LIST OF CONTRACTS IN [redacted]

The list of contracts which follows as Enclosure (I) is the Medical Sciences part of the Quarterly Project Summary for 1 October 1947. This summary is put out by the Office of Naval Research for the information of other military services interested in all types of research.

As will be seen, each contract carries with it its official Office of Naval Research number as well as its official Research and Development Board number, the location of the contractor, the principal investigator, and a short statement as to the proposed investigation as well as a progress report.

As has been indicated in several other places in this overall report, these are listed as to branch and are numerically so classified as to be easily found. [redacted] detailed information as to how to locate a particular project, see Enclosure (B), Current Programs.

[redacted]

LIST OF CONTRACTS OF THE
MEDICAL SCIENCES DIVISION
BY
RESEARCH AND DEVELOPMENT BOARD
NUMBER

Enclosure (I)

MEDICAL SCIENCES DIVISION

MEDICAL SCIENCES DIVISION

GENERAL

NR-100-486 Scientific Consultation Service (Medical) (Unclassified)

Contractor: National Academy of Sciences, Washington, D. C.
Contract: N7-onr-291, Task VII, (7/1/47 to 6/30/48)
Investigator: L. H. Weed

This project is a joint Army-Navy contract. The National Academy of Sciences has available specialists in practically all fields of science. The advice of these specialists will be made available as needed under this contract, for the purpose of assisting in the evaluation of research proposals and the direction of research activities into the most profitable channels.

Progress to 6/30/48: This is a consulting service and the progress is normal. This contract is in the process of being renewed.
Estimated Completion: Continuing

Physiology

GENERAL AND MISCELLANEOUS

NR-110-160 Scientific Consulting Service (Aviation Medicine and Aeromedical Research) (Unclassified)

Contractor: National Academy of Sciences, Washington, D. C.
Contract: N5-ori-177, Task IV, (7/1/46 to 12/31/48)

The purpose of this project is to provide additional research in the field of aviation medicine. The National Academy of Sciences will (when requested) supply necessary personnel, facilities, and temporary consultants; conduct investigations, surveys, and critical analyses; and prepare and furnish advisory and technical reports on problems in specific fields of sciences.

Progress to 6/30/48: The Committee on Aviation Medicine consulted with the armed services to determine what subjects they considered pertinent and wished to have discussed by leading authorities at the committee meetings. It was considered that by this means the Committee on Aviation Medicine would be informed of the important practical problems of the services and in turn could provide the Air Forces and Navy with educational symposia in these subjects.

The first meeting of the Committee for the fiscal year 1948 was devoted to biological effects of ultrasonics and explosive decompression. The second meeting was held at Randolph Field in consultation with the staff of the School of Aviation Medicine on their scientific program. Reports are being prepared on an evaluation of the research program at the school and concerning the educational program of the school for the Advisory Board of the Air University. The third meeting considered fatigue and physiological problems associated with jet aircraft. Civilian scientists, formerly associated with aviation medicine, are invited in order to keep this group interested in the subject.

The Committee is a clearing house of information for the services. The card index files of the Division of Medical Sciences has been microfilmed. Several sets of these films have been furnished to the Air Forces and the Navy. Copies of any article are supplied on request. The Committee also offers consultative service to the Services.

Several projects are being sponsored by the Committee including the Crash Injury Research Project. The Committee is also filing and evaluating information collected by the Civil Aeronautics Administration on medical problems associated with ultrasonics which are occurring in industry.

This Committee is supported jointly with the Air Forces and composed of the following members: D. W. Bronk, Chairman, E. J. Baldes, E. F. DuBois, W. O. Fenn, J. C. Flanagan, H. K. Hartline, A. C. Ivy, C. E. Kossmann, J. L. Lilienthal, Jr., G. L. Maison, and C. L. Taylor.
Estimated Completion: Continuing

NR-110-394 The Role of Phospholipids in Determining Semi-Permeability (Unclassified)

Contractor: Medical College of Virginia, Richmond, Virginia
Contract: N6-onr-254, Task II, (6/1/47 to 3/31/49)
Investigator: J. H. Weatherby

The purpose of this project is to further investigations for (1) oxygenation of the brain under anoxic conditions, and (2) susceptibility to malaria. This program will include (1) isolation and identification of the membrane constituents from as many different types of cells as possible; (2) extension of studies on permeability characteristics so as to include inorganic as well as organic compounds; (3) a study of the role of the phospholipids in processes of excitation and conduction, particularly with respect to the acetylcholine-choline esterase system; (4) a study of inflammation and edema from the point of view of changes in permeability; and (5) the

GENERAL AND MISCELLANEOUS, NR-110-394 (Cont.)

distribution of chemicals and drugs among various tissues of the organism as regulated in part by the behavior of cell membranes.

Progress to 6/30/48: Studies on the electrical and permeability characteristics of artificial membranes containing phospholipids indicate that these membranes are readily permeable to organic acids and bases, but highly impermeable to their ions. Non-electrolytes permeate with ease, regardless of the pH of the medium in which they are dissolved. Acidic and basic dye substances follow the same general pattern. Essentially this same relationship between pH and permeation or non-permeation of organic electrolytes (including dyes) exists in many living cells, whether protozoan or mammalian.

Extraction and analysis of phospholipids from human erythrocytes yield the following fractions: Lecithin 45%, phosphatidyl ethanolamine 28.6%, sphingomyeline 18%, and phosphatidyl serine 8.4%.

Studies on staining reactions of human erythrocytes as compared with permeability characteristics of artificial phospholipid membranes reveal that in general basic dyes stain at the higher pH value and not at the lower and the acidic dyes stain at the lower pH value and not at the higher.

Permeability studies on artificial membranes containing varying proportions of the several lipids indicate that all membranes are relatively impermeable to ions, both organic and inorganic, in the system, electrolyte/membrane/water. In the system 0.2M potassium chloride/membrane/0.2M sodium chloride, sodium and potassium may be exchanged or not depending on the composition of the lipid mixture in the membranes. Apparently phosphatidyl serine is necessary for ion exchange. Thus, membranes containing only 1.6% of phosphatidyl serine did not permit the interchange of sodium and potassium in measurable quantities in 70 hours, although the analytical procedures are sufficiently sensitive to measure with reasonable accuracy quantities as small as two to three parts per million. On the other hand, membranes containing 56% phosphatidyl serine permitted a rapid interchange of sodium and potassium (1.3×10^{-5} moles in two and one half hours). Membranes containing proportions of phosphatidyl serine between these extremes were intermediate in permitting the interchange of sodium and potassium. Sodium or potassium chloride permitted a similar ionic exchange with eosine, toluidine blue, nicotine, and salicylate when the membrane contained a significant quantity of phosphatidyl serine. Beef red cells contain phospholipids in proportions quite different from those in human cells.

Estimated Completion: Continuing

NR-110-473 Advisory Panel in Physiology (Unclassified)

Contractor: University of Chicago, Chicago, Illinois
Contract: N7-onr-440, Task I, (8/1/47 to 6/30/49)
Investigator: R. W. Gerard

All proposals are processed by the Physiology Branch through the interested bureaus of the Navy for approval and recommendation. Proposals are also sent to appropriate committee of the National Research Council for advice. There is need, however, for a panel more closely attached to ONR to decide which of the proposals approved by the above advisors are to be supported in view of the restricted funds available.

The Panel consists of five civilian members selected by both disciplinary and geographic distribution, and representatives of Naval bureaus and other Federal agencies.

Progress to 6/30/48: The members of this Panel are R. W. Gerard, Chairman, E. J. Baldes, Fred D'Amour, Clive McCay, and Carl F. Schmidt.

The Panel has met twice and will meet again in September.

Estimated Completion: Continuing

GENERAL AND MISCELLANEOUS (Cont.)

NR-110-757 Permeability of Certain Epidermal Membranes to Gaseous Carbon Dioxide (Unclassified)

Contractor: North Carolina State College of Agr. and Eng., West Raleigh, North Carolina
Contract:
Investigators: D. B. Anderson, H. T. Scofield

Although there is considerable indirect evidence that epidermal walls are permeable to carbon dioxide, no comprehensive study of this matter has been undertaken. It is proposed, therefore, to investigate the permeability of cutinized epidermal walls of the leaves and fruits of several species of plants and to study also the permeability of the uncutinized epidermal cells of roots by using radioactive carbon dioxide as a tracer.

It is hoped that this study may contribute to our understanding of the permeability of epidermal membrances to carbon dioxide, a matter of considerable fundamental importance, particularly in relation to problems of storage of living plant tissues.

Progress to 6/30/48: No progress to report.
Estimated Completion: Continuing

NR-110-758 The Physiologic and Pathologic Effects of Radioactive Cobalt (Unclassified)

Contractor: University of Denver, Denver, Colorado
Contract:
Investigator: F. E. D'Amour

The purpose of this project is to make a comparison of radioactive and non-radioactive cobalt. Since the brilliant original work of Orten it has been established that the administration of cobalt, in extremely small doses, has a powerful stimulating effect on red cell production. It is also known that radioactivity frequently produces the opposite result, namely anemia. It would therefore be interesting to study the opposing effects of radioactivity on hematopoiesis and to determine at what radioactive dosage the destruction action overcame the stimulating effect. As another phase of the study it would be possible to determine, by radiologic assay whether cobalt is actually a component of the red cell, which, on the basis of chemical assay, is usually denied.

Progress to 6/30/48: No progress to report.
Estimated Completion: Continuing

NR-110-761 Metabolism of Copper (Unclassified)

Contractor: North Carolina State College of Agr. and Eng., West Raleigh, North Carolina
Contract:
Investigator: J. A. Weybrew

The role of copper in catalyzing hemoglobin formation is well known. Furthermore, copper is associated with certain respiratory enzyme systems and is a constituent of the cytochrome C molecule. The possibility that copper might also be involved in the mechanism for the termination of pregnancy and/or the initiation of lactation might be inferred from the observation that there is an increased mobilization of copper as pregnancy approaches term. This study will elucidate this mechanism.

Progress to 6/30/48: No progress to report.
Estimated Completion: Continuing

PHYSIOLOGY

METABOLISM AND NUTRITION

NR-111-012 Nutritional Research (Unclassified)

Contractor: University of Chicago, Chicago, Illinois
Contract: N6-ori-20, Task VI, (6/1/46 to 6/30/49)
Investigator: P. B. Cannon

The purpose of this project is to make a study of amino acid utilization and the relation between amino acid deficiencies and appetite. An exploratory study of the precise roles of various food constituents--their relations to illness and health will be made; controlled experiments, directed at the interrelationships of amino acids, enzyme systems, vitamins, minerals, and calories by the utilization of isotope techniques, psychological testing methods and pathological procedures, will be undertaken. A large scale investigation is being made of interrelationships between amino acids, enzyme systems, and various nutritional entities in health and disease and under conditions of pharmacological treatment.

Progress to 6/30/48: Work on this contract has shown that adult, well-nourished white rats can be maintained with no loss of weight on rations adequate in calories, vitamins and minerals, and containing a mixture of 16 crystalline amino acids in the same proportions as in casein in 15 gm portions per day. However, if any one of nine essential amino acids is omitted from this ration, the animals lose weight, appetite, and total circulating plasma protein, and are consistently in negative nitrogen balance which parallels the weight loss. At the end of 20 days, if the missing amino acid is replaced, the animals start to gain weight. There is also much variation in the amount of each amino acid required for maintenance.

The effect of protein deficiency on the response of neutrophilic leucocytes to stimulation indicates that the cause of the leucopenia which ensues is probably in the bone marrow.

Comparative protein evaluation studies have been undertaken to determine the relative nutritive potentialities of several proteins under comparable conditions. The proteins tested ranked in the following descending order: Lactalbumin and casein (the reference protein), defatted egg albumin, dehydrated beef, defatted whole egg, casein, peanut protein, and wheat gluten.

It was found that cotton seed protein yields a value approximately 85% of that of a high quality casein-lactalbumin mixture.

Studies on the role of indispensable amino acids in the maintenance of the adult albino rat have been made using the criteria of preservation of appetite and weight as well as nitrogen balance in measuring qualitative amino acid requirements. It has been found that the normal adult rat maintains appetite and weight when receiving rations in which only the ten amino acids essential for growth are present. The removal of arginine from this mixture produces a variable depression of appetite--when appetite is maintained, weight and a positive nitrogen balance are preserved. The absence of each of the remaining nine essential amino acids from the basal ration, although producing a variable depression in appetite, always leads to weight loss and a negative nitrogen balance. The absence of tryptophane, methionine and threonine do not produce the marked loss of appetite observed with the same deficiencies in the protein-depleted rat. The absence of lysine led to only slight interference with voluntary food consumption in both the protein-depleted and normal adult rat. In most instances the effect on food consumption was not quite so acute or marked as that observed previously in the protein-depleted rat. Substitution of norleucine or lysine led to decreased appetite and weight loss similar to that produced by a deficiency of these amino acids. Substitution of tyrosine for phenylalanine resulted in a loss of appetite and weight somewhat less severe than that of phenylalanine deficiency. Despite equalization of the food intakes of rats deficient in lysine, leucine, histidine and phenylalanine with their controls by means of the force-feeding technique, animals on deficient rations lost weight and were in negative nitrogen balance. Results indicate that the same nine essential amino acids required for growth of the young rat are necessary for maintenance of appetite, weight and nitrogen balance in the adult rat.

Estimated Completion: Continuing

METABOLISM AND NUTRITION (Cont.)

NR-111-029 Basic Studies on Protein and Amino Acid Metabolism Requisite for Protein and Amino Acid Therapy (Unclassified)

Contractor: Rutgers University, New Brunswick, New Jersey
Contract: N7-onr-345, Task II, (6/1/46 to 6/14/49)
Investigator: J. B. Allison

This investigation is planned to secure basic knowledge of many details of protein and amino acid metabolism which is necessary for intelligent and effective clinical use of specific proteins, protein hydrolysates, and amino acid mixtures (natural or synthetic). This investigation involves the feeding of protein derivatives to experimental animals with the determination of nitrogen balance index and the effect on regeneration of tissue proteins. Studies are being made on the effects of methionine, cystine and other organic thio compounds on the development, growth, and composition of specific organs and on the hormonal relationships which may be involved; and effects of individual amino acids not containing sulfur on the nitrogen balance index of various proteins and protein hydrolysates and on the regeneration of tissue proteins.

Progress to 6/30/48: Experiments on the excretion of various forms of urinary sulfur, dogs fed Labco casein supplemented with methionine, show that the excretion of ethereal sulphate sulfur and of organic sulfur is independent of the sulfur intake. Methionine, however, in the region of negative sulfur balance, decreases the excretion of inorganic sulphate sulfur below that in control experiments. There is a marked increase of inorganic sulphate sulfur when dogs are in positive sulfur balance and from 70 to 100% of the sulfur absorbed, beyond that needed to maintain sulfur equilibrium, is excreted in the urine. Since no free methionine could be detected even at the highest methionine intakes, the methionine must have been retained as such, or, metabolized so that the sulfur was oxidized to inorganic sulphate. Methionine reduces the amount of both nitrogen and sulfur necessary to maintain equilibrium.

In investigating the effect of arginine on the toxicity of excess methionine utilization of sulfur in normal and protein depleted dogs, it was found that excretion of all forms of sulfur decreases below control values in the depleted animal. This decrease is not, however, as great as the decrease in nitrogen. After 30 days of repletion on whole egg protein, the excretion of inorganic sulfur returned to control values, but the excretion of other forms of sulfur remained depressed.

The urinary sulfur ratio was still elevated above control values. These data suggest that sulfur is conserved more than nitrogen in the depleted animal. It is believed that this conservation of sulfur is in the form, at least in part, of more reserves for methylation.

When excess methionine is added to casein, weight loss is greater than in control animals, a loss which is overcome in part, by adding arginine to the methionine diet; the nitrogen balance is reduced markedly and creatine excretion is increased.

When arginine is added to casein, these changes are not so marked, but the size of the liver is increased. When both arginine and methionine are added, the nitrogen balance index of casein is not reduced as much as it is in the presence of casein alone but the creatinine excretion is increased.

Feeding methionine plus casein increases the size of the kidney, but if both arginine and methionine are added, the kidney is not increased in size. This suggests an antagonistic effect between arginine and methionine which can be partly explained on the basis of the utilization of arginine and methionine in the formation of creatine.

Rats fed thiouracil or propylthiouracil have enlarged livers capable of releasing larger than normal amounts of protein, possibly contributing to the increase in polypeptide and to the globulin fractions of the plasma.

0.25% thiouracil is close to the maximum daily dose for adult rats. This dose will increase total plasma protein due to an increase in plasma globulin and will cause a rise in liver protein. After 40 days' thiouracil feeding, plasma protein and liver protein still exceed

METABOLISM AND NUTRITION, NR-111-029 (Cont.)

normal. The data suggest that the daily dosage of thiouracil is more important than the total amount fed since there is a more pronounced effect of 0.75% thiouracil fed for 20 days as compared with 0.1% thiouracil fed for 20 and 40 days. Thyroidectomy does not duplicate the effects of thiouracil on the liver. There was an increase in liver protein in thyroidectomized rats fed thiouracil.

A rise in non-protein nitrogen, plasma globulin concentration, and in total plasma protein occurred in male rats 20 to 25 days after thyroidectomy or thiouracil feeding. Plasma albumin concentrations simulated those of pair fed controls. Hematocrit decreased.

Castration in adult rats is followed by an increase in total plasma protein concentrations due to a rise in plasma globulin. Administration of testosterone propionate will prevent the rise in plasma globulin. In animals where thiouracil increases plasma globulin concentration, testosterone propionate will not restore globulin levels to normal. Thyroid and liver hypertrophy occurring in thiouracil-fed rats are not altered by concomitant androgen administration.
Estimated Completion: Continuing

NR-111-344 Properties and Metabolism of Natural Fats and Fatty Acids (Unclassified)

Contractor: Agricultural and Mechanical College of Texas, College Station, Texas
Contract: N7-onr-487, Task I, (1/1/48 to 12/31/48)
Investigator: P. B. Pearson

Under this project studies are being made on the deposition and metabolism of the naturally-occurring fatty acids and their isomers. Fat-deficient rats will be fed single pure fatty acids and the changes in the unsaturated components of the various tissue fats will be measured spectrophotometrically and by adsorption analysis to learn what effect each has upon the polyunsaturated fatty acids in tissue lipids. It is hoped by this means to learn what is the function of the essential fatty acids in metabolism.

Using purified lipoxidase, studies of the mechanism of oxidation of linoleic and related acids will be made with the view to gaining a knowledge of the processes of metabolism and rancidification of these acids. A study of the coupled oxidation of fat-soluble vitamins and antioxidants in oxidizing fat is also planned using lipoxidase to initiate the oxidation, in an effort to discover the mechanism of coupled oxidation and antioxidant activity.

Progress to 6/30/48: Study of the metabolism of essential fatty acids is under way. Rats maintained on a fat-deficient diet for three months are showing typical symptoms of the deficiency. Four groups with these symptoms are now receiving daily supplements of ethyl stearate, ethyl oleate, ethyl linoleate on ethyl linolenate. Some animals are being killed before the feeding of the supplements in order to serve as controls.

Investigations with chickens indicate that the requirements of riboflavin may be influenced by the kind and amount of fat in the diet. Chicks receiving high levels of Wesson oil show symptoms of riboflavin deficiency much earlier than chicks on a low fat diet or those fed lard when suboptimal amounts of riboflavin are included in the diet.
Estimated Completion: Continuing

SYSTEMIC PHYSIOLOGY

NR-112-002 Study of Effects of Anoxia and the Interrelationships Between Anoxia and Hyper- and Hypocapnia (Unclassified)

Contractor: Yale University, New Haven, Connecticut
Contract: N6-ori-44, Task VII, (4/1/46 to 4/30/49)
Investigators: J. F. Fulton, S. Gelfan

SYSTEMIC PHYSIOLOGY, NR-112-002 (Cont.)

The purpose of this project is to investigate the effects of anoxia and the interrelationships between anoxia and hyper- and hypocapnia. Detailed attention will be given to a comprehensive analysis of respiratory function, kidney function, endocrine function, and central nervous system function under anoxic stress; and the extent to which the disturbances in these various physiological mechanisms are ameliorated by controlling the carbon dioxide level of the blood.

Progress to 6/30/48: Rats and monkeys have been exposed to explosive decompression at high altitudes. It has been found that unanesthetized monkeys are as hardy as rats in withstanding such decompression. They can survive decompression in oxygen to altitudes as high as 75,000 ft if recompressed at free fall rate. They also survive decompression to 60,000 ft in air when recompressed at free fall rate. Heart changes following decompression are similar to those of rats. Exposure of rabbits and rats to anoxia at 25,000 ft for three to five hours leads to definite heart lesions similar to those produced in shock.

Bradycardia after decompression is not due to distention, decompression per se, or recompression (at least at high altitudes). It is presumed due almost entirely to anoxia following decompression at high altitudes. Reflex anoxic bradycardia is mediated by the vagus, since it is eliminated by administration of atropine. Evidence suggests that bradycardia produced during descent at free fall rate in oxygen from 42,000 ft is caused by impulses from the middle ear, arising from negative pressure resulting from recompression. Puncturing of the ear drums eliminated the bradycardia.

Fifty per cent of the monkeys sacrificed have various degrees of lung alveolar necrosis, presumably caused by rupture of the pulmonary capillaries during decompression. In all cases the right lung and especially the lower lobe of the right lung were severely affected.

From observations on an experiment concerning the repetitive discharges of the cortico-thalamic reverberating circuit, induced by afferent stimulation to determine whether the ascending pathway of the subsequent repetitive discharges uses the same fibers as those mediating the primary afferent volleys, two deductions are made: (1) If the impulses of the repetitive discharge arrive during the refractory period of an incoming afferent volley, they fail to proceed further. (2) If a primary afferent volley arrives in the refractory period of the repetitive discharges it keeps on propagating. From this it is concluded that the cortico-thalamic pathway for the repetitive discharges must be independent of that which conveys the great afferent volleys. Reverberating circuits of this kind are believed to exist not only between the sensory cortex and thalamus but also between the motor cortex and basal ganglia and possibly between the cortex and cerebellum or other subcortical structures. Considering that the electrical potentials circulating along different reverberating circuits have different frequencies and that these repetitive discharges can only be initiated by an afferent volley, it seems plausible to assume that EEG's are mainly a manifestation of concerted activities of numerous reverberating circuits initiated by incessant inflow of afferent impulses.

Cortical response is more highly susceptible to anoxia upon photic stimulation than optic nerve stimulation, obviously because of the involvement in the former of retina which is known to be extremely sensitive to oxygen shortage.

The evoked cortical potential consists of a rather brisk primary response and a train of rhythmic waves which, according to the analysis of the present investigator, are the repetitive discharges of a cortico-thalamic reverberating circuit induced by the great afferent volley. The succeeding repetitive discharges tended to disappear sooner during anoxia and return later during recovery than the primary response. The significance of the different components of the evoked cortical response in regard to consciousness is not yet known. However, the repetitive discharge is thought to be an important event underlying higher mental processes.
Estimated Completion: Continuing

NR-112-003 Study of Convalescence (Unclassified)

Contractor: University of Illinois, Urbana, Illinois

SYSTEMIC PHYSIOLOGY, NR-112-003 (Cont.)

Contract: N6-ori-71, Task XIII, (7/15/46 to 7/14/48)
Investigators: R. W. Keeton, W. H. Cole

As a result of trial and error doubt has been cast on certain methods (more specifically, prolonged bed rest and the neglect of the patient's nutritional requirements) of treating patients convalescing from surgical procedures. The purposes of the present studies are the establishment, experimentally, of objective criteria of convalescence, and the evaluation by means of these criteria of procedures designed to hasten convalescence. The difficulties of subjecting human subjects to adequately controlled studies is so great that a comprehensive long-time program is required. The physical and physiological status of patients must be assayed preoperatively, and their rate of return to the same or a better state of fitness must be measured. The role of preparative physical training has to be studied. The studies will be planned in such a manner that the individual experimental factors can be evaluated by means of statistical comparisons. It is hoped that some relatively simple indices of the progress of convalescence can be developed.

Progress to 6/30/48: Studies have been made on more than a 100 convalescent patients who underwent herniorrhaphies, cholecystectomies, radical mastectomies, etc. Measurements of circulatory efficiency have been made with such devices as the tilt table and the push-up test. Results suggest that for some time after operation, a weakness exists in certain compensatory cardiovascular mechanisms--namely those associated with the maintenance of the normal level of blood pressure in the face of a reduction in venous return.

Preoperative measurements are made of the amount of work (treadmill) which will induce anaerobic muscular metabolism as measured by accumulation of lactic acid in the blood and its rate of clearance. In fact, changes in urinary lactate following surgery appear to provide a sensitive test of the duration of convalescence. The day on which a patient is able to duplicate postoperatively his preoperative performance is regarded as in index of recovery of the muscular ability to perform mild non-exhausting work. Urinary lactate is reduced or kept at a low level by ambulation. It is increased by bed rest. It is not appreciably reduced nor maintained at a low level by a regimen in which increased quantities of food are fed but ambulation is omitted.

Studies on a variety of surgical cases with different postoperative regimens showed that: "Shotgun" and "early ambulation" regimens applied to cholecystectomies yield better performance and apparently speedier convalescence than regimens used in control gall bladders, spinal gall bladders, and control mastectomies respectively. Following cholecystectomy, there is evidence that high protein diets are deleterious.

In analyzing the nature of toxicity of large quantities of protein administered postoperatively into the jejunum of human subjects, it has been found that following herniorrhaphy, an uninterrupted administration into the stomach of a high caloric diet which contained large quantities of protein facilitates convalescence. When this plan was followed in patients submitted to cholecystectomy, with the exception that food was administered into the jejunum, two unexpected and unexplained deaths occurred. When the feedings were postponed 24 to 48 hours postoperatively and when they were interrupted with the rise of a rectal temperature to 102°F, the patients tolerated the feedings without untoward effects. A jejunostomy was established in dogs and they were allowed to recover. When 10 gm of enzymatic casein digest per kilo body weight were administered over a four-hour period into the jejunostomy of the dogs under light anesthesia, four of the five animals died. When the experiment was repeated without anesthesia five of the six animals survived. From the blood chemical studies, it was difficult to determine whether the deaths were to be attributed to dehydration induced by the protein and diarrhea, or to a toxicity of the protein when combined with the anesthetic.

Experiments in oral and tube feeding have set the limits of accuracy of the Atwater method of estimating the energy value of hospital diets at 9.5% at the 5% probability level, and at 11.3% at the 2% probability level, in the case of oral feeding. In the case of tube feeding, the

SYSTEMIC PHYSIOLOGY, NR-112-003 (Cont.)

Atwater method consistently overestimates the truth and may be totally unreliable if considerable diarrhea supervenes. The use of food composition tables in estimating the fuel value of these diets did not give good estimates of energy consumption, the errors being overestimations, generally, ranging up to 32%.
Estimated Completion: Continuing

NR-112-006 Prophylaxis of Experimental Renal Hypertension (Unclassified)

Contractor: University of Illinois, Urbana, Illinois
Contract: N6-ori-71, Task XII, (7/15/46 to 9/30/48)
Investigator: G. E. Wakerlin

The purpose of this investigation is to determine conditions under which maximum prophylaxis against experimental renal hypertension in dogs can be achieved by means of kidney extract injections with a view to the employment of the active principle of such extracts in the prevention and treatment of incipient essential hypertension in the human.

This will be done by investigation of the treatment of hypertension by means of various renal extracts and the mechanism of the action of these extracts.

Progress to 6/30/48: Successful prophylaxis against renal hypertension in dogs by means of injections of crude renal extracts had been reported by the investigator before this contract began. No correlation was found between prophylactic effect and the renin content of the extracts, the serum antirenin titres, or the plasma renin-hypertension systems.

Investigations under this contract indicate that there is no correlation between the success or failure of prophylaxis and the renal renin content and no difference at necropsy. The prophylactic effect of crude renal extracts may last for many months.

Comparison with therapeutic effect in established hypertension indicates that prophylaxis is a more sensitive test for the antihypertensive renal principle than therapeutic assay.

A highly purified renin (80 to 125 dog units per mg of N) has been prepared which is very effective in the prophylaxis and the treatment of experimental renal hypertension in dogs. Antirenin titres point to antirenin as the mechanism or the important part of the mechanism of the antihypertensive effect. Evidence has been obtained that the antihypertensive effect is antagonized by the non-renin fraction of crude hog renal extracts from which highly purified renin is prepared. Protection has been obtained against experimental malignant hypertension (including the vascular lesions) in dogs by means of partially and highly purified renins. Further study is necessary before trial in the prevention and treatment of incipient essential hypertension in man is warranted, but it is believed that another year of laboratory work will make it possible to transfer this problem to the clinic.
Estimated Completion: Continuing

NR-112-018 Metabolism of Steroids (Unclassified)

Contractor: Yale University, New Haven, Connecticut
Contract: N6-ori-44, Task VI, (5/1/46 to 12/31/48)
Investigator: W. T. Salter

Under this project micro-colorimetric methods are being developed to study the metabolism of steroids and phenanthrenes. These include the so-called "androgens" (17-ketosteroids), estrogens, "corticoids" and cardiac glycosides (digitoxin). In delayed adolescence, eunuchoidism, gyecomastia, pseudo-hermaphroditism, and perverted sex development of certain types characteristic changes can be demonstrated. These changes in urinary excretion involve both the absolute amounts and the ratios of antithetical steroids. The present methods permit the determination of these data over the course of a few hours.

SYSTEMIC PHYSIOLOGY, NR-112-018 (Cont.)

Because digitoxin is closely related chemically to other phenanthrenes the same techniques are being applied to cardiac drugs. It has been found that the response of failing myocardium to digitoxin congeners is a logarithmic function of the concentration of drug.

Progress to 6/30/48: In studying sex disturbances, chemical analysis of steroid hormones indicates that the steroid balance ratio of estrogen to 17-keto steroid excretion (E/A ratio) is useful in precise diagnosis of abnormal conditions. The "antithetical ratio" of normal males is usually less than 1.0. In normal females it is usually above 2.0. In males with prostatic hypertrophy or prostatic carcinoma, however, the E/A ratio is frequently in the female range, and occasionally above 10. It is postulated that the probable normal male hormone is 16.0 and the probable normal female hormone is 6.0.

Various cardiac glycosides have been compared with ouabain as a standard with respect to their action in increasing contractibility of the hypodynamic papillary muscle. Responses of all these drugs conform to a semi-logarithmic dosage response curve when the amplitude of contraction is expressed as per cent of maximal. It is hoped to show that therapy of cardiac cases can be controlled chemically similarly to the way sulphonamide therapy is controlled by means of blood concentration.

The hypodynamic myocardium will not respond to a given concentration of glycoside unless its degree of "fatigue" lies below the threshold of amplitude corresponding to the particular log-concentration concerned. The quantitative relationships can be explained, tentatively, by assuming the combination of the glycoside with an effector mechanism or structure in the cell. Further combination impeded the normal action, and thus included "toxicity".

Experiments with fluorescence produced from digitoxin indicate that the degree of fluorescence developed may be proportional to the concentration of digitoxin present.
Estimated Completion: Continuing

NR-112-089 Diffusion Respiration (Unclassified)

Contractor: University of Colorado, Boulder, Colorado
Contract: N6-ori-131, Task I, (6/15/46 to 6/30/49)
Investigators: R. W. Whitehead, W. B. Draper

Diffusion respiration (maintenance of gas-exchange between the atmosphere and lung alveoli in the absence of respiratory movements and of any type of artificial respiration, such as pulmotors, streams of air under pressure, etc.) is being studied with special reference to: (1) pH, oxygen saturation and carbon dioxide content of blood; (2) composition of alveolar gases; (3) survival of the experimental animals; (4) composition of urine and gastric juice under diffusion respiration; (5) behavior of dogs under diffusion respiration at simulated altitudes; (6) behavior of circulation; (7) occurrence of diffusion respiration under other anesthetics than pentothal sodium (which was originally used); (8) use of curare instead of pentothal sodium to produce respiratory arrest; and (9) aspects of carbon dioxide anesthesia.

Previous studies have shown that uptake of oxygen from the atmosphere continues essentially undiminished during respiratory arrest by pentothal provided (1) the circulation is efficient; (2) the airway is patent; and (3) the nitrogen of the atmosphere and respiratory tract is replaced by oxygen at the time breathing ceases. The entrance of atmospheric oxygen into the lung alveoli is explained as being due to suction inwards of the atmosphere as a consequence of the affinity for oxygen of the reduced hemoglobin in transit through the lung.

Progress to 6/30/48: During 45 min of diffusion respiration there are: (1) A marked accumulation of CO_2 in the pulmonary alveoli; (2) a consistent decrease in the venous blood pH to a level previously assumed to be fatal; and (3) animals subjected to this ordeal can be resuscitated and will, in the majority of cases, make a complete and permanent recovery.

SYSTEMIC PHYSIOLOGY, NR-112-089 (Cont.)

During the first 30 min of diffusion respiration, the oxygen content of arterial and venous abdominal blood is well maintained. Between the 30th and 45th min of respiratory arrest there is a progressive fall in the oxygen content of arterial and venous blood. After the initiation of lung ventilation, the arterial and venous oxygen content reach their control values within 15 min. There is, however, a temporary secondary fall in the oxygen content of venous blood at the 30th min post-diffusion.

During the 45 min of respiratory arrest there is a progressive rise in carbon dioxide content and a concomitant fall in the pH of arterial and venous abdominal blood. The average pH values at the 45th min of arrest are 6.72 for arterial blood and 6.84 for venous. After 60 min of lung ventilation, the carbon dioxide content and pH of both arterial and venous blood approximate their control values. The carbon dioxide content of the arterial blood during diffusion respiration becomes greater than that of the venous, and concomitantly the pH of the arterial blood becomes lower than the venous. Following resumption of lung ventilation, the normal relationships between these values reappear within 15 min.

There is almost complete anuria during diffusion respiration with a prompt return of urine secretion upon the resumption of spontaneous breathing. This anuria can be abolished by denervation of the kidney by means of pontocaine. It has been found that hydration will not prevent development of anuria during diffusion respiration.

Electrical activity in the brain of dogs begins to diminish promptly with the cessation of respiration and the institution of diffusion. Within five to 15 min after the beginning of diffusion, the electrical activity of the brain practically disappears. The extent to which this depression of electrical activity is due to pentothal sodium has not been determined as yet. This electrical activity returns rather promptly upon the beginning of spontaneous or artificial respiration but the return of the electroencephalogram to complete normality requires several days.
Estimated Completion: Continuing

NR-112-097 — Studies of the Physiological Disturbances Attending Bodily Injury — (Unclassified)

Contractor: Medical College of Virginia, Richmond, Virginia
Contract: N6-onr-254, Task I, (12/1/46 to 11/30/48)
Investigator: E. I. Evans

The purpose of this project is to study the physiological disturbances attending bodily injury including (1) the renal regulation of acid-base equilibrium in states of hypochloremia, base deficit, post-transfusion reaction, and sulfonamide crystalluria; (2) the physiological mechanisms involved in the post-anesthesia shock state; (3) the utilization of hemoglobin as a source of nutrition nitrogen; and (4) addition studies on vaso-excitatory and vaso-depressor substances.

Progress to 6/30/48: Dehydration, hypochloremia, and alkalosis as observed after severe loss of gastric juice by vomiting or gastric suction are being studied in dogs subjected to the total gastric pouch method and gastrostomy with pyloric ligation.

Despite alkalosis, urine is acid (pH 5 to 6.4). This acidity is attributed to the fact that body deficiency of sodium salts is so great that excretion of both NaCl and $NaHCO_3$ is almost completely stopped, apparently to preserve the body's remaining salts.

Sodium chloride infusions correct the alkalosis and dehydration, replace lost plasma sodium and chloride, and permit excretion of excess $NaHCO_3$ raising urine pH to 7.5-8.0.

It has been determined that resumption of chloride excretion is a better guide to diagnosis, treatment, and replacement of various types of dehydration than plasma chloride concentration.

Providing kidney and adrenal function are normal, water and salt balance will be properly maintained if daily urine volume exceeds 1500 cc and urine salt concentration approximates three grams per liter.

SYSTEMIC PHYSIOLOGY, NR-112-097 (Cont.)

Complete dependence on these simple measurements as quantitative guides to such a complicated physiological mechanism as water and salt equilibrium should be supplemented by clinical observations of edema, skin turgor, thirst, respiration, the appearance of the tongue and eyeballs, mental state, etc. Also once the urine is salt free, plasma chloride concentration must be determined in order to estimate the magnitude of salt depletion. If plasma chloride concentration is abnormally low, plasma CO_2 concentration must be measured. When kidney function is impaired it is safer to depend on plasma chloride than urine salt measurements. Evidence indicates that renal function may be depressed in conditions causing diminished blood volume, as in dehydration, during and immediately following shock, and postoperatively.

Massive infusion of a solution of NaCl plus glucose decreases plasma potassium to less than half the normal concentration, and apparently calcium also. These effects indicate the desirability of using a balanced electrolyte solution of Na, K, Ca, and Mg when large infusions are given.

Sodium bicarbonate infusion does not correct the plasma electrolyte pattern, it raises urinary pH above the physiological range (pH 8), and causes tetanic convulsions. These results indicate the possible dangers of: Using sodium bicarbonate to alkalinize the urine of patients suffering gastric fluid loss; the advisability of using NaCl infusions; and the desirability of guiding therapy of measurement of urine salt concentration (measured as chloride) and urine volume instead of plasma chloride concentration.

It is suggested that the term "dehydration" be substituted by its physiological components "primary water depletion", "primary salt depletion", and "mixed water and salt depletion".

Estimated Completion: Continuing

NR-112-104 Studies on Trypsin Shock (Unclassified)

Contractor: Indiana University, Bloomington, Indiana
Contract: N6-ori-180, Task I, (12/1/46 to 11/30/48)
Investigator: D. E. Bowman

The purpose of this project is to study the mechanism of shock associated with toxic proteins, and the mechanism of blood clotting by means of chemically modified trypsin (such as iodinated) or other agents which may lend themselves to such a study.

Progress to 6/30/48: The profound shocking properties of intravenously administered trypsin can be reduced to a low level by acetylating the enzyme with ketene or by partially iodinating it under standardized conditions. Iodination decreases the shocking properties considerably more than proteolytic or thromboplastic activity. Acetylation appears to decrease shock and proteolytic activity about equally.

In repeated observations, using normal plasma of dogs, it has been found that trypsin, which is iodinated sufficiently to eliminate, essentially, shocking properties, accelerates the clotting of the recalcified plasma to the same degree as untreated trypsin. The clotting influence is most striking in cases showing relatively long coagulation times in the absence of an accelerating agent.

Proteolytic and hypotensive activities of trypsin are not inseparable. Free amino groups and phenolic groups do not appear to be essential to either type of activity. There is a striking parallel between the properties which appear to be those of the chemical groups associated with trypsin shock and those of the indole nucleus of tryptophane.

Characteristics of the protein groups associated with the hypotensive activity of trypsin correspond with the properties of free tryptophane although participation of other groups is not excluded.

Estimated Completion: Continuing

SYSTEMIC PHYSIOLOGY (Cont.)

NR-112-118 Interrelationships Between Respiration and Circulation Under Anoxic Conditions (Unclassified)

Contractor: University of Denver, Denver, Colorado
Contract: N6-ori-194, Task I, (10/7/46 to 10/6/48)
Investigators: F. E. Blood, F. E. D'Amour

The title of this project was formerly "Efficiency of Various Types of Artificial Respiration and of Respiratory Stimulants at High Altitudes".

It is planned to study the causation of the apnea and hypotension occurring when the oxygen supply fails and the reason for the return of the blood pressure and respiration even though anoxic conditions continue. In general, the study falls into two main divisions, the investigation of nervous factors and chemical factors.

Progress to 6/30/48: It has been determined that the anatomy and histologic structure of the rat is similar to that of other species in that oxygen lack stimulates respiration through operation of a reflex in which the sensory receptors are located in the carotid body. (The cyanide-injection method is used to test the functioning of this reflex or for successful denervation of the carotid body.)

Rats were given various mixtures of inert gases and oxygen, records of respiration and circulation being taken simultaneously. After the normal response was recorded, the carotid bifurcation was excised and the test repeated. It was found that pure nitrogen, pure helium, 95% nitrogen plus 5% oxygen, 95% carbon dioxide plus 5% oxygen, all gave essentially the same results, namely a precipitous fall in blood pressure and an apneic period of from one to three minutes duration, followed by a spontaneous restoration of respiration and a rise in blood pressure and pulse pressure to normal, or greater than normal, levels. This occurred in spite of the fact that administration of the inert gas was continued. Following denervation there was no essential change in the above described happenings.

On 90% nitrogen plus 10% oxygen or 90% nitrogen, 5% oxygen and 5% carbon dioxide, the fall in blood pressure was somewhat less pronounced. Apnea did not occur with regularity, when it did, the apneic period was usually short. Following denervation no change in the animal's responses were observed, if no apnea had occurred before denervation, it did not occur afterward and vice versa.

Tentative conclusions based on the above results are:

That the vasomotor system is somewhat more sensitive to oxygen lack than is respiration since, with 10% oxygen in the mixture, the blood pressure fall is still prominent, while the apneic period frequently disappears.

That neither the vasomotor nor the respiratory response is mediated either through the carotid body or through the vagus nerves, since elimination of these in no way alters the response to anoxia.

Analysis of simultaneous records of respiration and circulation, both during the original and the "rebound" response and in normal, sinus-denervated and vagotomized rats, lead to the conclusion that the respiratory response is secondary to the circulatory. In most cases the fall in blood pressure precedes the return of respiration.

This has led to a study of the effect of pressor agents on respiration, i.e., to determine whether a rise in blood pressure during an apneic period of predictable length would re-start the breathing apparatus. The results obtained with adrenalin, the only agent so far tried, are peculiar but significant in several ways. No rise in blood pressure has ever been noted, although adrenalin is not considered a respiratory stimulant. This would apparently indicate that the cause of the hypotension is post-arteriolar, as it is in traumatic shock, in which adrenalin is also ineffective in raising the blood pressure. This finding is of interest in connection with the effectiveness of the Barospirator for use in the treatment of traumatic shock.

Estimated Completion: Continuing

SYSTEMIC PHYSIOLOGY (Cont.)

NR-112-124 The Hypophysis and Iron Metabolism (Unclassified)

Contractor: Boston University, Boston, Massachusetts
Contract: N6-ori-160, Task II, (7/15/46 to 7/1/49)
Investigator: R. C. Crafts

Hypophysectomy produces a microcytic hypochromic anemia in adult rats. Injections of thyroxine, iron, and copper have come very close to preventing this anemia. Accordingly, this project will study the possible relationships of the hypophysis to iron metabolism. Gastric acidity; intestinal acidity; plasma iron; stored iron in the kidneys, liver, and spleen; and iron intake are under investigation in hypophysectomized adult female rats and littermate controls.

Progress to 6/30/48: Animals tested for normal blood pictures were divided into two groups. One group was subjected to hypophysectomy and the other used as a control. Fifty days after hypophysectomy, the operated rats showed decreases in total erythrocyte counts, and hemoglobin values while the control animals remained normal.

After the anemia had become established in the hypophysectomized rats, the gastric contents were studied.

Results show that hypophysectomy produces a consistent decrease in gastric secretion not due to the anemia following removal of the hypophysis. In studying the effects of hypophysectomy on serum and stored iron it was found that in hypophysectomized rats, there was a decrease in serum iron, storage iron was elevated in concentration, but the total available was normal except for liver content. These effects are duplicable on rats kept on a diet level decreased to that of the hypophysectomized rats, but the latter show greater lack of ability to utilize available stored iron in the formation of hemoglobin.

Although no sign of infection occurred in the rats used in these experiments, the distribution of iron following hypophysectomy resembles that following infections in the human and in the dog. It has been postulated that although there is available iron in storage during infections, this iron is not utilized to combine with protoporphyrin to form heme, because the iron is diverted to the tissues where it is made unavailable for hemoglobin formation. That a similar occurrence would follow hypophysectomy is a possibility.
Estimated Completion: Continuing

NR-112-157 Role of the Islets of Langerhans in Diabetes Millitus (Unclassified)

Contractor: University of Minnesota, Minneapolis, Minnesota
Contract: N6-ori-161, Task I, (7/15/46 to 7/14/49)
Investigator: E. T. Bell

The purpose of this project is to determine the effects of high blood sugar upon the islets of Langerhans. The practical application would be to determine whether it is advantageous to keep the blood sugar of a diabetic at a normal level. The experiment is being conducted on rats and the diabetes is being produced by partial pancreatectomy and by alloxan.

Progress to 6/30/48: The Beta cells of the islets of Langerhans, the cells which form insulin, may be completely degranulated by three different procedures all of which increase the demand for insulin. Rat pancreas have been studied and it has been found that when rats are fasted for seven or eight days, nearly all the Beta granules disappear. When they are fed exclusively on olive oil or lard for two or three weeks, the Beta granules disappear completely. Rats given a daily injection of insulin show complete degranulation of the Beta cells within one week. It has previously been shown that rats fed as indicated above show a marked decrease in the insulin content of the pancreas. It therefore appears that the Beta granules represent stored insulin. It seems established also that insulin is not formed by the pancreas unless there is a demand for it.

SYSTEMIC PHYSIOLOGY, NR-112-157 (Cont.)

Forced feeding of extremely high levels of carbohydrate causes hyperglycemia (370 mg %) and glycosuria just preceding the death of animals; presumably, death is caused by other deficiencies. Studies are under way on a diet complete in protein, vitamins, and minerals but high enough in carbohydrates to cause abnormally high intake.
Estimated Completion: Continuing

NR-112-191 Relationship of Digestive Processes to the Endocrine System (Unclassified)

Contractor: University of Rochester, Rochester, New York
Contract: N6-ori-126, Task IV, (9/1/46 to 8/31/48)
Investigator: E. S. Nasset

This project will investigate the relationship of various hormones to the secretion of digestive juices. Part of the project is concerned with the isolation and identification of enterocrinin, an alimentary hormone which excites the glands of the small intestine. The non-alimentary hormones, insulin, thyroxin, and parathyroid hormone are being studied in reference to their effect on the intestinal glands.

Progress to 6/30/48: A new method has been developed for the preparation of enterocrinin, a hormone which is a potent excitant for the glands of the small intestine. Previous methods gave yields of five to 10% of the original active material in the final product whereas the present method yields 50%. Further modifications of procedure in the extraction and purification of this hormone have failed to yield significant results in purification.

Hypercalcemia induced in the normal dog either by parathyroid extract or large doses of crystalline vitamin D failed to produce significant alterations in the quantity or quality of intestinal juice.

Moderate amounts of insulin given to the fasting dog increase enzyme output in the small intestine. If the dog is fed before insulin injection, the effect is a sharp reduction in enzyme output. Fistulae used in these experiments have been denervated and observations are under way to determine the part played by extrinsic nerves in insulin response.

Continuous intravenous calcium gluconate administered to maintain blood calcium at 14 to 15 mg % had no significant effect on the secretion of intestinal juice.
Estimated Completion: Continuing

NR-112-198 Fluid, Electrolyte, and Protein Requirements of Patients with Surgical Disease (Unclassified)

Contractor: Harvard University, Cambridge, Massachusetts
Contract: N5-ori-76, Task XIII, (1/15/47 to 9/15/49)
Investigator: O. Cope

Under this project research is being conducted on the nutritional requirements of fluid, electrolytes, and proteins by individuals under conditions of stress. The particular condition in this study will be that of surgical disease but the information should be applicable to other stress conditions. (1) The balances of nitrogen, potassium, and sodium are determined in seriously ill surgical patients and normal controls. The effects of operations, sepsis, trauma, and dehydration are being studied. (2) The metabolic handling of single tracer doses of potassium is measured to discover the conditions in which avidity for potassium exists. (3) Equilibrium rates for an injected dose of radioactive potassium are being determined by measuring the specific activity of blood cells, serum, urine, muscle, and other tissues at varying periods after injection into patients. (4) The measurement of the body fluid spaces, including total body water with D_2O is carried out in conjunction with this program. A new type of constant temperature bath for the falling drop measurement has been developed.

SYSTEMIC PHYSIOLOGY, NR-112-198 (Cont.)

Methods have been developed for the study of total body constituents, cellular chemical changes and parenteral nutritional therapy based on isotope dilution studies in conjunction with more standard procedures such as metabolic balance studies. These procedures are to be applied to clinical research in the coming year.

Progress to 6/30/48: Studies with radioactive potassium have been concerned in one phase with the measurement of the total mass of exchangeable potassium in the body (K^{39}_{te}). This measurement is regarded as an anthropometric measurement to be considered in the same category as the measurement of plasma volume, extracellular fluid volume and total body water. Instead of expressing a phase volume of body fluid, the entity measured is a mass of ions both within and without cells. From a technical point of view, the measurement is based on isotope dilution; from an interpretive point of view, the entity measured is a function of the total mass of oxidizing cellular protoplasm in the body since, within cells, potassium is found in constant ratio to protein and glycogen. Measurement of the total amount of potassium in the body also becomes an indirect measurement of the total mass of protein-containing cellular matter in the body.

K^{39}_{te} may also be thought of as a measurement of the energy-producing "engine". From specific activity data on human tissues, the assumption would appear justified that the K^{39}_{te} is a measure of all the potassium in the body save a fraction of potassium in the red cell mass approximating 50 milliequivalents.

Patients given injections of radioactive potassium have also been studied with three other objectives: An observation of the rate of excretion of the injected radioactive potassium; observations of the basal rate of total potassium excretion (K^{39}_{te}); and a study of the exchange of potassium in tissues and body fluid to determine the rate at which equilibrium is reached within the body.

The outstanding usefulness of the studies on the measurement of metabolic balances in surgical patients has been to provide a framework within which the study of K^{39}_{te} could be carried out. During the tissue destroying phase of disease, the balances observed are apparently the result of the excretion of the product of tissue destruction in the urine. During the tissue-building phase of convalescence, potassium is retained in the body to a disproportionate extent. It is considered conceivable that this may be related to alterations in carbohydrate metabolism during recovery from depletion.

Observations of specific activity curves within the living patient have demonstrated that the permeability of the red cell to potassium is somehow different from that of other body cells. Analyses of the potassium content of the red cell have been made and significant variation between well and depleted individuals has been found. Patients with Cushing's syndrome have the highest mean erythrocyte potassium content. Studies have also been made of the permeability of the red blood cell to radioactive potassium in vitro. In vivo exchange of potassium into red cells is very slow in reaching equilibrium at 70 hours or later, an in vitro system which reproduces all the characteristics of the red cell in its natural environment within the living organism has not yet been produced. Investigation concerning how potassium may be administered intravenously at high concentrations with safety is being made. Investigation has been made of the fatal rate of potassium injections in rabbits and of quantitative studies of the use of potassium intravenously in human patients. The concomitant use of glucose, insulin and amino acid has also been studied. It is suggested that as long as infusion proceeds at rates in the neighborhood of one to two per cent of the threshold fatal rate in animals, unjustified risks are not being assumed.

Rather large amounts of insulin are required to prevent blood sugar elevations during the administration of 10% glucose intravenously. Urine sugar losses are not excessive even when no insulin is infused. When insulin is administered with glucose, the drop in serum potassium accompanying the intravenous infusion is not more striking than that observed when no insulin is given. In both cases, lowering of serum potassium concentration is observed. The presumptive reason for this drop in potassium concentration is to be found in the laying down of

SYSTEMIC PHYSIOLOGY, NR-112-198 (Cont.)

glycogen with potassium. Administration of potassium intravenously in these concentrations and rates did not produce significant elevation of plasma potassium and failed to alter the curve of plasma potassium concentration.

The rate at which amino acids must be infused to produce gross elevations of the plasma non-protein-nitrogen concentration has been studied. It was found that excessive rates of administration are necessary to produce gross elevations of plasma non-protein-nitrogen with the intravenous administration of amino acids.

Work is being done on a method to measure the total quantity of water in the human body by the dilution of heavy water, using deuterium.

Estimated Completion: Continuing

NR-112-214 Effects of Prolonged Bed Rest on the Respiratory and Circulatory Systems (Unclassified)

Contractor: Edward L. Trudeau Foundation, Saranac Lake, New York
Contract: N7-onr-307, Task III, (3/1/47 to 2/28/49)
Investigators: A. J. Vorwald, G. Wright

The purpose of this project is to study effects of enforced inactivity on the respiratory and circulatory systems, including measurement of arterial oxygen tension at rest and following or during exercise--in various diseases of the lungs. Maximum breathing capacity; pulse and blood pressure responses to change in posture; metabolic, respiratory and circulatory responses to graded exercise and application of methods of Riley et al to measurement of the arterial oxygen tension at rest and during and following exercise will be investigated.

Progress to 6/30/48: Observations regarding the interpretation of the resting calculated alveolar-arterial gradient indicate that this gradient shows great variations which are not easily correlated with disease states.

From correlation studies it appears that the calculated alveolar pO_2 is a function of the arterial pCO_2, being inversely proportional as a rule. It is believed that a need exists for some means of further differentiation between the various components which apparently combine in any given case to produce the total gradient.

Studies on the pathological physiology underlying exertional dyspnea in granulomatosis in beryllium workers indicate that overbreathing, especially during exercise, and loss of breathing reserve are the primary causes of exertional dyspnea in granulomatosis occurring in beryllium workers. Overbreathing is clearly the earliest, predominant and sometimes the sole cause of the dyspnea. Loss of breathing reserve is a late development and severely augments the dyspnea. A low arterial blood pO_2 and higher than normal gradient for oxygen across the alveolar membrane was observed in each case of granulomatosis. The possible role of this factor as a cause of overbreathing is postulated. Loss of total lung volume and the development of emphysemia were observed in several cases, and the role of these factors as a cause of loss of breathing reserve is suggested.

Other studies are being carried on concerning changes observed during convalescence; maximum breathing capacity; vital capacity; Schneider index; respiratory and metabolic status at rest; respiratory and metabolic response to exercise; and measurement of oxygen debt.

Although prolonged physical inactivity (not absolute in character) was associated with the usual symptoms of weakness, etc., during the earliest physical exercises, the measurable deviations of physiological function were inconstant and of unexpectedly small magnitude. There was evidence of circulatory unbalance (Schneider test) but during a steady state of activity the cardiovascular apparatus was found to be adequate to the demands placed upon it. While it was shown, by these studies, that these subjects possessed a capacity for physical work which was low and which improved with rehabilitation, they do not show clearly the underlying mechanism of this fact. Breathing reserves were shown to be adequate as was also the ability to use

SYSTEMIC PHYSIOLOGY, NR-112-214 (Cont.)

oxygen. Muscle weakness seems to be the limiting factor in their tolerance for exercise. Unbalance of the cardiovascular system may play a part in the low tolerance for work by virtue of inadequacy to raise and maintain a sufficiently high cardiac output. In the absence of more objective evidence of physiological subnormality, it appears that the uncomfortable sensations associated with exercise after prolonged physical inactivity are in part due to an unusual acuity of the cortex for these sensations. Relatively mild hyperventilation may be grossly exaggerated by the cortex which for a long period has been unaccustomed to the feeling of hyperventilation and a rapid heart rate. De-conditioning which accompanies prolonged physical inactivity is apparently a temporary phenomenon and restitution of function to normal occurs as exercise is gradually increased. Data are not completely correlated on the study of factors influencing oxygen tension of the arterial blood at rest, during exercise and in disease. The most striking increase in gradient for O_2 was observed in the cases of pulmonary granulomatosis. Other diseases studied have in some instances revealed an interference with gas transfer but these are almost always minor in severity. Many show no abnormality of gas transfer. Probable explanation is that, in general, with the exception of pulmonary granulomatosis, disease processes involving the lung destroy the blood vessels at the same time and in the same areas where involvement of the alveoli occurs, so that marked reduction of effective gas transfer between air and blood is unusual.
Estimated Completion. Continuing

NR-112-235 Studies on Human Beings in Respiratory, Cardiovascular, and Neurophysiology (Unclassified)

Contractor: Mayo Foundation, Rochester, Minnesota
Contract: N6-ori-226, (10/1/46 to 6/30/49)
Investigator: D. C. Balfour

The purpose of this project is to conduct general studies in respiration, cardiovascular physiology, and neurophysiology in the human being.

Progress to 6/30/48: This contract involves principally a "good-will" relationship at a token expenditure of $1.00 for three years. Reports are submitted only at the discretion of the contractor and none have been received to date.
Estimated Completion: Continuing

NR-112-250 Study of the Gaseous Exchanges in Pulmonary Alveoli (Unclassified)

Contractor: Ohio State University, Columbus, Ohio
Contract: N6-ori-225, Task VIII, (1/1/47 to 3/31/49)
Investigator: F. A. Hitchcock

The purpose of this project is to make a study of the volume and composition of the air expelled from the lungs during explosive decompression. The plan is to develop and construct apparatus by means of which the oxygen, carbon dioxide, nitrogen, and water vapor content of the air can be determined continuously. A method is already available for fractionation and analysis of the air expelled from the lungs during rapid decreases in barometric pressure. From data obtained, it is hoped to be able to calculate the rate at which various gases diffuse through the alveolar membranes. A study of the temperature changes in the lungs of animals during the rapid expansion which takes place following explosive decompression, is also being made.

Progress to 6/30/48: A mass spectrograph has been developed which records continuously the changing composition of the air expelled from the lungs during explosive decompression.

SYSTEMIC PHYSIOLOGY, NR-112-250 (Cont.)

An apparatus has also been constructed for mechanical partitioning of air leaving the lungs with subsequent chemical analysis of the various fractions. Extensive investigations of various methods and techniques for air analysis have been made. One apparatus developed for this problem consists of a means of dividing the expired air into two fractions of predetermined size. With this apparatus the composition of alveolar air expelled by the Haldane-Priestly method has been investigated. Results show that the percentage of CO_2 present in air increases toward the end of the collection which would indicate a change in composition of alveolar air during collection by conventional techniques. Other types of apparatus are being investigated including one based on the electrical resistivity principle for determination of water vapor.
Estimated Completion: Continuing

NR-112-335 Circulation of the Brain (Unclassified)

Contractor: University of Colorado, Boulder, Colorado
Contract: N6-onr-231, Task VIII, (2/1/48 to 1/31/49)
Investigator: E. A. Scharrer

The purpose of this project is to study the functional significance of regional variations of the capillary density in the central nervous system; the role of vascular factors in the selective vulnerability of the ammon's horn, the Purkinje cells, and other areas of the central nervous system; the reorganization of the vascular pattern around brain lesions; the drainage of the interstitial fluid from the nervous tissue; and the resistance of different parts of the neuron to ischemia. Further investigations will, it is hoped, better present understanding of pathological processes in the central nervous system due to circulatory disturbances, through study of the fundamental anatomical and physiological characteristics of the circulation of the brain and spinal cord, and the microanatomical relationships between nervous tissue and blood vessels, the significance of the Virchow-Robin spaces, and the reaction of nerve cells and glia cells to fluid imbalance.

Progress to 6/30/48: The contractor has just assembled his personnel and is still collecting necessary apparatus for these investigations. The first question he plans to work on is how fishes are protected against effects of sudden pressure changes during vertical movements from surface areas to deep regions. The saccus vasculosus appears to provide the mechanism by which changes of intracranial pressure can be recorded and equalized for the protection of the brain and its circulation.
Estimated Completion: Continuing

NR-112-601 Blood Flow Volume in Kidney and Liver (Unclassified)

Contractor: University of North Carolina, Chapel Hill, North Carolina
Contract: (5/1/48 to 4/30/49)
Investigator: H. D. Bruner

Under this project the investigations resolve themselves into two phases. One phase dealing with animal experimentation, and the other dealing with clinical application.

The problem is an application of a mathematical analysis of factors controlling humoral distribution and tissue uptake of agents. This was part of a method for measuring cerebral blood flow by means of N_2O and later radiokrypton. The curve of disappearance of a substance from the blood stream is a function of blood flow when the substance is completely cleared by the tissue. It is essential that the substance be completely extracted and this requirement is best met by following the disappearance of a radioactive compound specifically taken out by the tissue, particularly the liver and the kidney. Also, the isotope to be used, I^{131} emits a satisfactory gamma ray making it possible to follow the curve without taking blood samples.

SYSTEMIC PHYSIOLOGY, NR-112-601 (Cont.)

Progress to 6/30/48: No progress to report.
Estimated Completion: Continuing

ELECTROPHYSIOLOGY

NR-113-005 Functional Organization of the Human Cerebral Cortex (Unclassified)

Contractor: University of Illinois, Urbana, Illinois
Contract: N6-ori-71, Task III, (5/1/46 to 3/31/49)
Investigators: P. Bailey, G. von Bonin, W. S. McCulloch

The purpose of this project is to investigate the pattern of connections in Macaca mulatta, Pan satyrs, and Homo sapiens.

The relationships of various areas of the cerebral cortex to others are very imperfectly known and difficult to determine by the usual anatomical methods because of the complication of structure. The method of physiological neuronography has made it possible to attack this problem fruitfully within a reasonable period of time.

Progress to 6/30/48: Work on the completion of studies of the organization of the macaque brain have been under way, along with experiments on two dozen macaque monkey and one chimpanzee. The chimpanzee was studied in order to complete information already available and to be certain that this information can be extrapolated to the human. Equipment for extending observations on the human cortex during operations has been obtained and records of several cases are available.
Estimated Completion: Continuing

NR-113-007 Changes in Hyperoxic Convulsions (Unclassified)

Contractor: University of Illinois, Urbana, Illinois
Contract: N6-ori-71, Task II, (6/1/46 to 6/30/49)
Investigator: W. S. McCulloch

The purpose of this project is to apply to the cerebral cortex in the hyperoxic convulsion those techniques which have led to an understanding of what is going on in the brain in other convulsions.

Changes in electrical activity, blood flow, oxygen tension, acidity, and oxidation-reduction potential will be recorded synchronously from devices attached to the animal in a small pressure chamber. Connections through the chamber wall will all be electrical. Seizure will be observed and photographed through a window at the time indicated by changes in the synchronous recordings; liquid air will be discharged on to the animals' brains and these will be analyzed for concentrations of intermediary metabolites.

Changes will be correlated with the convulsions induced by hyperoxia in the hope that a better understanding of the mechanism of such convulsions may indicate therapeutic utility and means of prevention when unwanted.

Progress to 6/30/48: This project has been primarily devoted to the design and fabrication of suitable equipment to be used in this investigation. A pressure tank, accessory apparatus including a cathode ray unit, three direct-coupled amplifiers, a non-blocking capacity-coupled three channel electroencephalographic amplifier, and devices for measuring cortical blood flow, cortical pH, oxidation reduction potentials and O_2, have been constructed.
Estimated Completion: Continuing

ELECTROPHYSIOLOGY (Cont.)

NR-113-046 Investigation of the Functional Organization of the Extrapyramidal Systems of the Brain; Quantitative Study of the Reinnervation of Voluntary Muscle After Nerve Action (Unclassified)

Contractor: Northwestern University, Evanston, Illinois
Contract: N6-ori-96, Task V, (6/15/46 to 6/14/49)
Investigators: H. A. Davenport, H. W. Magoun

The purpose of this project is the investigation of the extrapyramidal systems in monkeys by stimulating each component and recording the electrical activity evoked at the next lower station in the pathway utilizing Horsley-Clarke technique.

The investigators will also section nerves to two muscles, prevent one from regrowing into either muscle, split the other into equal parts and study the ability of the divided one to reinnervate the muscles. After regeneration of nerves is completed, their functional capacity will be evaluated by electrical recording and histological sections of them will be prepared and fibers in both the regenerated ends and the original trunk enumerated.

Progress to 6/30/48: In cats and monkeys, after complete bilateral transection of the cerebral peduncles performed under pentothal or vinethene, electrical stimulation of caudate nucleus, putamen, pallidum, amygdala, ventral thalamus, or sub-thalamus and their interconnections, yielded complex repetitive movements usually starting proximally in a contralateral extremity and extending distally. Those of the hind limb have generally been elicited from dorsal, those of the fore limb from intermediate, and those of the mouth and tongue (lapping and swallowing) from amygdala and other ventral sites.

Acute decortication has not altered these responses. Their frequency increased with the voltage of stimulation until prevented by a tonic component. Extensor hypertonus produced by destruction of the fastigial nuclei replaced all of them (except lapping and swallowing) by postures maintained during stimulation followed by rebound at the end of stimulation.

At voltages just insufficient to elicit movement, dimunition of tone can sometimes be detected, and such stimulation frequently reduces shivering and some spontaneous movements.

It has been established that the visual areas (17,17,19) of the cerebral cortex are connected with the auditory-visual area of the cerebellum. Work is in progress to determine whether or not the auditory area of the cerebrum is also connected to this part of the cerebellum by studying the effects of cerebral stimulation on the electrical activity of the auditory and visual areas of the cerebellum.

Experimentation to determine the relationship between the sensory areas of the cerebrum and the sensory receiving areas of the cerebellum indicates that the cerebellar tactile areas discharge into the cerebral tactile areas via the thalamus.

In studying the regrowth of motor nerves, the severed distal end of the common peroneal nerve with a severed proximal stump was joined to the lateral head of the gastrocnemius muscle to determine whether a small nerve, by branching of its fibers, will regrow into a larger one and thereby maintain the well being of the muscles originally supplied by the larger nerve. A normal average of about 1800 fibers in the larger (common peroneal) nerve were counted. In the smaller nerve (leading to the lateral head of the gastrocnemius) there were 350 to 400 fibers. The animals were sacrificed two to six months postoperatively and the number of fibers regrown into the degenerated common peroneal were determined. (Regrowth from the proximal stump of the common peroneal was prevented by capping with methyl-methacrylate plastic.) Results indicate that considerable branching of fibers in the smaller nerve occurred. In 31 of 35 animals, the number regrown was greater than the number in the smaller nerve from which the fibers were derived. The numbers varied from 568 to 2912 and indicated that extensive branching of fibers occurred when those from the small nerve grew into the large one.

ELECTROPHYSIOLOGY, NR-113-046 (Cont.)

Stimulation of denervated muscles of guinea pigs by tantalum electrodes permanently fixed at each end of a muscle mass (peroneal group) resulted in the formation of rather large masses of connective tissue around the electrodes. Since tantalum is almost inert in living tissue, it appears that electrical excitation over periods of six to eight hours per day is responsible for the connective tissue formation.
Estimated Completion: Continuing

NR-113-099 Properties of Muscle Cell Membranes (Unclassified)

Contractor: Medical College of Virginia, Richmond, Virginia
Contract: N6-ori-198, Task I, (9/1/46 to 1/31/49)
Investigator: R. W. Ramsey

The purpose of this project is to study the properties of living cells.

Following excitation of a cell the membrane is depolarized for an interval and then regains its former state of polarization. At the instant of recovery of polarization the cell is completely inexcitable to electrical stimuli even though the membrane potential is of normal magnitude. Subsequently the membrane gradually becomes more and more susceptible to electrical stimulation until the original threshold level is regained. It is suggested that the function of many naturally occurring drugs such as acetylcholine, histamine, etc., may be in rendering the membrane unstable during this relatively refractory period.

Accordingly it is proposed to investigate first, the effect of drugs on the duration and kinetics of the relatively refractory period.

Progress to 6/30/48: Initial phases of the investigation concentrated largely on simple measurements including rectangular strength duration curves (excitability), and injury potentials of skeletal muscles of the frog, involving comparison of normal excitabilities and demarcation potentials of skeletal muscles with those observed after exposure to a drug or enzyme poison.

The principal drug investigated is sodium fluoracetate, since it is generally believed that because it poisons the pyruvate-acetate system, it probably greatly affects systems requiring acetylation, such as the synthesis of acetylcholin.

In the determination of chronaxie and rheobase from rectangular strength duration, the most common result was heightened curves of irritability and great fatigability. The rheobase usually fell appreciably but rapidly increased upon repetitive stimulation. With greater concentrations the muscle became inexcitable to electrical stimulation.

Demarcation potentials of muscles were treated in several different ways and then compared. The most direct positive fact was that sodium fluoracetate lowers the membrane potential of muscle cells, but only with surety at concentrations five to 10 times greater than those required for a demonstrable effect on excitability, i.e., the concentration has to be in the order of molar/10,000.

It is felt that much of the variability of demarcation ascribed to biological variability of muscles can probably be accounted for by the fact that for a given indicating instrument, muscles of large cross sectional areas will appear to have high demarcation potentials compared to muscles of small cross sectional areas.
Estimated Completion: Continuing

NR-113-128 Metabolism of the Nervous System in Relation to Function (Unclassified)

Contractor: University of Chicago, Chicago, Illinois
Contract: N6-onr-20, Task XIV, (11/15/46 to 6/30/49)
Investigator: R. W. Gerard

[redacted]

ELECTROPHYSIOLOGY, NR-113-128 (Cont.)

In appropriate animals, brain function (behavior and electrical stimulation) related to metabolism (oxygen usage, chemical analyses and tracers) as conditions are varied in normal development, induce over and underactivity (forced exercise convulsant, or depressant drugs, thyroid feeding or removal, etc.) and degeneration and regeneration. Metabolism of the nervous system in relation to function with emphasis on relation of carbohydrate to phosphoproteins and phospholipins and on use of tracer techniques is being made. This study is directed primarily to the elucidation of problems regarding neural metabolism as a basis for normal function and abnormal variations (better fiber regeneration), improving use of hypoglycemia and other chemical or shock therapies in the treatment of psychoses, ameliorating nervous system fatigue which limits performance under maintained physical stress.

Progress to 6/30/48: Research has been initiated on the changes in phosphoproteins and phospholipids in nerve during rest and activity; comparable determinations on free amino acids; the influence of some metabolic inhibitors on nerve conduction; the role of acenosine triphosphate and adenosine triphosphotase in conduction and membrane potentials; and the existence of DC potentials in the mammalian brain and the influence on these of chemical and other conditions. Radioactive tracer methods are being established.

The amount of free glutamic acid and non-protein glutamic acid in rat brains has been determined. Evidence suggests that strychnine convulsions decrease the amount of free or combined glutamic acid in brain.

It has been found that sodium fluoracetate does not affect conduction or resting respiration of frog sciatic nerve. Methylfluoracetate at .005M which should penetrate more readily, irreversibly abolishes the action potential in three and one-half hours, giving faster extinction at higher concentrations. Acetate, alcohol, pyruvate, or succinate at .01M do not prevent the fall in action potential but fumarate at this concentration protects it, while permitting a fall of 50% in resting respiration. .05M succinate also protects.

Tetraethyl pyrophosphate increases the amplitude and regularity of the normal rhythm of the electrical activity of isolated frog brain. Di-isopropyl fluorophosphate may slow the waves to two a second and render them more spikelike. DFP but not TEP completely suppresses spikes otherwise obtained with caffein alone.

Methylfluoracetate depresses the amplitude of the spontaneous rhythm, leaving the frequency unchanged, and reduces the period of surviving activity of the excised brain to about one-tenth of normal. This metabolic inhibitor fully suppresses caffein spikes. Sodium fluoracetate has no significant effect on the spontaneous or caffein induced activity; presumably because of poor penetration.

It has been postulated that a basic feature of nerve impulse conduction, the permeability change in the membrane, depends upon a structural change in certain membrane proteins. If the latter resemble the myosin system of muscle, they should be associated with ATP-ase activity.

To test this hypothesis, measurements were made of the ATP-ase activity to the axoplasm, extruded from cleaned giant axons of the squid and of the remaining sheath portion. Axoplasm splits phosphate from ATP at the rate of about 0.2 micrograms P/mg wet weight in 30 min at 26.5° while the average figure for the sheath is 19, about 100 times as much! Not only is the ATP-ase activity of the nerve fiber almost exclusively confined to the sheath portion, but the latter has an activity even greater than that of the squid muscle. Contrary to the case of cholinesterase, ATP-ase is not more concentrated in the optic ganglion than in the axon sheath. Nerve ATP-ase also resembles vertebrate muscle ATP-ase in its substrate specificity and in its sensitivity to CA^{++} concentration, though it is considerably less sensitive to sulfhydryl poisons.

Estimated Completion: Continuing

ELECTROPHYSIOLOGY (Cont.)

NR-113-133 Autonomic and Somatic Effects of Experimentally Induced Convulsions (Unclassified)

Contractor: University of Minnesota, Minneapolis, Minnesota
Contract: N6-ori-161, Task II, (7/15/46 to 7/1/49)
Investigator: E. Gellhorn

The purpose of this project is to investigate the following problems:

(1) Somatic effects of experimentally produced convulsions. The chief problems concern the influence of afferent impulses originating either in peripheral nerves or in the hypothalamus on the convulsive reactivity of the central nervous system, particularly of the motor and sensory cortex. The study includes convulsive reactions induced by drugs such as picrotoxin as well as convulsions produced by electrical currents.

(2) Autonomic effects of experimentally produced convulsions. The influence of procedures used in the shock therapy of mental diseases on the reactivity of autonomic centers of the rat as indicated by changes in blood sugar.

Progress to 6/30/48: Investigation, of the effect of optic and acoustic stimulation on cortical potentials and movements under the influence of increasing degrees of picrotoxin poisoning, revealed that progressing degrees of picrotoxinization elicit a response in the specific cortical projection areas which increases in amplitude and also becomes repetitive. Moreover, sensory responses similar in quality and quantity appear in previously nonresponding cortical areas (including the suppressor areas) and in the hypothalamus. The motor cortex is not particularly sensitive to picrotoxin discharges, since responses to an acoustic stimulus may appear in non-acoustic projection areas while they are absent in the motor cortex. Optic or acoustic stimuli may elicit or intensify convulsive movements but these reactions are mostly confined to the moment of stimulation. Generalized convulsive movements are not induced by these stimuli.

Studies on the differential action of anoxia, asphxia, and carbon dioxide in normal and convulsive potentials showed that: (1) Anoxia induced by inhalation of 4% oxygen or of nitrogen abolishes convulsive potentials at a time when normal potentials are practically unchanged; (2) on readmission of air, normal potentials appear in the previously convulsant areas before the convulsive spikes reappear; and (3) there is no indication of an excitatory phase in anoxia.

Asphyxia induced by cessation of artificial respiration similarily abolishes spikes before normal potentials, and leads to an earlier reappearance of the latter on readmission of air. In addition, asphyxia causes a temporary excitation characterized by an increased frequency of spikes and, in the normal cortex, by an increase in background and a decrease in dial-potentials.

When anoxia or asphyxia is carried out until convulsive and normal, grouped (dial) potentials are abolished, their restitution on reoxygenation is preceded by continuous small potentials which are considered to be the equivalent of the increased post-anoxic excitability.

Convulsive potentials may be replaced in the course of anoxia or asphyxia by dial potentials, which were absent in the same cortical area as long as convulsive activity persisted. Moreover, under favorable conditions progressive anoxia and asphyxia is accompanied by a decreasing spike amplitude while on reoxygenation their magnitude increases. These data seem to indicate that anoxia and asphyxia induce a progressive decruitment of cortical cells and re-oxygenation, a progressive recruitment. The limiting factor which determines the number of discharging neurons and the degree of their activity (convulsive versus non-convulsive) seems to be the supply of oxygen.

The restitution of normal oxygenation of the blood after anoxia and asphyxia is often accompanied by a rebound, which is shown in the normal cortex in the form of more frequently appearing groups of dial potentials and in the convulsant cortex as increase in frequency of spikes. During this rebound convulsive potentials may appear which were absent under control conditions due to the application of subthreshold concentrations of the convulsant drug.

ELECTROPHYSIOLOGY, NR-113-133 (Cont.)

Hypercapnia induced by inhalation of 10.6% carbon dioxide causes excitation of normal and particularly of convulsive potentials.

Investigation of the influence of repeated anoxia, electroshock and insulin hypoglycemia on the reactivity of the sympathetico-adrenal system indicates that:

Action of a standard anoxia test involving five periods of 25 min each at 280 mm of mercury was used as a method to evaluate the responsiveness of the centers of the sympathetico-adrenal and vago-insulin systems on the basis of blood sugar determinations. It was found that repeated convulsions induced electrically increased greatly the hyperglycemic response of rats to the standard test. This is interpreted as a sign of increased reactivity of the sympathetico-adrenal system and is accompanied by a marked dominance of this system as compared to the vago-insulin system. Similar results were obtained after frequent exposures to prolonged anoxia. However, repeated insulin comas failed to bring about this shift and showed actually a diminished or no hyperglycemic response to the standard anoxia test. It was shown that in these rats, the administration of adrenalin failed to induce glycogenolysis, which explains the reduction in the hyperglycemic response. Whether the reactivity of the centers of the sympathetico-adrenal systems is increased, as it seems to be by prolonged anoxia and electroshock, will be determined later. Effects were reversible after two to five weeks. Work on anoxia and electroshock lends support to the idea that procedures similar to those used in "shock therapy" of mental disease increase reactivity of the centers of the sympathetico-adrenal system.
Estimated Completion: Continuing

NR-113-154 — Effects of Chronic Tension on Peripheral Nerves, Skeletal Muscle, and Blood Vessels — (Unclassified)

Contractor: University of Texas, Austin, Texas
Contract: N6-ori-169, Task I, (7/1/46 to 6/30/48)
Investigator: D. A. Duncan

The purpose of this investigation is to ascertain the extent to which nerves, muscles and blood vessels may be lengthened by chronic mechanical tension in the repair of defects of these structures.

Progress to 6/30/48: This project has been terminated.

Tantalum retractors, suitable for putting tension on the sciatic nerve of cats, have been designed and used on six cats. Some of these animals have had the nerve stretched from one to four times without apparent damage to the nerve. One animal, in which all conceivable natural slack in the nerve has been taken up and true lengthening of the nerve is taking place, has reached the stage obtained in previous experiments in which the nerve was 50% longer than normal.

NR-113-232 — Measurement of Strength of Affected Muscles in Orthopedic Disabilities — (Unclassified)

Contractor: Springfield College, Springfield, Massachusetts
Contract: (7/1/48 to 6/30/49)
Investigator: H. Clarke

Tests will be made of various methods of measurement of muscle strength developed on normal control subjects and orthopedic patients. Techniques already developed will be extended and refined, testing apparatus will be further developed, and norm charts will be constructed for the various strength tests. Norm determinations concerning requirements of personnel in performing certain specific tasks (human engineering) will be made.

ELECTROPHYSIOLOGY, NR-113-232 (Cont.)

Progress to 6/30/48: This project expired on 14 March 1948, however, it has recently been reactivated. There is no progress to report at this time.
Estimated Completion: Indefinite

NR-113-241 Study of Nerve and Muscle Function (Unclassified)

Contractor: Johns Hopkins University, Baltimore, Maryland
Contract: N5-ori-166, Task VIII, (10/1/46 to 6/30/49)
Investigator: J. L. Lilienthal, Jr.

The purpose of this project is to investigate the electrical and chemical changes occurring during normal and abnormal activity of nerve and muscle. This includes measurements of contraction strength of muscle under influence of a variety of conditions. Results may be of importance to understanding neuromuscular disease as well as general tissue metabolism. Study of neuromuscular transmission and of the effects of intraarterial acetyl choline, neostigmine, epinephrine, and muscle enzymes, curare in the motor disturbances accompanying hyperthyroidism, hypoadrenalism, the muscular dystrophies, post-infection asthenia will be made.

Studies are being made on the effect of highly purified or crystallized nemotoxins of A. botulinus, B. tetanus, and C. diphtheria on neuromuscular function in experimental cats. Measurement--muscle of normal enzyme active levels of succinic dehydrogenase, cytochrome c, creatine phosphors, ATP-ase and related enzymes as required for purposes of comparison with the dystrophic muscle will also be made.

Progress to 6/30/48: Studies of the following subjects have been reported:

1. Vascular responses to curare in man.
2. Creatine metabolism.
   a. Relations between creatine and sodium metabolism.
   b. Renal factors in creatine excretion.
   c. Studies of the effects of various endocrine tubular reabsorbtion of creatine.
3. α-Tocopherol--investigation of the antithrombic and antiproteolytic activity of alpha tocopheryl phosphate.
4. Effects of 2-4 dichlorophenoxy acetate (2-4 D) which produces intense myotonia and of pentamethylene tetrazol (metrazol) which potentiates electrical activity and tension of muscle.
5. The problem of the distribution of potassium between serum and interstitial fluid in man has been studied. It has been found that contrary to previous studies, the potassium ion is freely diffusible across the vascular membrane in accord with the Gibbs-Donnan theory.
6. Two courses of desoxycorticosterone acetate in doses varying from five to 15 mg/day were given to a patient with myotonic dystrophy. During the second week of DCA administration, there was an increase in voluntary fluid intake, a diuresis with reduction in water balance, negative sodium and potassium balances, and loss of body weight. The glomerular filtration rate was unchanged. Reabsorption of water and of creatine was inhibited. During the week following withdrawal of DCA, after polydipsia, polyuria, and electrolyte loss had been established, the pattern of electrolyte balance resembled that of Addison's disease.

Estimated Completion: Continuing

NR-113-281 Narcotic Effects of High-Nitrogen Pressures in Cell Suspensions or Isolated Tissues (Unclassified)

Contractor: University of Rochester, Rochester, New York

ELECTROPHYSIOLOGY, NR-113-281 (Cont.)

Contract: N6-ori-241, Task II, (1/1/47 to 8/31/48)
Investigator: W. O. Fenn

The behavior of man exposed to high air pressures has given rise to the belief that high pressures of nitrogen have narcotic effects on the brain. There are, however, no experiments on isolated tissues which support this belief. The purpose of this investigation is to study isolated muscles, nerves and other tissues under high pressures of nitrogen in order to discover whether any of the effects can be attributed to specific nitrogen effects or whether they are all due to the effect of high pressure, per se. The initial experiments have been concerned with the effects of nitrogen pressures on phagocytosis of starch grains by white blood corpuscles of the rat. Pressures up to 800 lb of nitrogen were used but no changes in the rate of phagocytosis were observed. Experiments on the action potentials and injury current of nerve are now in progress. It is planned to investigate next any possible effects on reflex contraction of frog muscles.

Progress to 6/30/48: Evidence for a narcotic action of increased pressures of nitrogen has been sought along three lines: (1) Phagocytosis of rice grains by rat leucocytes; (2) injury potential and action potential of frog sciatic nerve; and (3) heart beat, body movements, and survival of the Crustacean, Daphnia.

These experiments on the phagocytosis of rice grains by rat leucocytes have failed to demonstrate a narcotic effect of nitrogen pressures up to 800 lb/in ^{2}. The injury potential of frog sciatic nerve was found to be depressed little or not at all by high tensions of nitrogen. Experiments still in progress on the heart beat, locomotion, and survival of Daphnia have as yet revealed no noteworthy difference between effects of 1000 lb/in ^{2} of nitrogen and the same pressure of helium. Narcotic effects have been lacking, and a hyperexcitability characterizes a later period in exposure. High pressure of air of less than 1000 lb/in ^{2} gives effects, presumably due to oxygen poisoning, which seem to bear some resemblance to narcosis.
Estimated Completion: Continuing

NR-113-300 Mechanisms of Muscular Contraction (Unclassified)

Contractor: New York University, New York, New York
Contract: N6-onr-279, Task VII, (5/15/48 to 9/30/49)
Investigator: A. Sandow

The purpose of this investigation is to determine the fundamental nature of the mechanochemistry of muscle action, i.e., to elucidate the means by which the muscle contractile proteins are energized for mechanical activity by coupling to and interaction with adenosinetriphosphate (ATP), the immediate source of chemical potential energy for the contractile material. This basic knowledge can then be applied to the understanding and possible treatment of certain muscular dysfunctions, especially in connection with muscular atrophy.

Progress to 6/30/48: No progress report has been received.
Estimated Completion: Continuing

NR-113-313 Anatomical Study of Afferency in the Sympathetic Innervation of the Extremities (Unclassified)

Contractor: Georgetown University, Washington, D. C.
Contract: N8-onr-552, (4/1/48 to 3/31/49)
Investigators: F. D. Threadgill, O. Solnitzky

ELECTROPHYSIOLOGY, NR-113-313 (Cont.)

The purpose of this project is to study retrograde cell degeneration, Wallerian degeneration, and terminal bouton degeneration in the nerve cells and fibers in the dorsal and sympathetic ganglia, following ramisectomy of the sympathetic ganglia innervating the lower extremities of cats. By this method it will be possible to determine: (1) If the sympathetic ganglion contains afferent nerve cells with axons passing to the dorsal ganglion (function of pericellular plexus of Dogiel); (2) if the sympathetic ganglion contains afferent fibers with the cell bodies in the dorsal ganglion (such as the viscero-sensory fibers of the abdomen); and (3) if there is no evidence of degeneration of cells or of fibers in the dorsal ganglion (indicating that afferency is not a property of the sympathetic nervous system).

This study is pertinent to the treatment of causalgic and related states in post-traumatic war injuries as well as for other injuries. It should also lead to better understanding of some of the peripheral vascular diseases, i.e., Raynaud's disease, and such other diseases as hypertension and angina pectoris.

Progress to 6/30/48: No progress report has been received.
Estimated Completion: Continuing

NR-113-336 Nerve Growth Under Stimulation of Continued Stretch (Unclassified)

Contractor: New York Medical College, New York, New York
Contract: N7-onr-401, Task I, (6/1/47 to 5/31/49)
Investigator: T. I. Hoen

The purpose of this project is to use animal experimentation to determine the extent to which nerves can be lengthened by prolonged traction, the effect of such lengthening on structure of nerves, including nerve volume, cellular reaction in nerve, nerve sheaths and Schwann's cells, axones and anterior horn cells. The physiological status of nerves will be followed during lengthening by means of electrical studies.

Progress to 6/30/48: Results of recent experiments indicate that it is possible to get gross lengthening of the nerve, to the extent of 300 to 400% without demonstrable anatomic damage to the axones. It is hoped that this will be confirmed with physiological data in the next phase of the work.
Estimated Completion: Continuing

NR-113-399 Cerebral Regulation of the Autonomic Nervous Functions (Unclassified)

Contractor: Medical College of Virginia, Richmond, Virginia
Contract: N6-onr-254, Task III, (9/1/47 to 8/31/48)
Investigator: E. C. Hoff

Under this project cortical and subcortical areas will be stimulated with a variable frequency and amplitude condenser discharger square valve stimulator through electrodes applied to brain surface or placed in deeper areas by a Horsley-Clarke stereotoxic instrument. Effects of stimulation on blood pressure, heart rate and rhythm, vasomotor, and other autonomic functions will be measured coincident with the recording of efferent volleys in various automatic nerves with a cathode-ray oscillograph with suitable amplification.

Progress to 6/30/48: Evidence has been obtained in cats of a topographical localization in the frontal cortex of the brain of an autonomic control mechanism chiefly concerned with phasic changes in vegetative activity mainly in the direction of sympathetic over-action. The gyrus proreus (lying most rostrally in the frontal lobe) is particularly concerned with this sympathetic activation. It is of physiological as well as of clinical significance that areas within the frontal

ELECTROPHYSIOLOGY, NR-113-399 (Cont.)

cortex are thus concerned not only with the regulation and modification of posture and phasic activity of skeletal muscles but also with the readjustment of the vascular supply and other sympathetic changes appropriate to the bodily movements to be carried out. Clear-cut evidence has also been adduced for a predominantly depressor mechanism localized within the cortex, posterior to the frontal lobes, in the anterior portions of the parietal and temporal lobes. This depressor mechanism appears to act by inhibition of the frontal lobe sympathetic mechanism, and in the intact organism appears to exert a constant as well as a phasic governing control over autonomic activity, preventing excessive rise of blood pressure.

In view of this topographical separation in the cortical regulation of pressor and depressor responses, it may become feasible (if a similar mechanism can be shown to exist in man) by accurate section of specific projection fibers from the cortex to reduce excessively high blood pressure associated with anxiety-tension states.

Specifications have been worked out for a multichannel oscilloscope which, it is believed, will permit adequate recording of action potentials from two autonomic nerves, blood pressure, stimuli, and timing simultaneously.

A blood pressure pick-up system is also being constructed. Blood pressure recording is done by means of a Statham pressure gauge. In place of a needle in the artery, indwelling polyvinyl plastic catheters may be used. This way the animal can be moved if necessary and there is no difficulty with coagulation.

Estimated Completion: Indefinite

TEMPERATURE REGULATION AND ENERGY METABOLISM

NR-114-108 Effects of Reduced Atmospheric Pressure on Respiration (Unclassified)

Contractor: University of Maryland, College Park, Maryland
Contract: N6-ori-147, Task I, (6/24/46 to 8/31/48)
Investigator: N. E. Phillips

The purpose of this project is to study the effects of different atmospheric pressures and temperatures on the water relation in animals as reflected in total weight loss, water loss, and water balance; the effect of atmospheric water vapor pressure on the respiratory exchange; the effects of different atmospheric pressures and temperatures on respiratory quotient, basal metabolism, heat loss, and body temperature; the factors affecting the composition of alveolar air; and oxygen transportation, oxygen utilization, respiratory enzyme systems, and acid-base balance.

Progress to 6/30/48: In studying the effects of humidity and temperature on the survival of albino mice exposed to low pressure it has been determined that mice in an atmosphere saturated with moisture are able to withstand significantly lower pressures than mice in dry atmosphere at temperatures from 20°C to -20°C. Between 30°C and 0°C, the ability of mice to withstand reduction in atmospheric pressure increases with reduction in environmental temperature. Reduction in temperature below 0°C, decreases the ability of mice to withstand pressure reduction. When exposed to reduced atmospheric pressure, mice in moist air lose less moisture by evaporation than do mice in dry air at temperatures below 20°C. The beneficial effect of moist air at low pressure is explained as being due to the decrease in the loss of heat from the animal by evaporation with a corresponding reduction in the demand for oxygen.

Studies on Japanese beetles exposed to low pressure for short periods indicate that the beetles are killed by the rapid loss of water through excessive evaporation rather than by anoxia. Because of the rapidly evaporating water, the body temperature of beetles falls rapidly during exposure to low pressure. Beetles are able to live for periods in the absence of atmospheric oxygen and in atmospheres of inert gases.

TEMPERATURE REGULATION AND ENERGY METABOLISM, NR-114-108 (Cont.)

Investigations of the physiological effects of increased respiratory dead space have been under way in order to determine the effects of large volumes of artificial dead space on the minute volume, tidal volume, breathing rate, and time required to reach respiratory equilibrium. A marked increase in ventilation rate occurred with each increase in external dead space. Increase in effective dead space with each increase in external dead space is considerably greater than figures suggest. There was a slight increase in the respiration rate with increased dead spaces up to 2000 cc, above which the rate was slightly reduced. Except where there is marked O_2 reduction, breathing is regulated to give a constant percentage of CO_2. The effect of adding artificial dead space was to increase the ventilation rates so that the CO_2 percentage in the alveolar air would be kept nearly constant. The time required to achieve respiratory equilibrium was roughly proportional to the dead space employed except at 2500 cc and 3000 cc, at which there was no further increase.

Research on the effect of humidity on the change in body temperature of the albino rat during exposure to low atmospheric pressures revealed that the adult male rat shows a reduction in body temperature. This reduction is less in rats exposed to moist air than in those exposed to dry air. This heat saving effect of moist air is considered to be due to the absence of water evaporation from the animal. In rats exposed to moist air, the rectal temperature remains normal as the pressure is reduces until about 560 mm of mercury is reached. Below this it falls moderately. In dry air, the drop in rectal temperature begins immediately and continues gradually until about 510 mm of mercury is reached, below which it falls more rapidly than in animals in moist air. As long as the oxygen tension is maintained at its sea level equivalent, there is no change in body temperature. There appears to be a constancy between each total pressure (or partial oxygen pressure) and the body temperature established at that pressure. Changes in skin temperature follow a pattern similar to those of rectal temperatures, but, under the same conditions, are not as great and are more variable. The greater the pressure reduction, the longer is the period necessary for the establishment of constant body temperature.
Estimated Completion: Continuing

NR-114-192 — Relation of the "Biological Value" of Proteins to Their Thermogenic or Heat-Producing Effect — (Unclassified)

Contractor: University of Rochester, Rochester, New York
Contract: N6-ori-126, Task IX, (10/1/46 to 9/30/48)
Investigator: E. S. Nasset

The investigation under this project involves detailed studies of the proteins in eggs, meat, and wheat as they represent a considerable spread in the biological value scale.

Quantitative determination of the amino acids contained in the proteins and carefully controlled nitrogen balance experiments for biological value will be made; also determination of heat production at proper intervals (for thermogenic effect). Experiments on native protein with equivalent mixtures of synthetic amino acids and variations thereon will be duplicated. It is hoped to determine why proteins give more heat than fat or carbohydrate. Expressions will be given in terms of definite mixture of amino acids (quantitatively).

Progress to 6/30/48: Control amino acid diets are compounded to simulate egg protein. The 10 essential amino acids are used for this purpose, employing the natural isomers when available. It is hoped that eventually a mixture can be used which simulates a protein in respect to every animal acid. Progress to date has shown that this mixture may have a higher biological value than egg protein itself. Heat production was significantly increased on an amino acid mixture partially deficient in one amino acid.

The non-essential amino acid, glutamic acid, used as a "filler" to provide the nitrogen not supplied by the mixture of essential amino acids, has no specific influence on the body nitrogen sparing effect of the whole mixture. If glycine is substituted for glutamic acid, the

TEMPERATURE REGULATION AND ENERGY METABOLISM, NR-114-192 (Cont.)

results are the same. When a complete amino acid mixture is fed to rats, which have previously been on a protein-free diet, the urinary excretion of nitrogen is decreased and the "spared" nitrogen does not accumulate in the blood non-protein nitrogen.

In nitrogen balance studies using amino acid mixtures, the amount of absorbed nitrogen required for nitrogen equilibrium is found to be a more consistent characteristic of the dies than is "biological value".

If the L-methionine content of a "complete" amino acid mixture is reduced to one-third, the biological value of the mixture is halved. If both isomers of methionine are fully utilized, the mixture contains two-thirds as much of this amino acid as egg. It is computed that adult rats require 4.8 mg DL-methionine nitrogen per day per $Kg^{3/4}$ for the maintenance of nitrogen equilibrium. The specific dynamic action of the food was not altered by reducing the methionine content. If the DL-valine content of the amino-acid mixture is reduced to one-third, the biological value of the mixture is unchanged. This indicates that the daily requirements of DL-valine are less than 5.0 mg of nitrogen per $Kg^{3/4}$. The specific dynamic action is not altered by reducing valine content.

Estimated Completion: Continuing

NR-114-293 — Respiratory Exchange in Man During Periods of Intense Muscualr Activity — (Unclassified)

Contractor: Swarthmore College, Swarthmore, Pennsylvania
Contract: N7-onr-380, Task II, (5/1/47 to 4/30/48)
Investigators: L. Irving, H. Erikson

Progress to 6/30/48: This project has been transferred to the Human Ecology Branch and combined with project number NR-162-430. Progress will be reported under that number.

ANATOMY

NR-115-016 — Study of Bone Repair — (Unclassified)

Contractor: Columbia University, New York, New York
Contract: N6-ori-110, Task II, (6/1/46 to 6/30/49)
Investigator: S. S. Hudack

This project involves a study of the influence of various artificial matrices on the formation of bone in healing tissue. The artificial matrix used as a vehicle to make calcium and bone salts available for bone formation will be so formed that the optimum properties of undifferentiated connective tissue will be utilized for deposition of bone. Optimum physical form and mineral content of the matrix is being studied in relation to the vascular supply. The study of artificial matrices may make possible an exogenous substitute for isogenous bone grafts. This can make possible the grafting of non-unions and filling-in of bone defects and cavities with greater probability of success and less further mutilation in reconstruction cases than is possible with present techniques.

Progress to 6/30/48: A crude process of making lucite filament for the artificial matrix has been developed and techniques for handling isogenous and non-isogenous collagen fibrils have been devised.

Studies are under way on articular replacement, wherein the diseased portion of the bone is removed (including even the ball and socket of the hip joint) and is replaced with an artificial bone and joint made of stainless steel and a plastic ball. This substitute works practically as well as a normal bone joint. Patients are able to walk without pain or stiffness--one after

ANATOMY, NR-115-016 (Cont.)

three years in bed with arthritis. Work has also been done on substituting for the shoulder joint.
Estimated Completion: Continuing

NR-115-070 Relationships of Function and Morphology of Blood Vessels; Acute Necrotizing Arteriolitis (Unclassified)

Contractor: Yale University, New Haven, Connecticut
Contract: N6-ori-44, Task XII, (6/1/46 to 5/31/49)
Investigators: M. C. Winternitz, H. B. Shumaker

The purpose of this project is to make microscopic studies of the repair of the intimal, elastic and muscular elements, the vasavasorum; the nutrition of free vein inserts, the anatomy and function of the neural elements; the best methods of vascular suture; the expansibility, contractility, and growth in immature animals of lines of anastomosis; and possible further application of the techniques of vascular suture. As a necessary corollary to these studies, the relative efficacy of various anticoagulant agents in preventing intramuscular clotting is being undertaken. Necrotizing arteriolitis is a vascular lesion occurring in diseases of man such as *malignant nephrosclerosis, periarteritis nodosa, rheumatic fever,* and allergic disorders. The plan of this project is to study the mechanism of production of these lesions experimentally beginning with the reaction of the blood-vessel wall to known chemical substances. Such lesions will be comparable anatomically and biochemically with those produced by simple allergic states. The relation of such experimental lesions to more chronic degenerative forms will also be investigated as well as the biology and biochemistry of lesion producing substances in relation to their observed anatomical and physiological effects--including the anatomy and function of blood vessels and the physiology of the heart from the standpoint of clinical surgery.

Progress to 6/30/48: Injection of allylamine in dogs affords a relatively simple concrete starting point for a study of the pathogenesis and fate of arterial lesions which are basically similar to those occurring in certain diseases in man.

Lipid accumulation occurs in these dogs. Hearts of animals dying during allylamine administration have been dilated, and scarred with fibrous vessels. Once the arterial media is destroyed, little change occurs in the intima unless reaction occurred at the time of the original medical necrosis. Hemorrhage, necrosis, and deposited pigment are found in thickened proliferated intimae. Only rarely does a vessel with a fibrous media show fresh subendothelial lesions.

Experiments have demonstrated that Grollman's "depressor" extracts are in reality a mixture of depressor and pressor substances. The total effect of these mixtures on injection is a marked fall in systemic blood pressure. Injection of these mixtures into nephrectomized dogs results in systemic arteriolar necroses.

These observations allow the conclusion that temporary systemic hypertension is not necessarily a factor in the pathogenesis of arteriolar necroses following injections of renal extracts into nephrectomized dogs.

Studies on the other phase of this contract include the following, results of which are too numerous to mention here: Healing of blood vessels with particular reference to arterial suture; effectiveness of anti-coagulant agents in inhibiting intra-vascular clotting; mechanisms and function of intrinsic innervation of blood vessels; frostbite; morphological study of vasa-vasorum; effectiveness of heparin and dicumarol in prevention of arterial and venous thrombosis; fibrinogen; coarctation of the aorta and aortic aneurysm; sympathectomy; causalgia; post-traumatic vasomotor disorders; and several related studies.
Estimated Completion: Continuing

ANATOMY (Cont.)

NR-115-182 Quantitative Measurements of Cells and Cell Types (Unclassified)

Contractor: University of Kansas, Lawrence, Kansas
Contract: N6-ori-220, Task I, (6/15/47 to 6/14/49)
Investigator: P. C. Roofe

The purpose of the project is to count, in normal male and female rats, the cell population of the areolar connective tissue, spleen, lymph nodes, and bone marrow under normal diets. The age limit of the rats will be three months after reaching sexual maturity. This same procedure will be executed on rats, on diets deficient in one or more of the essential animo acids. No attempts will be made to see the changes brought about by a deficient diet on older or aging individuals. Also no attempts will be made on effects of deficient diet in the early growth stages or upon fetuses carried by females on a deficient diet. Actual counts are to be made on sectioned material instead of smears. Stains will be used not only for recognition but also to bring out secretory granules both intracellular as well as extracellular.

Progress to 6/30/48: Three groups of rats have been studied. One group consisted of rats on a normal diet containing 18% protein, another group consisted of rats whose diet contained only two per cent protein, and a third group had no protein in its diet.

When these animals were dissected after being on the diet about 57 days, the hemopoietic organs were removed. To date the cervical lymph nodes of six rats on the normal 18% diet, nine rats on the two per cent diet and 10 on the zero per cent diet have been studied.

The camera lucida was employed for making quantitative cell counts. The graph paper was calibrated and an area 50 micron square was drawn and the cells in this area were sketched and counted.

Four different areas were studied: the nodule, the internodular area, the medullary cord, and the medullary sinuses. Cells were classified according to their size as they appeared in the field and the reticular cells were classified according to their morphology. Ten sections from each node were studied giving a volume of 250,000 cubic microns. This was then converted to one cubic millimeter. The average was taken of the total of the counts of each type of cell in each area for the three groups of rats.

The cell populations of the different types of cells in the lymph nodes of rats on the two per cent and zero per cent protein diet do not vary much from one another.

However, the deviation of these cell counts from those in animals on a normal diet is quite significant. The reticular cells vary but little from the normal, the large lymphocytes likewise remain close to the normal. The medium-sized and small lymphocytes are the most greatly affected by the depleted diets. The medium-sized cells in the nodule are depressed about 1,600,000 cells/cu mm from the normal, while the small lymphocytes in this area are increased in number over 2,000,000 in the two per cent animal and 2,500,000 in the zero per cent animals. In the internodular area, the medium-sized cells are increased about 500,000 in both depleted diet groups. The small lymphocytes in this area are depressed about 1,500,000 cells/cu mm in both depleted diet groups.

In the medullary cords, the medium-sized lymphocytes are depleted about a million cells below the normal in the two diet groups, while the small lymphocytes are increased about a million cells in each group of protein-deficient animals.

The medium-sized lymphocytes in the medullary sinuses are increased in population in the two groups above the normal, while the small type cells are diminished in number about two million cells. The largest variation of large lymphocytes appears here with a difference of about 200,000 cells above the animals on 18% or normal diet.

Estimated Completion: Continuing

ANATOMY (Cont.)

NR-115-245 Mass Cultivation of Human Tissues (Unclassified)

Contractor: New York City Cancer Institute, New York, New York
Contract: N7-onr-343, Task I, (6/1/47 to 5/31/49)
Investigator: J. Vogelaar

This study will attempt to determine the optimal growth conditions for human fibroblasts. A systematic study of the significance of various amino acids and vitamins for the growth in vitro of fibroblasts is being made. A similar study with regard to human skin epithelium is also under way. Methods will be worked out for the mass cultivation of both kinds of tissues. A special study will be made of those biological factors which may interfere with the successful implantation of the tissues into the human body. As well as a clinical study of the behavior of implants of tissue cultures into the human body.

Progress to 6/30/48: A number of synthetic culture media have been employed to study the behavior of human cells in vitro. Artificial feeding solutions of known composition (various combinations of essential amino acids, vitamins, purine and pyrimidine bases) failed to sustain the growth and development of human leucocytes. Media containing peptone in combination with glycine favor the growth of individual cells, their increase in number and their transformation into fibroblasts. Best results with monocytes were obtained with a medium prepared from 57 different chemicals (inorganic salts, alcohol, water-soluble vitamins, glucose and hemin also). These cells could be kept alive for several weeks during which time both cell multiplication and the transformation into fibroblasts were observed. Indications were that monocytes are only increased in size when certain essential amino acids are present in the medium.

Zinc and fluorine in a concentration of the order of 0.5×10^{-5} have a definite beneficial effect on the cultures. No such effect has been observed with manganese, nickel, and cobalt.
Estimated Completion: Continuing

Biochemistry

ADMINISTRATIVE

NR-120-475 — Advisory Panel in Biochemistry — (Unclassified)

Contractor: Columbia University, New York, New York
Contract: N7-onr-469, (8/1/47 to 8/1/48)
Investigator: E. Brand

The panel will consist of five civilian members, selected by both disciplinary and geographic distribution, and representatives of Naval bureaus and other Federal agencies. These members will work closely with the Biochemistry Branch and other branches of ONR, as requested, to assure maximum benefit from expenditures for biochemical research.

Progress to 6/30/48: The Panel met in February to discuss the proposals which had been submitted up to that period. Of the submitted proposals approximately 80% were rejected for one reason or another.

The Panel also discussed the general scope and plan of the research program of the Biochemistry Branch, as well as the philosophy of contract renewals.

The next meeting will be held on 27 August 1948.

Estimated Completion: Continuing

PHYSICAL CHEMISTRY AND METHODS

NR-121-289 — Solubility Coefficient of Carbon Monoxide — (Unclassified)

Contractor: Loyola University, Chicago, Illinois
Contract: N7-onr-337, Task I, (5/1/47 to 3/31/49)
Investigator: J. Sendroy, Jr.

The purpose of this project is to study and to evaluate the solubility coefficient of carbon monoxide in water, salt solutions, plasma, serum, whole blood, and cell suspensions at temperatures ranging from 20° to 40°C. The objective of the investigation will be attained by the use of physico-chemical procedures whereby the fluids mentioned will be subjected to initial states of under and over-saturation with respect to CO, the final value at equilibrium being necessarily the same from both directions. Data are available in the literature for water but are few for the effect of temperature and salt solutions. Data with respect to plasma are scant and are believed, with good reason, to be erroneous. No data are available for the solubility of CO in blood, owing to the difficulty of determining the relatively small amount of dissolved CO gas in the presence of the much larger amount bound to hemoglobin. It is proposed to study this, both directly on normal blood exposed to CO, and indirectly with the blood hemoglobin converted to other types, such as methemoglobin.

Progress to 6/30/48: CO gas was obtained from the National Bureau of Standards. It was found that hydrogen was present to a concentration of 2.1%. Analysis for CO_2 indicated a content of 0.16%.

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BIOCHEMISTRY

PHYSICAL CHEMISTRY AND METHODS (Cont.)

NR-121-476 Physical Chemical Studies of Biologically Important Molecules (Unclassified)

Contractor: Smith College, Northampton, Massachusetts
Contract: N8-onr-579, (6/1/48 to 5/31/49)
Investigators: G. A. Anslow, D. Wrinch

The purpose of this project is to study the structure of biological molecules, especially protein molecules. In one case the investigator expects to develop methods of interpreting X-ray intensity data from molecular, particularly mega-molecular crystals, and the study of the relation between distributions in atomic space S and vector space Sv. In the other case the investigator will undertake an intensive spectrophotometric study of the "end" absorption in native proteins and of the spectra of various protein degradation products, such as antibiotics, gramicidin, gramicidin soviet and tyrocidin, together with further studies of the spectra of peptides and of molecules containing -C-C-OH.

Progress to 6/30/48: No progress to report.
Estimated Completion: Continuing

NR-121-479 Kinetics and Energetics of Chemical Reactions in Biological Systems (Unclassified)

Contractor: Catholic University of America, Washington, D. C.
Contract: N8-onr-62100, (6/15/48 to 10/14/48)
Investigator: K. J. Laidler

The purpose of this project is to study the transfer of energy by means of experimental systems which reproduce some of the more fundamental processes essential to living systems. Transfer of chemical energy into diffusion through a membrane will be an important part of the program and will involve a study of the mechanism of enzyme-catalyzed reactions. It is intended to use isotopic tracers for this last phase of the work. Enzyme kinetics will be studied and enzymes will be prepared in crystalline form; molecular weights and other properties in solution will be determined. The kinetics of photosensitization in solution will be investigated and from the standpoint of biological photosynthesis the reaction of the photosensitized oxidation of water to oxygen will be studied using various kinds of solid sensitizers.

Progress to 6/30/48: No progress to report.
Estimated Completion: October 1948

NR-121-736 Metabolic Studies with Radioactive Isotopes (Unclassified)

Contractor: Duke University, Durham, North Carolina
Contract: (6/30/48 to 6/30/49)
Investigators: P. Handler, J. S. Harris

The purpose of this project is to (1) measure the turnover rates of organic phosphates (glucose-6-phosphate, adenosine triphosphate, etc.) in renal tissue under circumstances where the kidney is required to perform different degrees of "work", e.g., to excrete, dilute, and concentrate urine, acid or alkaline urine, after administration of pituitary, parathyroid adrenocortical extracts, etc., and the turnover rate compared with actual renal performance.

(2) Investigate mechanisms involved in the maintenance of fluid and electrolyte balance. Present knowledge of events occurring in the various pathological upsets in normal balance are largely limited to extracellular fluid and simply assume osmotic equilibrium with

PHYSICAL CHEMISTRY AND METHODS, NR-121-736 (Cont.)

cellular fluid. It is proposed to reinvestigate the entire situation. Both humans and dogs subjected to various processes calculated to produce 'dehydration', acidosis, alkalosis, etc., will be studied with the aid of radio Na and K to determine the extent to which the volume and composition of extracellular and intracellular fluids are affected.

Parathoromone is known to cause mobilization of bone salt but the rate, locus and mechanism is unknown. By studying the behavior of radio Sr and P in pretreated animals, after administration of parathoromone, some light should be shed on this problem.

(3) Study uptake and release of P by normal animals and animals overdosed with vitamins A and D. Both of these have profound affects on bone when given in large doses but no information regarding mechanisms is yet available.

Progress to 6/30/48: No progress to report.
Estimated Completion: June 1949

ENZYMOLOGY

NR-122-011 Cytochrome C Metabolism in Regenerating Liver (Unclassified)

Contractor: University of Pennsylvania, Philadelphia, Pennsylvania
Contract: N6-ori-168, Task I, (9/1/46 to 3/31/49)
Investigator: D. L. Drabkin

The purpose of this project is (1) to secure information upon the metabolism, hitherto unavailable, of the fundamental biocatalyst of tissue oxidation-reduction processes, and (2) to gain information upon basic aspects of tissue regeneration and growth (in regenerating liver).

The influence of diet (non-protein and high-protein) and the influence of anoxia, induced by simulated high altitude conditions, on the production of cytochrome c is being investigated, using the technique of partial hepatectomy in the young, adult, albino rat.

Progress to 6/30/48: In studying the effect of hormonal factors on cytochrome c metabolism, experiments disclosed an apparently significant influence of the thyroid gland on the cytochrome c content of all tissues. This effect suggests a mechanism whereby thyroxine helps regulate the oxygen consumption of tissues and the whole body.

Thyroidectomy of rats on a vitamin supplemented, high-protein diet induced a striking reduction in total body cytochrome c, reflected in the concentration of the pigment in individual organs and tissues. Decrease in cytochrome c was about twice as great in skeletal muscle as in liver, with intermediate decreased values in heart and kidney cortex. In thyroidectomized rats, liver regeneration was not strikingly interfered with, although it was of smaller magnitube than normally. Administration of thiouracil produced a reduction of similar magnitude, in the cytochrome c of tissues, as after complete thyroidectomy.

Investigation of the effect of thyroxine administration and of adrenalectomy is also under way. Metabolism studies using radioactive iron as a tracer, indicate that cytochrome c iron is only a relatively small part of total liver iron. Besides cytochrome c iron, there are ferriton iron, residual hemoglobin iron, as well as other irons.

Estimated Completion: Continuing

NR-122-101 Changes in Proteins and Enzyme Activities During Muscular Atrophy (Unclassified)

Contractor: Medical College of Virginia, Richmond, Virginia
Contract: N6-ori-198, Task II, (9/1/46 to 9/1/48)

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BIOCHEMISTRY

ENZYMOLOGY, NR-122-101 (Cont.)

Investigator: E. Fischer

The purpose of this project is to investigate (1) the changes in actin content and actomyosin formation in denervated skeletal muscles before and after treatment by electrical stimulation and/or massage; (2) the qualitative and quantitative differences in physico-chemical properties and in adenosin triphosphatase activity of myosin isolated from normal, atrophied, and treated muscles; and (3) myogen A, especially its enzymatic properties, and other muscle enzymes in relation to muscular atrophy and its retardation by appropriate therapeutical measures.

Progress to 6/30/48: Previous experiments on the relation between myosin and ATPase activity have been repeated using purified myosin.

Studies on the effect of electrical treatment and massage on the ATPase of denervated muscle have not shown any large effects in prevention of myosin deterioration. However, electrical treatment produces a greater beneficial effect than massage.

Investigation of the zymohexase content of normal and denervated muscle has shown that zymohexase activity starts decreasing only after a considerable loss in myosin and it is therefore not directly connected with the primary process of atrophy.

The exact time relation of the decrease in enzyme activity has been established. Up to 10 days after denervation, the enzymatic activity per gram muscle remains unaltered, although the weight loss reaches about 20%. From then on the enzymatic activity diminishes rather quickly, so that three weeks after denervation, the zymohexase activity is about 20% of that of the normal muscle, although atrophy has reached only about 50% weight loss. This delayed onset of the loss of zymohexase activity indicates its secondary nature. Appropriate electrical treatment of denervated muscle is able to retard considerably the secondary loss in zymohexase activity.

In order to shed light on the proteolytic process involved in muscle atrophy it has seemed desirable to investigate the glutathion content of degenerating muscle (reduced glutathion is an activator of proteolytic enzyme). The titration method for glutathion determination in muscle has been improved and checked against Woodward's method of micro-estimation of glutathion by its action as co-enzyme for glyoxalase. A distinct increase of glutathion with denervation has been found. This increase appears to be diminished by treatment about proportionally to the retardation of the weight loss.

In measuring the oxygen consumption and carbon dioxide liberation of denervated muscles, according to the method of Richardson et al, it was confirmed that the oxygen consumption markedly increases. However, these increases did not indicate any fixed relation to the time elapsed since denervation. The carbon dioxide liberation of an individual muscle is altered exactly as its oxygen consumption, and therefore the R. Q. of the muscles is not affected by denervation. Appropriate electrical treatment apparently did not diminish significantly the raised oxygen consumption of denervated muscle, and had no influence upon the R. Q.

In studying the relation between muscle atrophy and thyroid activity, it has been established that in rats on a diet extremely poor in iodine, thiourea will increase the thyroid weight much more in rats with one or both gastronemii denervated, than in the control rats. This is the opposite to observations on rats on a high iodine diet. It is assumed that if an iodine shortage exists, a relatively large fraction of the available iodine is required by the denervated muscle. In consequence, the antagonistic action of the iodine upon the thiourea effect on the thyroid is missing. Microiodine analyses of the tissues are being worked out to test this hypothesis.

The rate of atrophy is not influenced by shifting from a mixed diet to diets free of fat or free of carbohydrates, but otherwise sufficient. However, diets poor in protein diminish the atrophy rate significantly. This atrophy-retarding effect of protein lack might be due to the absence of the specific dynamic action of the protein.

Estimated Completion: Continuing

ENZYMOLOGY (Cont.)

NR-122-110 Influence of Stress on Potassium Metabolism; Enzyme Activity in the Psychotic State (Unclassified)

Contractor: Worcester Foundation, Shrewsbury, Massachusetts
Contract: N6-ori-197, Task I, (10/1/46 to 10/1/48)
Investigator: H. Hoagland

This project has been expanded in order to include studies formerly under project NR-122-111.

The purpose of this project is to study the influence of stress on potassium metabolism and enzyme activity in the psychotic state. It has been found that "normal" individuals vary considerably in adrenal cortical activity in response to a variety of experimental and field stress situations, and that there is a quantitative relationship in ability to withstand stress and adrenal cortex function. In psychotic patients the normal type of adrenal stress responses have not been found.

Because of the importance of potassium in determining nerve excitability and in the conduction of nerve impulses, and because of the role of the adrenal cortex in regulating potassium metabolism, a study of brain and muscle potassium in animals in relation to stress and adrenal function is being made. An investigation is also being made of the urinary potassium output in normal and psychotic persons during stress experiments in relation to several measures of adrenal cortical activity.

The probability that psychotic states may be associated with deficiencies of certain respiratory enzyme systems in the brain is also being investigated. At present, fresh brain plugs from schizophrenic patients, taken at the time of lobotomy operations, are being analyzed for their cytochrome contents. It is hoped to obtain some fresh brain material at the time of other types of brain operations from non-psychotic patients.

Large quantities of cytochrome c are also being extracted from beef heart to administer to psychotic patients, in order to study the effects of its administration in relation to psychotic states of patients. Some experiments on psychoneurotic dogs involving the administration of enzyme constituents are also in progress.

Progress to 6/30/48: The administration of adrenal cortex extract (ACE) to an isolated rabbit spleen, perfused with whole blood, induces a prompt discharge of splenic lymphocytes into the circulation. There is, secondarily, a tendency for the level of circulating lymphocytes in the perfusion medium to fall, which appears to be due to accelerated lymphocyte breakdown by ACE in the presence of spleen. The activity of ACE to produce the in vitro reaction upon spleen is not associated with alteration of mean arterial pressure or by changes in splenic flow, and can be demonstrated upon repetitive addition of ACE. The addition of ACE to perfused thymus, liver, or lung does not produce discharge of lymphocytes from these tissues; glucose, epinephrine, desoxycorticosterone acetate, and estradiol dipropionate do not provoke lymphocyte discharge from spleen. The view that spleen is a lymphocyte reservoir under control of adrenal cortical secretion is supported by in vivo findings that (1) the blood lymphocytosis observed in normal rats subjected to swim stress can be significantly reduced by adrenalectomy or splenectomy; (2) ACE induces lymphocytosis in swimming adrenalectomized rats, but not in splenectomized-adrenalectomized rats; and (3) desoxycorticosterone does not produce lymphocytosis in adrenalectomized rats subjected to swim stress.

Studies have been made of the adrenal cortical function in psychotic (schizoid) patients and in normal persons. The normal individual responds to stresses with an enhanced excretion of 17-keto steroids, cortical hormones, uric acid, sodium and potassium, and a circulating lymphopenia. The psychotic individuals, by and large, fail to show these responses to stress. This experience appears to be more clear cut at the biochemical and physiological level than any differences which have appeared in studies of psychotic patients. An attempt is being made to localize the source of the deranged adrenal function. In about half of the psychotic patients

ENZYMOLOGY, NR-122-110 (Cont.)

the adrenal cortex does not respond to injections of purified adrenocosticotrophin, which is in sharp contrast to the cortical responses of normal people. In the remainder of the psychotic group, while the adrenal cortex does not respond to the experimental stresses, it does respond to the cortiertrophins in a more or less normal fashion. This suggests that in these particular patients, the stress response failure is due to the pituitary or to the control of the brain over the pituitary. It is of interest to emphasize that the 24-hour 17-ketonteroid output of the psychotic group is not markedly different from that of the normal population. It is specifically the basic stress response mechanisms which are defective in the psychotic population.

In a recent publication on the affect of phosphates on flame photometer determinations of sodium and potassium in urine, homogenized muscle, or ashed muscle, it was found that the removal of phosphate by CaO does not significantly affect the determination of these two elements. The investigators, whose results are at variance with literature, explain the discrepancy as due to the use of more dilute aliquots than were previously used.

Estimated Completion: Continuing

NR-122-111 Enzyme Activities in Psychotic States (Unclassified)

Contractor: Worcester Foundation, Shrewsbury, Massachusetts
Contract: N6-ori-197, Task II, (11/15/46 to 11/14/48)
Investigator: H. Hoagland

Progress to 6/30/48: This project has been combined with project NR-122-110.

NR-122-195 Cardiorespiratory Physiology as Influenced by Respiratory Enzymes (Unclassified)

Contractor: Harvard University, Cambridge, Massachusetts
Contract: N5-ori-76, Task XII, (1/1/47 to 12/31/48)
Investigator: M. D. Altschule

The purpose of this project is to study the role of blood carbonic anhydrase in disease. It has been necessary to devise a method for estimating the activity of the enzyme at body temperature. Measurements of carbonic anhydrase activity in the blood of patients with anemias and cardiac and pulmonary diseases are being made.

Progress to 6/30/48: Convulsions induced electrically for the treatment of mental disease give rise to marked anoxia, hypercarbia, and acidosis. These changes constitute a severe load on the respiratory mechanisms of blood, and it was therefore considered important to ascertain whether blood carbonic anhydrase activity might be affected. A study of this sort has additional interest in view of the emphasis placed upon brain carbonic anhydrase activity in mental disease.

Twelve patients ranging in age from 38 to 67 years were studied, nine were women. None showed evidence of cardiovascular or respiratory disease, except for mild hypertension or emphysema in several. In two of the patients the violence of the convulsions was moderated by means of curare (solution d-Tubocurarine Squibb). Blood carbonic anhydrase activity increased in some of the patients. The violence and frequency of the seizures determined whether or not carbonic anhydrase increased.

Such changes may not be the cause of therapeutic response to electro-shock therapy, but are probably due to secondary effects such as muscular activity and the problem of training.

Recent studies on blood carbonic anhydrase in diseases of the heart and lungs show no change in anhydrase activity in the blood of patients with dyspnea due to congestive heart failure, or chronic pulmonary disease, unless polycythemia develops in which case the enzyme is increased.

Estimated Completion: Continuing

ENZYMOLOGY (Cont.)

NR-122-212 Clinical and Biochemical Aspects of Chronic Occupation Diseases (Unclassified)
(Formerly NR-126-212)

Contractor: Edward L. Trudeau Foundation, Saranac Lake, New York
Contract: N7-onr-307, Task I, (3/1/47 to 1/7/50)
Investigators: F. W. Klemperer, A. J. Vorwald

The purpose of this project is to study respiration under conditions of an increased alveolararterial pulmonary gradient.

It appears that exposure to beryllium produces a diffuse pulmonary granulomatosis. This condition, simulating military sarcoidosis of the lungs is widely distributed in industries manufacturing or fabricating various compounds of beryllium. It has been discovered in such widely diversified places as fluorescent lamp factories, brass foundaries making beryllium copper, radio tube plants, etc.

The study of the rather unique fibrosing disease will contribute to a fuller understanding of the mechanisms of fibrosis and may lead to the solution of many fundamental problems bearing on fibrosis, tissue damage due to the inhalation of toxic dusts and tissue repair.

Progress to 6/30/48: An analytical procedure for beryllium has been developed. An investigation of the mechanism by which silica produces the histological changes of silicosis has been started, testing the hypothesis that silica dust may catalyze the destruction or alteration of tissue proteins.

Experiments show that the enzymatic activity of the protein urease, which releases ammonia from urea, is significantly decreased by incubating urease with biologically active silica. This inactivation may be an index of the molecular destruction of urease by the silica dust.

Estimated Completion: Continuing

NR-122-243 Biological Synthesis of Lactose (Unclassified)

Contractor: University of Oregon, Eugene, Oregon
Contract: N6-onr-218, Task II, (2/1/47 to 3/31/49)
Investigator: F. J. Reithel

The purpose of this project is threefold. First, to develop a satisfactory method for determining lactose in the presence of glucose and galactose. Second, to obtain a homogenate or cell free extract of mammary tissue that will synthesize lactose. Third, to discover what is the precursor of lactose in vivo.

Progress to 6/30/48: Analytical methods, of sufficient sensitivity and selectivity so that lactose synthesis can be determined, have been devised. By using three strains of yeast, it is possible to determine small quantities of lactose in the presence of interfering substances. Several organic compounds, which might logically be expected to act as precursors of lactose, have been synthesized.

The investigator is attempting to prepare a cell free mammary gland extract capable of synthesizing lactose from a glucose substrate. Viable homogenates of lactating guinea pig mammary gland fortified with ions, co-enzymes and ATP have been prepared and the rates of oxygen consumption under varying conditions of temperatures and pH have been studied. O_2 uptake of the hemogenate appears to be as great in the presence of added lactose as it is with added glucose. (The homogenate also contains about 1 mg lactose per gram tissue, dry weight.) Aerobic metabolism does not change appreciably in the range of pH 6.5 - 7.3. The succinate levels of the incubated mixtures seem to be a determining factor. Respiration can be inhibited at least 50% by malonate. Dialyzed as well as undialyzed hemogenates are being tested; the

ENZYMOLOGY, NR-122-243 (Cont.)

former has approximately 1/3 the O_2 uptake of the latter.
Estimated Completion: Continuing

NR-122-278 The Pathological Physiology of the Liver (Unclassified)

Contractor: University of California, Berkeley, California
Contract: N7-onr-295, Task V, (1/15/47 to 6/30/49)
Investigator: L. W. Kinsell

The purpose of this project is to determine (1) the protein balance in liver disease; (2) the effects of therapeutic procedures on liver physiology; (3) the usefulness of standard and new liver function tests; (4) the role of the liver in the conjugation of steroids; and (5) the effectiveness of protein anabolic steroids in liver disease.

Progress to 6/30/48: Lipotropic agents were shown to be of benefit in the treatment of patients with chronic liver disease and possibly with acute liver disease, over and above the benefit derived from a high protein intake.

Glycogen storage tests were shown to have value as tests for liver function.

Modifications have made the cephalin cholesterol flocculation test more dependable, and have eliminated the disadvantages which discouraged its use as a routine test in the past.

Protein anabolic steroids appear to be of significant value in the treatment of liver disease.
Estimated Completion: Continuing

NR-122-385 Histochemistry of Nerves and Associated Tissues (Unclassified)

Contractor: University of South Dakota, Vermillion, South Dakota
Contract: N7-onr-456, Task I, (9/1/47 to 8/31/48)
Investigator: W. L. Hard

The purpose of this project is to conduct (1) a detailed survey of phosphatases in the various types of neurons of the central and peripheral nervous system; (2) a study of the fetal development of various types of neurons, to be correlated with the first appearance of phosphatase and its concentration; (3) a quantitative analysis of phosphatase in normal and degenerating peripheral nerves; and (4) a study of the "blood-brain barrier" as revealed by enzyme localization in the vascular bed of the nervous system, including the choroid plexus.

Progress to 6/30/48: Histochemical phosphatase and glycogen studies of the choroid plexus have been made in rabbit fetuses beginning on the twelfth day of gestation and extending at two-day intervals, to birth. Studies have also been made on post-natal animals at 12 intervals ranging from the first post-natal day to the six-month adult. The significant observations on the choroid plexus may be summarized as follows:

Villi first appear in the roof of the fourth ventricle on the 16th fetal day. Both alkaline phosphatase and glycogen appear at this time in these villi. The glycogen is limited to the ependymal cells, while the phosphatase occurs only in the connective tissue elements of the pia supporting the ependyma. It is noted that phosphatase occurs in the pia only in villi; the non-villous portions of the pia are negative.

By the 18th day an obvious increase in both phosphatase and glycogen has occurred in the same areas. A progressive increase, as indicated by the intensity of the reaction, occurs for both phosphatase and glycogen on the 24th day. By the 26th day there is a marked reduction in the amount of glycogen, with some villi practically free of it. The phosphatase reaction has, if anything, increased. By the 28th day, two days prenatal, the plexus is essentially free of glycogen, and the condition as seen in the adult plexus results. This is, namely, a glycogen

ENZYMOLOGY, NR-122-385 (Cont.)

free ependyma, but an intense alkaline phosphatase concentration is the supporting pia.

Further studies in progress are designed to identify, more accurately, the physiology of these constituents in the choroid plexus.

Estimated Completion: Continuing

NR-122-490 Study of Enzyme Systems Involved in Biological Oxidations and Synthesis in Animal Tissue (Unclassified)

Contractor: New York University, New York, New York
Contract: N6-onr-279, Task VI, (4/15/48 to 4/14/49)
Investigator: S. Ochoa

The purposes of this project are:

(1) Further purification of the enzyme from pigeon liver which brings about fixation of carbon dioxide by pyruvic acid.
(2) Purification of the various enzymes involved in the fixation of carbon dioxide by ketoglutaric acid (oxalosuccini carboxylase, isocitric dehydrogenase, aconitase).
(3) Investigation of the relationship biotin to carbon dioxide fixation and more specifically to the liver enzyme mentioned in (1).
(4) A study of the mechanism of the synthesis of tricarboxylic acids by C_4, or, C_3 and C_4 condensation.
(5) Further investigation of the mechanism concerned in the synthesis of arginine and urea from citrulline by mammalian tissues, i.e., step 2 of Krebs cycle. (a) Separation and purification of the participating systems. (b) Further investigation of substrate dependences and co-factor requirements.
(6) Investigations of the enzymes concerned in the synthesis of citrulline from ornithine by mammalian tissue, i.e., step 1 of Krebs cycle. On the basis of preliminary work on step 2 it is expected that anaerobic synthesis by a soluble system can be attained by analogous procedures.

In these studies manometric, spectrophotometric, and chemical methods will be employed along with the general techniques of protein and enzyme fractionation.

Progress to 6/30/48: No progress has been reported.
Estimated Completion: Continuing

NR-122-508 Studies of Organic Acid Metabolism (Unclassified)

Contractor: Indiana University, Bloomington, Indiana
Contract: (5/31/48 to 6/1/49)
Investigator: I. C. Gunsalus

The purpose of this project is to explore the mode of breakdown and formation of organic and amino acids. Those so far studied include the fermentative breakdown of citric, malic, fumaric, lactic, and pyruvic acids, and the energy coupling processes involved. In addition, the anaerobic metabolism of tryptophane and serine, both of which yield pyruvic acid as an intermediate product, have been studied. These reactions lie only one step from organic acid metabolism. The proposed research would be directed at a determination of the mechanism, the cofactors involved, and their relationship to known vitamins or to unidentified accessory substances.

Among the difficulties involved in the immediate attack of these problems is the unavailability of the coenzyme forms of several of the vitamins. A study of the form of these cofactors and their isolation or synthesis would be highly desirable and would remove one of the present bottlenecks in biochemical research.

ENZYMOLOGY, NR-122-508 (Cont.)

It is proposed to study these reactions with the lactic and coliform organism now in use, and also to use several strains of aerobic spore-forming organisms to study the more strictly aerobic phases.

Such a study will lead to a better understanding of the biochemical and physiological processes taking place in the human organism, and will throw light on mechanisms of approach and a better understanding of health and disease in man.

Progress to 6/30/48: No progress to report.
Estimated Completion: Indefinite

NR-122-551 Metabolism of Glutamic Acid in Children and Animals (Unclassified)

Contractor: Children's Hospital Research Foundation, Washington, D. C.
Contract: N8-onr-62201
Investigator: S. P. Bessman

The purpose of this project is to conduct studies which will attempt to elucidate (1) the fate of the NH_2 group which is removed from the glutamic acid which is converted to ketoglutarate. The first step would be a dismutation between citric and glutamic acid with the formation of succinic and ketoglutaric acids and glycine. This would increase the rate of formation of the keto acid by the Krebs cycle, and the increase in succinate and ketoglutarate could account for the increase in O_2 uptake noted on the addition of glutamic acid. The glycine might give a lead to the two carbon molecule suggested by Lipmann as part of the carbohydrate cycle. (2) a study of the effect of an environment, of the nature of intracellular fluid, on the reactions of glutamic acid in brain slices which have already been studied by Weil-Malherbe in Ringers, to perhaps, throw new light on the problem of Roberton's demonstration of glycogen synthesis. (3) a study of the effect of various substances peculiarly toxic to brain on the oxidation of glutamic acid. Clinical investigations will also be undertaken.

Progress to 6/30/48: No progress to report.
Estimated Completion: Indefinite

NR-122-725 The Translocation of Mineral Substances in Plants (Unclassified)

Contractor: University of Missouri, Columbia, Missouri
Contract: (6/30/48 to 6/30/49)
Investigator: J. Levitt

The purpose of this project is to investigate the translocation of mineral substances in plants - into which tissues the mineral substances are moved, the mechanism by which they are moved, and the physiological relationships existing between these mechanisms and other processes.

It is anticipated that radiophosphorus and sulfur will be employed as tracer substances. The movement of substances under investigation will be followed by Geiger counters and in some cases by the diamond method.

It is hoped that data obtained will throw some light on the mechanism and role played by the muscles in the biological organism.

Progress to 6/30/48: No progress to report
Estimated Completion: June 1949

[redacted]

BIOCHEMISTRY

NUTRITION

NR-123-028 — Relation of Vitamin A to the Utilization of the Essential Amino Acids — (Unclassified)

Contractor: Rutgers University, New Brunswick, New Jersey
Contract: N7-onr-345, Task I, (6/1/46 to 12/31/48)
Investigator: W. C. Russell

In contrast with the other vitamins, it seems likely that vitamin A is concerned with the formation and maintenance of body cells rather than the chemical reactions which go on within the cells. Since the essential amino acids are also concerned with the formation and maintenance of cells it is important to determine whether any relationship exists between the functions of vitamin A and the essential amino acids. By means of the microbiological procedure for the determination of the essential amino acids, the fate of each of these acids will be determined, by balance studies, when they are fed (1) in adequate quantities to the white rat receiving adequate vitamin A and in various degrees of vitamin A deficiency, and (2) when adequate vitamin A is supplied and the quantities of essential amino acids varied. The amino acids in the experimental diets of the purified type will be supplied in the crystalline form and for some experiments as proteins of known amino acid content. From the practical standpoint the results may be of interest in the utilization of vitamin A in such phenomenon as nightblindness and of purely scientific interest in the field of the interrelationship of nutrients.

Progress to 6/30/48: The lowest food intakes, the smallest gains in body weight, and the smallest nitrogen balances occurred more frequently among rats receiving vitamin A at the one unit level as compared with those for the animals receiving three units. The relationship between nitrogen consumption and nitrogen balance is what one would normally expect to find. The tendency for the rats supplemented with one unit of vitamin A to have lower nitrogen balances than the three unit animals may be due to the fact that the one unit rats, because of a relatively greater deficiency of vitamin A, did not eat as much food as the others.

Excretion of amino acids in the urine was of a low order, being about one per cent of the total intake. There is no apparent correlation between nitrogen consumption or balances and amino acid excretion. The urinary excretion pattern of amino acids reflects the dietary pattern for both the one and the three unit levels of vitamin A. This excretion pattern may be considered a valid criterion, it may be concluded that an inadequate intake of vitamin A does not disturb the metabolic utilization of essential amino acids in the case of the white rat. That higher urinary amino acid values were not found for the one unit vitamin A rats, may mean that the subminimal level of vitamin A did not cause damage to kidney tissue.
Estimated Completion: Continuing

NR-123-068 — Vitamin A Content of Fish Liver Oils — (Unclassified)

Contractor: Yale University, New Haven, Connecticut
Contract: N6-ori-166, (7/1/47 to 12/31/48)
Investigator: D. Merriman

The purpose of this project is to investigate the variations in vitamin A content of the oils of different species of fish at regular periods throughout the year. It is hoped that correlations will be established between the vitamin variation and the food, sex, stage of maturity, etc., of the various species.

This survey is planned to provide a rational basis for a future attack on the problem of how and why vitamin A is accumulated in fish oils, and its physiological significance.

Progress to 6/30/48: No progress report has been received.
Estimated Completion: Continuing

NUTRITION (Cont.)

NR-123-075 Molecular Isosterism of Antivitamins and Other Specific Antagonists (Unclassified)

Contractor: University of Colorado, Boulder, Colorado
Contract: N6-ori-131, Task II, (6/15/46 to 12/15/48)
Investigators: K. Dittmer, I. Goodman

From reported results on specific metabolite antagonists, especially those of the vitamins, certain major structural changes which should produce antagonists have been suggested. Some of these changes are (1) a carboxyl group to a sulfonic acid or sulfonamide; (2) a carboxyl group to an aromatic ketone; (3) a pyrimidine nucleus to a benzene ring; (4) an aromatic sulfide to a vinylene group; (5) a chlorine atom for a methyl group; and (6) other miscellaneous changes.

This research program was undertaken to apply some of the above structural changes to other compounds for example, amino acids, nucleosides, pyrimidines, purines, and maybe vitamins. The new compounds will then be tested with microorganisms, enzyme systems in the mammal to determine whether they are antagonists of the parent substances. Wherever possible a physical-chemical study of these and known antagonists will also be made.

It is hoped that this research will lead to a more rational approach to the synthesis of new specific antagonists. Furthermore, the results from this investigation should either support or disprove some of the present hypotheses, and may suggest new hypotheses, concerning the basis for building antagonistic compounds.

Progress to 6/30/48: A report has been received on the growth-inhibitory properties of the vinylene analogue of cysteine, allylglycine, and the two closely related unsaturated amino acids, methallyl-glycine and crotylglycine. Three strains of Escherichia Coli and strain 139 of Saccharomyces cerevisiae were used.

Allylglycine and methallylglycine were the most equally effective inhibitors of E. Coli, producing complete inhibition of growth for 16 hours in very small concentrations. Crotylglycine was less active on the growth of all three strains of E. Coli. For S. cerevisiae, allylglycine was the most effective inhibitor of the three unsaturated amino acids, and crotylglycine showed only low inhibitory action.

The reactions involved in syntheses of allylglycine and methallylglycine from allyl chloride and methallyl chloride and ethyl acetamidomalonate have been investigated. By similar methods crotylglycine was synthesized.

Acid hydrolysis of ethyl methallylacetamidomalonate resulted in complete lactonization yielding α-amino-γ-methyl-γ-valerolactone hydrochloride. This was converted by base to γ-hydroxyleucine.

Acid hydrolysis of ethyl allylacetamidomalonate resulted in the formation of α-amino-γ-valerolactone hydrochloride in 26-33% yield and allylglycine in 30-35% yield. The α-amino-γ-valerolactone hydrochloride was converted to α-amino-γ-hydroxyvaleric acid.

Crotylglycine was prepared by basic hydrolysis of ethyl crotylacetamidomalonate and ethyl crotylacetamidocyanoacetate in 30 and 50% yields, respectively.

The structures of these three amino acids have been established by reduction to known compounds and by ozonolysis.

Estimated Completion: Continuing

NR-123-076 Studies of the Newer Members of the B Group of Vitamins (Unclassified)

Contractor: Cornell University, Ithaca, New York
Contract: N6-ori-91, Task V, (6/1/46 to 12/31/48)
Investigators: L. C. Norris, C. K. Cain, N. S. Moore

NUTRITION, NR-123-076 (Cont.)

The purpose of this project is to conduct studies to (1) ascertain more completely the physiological functions of the newer members of the B group of vitamins and their importance in applied nutrition, and (2) isolate, identify, and synthesize the newer members, not yet identified chemically, and determine their physical and chemical properties. The newer members of the B group of vitamins are (1) folic acid, required for the prevention of anemia and for certain other physiological functions; (2) a second antianemic factor required by the chick; and (3) a factor required for growth and reproduction in the chicken. The results of recent work suggest the existence of still another unknown growth factor. Beta-pyracin, a derivative of pyridoxine, has been found necessary, under certain conditions, to free folic acid in the bound forms of this vitamin and render it available to the chick. Because of desirable physiological characteristics, the chick is being used in most of the basic research work on these vitamins. As in the case of folic acid, the other newer members of the B group of vitamins are expected to be found of importance in human nutrition.

Progress to 6/30/48: A number of pterins, related to the pterin nucleus of folic acid, were synthesized and tested for folic acid activity with microorganisms and chicks. Several of these, all containing the 2,4-diaminopterin structure, were found to possess marked anti-folic acid activity for bacteria, but markedly decreased growth and hemoglobin formation in the chick, effects which were counteracted by additional folic acid. A possible explanation of the effects of these compounds is that they act by combining with a specific protein (apoenzyme), thus preventing the normal attachment of folic acid in the formation of an enzyme required for the growth of bacteria and for growth and hemoglobin formation in animals.

Using an amino acid basal medium, two unknown factors required by Lactobacillus casei were found to be present in antipernicious anemia liver extracts, and a third factor, believed to be strepogenin, was found in casein. Studies with Streptococcus faecalis showed, on the other hand, that only the two factors in liver are required for growth on an amino acid basal medium. One of the factors in liver extracts occurred in a rather constant amount in all of the extracts, while the other was present in varying quantities. One of these factors is believed to be the animal protein factor, and an attempt is, therefore, being made in studies with S. faecalis to correlate the microbiological results with the chick results on the animal protein factor.
Estimated Completion: Continuing

NR-123-150 Metabolic Changes Which Occur During Feeding by Intravenous Injection Alone (Unclassified)

Contractor: Johns Hopkins University, Baltimore, Maryland
Contract: N6-ori-243, Task I, (11/1/46 to 7/1/49)
Investigator: J. E. Howard

The purpose of this project is to determine the physiological activity of the G.I. tract during total intravenous alimentation (especially secretory activity by (1) direct means, and (2) indirect means by determination of electrolytes and nitrogen of colonic washings taken at appropriate intervals. Urinary excretion of certain vitamins during total intravenous alimentation is also to be carried out, as well as bacteriological studies of the colon. Studies in calcium and phosphorus metabolism are also projected, especially in regard to obscure rarefying diseases such as "menopausal osteoporosis".

Progress to 6/30/48: Determinations of intestinal secretions at various levels of the intestinal tract by means of two and three-way balloons did not prove satisfactory. Therefore, an indirect approach was attempted. Patients were given total intravenous feeding before and after surgery, and the physiological effect on the intestine was studied by colonic washings. Analyses of the colonic washings were made for Ca, P, N and K, and the total bacterial content was determined.

Results showed that in total intravenous feeding without enemata, little or no material reaches the colon, if intestinal juices are secreted, most of their contents are resorbed. Daily

NUTRITION, NR-123-150 (Cont.)

enemata (normal saline) greatly increase calcium and phosphorus content of colon during total intravenous feeding, either by reflexes which cause upper tract secretion, or by directly stimulating the colon to secrete. Daily saline enemata increase the bacterial count. Improvement in the post-operative course of patients so treated seems likely due to lowered intestinal secretions as compared with patients fed orally.

Tests are also being made on vitamin excretion during total intravenous feeding, daily analyses being made of the intake and urinary output of thiamine, n-methyl nicotinamide, calcium pantothenate, riboflavin and folic acid. Urinary analyses showed the group to have been excreting low normal amounts when the experiment began. Output of all substances diminished until operation. The urinary thiamine continued to fall after operation, but the others showed no further fall, or actual rise in three to five days after operation. These results are contrary to certain published studies of urinary vitamins after trauma. These studies will be continued with extended post-operative observations on total intravenous feeding.
Estimated Completion: Continuing

NR-123-252 A Study of the Metabolic Effects of Folic Acid (Unclassified)

Contractor: Ohio State University, Columbus, Ohio
Contract: N6-ori-225, Task VII, (1/1/47 to 9/30/48)
Investigator: F. A. Hitchcock

The purpose of this project is to conduct research designed to determine the metabolic effects of folic acid on normal human beings and on patients being treated for various blood disorders. The investigation will include the effects of folic acid on nitrogen balance, utilization of carbohydrates and fats, and gaseous exchanges and respiratory quotient.

Studies are also being carried out to determine the effect of folic acid on the metabolism on bone marrow in vitro. All these studies will be correlated with the effects of folic acid on the blood picture. A comparison of the effects of folic acid with the effects of liver extracts will also be made.

Progress to 6/30/48: Folic acid seems to improve the appetite with a resultant increase in total calories consumed, increased retention of nitrogen, and increased utilization of carbohydrate. While there is a tendency for the specific dynamic action of food to be increased with hospital patients, there is also the possibility of a slight decrease in basal oxygen consumption.
Estimated Completion: 30 September 1948

NR-123-298 Nutritional Content of P.O.W. Diets (Unclassified)

Contractor: Massachusetts Institute of Technology, Cambridge, Massachusetts
Contract: N7-onr-297, (5/6/47 to 5/5/48)
Investigator: S. A. Goldblith

The purpose of this project is to make an analysis of data on the nutritional condition of American prisoners of war at the Zentsuji Prisoner of War Camp, Shihoku, Japan.

Progress to 6/30/48: This project has been completed. An analysis of total food intake of officer prisoners of war at Zentsuji, Japan have been made. These calculations are based upon the composition of the raw foods. The actual intake of the various nutrients was undoubtedly less than these calculations indicate, because vitamins are destroyed during cooking and vitamins and minerals are extracted into the cooking water and discarded. The data presented here therefore reflect a condition which is quite optimistic.

The diet consisted almost entirely of vegetable foods with rice, barley, and to a lesser extent, soybeans as the staple foods.

NUTRITION, NR-123-298 (Cont.)

Due to the large amount of green vegetables in the diet there was no lack of vitamin A, ascorbic acid or iron. There were clinical evidences of hypoproteinemia which may be ascribed to the fact that there was very little animal protein in the dietary.

The monthly average weights of the officers correlate quite well with the calories received. The National Research Council's recommended daily allowances for a moderately active, 70 km man are 3000/calories/day. It was observed that body weight was maintained when the calorie intake was approximately 3000 calories.

Fat intake was below a desirable level. It is suspected that the dry scaly skin observed in all of the prisoners is a manifestation of a deficient intake of essential fatty acids.

The calcium intake was sufficient for only seven months of the 31 months studied.

There was sufficient thiamine in the diet until the last 12 months of the period studied Suspected cases of beri-beri were observed during this period of low thiamine intake.

The riboflavin was not adequate during the entire period of the study. The clinical manifestations of riboflavin deficiency were apparent.

Pellagra was observed intermittently during the 31 months of incarceration between December 1942 and June 1945. Since the exact niacin intake is not known it is difficult to determine whether the development of pellagra in subjects, on a diet which calculates to contain approximately 16 mg, is proof that the National Research Council's allowance of 15 mg per day is inadequate.

NR-123-324 — Plasma Proteins and Protein Metabolism in Premature and New Born Infants — (Unclassified)

Contractor: George Washington University, Washington, D. C.
Contract: N7-onr-419, Task I, (5/1/47 to 6/18/49)
Investigators: L. K. Sweet, J. H. Roe

This project constitutes a part of the general program on protein metabolism. Many of our most fundamental and important findings in the field of physiology have originally been observed in studies on the developing organism (in fetal life and infancy) when the demands for anabolic metabolism are great and new organs and organ systems are just beginning to function.

Progress to 6/30/48: Data are being accumulated on the blood protein concentration of newborn babies both premature and full term. The blood analyses and body weights are followed for several months while the infants are fed on either the customary formulas or the basic formula with added protein. More studies are needed before it can be determined whether the protein feeding establishes a more satisfactory rate of growth for the newborn.
Estimated Completion: Continuing

PROTEIN CHEMISTRY AND IMMUNOCHEMISTRY

NR-124-015 — The Fractionation of Plasma Proteins of Diseased and Traumatized Animals and Patients, Including Those Exposed to Radiation — (Unclassified)

Contractor: University of Virginia, Charlottesville, Virginia
Contract: N7-onr-372, Task I, (6/15/47 to 6/30/49)
Investigator: A. Chanutin

The purpose of this project is to investigate fractionation of the blood plasma by the alcohol precipitation procedure with studies of the fractions obtained by chemical and electrophoretic methods.

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BIOCHEMISTRY

PROTEIN CHEMISTRY AND IMMUNOCHEMISTRY, NR-124-015 (Cont.)

Progress to 6/30/48: Sera from control and injured dogs, goats, and rats were fractionated. The animals were injured by turpentine, burning, or gassing with vesicants. Sera from turpentine-injured dogs yielded two new fractions, both α-globulins, neither of which was found in the normal dog serum. IV-4B is obtained from IV-4 by isoelectric precipitation and is high in lipide content. IV-4 fl is a fraction of low density and has a relatively high content of carbohydrate. In injured dogs, the yield of fractions rich in α- and β-globulins, such as III-0 and IV-4, was greatly increased, while the yield of fractions rich in γ-globulin decreased considerably.

General fractionation procedures had to be altered for goat sera, principally because of the low solubility of albumin in the presence of alcohol. Further modifications concerned the preparation of α_1- and α_2-globulins. Two fractions containing electrophoretically pure γ-globulins were obtained. α_1- and α_2-globulins, approximately 90% pure, were isolated. Electrophoretically pure albumin was isolated and crystallized. The goat serum usually showed an increase in β-globulin upon injury. In contrast to dogs, goats did not show the marked changes in the electrophoretic patterns of sera after injury.

Rat plasma was fractionated into four fractions. Electrophoretic analyses of these fractions revealed several protein components which could not be observed in whole plasma. All types of injury showed striking changes in the electrophoretic patterns of II + III and IV-4. These changes could not be seen in the whole plasma of injured rats.
Estimated Completion: Continuing

NR-124-156 Mineral Element Binding Properties of Intra-Cellular Constituents (Unclassified)

Contractor: Oberlin College, Oberlin, Ohio
Contract: N6-ori-157, (7/15/46 to 9/15/48)
Investigator: G. T. Scott

The purpose of this project is to make a basic study of the activity of potassium in the tissues.

Studies are in progress on the potassium and sodium binding properties of myosin, liver-cell components and mammalian erythrocytes. The influence of ionic strength, pH, and adrenal hormones on these bindings are included in the investigations.

Progress to 6/30/48: It was found that there is competition between calcium and magnesium for cellular components. In the absence of one, there is an equivalent replacement by the other. Sodium can replace calcium and magnesium to some extent, but not potassium.

Significant modifications have been made in the flame photometer.

A study is in progress of the binding of intra-cellular cations (Na, K, Ca, Mg) by components of liver cell brei, the criterion of the bound state being the inability to remove and washout specific ions by dialysis. It is observed that the dialysis of myosin against solutions hypotonic with respect to three of the cations and deficient in the fourth usually removes some of the former cations, and a large proportion but not all of the fourth. A comparable dialysis of liver cell brei washes away potassium completely, indicating that by this definition the intra-cellular potassium alone of the ions is not bound to the cell components.
Estimated Completion: Continuing

NR-124-225 The Electrophoretic Ultracentrifugal Investigation of High Polymers (Unclassified)

Contractor: Ohio State University, Columbus, Ohio
Contract: N6-ori-225, Task VI, (12/1/46 to 11/30/48)
Investigator: Q. Van Winkle

PROTEIN CHEMISTRY AND IMMUNOCHEMISTRY, NR-124-225 (Cont.)

The purpose of this project is to conduct a study of the physical and chemical properties of the non-virus type nucleoproteins, with the aid of the electrophoretic ultracentrifuge, the Tiselius electrophoresis apparatus, the electron microscope, and the ultraviolet microscope. The nucleoproteins are being obtained from various mammalian glands such as the liver, pancreas, spleen, appendix, etc. This investigation will yield information concerning (1) the sizes and shapes of a number of types of nucleoprotein molecules as determined by the ultracentrifuge, and the electron microscope; (2) the nature of the bonds which link nucleic acid and protein together in the nucleoprotein molecule; and (3) the number and identity of the different types of nucleoproteins in various cells.

Progress to 6/30/48: Nucleoproteins from rabbit appendices were investigated by the following methods: Electrophoresis, diffusion, and ultracentrifuge.

These nucleoproteins are quite labile, showing complexes between nucleic acid and proteins, the compositions being a function of pH and salt concentration.

Molecular weights varied with the method of preparation. The electrophoretically purified material had a molecular weight of 4,600,000 and an axial ratio of 150/1. The chemically prepared material had a molecular weight of 1,800,000 and an axial ratio of 100/1.

Sedimentation, velocity, diffusion constant were studied. These results show very marked differences in the fundamental physical and chemical properties of the nucleoproteins obtained from various mammalian organs. Previous investigations on rabbit liver proteins have disclosed that molecular weights of electrophoretically purified materials are lower and that the axial ratio is smaller than for the appendices.

Estimated Completion: Continuing

NR-124-260 Composition, Properties and Structure of Proteins (Unclassified)

Contractor: Columbia University, New York, New York
Contract: N6-onr-271, Task I, (12/13/46 to 6/30/49)
Investigators: E. G. Miller, Jr., E. Brand

The purpose of this project is to make a quantitative analysis of the amino acids comprising the protein fractions of blood of man, horse, ox, and of certain enzymes. This will involve improvement of existing methods and development of new analytic methods. Particular emphasis will be placed on determination of the structure of the terminal groups of the polypeptide chains of practically or theoretically important proteins.

Progress to 6/30/48: Methods for the Determination of Amino Acids. Attempts to develop a satisfactory microbiological assay for alanine are being continued. A number of strains of Lactobacillus are being tried. The isoleucine content of a number of previously reported proteins is being reinvestigated. A number of different preparations of D, L-isoleucine and also one of L-isoleucine are being used for comparison. The isoleucine content of B-lactoglobulinis is appreciably lower than was originally reported (6% against 8.4%). Microchemical and photometric determinations of protein constituents and amino acids were carried out as previously. A microphotometric method for the determination of histidine was developed. Additional microbiological values on certain proteins are being collected for comparison.

Determination of Sulfate in Proteins. Many highly purified proteins contain appreciable amounts of sulfate, partly as a result of their preparation which frequently involves the use of sulfates. The sulfate content of a considerable number of proteins was determined. This determination always involves hydrolysis or at least mild hydrolysis. It is not always possible to tell whether the sulfate has been present in these preparations as a salt or perhaps in ester form.

Determination and Properties of Specific Side Chain Groups in Proteins. The dependence of the ultraviolet absorption of tyrosine on the dissociations of charged groups, particularly,

PROTEIN CHEMISTRY AND IMMUNOCHEMISTRY, NR-124-260 (Cont.)

the phenolic group, was investigated in great detail. All the microscopic dissociation constants of tyrosine were established by ultraviolet spectrophotometry. The ultraviolet absorption of a number of proteins at different hydrogen ion concentrations were also studied. In some cases, the interpretation of these results depends on a detailed study of the ultraviolet absorption of tryptophane. In most cases, it is already clear that the ultraviolet absorption of the phenolic group in proteins is not the same as that of the isolated amino acid tyrosine. It has been concluded that the pK of the phenolic group in certain proteins is appreciably different from that of tyrosine.

Detailed studies of the pH Dependency of the ultraviolet absorption of tryptophane were made. The pH dependence of the ultraviolet absorption of most amino acids has been studied but not in sufficient detail. It was observed that there is a definite difference in ultraviolet absorption of cystine between acid and alkaline pH. This phenomenon may be related to the hydrolysis of cystine in an alkaline medium: $SS + H_2O = SH + SOH$. Since cystine is only slightly hydrolyzed, dithiodiglycollic acid, which is markedly hydrolyzed, was tried. This compound was found to have marked ultraviolet absorption with a peak at 3200 Å in an alkaline medium. The absorption completely disappears on acidification. The hypothesis is advanced that the so-called "unspecific" absorption of certain proteins in an alkaline medium may be due to the hydrolysis of SS linkages, as shown above. These observations are being extended.

Preparation of the L and D Forms of Amino Acids. Certain amino acids, such as valine, isoleucine, phenylalanine, methionine and particularly threonine are available only in synthetic form as racemic compounds. They are needed in their natural forms for many aspects of the investigations. Preparation by resolution of both the L and D forms are under way. Threonine has been synthesized on a fairly large scale and the first batch of about 15 gms of L-Threonine is available for experiments. The rest of the material including D-Threonine and allo-Threonine are at various stages of preparation. In view of the occurrence of D-amino acids in certain peptides, it is intended to utilize the D-amino acids obtained by resolution for synthesis of D-peptides and for nutritional investigations.

Composition of Proteins. The data for gelatin are complete. A considerable number of data have been assembled on the composition of the following proteins: a, B and Y chymotrypsin; human a and B serum globulin; human, adult and fetal bovine hemoglobins; crystalline mercury salt of human serum albumin; crystalline iron-binding protein of human plasma; crystalline yeast protein; crystalline trypsin; crystalline trypsinogen and crystalline trypsin inhibitor from soybean; human blood group substances; also crystalline egg albumin, edestin, and elastin.

Recently published bioessays seem to indicate that certain strains of Lactobacilli contain all of the glutamic acid in DL form. A study is under way to attempt to confirm this claim by isolation of DL glutamic acid from Lactobacillus arabinosus 17-5 and to ascertain whether other amino acids are present in these bacteria in racemic form.

Protein Nutrition. A sufficient supply of crystalline and recrystallized B-lactoglobulin preparation is available, and will continue to be available, not only to carry out nutritional experiments but also for further studies on the chemical structure of B-lactoglobulin.

In feeding experiments, on weaning mice, the growth response of the mice to purified casein, purified lactalbumin, crystalline B-lactoglobulin and amino acid mixtures corresponding to B-lactoglobulin was compared. The experiments also included a comparison of the effect of different salt mixtures. In order to make the experiment strictly comparable, the mice were put on a starting diet containing an amino acid mixture instead of protein. It was found that somewhat better growth and "protein efficiency" was obtained with casein and lactalbumin than with B-lactoglobulin. It is known that casein and lactalbumin still contain certain growth factors which are not present in the crystalline B-lactoglobulin. The amino acid mixture corresponding to B-lactoglobulin which has been used in these experiments was made up in such a way as to replace all the rare L-amino acids by twice the amount of the DL forms. The growth response of the mice to these amino acid mixtures was much higher than reported in the literature for somewhat different mixtures, but still amounted to only about 70% of the growth response to B-lactoglobulin.

PROTEIN CHEMISTRY AND IMMUNOCHEMISTRY, NR-124-260 (Cont.)

These experiments are being continued by gradually replacing all the DL amino acids by their L forms. (The reason for the synthesis of L-threonine.)
Estimated Completion: Continuing

NR-124-482 Amino Acid Metabolism of Infants (Unclassified)

Contractor: New York University, New York, New York
Contract: N6-onr-279, Task VIII, (4/15/48 to 4/14/49)
Investigators: L. E. Holt, A. A. Albanese

The purpose of this project is to make amino acid requirement studies on both the normal and diseased infant.

These studies are an extension of studies undertaken in 1941. To date the investigators have attempted to produce specific amino acid deficiencies. The general procedure has been to eliminate a single amino acid from the diet and follow the N_2 retention, weight curve, and plasma protein level, and by step-wise replacement of the missing factor to determine the minimum amount required to restore these criteria to normal values. It is further proposed to use tagged amino acids as supplements and to assay the said amino acid in the urine, blood, and tissue by the Geiger counter technique. The infant, a growing organism, makes an ideal experimental situation to study both normal and abnormal growth. On a weight basis it has been found that the protein requirement is five times greater than that of the adult.

Progress to 6/30/48: No progress has been reported.
Estimated Completion: Continuing

SECRETION AND EXCRETION

NR-125-031 The Role of the Liver in Traumatic Shock (Unclassified)

Contractor: Harvard University, Cambridge, Massachusetts
Contract: N5-ori-76, Task VI, (6/1/46 to 12/30/48)
Investigator: J. Fine

There is cumulative evidence to show that damage to the liver is responsible for the failure of advanced traumatic shock to respond to therapy. Recent animal experiments have demonstrated that this liver injury can be repaired by cross-circulation of the liver with a healthy donor.

The purpose of this project is to determine (1) whether repair of the liver damage is due to some contribution by the donor animal apart from supplying additional arterial blood to the shocked dog's liver; and (2) whether the liver injury results in the production of a toxic agent or in the loss of a normally available substance affecting the integrity of the peripheral vascular system.

Progress to 6/30/48: Shock. In a previous report it was stated that the recovery of a dog in irreversible hemorrhagic shock by perfusion of the liver with a healthy donor animal was due to a contribution not only of arterial blood, but to some additional factor. Several dogs, whose livers were damaged by chloroform to an extent which was not obvious clinically but could be detected by liver excretion tests, were used as donors. The method of depriving the donor of organs whose continued normal function might be an essential part of his contribution to the recipient was used. These donors failed to sustain the shocked dog and it was tentatively concluded that the donor's liver must be healthy if he is to restore integrity to the shocked dog's liver. It was noted that the shocked dog in these experiments died with a massive

[redacted]

BIOCHEMISTRY

SECRETION AND EXCRETION, NR-125-031 (Cont.)

hemoperitoneum. The hemoperitoneum had been observed many times before and it was finally concluded that it was not due to technical error, but to a large increase in portal venous pressure which was not manifest until the irreversibly shocked dog was given massive transfusions, whether by cross-circulation, auto-perfusion or otherwise.

Peritoneal Irrigation for Acute Renal Failure. Improvements in technique have been developed so that it is now possible to restore and maintain fluid and electrolyte balance. Pulmonary edema, hypocalcemia and other complications can now be avoided or minimized. Moreover, the investigators are becoming increasingly convinced that the uremic state itself imposes further suppression of renal function. This follows from the repeated observation that diuresis is often abruptly initiated by irrigation for 48 to 72 hrs.

The safeguards against bacterial contamination of the peritoneum have also been improved, but by no means eradicated. This involved a thorough study of the possible source of organisms from the intestine of the normal and uremic animal. Frank peritonitis has not been produced in the animal, though E. coli has been recovered from the peritoneum. In a recent case of recovery from postpartum eclampsia and renal failure, B. subtilis, a non-pathogenic organism, obviously an air or skin contaminant, was the only bacteria cultured from the peritoneal drainage. It is obvious that the technique to prevent infection requires improvement and until one can be certain of preventing peritoneal infection, the method must not be regarded as a safe clinical procedure.

Estimated Completion: Continuing

NR-125-136 Renal Factors Influencing the Accumulation of Edema Fluid (Unclassified)

Contractor: Washington University, St. Louis, Missouri
Contract: N6-ori-202, Task II, (10/15/46 to 6/30/49)
Investigator: P. H. Futcher

The purpose of this project is to make a study of the effect of the intake of varying amounts of sodium chloride upon renal glomerular filtration rate, (mannitol clearance), and upon the degree of reabsorption of water and salt by the renal tabules. The renal blood flow and the urinary excretion of salt-and/or water- retaining adrenal and pituitary hormones will also be measured if the dependability of available techniques is substantiated. Normal human subjects will be thus studied, as will patients with edema due to cardiac insufficiency and cirrhosis of the liver.

Progress to 6/30/48: Unilateral sympathectomy and unilateral adrenalectomy produce the same effect upon the excretion of water, chloride, mannitol, and sodium para-aminohippurate in dogs under nembutal anesthesia. Namely an excess in excretion of all these substances by the left kidney several weeks after left adrenalectomy, and several weeks after left supradiaphragmatic sympathectomy with intact adrenals.

In some instances, the increase in glomerular filtration rate (mannitol clearance) sufficed as a possible explanation for the increased excretion of water and chloride by the kidney homolateral to the site of the operation.

This gives evidence of a hitherto unsuspected homolateral relationship between the adrenal gland and the kidney.

Estimated Completion: Continuing

PHARMACOLOGY AND TOXICOLOGY

NR-126-129 Research in Anesthesiology (Unclassified)

Contractor: University of Chicago, Chicago, Illinois

PHARMACOLOGY AND TOXICOLOGY, NR-126-129 (Cont.)

Contract: N6-ori-20, Task XI, (7/15/46 to 7/15/49)
Investigators: E. M. K. Geiling, H. M. Livingstone

The purpose of this project is to make a study of the effect of narcotics upon histamine metabolism. Urethane causes a marked decrease in the blood histamine of the rabbit. This work is being extended to other anesthetic agents and other animals, and the influence of analeptics and antihistamine agents will be determined. Acetyl choline metabolism and its relation to anesthesia is being investigated. An attempt is being made to clarify the mode of action of histamine and its relation to acetyl choline and choline asterase in order to explain various problems related to anesthesia.

Methods for the intravascular administration of oxygen are under investigation. It has been found that intravenous hydrogen peroxide supplies more oxygen than can be made available by the injection of oxygen itself. The effects of intravenous subcutaneous and intraarterial administration of hydrogen peroxide, are being observed with a view to possible clinical uses.

Blood gas analyses have been made following the intravenous administration of the gaseous anesthetics. Observations are being made on a new respiratory stimulant derived from a plant extract.

Further work will be done to study the absorption and effects of drugs when inhaled in aerosol form. Thus far the results have not been very promising, but improvements in technique are being explored.

Progress to 6/30/48: Ethylurethane causes a marked drop in the blood histamine level of rabbits. In prolonged narcosis, blood histamine reaches its initial level two to three hours after urethane injection. Repeated injection of urethane causes a similar decrease in blood histamine as observed after the first dose. Experiments with procaine reveal that intravenous administration, elicits rapid fall in the blood histamine of the rabbit, which, shows a maximum at the time when convulsions caused by procaine occur. At present experiments are being performed in which the enzymatic split products of procaine are tested for their effects on histamine metabolism.

Basic studies show that narcotics interfere with enzyme-catalyzed reactions of the tissues. Experiments have given evidence that bacterial toxins have a marked effect on histamine and carbohydrate metabolism of animals. Findings in histamine experiments showed striking similarity to those observed in previous histamine anesthetic experiments. Together with changes in histamine metabolism, there was inhibition of glycogen resynthesis in the toxin-poisoned animals.

Experiments based on these similarities are under way, in order to study the effect of anesthetics (procaine first) on enzymes and metabolites.

Succinic dehydrogenase and cytochrome oxidase have been tested and other metabolic experiments are in progress. The effect of anti-histamine substances on metabolism in the light of previous considerations will be the subject of further investigations.

A teaching movie film on "Deleterious Effects of Drugs Used in Anesthesia", being made in conjunction with the American College of Surgeons, is nearing completion.
Estimated Completion: Continuing

NR-126-134 Studies on the Pharmacology of Para-Aminobenzoic Acid (Unclassified)
(Formerly 135-134)

Contractor: George Washington University, Washington, D. C.
Contract: N6-ori-163, Task I, (7/1/46 to 1/1/49)
Investigator: P. K. Smith

Under this project work is divided into three parts.

(1) Determination of the toxicity of para-aminobenzoic acid in various animals when given orally in single doses and when mixed with the food. This includes determination of any pathological changes produced by the drug.

PHARMACOLOGY AND TOXICOLOGY, NR-126-134 (Cont.)

(2) Administration of the drug in large single and in large continued doses to patients to determine the best means of administration and whether or not the drug exerts any deleterious effects with special reference to the kidneys, liver, and blood.

(3) Screening of drugs for the treatment of rickettsial diseases. This study is being carried out in a search for other drugs that may be more effective than para-aminobenzoic acid in rickettsial diseases. The method of testing involved the use of chick embryos, infected with endemic typhus rickettsial. The drugs are then administered to the egg and after a suitable time determination is made to see whether or not the animals have survived.

Progress to 6/30/48: Dr. Smith has reported on the pharmacology of Para-Aminobenzoic Acid (PABA). Most of the drug is excreted as a conjugation product with glycine (para amino hippuric acid). Part of this is acetylated as are the sulfanamides. No toxicity was observed in normal subjects with dosages up to four grams. Studies of patients with liver disease show that the metabolism of PABA is inefficient and parallels that of benzoic acid.

Dr. Smith is also screening drugs for anti-rickettsial action. Walter Reed Hospital is furnishing the rickettsia and the National Institute of Health, the drugs which were previously collected for anti-malarial screening.

Estimated Completion: Indefinite

NR-126-158 Intravenous Anesthesia (Unclassified)

Contractor: Indiana University, Bloomington, Indiana
Contract: N6-ori-180, Task II, (12/1/46 to 11/30/48)
Investigators: H. R. Hulpieu, V. V. Cole

The purpose of this project is to study detoxication of procaine in intact dogs as influenced by length of administration, partial asphyxia, and preliminary medication with depressant drugs; and the influence of intravenous procaine on the action of autonomic and stimulant drugs as compared with the action of these drugs when anesthesia is produced by ether and by the barbiturates. The effect of intravenous procaine on the inhibitory influence of the sulfana mides on bacterial infection will be investigated. Other likely local anesthetic agents will be compared with procaine as measured by the above experimental procedures.

Progress to 6/30/48: Metabolism and distribution of procaine hydrochloride was studied in animals anesthetized with ether, chloroform, and sodium thiopental. In rats, ether increased the toxicity of procaine, the addition of epinephrine increased this toxicity still further. Dogs, under sodium thiopental withstood larger procaine doses than did those under chloroform. Those under chloroform were more resistant to death than those under ether.

The distribution and storage of these agents was studied in tissues and organs.

Estimated Completion: Continuing

NR-126-212 Clinical and Biochemical Aspects of Chronic Occupation Diseases (Unclassified)

Contractor: Edward L. Trudeau Foundation, Saranac Lake, New York
Contract: N7-onr-307, Task I, (3/1/47 to 1/7/50)
Investigators: F. W. Klemperer, A. J. Vorwald

This project number has been changed to NR-122-212.

PHARMACOLOGY AND TOXICOLOGY (Cont.)

NR-126-299 Effects of High Partial Pressures of Oxygen on Man (Unclassified)

Contractor: University of Pennsylvania, Philadelphia, Pennsylvania
Contract: N6-onr-249, Task I, (3/1/47 to 2/28/49)
Investigators: C. J. Lambertsten, C. F. Schmidt

The purpose of this project is to make observations of the effects on normal man of exposure to pO_2 ranging from one to five atmospheres with reference to the nature and incidence of symptoms, course of recovery, effect of CO_2 temperature and repetition of exposure.

Progress to 6/30/48: No progress report has been received.
Estimated Completion: Continuing

NR-126-451 The Role of Electrolytes in Metabolism and the Hazards to Health of Exposure to Manufacturing Processes of Explosives (Unclassified)

Contractor: Temple University, Philadelphia, Pennsylvania
Contract: N7-onr-407, Task I, (1/1/46 to 8/1/49)
Investigator: F. W. Sunderman

This project has been declassified since the 1 April 1948 issue of this Summary.

DINA is a component of the flashless propellant, albanite. Observations on human subjects exposed to DINA revealed that the outstanding complaint was that of headache.

The present investigation pertains to the study of headaches, especially headaches produced from exposure to aliphatic nitrate and nitrite asters. Essentially six types of approach are at present being undertaken: (1) The characterization of the blood pigment observed in animals poisoned by aliphatic nitrate and nitrite esters; (2) the characterization of the electroencephalographic patterns in experimental animals poisoned by such compounds; (3) direct observation of the changes in the cerebral blood vessels in monkeys following exposure; (4) metabolic changes occurring in humans suffering from headaches following exposure; (5) the effect of barbiturates, oxygen, and other agents in experimental animals exposed to such compounds; and (6 measurements of changes in the cerebral blood flow. If feasible they will be correlated with changes in the cerebral capillaries and electroencephalographic patterns.

Progress to 6/30/48: No progress report has been received since this project was declassified.
Estimated Completion: Continuing

NR-126-489 Biological Action of Fluorine Compounds (Unclassified)

Contractor: University of California, LaJolla, California
Contract: N8-onr-519, Task I, (4/1/48 to 3/31/49)
Investigator: E. M. MacKay

The purpose of this project is to conduct a general investigation of organic fluorine compounds with emphasis on the two peculiar "fluorine properties" (1) biological inertness, and (2) structural competitive inhibition - the latter emphasizing enzyme effects. Physiological and pharmacological studies will be correlated with indications from enzyme reactions. Physiological tests will be devised to show the mechanism of action of the compounds as indicated from enzyme studies and to utilize specific inhibitors to provide more knowledge of the details of normal and pathological metabolism. The principal method of approach of this program being the chemical synthesis of organic fluoride derivatives which might be expected to act as competitive inhibitors. Industrially important fluorine derivatives can be tested for degree of toxicity or degree of inertness.

PHARMACOLOGY AND TOXICOLOGY, NR-126-489 (Cont.)

Progress to 6/30/48: No progress has been reported.
Estimated Completion: Continuing

GENERAL AND MISCELLANEOUS

NR-129-509 Development and Construction of a Human Calorimeter (Unclassified)

Contractor: American Society of Heating and Ventilating, Cleveland, Ohio
Contract:
Investigator: T. H. Benzinger

The Society's laboratory will procure and/or construct all materials, equipment instruments, and apparatus needed in the investigation of the principle of a human calorimeter; and for the construction of a calorimeter large enough to hold a man and to allow him room for exhaustive physical excercise in the supine position.

Progress to 6/30/48: No progress to report.
Estimated Completion: June 1950

NR-129-759 Biological Synthesis of the Peptide Bond: Fellowship Training Program (Unclassified)

Contractor: Reed College, Portland, Oregon
Contract: (6/30/48 to 6/30/49)
Investigators: F. Hungate, A. Livermore

The purpose of this project involves the biological synthesis of the peptide bond. Interesting research on some phases of this problem has already been made in several laboratories, but in spite of this work knowledge of the mechanism of peptide bond (and protein) synthesis remains scanty. It is proposed to attack the problem by studying the synthesis of small, naturally, occurring di- and tripeptides, such as glutathione. Then it is expected to experiment with intact animals and also to make some in vitro experiments with surviving tissues, tissue breis and tissue extracts. It is proposed to use amino acids and amino acid derivatives labeled with isotopic atoms in order to follow the reactions which take place. The isotopically labeled compounds will be particularly useful in cases where there is only a small amount of synthesis accompanied by a large amount of hydrolysis of the peptide. It is expected to use radio isotopes of carbon, sulfur and iodine (perhaps others later).

Progress to 6/30/48: No progress to report.
Estimated Completion: June 1949

Microbiology

GENERAL

NR-130-013 Meningococcal Infection (Unclassified)

Contractor: University of Chicago, Chicago, Illinois
Contract: N6-ori-20, Task V, (5/1/46 to 4/30/49)
Investigator: C. P. Miller

Under this project two problems are being attacked:

(1) Preparation and investigation of toxins produced by meningococcus, including:
   (a) Comparison of the toxigenic potencies of different strains of meningococcus, especially comparison of strains from acute fulminating cases and from non-fatal cases;
   (b) action on experimental animals - physiological and pathological; and
   (c) protective action of penicillin against the lethal effect of toxins on experimental animals.
(2) Development by meningococcus of penicillin resistance and streptomycin resistance.

Progress to 6/30/48: Studies are under way to explain the rapidity with which, and conditions under which, meningococci develop a very high degree of streptomycin resistance during two or three subcultivations on media containing increasing concentrations of the drug. Sixteen to 18 strains of meningococcus on 25 preparations of streptomycin consistently developed two mutants, which markedly differ in appearance, viability, and virulence from the original strains.

It has been repeatedly demonstrated both in the clinic and in the laboratory that bacteria, initially sensitive to streptomycin, can very quickly acquire resistance to high concentrations of the drug. Search for an explanation of this fact, showed that (1) the rapid development of resistance is due to the multiplication of resistant variants which appear in small numbers in the original bacterial population by the process of random mutation; and (2) these streptomycin resistant variants are of at least two types. One type will grow on ordinary media as well as on streptomycin-containing media. The other type requires streptomycin for its growth in vitro and in vivo.

Certain impure preparations of penicillin have been shown to exert a marked protective action against the lethal effect of sterile bacterial endotoxins in mice. Maximal protective action requires crystalline penicillin plus some impurity factor, the isolation of which is now being attempted.

Streptomycin--dependent organisms have been recovered from the pharynx and large bowel of mice and rabbits during the second week of treatment with large doses of streptomycin.

Streptomycin--resistant bacteria have been cultured in large numbers from the throats of 98.4% of 61 patients receiving one to four grams of streptomycin a day; streptomycin-dependent bacteria were recovered from the throats of 2/5 of them. Streptomycin-resistant bacteria do not occur with such frequency in hospital staff members or untreated patients. They were found in only four per cent of the first group and 10% of the second group.

Approximately 12 manuscripts have either been published or submitted for publication.

Estimated Completion: Indefinite

NR-130-044 Bacteriophage (Unclassified)

Contractor: Yale University, New Haven, Connecticut
Contract: N6-ori-44, Task IX, (6/1/46 to 8/31/48)
Investigator: P. B. Cowles

GENERAL, NR-130-044 (Cont.)

The purpose of this project is to investigate (1) the affect of various growth factors and similar substances upon the elaboration of bacteriophage by several species of bacteria, and (2) the availability of substances derived from the products of bacterial disintegration for bacteriophage growth.

Progress to 6/30/48: Studies of the affects of alpha amino acids on bacterial suspensions showed that glycine causes an immediate increase in turbidity followed by clearing of the suspension. The mechanism of action of the glycine was studied. The first approach was to establish the rate of enzyme formation in the bacterial lysis and the concomitant effects of glycine. However, since the usual enzyme inhibitors, cyanide, fluoride, iodoacetate, citrate and cuprous, mercurous, and silver ions failed to prevent or stop the reaction, the theory of lysis based upon enzyme activity is not likely. The results of this research challenge the present concept of the lysis of bacterial cells by amino acids and invite further theorization and research to explain the phenomenon.

Progress has also been reported on factors underlying the growth of viruses. It has been known for several years that bacteriophage, the virus family affecting bacteria themselves, can increase in numbers without a concomitant increase in growth of the host bacterial cells.

The present research concerns itself with this problem of the stimulation or inhibition of bacterial and bacteriophage growth and their interdependence. For instance, glycine will allow increase in growth of the 'phage and prevent bacterial growth. An analogue of glycine amino methane sulfonic acid prevented 'phage growth. The inference is that 'phage utilized glycine without the participation of the bacteria as expressed as growth.

Additional observations (such as in the presence of penicillin) showed that 'phages increase but the growth of the host bacteria are inhibited. However, with streptomycin the 'phage as well as the susceptible host cells are inhibited. Chloromycetin has an effect similar to that of streptomycin. Along these same lines the factors influencing the size of 'phage plagues have been investigated.

This research opens new fields of inquiry in respect to mechanism of action of antibiotic and chemotherapeutic agents and the essential growth factors of bacteriophages.

It has been observed that bacteriophage produced in synthetic medium is very often held back by the usual bacteriological filters. The addition of small amounts of nutrient broth or of such substances as sodium desoxycholate or sodium lauryl sulfonate to bacteriophage preparations immediately prior to filtration permit the lytic agent to pass through. The reasons for this are not as yet apparent and the phenomenon is being further investigated, to see whether the effect is due to surface tension changes or to some other factor. It seems probable that the failure to detect bacteriophage, and perhaps other viruses as well, in certain filtrates may have been due to characteristics of the suspending mediums similar to those mentioned here.

An observation made in the early days of the study of bacteriophage is being investigated. Twenty five years ago Wollman reported that by the use of collodion membranes of the proper permeability bacteria could be grown in broth on the one side and bacteriophage could be shown to increase in amount on the other. Presumably, materials produced by the bacteria could pass the membrane and serve as pabulum for the virus. This finding was at once confirmed by several investigators, but serious objections were raised, namely, that the collodion membranes might have allowed the bacteriophage to pass back and forth undetected. In several of numerous experiments these results have been reproduced, and rigorous controls failed to disclose any contamination of culture with bacteriophage, or of bacteriophage with culture. If further work upholds these results it should be possible and distinctly important to obtain the metabolites responsible for the virus increase.

In connection with Dr. Krueger's recent announcement (NR-133-096) of succes in growing bacteriophage in filtrates of lysozyme lysates of staphylococci it is pertinent to recall that in the past efforts to obtain growth with similar preparations derived from B. megatherium and B. mesenterious were unsuccessful. Further attempts will be made when details of Krueger's methods are available.

GENERAL, NR-130-044 (Cont.)

A copy of a manuscript designed for the Journal of Bacteriology has been prepared. Since this subject bears no obvious relation to the problems of the contract, it may be mentioned that nitrophenols were being used as inhibitors of cell growth in certain phases of the work, and it seemed desirable to determine something of their behavior.

A Publication on "The Use of Glycene in the Disruption of Bacterial Cells" appeared in Science vol 107:376-377 Apr. 9, 1948.

Estimated Completion: Indefinite

NR-130-055 Virus Diseases (Unclassified)

Contractor: The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania
Contract: N6-ori-188, Task I, (9/1/46 to 8/31/48)
Investigators: T. F. McNair Scott

The purpose of this project is to (1) establish and operate a Virus Diagnostic Research Laboratory, involving preparation and standardization of biological materials for diagnostic tests, such as antigens for complement-fixation and corresponding control sera; the study of specimens submitted from patients suspected of virus infections, i.e., attempts to isolate and identify the causative agents and to demonstrate antibody responses; the search for the source of infection in the studied cases and the analysis of data collected during epidemics; and the adaptation and development of new diagnostic tests and research toward their interpretation. (2) Studies are concerned in the main with metabolic phenomena appearing in virus-infected cells of bacterial, plant and animal types; in the energetics and nutritional requirements of virus synthesis and investigations into the pathways employed in the formation of virus substance. The use of inhibitory substances for the specific inhibition of essential steps in virus multiplication is also being studied.

Progress to 6/30/48: Viruses of the bacteriophage-escherichia coli system have been isolated, and their composition and chemical reactivities extensively studied. All viruses have been shown to contain nucleic acid and several building blocks, nucleotides have been identified together with characteristics of their metabolism. An immediate end in view is the explanation of the phenomenon of multiplication. The latest paper from this research group is on this problem, "The Synthesis of Nucleic Acid and Protein in Escherichia coli B infected with T_2 T Bacteriophage" which will appear in the Journal of Biological Chemistry.

GENERAL, NR-130-067 (Cont.)

(1) The animals are being studied at Lobund as unique biological specimens from the pathological, bacteriological, physiological and biochemical viewpoints. Their usefulness is also being investigated in the etiology of dental caries. They are being used as test animals in nutrition and virology.
(2) Building, testing, and putting into operation large-scale apparatus in which numerous animals can be reared germ-free through many generations.

Progress to 6/30/48: At this time the long disputed question of whether germ-free vertebrate life is possible has been fairly answered in the affirmative.

An experiment is reported in which 17 chicken eggs were passed into the germ-free system. Twelve hatched. One chick died after hatching and 8 were sacrificed for examination. The three remaining, two cocks and a hen, were reared to maturity and are presently nearly 300 days old. Growth and general appearance are satisfactory. The hen started to lay when 190 days old.

The significance of this event lies in the fact that it marks a new era in experimental biology. Now, for the first time, there is a normal germ-free animal; the exact picture for this type of germ-free animal can be charted without running into the danger of describing other deficiencies and having them ascribed to germ-freeness.

From a nutritional point of view, the laying of an egg by a germ-free chicken indicates that the nutrition of such animals is adequate. Essentially, it may be assumed that there is now a normal chicken for nutritional research; and procedure to chart out the exact utilization of vitamins and other foodstuffs in the absence of microbes may now be carried out.

From virological, bacteriological, and serological points of view, the completion of a germ-free cycle and the start of a new cycle originating from germ-free parents (the eggs are fertile and are now being incubated) are tremendously exciting. Here the questions of the origin of normal antibodies, problems of resistance to infection, the possibility of egg transfer of viral and microbial agents, etc., all become accessible with direct techniques.

From a historical point of view, this is important if for no other reason that it, for the first time, answers the original query of Pasteur (Pasteur, L. 1885 Observations relative à la note de M. Duclaux. Compt. Rend. Acad. Sci., 100 68.) and refutes his supposition: That life is probably dependent upon intestinal bacterial saprophytes. The work of earlier authors has not answered the question of whether normal life was possible without the presence of microbes.

Three of the first eggs laid by the germ-free hen were incubated in a G-F system. Two were cracked, one yielded a dead 15 day embryo. The uncracked egg hatched on 12 April, 1948.

This chick has been maintained on a diet similar to the one fed the parent animal. Microbiological tests on the animal have been negative to date. The chick appears normal and is growing at a rate comparable to control animals.

Egg production has been better than in non-germ-free hens reared on the same sterilized diet. Microbiological tests on the animals are negative.

Control chicks receiving the same diet, but not sterile, began laying about one month earlier than the germ-free birds or the control animals fed the sterilized ration.

This work will lead to research on germ-free life in such fields as nutrition, genetics, immunology and other fields influenced by the uncontrollable variable of microbic contamination.
Estimated Completion: Indefinite

NR-130-137 Infectious Hepatitis (Unclassified)

Contractor: Johns Hopkins University, Baltimore, Maryland
Contract: N6-ori-166, Task VII, (6/15/46 to 7/15/49)
Investigator: G. S. Mirick

Progress in the study of infectious hepatitis or homologous serum jaundice has been limited by the fact that the disease has never been established in laboratory animals. This is

GENERAL, NR-130-137 (Cont.)

the principal purpose of the present research project. M. rhesus monkeys are thought to be susceptible because the infection of their serum into human beings has resulted in jaundice. Infectious material obtained from two distinct outbreaks of jaundice in Naval personnel at Cleveland and Great Lakes is being inoculated into M. rhesus monkeys together with lactophenin, a drug which has been reported to produce in human beings a disease similar to infectious hepatitis. The liver function of these monkeys is being studied by various tests.

Because of the long incubation period in homologous serum jaundice in humans, other studies concerning hepatitis are being followed. These concern the use of the thymol turbidity test of liver function in human beings and studies of proteolytic enzyme concerned in blood clotting and clotolysis in liver disease.

Progress to 6/30/48: Plasma has the property of lysing or dissolving clotted blood. The ability of plasma to lyse clots is increased markedly with liver disease, toxemia of pregnancy, shock, after typhoid vaccine, and pre and post operatively.

The clot presumably is lyzed or digested by proteolytic enzymes present in the blood. Dilute acetic acid precipitates one proteolytic enzyme from plasma from the englobulin fraction, and chloroform activates another in the acid insoluble englobulin fraction. A third source of enzyme effective in lysing plasma and fibrin clots is from filtrates of Beta hemolytic streptococci cultures.

Dr. Ratnoff of Johns Hopkins has shown that plasma proteolytic enzymes from streptococcal filtrate are identical with the enzyme activated by chloroform. The precursor of this plasma proteolytic enzyme is precipitated with the englobulin fraction of plasma at Ph 5.2.

Two articles have been published and three others were submitted for publication. All deal with problems in the general field, factors influencing incidence and etiology of infectious hepatitis. Considerable interest is centered around metabolic products of hemolytic streptococci and their effect on liver cells.

Estimated Completion: Indefinite

NR-~~130~~-146 — Intermediate Metabolism of Carbohydrates of Bacteria — (Unclassified)

Contractor: Western Reserve University, Cleveland, Ohio
Contract: N6-ori-208, Task I, (10/1/46 to 9/30/48)
Investigator: H. G. Wood

Under this project investigations of the intermediary metabolism of carbohydrates are being conducted along four different lines:

(1) An attempt is being made to determine whether or not adenosine triphosphate is a necessary component for fixation of carbon dioxide in oxalacetate with enzymes from bacteria, comparable to the findings with the enzymes from pigeon liver. It seems probable that phosphate esters may be formed in the reaction and efforts are being made to demonstrate such esters.

(2) The conversion of pyruvate to acetyl methyl carbinol lactic and acetic acids and the fixation of carbon dioxide are being investigated. The possibility of a common intermediate which may be broken down to the above named compounds and in which carbon dioxide may be fixed is being studied.

(3) A test is being conducted to determine whether or not acetyl phosphate is an intermediate in the phosphoclastic reaction ($CH_3.CO.COOH\ H_3PO_4 \longrightarrow CH_3CO.OPO_3H_2\ HCOOH$). To do this, C^{13}- acetyl phosphate and C^{13}-formic acid are being synthesized and their relative rates of exchange in pyruvate are being determined. It is known that C^{13}- formate is rapidly converted to the carboxyl of pyruvate. Acetyl phosphate should exchange as rapidly if it is an intermediate.

GENERAL, NR-130-146 (Cont.)

(4) The possible role of acetate condensation to form succinate and the part this reaction plays in respiration is being investigated. Tests are being made to isolate the enzyme and C^{13}-acetate will be used in the investigation.

Progress to 6/30/48: During the biochemical conversion of pyruvic acid to acetylmethylcarbinal by micro-organisms and mammalian tissues, alpha-acetolactic acid is probably an intermediate. The synthesis of alpha acetolactic acid was accomplished by the oxidation of the labile hydrogen on methyl substituted ethyl acetoacetate.
Estimated Completion: Indefinite

NR-130-169 Virucidal Agents (Unclassified)

Contractor: Western Reserve University, Cleveland, Ohio
Contract: N6-ori-208, Task II, (10/1/46 to 1/14/49)
Investigator: H. J. Carlson

Screening by in vitro technics of extracts of a considerable number of higher plants for anti-biotic activity against microorganisms (bacteria and fungi) and viruses has been carried out. This work is being extended to include plants from different parts of the United States. Several plants have already shown promise. Extracts of these as well as of others that are discovered will be further purified and used in vivo against bacteria and viral infections in experimental animals. A similar search is being made for possible antibacterial and antiviral substances in cultures of protozoa. Testing technics are used on the material of protozoal origin similar to technics developed for testing extracts of plant origin.

Progress to 6/30/48: Five publications have evolved from this project:
(1) Screening Methods for Determining the Antibiotic Activity of Higher Plants.
(2) Antibacterial Substances from Plants.
(3) Antibiotic Substances Separated from Sumac.
(4) Antibiotic Agents from Leptotaenia.
(5) Antibiotic Extracts from Yellow Adder's Tongue.

Dr. Carlson has derived substances from plants that are analogous to penicillin and streptomycin in the test tube. The general effect covers a much larger group of microorganisms including the viruses of influenza and poliomyelitis. The extracts show definite promise of contributing to the armamentarium against disease.

In an attempt to find a substance to replace quinine or other substances commonly used in the treatment of malaria, aqueous extracts have been made from many plants. So far, 1,500 plants have been secured for antibiotic activity. There are at present 300 plant extracts which have demonstrated some antibacterial activity. Forty have in vitro antiviral activity. Many of these are being tested for in vivo activity. Recently, the interest of the investigators in antituberculosis compounds has been aroused, and all active extracts are being tested against recently isolated non-pathogenic strains of mycobacteria. Some very promising leads have been found. The bacterial spectrum of these extracts is much greater than antibiotics obtained from lower forms. The experiments to date have indicated that the green portions of the plants have the greater antibiotic activity, and that dry ice preserved specimens of plants do not have activity comparable to that of freshly obtained specimens.

In the very early stages of this investigation there was considerable interest in studying protozoa as sources of antibiotics. Certain protozoa apparently do produce antibiotics, but in general they require bacteria for growth and the difficulty of training protozoa to grow in the absence of bacterial contaminants leads to questions as to the value in pursuing this lead any further.
Estimated Completion: Indefinite

GENERAL (Cont.)

NR-130-176 Experimental Streptococcal Infection in the Embryo (Unclassified)

Contractor: University of Kansas, Lawrence, Kansas
Contract: N6-ori-164, Task VII, (10/1/46 to 9/29/48)
Investigator: N. P. Sherwood

Under this project six problems are being investigated:

(1) A study of the ability of 60 or more strains of hemolytic streptococci, representing all of the Lancefield groups, to produce hyaluronadase, pro-invasin, etc. Both intradermal and chemical methods are being employed. Hyaluronic acid prepared from human umbilical cord and from chick embryos are being used.
(2) A study of capsule and hyaluronic acid formation by the same streptococci.
(3) A study of various toxins and toxic substances produced by these streptococci with an attempt to determine if cardiotoxic substances are produced by other than Group "A" streptococci.
(4) A comparison of the host-parasite relationship, including hematological and other phenomena observed in the embryonic chick and the C-A membrane, with infections observed in the rat, mouse, and perhaps the rabbit.
(5) A study of the phenomenon of synergism to see whether such exists between the streptococcus and certain viruses. Can streptococci act as carriers of virus either by adsorption or as host cells? Is there a synergistic effect in streptococcal and diphtheria infection and also staphylococcal infection?
(6) A study of selected antibiotics and chemotherapeutic agents on selected strains of streptococci.

Progress to 6/30/48: This is the first experimental work in which all of the physiological products of streptococci presumed to relate to their virulence have been studied in a fairly long series of strains including representatives of the first nine Lancefield groups. The following observations have been made.

Hyaluronidase activity is frequently associated with the virulence of streptococci, but it is not essential for virulence.

Many streptococci which fail to produce hyaluronidase do produce a skin spreading factor as determined by intradermal tests.

Streptococci are more virulent for mice when infection is produced by the intraperitoneal route than by either the intradermal or the intranasal route.

Group C streptococci are, in general, more virulent for mice than any other group.

Some strains of hemolytic streptococci seem to have an ability to invade through the mucous membrane of the respiratory tract and establish themselves in the blood stream of the host (mouse).

Testicular extracts and streptococcal hyaluronidase withstand considerable shaking and are not injured by iodine, cyanide, fluoride, or hydrogen peroxide.

Some hemolytic streptococci are able to inhibit the growth of other hemolytic streptococci as a result of the production of an antibiotic substance which we have named Streptostasin. Streptostasin is a new antibiotic.

All of the streptococcal strains tested against mouse plasma for fibrinolysin failed to show this activity.

Evidence has been obtained to show that the capsule of group A streptococci, at least, is composed of hyaluronic acid since it disappeared following treatment with hyaluronidase.

Capsules as distinct structural entities are not widespread among hemolytic streptococci although some strains of virulent and avirulent streptococci form capsules. Some virulent streptococci do not form capsules.

Hyaluronic acid production by hemolytic streptococci does not give a satisfactory correlation with capsule production or with colony type.

Most streptococci are not virulent when introduced intranasally into mice.

GENERAL, NR-130-176 (Cont.)

The various physiological products of streptococci which have been associated with the virulence of streptococci cannot act as more than accessory substances perhaps altering the course of an infection somewhat. None of these factors, as determined by in vitro experiments, are essential for virulence of a strain.

Preliminary experiments using bacterial cell and supernatant preparations from cultures of a streptococcus Lancefield group A, type 6, have indicated the presence of an active substance which will cause a fatal cardiovascular response in the rabbit. The mechanism of this response is not known. The active substance shows its greatest activity in neutralized supernatant preparations, but the factor itself is not known, nor has it been isolated. The activity of the cell itself indicates that it is the same factor as is present in the neutralized supernatant but this is not definitely established. Further work on the factor itself and on the mechanism of its action is needed before any conclusions can be drawn regarding the pharmacological activity.

Estimated Completion: Indefinite

NR-130-190 Physiology of the Meningococcus (Unclassified)

Contractor: University of Rochester, Rochester, New York
Contract: N6-ori-126, Task III, (9/1/46 to 8/31/48)
Investigator: H. W. Scherp

The purpose of this project is to determine the meningococcal metabolic requirements particularly CO and CO substitutes, with the end in view of being able to inactivate essential enzyme systems and thus produce bacteriostasis. Second object of the research is to isolate and determine the chemical nature of the type and group specific polysaccharides from types I and II alpha meningococcus. This would be a step toward a further understanding of antigencity and production of artificial immunity against meningococcal meningitis.

Progress to 6/30/48: Dr. Scherp has defined an essential growth factor for the meningococcus required in trace amounts. The factor can be substituted by a CO_2 environment. Chemical analysis has failed to identify it. The active principle does not include the known micronutrients such as thiamin, riboflavin, niacin, pyridoxine and its congeners, pantothetic acid, biotin, folic acid, Co-enzymes I and II, glutathione, glutamine, and fatty acids.

Estimated Completion: Indefinite

NR-130-194 Investigation of Changes Which Take Place in Foods During Storage in Frozen Conditions (Unclassified)

Contractor: University of Minnesota, Minneapolis, Minnesota
Contract: N6-onr-246, Task II, (2/1/47 to 1/31/49)
Investigator: H. O. Halvorson

The purpose of this project is to obtain fundamental information on the activities of microorganisms and enzymes at various temperatures below freezing so that such information will be available for the analysis of methods of freezing food and the processing of frozen food. Studies will be made of the changes in the microbial population which take place in food during storage in the frozen condition. Enzymatic changes which take place during the storage period will also be investigated.

Progress to 6/30/48: It has been shown that organic acids promote a greater destruction of bacteria during freezing and thawing than mineral acids. Of the organic acids tested, acetic acid seems to cause greater destruction to more organisms than lactic acid at a similar pH. The reaction of various organisms to acids on prolonged storage appears to differ with the organism being studied and the type of medium in which it is suspended.

GENERAL, NR-130-194 (Cont.)

The medium in which an organism is suspended plays an important part in its survival. It appears that the greater the amount of colloidal or other solid amorphous material which is present the greater is the protective effect of the medium and in this respect broth appears to allow greater destruction of microorganisms than milk or liver agar paste. In turn, milk is not as efficient as liver agar paste in protecting organisms suspended in it. This appears to be true for both freezing, thawing, and prolonged storage. Storage temperature appears to be of importance in the survival of microorganisms. This was demonstrated with specific examples. Just as organisms vary in their resistance to freezing and thawing, so do they in their ability to withstand storage at low temperatures.

Repeated freezing and thawing have no effect on enzyme activity when measured at standard conditions of pH 5.8 at 40° C.

Estimated Completion: Indefinite

NR-130-197 Virus Research - Biophysics (Unclassified)

Contractor: University of Pennsylvania, Philadelphia, Pennsylvania
Contract: N6-ori-168, Task II, (9/1/46 to 8/31/48)
Investigator: T. F. Anderson

The purpose of this project is to study the mode of multiplication of the bacterial viruses T1 to T7 on their host, E. coli strain B. Special emphasis is placed on the nutrient co-factors required by the several viruses for adsorption on their host cells as related to the enzymatic structure of the cells. The reduplication of virus within the host and lysis of the host is also being studied. Special techniques used include sonic vibration, electron microscopy, ultraviolet irradiation and spectrophotometry.

Progress to 6/30/48: A study is being made of the mechanism of specific absorption of viruses on their host cells. This phenomenon is particularly interesting because bacterial viruses are absorbed only on those host cells which can support their growth. It is apparent that the surface of the bacterial cell contains all of those elements which are required for the multiplication of each of the 100 or more different viruses which can multiply within it.

Estimated Completion: Indefinite

NR-130-240 Tuberculosis (Unclassified)

Contractor: University of Pennsylvania, Philadelphia, Pennsylvania
Contract: N6-ori-168, Task III, (11/1/46 to 10/31/48)
Investigator: E. R. Long

The purpose of this project is to investigate the various factors concerned in the progressions and regressions of minimal pulmonary tuberculosis infiltrations.

A review has been made of approximately 2,000 case histories at the Henry Phipps Institute in order to extract information on minimal pulmonary tuberculosis. The material extracted consists of 1,131 cases of minimal pulmonary tuberculosis of reinfection type, composed of 650 white patients and 481 colored patients.

Isolation of characteristics enabling differentiation of those patients who had the progressive disease from those who had the non-progressive disease was attempted on the basis of (1) radiological interpretation, (2) symptomatology, (3) contact history, and (4) sputum analysis.

The significance of environmental factors in relation to progression rates and mortality was investigated.

The effect of associated disease upon progression of tuberculosis is to be determined.

The "follow-up" of patients rejected for military service, to determine progression and mortality rates, will be attempted.

GENERAL, NR-130-240 (Cont.)

Progress to 6/30/48: The analysis of 1200 minimal cases was completed from the point of value of and error in radiological prognosis.

Also completed was the analysis of factors influencing the rate of progression in radiologically active minimal tuberculosis. The following factors were considered: Age, race, sex, rest, contact with positive sputum, and economic status, both at the time of diagnosis and during the first year after diagnosis.

Two manuscripts, "The Value of Radiology in the Prognosis of Pulmonary Tuberculosis" and "Factors Influencing the Rate of Progression of Mortality among Minimal Cases of Tuberculosis Diagnosed Radiologically as Active" are being prepared for publication in two different journals devoted to tuberculosis and epidemiology. Another paper in the course of preparation includes statistical evaluation of such factors as (1) loss of weight, (2) fatigue, and (3) cough, expectoration, and other pulmonary symptoms together with an exact correlation of symptoms, prognosis and certain objective laboratory data.

A study on prevalence rate in pulmonary tuberculosis is still in progress.

Estimated Completion: 1950

NR-130-358 Tracer Elements in Tubercle Bacillus Metabolism (Unclassified)

Contractor: University of Pennsylvania, Philadelphia, Pennsylvania
Contract: N6-onr-249, Task VI
Investigator: E. R. Long

The purpose of this project is to conduct research which will constitute a pilot study in the adaptation of isotopes to the elucidation of the biochemical mechanisms in the metabolism of the tubercle bacillus.

If the study clarifies the synthesis of the lipid fraction, then it is logical that the other bacterial fractions may be similarly investigated and the methods subsequently applied to bacteria in general.

The ultimate goal of the research is in the identification of essential enzyme systems which may be blocked by agents which would consequently turn out to be bacteriostatic and bacteriocidal in clinical medicine.

This project will be carried out by the Henry Phipps Institute of the University of Pennsylvania where the tubercle bacillus will be provided, the Department of Chemistry at Yale University where chemical analysis will be carried out, and the Biophysics Laboratories at Columbia University where isotopic determination will be done.

Progress to 6/30/48: Sodium acetate containing $carbon_{13}$ in the carboxyl radical is added to a modified Long's culture medium for the growth of Mycobacterium-tuberculosis.

Excellent growth occurs on a medium containing $carbon_{13}$. The growth is appreciably more luxuriant than on a medium containing carbon in the normal $carbon_{12}$ form.

Estimated Completion: 1950

NR-130-469 Physiology of Dermatophytes (Unclassified)

Contractor: University of Kansas, Lawrence, Kansas
Contract:
Investigator: A. J. Mix

The purpose of this project is to study the physiology of the dermatophytes using the organisms, Tricophyton mentagrophytes and Microsporum canis (Milanosum).
The following methods are being employed:

(1) Ion-substitution in nutrient solutions to determine the optimum medium for the fungi concerned as measured by growth and respiration.

GENERAL, NR-130-469 (Cont.)

(2) Employing this optimum medium as a test solution to determine optimum conditions of (a) hydrogen-ion concentration, (b) temperature for growth and respiration of these fungi.
(3) Using results obtained from procedures 1 and 2, to study nitrogen requirements of these fungi and the availability of various nitrogen compounds to them.
(4) Using the optimum medium to study keratin-utilization by these fungi.
(5) Study of the effect of various poisons and growth repressants on growth and respiration and keratin-utilization by these fungi.
(6) Study of the effect of known antibiotics on these fungi, and search for new and specific antibiotics.
(7) Study of the applicability of the facts learned to methods of treatment of the mycoses concerned.
(8) Study of factors conditioning sporulation of these fungi in culture.

Progress to 6/30/48: No progress to report.
Estimated Completion: November 1950

NR-130-535 Advisory Panel in Microbiology (Unclassified)

Contractor: University of Michigan, Ann Arbor, Michigan
Contract:
Investigator: W. J. Nungester

The Panel will consist of six civilian members selected by both disciplinary and geographic distribution, and representatives of Naval Bureaus and other Federal agencies. These members will work closely with the Microbiology Branch and other branches of ONR, as requested, to assure maximum benefit from expenditures for microbiological research.

Progress to 6/30/48: The panel met in February and reviewed the program of the Microbiology Branch. Recommendations were made for renewing, discontinuing, or, referring to other groups some 55 projects. The second meeting of the panel was held on May 15 and 16. Nineteen proposals were considered. Active projects were reviewed and evaluated. Interviews were held with nine principal investigators who presented verbal progress reports and plans for future study.
Estimated Completion: Indefinite

NR-130-713 Influenza Vaccine (Unclassified)

Contractor: Johns Hopkins University, Baltimore, Maryland
Contract: (6/30/48 to 6/30/49)
Investigator: T. G. Ward

The purpose of this project is to attempt to develop an effective influenza vaccine by (1) determining the antigenic relationship of strain P46A-1 to other strains of influenza virus, and (2) determining the antigenic response in man to influenza strain P46A-1.

It is hoped that conclusions will be reached regarding the feasibility of a field study utilizing P46A-1 as a human influenza vaccine.

Progress to 6/30/48: No progress to report.
Estimated Completion: June 1949

[redacted]

MICROBIOLOGY

IMMUNOLOGY

NR-131-163 Investigation of Reticulo-Endothelial Immune Serum (Unclassified)

Contractor: University of Texas, Austin, Texas
Contract: N6-onr-266, Task V, (2/1/47 to 1/31/49)
Investigator: C. M. Pomerat

This project is conducting fundamental research in immunology which will contribute significantly to the understanding of auto-immunization as in the aging process and in the rheumatic fever sequels.

Experimental work in this laboratory established significant shifts in the activity of blood and tissue cells, both in vitro and in vivo, by homologous anti-spleen and bone marrow prepared according to Bogomolets and his group in the U.S.S.R. Moreover, the active agent has been identified in a globulin fraction.

Further studies are planned to determine the essential antigenic factor of spleen and bone marrow which is involved in the development of such immune sera. Preliminary work indicates that the migration of cells from the buffy layer of the blood and from explanted fragments of embryonic spleen in vitro can serve as an efficient quantitative method in screening and assaying both antigenic and antibody activity.

Progress 6/30/48: Pomerat and Anigstein showed that the Reticulo-Endothelial Immune Serum (in the course of this report referred to as REIS), in strong concentrations reduces, in tissue cultures, the migration of cells and provokes their clumping. These experiments were carried out on spleens of chick embryos and of new born chicks.

Pomerat also demonstrated that strong concentrations of REIS have an inhibitory action upon migration of malignant cells (Walker rat sarcoma #319) in vitro. On the other hand, there are indications that weaker doses of REIS and other anti-organ sera may act as stimulators for the outgrowth of the fibroblasts, as hinted by studies in tissue cultures.

The aim of the present research was to find out whether these morphological changes influenced by anti-organ sera might be correlated with corresponding changes in the cell metabolism and, if so, to establish the nature of such changes.
Estimated Completion: Indefinite

NR-131-167 Universal Serologic Reaction (Unclassified)

Contractor: University of Michigan, Ann Arbor, Michigan
Contract: N6-ori-190, Task I, (8/15/46 to 8/14/48)
Investigator: R. L. Kahn

Work under this project is based on an observation made at the University of Michigan that positive serologic reactions can be obtained in practically all human beings (and in animals) with various antigens used in tests for syphilis by properly modifying the techniques of these tests. Because these reactions are biologically widespread, they are referred to as universal reactions. Efforts are being directed to study the nature of these reactions and to determine whether the reactions show distinctive characteristics, or patterns, in health and in various diseases.

Progress to 6/30/48: It has been demonstrated that the lipid antigen (Kahn) and serum employed in tests for syphilis can be treated technically so as to elicit positive reactions in sera from patients with leprosy. Therefore, this could be a new diagnostic test for leprosy.

Studies carried out thus far on serologic patterns in tuberculosis patients indicate that the universal reaction may prove of value in prognosis if the patients are repeatedly tested. Some evidence that tissue lipids may be liberated through natural processes and become antigenic has been found. This may lead to an explanation for the universal serologic reaction.
Estimated Completion: Indefinite

IMMUNOLOGY (Cont.)

NR-131-174 Immunological Studies of Red Cells (Unclassified)

Contractor: University of Rochester, Rochester, New York
Contract: N6-ori-126, Task V, (9/1/46 to 8/31/48)
Investigator: L. E. Young

Under this project immunological studies of red blood cells are being conducted along three lines:

(1) Investigation of mechanisms of erythrocyte destruction in hemolytic disorders. The splenic and peripheral blood of transfused splenectomized patients is being subjected to combined fragility and differential agglutination tests in an effort to demonstrate a selective action of the spleen of abnormal cells. Search is being made for abnormal antibodies. Hemolytic anemia is being produced artificially in animals and observations made on the spleen, liver, bone marrow and most accessible capillary beds.
(2) An attempt is being made to inhibit the production and activity of antibodies active against red cells.
(3) The use of erythrocytes of various species and of hemagglutinin absorption tests in the laboratory diagnosis of certain infectious diseases is being explored.

Progress to 6/30/48: Dr. Young has developed the incubation test as a technique for elucidating latest hereditary blood dyscrasios.

Twenty one patients from 13 families with hereditary spherocytic disease (congenital hemolytic anemia) were subjected to intensive hemological and immunological study. It was found that incubation of sterile defibrinated blood from these individuals increases both osmotic and mechanical fragilities of their red cells to a greater extent than is true in the normal individual.

This incubation test is valuable in detecting inapparent abnormalities of the erythrocyte and in charting the hereditary pattern of the disease.
Estimated Completion: Indefinite

NR-131-224 Biochemistry and Kinetics of Toxins and Toxin-Antitoxin Reactions (Unclassified)

Contractor: Montana State College, Bozeman, Montana
Contract: N6-onr-237, Task II, (1/1/47 to 12/31/48)
Investigator: K. F. Swingle

The purpose of this project is to make a fundamental research on the chemical pathology and immune chemistry of toxins using enzyme system and cellular respiration studies as well as the usual chemical analysis techniques. The application of this research will be toward the development of new methods of immunization and greater efficacy of therapy of diphtheria tetanus, food poisoning (botulism) and other diseases.

The exact manner, chemically speaking, by which bacterial toxins (also those of other pathogenic microorganisms) injure the structural substances or metabolic functions of the host has been worked out in only a few instances, and in these incompletely. It is the purpose of this project to launch a systematic investigation of the chemical reactions by which various bacterial toxins injure the host animals. This study includes investigations of the chemical effects of each toxin studied on the structural substances and on the metabolic functions of the host.

The elucidation of the mechanism of a toxic reaction is being followed normally, by a detailed study of the characteristics of the reaction involved, establishment of a precise in vitro method for assay of the toxin, purification of the toxin, study of the reaction of the toxin with its homologous anti-toxin, development of in vitro methods for anti-toxin assay, attempts to develop appropriate chemotherapeutic methods for inhibiting or modifying the reaction of the toxin in the diseased animal, and development of improved methods for immunization.

IMMUNOLOGY, NR-131-224 (Cont.)

The initial phase of this work is being done with microorganisms of veterinary importance, some of which are also of importance to human medicine. The principles and methods developed should be useful, generally, in both branches of medical science.

Progress to 6/30/48: The method for determining the lecithinase (a yardstick for measuring toxin activity or toxicity) value of a toxin preparation was simplified and at the same time refined and made highly reliable, reproducible, and precise.

A similar simplification and refinement was achieved for determining the anti-lecithinase value of an immune serum.

Conditions under which the toxin can be dried without loss of activity were established.

Preliminary studies on the nature of the active groups in the lecithinase molecule by the use of specific protein reagents were made.

Estimated Completion: Indefinite

NR-131-259 Globin, Preservation of Dried Plasma and Blood (Unclassified)

Contractor: Bryn Mawr Hospital, Bryn Mawr, Pennsylvania
Contract: N7-onr-326, (4/1/47 to 3/31/49)
Investigator: M. H. Strumia

The purpose of this project is to increase present knowledge of the effects of preservation on plasma.

So far, data have been assembled on the preservation of plasma in the dried as well as in the frozen state, for periods up to four years. These studies include titration of complement, prothrombin, determination of solubility, turbidity, stability, pH, viscosity, protein concentration, physiological effect in humans, etc. It is considered important to continue these studies for a period up to 10 years since it is likely that dried plasma will remain standard material for the Navy for the treatment of shock. Work so far shows that the period of preservation of plasma packaged according to the standard method developed for the Armed Forces is probably well over five years.

Progress to 6/30/48: A modified globin can be prepared from human erythrocytes left over from plasma preparation. It is safe in humans. And it has been used satisfactorily as a plasma substitute to restore lost blood volume in humans suffering from secondary shock, and as a source of nitrogen for intravenous feeding, particularly to maintain an adequate volume of circulating proteins.

Estimated Completion: Indefinite

NR-131-375 Applied Immunology (Unclassified)

Contractor: Stanford University, Stanford, California
Contract: (5/1/48 to 5/1/49)
Investigator: J. J. Miller

The purpose of this project is to study (1) the speed of response in individuals, who were actively immunized four or more years ago to a stimulating dose of tetanus toxoid; and (2) the problem of the poor reactor.

Progress to 6/30/48: No progress to report.
Estimated Completion: May 1949

IMMUNOLOGY (Cont.)

NR-131-406 Experimental Study of the Etiologic and Immunologic Basis for the Rheumatic Fever Complex (Unclassified)

PARASITOLOGY AND MEDICAL ZOOLOGY, NR-132-122 (Cont.)

The purpose of this project is to make a new approach to the malarial problem, placing the emphasis on the physiological and biochemical aspects of the environment of the parasite in its different host relationships. The end in view is to alter the ionic, molecular, and enzymatic characteristics and hence create an unfavorable environment for the parasite without seriously affecting the final host, man.

Progress to 6/30/48: Methods are being devised for the preparation of pure amino acid solutions corresponding to the high percentage found in insect hemolymph. The difficulty in using some of the commercial preparations such as Stearn's "Parenamine" rests in their low pH (4.4). The amount of base required to bring the pH to a level equal to that of insect hemolymph (6.8) is greater than the total base in insect blood. It is probable that insect hemolymph contains a much higher percentage of arginine than the commercial preparations. Attempts are now in progress to prepare arginine as free base and add it to the commercial preparations in amounts sufficient to bring the pH to 6.8.
Estimated Completion: Indefinite

NR-132-161 Chagas' Disease (Unclassified)

Contractor: University of Texas, Austin, Texas
Contract: N6-onr-266, Task IV, (2/1/47 to 1/31/49)
Investigator: A. Packchanian

The purpose of this project is to develop and standardize the laboratory methods for the diagnosis of Chagas' disease in man and in animals. Special attention is being given to serological and cultural tests and electrocardiographic studies. Antigenic characteristics of various carbohydrates and protein fractions of Trypanosoma cruzi are being studied. Field studies are being conducted to study the possibility of human cases in the United States where the reservoir host and insect vectors of Chagas' disease are known to occur. Chemotherapeutic studies of the disease both in vitro and in vivo are also being undertaken.

Progress to 6/30/48: The development of techniques for agglutination, precipitation, complement fixation, and skin tests for Chagas' disease have been reported. Various types of antigen were made by utilization of Trypanosoma cruzi cultures. The antigens were used for complement fixation and precipitation tests in diagnosis of known and suspected cases of Chagas' disease. It was found that a water soluble fraction prepared according to Packchanian was the most potent for complement fixation tests. Further studies on additional samples, carbohydrate fractions of water soluble antigen, and the standardization of the technique are in progress. The precipitation test was clear-cut and diagnostic with water soluble antigen. Acetone and alcohol fractions of the antigen are not suitable for clinical diagnosis.
Estimated Completion: Indefinite

NR-132-162 Weil's Disease (Unclassified)

Contractor: University of Texas, Austin, Texas
Contract: N6-onr-266, Task III, (2/1/47 to 1/31/49)
Investigator: A. Packchanian

Under this project serological and immunological studies are being carried out on a collection of various strains of Leptospira collected from Europe, America, Asia, and Australia. These strains then will be grouped according to their serological characteristics. Attempts will be made to develop a simple serological procedure for diagnosis of Weil's disease which can be used in any small laboratory. Chemotherapeutic studies of Weil's disease also will be carried out.

PARASITOLOGY AND MEDICAL ZOOLOGY, NR-132-162 (Cont.)

Progress to 6/30/48: Many strains of the causative agent, Leptospira, were collected from various parts of the world, i.e., Holland, England, Japan, Australia, India, etc. These stock cultures are maintained in suitable culture medium and at the present time are subjected to serological and immunological studies.

Diagnostic aid for Weil's disease was given to various institutions and physicians in Texas, Georgia, and Maryland.

Various strains of Leptospira were suspended in a few chemicals and their solubility or insolubility in a given chemical was determined. The strains which were found soluble in bile or bile salts and not in saporin were utilized in precipitation tests using dissolved Leptospira in bile salts as antigen and positive antiserum as antibodies.
Estimated Completion: Indefinite

NR-132-185 Biology of Trombiculid Mites (Unclassified)

Contractor: University of Kansas, Lawrence, Kansas
Contract: N6-ori-220, Task II, (2/1/47 to 1/31/49)
Investigator: H. B. Hungerford

The purpose of this project is to study the life cycles of the local trombiculid mites, host relations of their larvae, ecologic requirements and relations of the various stages in the life cycles of these mites, and geographic distribution of these species. It is expected that the results of an intensive study will contribute to the understanding of the principals of geographic and ecologic distribution of chiggers and to an understanding of their role in the transmission of disease.

Progress to 6/30/48: A total of 739 vertebrate animals belonging to 73 species have been examined for chiggers. Of this number, chiggers were found and preserved from 70 host animals belonging to 18 species. An attempt is being made to correlate the distribution of chiggers and their hosts with soil and vegetable types.
Estimated Completion: Indefinite

NR-132-380 Taxonomy of Decapod Crustaceans (Unclassified)

Contractor: University of North Carolina, Chapel Hill, North Carolina
Contract: N7-onr-368, (4/1/47 to 3/31/49)
Investigator: D. G. Frey

The purpose of this project is to (1) study the taxonomy and ecology of Palaemonidae and Atyidae in order to demonstrate the paths of distribution throughout the pacific; and (2) elucidate the role of the fresh water shrimp in the transmission of the lung fluke, paragonimus westermani.

Progress to 6/30/48: No progress has been reported.
Estimated Completion: Indefinite

NR-132-495 Filariae of the Cotton Rat (Unclassified)

Contractor: University of Texas, Austin, Texas
Contract: (5/1/48 to 11/1/50)
Investigator: J. A. Scott

The purpose of this project is to conduct biological studies on the tropical rat mite in relation to its role as vector of filariae of the cotton rat.

[redacted]

MICROBIOLOGY

PARASITOLOGY AND MEDICAL ZOOLOGY, NR-132-495 (Cont.)

Until recently experimental studies on filariasis were handicapped by lack of a suitable laboratory animal. During the war naturally infected rats were used for testing antifilarial drugs. Dr. Scott developed a method of infecting rats for this purpose. The object of the proposed research is to determine the factors involved in controlling the development of the mites, the larvae (filariae) within the mites and the subsequent transmission of the filariae to the rat.

Progress to 6/30/48: No progress to report.
Estimated Completion: 1 Nov. 1950

EPIDEMIOLOGY

NR-133-095 Chemical-Biological Coordination Center (Unclassified)

Contractor: National Academy of Sciences, Washington, D. C.
Contract: NA-onr-10-47, (6/1/46 to 6/30/49)
Investigator: A. N. Richards

The Chemical Biological Coordination Center is a service organization without funds for the support of research and with no intent of directing research. Its principal functions are to gather information on the biological actions of chemical agents with a view to using such information to coordinate chemical structure with biological effect and to furnish laboratories with chemical compounds that might be used in their investigations.

Progress to 6/30/48: The organization of the information will be facilitated through the use of punched cards and the adoption of chemical and biological codes which will permit the Center to furnish, upon request, information concerning structure and action. The Center has already functioned in assisting university, government, and industrial laboratories.

A questionnaire has recently been sent to investigators in an attempt to learn whether they are doing virus research, screening compounds, and if they would like additional compounds for screening. Two publications from N.A.S. of educational nature have been received.
Estimated Completion: Indefinite

NR-133-096 Airborne Infectious Diseases (Unclassified)

Contractor: University of California, Berkeley, California
Contract: N6-ori-111, Task V, (7/1/46 to 7/14/48)
Investigator: A. P. Krueger

The purpose of this project is to make (1) epidemiologic, bacteriologic, immunologic, and statistical studies on herd infections transmitted via the respiratory tract, such as pneumonic plague, psittacosis, coccidiodomycosis, etc; (2) studies on contagion under conditions of controlled temperature, humidity, and air disinfection; (3) the respiratory system as a route for the introduction of pathogenic, immunogenic, chemoprophylactic, and chemotherapeutic agents; and (4) comparative pathogenesis of selected viral and bacterial infections induced by quantitative exposure of the respiratory tract to single or combined disease agents in normal and protected experimental animals.

Progress to 6/30/48: One publication, "The Relation of the Oil Treatment of Floors and Bedding to the Control of Respiratory Diseases Among Naval Personnel" was published in The American Journal of Hygiene 46:376-407, 1947. Other reports are in the manuscript stage.

Important contributions resulting from this investigation are shown in a documentary film prepared by this group on "The Application of New Instruments and Technics in the Laboratory".

EPIDEMIOLOGY, NR-133-096 (Cont.)

Some interesting and valuable observations have been made on the "Effect of Penicillin on the Reaction Between Phage and Staphylococci"

Dr. Krueger has recently reported that they have been able to cultivate bacteriophage in the absence of living cells. This is the first time such an accomplishment has been made. Application of principles involved in this work to the study of other viruses may lead to discoveries of extreme importance.

Estimated Completion: Indefinite

NR-133-140 Natural Reservoirs and Vectors of Tularemia (Unclassified)

Contractor: University of Kansas, Lawrence, Kansas
Contract: N6-ori-164, Task II, (9/1/46 to 3/31/49)
Investigator: C. M. Downs

This project has been combined with project NR-134-142.

NR-133-321 Rheumatic Fever (Unclassified)

Contractor: Northwestern University, Chicago, Illinois
Contract: N7-onr-450, Task II, (9/15/47 to 9/15/49)
Investigator: A. F. Coburn

Rheumatic fever is a common disease of urban populations. There are annual outbreaks of streptococcal infections of the upper respiratory tract (scarlet fever, tonsillitis, pharyngitis, sinusitis, etc.). Available statistics indicate that in the United States 1,000,000 attacks occur annually, with a mortality of 40,000. The onset of the disease is between the ages of five and puberty. It is recurrent in 75% of instances, and the average age at death is 30 years. The serious aspects include the rate of recurrence, incidence in the young, the crippling effects on the heart, kidneys, and joints during the most active years of life.

Dr. Coburn proposes immunological, biochemical, and epidemiological techniques for the identification of the bacterial factor of communicability in the hemolytic streptococcus. This in turn would have direct application to the development of techniques for preventing the dangerous carrier state and hence would aid in combating rheumatic fever.

Progress to 6/30/48: No progress has been reported.
Estimated Completion: Indefinite

PATHOLOGY AND CANCEROLOGY

NR-134-042 Pulmonary Pathology (Unclassified)

Contractor: Yale University, New Haven, Connecticut
Contract: N6-ori-44, Task XI, (6/1/46 to 2/28/49)
Investigators: M. C. Winternitz, G. E. Lindskog

The purpose of this project is to conduct: (1) a study of the collateral bronchial arterial circulation of the lung after pulmonary artery ligation, and of the function of this lung in gas exchange. (2) a study of the physiological effects of graded obstruction to the respiratory tract, with special emphasis on the point at which decompensation occurs: Arteriovenous O_2 and CO_2 differences and cardiac output; respiratory and cardiac rates; intratracheal pressure; blood pressure.

PATHOLOGY AND CANCEROLOGY, NR-134-042 (Cont.)

(3) Studies of bronchiectasis with special emphasis on pathogenesis including (a) experimental work designed to produce atelectasis without persistent bronchial obstruction, and (b) observations on human surgical specimens made by obtaining casts of the bronchial tree, in correlation with the microscopic changes. (4) Experimental studies of pulmonary edema induced by ANTU, and attempts to prevent edema with BAL and other agents.
The title of this project was formerly "Thoracic Surgery".

Progress to 6/30/48: Research to date has resulted in 11 excellent papers. Progress on various aspects of the research is as follows:

(1) Experimental Studies of the Collateral Circulation of the Lungs: After ligation of the main pulmonary artery in the dog the bronchial arterial circulation increases progressively (as demonstrated in vinylite injection casts) and assumes a respiratory function of increasing magnitude as measured by bronchospirometry.

(2) Anatomical Investigations of the Respiratory Tract: (a) With the recent developments in thoracic surgery there has arisen a need for detailed and accurate knowledge of the anatomy of the lungs. To meet this need, and to supplement the valuable studies of Brock, and of Boyden, multicolored broncho-vascular casts of the lungs (the bronchi, arteries, and veins) are being made from autopsy material. (b) A new operative technique for bronchiectasis, "bilobectomy" for removal of the right middle and lower lobes en masse, has been developed in part on the basis of the study of 25 casts prepared to show the relations and variations of the blood vessels and bronchi.

(3) An Evaluation Study of the Cytological Method for the Diagnosis of Carcinoma of the Lung: Sputum or bronchial secretions, or both, were studied cytologically from 51 patients with carcinoma of the lung and from 80 persons with other types of pulmonary disease. The cytological diagnoses were rendered without knowledge of the clinical diagnoses. The cytological technique increased the percentage of preoperative microscopic diagnoses to 76%, from the 38% available from bronchoscopic biopsies alone.

(4) Studies on the Histamine Content of Neoplastic (Cancerous) Pulmonary Tissues: The results demonstrate a decreased content of extractable histamine in neoplastic pulmonary tissue. Three possible explanations for this phenomenon are suggested. (1) It has been shown that fetal lung tissue is especially low or wanting in extractable histamine (38). The low content in neoplastic tissue may represent a reversion of growth and biochemical characteristics toward those of embryonal lung tissue. (2) That the histamine in lung is found largely in stromal cells not present in great abundance in the tumors, which consisted primarily of epithelial derivatives. (3) Neoplastic lung tissue may be especially rich in histaminase, a possibility which deserves to be investigated further.
Estimated Completion: Indefinite

NR-134-142 Pathogenesis and Immunity in Tularemia (Unclassified)

Contractor: University of Kansas, Lawrence, Kansas
Contract: N6-ori-164, Task IV, (9/1/46 to 3/31/49)
Investigator: C. M. Downs

In the 1 January 1948 issue of this summary it was incorrectly stated that this project had been terminated. This project includes studies formerly under projects NR-130-141 and NR-133-140.

The purpose of this project is to study the invasion and multiplication of Pastuerella tularense in the normal and immune animal; the comparison of vital, metabolic processes in virulent and avirulent organisms; and a study of immunity with emphasis on the role that the spleen plays. The growth requirements of Pastuerella tularense and the determination of effect of certain factors on growth and multiplication are being studied. The ultimate aim of this phase of the study is to find a chemically defined medium on which blocking of essential enzyme systems may be studied and chemotherapeutic agents may be examined.

PATHOLOGY AND CANCEROLOGY, NR-134-142 (Cont.)

It also includes an investigation of the animals in endemic areas to determine the role they may play as natural reservoirs and vectors of tularemia.

Progress to 6/30/48: The study of the pathogenesis of tularemia in white rats continues. The following summary includes observations that have been made.

(1) Recovered rats are more solidly immune than vaccinated rats as indicated by a greater survival rate and the smaller amount of multiplication of the organisms in the tissues.

(2) Normal rats are highly susceptible to infection with P. tularense. The organisms multiply in the tissues and invade the blood until death occurs or recovery begins on the third to fifth day. The rise in agglutinating antibodies four to five days post-infection coincides with the improvement in clinical appearance and the onset of recovery. In recovered and vaccinated rats or in convalescent control rats, the organisms decrease and disappear from the tissues in the following order: Blood, liver, lymph nodes, spleen.

(3) Serum from vaccinated and recovered rats and serum from vaccinated rabbits and from recovered humans confer little passive immunity.

(4) The serum from recovered and vaccinated rats is no more bactericidal in vitro than that of normal rats.

(5) Rats which have recovered from infection continue to harbor the organisms in the spleen for at least 46 days after infection.

(6) Immunity persists at a high level in vaccinated rats for at least 99 days after vaccination and in recovered rats for 128 to 223 days after recovery from the initial infection.

(7) Some strains of P. tularense of low virulence are effective immunizing agents in white mice.

(8) In field work investigations of the cotton tail rabbits and cotton rats collected, showed no evidence of tularemia in themselves or their ectoparasites. Cotton rats were found to be as susceptible to tularemia as mice or guinea pigs but were not protected by vaccination which is effective in white rats.

Estimated Completion: Indefinite

NR-134-202 Arthritis (Unclassified)

Contractor: Stanford University, Stanford, California
Contract: N6-onr-251, Task I, (10/15/46 to 10/14/48)
Investigator: P. J. Hanzlik

The purpose of this project is to check various methods of producing arthritis in animals. It is hoped to develop a procedure for a regularly reproducible progressive polyarthritis which can be used for studying possible variables affecting the process, such as temperature changes, immersions, etc., and for trials with chemotherapeutic agents, including the nature of their action.

Progress to 6/30/48: Much work on induced and natural arthritis in rats and man has been done using various agents to induce the syndrome. The use of gold has been studied in therapy of this condition and effects of various agents for neutralizing the effect of gold have been studied.

The following papers have been published:

"Production of Experimental Polyarthritis by Pleuropneumonia-Like (L-4) Organisms in Rats and Preliminary Results on Protective Effects of a Gold Product". Helen B. Tripi and William C. Kuzell. Stanford Medical Bulletin Vol. 5 May 1947.

"The Effects of 2, 3 - Dimercaptopropanol (BAL) on Toxicity and Excretion of Gold". Stanford Medical Bulletin, Vol. 5 November 1947, William C. Kuzell, Philip L. Pillsbury and Selig A. Gellert.

"Tests of Possible Antagonism of Gold for Histamine Toxicity and Certain Allergic Reactions". William C. Kuzell and Robert H. Dreisbach, Proc. Soc. for Exper. Biol. & Med. Vol. 68, 157-158, 1948.

PATHOLOGY AND CANCEROLOGY, NR-134-202 (Cont.)

"Diffuse and Nodular Hyperplasia of the Thyroid Gland in Thiouricil - Treated Rats". William C. Kuzell, Helen B. Tripi, Grace M. Gardner and Gert L. Laquer, Science Vol. 107, 374-375, 1948.

"Ankylosing Spondylarthritis". William C. Kuzell. Medical Bulletin (in press).

"Effect of Roentgenotherapy on Urinary 17 - Ketosteroid Excretion in Ankylosing Spondylarthritis". Ronald A. Davison, Peter Koets and William C. Kuzell (in press).

Estimated Completion: Indefinite

NR-134-261 Follow-Up Studies of Patients Treated for Malignancy (Unclassified)

Contractor: U. S. Naval Hospital, Bethesda, Maryland
Contract: P.O. 8-47, (8/1/46 to 2/1/49)
Investigator: R. Parsons

Under this project it is planned to select, from 20,000 cases, a significantly large series with adequate pathologic material and with sufficient clinical history and identification for follow-up studies. In these selected cases, letters of inquiry will be sent, personal calls will be made, re-examination will be performed and other studies carried out to determine the subsequent clinical course of the patient and the ultimate results of treatment. Where follow-up studies are successful, additional sections and photomicrographs will be made and other records of a permanent nature will be elaborated in order to secure a permanent library of maximum diagnostic work. This material will become the property of the Naval Medical School, and, if desired, duplicate material will be prepared for the cooperating activities in the project.

Progress to 6/30/48: Follow-up studies including histological sections and tabulations were completed on 650 cases of cancer of the stomach, 300 cases of lymphomas, 406 bone tumors, and 827 breast tumors.

Estimated Completion: Indefinite

NR-134-391 Pathology of Streptococcosis (Unclassified)

Contractor: Boston University, Boston, Massachusetts
Contract: N7-onr-418, Task I, (4/1/47 to 6/30/49)
Investigator: L. Weinstein

The purpose of this project is to study the mode of infection and invasion by streptococci mainly with respect to the type of cellular response evoked; the alterations produced in tissues in the initial infection; the spread of bacteria; the changes in these reactions produced by various therapeutic measures; and by the addition of materials which make the streptococcus more invasive.

Progress to 6/30/48: Attempts have been made to produce streptococcal pneumonia in various animals. When the organisms were introduced directly into the pharynx, there was no evidence macro or microscopically of pulmonary infection, although 50% of the animals regularly developed acute purulent pleurisy with empyema and died.

The inference is that the following is a mechanism of developing systemic streptococcal infection. The organisms enter the blood and the body via the respiratory tree without causing any infection of the pulmonary tissue itself.

Estimated Completion: Indefinite

PHARMACOLOGY AND TOXICOLOGY

NR-135-043 Staphylocoagulase (Unclassified)

Contractor: Yale University, New Haven, Connecticut
Contract: N6-ori-44, Task X, (6/1/46 to 5/31/48)
Investigator: M. Tager

The purpose of this project is to study staphylocoagulase from two angles.

(1) Concentration and purification of the agent, with a consideration of its methods of optimal production, properties, and mode of action on human plasma.
(2) Possible activity in vivo, with special interest in its (a) local, and possibly general, effects on the coagulation of blood, (b) toxicity, and (c) role in staphylococcal infection.

Progress to 6/30/48: This project has been completed. A final report is being prepared and will be distributed in the near future.

NR-135-051 Chemotherapeutic Agents in Ocular Tissues and Fluids (Unclassified)

Contractor: Northwestern University, Evanston, Illinois
Contract: N6-ori-96, Task I, (5/1/46 to 6/30/48)
Investigators: C. Farmer, J. Bellows

The high incidence of ocular infections in both military and civilian life suggest the need for a study of the effect of the new antibiotic and chemotherapeutic agents in these conditions. It was, therefore, decided to investigate the effect of the drugs per se upon ocular tissues when injected into the vitreous and aqueous, and to study their antibacterial actions in situ. Studies are also being made to determine the best method of application to control ocular infections, i.e., direct injection to the site of infection, intravenous and intramuscular injection, and local application. The rate of diffusion through the cornea into the anterior chamber is being measured with and without wetting agents, and also by means of iontophoresis. The initial studies are being conducted on rabbits, and then applied to clinical cases. Various drugs and organisms are being systematically investigated.

Progress to 6/30/48: This project has been completed. A final report is being prepared and will be distributed in the near future.

NR-135-054 Antibacterial Agents (Unclassified)

Contractor: Northwestern University, Evanston, Illinois
Contract: N6-ori-96, Task III, (5/15/46 to 5/14/49)
Investigator: I. M. Klotz

The purpose of this project is to study the structural and environmental factors which influence the combination of proteins and enzymes with drug molecules.

Studies are being made of the rates of growth of microorganisms in media containing a series of structurally related antibacterial agents. The series which are being studied include known compounds of the sulfonamide type as well as some new substances of related nature. The kinetics of growth in the presence of detergents are also being followed.

The combination of various molecules and metal ions with proteins is being studied by dialysis-distribution techniques. Related information on enzymes is being obtained by kinetic studies using a manometric technique.

Progress to 6/30/48: Emphasis has been placed on (1) studies of factors which influence the binding of ions by proteins, and (2) protein synthesis in microorganisms using radioactive tracers.

PHARMACOLOGY AND TOXICOLOGY, NR-135-054 (Cont.) (Unclassified)

In copper protein complexes the carboxyl groups on the protein is the site of binding. Several proteins beside serum albumin; in particular hemocyanin, Beta lactoglobulin, and lysozyme bind organic anions. Measures, which, denature protein such as heat, dilute hydroxide, urea and urethane, also decrease the binding ability for organic ions.

The synthesis of peptide bonds has been isolated from the more complex processes of growth in microorganisms by studying the uptake of the amino acid methionine labeled with radioactive sulfur 35.

Two papers have been published and one manuscript has been submitted for publication.

Estimated Completion: Indefinite

NR-135-125 Staphylocoagulase (Unclassified)

Contractor: Boston University, Boston Massachusetts
Contract: N6-ori-160, Task I, (7/15/46 to 1/1/49)
Investigator: B. S. Walker

The purpose of this project is to study the coagulase of staphylococci (together with related substances) in respect to (1) isolation and purification, (2) mode of action, (3) chemical nature, (4) possible medical and surgical applications of coagulase and related substances, and (5) possible evidence bearing on the mechanism of blood coagulation.

Progress to 6/30/48: Coagulase is a glycoprotein with isoelectric point near pH 4, having the special enzymatic property of converting fibrinogen into an insoluble protein similar to fibrin, but not identical with it. The enzymatic property is slowly destroyed by heat, rapidly by peptic or tryptic digestion, less rapidly by exposure to formaldehyde (Gengou). The conversion of fibrinogen to the insoluble clot follows a modified unimolecular reaction; velocity curves indicate an activation with resulting increase of clotting rate, and a loss of activity proportional to the amount of clot formed. Preparations of coagulase purified by repeated precipitation at pH 4 check bleeding from surface wounds on an experimental animal, but do not produce intravascular clotting. Coagulase can also be concentrated by chromatographic adsorption on activated alumina.

Recently, concentrates of coagulase (prostaphylocoagulase) have been made from culture filtrates of Staph, Aureus in which the coagulase titre per milligram of nitrogen has been increased over a thousand fold. The coagulant activity of such partially purified staphylocoagulase has been found to be inhibited by streptomycin, propylene glycol, and sodium azide. It is not inhibited by penicillin, zepheran, bacitracin, tyrothricin, gramicidin, tyrocidin, sulfathiazole or sulfadiazine.

A manuscript describing the work on which the above conclusions are based has been submitted to the Journal of Bacteriology for publication. Additional studies have shown that the coagulation of plasma by coagulase is enzymatic but does not follow the simple first order curve. Complications include the reaction of the bacterial substance with a co-factor in plasma, the loss in potency of coagulase as the reaction proceeds, and the time for the polymerization of activated fibrinogen into the final clot.

Estimated Completion: Indefinite

NR-135-134 Studies on the Pharmacology of Para-Aminobenzoic Acid (Unclassified)

Contractor: George Washington University, Washington, D. C.
Contract: N6-ori-163, Task I, (7/1/46 to 6/30/48)
Investigator: P. K. Smith

This project has been transferred to the Biochemistry Branch and will be reported under Project NR-126-134.

PHARMACOLOGY AND TOXICOLOGY (Cont.)

NR-135-178 Synthesis of Fluorine-Substituted Insecticides, Anti-Malarials, and Other Chemotherapeutic Agents (Unclassified)

Contractor: University of Kansas, Lawrence, Kansas
Contract: N6-ori-164, Task V, (2/1/47 to 1/31/49)
Investigator: C. A. Vanderwerf

The purpose of this project is the synthesis and pharmacological testing of a series of fluorine-containing compounds of potential value as chemotherapeutic agents, with the ultimate aim of determining the effect on the properties of various medicinals produced by the substitution of fluorine atoms for other groups in the molecule. Particular emphasis will be placed on new compounds isosteric with antimalarials and arsenicals of proved value, which will differ from these known compounds only in the replacement of fluorine atoms for amino- or hydroxy-groups. To a lesser extent, compounds will be studied in which fluorine atoms replace chlorine atoms or methoxy-groups in the molecules of known chemotherapeutic agents.

Progress to 6/30/48: The classical work of Ehrlich indicated the superior activity of arsphenamine (3,3' diamino 4,4' dihydroxyarsenobenzene) in the therapy of syphilis. The dihydroxly group of this compound has been replaced by fluorine atoms and the resultant 3,3' diamino 4,4' - difluoroarsenobenzene is being pharmacologically tested.
Estimated Completion: Indefinite

NR-135-211 Chemotherapy in Tuberculosis and Silico-Tuberculosis (Unclassified)

Contractor: Edward L. Trudeau Foundation, Saranac Lake, New York
Contract: N7-onr-307, Task II, (3/1/47 to 2/28/49)
Investigator: A. J. Vorwald

The purpose of this project is to investigate "chemotherapy in chronic tuberculosis and silico-tuberculosis". Experimental production of tuberculosis lesions which are chronic in type. Susceptible animals are to be exposed to the tubercle bacillus and to silica and at intervals thereafter are to be treated with streptomycin and/or other antibiotics and chemotherapeutic agents having possible good effect on chronic tuberculosis complicated by pneumoconiosis.

Progress to 6/30/48: From experiments with guinea pigs it has been demonstrated that:
(1) Streptomycin is a useful therapeutic agent in cases of tuberculosilicosis.
(2) Treatment of a tuberculo-silicoatic process in the guinea pig with aluminum and streptomycin is more effective than with streptomycin alone.
(3) Aluminum alone used in treatment accomplishes no significant results.
(4) Immunization with B.C.G. vaccine apparently minimizes pathological changes occurring when guinea pigs are subjected to injections of quartz.
Estimated Completion: Indefinite

NR-135-762 Experimental Study of the Etiologic and Immunologic Basis for the Rheumatic Fever Complex (Unclassified)

Contractor: University of Minnesota, Minneapolis, Minnesota
Contract:
Investigator: J. T. Syverton

The purpose of this project is to make preliminary investigations of fundamental nature as an approach to the study of the rheumatic state. These studies are of an exploratory

PHARMACOLOGY AND TOXICOLOGY, NR-135-762 (Cont.)

nature to determine by means of immunologic techniques the role of natural antibacterial mechanisms, homologous tissue antibodies, heterologous antibodies, and streptococcal derivatives in the pathogenesis of the rheumatic state. Included in the variety of methods and techniques to be utilized in this work are phagocytosis, bactericidal tests, radioactive isotopes, and modified tissue cultures.

Progress to 6/30/48: This project represents a continuation of studies started by Dr. Syverton under project number NR-131-406. Dr. Syverton was recently transferred to the University of Minnesota; no progress has been reported since his transfer.
Estimated Completion: Indefinite

Psychophysiology

INTERACTION BETWEEN SENSES

NR-140-181 *Development of Neuromuscular Mechanisms* (Unclassified)

Contractor: University of Kansas, Lawrence, Kansas
Contract: N6-ori-164, Task VIII, (10/1/46 to 9/30/48)
Investigator: H. C. Tracy

The purpose of this project is to extend an earlier study on the development of embryonic behavior, using embryos of the Toad Fish, Opsanus Tau, a salt water teleost obtainable at Marine Biological Laboratory, Woods Hole, Massachusetts. It is proposed to study the relation of anatomical structure to observed behavior development particularly with regard to: (1) Relation of nervous system to first body movements; (2) histogenesis of muscle in relation to first movement; (3) relation of sensory nerves to first response to external stimuli; (4) development of eye and body movements on rotation, and their relation to nervous system; (5) histogenesis of sensory maculae in relation to reactions stated in (4); (6) test effects on motility and muscle histogenesis by removal of neural tube in earliest stages possible, and test effect on eye muscle developments by cutting eye muscle nerves; and (7) test effect of certain drugs on development of motility.

Progress to 6/30/48: Embryos of Opsanus Tau, collected at the Marine Biological Laboratory, Woods Hole, have been sectioned, stained, and classified according to developing stages of behavior. Various staining techniques were used. Aceticholine and cholinesterase in the embryo and the relationship between these substances and the development of behavior have been studied. The relationship of the earliest differentiation in the nervous system to the first movements in the embryo is being investigated, systematically.
Estimated Completion: 31 March 1949

NR-140-455 *Influence of the Non-Auditory Labyrinth on the Effective Function of the Human Organism* (Unclassified)

Contractor: Tulane University, New Orleans, Louisiana
Contract: N7-onr-434, Task I, (6/20/47 to 9/30/48)
Investigator: R. Brown

Under this project the research is divided into two parts: (1) A study of both normal persons and patients with nonfunctioning labyrinths in various tilting and rotating devices (including the human centrifuge) on the ground and, insofar as possible, in the air; (2) a study of the physiological aspects of (1) above, with particular attention to the nature and effects of conflicts and rivalry between the perceptions and the directives for action related to the labyrinths and those related to other sense organs, especially vision.

Progress to 6/30/48: Linear and angular accelerometers were modified and calibrated for analysis of flight patterns in aircraft, as well as for use in the laboratory. A motor driven tilt chair with remote indicator was installed at the University laboratory. A study of one aspect of the oculo-gyral illusion was completed. Results indicate that apparent motion involves, primarily, vestibular nystagmus following rotation, whereas apparent displacement of a visual target is influenced by other factors. Translations and abstracts of the literature on vestibular functions are being collated in preparation for a critical review.
Estimated Completion: Indefinite

[redacted]

PSYCHOPHYSIOLOGY

ANATOMY, PHYSIOLOGY, AND NEUROMUSCULAR FUNCTIONS OF VISION

NR-141-017 — Human Vision — (Unclassified)

Contractor: University of Pennsylvania, Philadelphia, Pennsylvania
Contract: N6-onr-249, Task II, (4/15/46 to 4/15/49)
Investigator: H. K. Hartline

The purpose of this project is to investigate the physiology of vision by recording electrical activity in the optic nerve fibers of lower animals. Photoreceptor mechanisms of the visual sense cell and the organization of nervous activity in the layers of the vertebrate retina will also be studied. Specific problems will include brightness discrimination, light-and-dark-adaptation, "fatigue", threshold uncertainty, relation between spatial and temporal summation, and relation between rod and cone functions. Extension of methods to human eyes available from enucleation operations will be attempted. Parallel studies, by standard methods, of subjective observation will be made on human subjects. Consultative and other assistance to service laboratories will be furnished according to request. Specific problems on which assistance can be given include lighting problems, problems of night vision, optical distortion, characteristics of binoculars.

Progress to 6/30/48: A technical report, "Light and Dark Adaptation of Single Visual Sense Cells", was published in the Journal of Cellular and Comparative Physiology. Experiments are continuing upon the relation between the slow cellular action potential of small isolated groups of retinal cells and the discharge of nerve impulses in their axones for the eye of Limulus.

Dr. Hartline is continuing his study of the processes of light and dark adaptation in single photoreceptor elements for which he received the Howard Crosby Warren Medal from the Society of Experimental Psychologists. He was elected, also, to membership in the National Academy of Sciences.

Estimated Completion: Indefinite

NR-141-022 — Binocular Neuromuscular Mechanisms — (Unclassified)

Contractor: Washington University, St. Louis, Missouri
Contract: N6-ori-202, Task I, (9/1/46 to 8/31/48)
Investigator: R. Scobee

The purpose of this project is to make (1) a study of all of the known variables in the Maddox Rod test of heterophoria; (2) a comparison of other tests of heterophoria with the Maddox Rod; (3) a study of the basic factors which influence heterophoria; (4) the relationships of the various portions of the muscle balance examination to the evaluation of the "muscle balance" as a whole; and (5) a study of the present diagnostic methods used in the measurement of heterotropia with the possible discovery of some better and more reliable diagnostic criteria.

Progress to 6/30/48: A technical report, "The Fascia of the Orbit, Its Anatomy and Clinical Significance", was submitted to the American Journal of Ophthalmology. A non-technical article, "The Future of the Cross-Eyed Child", appeared in the 15 June 1948 issue of the ONR Research Reviews. Studies of intermittent exotropia are awaiting the securing of a competent orthoptist to complete the visual training of the 25 selected cases. A study of the surgical treatment of vertical phoria has been initiated, and the study of heterotropia is being continued.

Reprints of a technical report, "Relationships between Lateral Heterophoria, Prism Vergence, and the Near Point of Convergence", published in the American Journal of Ophthalmology, Vol. 31, No. 4, April 1948, have been distributed.

Estimated Completion: Indefinite

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PSYCHOPHYSIOLOGY

ANATOMY, PHYSIOLOGY, AND NEUROMUSCULAR FUNCTIONS OF VISION (Cont.)

NR-141-277 Chemistry and Physiology of Vision (Unclassified)

Contractor: Harvard University, Cambridge, Massachusetts
Contract: N5-ori-76, Task XI, (10/1/46 to 9/30/48)
Investigator: G. Wald

Under this project two lines of investigation are being pursued in close association with each other: (1) Measurements of the spectral sensitivity of human vision, cone and rod, in various physiological states, and in normal and aphakic eye, and (2) the chemistry of the photoreceptor systems of the rods and cones and of other retinal components.

Progress to 6/30/48: Dr. Wald attended the various International Congresses in England and France during the summer of 1947. He wrote a summary of his impressions of European scientists and laboratories, and he edited the notes and reports made by the late Dr. Selig Hecht, on the same subject.

Work is continuing on the chemistry, physics, and physical chemistry of the visual process. Dr. Wald has also written two technical reports, "Galloxanthin, A Carotenoid from the Chicken Retina", and "The Synthesis from Vitamin A_1 of 'Retinene$_1$' and of a New 545 mu-Chromogen Yielding Light-Sensitive Product".
Estimated Completion: Indefinite

NR-141-359 Study of Electrical Activity of the Human Retina (Unclassified)

Contractor: Brown University, Providence, Rhode Island
Contract: N7-onr-358, Task II, (9/29/47 to 9/30/49)
Investigator: L. Riggs

The purpose of this project is to study the perception of colors under low levels of illumination and conditions of fog, and to investigate color blindness by this new technique. It is hoped that this study will lead to basic understanding of the process of color vision and to practical application of these findings in the selection of personnel for night look out duty, and the elimination of the color blind from the Naval service.

By means of recording the retinal action potentials picked up by an electrode fastened to the living eye by a contact lens, the response activity of the retina to light will be studied in both normal and color blind subjects. This will determine whether the deficiency occurs in the retina or in the higher brain centers. Similarly, the function of dark adaptation and of visibility for both normal and color blind eyes will be studied by measuring the electrical response of the retina to light of different wave lengths and of different intensities.

Progress to 6/30/48: Special facilities and equipment have been obtained to provide for recording the retinal response to light of various wavelengths. Subjects have been recruited and contact lenses fitted to their eyes to facilitate the electrical recording. Full scale experimental work will be undertaken during the summer.
Estimated Completion: Indefinite

PHYSIOLOGICAL OPTICS

NR-142-404 Visual Research (Unclassified)

Contractor: Columbia University, New York, New York
Contract: N6-onr-271, Task IX, (9/2/47 to 8/31/48)
Investigator: C. H. Graham

PHYSIOLOGICAL OPTICS, NR-142-404 (Cont.)

The purpose of this project is to make a study of vernier acuity in its various time and intensity relations. An apparatus and technique, developed at the Columbia Laboratory, will be used to measure instantaneous thresholds of a single retinal area while it is adapting to illumination. The data obtained will have a direct bearing upon the theory of visual photochemical processes.

The electrical activity which occurs when a single sense cell is illuminated will be studied by electrical recording methods using the horseshoe crab. Results with this preparation are not complicated by the activity of neural synapses, hence it is important to explore the effect of all parameters of the visual stimulation functions.

Neither theory nor data on the problem of monocular movement parallax are available in the literature on space perception. Experiments will be conducted on the effect of illumination, rate of movement, retinal position, size of target, and symmetry of object relations upon the threshold.

Progress to 6/30/48: Under the leadership of Dr. C. H. Graham important scientific contributions in the field of vision have been made on the following subjects: (1) Temporal and intensity relationships in coincidence acuity; (2) light adaptation and photochemical theory; (3) paramenters of monocular movement parallax thresholds; (4) figural after effects; and (5) the effect of illumination upon stereoscopic acuity. In addition, a monograph on "Visual Perception" has been completed by the Director for inclusion in the Handbook in Experimental Psychology.
Estimated Completion: Indefinite

NR-142-526 Screening Devices for Rapid Testing of Visual Functions (Unclassified)

Contractor: Johns Hopkins University, Baltimore, Maryland
Contract: N6-onr-243, Task VII, (3/1/48 to 2/28/50)
Investigator: L. L. Sloan

The purpose of this project is to make an investigation of the basic factors involved in measuring certain aspects of visual function, in particular acuity, phoria, depth perception, and color discrimination. One purpose of the studies is to determine the experimental condition necessary to obtain reliable and valid measures of visual functions by means of visual screening devices. Other visual tests will be evaluated, i.e., night vision, peripheral vision, etc.

Progress to 6/30/48: Several instruments for visual screening procedures have been obtained. New test plates have been designed and are being manufactured.
Estimated Completion: 28 February 1950

NR-142-565 The Influence of Certain Sunglasses on Object-Color Perception (Unclassified)

Contractor: Temple University, Philadelphia, Pennsylvania
Contract: N8-onr-560, (3/1/48 to 2/28/49)
Investigator: R. H. Peckham

The purpose of this project is to determine, by experiment, the perception of object-colors through colored or tinted sunglasses. Standard sunglasses will be used in varying thicknesses in order to change the transmission from five per cent to 50%. The adaptation of the eyes to the sunglasses will be computed by both the Munsell and Judd methods. The relative completeness of adaptation will be checked empirically and the effect of the lenses on color perception will be determined experimentally.

Progress to 6/30/48: No progress to report.
Estimated Completion: 30 June 1949

PHYSIOLOGICAL OPTICS (Cont.)

NR-142-710 Visibility of Submerged Objects (Unclassified)

Contractor: Massachusetts Institute of Technology, Cambridge, Massachusetts
Contract: N5-ori-78, Task XXXI, (6/1/48 to 11/30/48)
Investigator: S. Q. Duntley

The purpose of this project is to obtain adequate data on various physical factors so that engineering methods can be applied to the visibility of submerged objects. In particular, it is necessary to investigate the refractive effects of the surfaces of bodies of water and the contrast reduction by reflections from such surfaces. Photometric observations will be made of a variety of submerged objects at various depths and azimuths under a wide range of lighting and weather conditions. Both photographic and visual photometry will be used. From these exploratory experiments a means for specifying the physical factors in question in terms of the state of the sea and the state of the sky, measured by parameters which can be evaluated easily, on shipboard or estimated from meteorological data, will be evolved.

Progress to 6/30/48: No progress to report.
Estimated Completion: 30 November 1948

PERCEPTUAL FUNCTIONS OF VISION

NR-143-106 Probability of Detection and Recognition of Visual Targets (Unclassified)

Contractor: University of Michigan, Ann Arbor, Michigan
Contract: N5-ori-116, Task V, (7/15/46 to 10/15/49)
Investigator: H. R. Blackwell

The purpose of this project is to obtain engineering data for normal human binocular vision, to be used in various practical military situations in which visual detection and recognition are involved. Initial studies will be made in which the relation between brightness contrast and stimulus exposure is determined for objects differing in size, shape, and location in the visual field. Data are to be obtained utilizing the psychophysical method of constant stimuli so that the entire curve of probability can be determined. The relation between binocular and monocular thresholds will also be determined. An investigation will be made of the effect of the steepness of the stimulus gradient and the effect of training upon visual thresholds.

Initial work will be designed to establish the most valid use of psychophysics. In addition, the validity of observations made at a short viewing distance in predicting results at long viewing distances will be established.

Progress to 6/30/48: New quarters for the Vision Research Laboratory were completed and improved equipment for the automatic administration and recording of psychophysical experiments was installed. Experiments on psychophysical methods and on detection and resolution thresholds relative to viewing distance were completed. Technical reports on these subjects will be available in the near future. Field studies on visibility and atmospheric optics are under way at Akron, Ohio and Roscommon, Michigan, under the guidance of the Sub-Committee on Visibility and Atmospheric Optics of the Armed Forces-NRC Vision Committee.
Estimated Completion: Indefinite

NR-143-151 Estimation of Speed and Angle of Approach of Aircraft (Unclassified)

Contractor: Denison University, Granville, Ohio
Contract: N6-ori-189, Task I, (9/15/46 to 9/14/48)

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PSYCHOPHYSIOLOGY

PERCEPTUAL FUNCTIONS OF VISION, NR-143-151 (Cont.)

Investigator: W. C. Biel

In the use of certain types of fire control equipment estimations of the speed of an aerial target must be made. Occasionally angles formed by the line of sight and the target fuselage must also be estimated.

In the first half of 1945 a group of 20 commissioned Army anti-aircraft artillery officers were tested for the accuracy with which they could make these judgments. They were then given training in speed estimation by being told the "true" target speed for each course a short time after they had made their judgments. Following this, the observers were again tested in estimating speed and angle of approach to see if this type of training had any effect. During the experimental periods, courses varying in speeds, ranges, elevations, and direction were flown by the following planes: AT-11, PQ-14, B-25, B-26, P-47, and P-63. Criteria for true speeds and approach angles were obtained from computations based on continuously recorded azimuth and elevation angles (from M9 Director tracking) and slant range (SCR 584).

Under the present contract the speed estimations and angle estimations made by the observers are being compared separately with the criteria for the different types of planes, varying speeds of a particular plane, types of courses, before training, after training, etc.

Progress to 6/30/48: Summary tables for the results showing the accuracy of speed estimation are nearly complete. Computations relative to the estimation of angle of approach are still in progress.
Estimated Completion: 14 September 1948

NR-143-153 Test of Color Vision (Unclassified)

Contractor: University of Minnesota, Minneapolis, Minnesota
Contract: N6-onr-246, Task I, (12/1/46 to 11/30/48)
Investigators: D. G. Paterson, M. A. Tinker

Under this project various color vision tests will be studied to determine (1) the amount of agreement in identifying color defective persons; (2) the reliability of these tests; and (3) the influence of other factors such as illumination, age, and socioeconomic status of subjects on these tests.

Progress to 6/30/48: Routine testing of subjects is continuing, and about 179 men have been tested to date. No analysis of data will be attempted until many more subjects have been tested.
Estimated Completion: 30 November 1948

NR-143-253 Response Mechanism of the Visual Threshold (Unclassified)

Contractor: Indiana University, Bloomington, Indiana
Contract: N6-onr-180, Task IV, (6/1/47 to 9/30/49)
Investigator: W. S. Verplanck

The measurement of sensory thresholds is the basic technique for investigating the sensory capacities of the human. The present program will examine each of the methods carefully, using standard instruments and stimuli, on a group of subjects who are young, healthy, of normal vision, and representative of service personnel. The variables to be investigated include inter-trial interval, spacing of steps, use of "vexir fehlen", conditions of reinforcement, shutter sounds, and "ready" signals. It is expected that many of the difficulties encountered in making psychophysical measurements may be accounted for by the basic dynamics of behavior, and may be eliminated by using knowledge of these processes.

PERCEPTUAL FUNCTIONS OF VISION, NR-143-253 (Cont.)

Progress to 6/30/48: Four dark rooms and one sound-proof dark room were constructed. Two assistants were selected and trained in psychophysical methods and experimental procedures.

Facilities and equipment were obtained and installed to permit the routine measurements of dark adaptation under various controlled conditions. Experiments will continue until the variables named above are investigated.
Estimated Completion: Indefinite

NR-143-262 Peripheral Vision (Unclassified)

Contractor: Johns Hopkins University, Baltimore, Maryland
Contract: N6-onr-243, Task III, (2/1/47 to 6/30/49)
Investigator: F. N. Low

Under this project a study will be made of the effects of changing the illumination upon the peripheral vision of human subjects under both scotopic and photopic conditions. Special attention will be directed to the differences in apparent visibility which occur at dusk and dawn.

Progress to 6/30/48: Dr. Low has demonstrated that more time is required to perceive objects falling upon the peripheral retina than upon the para-central region. Momentary diminution of brightness at low levels of illumination causes a temporary impairment of peripheral form perception. A significant decrease in peripheral acuity was caused by both increased angular deviation from the line of sight and decreased time of exposure.
Estimated Completion: 30 June 1949

NR-143-292 Field Tests of Optical Equipment (Unclassified)

Contractor: Indiana University, Bloomington, Indiana
Contract: N6-onr-180, Task III, (3/1/47 to 12/31/48)
Investigator: W. S. Verplanck

Under this project the statistical analysis of the results of field tests of optical equipment conducted at the U. S. Submarine Base, New London, Connecticut, during 1945, will be completed. The objective is to determine the practical and relative values of various optical instruments under various conditions of visibility, visual performance, and Naval operations.

Progress to 6/30/48: Computations relative to sightings of targets and atmospheric attenuation are practically complete. Further statistical analyses will be completed during the summer and preparation of the final report will begin.
Estimated Completion: 31 December 1948

NR-143-325 Color Sense Measurement in Normal and Abnormal (Unclassified)

Contractor: Cornell University, Ithaca, New York
Contract: N6-onr-264, Task VII, (2/1/47 to 3/31/49)
Investigator: E. Murray

The purpose of this project is to secure a more sound empirical basis, through accumulated observations, for the science of color vision and its practical applications. The determination of the chromatic thresholds of normal and abnormal subjects will be made of critical points on the spectrum for the light adapted eye. Later, a distribution curve for each critical hue showing the range of high and low sensitivity and the median in normal and abnormal subjects will be established.

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PSYCHOPHYSIOLOGY

PERCEPTUAL FUNCTIONS OF VISION, NR-143-325 (Cont.)

Progress to 6/30/48: Testing of normal and color anomalous subjects is continuing using standardized procedures. A technical report will appear in the July, American Journal of Psychology.
Estimated Completion: 31 March 1949

NR-143-410 Effect of Illumination of One Eye Upon the Visual Thresholds of the Other Eye (Unclassified)

Contractor: Michigan State College, East Lansing, Michigan
Contract: N8-onr-516, Task I, (3/1/48 to 5/30/48)
Investigator: S. H. Bartley

Various threshold measurements for one eye will be made, while the illumination in the other eye will be varied systematically from near threshold limits to very high levels of illumination.

Progress to 6/30/48: This project has been terminated. No work was done.

NR-143-497 Study of Certain Aspects of Lookout Technique (Unclassified)

Contractor: Yale University, New Haven, Connecticut
Contract: N7-onr-288, Task V, (10/1/47 to 9/30/48)
Investigator: W. R. Miles

Eye movements of controlled groups will be photographed, under infrared light, to determine the occurrence of suspected over-convergence during the detection of faint targets under low levels of illumination.

Different methods of using binoculars for the determination of the orientation of distant targets under low levels of outdoor illumination will be tested.

This project is supported by the Bureau of Medicine and Surgery under project number NM-003-033.

Progress to 6/30/48: No progress report has been received.
Estimated Completion: 31 March 1949

NR-143-638 Individual Constants of Luneberg's Metric of the Visual Space (Unclassified)

Contractor: Columbia University, New York, New York
Contract:
Investigator: L. H. Hardy

By mathematical analysis Dr. Rudolph Luneberg has established a correlation between physical space and the corresponding visual perception, using non-Euclidian geometry. From this analysis, he derived a metric of visual space as a function of physical coordinates and two individual constants. It is proposed to conduct experiments in space perception which will provide empirically determined values for these constants. Such constants, when substituted in Luneberg's equations, will provide an empirical check on his theory.

Progress to 6/30/48: No progress to report. This project will get under way on 1 September 1948.
Estimated Completion: August 1949

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PSYCHOPHYSIOLOGY

PERCEPTUAL FUNCTIONS OF VISION (Cont.)

NR-143-669 Armed Forces-NRC Vision Committee (Unclassified)
(Formerly NR-014-009)

Contract: University of Michigan, Ann Arbor, Michigan
Contract: N5-ori-116, Task I, (10/1/45 to 9/30/48)
Investigator: D. G. Marquis

The Armed Forces National Research Council Vision Committee, formerly known as the Army-Navy-NRC Vision Committee provides consultative services in all aspects of the field of vision to the Army, Navy, and the Air Force upon request. By means of semi-annual meetings, the Committee brings together personnel from the Army, Navy, and Air Force research laboratories, the medical profession, university laboratories, and engineers to discuss visual problems of special interest to the military services. Both fundamental and applied research projects are reviewed and specific recommendations are made relative to research and development in the field of vision. This project is placed with the University of Michigan for the purpose of handling the administrative details of the Committee. The civilian members are appointed by the National Research Council. This project, formerly carried by the Physics Branch, under NR-014-009, has been transferred to the Psychophysiology Branch.

Progress to 6/30/48: Two formal meetings were held. On 20-21 October 1947, the Committee met at the Special Devices Center, where technical papers on testing of visual acuity, visibility, instrumentation in supersonic flight, and sunglasses, were presented. Recommendations for visual standards for the military services and manuals for testing visual acuity and heterophoria were also presented.

On 27-28 May, the Committee met at the Medical Research Laboratory, Submarine Base, New London, Connecticut. Technical reports on visual screening devices, studies of visual acuity, night vision, color blindness, the Navy Color Lantern, specifications for red and green signal lights, effects of illumination upon visual acuity, and the relationship between vision and audition, were presented.

Recommendations concerning color vision testing, vision testing, research in visibility and atmospheric optics and illumination were made. The following sub-committees have been active during the year: Visual Tests and Procedures, Color Vision, Visibility and Atmospheric Optics and Illumination. Dr. Richard G. Scobee, Washington University Medical School, St. Louis, Missouri, was elected Chairman, succeeding Captain C. W. Shilling (MC) USN.
Estimated Completion: Indefinite

NR-143-715 Naval Research Advisory Panel for Psychophysiology (Unclassified)

Contractor: University of Pennsylvania, Philadelphia, Pennsylvania
Contract: (7/1/48 to 6/30/49)
Investigator: H. K. Hartline

Under this project the University of Pennsylvania will provide an Advisory Panel for Psychophysiology, acceptable to the Office of Naval Research and to have as its Chairman, Dr. Haldane Keffer Hartline of the Eldridge Reeves Johnson Foundation for Medical Physics. The University will provide consultative services, meeting place, office space for the Chairman, secretarial service, and communication facilities. The University will arrange for transportation, subsistence, reimbursement and communication for the membership.

Progress to 6/30/48: No progress to report. This project will get under way on 1 July 1948.
Estimated Completion: Continuing

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PSYCHOPHYSIOLO

REHABILITATION, VISION

NR-144-323 Research for Purpose of Improving Wearing Qualities of Contact Lenses (Unclassified)

Contractor: H. J. Hoff, Washington, D. C.
Contract: N7-onr-289, (2/1/47 to 1/31/49)
Investigator: H. J. Hoff

All contact lens research in the past 15 years has been aimed at delaying onset of haze in vision by using various aqueous solutions between the lens and eye. Results have been negative. A new contact lens is being designed to permit a rapid rate of flow of lacrimal fluid under the lens.

Progress to 6/30/48: Several contact lenses have been made under a new design and are being tried out on private patients.
Estimated Completion: 31 January 1949

ANATOMY, PHYSIOLOGY, AND NEUROLOGY OF HEARING

NR-145-233 Anatomy and Physiology of the Auditory System (Unclassified)

Contractor: University of Oregon, Eugene, Oregon
Contract: N7-onr-287, Task I, (1/1/47 to 1/1/49)
Investigator: A. R. Tunturi

The purpose of this project is to conduct basic research on the anatomy and physiology of the acoustic system in the brain and the mechanism of the ear. This includes a study of the distribution of nerve fibers from the ear to the brain, the pathways in the brain involved in binaural localization, and the masking effects of pure tones and noises on the nerve responses of the brain to sounds.

Progress to 6/30/48: The ten-channel cathode ray oscillograph has been in use for several months and experiments have been continued on the investigation of the cortical response area in relation to frequency and intensity of the sound pulse. Microscopic studies of the neural pathways in the brain are also being continued.
Estimated Completion: Indefinite

NR-145-322 Nature of Sound Conduction in the Ear (Unclassified)

Contractor: Princeton University, Princeton, New Jersey
Contract: N6-onr-270, Task III, (4/1/47 to 9/30/49)
Investigator: E. G. Wever

The purpose of this project is to investigate the passage of sound through the ear and the modifications of the vibratory patterns produced in the process of transmission with exact measurements of the pathways of conduction. The plan includes four closely related problems, all employing a similar method. These problems are (1) the routes of transmission of sound through the ear; (2) the functions of the ossicular chain; (3) the effects of air pressure upon sound conduction through the middle ear; and (4) the nature and limits of distortion in the ear. The method will consist of measurements of the electrical potentials of the cochlea in experimental animals during stimulation with sounds. Wherever possible, the studies on animals will be checked by observations in man.

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PSYCHOPHYSIOLOGY

ANATOMY, PHYSIOLOGY, AND NEUROLOGY OF HEARING, NR-145-322 (Cont.)

Progress to 6/30/48: Three reports have been made by Professor E. G. Wever on the effects of negative pressure in the middle ear, sound conduction in the middle ear, and the functions of the round window. A cooperative investigation on auditory hazards in connection with the use and testing of jet engines has been undertaken with the Aero-Medical Equipment Laboratory at Philadelphia. Preliminary studies of animals exposed in the vicinity of jet engines reveal a marked and general loss for frequencies in the audible range.
Estimated Completion: 30 September 1949

NR-145-398 Study of Activity of Single Fibers of Auditory Nerve, Acoustic Tracts, and Nuclei in the Brain Stem (Unclassified)

Contractor: University of Rochester, Rochester, New York
Contract: N6-onr-241, Task VII, (9/1/47 to 8/31/49)
Investigators: E. H. Kemp, G. R. Wendt

The purpose of this project is to study the basic physiological phenomena, associated with single elements of the auditory system, and the responses to frequency and intensity. An analysis will be made of complex sounds, interference, masking, etc. Microelectrode techniques may make possible a much clearer picture of synaptic activity in auditory centers than that obtained in earlier studies.

Progress to 6/30/48: Experimental equipment has been assembled and assistants trained in the procedures. Preliminary research has been initiated, but no technical results will be available for some time.
Estimated Completion: 31 August 1949

ACOUSTICS

NR-146-608 Studies on the Function of the Inner Ear (Unclassified)

Contractor: University of Chicago, Chicago, Illinois
Contract: N6-onr-20, Task XXIV, (4/1/48 to 3/31/49)
Investigator: J. R. Lindsay

The function of the inner ear will be investigated by altering the receptor cells, nerve supply, and the fluid system of the cochlea, using various experimental procedures. Changes in hearing and in the electrical response of the cochlea will be measured. A method will be developed to make possible a more exact analysis of the forces acting upon the fluids of the inner ear through the conducting mechanism of the middle ear. Studies will be made, specifically, upon the hearing losses produced by blast injury, upon the effect of partial sectioning of the auditory nerve, upon the effect of interruption of the blood supply to the cochlea, and upon the effect of surgical treatment of Meniere's disease on hearing.

The changes in hearing, in cochlear microphonics, and in the degeneration of nerve and sensory cells in the cochlea following partial section of the auditory nerve and interruption of the blood supply to the cochlea will add to the knowledge of the analytical function of the cochlea and the resulting pattern of impulses in the auditory nerve. Since hearing loss may occur prior to histological changes in the sensory cells or nerve elements of the cochlea, a study of the intralabyrinthine fluid system in cochlea function may lead to the answer to an important clinical problem. Motion picture recordings, using a high speed camera and stroboscopic illumination, of the vibration of the eardrum in situ will aid in these investigations.

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ACOUSTICS, NR-146-608 (Cont.)

Progress to 6/30/48: Equipment and facilities are available and the research staff is proceeding with the investigation.
Estimated Completion: Indefinite

PERCEPTUAL FUNCTIONS OF HEARING

NR-147-201 Communications (Unclassified)

Contractor: Harvard University, Cambridge, Massachusetts
Contract: N5-ori-76, Task II, (1/1/46 to 1/31/49)
Investigator: S. S. Stevens

Under this project the Psycho-Acoustic Laboratory of Harvard University will undertake studies in psychological and physiological acoustics with special reference to (1) the principles governing the effectiveness of voice communication equipment, especially as revealed by articulation tests; (2) the masking effects of various kinds of noise and their relation to speech communication; (3) the principles governing the behavior of personnel in communication activities; and (4) the psychology of hearing and the physiological nature of the auditory process, including monaural versus binaural hearing, differential sensitivity, auditory fatigue, deafness, growth and decay of excitation, sound localization, etc.

Progress to 6/30/48: A most productive fundamental research program has been conducted at the Psycho-Acoustic Laboratory of Harvard University under the directorship of Professors S. S. Stevens and E. B. Newman.

Considerable progress has been made on the investigation of the interaction, summation and inhibition of the innervations of the two ears, the effect of masking, filtering, and interrupting upon the intelligibility of speech against a background of noise, and the perception of bursts of noise. All of these have important bearing upon the theory of hearing and have practical applications as well. The addition of Dr. G. v. Bekesy and Dr. Galambos to the staff has made possible investigations of the physiology of hearing. They are making mechanical measurements on the basilar membrane of the inner ear, applying slit-lamp microscopy to the study of the fine structure of the inner ear, and taking high speed motion pictures of the middle ear to obtain precise measurement of the amplitude of motion of the various components under various stimulus conditions in the living animal. A very practical study has been completed on the size of earphones to be used under the combat helmet. A number of contributions are being made by the staff to the forthcoming Handbook of Experimental Psychology.
Estimated Completion: Indefinite

REHABILITATION, HEARING

NR-148-170 Aural Rehabilitation (Unclassified)

Contractor: Central Institute for the Deaf, St. Louis, Missouri
Contract: N6-onr-272, Task III, (1/1/47 to 12/31/48)
Investigator: H. Davis

The basic aspects of this research are directed at the psychophysiological acoustics of the middle and inner ear, including a study of the aural microphonic, the function of the round window, the neural physiology of the basilar membrane and the function of the intra-aural muscles.

REHABILITATION, HEARING, NR-148-170 (Cont.)

A study of binaural hearing, especially for hard of hearing subjects following fenestration operations for otosclerosis, will be made in order to validate tests for the perception of speech. These tests will be used for (1) selection of suitable cases for fenestration surgery, and (2) judging the ultimate success of the operation.

A study of diagnostic methods for impaired hearing will be made using (1) threshold for speech in quiet, (2) threshold for speech in noise, and (3) articulation scenes at various signals to noise ratios.

A critical survey will be undertaken concerning the effects of noise upon human beings, with particular emphasis upon working efficiency, audition, and annoyance.

Progress to 6/30/48: A test for hearing, involving a new concept called social adequacy index for the hard of hearing, has been developed. This involves a measurement of the efficiency of hearing for connected discourse as compared with earlier tests involving musical tones or nonsense syllables. An evaluation of fenestration surgery has been presented in a technical report. Specifications for performance tests of hearing aids are being prepared for the Council on Physical Medicine. A survey of the effect of noise upon human beings for the Bureau of Ships is nearing completion. The Director of Research has completed a Monograph on the "Psychophysiology of Hearing and Deafness" for the new Handbook of Experimental Psychology. Dr. Davis was elected to the National Academy of Sciences.
Estimated Completion: Indefinite

OTHER SENSES

NR-149-598 Vibratory Research (Unclassified)

Contractor: University of Virginia, Charlottesville, Virginia
Contract: N7-onr-372, Task II, (4/1/48 to 9/30/48)
Investigator: F. A. Geldard

The purpose of this project is to study the cutaneous mediation of vibratory forces, the upper and lower limits of vibratory response, the frequency intensity function, differential intensity and frequency discrimination, and electrical versus mechanical arousal of vibratory sensations.

Progress to 6/30/48: No progress has been reported.
Estimated Completion: Indefinite

NR-149-721 Psychophysiology of Taste (Unclassified)

Contractor: Brown University, Providence, Rhode Island
Contract: (7/1/48 to 6/30/49)
Investigator: C. Pfaffman

The purpose of this project is to investigate the psychophysiology of gustatory sensation by two methods:

(1) Using groups of rats in an adequately controlled experimental design, the influence of partial and completion denervation of the tongue and mouth upon the taste preferences and aversions of the white rat will be studied. Using the method of Richter, threshold concentrations of various chemical solutions at which the animal shows either a preference for, or an avoidance of, the taste solution will be determined. These experiments will be conducted on normal animals and several groups of animals in which the nerves to the tongue and mouth have

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PSYCHOPHYSIOLOGY

OTHER SENSES, NR-149-721 (Cont.)

been removed by surgical means. Histological control to determine the efficacy of the denervations will be used.

(2) Using human subjects and psychophysical methods, the absolute and differential thresholds for four sweetening agents, suchrose, saccharine, glucose, and fructose together with a determination of their equal sweetness concentrations, will be obtained.

Progress to 6/30/48: No progress to report. This project will get under way on 1 July 1948.
Estimated Completion: 30 June 1949

Psychology

SELECTION AND TRAINING OF PERSONNEL

NR-151-039 An Empirical and Factorial Study of Mechanical Aptitudes (Unclassified)

Contractor: University of Chicago, Chicago, Illinois
Contract: N6-ori-20, Task XII, (10/1/46 to 9/30/48)
Investigator: L. L. Thurstone

The purpose of project is to isolate the component abilities in the complex which are known as mechanical aptitude. Mechanical aptitude is mostly in the head rather than in the finger tips as is commonly believed. It is known that the space factor S is one of the components which represents ability to visualize two and three-dimensional space, but this is only one of the components. The study is being made with batteries of psychological tests, designed to test various hypotheses concerning the fundamental nature of mechanical aptitude. By means of factorial analysis, the component abilities should be isolated and identified. If these abilities can be identified, it will be possible to (1) describe in a practical, useful way the various kinds of mechanical aptitude; (2) appraise these abilities in each individual by properly designed tests; and (3) adjust the selection and training in accordance with the individual profiles of abilities.

Progress to 6/30/48: During the past year the tests which had previously been developed to measure the various factors of space, experience, movement, visual memory, closure, perception, reasoning, and interest analyses were administered to groups of boys of high school age and a selection made of those which seemed most comprehensive. These tests were then administered to groups and individuals.

All the testing has been completed and the factor analysis of the group tests is well under way. Two factors have been extracted and the work is progressing satisfactorily, and the analyses should be completed by the end of September. The results of these analyses should provide a basis for the construction of practical tests for use in measuring the primary factors which have been isolated.

Estimated Completion: 30 September 1949

NR-151-060 Motion Sickness (Unclassified)

Contractor: University of Rochester, Rochester, New York
Contract: N6-ori-126, Task I, (6/1/46 to 10/31/48)
Investigator: G. R. Wendt

The purpose of this project is to extend present knowledge and understanding of factors underlying motion sickness. By coordinating studies of normal humans and physiological and functional studies of dogs it is proposed to obtain information about the relation of wave-characteristics to sickness rates, the role of vestibular, postural, vascular, temperature, and visual factors in sickness, and the mode of action of the vestibular apparatus during wave motion.

By means of collateral data taken on human subjects, data will be obtained on procedures for personnel selection, effects of sickness on performance, and subjective reactions to motion.

Progress to 6/30/48: The results of studies made to date seem to indicate that non-psychological factors such as the character of the motion, the posture of the head, and the physiological state as affected by drugs are demonstrably major determiners of motion sickness rates. The Army and Navy personnel who were the subjects of these experiments did not get sick, even though psychological factors were present, unless the combination of physical and physiological factors was appropriate.

SELECTION AND TRAINING OF PERSONNEL, NR-151-060 (Cont.)

The evidence suggests that the most promising lines of development for prevention of sickness are in a better understanding of the kinds of motion which produce sickness, followed by changes in design and operating procedures to avoid the worst conditions; a better understanding of the role of posture, followed by routine adoption of favorable postures when the motion becomes unfavorable; and better understanding of the physiology of motion sickness so that prophylactic drugs may be rationally selected for study.
Estimated Completion: Indefinite

NR-151-082 Relation of Muscular Tension to Effort and Fatigue (Unclassified)

Contractor: Cornell University, Ithaca, New York
Contract: N6-ori-91, Task III, (5/10/46 to 5/31/49)
Investigator: T. A. Ryan

The general problem is to study the location and patterning of muscular tensions in various kinds of skilled and mental work; to study the changes in these patterns in prolonged effort in each task; and to seek the common characteristics of the muscular tensions involved in dissimilar kinds of work and fatigue.

Within this general problem, the first task is to determine the affects of ocular strain upon muscular tensions in other parts of the body, and to compare these affects with the affects of other types of work which involve similar amounts of effort but do not involve visual strain.

Muscle tension is being recorded by means of amplifiers, rectifiers, and an integrating circuit which produces a record showing the average rectified voltage developed in a muscle group in a given period of time.

Progress to 6/30/48: Two experimental series have now been completed. In the first first, subjects worked on a difficult visual test under three conditions: (1) Normal or control, (2) severe glare, and (3) loud noise as a distractor. Electric potentials were recorded from three areas of the body: Upper inactive arm, upper active arm, and the potentials developed between the two ear lobes. Twenty-four subjects participated in this series. The conditions were presented in counterbalanced order to eliminate the affects of the general trends in muscle tension during the experimental series.

Potentials developed in the ear showed a significant increase during the glare and distraction periods as compared with the normal control. Potentials in the arms were not significantly different during the conditions of glare and distraction as compared with the normal control. All areas showed marked increases in potentials during work as compared with rest, but evidently the only area which was differentially affected by the severity of the conditions of work was the head area as recorded through ear lobes.

The second series, with a total of 12 subjects, consisted of normal reading, with a statement to the subject that he would be tested on what he read. Otherwise conditions were the same as those in the first series. In this case, no significant influence of glare and distraction appeared in the measures of muscle potential. The second series was an attempt to duplicate the experimental conditions, used by Luckiesh in his studies on the effects of illumination. Here, however, there is no measure of accomplishment possible and it is quite likely that glare and distraction had no affect on muscle tension because the subjects slowed down their performance thus maintaining a more or less constant level of effort.

Work is presently under way on a continuation of the first series. Investigations will explore the potentials developed in the neck and shoulder, the leg, and the forearm in both the active and inactive areas.

Another series, to be started soon, will compare potentials developed during work for different levels of illumination.

Significant improvements have been made in the apparatus used for these tests and as a result the collecting of future data will be greatly facilitated.
Estimated Completion: Indefinite

SELECTION AND TRAINING OF PERSONNEL (Cont.)

NR-151-098 Psychological Effects of Accelerative Forces (Unclassified)

Contractor: University of Southern California, Los Angeles, California
Contract: N6-ori-77, Task III, (10/1/46 to 12/31/48)
Investigator: N. Warren

The purpose of this project is to investigate effects of acceleration on psychological and psychomotor functions of human subjects. This includes changes in speed and accuracy of response and skilled movements, and changes in the speed and accuracy of the perception of both visual and kinesthetic stimuli. Determination also is to be made of the degree to which various protective devices modify the psychological effects of acceleration.

Progress to 6/30/48: Two studies have been completed and reports submitted to this office, one on stick force estimations and one on maximum stick force. A study of spacial orientation has been completed and the report is in preparation. Further work has been started on maximum stick forces with 10 subjects being tested on the maximum force applicable under g forces ranging from one to five.

Additional time has been obtained on the centrifuge during the past six months and various studies are being planned and developed. Some of these are: A study of perceptual speed; reaction time to relatively simple stimulus patterns; dial reading; maximum stick forces in forward and right aileron directions; and a study of pupillary size as related to increased positive radial acceleration.
Estimated Completion: Indefinite

NR-151-126 Development of Several Equated Forms of a Brief Individual Intelligence Test (Unclassified)

Contractor: Northwestern University, Evanston, Illinois
Contract: N6-ori-158, Task I, (7/15/46 to 7/14/48)
Investigator: W. A. Hunt

The purpose of this project is to validate and standardize some of the abbreviated individual intelligence scales used as screening devices during World War II, as well as the possible development of new individual intelligence scales of an abbreviated nature.

Progress to 6/30/48: Three studies, in addition to previously reported work, are now well under way. One involves an investigation of the possibilities of the Hebb-McGill Verbal Situations Test in picking up psychopaths. The importance of this in a Navy test battery is obvious. With the cooperation of the Chicago Municipal Court Clinic and the Disciplinary Barracks of the Great Lakes Training Station some 60 psychopaths have been tested to date.

Another study has investigated the ability of clinicians to make successful qualitative judgments (without objective scoring procedures) on the CVS. This study is now being written up and demonstrates that CVS is not too brief to offer a basis for such judgments.

A final study is investigating the technical effects of test abbreviation, i.e., fatigue, boredom, and affect on the item of a change in the context in which it is presented. This technical study has involved the group testing of 1,000 subjects and the individual testing of 400 more. The testing is about finished and calculation of the data is about to begin.
Estimated Completion: Indefinite

NR-151-127 The Follow-Up Study of Certain Administrative Procedures of the Bureau of Medicine and Surgery (Unclassified)

Contractor: Northwestern University, Evanston, Illinois
Contract: N7-onr-450, Task I, (9/2/47 to 3/2/49)
Investigator: W. A. Hunt

SELECTION AND TRAINING OF PERSONNEL, NR-151-127 (Cont.)

The purpose of this project is to make follow-up studies of several hundred cases screened, at several Naval stations, during the war years. Their screening records will be compared with their education, health, and general service records now on file in the Navy Department. Thus, it will be possible to determine the effectiveness of the screening procedures to eliminate individuals who might become liabilities, rather than contributing members of the Naval service.

Progress to 6/30/48: This project was slow in getting under way due to the moving of service records to Garden City, L. I. It has accordingly been extended without additional funds to 2 March 1949.

A competent assistant has been obtained and analysis of records has been begun. Preliminary indications are that there is a relationship between neuropsychiatric screening and later discharge, i.e., screening seems to cut down later discharges for neuropsychiatric reasons. It is interesting to note, however, as a trend that the differences in subsequent discharge are not as great as those in original aptitude discharge. In other words, increasing the number of training aptitude discharges decreases attrition, but at a lesser rate.

Work is progressing favorably in spite of numerous difficulties encountered in this type of research, and a formal report will be submitted in the near future.
Estimated Completion: 2 March 1949

NR-151-132 Development of Basic Measures of Precision In Psychomotor Skills (Unclassified)

Contractor: Northwestern University, Evanston, Illinois
Contract: N6-ori-158, Task II, (7/15/46 to 7/14/49)
Investigator: R. H. Seashore

The purpose of this project is to design a battery of psychomotor tests to sample performance emphasizing: (1) Precision in static and dynamic equilibrium; (2) coordination of arm and hand movements in aiming, thrusting, and tracing movements; and (3) simultaneous coordinations of hands and feet in complex operations such as operating planes, gunsights, computing devices, and other complex mechanisms.

After determining optimal test procedures for administering each test, the interrelations of the various psychomotor factors underlying these skills will be analyzed. A revised portable battery of psychomotor tests to measure each factor discovered should then be prepared for work on selection of personnel and for measuring effects of extreme working conditions, e.g., temperature, altitude, fatigue, drugs, and diets.

Progress to 6/30/48: Many difficulties were encountered with personnel and equipment in this project, and results were not obtained in quantity until recently. Accordingly the project has been extended one year, without additional funds.

Using the Thurstone centroid method of analysis, three factors have so far been isolated: (1) Arm-hand steadiness and aiming; (2) arm-hand precision in thrusting and tracing with a stylus; and (3) arm-hand precision in moving a ring over a rod in three dimensions, including wrist rotation.

A photoelectric ataxiameter, for measuring steadiness, has now been redesigned, and will be the first unit of a portable battery of psychomotor precision tests for measuring standing, and sitting postural sway, and arm-hand steadiness. The test of dynamic equilibrium has been redesigned and is being calibrated for accuracy on the new electrical scoring circuit.

The end result of this study is hoped to be the construction of a battery of portable tests measuring each of the various factors isolated in one experiment. This battery should be useful in determining aptitudes which may be necessary for operating various machines or instruments which call for precision in complex performances. It will also be useful as a set of criteria of benefits or impairments of coordination under extreme conditions of altitude,

temperature, pressure, oxygen, air-conditioning, etc., and the effects of drugs, fatigue, recovery from illness, and other experimental conditions.
Estimated Completion: 14 July 1949

NR-151-200 A Proposal for the Further Investigation of Vertigo (Unclassified)

Contractor: Brooklyn College, Brooklyn, New York
Contract: N7-onr-323, Task I, (2/15/47 to 7/31/49)
Investigator: H. A. Witkin

The purpose of this project is to study the role of visual stimuli in vertigo, the affects of fatigue on the incidence and duration of vertigo, individual differences in the mode of orientation, with reference to bodily factors, labyrinthine sensitivity, pressure sensitivity, the role of kinesthetic factors, etc. A study will be made of the personality correlates of space orientation.

Progress to 6/30/48: The administration of the battery of orientation and non-orientation perceptual tests was continued, using 100 subjects. The purpose of this area of investigation is to determine whether the features which characterize a person's space orientation are found in all of his perceptual activities. In each test, pretesting was carried out to establish a final procedure for administration of the test and to determine its reliability. Each subject was also tested again on the Stability of Orientation Tests and the Dark Room Test which were administered over a year ago. In this way it is possible to determine the stability of an individual's mode of orientation over a relatively long period of time.

Work on the Personality Correlates of Mode of Orientation was begun by testing a group of 211 subjects in the Stability of Orientation Test and the Dark Room Test and then carrying out personality analyses of segments of the distribution obtained. The earliest work centered upon subjects at both ends of the distribution. Subsequently a personality study was made of subjects who gave more intermediate performances on the orientation tests. This group was not a representative one and it was decided to enlarge the group to obtain adequate sampling. Thirty-five additional members of the original group were tested. Analyses of these data are being made.

Fifteen athletes and eight dancers have been tested on the perceptual battery. These persons, it is presumed, are more alert to kinesthetic experiences than any other group due to their particular concern with postural matters. Other groups with specific experiences or with specific lacks in sensory equipment will be investigated, among these being persons with dead labyrinths and a group of near blind individuals.

Two reports are being prepared for publication, one concerning the role of visual factors in the maintenance of upright posture and one dealing with the ataxiameter technique used in the investigations.
Estimated Completion: Indefinite

NR-151-248 Measurement of Interest Patterns of Naval Personnel (Unclassified)

Contractor: University of Minnesota, Minneapolis, Minnesota
Contract: N6-ori-212, Task III, (10/15/46 to 10/14/48)
Investigator: K. E. Clark

This project will make an attempt to develop a scale which will provide an objective and quantitative measure of the interests of enlisted personnel, and which may be used in assigning these personnel to training and duties. The project will develop an interest scale, and will then administer it to civilian high school seniors, to persons in several civilian occupations, and to enlisted Naval personnel who have made progress in one of several rating groups. By comparison of responses of persons in different occupations, scoring keys will be

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developed to show the extent to which a given person's interests are similar to those of a person making a success in a like occupation. This research will be similar to that which resulted in the Strong Vocational Interest Blank, except that emphasis will be placed on Naval enlisted rating groups, and related sub-professional civilian occupations, rather than on the occupational fields usually entered by college graduates.

Progress to 6/30/48: An interest scale has been developed and administered by mail to 3,763 persons in eight different occupational groups which include electricians, painters, sheet metal workers, plasterers, cement workers, printers and allied trades, milk wagon drivers, bakers and confectioners, and miscellaneous trades. Returns are not complete, but to date over forty per cent returns have been received. Ten people have worked on the project, most of them were graduate assistants, some part time and some full time.

Data from Navy rates are being obtained through the cooperation of the research facility of the Bureau of Naval Personnel. These data are presently being analyzed. The entire male student body of a local high school is also being tested, and day and night school apprentices are being tested in the St. Paul area.

Preliminary analysis of the data obtained from four of the above occupational groups, namely printers, electricians, painters, and milk wagon drivers, indicates that less than five per cent of individuals score above the median score obtained by individuals of another occupational group. If letter grades were assigned in terms of those used in the Strong Vocational Interest Blank approximately 10% of employed adults would score A on keys for occupations in which they are not engaged, whereas 75% would score A on their own occupational keys.

Plans are being made for increasing the scope of the work by sampling more occupational groups and by obtaining additional cases in the groups already under study.
Estimated Completion: Indefinite

NR-151-345 Identification of Persons Unfit for Military Service (Unclassified)

Contractor: University of Maryland, College Park, Maryland
Contract: N7-onr-397, Task III, (12/1/47 to 11/30/48)
Investigator: C. N. Cofer

This project will attempt to correlate the responses given on personality tests with physiological changes associated with emotional upsets occasioned by giving "right" or "wrong" responses. Records will be made of heart, breathing, blood pressure, etc., during the administration of the tests, and changes will be noted. These changes will be related to the items answered at the time the disturbances occurred, and the subjects will be interviewed concerning their reasons for the responses they gave. In this way, it will be possible to determine the degree to which falsification occurred as well as the reasons for the falsification.

Progress to 6/30/48: Data were obtained from 25 subjects who have responded to items from the Minnesota Multiphasic Personality Inventory while simultaneous recordings were made of the electro-dermal response. Each of these subjects was subsequently interviewed to determine the "emotional significance" of the personality test items. These data are being analysed and will be completed by the end of the next quarter.

A second study was designed to determine how much effect conscious malingering would have on scores made on the above mentioned inventory and whether malingered records could be differentiated from honest records by the study of several special scores routinely available on this inventory. Control subjects took the test twice honestly and the experimental subjects took the test either with an attitude of positive malingering or with one of negative malingering in addition to taking the test once honestly. Analysis of the data will be made during the coming quarter and will be directed at the following problems: Gross score changes from malingering; detection of malingering by study of the K and L scales as well as by other

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methods; and item analysis in order to determine whether certain items are more unreliable than others and whether certain items are more susceptible to malingering than others.
Estimated Completion: Indefinite

NR-151-698 Experimental Studies on Group Productivity and Communication Within Groups (Unclassified)

Contractor: University of Michigan, Ann Arbor, Michigan
Contract:
Investigators: D. Cartwright, R. Lippitt

The purpose of this project is to study group productivity during a three week training laboratory for administrators, training officers, etc. Techniques of conference leadership, staff relations, and training procedures will be examined. Intensive studies will be made of: (1) Differential capacities of different personality types to contribute to productive group thinking; (2) leadership techniques most effective in creating efficient committee process; (3) potentialities for change toward higher levels of productivity of different types of group members. A small study of productivity is being conducted to develop techniques for studying the relation between the "we feeling" and group productivity in industrial and Naval establishments.

Progress to 6/30/48: This project represents a continuation of studies undertaken under project number NR-153-267. No progress has been reported under this new project number.
Estimated Completion: Indefinite

STUDY OF ABERRANTS

NR-152-040 Investigation of Fatigue Elements and Their Relation to General Psychoneurotic Function (Unclassified)

Contractor: Harvard University, Cambridge, Massachusetts
Contract: N5-ori-76, Task VIII, (7/1/46 to 3/31/49)
Investigator: R. S. Schwab

The purpose of this project is to determine if fatigue symptoms are (1) muscle fatigue; (2) a basic chemical or biophysical imbalance or dysfunction; or (3) a psychological component of a more generalized personality reaction. A group of Naval subjects whose complaint is fatigue will be studied by means of appropriate tests. In addition a group of controls free from these fatigue symptoms will be studied.

Progress to 6/30/48: This study reports the observations of quantitative ergographic studies including electromyograms on the effect of prostigmine injections (1 mgm to 1-1/2 mgms) in 10 normal control subjects; in 10 patients with pyschoneuroses; and in 10 proven cases of myasthenia gravis.

It was shown that prostigmine has little effect on the normal controls as far as muscle power goes. It reduces the muscle power in psychoneurotics by a small but definite amount in the majority, and in some, by a considerable amount (this is due, in part, to the increased sensitivity of these individuals to this drug and to side effects). The effect in myasthenia gravis is a marked increase in efficiency and power that is well known and has been clearly proven.

In most of these determinations, there were lactic acid measurements on the blood. The resting lactic acid values are obtained before the exercise, and the lactic acid values are determined three minutes after the exercise and 15 minutes after the exercise. In most of the neurotics, the lactic acid produced is higher than in the normal and goes down to its previous

STUDY OF ABERRANTS, NR-152-040 (Con.)

level more slowly. It is not only higher than in normals, but the amount of work is less. In myasthenics, on the other hand, the amount of lactic acid produced is directly proportioned to the amount of work done and the shape of the curve is the same as the normals. After prostigmine, there is a reduction in the amount of work done in the normals, but the lactic acid produced is about the same. In myasthenics, the amount of work increases, as well as the lactic acid. In psychoneurotics, the work-lactic acid disassociation is greater.
Estimated Completion: Indefinite

NR-152-237 Investigation of the Effect of Anoxia On the Electro-Encephalagram and on Behavior of Patients with Combat Fatigue (Unclassified)

Contractor: Harvard University, Cambridge, Massachusetts
Contract: N5-ori-76, Task XIV, (3/1/47 to 2/28/49)
Investigator: J. E. Finesinger

The purpose of this project is to (1) investigate, in a series of patients with combat fatigue and psychoneurosis, and in a series of normal control subjects, the affects of breathing low oxygen upon the E.E.G., heart rate, ventilation, verbal and gestural activity, and motor performance; (2) investigate the role of psychological and clinical factors in anoxia tolerance; and (3) test the affects of various physical and chemical agents in combating the affects of low oxygen as reflected in the functions described in (1).

Progress to 6/30/48: Studies have been made which deal with the affects of anoxia upon the electroencephalagram, interaction chronograph, adrenal cortical hormones, pulmonary ventilation, heart rate, blood pressure, and certain psychological tests in patients and healthy adult control subjects. The patients were from the U. S. Naval Hospital and the Massachusetts General Hospital; the controls were obtained from the Naval receiving station and from hospital personnel. Observations indicate that the inhalation of mixtures low in oxygen brings about the gradual slowing of brain waves as measured manually and by analysis by the Walter electronic analyser. These changes are neutralized by the inhalation in addition to the mixture of small amounts of CO_2--, 3 and over. Cytochrome C does not neutralize the changes. Low oxygen is associated with a decrease in verbal and gestural activity. Patients show significantly greater changes than controls. Breathing low oxygen is often, but not always, associated with an increase in pulmonary ventilation, an increase in heart rate, a slight increase in systolic blood pressure, and a decrease in pulse pressure. Low oxygen is associated with an increase in adrenal cortical hormone as measured by its depressing effect on the circulatory lymphocytes, and eosinophils and a slight increase in urinary 17 keto-steroids.
Estimated Completion: Indefinite

NR-152-301 Research on Process of the Administrative Conference (Unclassified)

Contractor: University of Michigan, Ann Arbor, Michigan
Contract: N6-onr-232, Task VII, (9/1/47 to 8/31/48)
Investigator: D. Marquis

This project number has been changed to NR-153-301.

NR-152-431 Psychiatric Research (Unclassified)

Contractor: Washington School of Psychiatry, Washington, D. C.
Contract: N6-onr-521, Task I, (1/1/48 to 6/30/49)
Investigator: H. S. Sullivan

STUDY OF ABERRANTS, NR-152-431 (Cont.)

The purpose of this project is to make detailed personality studies of a number of Naval officers and men who were outstandingly successful in their military careers. The data secured will be used to improve methods for the selection and training of combat leaders; the development of new therapeutic techniques for rehabilitation; and new procedures for the prevention of combat neuroses.

Progress to 6/30/48: This project has been delayed due to difficulties in obtaining subjects, and no report has been issued.
Estimated Completion: 30 June 1949

HUMAN RELATIONS

NR-153-123 A Study of Leadership in Naval Establishments (Unclassified)

Contractor: Ohio State University, Columbus, Ohio
Contract: N6-ori-17, Task III, (6/1/46 to 4/30/49)
Investigator: C. Shartle

The purpose of this project is: (1) To conduct a study of leadership in Naval establishments by employing job analysis methods, sociometrics, and individual testing for leadership activities in relation to organization structures; (2) to determine the value of the various methods of appraising leadership ability, and derive principles and methods which may be applied by Naval officers in evaluating the leadership requirements of various group situations; and (3) to develop information and techniques which may be useful in the selection, training, transfer, and assignment of personnel serving in leadership capacities, including leadership positions in civilian life.

Progress to 6/30/48: Naval staff organizations have been studied in three centers and analyses of the relationships among rank, department, time-distribution, R.A.D., and staff methods have been completed.

Revisions have been made in the original interview schedule, extending it and emphasizing these aspects of leadership: Methods of working with staff, qualifications, internal communications, and group morale. The project has also cooperated in the collection of new data on factors associated with leadership and personality, in a study involving 310 persons of college age.

New approaches to the objective quantitative study of internal communications are being made and will be reported in the near future.

The project has benefited from the work of several graduate students who have completed either Ph.D. theses or other papers on some aspect of this research. Some of these are related to the R.A.D. scales, a study of internal attitude communication and leadership, and field testing of both the old and revised forms of the responsibility, authority, and delegation scales.
Estimated Completion: Indefinite

NR-153-263 Cultural Study of American Minorities of Foreign Origin (Unclassified)

Contractor: Columbia University, New York, New York
Contract: N6-onr-271, Task III, (4/1/47 to 3/31/49)
Investigator: R. Benedict

The purpose of this project is to improve techniques for handling and selecting personnel of foreign origin with widely diverse cultural backgrounds. It is planned to examine historical, economic, political, and literary studies that have bearing on the habits of the groups

HUMAN RELATIONS, NR-153-263 (Cont.)

studied, and to integrate this material with data obtained through interviews and observation. A careful recording of behavior in analogous situations, of interviews, tests, psychiatric data, etc., analysis of novels, cartoons, plays and action pictures, and other materials will also be made. On the basis of such material, national habits of thought and behavior become more intelligible and relations with these groups can be more intelligently planned.

Progress to 6/30/48: Work begun last year on French, Czech, Chinese, and Russian cultures has been continued and studies of Syrian cultures have been recently started. Seven papers have been prepared for publication and will appear in various journals during the coming months.

Studies of quarreling patterns, attitudes toward the stranger, and friendship patterns for intra-project use have been prepared and will later be combined with other studies. Another cross cultural topic, on which work is starting, is housing in relation to culture behavior.

Estimated Completion: Indefinite

NR-153-267 Experimental Studies on Group Productivity and Communication Within Groups (Unclassified)

Contractor: Massachusetts Institute of Technology, Cambridge, Massachusetts
Contract: N5-ori-78, Task IX, (12/1/46 to 6/30/48)
Investigators: D. Cartwright, R. Lippitt

The purpose of this project is to study group productivity during a three-week training laboratory for administrators, training officers, etc. Techniques of conference leadership, staff relations, and training procedures will be examined. Intensive studies will be made of: (1) Differential capacities of different personality types to contribute to productive group thinking; (2) leadership techniques most effective in creating efficient committee process; and (3) potentialities for change toward higher levels of productivity of different types of group members. A small study of productivity is being conducted to develop techniques for studying the relation between the "we feeling" and group productivity in industrial and Naval establishments.

Progress to 6/30/48: This project has been terminated. A new contract is being negotiated with the University of Michigan. Further studies will be conducted under project number NR-151-698.

Analysis of the data from a student-veterans housing project dealing with the affects of communication and group structure on the development of group standards has been completed and the technical report is nearing completion. It will contain chapters headed (1) The Study of Group Formation and Functioning; (2) Description of a Housing Community; (3) The Ecology of Group Formation; (4) The Growth of the Tenant Organization; (5) The Development of Group Standards; (6) The Social Status of the Deviate; (7) The Process of Communication; (8) Patterns of Group Structure; and (9) A Theory of Group Structure and Group Standards.

Analysis of data from a F.P.H.A. housing project dealing with the effects of communication on attitudes and the spread of attitudes has been advanced, and preliminary work has been started to develop techniques for studying in the laboratory the process of social communication and its effects. Once these techniques and measuring instruments are perfected a number of theories developed from the preceding studies will be put to laboratory test.

In the studies of group productivity and change of group productivity work has proceeded on five related studies; (1) the training laboratory; (2) a laboratory experiment on directive and non-directive training; (3) an experimental comparison of the affect of cooperation and competition on group productivity; (4) a field study of cohesiveness of work groups in a factory; and (5) a laboratory experiment stemming from this industrial study.

Estimated Completion: Indefinite

HUMAN RELATIONS, (Cont.)

NR-153-272 Research on Fundamental Problems of Organizing Human Behavior (Unclassified)

Contractor: University of Michigan, Ann Arbor, Michigan
Contract: N6-ori-232, Task II, (3/1/47 to 4/30/49)
Investigator: R. Likert

The purpose of this project is to increase present knowledge of how human groups are organized and how men may be trained to make practical use of this knowledge. Intensive observations will be made of existing groups under normal conditions of operation. Using a wide variety of techniques, the research staff will seek to evolve or gain dependable information on such topics as how groups set up their objectives, what factors influence their success or failure in moving toward these objectives, and what forces tend to weld the group together or split it apart.

Progress to 6/30/48: The final report of the first study in this series is in preparation. It is a study of several hundred employees and their supervisors and managers in the home office of a large insurance company. In this company several sections of employees do comparable work. Some sections turn out more work per man-day than others. The kinds of human relations and other causes that produce this greater productivity were studied. Factors affecting job satisfaction were also studied.

The second study in the series is well under way in a large utility corporation. The third study, which is being conducted in a corporation manufacturing automobiles, is getting started.

A survey was made of ground school instructors attitudes toward their jobs at NATB Pensacola and the report has been submitted to the Chief of Naval Air Training. This study was done in conjunction with another project conducted at Pensacola which is studying the training program and its effectiveness.
Estimated Completion: Indefinite

NR-153-301 Research on Process of the Administrative Conference (Unclassified)
(Formerly 152-301)

Contractor: University of Michigan, Ann Arbor, Michigan
Contract: N6-onr-232, Task VII, (9/1/47 to 8/31/48)
Investigator: D. G. Marquis

The purpose of this project is to conduct basic research on the conference process related to group dynamics and the mechanisms involved in inter-personal behavior. It is hoped to derive answers to questions concerning the type of personnel which can be used to advantage in conferences and committees, what procedures facilitate the discovery and acceptance of new solutions to problems, and what types of material conferences deal with most effectively and least effectively.

The research will be divided into three parts: (1) Representative samples of conferences will be observed and analyzed; (2) hypotheses will be developed during this analysis; and (3) these hypotheses will be tested experimentally.

Progress to 6/30/48: A survey of administrative conference practices has been completed and progress has been made in the development of instruments in a cross-sectional study. Laboratory and field experiments have been set up to explore further aspects of conference process theory.

A complete survey of the literature concerning conference process has been compiled and two investigators have attended conferences in the Department of the Navy and other government offices and have interviewed many persons who have wide experience in conference management.

HUMAN RELATIONS, NR-153-301 (Cont.)

Four experimental conferences have been held and the data are being analysed. The development of category descriptions in the area of problem-solving behavior has been completed and the reliability of coders has been found to be .85.

A special experiment was conducted to test the hypotheses concerning the influence of goal congruence on conference outcome. The data are in the process of being analysed.

Arrangements have been made with the Michigan Unemployment Compensation Commission to carry out field studies of a quasi-experimental nature during the coming months. This will be directed at an understanding of some pre-conference variables such as manager competence, pre-conferences cliques, and spread of participation.

Estimated Completion: Indefinite

NR-153-342 — Basic Studies of Leadership — (Unclassified)

Contractor: University of Rochester, Rochester, New York
Contract: N6-onr-241, Task V, (7/1/47 to 6/30/49)
Investigator: L. Carter

The purpose of this project is to study the leadership situation at a primitive level for the purpose of determining the factors which operate to produce a leader. Small groups will be asked to work on a common task which requires cooperation between the participants. There will be a diversity of intellectual, mechanical, and social tasks. Leaders will be assigned in some instances, not in others. Comparisons will be made of work output, cooperativeness, efficiency, and solidarity of the groups under these various conditions, etc.

Progress to 6/30/48: Fifty pairs of subjects selected from two high schools in Rochester have completed the work tasks assigned in the experimental situation. These consist of a task which requires mechanical manipulation, clerical aptitude, and intellectual performance. Each of the subjects has been given a battery of tests; and criterion data have been collected from the high schools, consisting of marks, extra-curricular activities, socio-economic status, etc.

Analysis of the recorded conversations obtained during the experiments has been completed, and a report will be submitted in the near future.

A paper was read at the Easten Psychological Meeting which indicates that "Leadership is Specific to the Situation", but that it is possible in this experiment to predict with some degree of accuracy which of the pair of subjects will assume leadership in a second situation after they have been observed in one situation.

Estimated Completion: Indefinite

NR-153-348 — The Effect of Media of Mass Impression on Public Attitudes and Behavior — (Unclassified)

Contractor: University of Minnesota, Minneapolis, Minnesota
Contract: N6-onr-246, Task IV, (9/15/47 to 9/14/48)
Investigator: R. Nafziger

Under this project investigations will be made of factors producing differences in readership and listnership habits among segments of the population. The differences in readership of various content categories among elements of the population will be studied and an intensive study of individual differences in readership and listnership habits among individuals in various economic, educational, and age groups will be made, including pertinent tests of attitude personality, interest, knowledge and ability. In short the study will explore the question: What in the individual is related to his choice of media categories and what is the effect of exposure to various categories.

HUMAN RELATIONS, NR-153-348 (Cont.)

Progress to 3/31/48: A detailed report of the work conducted at the School of Journalism has been received. Much of the report deals with studies completed prior to the granting of this contract. Studies reported include effects of position, length; content upon readers of both sexes; socio-economic breakdowns of readership of the Minneapolis Sunday Tribune; and a summary and comparison of results of readership studies made by the Division during 1944-1947. These studies are being continued.
Estimated Completion: Indefinite

NR-153-363 The Measurement of Human Needs (Unclassified)

Contractor: Wesleyan University, Middletown, Connecticut
Contract: N6-onr-262, Task II, (5/1/47 to 12/31/48)
Investigator: J. W. Atkinson

Using a new projective technique, the investigator hopes to gain information relative to the relationship between motive and percept. Previous studies of projection have assumed certain relationships between the person and his projections without experimentally studying these relationships. This experiment will set up a controlled state of need, e.g. hunger, and will study the extent to which projections indicate the presence and strength of this need. Analysis of the projections will be made in order to determine precisely what is projected by people in a state of need (hunger, et al), the goal (food), the instrumental act (seeking food), the subjective state (hunger), etc.

Progress to 6/30/48: There have been four publications on the work of this contract. These are:

(1) McClelland, D. C. and Atkinson, J. W. "The Projective Expression of Needs. I. The Effect of Different Intensities of the Hunger Drive on Perception". Journal of Psychology, 1948, 25, 205-222.
(2) Atkinson, J. W. and McClelland, D. C. "The Projective Expression of Needs. II. The Effect of Different Intensities of the Hunger Drive on Tehmatic Apperception", Journal of Experimental Psychology.
(3) McClelland, D. C., Atkinson, J. W., and Clark, R. A. "The Projective Expression of Needs. III. The Effect of Different Intensities of Need Mastery on Thematic Apperception", technical report submitted to ONR, Dec. 3, 1947.
(4) Clark, R. A., McClelland, D. C. and Atkinson, J. W. "The Projective Expression of Needs. IV. The Relationship Between Objective Test Measurement and Thematic Measures of Need Mastery", technical report submitted to ONR Dec. 3, 1947.

One more report is under preparation and will be issued during the summer.
Estimated Completion: Indefinite

NR-153-373 Field Evaluation of Materials on Leadership (Unclassified)

Contractor: University of Maryland, College Park, Maryland
Contract: N6-ori-147, Task II, (1/1/47 to 8/31/48)
Investigator: J. G. Jenkins

The purpose of this project is to improve leadership training courses at Naval Training Centers. Data on leadership will be collected and developed into a manual for use in a leadership course to be given in NROTC units at the Naval Academy, Annapolis. This material will be evaluated by measuring attitudes, opinions, and ideas before and after the presentation of the materials. Control groups will be used throughout, and follow up studies will be made, whenever possible, in later years to determine the effectiveness and permanence of the training procedures and materials.

HUMAN RELATIONS, NR-153-373 (Cont.)

Progress to 6/30/48: Data on leadership have been collected and compiled into a text which is at present in use at Annapolis. It is being given to the 1st class as a part of a leadership training course.

Four tests are being used in the evaluation study: (1) The Watson-Glazer Test of Critical Thinking; (2) The GW Social Intelligence Test; (3) A Social Situation Test, devised by the investigators; and (4) A Common Sense Test, also devised by the investigators. (This test is one concerning psychological superstitutions). These tests are being given to men who are taking the leadership course before and after the course and to others who are not taking the course at the same interval without the intervening course material.

Preliminary analysis indicates that there are significant changes in attitudes, information, and adaptiveness of thought in the various areas tested.

Estimated Completion: Indefinite

Human Ecology

ENVIRONMENTAL PHYSIOLOGY

NR-160-079 Quick Freezing of Precooked Foods (Unclassified)

Contractor: Cornell University, Ithaca, New York
Contract: N6-ori-91, Task VII, (6/1/46 to 6/30/48)
Investigator: W. A. Gortner

The purpose of this project is to study the types of precooked foods best adaptable to freezing preservation and also point up and investigate certain problems which need to be solved in the preparation, precooking and subsequent chilling, freezing, storage, thawing, and cooking of precooked frozen meals. Selection of attractive and successful menus will receive attention.

A second phase of these studies will investigate factors influencing rancidity in precooked meats such as pork. The effect of diet in altering fatty acid composition or antioxidant deposition will be studied as it bears on fat stability.

Time-temperature relationship in development of food poisoning and spoilage agents are being studied with a view to developing a "thawing indicator" and simple means of detecting undesirable amounts of microorganisms or their metabolic products in precooked frozen foods.

Progress to 6/30/48: Work on the development and storage of precooked frozen meals is continuing and a number of promising meal combinations have been developed. The need for storage at a maximum of 0° F. is indicated.

Studies on laboratory animals indicate that animal food fats may vary greatly in tendency to go rancid, depending on the nature of the fat and the amount of antioxidants in the diet.

Bacteriological studies indicate that a potential health hazard exists if precooked frozen foods are allowed to thaw for several hours before being consumed. Anaerobic fermentation of mannitol has proved a good presumptive test for potential food poisoning bacteria. Preliminary results in the development of an indicator which will show when frozen foods have been thawed to a dangerous point seem to be promising.

At this time it is not yet known whether or not this contract will be renewed.
Estimated Completion: Indefinite

NR-160-307 Function of Liver in Carbon Monoxide Metabolism (Unclassified)

Contractor: University of California, Berkeley, California
Contract: N7-onr-295, Task IV, (2/1/47 to 6/30/49)
Investigator: N. Pace

The purpose of this project is to study the role of liver in carbon monoxide uptake with the use of radioactive carbon employing isotope C^{11} or C^{14}. Studies are to be conducted on standardized liver brei in vitro. Measurements of CO concentration in the liver will be made in vivo while simultaneous measurements are made on various aspects of general circulation. Animals under study will be exposed to various concentrations of carbon monoxide in respired air. This fundamental approach is an effort to clarify knowledge concerning the body absorption of carbon monoxide.

Progress to 6/30/48: The specific activity of the C^{11} used in tagging CO is being increased by two methods, (a) by using proton bombardment rather than deuteron bombardment, and (b) by using pure boron 10 in the form B_2O_3 as the target material. Method (a) is expected to increase the yield of C^{11} by two, and method (b) by five; hence, an over-all factor of 10 may result. This should substantially improve the experimental possibilities of C^{11} in these studies.

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HUMAN ECOLOGY

ENVIRONMENTAL PHYSIOLOGY, NR-160-307 (Cont.)

The counting field efficiency for the tube and shield assemblies, currently being used for C^{11}, was measured experimentally and agrees well with a theoretically derived curve. This final result is somewhat different from the values given in the investigator's Status Report No. 1.

The rate of release of CO by human subjects was found to be slower with increasing age. The effect is approximately one per cent longer half time of desaturation with each increased year of age. The factor of age in treatment of individuals suffering from CO poisoning appears, therefore, to be of importance.

Estimated Completion: Indefinite

NR-160-615 Attraction of Flying Insects to Surfaces Treated with Residual Insecticides (Unclassified)

Contractor: University of Wisconsin, Madison, Wisconsin
Contract: N8-onr-60000, (5/1/48 to 4/30/51)
Investigator: R. J. Dicke

The purpose of this project is to investigate a theory that a combination of chemical attractants combined with residual insecticides (i.e., DDT) might induce insects to contact concentrated spray deposits on limited control areas or panels.

Residual insecticides are effective only when flying insects come to rest upon treated surfaces. The attraction of insects to limited areas treated with concentrated residual insecticides offers some rather unusual possibilities for more effective and economical utilization of residual insecticides for the control of several kinds of insects.

Progress to 6/30/48: No progress to report.
Estimated Completion: Continuing

ACCELERATION

NR-161-014 Physiological, Biochemical, and Anatomical Effects of Body Acceleration Relative to Pilot Position in High-Speed Aircraft (Unclassified)

Contractor: University of Southern California, Los Angeles, California
Contract: N6-ori-77, Task I, (4/9/46 to 10/30/50)
Investigator: D. R. Drury

Under this project the human centrifuge is being used for studies of physiological, biochemical, and anatomical effects of acceleration on the body relative to body orientation. The physiological problems include the mechanism involved in blood pooling, the dynamics of intracranial circulation and intracranial pressures, and the capacity of the cardiovascular sys

ACCELERATION, NR-161-014 (Cont.)

pulling effort. The involuntary pull of the subjects' arms, at one G, increases as the angles of the members increase in relation to the direction of G force, due to their own mass and leverage system.

The point at which increased pulling effort, as it approaches maximum, converts the arm system from a jointed G-responsive leverage system to an apparently rigid, non-jointed functional condition, remains to be determined.

Involuntary pull for two arms, at one G, was found to exceed 10 lb, in more than 50% of the arm angles tested in these experiments. This involuntary pull may exceed the force per G required by a pilot to "pull G", which is currently engineered into aircraft controls. Thus it is possible for apparent "stick reversals" to originate in the pilot and not in the aerodynamic forces acting on the control surfaces of the airplane. Due to the ease of unconsciously exerting mild corrective muscular forces at low G, to balance the involuntary pull, stick reversals of anatomical origin may not be apparent to the pilot until high G forces are encountered. Confusion to the pilot can result.

The increased intravascular pressures, developed during exposure to increased acceleration, cause a rapid and significant outward filtration of fluid from the circulation.

At peak concentration there is evidence of significant leakage of protein from the circulation, as calculated from the hematocrit and plasma protein values.

Estimated Completion: Indefinite

NR-161-058 Physiological Reactions to the Stresses Imposed by High-Speed Aircraft (Unclassified)

Contractor: University of Pennsylvania, Philadelphia, Pennsylvania
Contract: N6-onr-249, Task IV, (4/1/46 to 6/29/49)
Investigator: H. C. Bazett

Stresses likely to be imposed in aircraft include acceleration and exposure to abnormal atmosphere pressures. Laboratory study is therefore being directed to the analysis reactions to very brief application of such stresses. Such analysis demands new methods. The Lilly electrical capacity manometer has been adapted so that blood pressure may be recorded directly, utilizing a plastic tube connection with the artery. The tube is of about 0.45 mm external diameter and may be introduced into vessels through a hypodermic needle without incision. Thus the subject can move without danger of a needle either piercing the artery or being withdrawn inadvertently during the experiment. This procedure should greatly facilitate recording of blood pressure on a centrifuge. Present work is directed towards obtaining accurate records under the conditions of a tilt-table. The manometer cannot as yet be moved vigorously without the appearance of artifacts.

Progress to 6/30/48: The electrical manometer has been improved and has been in constant use for the past six months. The instrument has been adapted for use with the Brush ink-writer which has greatly increased its usefulness. The amplifier has also been improved so that the instrument may now be moved without the introduction of artifacts. Further modification is being attempted in order to make the manometer smaller.

The plastic tube technique has been adapted for use with thermocouples which have been enclosed in the tubing and inserted in man into various vessels including the brachial, radial, femoral, dorsalis pedis, and common iliac arteries. The temperatures so measured are being reported in papers in the course of publication.

Estimated Completion: Indefinite

NR-161-059 Acceleration and Anoxia (Unclassified))

Contractor: University of Virginia, Charlottesville, Virginia

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HUMAN ECOLOGY

ACCELERATION, NR-161-059 (Cont.)

Contract: N6-ori-116, Task I, (6/1/46 to 6/30/49)
Investigator: S. W. Britton

Under this project the effects of negative and positive acceleration on blood flow and blood pressure in carotid and femoral arteries are being tested at forces one to six G, and for five to 10 sec. Monkeys, dogs, cats, and rats are being used in these experiments.

Influence of high deceleratory forces between 100 to 1000 G, of very brief duration, are being studied using a suspended sledge hammer type device, 11 ft long. Respiration, blood pressure, E.C.G., and possibly E.E.G. are being recorded.

Changes in circulation (B.P., E.C.G., etc.) under severe anoxia and on giving CO_2, O_2, glucose, etc., are being studied.

In explosive decompression tests between 0 to 80,000 ft altitude equivalent, respiration, circulation, and pathology, are being studied. Consideration is also being given to the physical principles involved.

Progress to 6/30/48: A 20 ft diameter heavy steel centrifuge with blood pressure and other devices attached, for determining effects of accelerations up to 50 G's, has been described. Results of tests on a large number of monkeys, dogs, and cats have been received.

Acceleration of the heart rate (five to 30 beats) on exposure to positive G forces shows a proportionality to the intensity and time of application of the force. Under prolonged exposure (five to 10 min, three and four G's) bradycardia and irregularity set in, but recovery was rapid on stopping the centrifuge. Negative G forces produced no significant change in heart rate (dog).

E.C.G. records derived from the left precordium showed marked RS_4 voltage reduction during positive G exposure, while increase in voltage was shown by the right chest record obtained simultaneously. Experiments indicated heart position and blood content were the responsible factors.

Carotid (or brachial) blood pressure fell sharply under positive G forces, and the femoral pressure rise was even more abrupt. Arterial pressure changes (carotid, brachial, femoral) showed a linear relationship to applied G stresses. A given change in acceleration produced the same unit change in arterial pressure at all force levels up to six G.

The carotid pressure of monkeys under G forces was affected significantly less than that of cats and dogs. At forces between one and six G's, monkeys showed about one G advantage over the latter animals.

Changes in pressure in a hydrodynamic model under acceleratory forces were similar to arterial pressure changes found in animals.

A carotid sinus reflex response affecting arterial pressure appears to be initiated six to eight sec after starting exposure to high G forces.

Blood flow reductions in the carotid artery occurred within a second or so after starting the centrifuge, and showed a proportionality to the acceleration applied. Under a force of three or four G's for 10 sec, flow in the carotid or brachial vessel usually reached the zero level.

Transverse forces (across the body) of four to eight G's produced moderate increases in heart rate and carotid pressure and flow.

On starting centrifugation high-voltage low-frequency "delta" brain waves appeared in 75% of the monkeys tested, within a second or so; sometimes they disappeared toward the end of a 10 sec run, and appeared again when the centrifuge stopped. The probability of occurrence of "deltas" was almost 1.0 on exposure to six G's for 30 sec.

Attempts to produce conditioned reflex responses and "experimental neuroses" by exposure to high G forces, applied frequently over several months, were negative.

Considerable protection against G forces was afforded by a belt or cuff around the abdominal area inflated usually up to 300 mm. Hg pressure. Survival time, E.C.G. and E.E.G., values, and arterial pressure and flow levels were all significantly affected. The advantage afforded by abdominal belt pressure varied between one and three G's, inversely to the severity of the exposure. Adrenalin gave moderate and very brief protection.

ACCELERATION, NR-161-059 (Cont.)

It was demonstrated that the reduction in carotid pressure observed during exposure to acceleratory forces (monkey, dog; one to four G, five to 30 sec) may be considered as a blood pressure deficiency area (pt_p). Thus, one may determine the carotid arterial pressure deficiency as a function of time. This area was found to be directly proportional to the intensity and duration of centrifugation (gt_g), and for a given acceleratory area the circulatory deficiency area was a constant.

Monkeys were found to be much more resistant to acceleration than dogs. In the monkey the arterial pressure deficiency areas on exposure to one, two, and four G were only about half as great as those in the dog; further, the recovery areas (rebound) were marked in the former and usually absent in the latter case.

A comparison of dog and monkey responses under positive and negative G forces also indicated that circulation through the cerebral tissues was maintained better in the anthropoid type. The differences in response may be referable to the different stance and thus the reflex development of the two animal types.

Estimated Completion: Indefinite

ARCTIC BIOLOGY

NR-162-218 Encyclopedia Arctica (Unclassified)

Contractor: Stefansson Arctic Institute, Inc., New York, New York
Contract: N6-onr-265, Task I, (12/1/46 to 12/31/50)
Investigator: V. Stefansson

The purpose of this project is to compile an encyclopedia of the Arctic, the sub-Arctic and related subjects. This will include the history, the natural conditions, and problems associated with living and operating in the Arctic.

Progress to 6/30/48: The total wordage to date under all heads is 915,639. Arrangements have been made with a large number of contributors for further articles in all classifications. Contributions during the next few months should be especially strong in natural sciences, botany, zoology, etc.

Because of the great amount of field work which was carried on in the Arctic during the year 1947, arrangements for most of the articles on the technical branches were postponed, so that as much recent information as possible could be included. Plans have been made for securing many of these scientific data. High on the list are engineering, medicine, and physiology, meteorology and climate, mechanical forces, and new techniques.

Estimated Completion: Indefinite

(Unclassified)

NR-162-295 Bibliography on the Arctic

Contractor: Arctic Institute of North America, New York, New York
Contract: N7-onr-367, Task II, (6/1/47 to 3/31/49)
Investigator: A. L. Washburn

The purpose of this project is to compile a partially annotated and thoroughly cross-indexed bibliography of Arctic literature.

Progress to 3/31/48: For full effectiveness of the Bibliography, attention is directed especially to Russian, Scandinavian, and to the parts of English language publications, whose content is not otherwise accessible to research workers through library catalogues and indexes. The variety of subject matter entails a great number of index headings, therefore analysis and indexing were slow at first. However, they are gradually increasing in speed as the index heads are developed.

ARCTIC BIOLOGY, NR-162-295 (Cont.)

Terrain Studies of the Northeastern Arctic: Toward the end of July, 1947, Dr. T. T. Patterson of Trinity College, Cambridge University, spent two weeks on Southhampton Island examining the contact between the Palaeozoic limestones and the Archaean crystallines. The fossils collected are being studied by palaeontologists of the Canadian Department of Mines and the University of Western Ontario.

Experiments were carried out in the use of aerial colour photography to determine the possibility of elucidating the character of the major rock structures. There are indications that this method may be of value in the analysis of superficial deposits.

Extensive additions were made to the existing map of the coastline of Pelly Bay and the southerly limits of the Palaeozoic sediments of Simpson Peninsula were more accurately placed.

Mammalian Population Studies of Northern Canada: This project has been outlined as providing a reference work in which as much detailed and accurate information as practical would be made available and indexed for ready reference. The status of this reference work consists of a file of 576 titles, cross-indexed and where necessary, abstracted, in addition to a file already in existence, and 200 pages of manuscript (about 40,000 words) prepared to cover 20 of the 77 species occuring.
Estimated Completion: Indefinite

NR-162-411 Arctic Biology, Colias (Unclassified)

Contractor: Arctic Institute of North America, New York, New York
Contract: N7-onr-367, Task I, (4/1/47 to 3/31/49)
Investigator: W. Hovanitz

The purpose of this project is to make an analysis of population structure, gene frequencies and hybridization of Arctic and sub-Arctic species of Colias (a genus of butterflies). The study, while dealing directly with Colias, is of basic interest since the genus has species ranging from tropics to 82° north latitude. It should reveal pertinent data on the manner in which biological populations of an organism become adjusted to differing environments. The correlation of biotic and climatic characteristics, on the basis degree of natural hybridization and transference of colar genes, can be done on statistically valid numbers by using this genus.

Progress to 6/30/48: During the past few months a collection of data from the major museums of North America has been under way as an adjunct to the field work which has been carried out. The frequencies of the W gene in many populations have been determined in a rough way from these collections.

It has been found almost impossible to differentiate four species of Colias in the Arctic of the Yukon and Alaska on morphological grounds. Further field work is therefore required. The differentiation is largely physiological in nature.

Plans are being made to analyze the field populations of five species of Colias in Yukon Territory, adjacent Alaska and northwest territories during the present season.

It is noted that the nature of the physiological adaptation to the environment of these Colias requires more complete control of the environmental factors such as temperature, and humidity than are at present available for these studies.
Estimated Completion: Indefinite

NR-162-429 Investigation of the Physiological Basis of Orientation of Migratory Birds in Arctic and Sub-Arctic Regions

Contractor: Cornell University, Ithaca, New York
Contract: N6-onr-264, Task IX, (5/30/47 to 1/31/49)
Investigator: D. R. Griffin

ARCTIC BIOLOGY, NR-162-429 (Cont.)

The purpose of this project is to investigate the physiological basis of orientation on the part of migratory birds in Arctic and sub-Arctic regions. The basic biological problem is one of sensory physiology -- what sense organ tells the bird in which direction it should fly? In the Arctic practically all species are migratory, and phenomenon of bird migration reaches its highest development. The work will be divided into three phases: (1) Preliminary work with gannets on the East Coast on the shores of the Gulf of St. Lawrence; (2) operations at Point Barrow studying the golden plovers; and (3) completion of work and analysis of results at Cornell University.

Progress to 6/30/48: Spring and summer studies of gannets, conducted in the Gulf of St. Lawrence proved valuable, not only because of basic data regarding the migration of these birds, but also for the validation and testing of equipment which was later transferred to Point Barrow for use at the Barrow Science Station.

Airplane observations of gannets showed that these birds find their way home from unknown territory by a process of exploration. The more general implications of these observations are that birds do not have any special sensory mechanism such as a sensitivity to the earth's magnetic field, and that their methods of navigation are based on sensory equipment common to all higher vertebrates, and thus presumably available, if properly understood and exploited, to men who are forced to rely on rough and ready means of orientation.

More experimental evidence is being obtained in order to substantiate further the above observations.

This work is coordinated with the general work on metabolism being carried out under the direction of Doctor Laurence Irving under project NR-162-430.
Estimated Completion: Indefinite

NR-162-430 Physiology Basic to the Acclimatization of Life to Arctic Environments (Unclassified)

Contractor: Swarthmore College, Swarthmore, Pennsylvania
Contract: N7-onr-380, Task I, (9/1/47 to 11/1/48)
Investigator: L. Irving

Under this project an investigation will be made of the metabolism of Arctic cold-blooded animals in comparison with the metabolic activity of temperate and tropical forms. A study will be made of the rate of the loss of heat from the surfaces of Arctic warm-blooded animals and of the insulation and vascular adjustments which conserve heat and maintain the temperature of the body. Measurements will be made of the metabolism of small Arctic hibernating mammals, and of migratory animals before departure from the Arctic and after their return.

Progress to 6/30/48: It was found that some warm blooded animals in the Arctic appear to be quite unaffected by exposure to low temperatures. Caribou, reindeer and Dall's sheep are not observed to seek shelter and are not known to suffer from exposure to Arctic low temperature and wind. Polar bears, wolves, moose, ptarmigan and foxes are not apparently affected by exposure, but at rest are sheltered in snow. Dogs are said to show dislike for exposure to temperatures below -40°, but no cases are reported in which healthy dogs accustomed to the Arctic climate have frozen. There is no question, however, that these dogs seek and enjoy warm housing.

In these animals the insulation afforded by fur and feathers is evidently sufficient to maintain suitable operating temperatures without undue expenditure of energy.

Certain small animals, such as weasels, lemmings, and mice take shelter from wind beneath the snow. It is probable that in their burrows moderate temperatures can be maintained, and that they thus avoid stress of extreme low temperatures.

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ARCTIC BIOLOGY, NR-162-430 (Cont.)

Studies upon insulation have been extended. Insulation is measured as the reciprocal of the electrical power required to maintain a plate at 37° between two layers of fresh skin against an outside temperature of 0°C. Insulation is approximately proportional to thickness of fur.

It is suspected that exposed areas such as the hooves, feet, legs, ears, and eyes are relatively poorly insulated, but it is likely that these tissues are preserved in part at the expense of metabolic heat. It is also suspected that the exposed tissues are able to operate steadily at lower than body temperature.

Wind, measured at about 17mph induced by a fan, increased the rate of heat loss differently in the different animals, but the order has not yet been clearly related to measureable properties of the fur or known habits of the animals.

Areas of subcutaneous fat obtained from reindeer and blubber of ringed and bearded seals were inferior in insulation to an equivalent thickness of fur or feathers. In still air the insulation provided by the blubber was roughly half that of the same thickness of fur. In none of the land animals does subcutaneous fat appear to be an important insulator. In most of the land animals the fat is unequally distributed, being frequently thickest over the hind quarters.

In studying the metabolism of cold-blooded animals at temperatures above freezing, it was found that the resting metabolic rate of Arctic animals at 0° corresponded with those known for a few animals of temperate regions at 10 to 15°.

Estimated Completion: Indefinite

NR-162-586 Peabody Aleutian Expedition (Unclassified)

Contractor: Harvard University, Cambridge, Massachusetts
Contract: N5-ori-76, Task XXIII, (5/1/48 to 6/30/49)
Investigator: J. B. Brew

The purpose of this project is to investigate physical and cultural adaptations in response to particular environment.

Medical studies will include: (1) Blood group (A, O, B, AB, N, and Rh); (2) carries occlusion; (3) tooth composition (analyses to be made in Boston); (4) cholesteral blood level; (5) cardiovascular studies; (6) blood chemistry; (7) food analyses; (8) BMR; (9) anthropometry; (10) visual field; (11) Rorschach; (12) thematic aperception; and (13) Horn-Hellersberg tests.

In addition, a folio on each Aleutian Island will be attempted and should include: Geneology, life history, medical and dental history (including tests above), occupation, economic welfare, attitudes toward white men (Americans and Russians), attitude to United States Government.

Progress to 6/30/48: No progress to report.
Estimated Completion: June 1949

NR-162-671 Distribution and Ecology of Arctic Marine Organisms (Unclassified)

Contractor: California Institute of Technology, Pasadena, California
Contract: N6-onr-244, Task XV, (6/1/48 to 6/30/49)
Investigator: G. E. MacGinitie

The purpose of this project is to make a survey of marine forms in the Point Barrow region and to complete, wherever possible, the distribution picture between the Atlantic and the Pacific. This will afford two distinct features:

(1) The added knowledge of marine forms to permit hydrobiological analysis of the Arctic sea, and

(2) determination of available animals for further study of physiological aspects of the Arctic.

ARCTIC BIOLOGY, NR-162-671 (Cont.)

Progress to 6/30/48: No progress to report.
Estimated Completion: 1949

NR-162-683 Immunology and Blood Chemistry of Arctic Animals (Unclassified)

Contractor: California Institute of Technology, Pasadena, California
Contract: N6-onr-244, Task XVII, (6/1/48 to 12/31/48)
Investigator: D. H. Campbell

The purpose of this project is to study immunology and blood chemistry of Arctic animals.

The immunological problems to be considered are (1) the rate of antibody formation in warm-blooded animals under Arctic conditions and in particular the effect of dormancy and hibernation on antibody formation, hypersensitivity, and immunity; (2) anaphylactic and skin reactions in hypersensitive animals; and (3) a study of blood types of local animals and their relation to similar species of animals in the temperature zone.

The blood chemistry problems to be considered are (1) the physical properties of blood proteins of Arctic animals, such studies would involve gross properties such as viscosity, pH, protein and lipid concentrations, and the physical properties of serum proteins such as molecular weights, electrophoretic properties, and stability toward denaturing agents; and (2) the physical properties of erythrocytes with particular emphasis on fragility, stability, and conditions of intracellular hemoglobin.

Progress to 6/30/48: No progress to report.
Estimated Completion: 3 June 1949

NR-162-684 Tissue Metabolism of Arctic Tissue (Unclassified)

Contractor: Stanford University, Stanford, California
Contract: N6-onr-251, Task XIV, (6/15/48 to 6/30/49)
Investigator: John Field, II

The purpose of this project is to study tissue metabolism in the Arctic.

Progress to 6/30/48: No progress to report.
Estimated Completion: Continuing

NR-162-688 Vitamin Content of Arctic Flora and Fauna (Unclassified)

Contractor: Creighton University, Omaha, Nebraska
Contract: N8-onr-603, Task I, (5/1/48 to 6/30/49)
Investigator: V. E. Levine

The purpose of this project is to study the vitamin C content of the plant and animal foods used by Eskimos. It is not generally known that Eskimos use plant foods in their diet. However, although these foods form an inconspicuous part of their diet, they are used at a time when there is a lack of fresh meat.

Progress to 6/30/48: No progress to report.
Estimated Completion: Continuing

HUMAN ECOLOGY

CLIMATE AND MAN

NR-163-023 Infrared Radiation and Thermal Measurement in Animal And Human Physiology, Medicine, Heating, and Ventilation (Unclassified)

Contractor: Cornell University Medical College, New York, New York
Contract: N6-ori-91, Task X, (6/15/46 to 4/30/49)
Investigator: E. F. DuBois

The purpose of this project is to investigate heat exchange by (1) a study of indoor radiation exchanges which will enable a more accurate estimation of heat loss between man and his environment; (2) a comparison of all the skin thermometers now available commercially, or which can be constructed in the laboratory, to determine their relative merits; (3) the procurement of infrared absorption spectra of biologically important compounds since these spectra are essential to the effective use of infrared methods in biological chemistry and medicine; (4) development work on rapidly responding radiation receivers with the intention of employing this method for the study of skin temperature changes during production of flash burns and other radiation burns; and (5) investigation of the physiology of hibernation and awakening in the marmot with the intention of throwing some light upon the functioning of vital organs and glands at low temperature and their greatly increased activity during recovery.

Progress to 6/30/48: A portable "ball radiometer" was completed for the use of the Navy and is now being calibrated. The radiation calibration was checked to within plus or minus one per cent and the anemometer calibration for wind velocity was completed, from 50 ft/min to about 2000 ft/min.

Comparative studies of the various skin thermometers on human skin have as yet been unsuccessful. This is due to the great variability in skin temperature within a very small skin area.

An investigation of the infrared spectra of tocopherals (Vitamin E) was completed and copies of the paper will be forwarded to ONR in the near future.

Studies of the ketosteroids and nucleic acids with the Baird Infrared Spectrophotometer are continuing.

Study of pain sensation and pain thresholds in patients with skin lesions has continued. It was ascertained that patients may perceive painful stimuli more intense than those on the normal skin.

The small animal calorimeter designed for the study of heat exchange was completed and calibrated. Experimental runs have been made on cats and marmots. The apparatus is also proving useful for studies of temperature regulatory mechanisms and peripheral blood flow. This is made possible by taking rectal and skin temperatures during the experimental period.

A constant temperature room is now in operation for animal heat regulatory studies in a wide range of temperature.

It is planned to produce lesions in the temperature regulatory center of the hypothalamus of cats in order to study their effect on heat loss and heat production.

Temperature regulation in aged women is being studied in the Russell Sage calorimeter in an attempt to discover whether or not the differences observed in the response to heat between men and women are carried beyond the menopause.

The construction of the housing around the Kold-Hold Walk-In Chamber is almost completed. An attempt to carry out investigations was made earlier in the year, but they proved to be impracticable without the protection afforded by this housing.

Estimated Completion: Indefinite

NR-163-052 Survival on a Raft

Contractor: Northwestern University, Evanston, Illinois
Contract: N6-ori-96, Task II, (5/1/46 to 6/30/48)
Investigator: J. S. Gray

CLIMATE AND MAN, NR-163-052 (Cont.)

Rats under conditions of water deprivation are being given diets with various proportions of fat, carbohydrate, and protein, and various proportions of tap and sea water. The objective is to establish the particular compositions of the solid and liquid components of the diet which are optimal from the standpoint of retarding weight loss and prolonging survival time.

Progress to 6/30/48: This project has been terminated. A final report is being prepared and will be distributed in the near future.

NR-163-173 Research in Environmental Medicine (Unclassified)

Contractor: University of Rochester, Rochester, New York
Contract: N6-ori-126, Task VII, (9/1/47 to 8/31/48)
Investigator: H. R. Brown, Jr.

Changes in environmental temperature and humidity have profound effects upon the physical dynamics of man. Approximately 80% of the world's population lives above 35° north latitude and in an area representing about 45% of the world's land. It is accordingly of great importance to know more concerning the human reaction to changing environments, and more particularly about the effects of cold. Changes in blood volume, oxygen consumption and utilization, and circulatory dynamics occur as a result of changing temperatures. It is the purpose of this project to make a complete study of these factors by means of newly adapted continuous recording types of apparatus. The knowledge thus obtained should bring about a better understanding of the action of such phenomena not only in normal subjects, but in subjects who are diseased. Special attention will be given to cardiovascular diseases.

Progress to 6/30/48: Means of recording various cardiovascular phenomena continuously have been developed. These are ballistocardiograph, electrocardiograph, pneumocardiogram, tachocardiogram, pressure-pulse waves, heart sounds, respiratory cycle, and right heart pressures.

The different reaction of the normal adult to the unit of cold stress points to an important measuring device of the physiological state.

Preliminary studies have been made on the use of curare and erythroidin in an attempt to lower body metabolism, and studies have been made of the use of environmental cooling in the therapy of hyperthermia.

It has been noted that interference with the human body's ability to lose heat will result in hyperpyrexia which may be fatal, unless effectively treated. In one patient the extreme elevation of the body temperature was lowered to the normal range and maintained at levels below 101°F, by placing the patient in a cold room. Thus a controlled environmental chamber is shown to be of value with especial reference to use in tropical and subtropical areas.

Estimated Completion: Indefinite

NR-163-177 A Physico-Chemical Investigation of Ion-Exchangers (Unclassified)

Contractor: University of Kansas, Lawrence, Kansas
Contract: N6-ori-164, Task VI, (2/1/47 to 6/30/49)
Investigator: D. N. Hume

The purpose of this project is to make a systematic study of the physico-chemical principles of ion-exchange systems. Examinations will be made of the equilibria between aqueous solutions of simple electrolytes and ion exchangers, such as the artificial zeolites and synthetic resins, in the hope of deducing laws governing such equilibria. Special studies of equilibria involving ions of different charge types will also be made.

CLIMATE AND MAN, NR-163-177 (Cont.)

Progress to 6/30/48: It has been shown that 6M hydrochloric acid, when used to condition the ion-exchange resin known as Dowex-50 is no more deleterious than 1 M hydrochloric acid.

A preliminary investigation of the silver-hydrogen ion exchange on Dowex-50 has been completed. Adsorption of silver ion on the solid resin has been found to take place, and has been evaluated semi-quantitatively. When the adsorption and the hydrolytic effects are taken into account, the equilibrium constant for the exchange occurring in solutions of unit ionic strength has been found to range in value from 16 to 22, varying with the equilibrium composition of the solid.

It is planned to study extensively the adsorption occurring when solutions of various concentrations of silver ion are placed in contact with silver resin, in an attempt to separate as far as possible the "hydrolytic" and adsorption effects from the true equilibrium exchange.
Estimated Completion: Indefinite

NR-163-203 The Production of Vegetables Under Total Artificial Radiation (Unclassified)

Contractor: Purdue University, Lafayette, Indiana
Contract: N7-onr-394, Task I, (6/1/47 to 5/31/48)
Investigator: A. P. Withrow

The purpose of this project is to investigate the possibility of producing fresh vegetables in Arctic areas, where winter light intensity and duration is insufficient for plant growth, and where electricity may be produced cheaply. Devotion of off duty hours to such activity may reduce the tedium and boredom of personnel in isolated areas and so reduce neuropsychiatric disorders.

The optimum of each of the following variables in the growth of vegetables under total artificial light will be studied: (1) Type of light, (2) Day length, (3) Light intensity, (4) Temperature, and (5) Nutritional elements as CO_2, minerals, vitamins.

Progress to 6/30/48: This project has been terminated. A final report is being prepared and will be distributed in the near future.

NR-163-270 Myelination and Other Factors in the Hypothalamus in Relation to the Maintenance of Body Temperature (Unclassified)

Contractor: Colorado Medical School, Denver, Colorado
Contract: N6-onr-231, Task IV, (4/1/47 to 3/31/49)
Investigators: A. R. Buchanan, R. M. Hill

Under this project cytochemical methods, both microscopic and microchemical histology, are being used in an effort to determine the development of a temperature control center in the hypothalamus of the homothermal animal.

Progress to 6/30/48: Four separate determinations of myelin densities in the hypothalami of 18-day-old rats maintained on the 14 diets previously reported, have shown that there are no consistent differences attributable to any one of the various diets. Mitochondrial differences have also failed to appear between the animals of one group and those of another. Similar studies have been made with adult rats, with similar results.

Second generation temperature studies in the adult animal are under way. These animals have been on their respective diets during their lives, including their in utero lives. These rats are being studied in the following respects: The effect of diet on temperature regulation; the effect of diet on myelination; the effect of diet on the thyroid; the effect of diet on acid phosphatase; the differences of the previous factors in the stressed and the non-stressed animals.

CLIMATE AND MAN, NR-163-270 (Cont.)

All diets represented vitamin A intakes greater than the normal requirement of the rat. The different levels of the dietary vitamin A did not cause any change in the serum level- the average value of each diet is about the same. The serum vitamin A level of male rats is higher than that of female rats. No carotene was found in any of the sera.

Methods of the analysis for vitamin C and manganese are ready for use, and analysis of serum vitamin C of the adult rat and carcass manganese of the 18-day-old rat are now under way.

Lactic acid determinations are being made on animals that have been injected intraperitoneally with particulate substances; the determinations are being run with the purpose of checking shock as the possible factor in the lowering of body temperature.

Preliminary work has been completed on enzyme studies in the Warburg apparatus. Studies will soon begin on the animals of the various diets, immature and adult.

Studies concerned with Ergotoxine Hyper-and Hypothermia in albino rats have shown that intraperitoneal administration of ergotoxine to albino rats has resulted in hyperthermic reactions when the environmental temperature has been 28°C or higher. When ergotoxine-treated rats were placed in an environment the temperature of which varied between 5° and 8°C, hypothermia always resulted; this was true of immediate exposure and of exposure subsequent to and during hyperthermia. Environmental temperatures between 22° and 25°C were sometimes conducive to moderate rises in temperature and sometimes to moderate falls. These changes were of short duration and were followed by long periods in which the body temperature remained within a very narrow range. Urethane given in conjunction with ergotoxine eliminated the hyperthermic effect. Subcutaneous administration of ergotoxine gave rise to less dramatic hyperthermic responses and to hypothermia (in cold environments) which was essentially the same as that elicited by intraperitoneal injection.
Estimated Completion: Indefinite

NR-163-329 Climatic Factors and Work Capacity

Contractor: University of Missouri, Columbia, Missouri
Contract: N7-onr-292, Task IV, (8/11/47 to 8/11/48)
Investigator: S. Brody

Under this project basic physiologic data are to be assembled in an attempt to arrive at an index of work (or physical fitness) and to determine the influence of climatic factors on this index. Sweating animals are to be studied and efficiency of muscular work will be measured.

Progress to 6/30/48: At present, investigations are being made on 12 cows, six of which are kept in a chamber at approximately 50°F. and 60% humidity. The other six are kept in a chamber in which the temperature is increased by five degrees to 10° F at approximately two-week intervals. The following measurements taken daily on each cow: Food, water consumption, and body weight; rectal, skin, and blood temperatures; cardiorespiratory activities including: pulse rate, respiration rate, tidal air, pulmonary ventilation rate, oxygen consumption, carbon dioxide, and methane production; heat production for the purpose of developing relations between the heat production and environmental temperature; heat dissipation by: radiation, convection, conduction, and vaporization from exhaled air and the skin.

Within a short period additional measurements will be made on the frequency of drinking, urine, and feces output.
Estimated Completion: Indefinite

HUMAN ECOLOGY

TROPICAL BIOLOGY

NR-164-468 "Bibliography on Army Ant Research" (Unclassified)

Contractor: American Museum of Natural History, New York, New York
Contract: N8-onr-505, (12/1/47 to 11/30/48)
Investigator: T. C. Schneirla

The purpose of this project is to study the behavior of representative species of ants in relation to reproductive processes; to continue the investigation of various subordinate problems; and to obtain data on the ecological conditions of the ant colonies during a time of year as yet univestigated - the transition from rainy-season to dry-season(November to March). The field work is planned to run from 5 November 1947 to about 15 March 1948. Basic investigation will be conducted continuously on Barro Colorado Island, C.Z. with supplementary investigations elsewhere (e.g. Chiriqui region of Panama; Costa Rica). Records will be taken of the ecological situation of the colonies in their two principal conditions of activity, the "nomadic" and the "static", in comparison with records from non-optimal situations, (atmospheric conditions, etc.). Barro Colorado Island will be patrolled as thoroughly as possible to map the movements and situations of army-ant colonies in its seven square mile area.

Progress to 6/30/48: No progress report has been received.
Estimated Completion: Continuing

NR-164-472 Insect Control Problem in the Micronesian Area (Unclassified)

Contractor: National Academy of Sciences, Washington, D. C.
Contract: N7-onr-291, Task VI, (8/1/47 to 7/31/48)
Investigator: C. E. Pemberton

This project constitutes a portion of the study of the ecological biology of the tropics. It is integrated with studies of a similar nature, life history and ecological relationships of other biological entities in the Arctic and temperature zones. Studies will be made of control methods for the following agricultural pests: banana root borer (Cosmopolitus sordidus), rhinoceros beetle (Oryctes rhinoceros), the giant African snail (Achatina fulica), and the Saipan coconut beetle (Brontispa mariana).

Progress to 6/30/48: Insect pests in Palau and Yap have been investigated, and natural enemies of insect pests have been liberated in Palau and Saipan.

The presence of the Oriental fruit fly in Guam was disclosed and control measures have been suggested.

Several kinds of parasites to control the mariana coconut beetle were imported from the Philippines, Siam, Malaya and Java. Scolia wasps were obtained for liberation against the rhinoceros beetle in Palau.

Collections of insect specimens are being made in Ponape, and control measures for encephalitis are also being instituted there.

A periodic report prepared by the Secretary of the Insect Control Committee for Micronesia has been received and summarizes the studies which have been carried out under this contract.

Regarding the danger of transporting destructive insects from Palau and Yap to other Islands of the area, one of the entomologists notes that the pests most likely to be transported include the giant African snail and the rhinoceros beetle in the Palaus and the cocoanut leaf-beetle, moth, and the weevil of breadfruit, and possibly the termite on Yap. The snail is likely to hide in any object which provides a hiding place while the rhinoceros beetle might be carried in the egg or larval stage in logs, tree fern stumps, etc. The cocoanut leaf-beetle might well be carried on green cocoanut leaves used for making baskets. There is found to be little danger of spreading the insects to new areas through shipments of taro, bananas or garden vegetables.
Estimated Completion: Indefinite.

Biophysics

BIOPHYSICS

NR-170-020 Amplification of the Fluoroscopic Image to Facilitate Greater Usefulness of Clinical Fluoroscopic Procedures (Unclassified)

Contractor: University of Chicago, Chicago, Illinois
Contract: N6-ori-20, Tasks VII and VIII, (5/1/46 to 4/30/49)
Investigator: P. C. Hodges

The purpose of this project is to investigate suggestions made by Langmir and Farnsworth and to attempt to develop operating models of image tubes by which the faint image of the fluoroscopic screen, used in clinical radiology, can be amplified to a brillance which will allow it to be photographed by ordinary photographic means.

Concentrated catadioptric cameras of the general type developed by Bernhard Schmidt in 1931 provide great speed (approaching f/0.5) and at the same time good resolving power over the entire film. They have had wide application in astronomy and more recently in television but until now have not been applied to clinical radiology. During the war a lens-mirror system was constructed at the Yerkes Observatory and under the present contract this lens system has been built into a 35 mm camera which is being used to film the small bowel. The development of a 70 mm camera is contemplated. In recent months a Danish development of the Schmidt camera, adapted for roentgenology, has been brought to the United States and is being tested by the U. S. Public Health Service. The lens system developed at Yerkes may have technical advantages over the original Schmidt system employed by the Danes, and in addition, may be more readily adaptable to mass production should this project demonstrate a widespread need for it in clinical radiology.

Progress to 6/30/48: Some of the optical equipment which had been delayed because of the technical difficulties of manufacture, has been delivered. No formal progress report has been received.
Estimated Completion: Indefinite

NR-170-560 Electro-Magnetic Induction Plethysmograph (Unclassified)

Contractor: Columbia University, New York, New York
Contract: N6-onr-271, Task XIV, (5/1/48 to 4/30/49)
Investigator: H. Grundfest

The purpose of this project is to attempt to develop an instrument for the accurate and simple measurement of the total quantity of blood flowing into a portion of an extremity per unit of time. It would then be possible to measure normal flow, as well as flow in cases of deformations of the body, and in parts of the body under stresses such as extremes of temperature and pressures.

The initial six months will be devoted to refinement of the instrument and in a clinical "shakedown" of the device. The estimated next year's program will consist of a study of peripheral circulation with the plethysmograph. It is highly probable that the instrument will eventually be used on the Johnsville centrifuge.

Progress to 6/30/48: No progress to report.
Estimated Completion: Continuing

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BIOPHYSICS

RADIOBIOLOGY

NR-171-030 — Cancer Research — (Unclassified)

Contractor: Memorial Hospital, New York, New York
Contract: N6-ori-99, Task I, (6/1/46 to 6/30/49)
Investigator: C. P. Rhoads

The purpose of this project is to use radioactive isotopes P^{32}, I^{130}, and I^{131} in combination with new organic complexes for developing greater tissue selectivity in the parenteral therapy of malignancies.

Progress to 6/30/48: The group has moved into a new laboratory and has accomplished much in the way of installing equipment and putting it in operating condition. This work is still continuing.

The synthesis of isoguanine has been completed with isotopic nitrogen. In addition, the isotopic sample has been fed to rats and the appropriate isolations of metabolites carried out. Because of the lack of a mass spectrometer no data on the biological experiments are yet available.

Results of the studies of the preparation of nucleic acids from the Neurospora crassa have so far been inconclusive. This is because of the apparent occurrence of orcinol reacting material which is not nucleic acid. The question of whether to enter into an exhaustive study of the nucleic acids of the neurospora is being considered.

Studies of the isolation of both adenosine and guanosine from the same sample of yeast nucleic acid have led to satisfactory isolations. Other possible approaches to the original goal of a preparation of isotopically labeled guanosine are also being considered.

The triazoles related to certain of the purines, the preparation, spectra, and purity of which have been studied, have been tried for their biological effect on L. casei. Other biological tests on these compounds are being made by the Chemotherapy Department of the Institute.

Owing to a lack of isotopic analyses, the biological experiments on hypoxanthine, xanthine, isoguanine, the incorporation of adenine into PNA and into DNA, and the incorporation of adenine into various organs of the rat are being held in abeyance. Attempts are being made to obtain these analyses outside of the Institute.

Preliminary work with radio-carbon determination by the solid barium carbonate method, in conjunction with a thin window G-M counter, has been carried out and a series of satisfactory results are being obtained. No biological experiment has yet been completed with radioactive carbon.

Estimated Completion: Indefinite

NR-171-105 — Isotope Research and Medicine — (Unclassified)

Contractor: Harvard Medical School, Boston, Massachusetts
Contract: N5-ori-76, Task VII, (6/1/46 to 6/30/49)
Investigators: A. B. Hastings, J. C. Aub, S. Warren

Based on past work employing C^{11}, a study is being made of the following using C^{14}: (1) Glycogen synthesis, in vitro, as influenced by the ionic environment, substrates and hormones, such as insulin and cortical steroids; (2) $C^{14}O_2$ incorporation in glycogen, fatty acids, certain amino acids and related compounds comprising the metabolic pool; and (3) the position of the labeled carbon atoms in the glucose molecules of newly formed glycogen (alpha carbon labeled lactic and pyruvic acid will be used as substrates). If possible, labeled amino acids will also be studied.

Such experiments should provide new information on the conditions which affect synthetic enzymatic reactions important to the metabolism of foodstuffs, and should also provide basic information on normal tissues upon which a study of pathological tissues may be based in the future.

RADIOBIOLOGY, NR-171-105 (Cont.)

Progress to 6/30/48: Chick embryos and young chicks were radiated continuously by injections of P^{32}, and examined in order to determine the effects of this radiation on embryonic and young chick tissue.

Injected P^{32} gradually concentrated in the bones. At first the concentration was not marked and the P^{32} was distributed in all of the tissues. After a few days the bones contained most of the radioactivity. This concentration increased, reaching a stable value of 10 to 20 times within two weeks.

Constant radiation retarded the growth rate of both the incubated embryos and chicks after hatching. Well formed and proportioned miniatures resulted. After the significant radiation had disappeared, the chicks resumed a near normal growth rate but did not attain the size of their non-radiated mates.

Chick gonads were very sensitive to radiation. The testis was more so than the ovary. The spermatogenic cells of both embryos and chicks were destroyed by even the smallest amounts of radiation. The developing ova were the most radiosensitive element of the ovary; their radiosensitivity decreased with age.

Of the components of bone, the cartilaginous epiphysis and especially the zone of proloferating cartilage were most sensitive to radiation. The osteoclasts and osteoblasts were relatively resistant.

Small doses of radiation inhibited proper maturation of the immature hematopoietic cells and reduced mitotic activity. Larger amounts of radiation produced an immediate and virtually complete cessation of mitotic activity and maturation.

The lymphoid tissue of the thymus was very sensitive to radiation and showed an almost immediate marked reduction of mitotic activity which lasted until most of the P^{32} had been concentrated in the bones. All but the most severe of these thymic injuries were reversible after radiation had decreased.

Antigen Tracer Studies and Histologic Observations in Anaphylactic Shock in the Guinea Pig: In anaphylactic shock caused by intravenous injection of minimal lethal shock doses of iodinated bovine gamma globulin, about 70% of the antigen is found in the blood at the time of death. This represents a removal of twice as much of antigen from the circulation as occurs in non-sensitized animals in the same time interval.

There was a specific increase in antigen uptake in the lungs after sensitization. The other organs did not show any change in affinity for antigen after sensitization.

No satisfactory histologic evidence to support the usual assumption that bronchial obstruction in anaphylactic shock is due solely to smooth muscle contraction.

Investigations are under way to study interim stages of the edema formation and antigen uptake in the bronchial walls during anaphylactic shock and the effects of various shock preventing drugs on antigen localization and edema formation.

Study of Skin Lesions of Persons Exposed to Beryllium Compounds: Several cases of subcutaneous granuloma arising in persons who have cut themselves on broken fluorescent lamps coated with beryllium - containing phosphor - have been studied. The pathology of these lesions is similar to that seen in the skin lesions of two beryllium workers who had pulmonary granulomatosis and essentially similar to the lung lesions seen in this disease.

It has been found that because of the danger of recurrence, treatment should involve complete excision. It is suggested that if other cases of subcutaneous granuloma arising in this way are to be avoided, caution must be exercised in the disposal and salvage of burnt out fluorescent lamps.

Incorporation of C^{14} Into Liver Proteins: The rate of incorporation of C^{14} carboxyl labeled dl-alanine into the proteins of rat liver slices was seven times greater in surviving slices of hepatoma nodules than in slices of normal livers, and two and one-half times that of slices from the non-malignant portions of the hepatoma-containing livers.

A preponderance of the activity incorporated was accounted for in the alanine fraction of the proteins. An increased rate of uptake of activity into hepatomas was likewise found when C^{14}-carboxyl labeled glycine was used. It is concluded that under the conditions used, the

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RADIOBIOLOGY, NR-171-105 (Cont.)

primary p-dimethylaminoazobenzene induced rat hepatoma incorporated alanine more rapidly into protein than does normal resting adult rat liver.

Radiation-Induced Hemorrhagic Disease in Chickens: The thrombocytopenia developing after radiation and the associated poor clot and loss of clot retraction would seem to be factors of importance in the hemorrhagic disease in chickens following P^{32} radiation. Since the blood coagulation time was not significantly altered even after severe radiation injury, it seems that the presence of a heparin-like substance similar to that found in dogs would be unlikely.

The following is a report on the status of various phases of "Research with Isotopes on Medical Problems" prepared by the Harvard Medical School.

A.1 Project 7(a)

A.1.1 Dr. Seymour J. Gray

(1) Papers published or in process between writing and publication:

The Phosphorus Turnover of Carcinoma of the Human Stomach as Measured with Radioactive Phosphorus. J. Schulman, Jr., M. Falkenheim and S. J. Gray.

(2) Research completed:

Work described in paper listed above.

(3) Research continuing:

(a) Work on the intragastric counter is continuing, with numerous modifications and changes in design.

(b) Spectrographic studies of gastric tissues and gastric tumors and other types of biological tissue are being carried on.

(c) Methods for determining and measuring small amounts of chromium in tissue are being perfected.

(d) Partition studies with radioactive phosphorus on the blood of patients with cancer are being carried on.

(4) New research undertaken:

(a) Uptake of radioactive phosphorus by gastric juice of patients with cancer and with benign lesions of the stomach are being studied.

(b) Determination of lysozyme in blood and tissues of experimental animals and humans with peptic ulcer and ulcerative colitis.

A.1.2 Dr. DeWitt Stetten, Jr.

(1) Research completed: (except for isotope analyses)

(a) The mechanism of obesity in rats subjected to hypothalamic injury (with Drs. C. N. H. Long and H. Mankin).

(b) The turnover of uric acid in the normal human (with Mrs. Jean Benedict and Dr. P. Forsham).

(c) The metabolism of dl-hydroxyproline (with Dr. M. R. Stetten).

(2) Research continuing:

(a) The fate of injected uric acid in the gouty and hyperuricemic human, in the rat and in the Dalmatian coach-hound.

(b) The metabolism of sorbitol and gluconic acid in the diabetic rat.

(c) A study of the possible hormone of the alpha cells of the Islets of Langerhans.

(d) The turnover of myocardial glycogen in the isolated (heart-lung preparation) heart.

(e) The mechanism of gastric HCl formation by the isolated gastric wall.

(f) The metabolism of methylene-labeled succinic acid.

(3) New research undertaken:

(a) Study of a possible purine precursor.

(b) Metabolism of ornithine, variously labeled.

A.1.3 Dr. Arthur K. Solomon

(1) Papers published or in process between writing and publication:

(a) The Measurement of Radioactivity in Solution, Rev. Sci. Instruments, January, 1948. A. K. Solomon and H. D. Estes

RADIOBIOLOGY, NR-171-105 (Cont.)

(b) Range and Energy of Beta Radiation from Calcium 45, Phys. Review, February 15, 1948. A. K. Solomon and L. E. Glendenin.

(c) Recoil-Activated and Thermal Exchange Reactions Between Sulfur-35, and Carbon Disulfide, Jour. Am. Chem. Soc. (Letter to Editor, Raymond R. Edwards, Frances Nesbett and A. K. Solomon.

(d) Radioautograph Technique with C^{14}. A. M. MacDonald, Jock Cobb and A. K. Solomon (to be published May 21, 1948 in Science).

(e) The Detection of Beta Radiation by Photographic Film. Jock Cobb and A. K. Solomon (to be published in Rev. Sci. Instruments in July, 1948).

(f) A Hood for Work with Radioactive Isotopes. A. K. Solomon and C. A. Foster (submitted to Analytical Chemistry).

(2) Research completed:

(a) The absorption spectrum of Ca^{45} (with L. E. Glendenin); as described in (b) above.

(b) The effect of beta radiation from C^{14} (with A. M. MacDonald and Jock Cobb); as described in (d) above.

(3) Research continuing:

(a) Studies relating to the formation of CS*S (with R. R. Edwards and Frances Nesbett).

(b) The perfection of techniques for high resolution radioautographs (with K. R. Kaess).

(c) The separation of radioactive I from Te. Studies relating to organic synthesis by recoil of radioactive elements (with R. R. Edwards).

(d) The preparation of radioactive S^{35} cystine by failure of the Szilard-Chalmers reaction. Biochemical and radiochemical studies of CO_2 metabolism in the retina (with E. G. Ball).

(e) Studies relating to the toxicity of small doses of CS^{2}_{35}. (with Philip Drinker, R. R. Edwards and Frances Nesbett).

(f) Studies relating to the formation of cerebro-spinal fluid using Na^{24} and other radioactive isotopes (with W. H. Sweet and Bertram Selverstone). Also the uptake of radioactive phosphorus in normal brain as compared with brain tumor.

(g) The turnover of Ca^{45} in lobster nerve (with J. H. Welsh and S. Soloway).

(Problems undertaken in collaboration with Dr. A. B. Hastings will be found in the next section.

A.2 Project 7(b) - (Under A. Baird Hastings)

(1) Papers published or in process between writing and publication:

(a) Incorporation of $C^{14}O_2$ in Rabbit Liver Glycogen In Vitro. A. Baird Hastings, A. K. Solomon, Christian B. Anfinsen, R. Gordon Gould, and I. N. Rosenberg.

(b) Metabolism of C^{14} α-labeled Pyruvate and C^{14} Carboxyl-labeled Acetate in Rabbit Liver Slices In Vitro. R. Gordon Gould, A. Baird Hastings, I. N. Rosenberg, A. K. Solomon and Yale J. Topper.

(c) Radioactive Carbon Dioxide Incorporation into Liver Proteins, In Vitro. Christian B. Anfinsen, Anne E. Beloff, A. Baird Hastings and A. K. Solomon.

(d) The In Vitro Incorporation of Carboxyl-labeled Acetic Acid in Liver Protein. Christian B. Anfinsen, Anne E. Beloff, A. Baird Hastings, A. K. Solomon.

(e) Note on the Synthesis of Succinic Acid Labeled in the Carboxyl Position with C^{14}. Yale J. Topper.

(f) $C^{14}O_2$ Excretion by Rats After Administration of Isotopic Bicarbonate, Acetate, and Succinate. R. Gordon Gould, F. M. Sinex, I. N. Rosenberg, A. K. Solomon and A. Baird Hastings.

(g) The In Vitro Utilization of Glucose by Rat Diaphragm Muscle. C. A. Villee, F. M. Sinex and A. K. Solomon.

RADIOBIOLOGY, NR-171-105 (Cont.)

(h) The In Vitro Utilization of C^{14}-labeled Glucose by Rat Diaphragm Muscle. C. A. Villee.

(2) Research completed:

(a) A comparison of the rate of oxidation of carboxyl-labeled succinate in the normal and the adrenalectomized rat. (F. M. Sinex and A. Baird Hastings.)

(b) A comparison of the rate of incorporation of C^{14} bicarbonate into the liver slice protein of the normal and adrenalectomized rat. (F. M. Sinex and A. Baird Hastings.)

(c) The utilization of C^{14}-labeled glucose by isolated muscle from hypophysectomized rats. (C. A. Villee and A. Baird Hastings.)

(3) Research continuing:

(a) A comparison of the rate of incorporation of labeled amino acids into tissue protein of the normal and adrenalectomized animal and the influence of cortical steroids upon this process. (F. M. Sinex and A. Baird Hastings.)

(b) A search in muscle mince, liver slices, and erythrocytes for a system sensitive to the in vitro addition of adrenal cortical steroids. (Isotopic $C^{14}O_2$ is being used in this work.) (F. M. Sinex and A. Baird Hastings.)

(c) The in vitro utilization of -labeled pyruvate and carboxyl-labeled acetate by rat diaphragm muscle from normal, diabetic, and adrenalectomized rats. (C. A. Villee and A. Baird Hastings.)

(4) New research undertaken:

(a) The effects of insulin and adrenal cortical hormones on the in vitro utilization by rat muscle of C^{14}-labeled glucose, pyruvate and acetate. (C. A. Villee and A. Baird Hastings.)

(b) The in vitro synthesis of lipids and proteins from C^{14}-labeled glucose, pyruvate, and acetate by rat diaphragm muscle. (C. A. Villee and A. Baird Hastings.)

(c) An analysis of the time relations in the utilization of C^{14}-labeled glucose by rat diaphragm muscle. (C. A. Villee and A. Baird Hastings.)

A.3 Project 7(c) - (Under Shields Warren)

(1) Papers published or in process between writing and publication:

(a) Antigen Tracer Studies and Histologic Observations in Anaphylactic Shock in the Guinea Pig, Am. Journal of Medical Sciences. Shields Warren and Frank J. Dixon.

(b) The Technique of Parabiosis in Rats and Mice, Proc. of the Society of Experimental Biology & Medicine. Jane C. MacMillan.

(2) Research completed:

(a) A method of obtaining parabiosis in adult rats and mice has been proved, a procedure which previously has been difficult to carry out except in relatively young animals. (Jane MacMillan.)

(3) Research continuing:

(a) Work on radioactive antigens in anaphylaxis has been continued using bovine albumen and radioactive iodine. (Frank J. Dixon.) A paper on this problem was presented before the American Society for Experimental Pathology at Atlantic City, March 18, 1948.

(b) The studies on the uptake of radioactive phosphorus from the egg yolk and its effect on the developing chick have been continued. Detailed histologic studies are being carried out.

(c) Studies on the uptake of radioactive phosphorus and radioactive sodium by the tissues in cases of disturbance of the peripheral circulation, particularly cases of diabetic gangrene, have been continued. In addition to this, circulation time studies in various conditions of impaired circulation have been carried out with these same substances. (Earl B. Wert.)

(d) The studies on the therapeutic value of radioactive phosphorus in leukemia and in plasma cell myeloma as well as polycythemia vera have been continued. (With William B. Stevens.)

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(e) Experiments have been carried out on the efficacy of various counting techniques and the suitability of various types of x-ray film for detection of small amounts of radiation. (With Russell F. Cowing.)

(f) The film badge service and the hemotologic service for the personnel of Harvard University projects in the field of nuclear energy are being continued.

A.4 Project 7(b) - (Under Joseph C. Aub)

(1) Papers published or in process between writing and publication:

(a) The Effect of Dinitrophenol on the Incorporation of C^{14}-labeled Alanine into the Proteins of Slices of Normal and Malignant Rat Liver. Ivan D. Frantz, Jr., Paul C. Zamecnik, J. W. Reese and Mary L. Stephenson.

(b) Incorporation In Vitro of C^{14} from Carboxyl-labeled dl-Alanine and Glycine into Proteins of Normal and Malignant Rat Livers. Paul C. Zamecnik, Ivan D. Frantz, Jr., Robert B. Loftfield and Mary L. Stephenson.

(c) Skin Lesions in Persons Exposed to Beryllium Compounds. Robert S. Grier, Peter Nash and David G. Freiman. (In press.)

(2) Research completed:

(a) Work described in papers listed above. (Ivan D. Frantz, Jr.)

(b) A series of seven cases of acute pneumonitis in persons exposed to extremely pure beryllium oxide and beryllium metal. Work in process of writing prior to publication. (Robert S. Grier.)

(3) Research continuing:

(a) Investigation of the mechanism of the synthesis of protein and of the peptide bond. The effect of a variety of substances on protein synthesis in normal and malignant tissues in vitro is being studied. (Ivan D. Frantz, Jr.)

(b) Attempt to produce bone tumors in rabbits by injection of beryllium compounds. (Robert S. Grier.)

(c) A study of the effects of beryllium on osteogenic sarcoma induced in rats by radium. (Robert S. Grier.)

(d) Continuation of the study of effects of beryllium on alkaline phosphatase. (Robert S. Grier.)

(e) Continuing attempt to procure radioactive beryllium-7 for tracer work. (Robert S. Grier.)

(4) New research undertaken:

(a) Separation of the amino acids derived from hydrolysis of C^{14}-labeled proteins. These separations are being carried out by means of starch column chromatography. (Ivan D. Frantz, Jr.)

(b) Study of the relative importance of altered rates of degradation and synthesis on the control of growth in regenerating rat livers. (Ivan D. Frantz, Jr.)

(c) Study of the synthesis of amino acids from carbon dioxide by surviving liver slices. (Ivan D. Frantz, Jr.)

(d) Study of the effects of intravenous beryllium sulfate in animals on calcium, phosphorus, phosphatase, nitrogen and blood sugar. (Robert S. Grier.)

Estimated Completion: Indefinite

NR-171-107 Biological Synthesis of Protein With Use of Isotopes (Unclassified)

Contractor: California Institute of Technology, Pasadena, California
Contract: N6-ori-102, Task II, (6/19/46 to 6/30/49)
Investigator: H. Borsook

The purpose of this project is to study protein synthesis in vitro by tissue slices using lysine and leucine, labeled by means of C^{14} as tracers. The labeled amino acids with a complete mixture of other unlabeled amino acids will be added to Ringer's solution or serum containing

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the slices. After four to 24 hours incubation, the reaction will be stopped, the protein and non-protein fractions separated, the labeled amino acids isolated and their content of C^{14} determined in a Geiger counter. The content of C^{14} in the lysine and leucine in the protein fraction will indicate the degree of protein synthesis. The quantities of tissue and reactants will be on a micro scale.

Progress to 6/30/48: Leucine has been synthesized with C^{14} in the carboxyl group and after submission to the action of liver homogenate was fractionated on a starch column. All of the radioactivity was found concentrated in three fractions. One was the unused leucine; one or both of the other two radioactive fractions may be different peptides. The first experiment with the labeled leucine demonstrated that starch column chromatography enables one to locate and isolate all of the products of a radioactively labeled amino acid quickly and surely.

Plans are being made to use starch column chromatography in the isolation and identification of the peptide of lysine. Plans are also being made to build fraction cutters for at least eight starch columns, as well as two automatic counters, so that the radioactivity measurement can go on continuously 24 hours in the day without human operation. Studies are continuing on the incorporation of labeled amino acids into proteins.

The following scientific reports were published in the Journal of Biological Chemistry (1) "Synthesis of Hippuric Acid in Liver Homogenate", by H. Borsook and J. W. Dubnoff, (168,397-1947), (2) "Ornithine-Catalyzed Urea Formation in Liver Homogenate", by H. Borsook and J. W. Dubnoff, (169,461-1947), (3) "On the Role of the Oxidation in the Methylation of Guanidoacetic Acid", by H. Borsook and J. W. Dubnoff, J. Biol. Chem. (171,363-1947). A new analytical instrument and ionophoresis apparatus similar to that described by Consden, Gordan, and Martin (Biochemical Journal 40,33-1946) is being built.
Estimated Completion: Indefinite

NR-171-138 Immediate and Delayed Biochemical and Biological Effects of Irradiation on Animal Tissues (Unclassified)

Contractor: University of California, Berkeley, California
Contract: N6-ori-111, Task III, (6/21/46 to 6/30/49)
Investigator: J. H. Lawrence

The purpose of this project is to increase medical and biological knowledge of (1) cancer, and (2) the effects of radioactive substances. Nucleic acid metabolism of neoplastic tissues has been followed with and without specific irradiation of the liver of approximately 3400 r. The desoxyribose-nucleic acid synthesis, under these conditions, is depressed five to six times. These studies and those of Hevesy suggest the probability of a chemical substance which mediates the effect of ionizing radiation upon nucleic acid metabolism. It is thought that the desoxyribose-nucleic acid is essential to tissue growth. In the presence of long continued liver irradiation of this intensity, neoplastic tissue transplants did not increase in size. Nucleic acid metabolism of normal tissues is apparently similarly depressed although results are not sufficient at this time to be statistically valid.

Progress to 6/30/48:

(1) (Research to develop methods by which tissues in situ can be selectively irradiated.

(a) The research supported by this contract has developed new colloids of yttrium and zirconium which can be controlled with respect to the site of deposition in the reticulo-endothelial system.

(b) By varying the size of the colloidal yttrium and zirconium particles, it has been possible to produce uniform smaller sized particles of the same colloids. These are only slightly deposited in the liver and spleen and the bulk of the deposition occurs in the bone marrow. The relative difference in the efficiency of colloid screening of the liver and

RADIOBIOLOGY, NR-171-138 (Cont.)

bone marrow for these different colloids remains unexplained, and it is likely that there are more factors involved than the obvious one of particle size.

Animals with specifically irradiated bone marrows are now being compared to similar studies of animals with specifically irradiated liver and spleens.

Techniques for specifically irradiating other tissues are being explored in the laboratory. As yet there are no other methods perfected except for the above.

(2) The study of specifically irradiated tissues is important because of the desirability of following changes in the intact irradiated animal. There is an apparent difference in the response of irradiated isolated tissue and irradiated tissue in situ. It may be impossible to ascertain the basis of these differences in view of the complexity of the relationships between tissue and host.

(a) It is already apparent that there is a major effect upon nucleic acid metabolism from specifically irradiated liver which is apparent in other non-irradiated tissues as though the irradiation itself had extended to these tissues.

(b) Specific irradiation of the liver at 1000 r/week is sufficient to depress tumor growth for three months. This may be due to the lack of desoxyribose nucleic acid in the tumor cells from which new chromatin is made. Specific irradiation of approximately 3400 r to the liver is sufficient to depress desoxyribose nucleic acid formation to 20% of the normal rate in neoplastic tissues.

(c) The administration of two substances which inhibit tumor growth were shown to have no effect upon desoxyribose nucleic acid metabolism in doses necessary to cause depression of growth.

(d) No clue has been found as to the nature of the substance produced in liver irradiation which remotely depresses nucleic acid formation.

(e) Irradiation of the bone marrow is being studied. The nucleic acid metabolism is not affected by 150 r of specific irradiation in spite of the rather great changes induced in the rate of hematopoiesis. The effect on the rate of depression of hematopoiesis is being studied and the larger marrow irradiation doses will be used to study the possible remote effects of marrow irradiation on nucleic acid metabolism. An experiment is to be started which will compare indirect effects of irradiation in non-irradiated tissues in animals in which either the bone marrow or the liver were specifically irradiated with equal ionization.

(f) The thyroid gland functions well in thyroxine synthesis in spite of thousands of r units of irradiation. The enzymatic mechanism of the thyroxine formation is apparently not at all comparable to the sensitivity of nucleic acid metabolism in the case of liver irradiation. Subsequent work will be attempted to match the histological changes in the gland with some of the detectable changes in the pattern of thyroid iodine metabolism.

(g) Survival experiments involving specific liver irradiation will be summarized and reported soon. Additional experiments of this type will continue.

(h) Radioactive carbon compounds are available and methods have been worked out for the study of the rate of utilization of acetate, succinate, glucose, phenyl-alamine, glycine, and tyrosine. The utilization rate of these substances will be followed in animals with acutely and chronically irradiated livers and compared to normal animals. Differences evident in liver metabolism will be compared with the metabolism of these substances in liver slice work.

(i) Chromatographic separation techniques for amino acids have been perfected in the laboratory which will immediately permit a detailed study of amino acid metabolism in tissue slice work. A study comparing slices from normal and chronically irradiated livers as well as acutely irradiated livers, is proposed.

The metabolism of carboxy labeled glycine has been studied and compared with the metabolism of acetate, and no differences were detected in acetate metabolism in animals in which the livers had been specifically irradiated to the level of 1,000,000 r. The indirect effect of liver irradiation upon desoxyribose-nucleic metabolism of tumors is established. One final check is being made to determine whether the small dosage of irradiation which, unavoidably

RADIOBIOLOGY, NR-171-138 (Cont.)

given the tumor, might account for the effect. This is rather unlikely from the original report of Hevesy and Hahn on the depression of desoxyribose-nucleic acid of directly irradiated tumors when the dosage required was a factor of 20 greater than the tumors of this experiment could have received.
Estimated Completion: Indefinite

NR-171-184 The Biological Effects of Ionization (Unclassified)

Contractor: University of Kansas, Lawrence, Kansas
Contract: N6-onr-260, Task I, (2/1/47 to 6/30/49)
Investigator: F. E. Hoecker

The purpose of this project is to study the biological responses in tissue to various density concentrations of ionization.

Progress to 6/30/48: Studies of radium metabolism in rats have been made and are being continued, in order to prepare radioactive tissue for microscopic study; to determine the optimum time of injection of radium; and to achieve maximum deposit at the site of bone injury. Radium metabolically deposited in the body, so that the radon is not eliminated, is found to increase continuously for more than 100 days after injection. Only 10% to 15% of the radium in the body is in this condition. Approximately one-third of the radium originally injected remains in the body for at least 100 days. Portions of the skeleton have been sectioned and autoradiograms are being studied.

Apparatus has been designed and a method developed for the measurement of the range of alpha particles in biological tissue. Preliminary measurements of range in organic materials were successful. A method for eliminating errors due to the nonuniformity of biological films is being developed.
Estimated Completion: Indefinite

NR-171-196 A Study of Plasma Proteins With Labeled Amino Acids (Unclassified)

Contractor: University of Rochester, Rochester, New York
Contract: N6-ori-126, Task VIII, (9/1/46 to 6/30/49)
Investigator: G. H. Whipple

It is known that plasma proteins show a very rapid rate of turn-over within the body protein metabolism. In fact they may represent intermediary proteins which are stores or used for various purposes within body cells. Under this project isotopically-labeled amino acids will be used to study, within the body, the use of amino acids and related plasma proteins containing the labeled acids. Such experiments should clarify normal protein metabolism and abnormal protein metabolism experimentally produced in the laboratory animal.

Progress to 6/30/48: Determination of the role of plasma proteins as intermediaries in the protein metabolism of the body has been contingent upon development of techniques of synthesis of labeled amino acids, and methods of measurement of radioactivity in biological samples.

Lysine has been synthesized with C^{14} in the epsilon position. Most satisfactory results were obtained from a modified Fisher and Weigert procedure in which the initial transformation

$$Cl(CH_2)_3Br \longrightarrow Cl(CH_2)_3C^{14}N$$

is effected by addition of KCN solution containing dissolved $AgC^{14}N$, prepared by the method of Cramer and Kistiakowsky. Since five subsequent steps are required, the overall yield does not exceed 20% to 25% of initial activity

RADIOBIOLOGY, NR-171-196 (Cont.)

Biological material has been sampled for radioactivity measurements by wet oxidation with Van Slyke chromic, phosphoric and sulfuric acid mixtures, and collection of evolved CO_2. Assay for $C^{14}O_2$ content employed either bell type mica window (1.1 mg/cm^2) with dry $BaCO_3$ samples, or direct measurement of dried gas after condensation in a metal liquid nitrogen cooled trap. For this a dynamic electrometer was developed with a recording FP-54 circuit for current measurement. For a 0.5 gm sample the gas method is about twice as fast as, and 40 times more sensitive than the solid sample method, and has a limit of 4×10^{-4} microcuries/gm carbon.

Preliminary trials on C^{14} labeled lysine fed to rats indicate that about 90% of the ingested C^{14} is exhaled as CO_2 within six hours. Forty-eight hour tissue levels show the liver to contain about 0.2% of the ingested dose at that time.

Estimated Completion: Indefinite

NR-171-256 The Design and Construction of a Microbeam of Light Atomic Nuclei for Biological Investigations (Unclassified)

Contractor: University of Chicago, Chicago, Illinois
Contract: N6-onr-20, Task XVII, (3/31/47 to 6/30/49)
Investigator: R. E. Zirkle

The purpose of this project is to develop and construct a microbeam cross section area less than 10^{-8} cm^2, and a study of the biological effects of protons, deuterons, and alpha particles on single cells. The modified cyclotrons at the University of Chicago will produce deuterons of energies up to 1.2 x 107 electron volts. Shielded beams will be directed to cells which are being studied while mounted on micromanipulators. The volume of irradiated cells and the number of traversing deuterons will be determined. This study is a fundamental approach to cellular physiology.

Progress to 6/30/48: An improved radiation measuring device, which differentiates between electrons passing through it at intervals of less than one ten millionth of a second, has passed preliminary tests.

The instrument is especially efficient in counting high-speed gamma rays. It is known as a scintillation counter and is a box containing fluorescent matter and an extremely sensitive photoelectric tube. Nuclear particles admitted to the box through a small hole produce bursts of light in the fluorescent matter (usually naphthalene). The light is picked up by the photoelectric tube and converted into a momentary current of electricity which can be amplified and measured.

Estimated Completion: Indefinite

NR-171-294 Radioactive Iodine Therapy of Graves Disease (Unclassified)

Contractor: Harvard University, Cambridge, Massachusetts
Contract: N5-ori-76, Task XV, (2/15/47 to 6/30/49)
Investigators: H. L. Blumgart, S. Hertz

The purpose of this project is to use isotopes of iodine in a basic study of iodine metabolism in blood, urine, body fluids, and thyroid. Special attention will be given to (1) the relative effectiveness of the I^{130} and I^{131} and short and long-life isotopes for irradiation therapy; (2) the preparation of cardiac patients for radiation (non-surgical) controlled thyroidectomies; and (3) the effectiveness of various goiterogens on iodine metabolism.

Progress to 6/30/48: Work is progressing on the following phases of the program:

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(1) To determine the accuracy of the measurement of retained RaI^{131}, the accuracy of measurement of urinary excretion of RaI^{131}, and measurement of retained RaI^{131} in the thyroid gland.
(2) Use of RaI^{131} in the diagnosis and treatment of disorders of the thyroid.
(3) Treatment of patients with congestive heart failure of angina pectoris by medical measures designed to produce profound lowering of the metabolic rate.

Estimated Completion: Indefinite

NR-171-340 Biological Effects of Radiation on Neurospora (Unclassified)

Contractor: California Institute of Technology, Pasadena, California
Contract: N6-onr-244, Task V, (6/1/47 to 6/30/49)
Investigator: G. W. Beadle

The purpose of this project is to make an investigation of the biological effects of atomic bomb radiation on the neurospora. Neurospora were exposed to radiation at Bikini. Mechanism for this study will be the determination of the changes in the metabolic requirements of the neurospora that were caused by the radiation.

Progress to 6/30/48: Large numbers of strains derived from material exposed at Bikini have been investigated. Numerous mutant types were found among them. This material is now being studied in regard to the biochemical characteristics of the mutant strains, comparison of the types of biochemical mutants produced in controlled material and in material exposed to controlled radiation of various kinds, including those from radioactive isotopes and those non-radioactive chemicals which may be expected to have mutagenic properties.
Estimated Completion: Indefinite

NR-171-352 Screen Test for Urinary Porphyrin Excretion (Unclassified)

Contractor: University of Maryland, College Park, Maryland
Contract: N7-onr-397, Task II, (6/1/47 to 5/31/48)
Investigators: H. J. Figge, J. E. Bowers

This project is part of a program designed to protect personnel from ionizing radiation. A number of important basic physiological considerations may be elucidated by the potential discrimination.

Progress to 6/30/48: This contract has expired.
A screen test for urinary porphyrin was made on 700 samples and has been found to be of practical value. It was able to detect several cases of porphyria as well as to determine the rate of porphyrin excretion in normal human subjects. The screen test has also been utilized on patients receiving radiation to study the porphyrin excretion. More studies are needed to determine conclusively whether cancer patients excrete excessive amounts of urinary porphyrin, as well as the effects of radiation upon porphyrin excretion.

NR-171-424 Micro-Spectrophotometry (Unclassified)

Contractor: Polaroid Corporation, Cambridge, Massachusetts
Contract: N7-onr-391, Task I, (6/1/47 to 5/1/49)
Investigator: E. H. Land

Progress to 6/30/48: This project has been transferred to the Physics Branch and will be reported under project Number NR-016-149.

RADIOBIOLOGY (Cont.)

NR-171-556 Response of Cells (Desquamate) to Deep Radiation (Unclassified)

Contractor: Massachusetts General Hospital, Boston, Massachusetts
Contract: N8-onr-597, (1/1/48 to 12/31/48)
Investigator: J. V. Meigs

The purpose of this project is to investigate the reaction of individual cells to deep X-ray radiation.

Guinea pigs, rabbits, and mice will be sprayed by a deep-therapy machine after which a careful examination of vaginal and oral secretions will be made. (Vaginal secretion studies developed by G. Papanicolan are the basis for a method of early cancer diagnosis.)

Progress to 6/30/48: No progress has been reported.
Estimated Completion: Continuing

NR-171-581 Biological Effects of High Voltage Radiation (Unclassified)

Contractor: Union College, Schenectady, New York
Contract: N8-onr-534, Task I, (7/1/48 to 6/30/49)
Investigator: L. B. Clark

The purpose of this project is to study the biological effects of high voltage X-ray radiations. Research will be focused on the X-ray range of one million to one hundred million volts as emitted by the hundred million volt betatron. Observations will be made concerning the effects of this X-ray range in tissues and upon individual enzyme systems in cells. This research should therefore be of value in determining personnel safety factors against high voltage radiation and should also provide a valuable fund of information concerning the therapeutic possibilities of these radiations.

Progress to 6/30/48: No progress to report.
Estimated Completion: Continuing

NR-171-604 Radio Autographs (Unclassified)

Contractor: Ohio State University, Columbus, Ohio
Contract: N6-onr-225, Task XVI, (3/1/48 to 2/28/49)
Investigator: M. L. Pool

Under this project the experimentation plan is as follows:

(1) For beta rays: A magnetic field of not more than 25,000 oersteds would be placed perpendicular to the surface of the objects to be investigated.
(2) For monoergatic electrons: A focussing magnetic field of low strength could be used in a limited number of cases.
(3) For alpha rays: A magnetic field much stronger than that used in (1) above would be placed perpendicular to the surface to be investigated.

Perhaps some sharpening would be obtained when the film is in contact with the surface to be investigated. However, it is probable that a magnetic lens would have to be employed to obtain satisfactory sharpness.

Progress to 6/30/48: No progress to report.
Estimated Completion: Indefinite

RADIOBIOLOGY (Cont.)

NR-171-642 Body Retention of Carbon 14 (Unclassified)

Contractor: Southern Research Institute, Birmingham, Alabama
Contract: N7-onr-385, Task II, (7/1/48 to 6/30/49)
Investigator: W. A. Lazier

The purpose of this project is to study the retention of C^{14} in the body. Less than lethal doses of radioactive compounds will be administered to mice. Especial attention will be given to carbon fixation in bone, in carbon-inohemoglobin in the liver and other tissues thought to be concerned with carbon fixation. Studies will be made to determine whether C^{14} activity retained in the animals will catalyze the appearance of neoplastic conditions.

Progress to 6/30/48: No progress to report.
Estimated Completion: Indefinite

NR-171-643 Role of Iron, Zinc and Other Metals in the Metabolism of Human Erythrocytes and Leukocytes with Reference to the Blood Dyscrasias (Unclassified)

Contractor: Massachusetts Institute of Technology, Cambridge, Massachusetts
Contract: N5-ori-78, Task XXVIII, (7/1/48 to 6/30/49)
Investigator: R. D. Evans

The purpose of this project is to investigate dietary components, blocking substances, accelerators, vitamin, and protein components to determine their influence on iron absorption in animal experiments. A metal binding globulin labeled with radioactive iron will provide an accurate tracer method. Differences in the rate of clearance of iron given, bound to the globulin, may throw some light on the site of breakdown in the iron cycle in blood dyscrasias. Results will be applied to clinical problems in iron therapy.

Another phase of the project will be concerned with a study of leukocytes. Efforts will be made to obtain separation of the various classes of leukocytes after the initial separation from whole blood. Pure colonies of granulocytes and lymphocytes will be obtained. This will permit analysis of the zinc content of the two main types of white cells in the normal state and in the leukemias and leukopenias, expressed by the ratio of Zn^{65} to total zinc.

Progress to 6/30/48: No progress report has been received.
Estimated Completion: Indefinite

NR-171-650 Treatment of Neoplasms by Direct Infiltration with Radioactive Colloids (Unclassified)

Contractor: Meharry Medical College, Nashville, Tennessee
Contract: N8-onr-561, Task I, (3/1/48 to 2/28/49)
Investigator: P. F. Hahn

The purpose of this project is to study the effectiveness of gold colloids in the treatment of various tumors by direct infiltration. Data will be simultaneously obtained on the tolerance to beta radiation exhibited by various body organs and tissues and their components of animals. A study will be made of the limits of tolerance of the hematopoietic system to beta radiations. At the same time a study will be made of the phagocytic system of the body and those factors which influence the relative degree of phagocystosis by different parts of the lymphoid-macrophage system.

RADIOBIOLOGY, NR-171-650 (Cont.)

Progress to 6/30/48: No progress to report.
Estimated Completion: Indefinite

NR-171-652 Study of the Use of Gamma Ray (Radioactive Isotope) as a Therapeutic Agent in Carcinoma (Unclassified)

Contractor: Washington University, St. Louis, Missouri
Contract: N8-onr-62400, (7/1/48 to 6/30/49)
Investigator: J. F. Nolan

The purpose of this project is to attempt to augment or complement present radiobiological techniques by directing itself against residual carcinoma in the fields of lymphatic drainage. Artificial radioactive material will be used in certain malignant tumors on the basis of their chemical characteristics and their affinity for specific cellular physiology. The technique will utilize a gamma ray emitter in colloidal form. Radioactive gold will be investigated. The tumor to be used will be a transplantable spontaneous mammary adenocarcinoma of a strain of brown mice. Data obtained on the dose factors and modes of administration will be evaluated and utilized in duplicate experiments using large animals, perhaps dogs or monkeys.

Progress to 6/30/48: No progress to report.
Estimated Completion: Continuing

NR-171-653 The Effects of Radiations Associated with Growth (Unclassified)

Contractor: Tufts College, Medford, Massachusetts
Contract: N8-onr-61400, (7/1/48 to 6/30/49)
Investigator: D. Rapport

The purpose of this project is to make an investigation which will include a study of the basic catabolic aspects of metabolism. In this respect, the work is being extended to include a synthesis of both ribo and desoxyribonucleic acid from specific substrates, especially histidine and pyrimidines, as well as in the relation of phosphatases to these reactions. It is in connection with these basic reactions that an attempt will be made to study the effect of radiation, both in normal tissues, and in rapidly and abnormally growing ones, as in regeneration and tumors. This study will include not only the effect of ionizing radiation but also monochromatic ultraviolet light upon tissues in various degrees of dispersion, but at first, primarily as homogenates.

Progress to 6/30/48: No progress to report.
Estimated Completion: Continuing

NR-171-654 Development and Construction of a Radiocobalt Applicator for Radiobiology (Unclassified)

Contractor: University of Illinois, Urbana, Illinois
Contract: N6-ori-71, Task XXII, (1/1/48 to 3/31/49)
Investigator: S. H. Quastler

The purpose of this project is to develop and construct a radiocobalt applicator to be used in conjunction with a 100 kv machine already being used in the physics department of the University of Illinois. The combination of the two machines would open a wide field of possibilities in which X-ray machines are of little use. Several types of projects would profit from the proposed applicator. An analysis of the lethal effect in mice, e.g., the split dose effects

RADIOBIOLOGY, NR-171-654 (Cont.)

could be made and along the same lines, the split dose effects could be studied in the discoloration of hair. Histological changes in the brain and liver, as well as combination effects of rays and fat-stored toxic hydro-carbons in mice, could be studied.

Progress to 6/30/48: No progress report has been received.
Estimated Completion: Continuing

NR-171-676 — The Nutrition of Tapeworms: The Effect of Relaxin Extract on Blood — (Unclassified)

Contractor: Rice Institute, Houston, Texas
Contract: (7/1/48 to 6/30/49)
Investigator: A. C. Chandler

One of the primary objectives of this project will be to orient and familiarize the investigators with radioactive isotope techniques. The actual studies are to be divided into two phases. An attempt will be made, using radioactive isotopes, to study the rate and amount of absorption of certain intestinal materials by the tapeworm. In the second phase, an attempt will be made to determine more completely the function of relaxin, a hormone of early pregnancy, in relation to kidney malfunction.

It is possible that tapeworms absorb vitamins from the host tissues. If this is true, many of the symptoms of tapeworm infection might be due to induced vitamin deficiences in hosts on a marginal supply in the diet and might be corrected by administration of vitamins.

Progress to 6/30/48: No progress to report.
Estimated Completion: Continuing

NR-171-677 — Distribution and Turnover of Sodium and Potassium in Acute Infections — (Unclassified)

Contractor: Wake Forest College, Wake Forest, North Carolina
Contract: (7/1/48 to 6/30/49)
Investigator: G. T. Harrell

Under this project serum sickness will be induced in animals. When edema develops, radio sodium and thiocyanate could be given. The plasma, urine, and intestitial fluid for total sodium would be compared with radio sodium and correlated with thiocynate space. A similar experiment will be made administering radioactive potassium. The experiments will be repeated with human beings.

Progress to 6/30/48: No progress to report.
Estimated Completion: Continuing

NR-171-678 — The Hormonal and Pharmacological Actions on the Formation of Phospholipides — (Unclassified)

Contractor: Wake Forest College, Wake Forest, North Carolina
Contract: (7/1/48 to 6/30/49)
Investigator: C. Artom

Under this project the synthesis of phospholipides will be followed with the aid of radioactive phosphorus as a tracer for the phosphate part of the molecule. By labeling the

[redacted]

BIOPHYSICS

RADIOBIOLOGY, NR-171-678 (Cont.)

methyl group of choline with C^{14}, the formation of lecithins, after administration of choline, could also be studied.

Progress to 6/30/48: No progress to report.
Estimated Completion: Continuing

NR-171-679 Biological Effects of Radiation from Excessive Amounts of I^{131} (Unclassified)

Contractor: Columbia University, New York, New York
Contract: N6-onr-27115, (7/1/48 to 6/30/49)
Investigator: A. Gorbman

The purpose of this project is to attempt to determine whether thyroid hormone synthesis is developed in a stepwise manner or whether the ability to form the new hormone develops suddenly.

The investigation is divided into two phases: (1) The effects upon the thyroid and neighboring tissues of radiotoxic doses of I^{131} are being studied; and (2) an analysis will be made of the function of the thyroid in the fetal mouse.

Progress to 6/30/48: No progress to report.
Estimated Completion: Continuing

NR-171-694 Beryllium Experimentation (Unclassified)

Contractor: University of Cincinnati, Cincinnati, Ohio
Contract: N7-onr-47902, (7/1/48 to 6/30/49)
Investigator: R. A. Kehoe

Under this project the quantitative relationships of beryllium dust inhaled into the lungs and the rate of removal from the lungs along with subsequent elimination from the body will be determined in experimental animals.

Progress to 6/30/48: No progress to report.
Estimated Completion: Continuing

MECHANICAL FORCES

NR-172-092 Physiological Study of Disability Evaluation (Unclassified)

Contractor: Medical College of Virginia, Richmond, Virginia
Contract: N6-ori-198, Task III, (9/1/46 to 8/31/49)
Investigator: F. A. Hellebrandt

The purpose of this project is to devise, construct, and validate a series of self-contained indicating and/or recording instruments for the study of the functional status of the upper extremities. Valid and reliable measures of physical capacity would expedite the quantitative study of progress under various forms of therapy following injury or disease, which would provide objective end-points of treatment, and would add demonstrable evidence to clinical judgment in support of estimates of disability.

Progress to 6/30/48: Instruments which have been completed include the wrist and radio ulnar ergographs, the squeeze or grip ergograph, the thumb ergograph, and electrodynamic brake

MECHANICAL FORCES, NR-172-092 (Cont.)

upper extremity ergometer. A major experimental study of the reliability of goniometry has been completed. The data are now being subjected to statistical analysis. Two incidental papers are being prepared for the technical group (physical and occupational therapists). One is a critical review of the literature on goniometry; the other is a description of a clinically feasible technique of goniometry, of probable value to training school groups.
Estimated Completion: Indefinite

NR-172-175 Crash Injury (Unclassified)

Contractor: National Academy of Sciences, Washington, D. C.
Contract: N5-ori-177, Task V, (7/1/46 to 6/30/48)
Investigator: H. DeHaven

The purpose of this project is to increase the understanding of human tolerance of physical forces and provide information upon which to base improvement in the designed relationship of the mechanical structures in aircraft to the human body.

Progress to 6/30/48: Informative accident No. 7 under Crash Injury Research has been received. This report points out that cases of free fall in which the velocity and the stopping distance can be judged with considerable exactness provide valuable evidence on the ability of the human body to tolerate severe jolt loads.

Actually, in many crashes, the chance of surviving as well as the danger of being killed are determined when a ship is built, for at that time two principal factors which limit "crash worthiness" are definitely established: (1) The energy absorbing characteristics of forward structures, wings, and landing gear; and (2) the distance between the nose of the ship and the pilot's seat. These features determine the magnitude of crash decelerations transmitted to the pilot and passengers and the maximum velocity at which a ship can crash and absorb enough energy to prevent the cabin from hitting bottom and collapsing.

All the progress reports of this project are widely distributed to interested individuals and agencies, and detailed examination of the work can be made by reference to these reports.
Estimated Completion: Indefinite

NR-172-384 Crash Injury Potentials of Aircraft Cabin Installation (Unclassified)

Contractor: Cornell Aeronautical Laboratory, Buffalo, New York
Contract: N6-ori-119, Task VIII, (1/1/48 to 12/31/48)
Investigator: C. C. Furnas

In order to evaluate the inherent danger of various types of structure, it is proposed that a standardized fragile, headlike object be projected against typical structures, and that the resulting blows, (jolt loads and impact forces) be recorded; the damage sustained by the projected objects would also be observed. The closer the relationship between the mechanical characteristics of the projected objects and the human head the more valuable these observations would be.

A useful and sufficiently close mechanical relationship between the plastic form and the human skull will be reached if plastic material is used which will (when covered with a fresh hide or other suitable material and filled with a gelatinous mass) show somewhat typical lineal fractures when the "head form" is dropped about five feet onto a hard flat surface.

Data obtained will be interpreted by medical experts and those experienced in the field of mechanical design, in order, to provide basic information whereby causes of dangerous injuries can be moderated by alterations in causative structures.

MECHANICAL FORCES, NR-172-384 (Cont.)

Progress to 6/30/48: A literature survey of the size, weight, and strength characteristics of human head forms was made. Thought has been given to the actual plastic head form that would approximate the characteristics of the human skull. The methods for the testing of such simulated head forms have been considered and evaluated. The preliminary design of a catapult mechanism was made.
Estimated Completion: Indefinite

NR-172-428 The Electrostatic Forces in Blood and Their Relationship to the Coagulation Mechanics (Unclassified)

Contractor: Cornell University, Ithaca, New York
Contract: N6-onr-264, Task X, (9/1/47 to 4/31/49)
Investigators: I. S. Wright, L. Wood

The purpose of this project is to investigate the bioelectrical and the physiological aspects of blood. Data are being obtained on the measurement of electrical potentials in the various components of blood and the changes of the potentials during thrombosing. An electrical circuit has been constructed which will make possible the determination of zeta potentials by the streaming potential technique. Studies show that the conductivity of blood is properly inherent to the plasma and that cellular elements are almost pure resistances. It has also been shown that the specific conductivity of blood and plasma is a function of temperature. Investigations will continue on the study of zeta potentials in whole blood, plasma erythrocyte suspensions, blood containing anticoagulants, tocopherols, and changes in zeta during clotting.
The title of this project was formerly "Electrostatic Aspects of Blood."

Progress to 6/30/48: An apparatus consisting of a combination bridge circuit, which will measure the electrical resistance of a capillary filled with solution, has been constructed. The EMF can also be measured as it is generated by the flow of the solution through the capillary. The solution is motivated by applying nitrogen gas under pressure to the ends of the capillary. Since the voltages are small, almost perfect shielding, contact, and insulation are demanded. As a result considerable difficulty is always experienced in getting such an apparatus into satisfactory working condition. The apparatus is now in the process of final adjustment.
Estimated Completion: Indefinite

NR-172-628 The Electrostatic Forces in Blood and Their Relationship to the Coagulation Mechanics ((Unclassified)

Contractor: Cornell University, Ithaca, New York
Contract: N6-onr-264, Task X, (9/1/47 to 4/31/49)
Investigators: I. S. Wright, L. Wood

This project number has been changed to NR-172-428.

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Dentistry

GENERAL AND MATERIALS

NR-180-360 Dental Materials (Unclassified)

Contractor: University of Michigan, Ann Arbor, Michigan
Contract: N6-onr-232, Task VIII, (2/1/48 to 2/1/49)
Investigator: N. O. Taylor

The purpose of this project is to develop the best combination of dental impression and model material for the production of indirect inlay castings, and partial and complete dentures. A study will be made of the most satisfactory combination of present material for production of models involving data on dimensional accuracy of end product and effect of manipulative procedures applied to accessory materials. After determining the most desirable cominbation of materials, the development of improved materials will follow without delay.

Progress to 6/30/48: This project was initiated 1 February 1948. Organizational details of personnel and materials are in progress and the work is about ready to get under way.
Estimated Completion: Indefinite

PROSTHESIS, OPERATIVE TECHNOLOGY, AND ORAL SURGERY

NR-181-396 Determination of Masticatory Efficiency (Unclassified)

Contractor: Tufts Dental School, Medford, Massachusetts
Contract: N7-onr-463, Task II, (11/1/47 to 10/31/48)
Investigator: A. S. Manly

The purpose of this project is to develop new devices, and to find new applications for existing ones, for use in measuring the effect of food types, the manner of chewing, and the presence of diseases on the attachment tissues of the human dentition "in vivo". A study will be made to determine minimal dental conditions essential for reasonably rapid and effective mastication of proper diet. Data collected under this program should lead to a more scientific approach to the business of designing dental prosthetic appliances for the individual.

The human subjects to be used for experimental purposes will be grouped according to age and clinical condition of the dentition and attachment tissues. Test material will be used for unit periods and the resultant size particles will be measured by hydrolysis, sieves, or by devices which may be developed. A measurement will be made of pain thresholds in dental attachment tissues in varying clinical states of health as different forces are applied by the muscles of mastication. The forces applied will be measured by a gnathodynamometer and spring gauge, or, by new instruments developed for such measurements, while the tactile sensitivity of the dental attachment tissues will be measured by the calibrated hair method. Measurements will be made with and without anesthesia. It is planned to develop a means of applying vibrations of certain periods to the teeth and then measuring the amplitude or resonant frequency of the tooth. A correlation will be made between this measurement and the clinical state of health of the dental attachment tissue.

Progress to 6/30/48: A series of calibrated hairs ranging in force from 0.6 to 5000 mg, for determining the tactile sensitivity of teeth and oral mucosa, was prepared.

Seven subjects were tested by a gnathodynamometer, for maximum biting force on all maxillary teeth, on several different days. The forces range from less than 20 to 260 lbs depending upon the position of the tooth and the condition of the periodental membrane. The standard deviation of a single determination was calculated for one of the subjects. This value ranges from 10 to 30% with different teeth.

PROSTHESIS, OPERATIVE TECHNOLOGY, AND ORAL SURGERY, NR-181-396 (Cont.)

Prior to the initiation of this project an instrument was developed which shows promise of measuring the degree of tooth mobility. A single generator was connected to a record cutter which drove a wire 1 mm in diameter producing a longitudinal vibration at a frequency ranging between 20 to 15,000 cycles. The amplitude of vibration of the wire is measured by phonographic pickup which is placed in contact with the wire. The output of the phonograph pickup is amplified and measured on a decibel meter. The frequency range from 800 to 1200 cycles/sec proved to be most useful in separating loose from stable teeth. When this range was tried on several periodental patients it was found that the dampening effect of a tooth in contact with a rod varied inversely according to the degree of the mobility of the tooth. This finding seems to establish the soundness of the principle involved. However, certain modifications in the equipment will have to be made, in order to bring about satisfactory precision of measurement.

Preliminary tests with carrots and peanuts indicated that moderate chewing produces particles ranging in size from those larger than 10 mesh to finer than 100 mesh. Analysis of the particle size distribution will be determined by plotting the data on logarithmic probability paper and by interpolating to estimate the median particle size.

Information is now needed on the precision and reproducibility of the method, and on which foods it should be used to evaluate the influence of hardness and toughness in mastication.

The measurement of size, shape, and hardness discrimination in the mouth was discussed in conferences. Rubber specimens with different and known sure hardness values, will be used on the subjects, who will be asked to determine their relative hardness. The ability to discriminate shape is to be determined by use of spheres of lucite which have two flat spots set at varying angles to each other. Just recently the director of the project J. T. O'Rourke died suddenly and Dr. A. S. Manly has assumed responsibility of the project with support of the Dental Branch ONR.

Estimated Completion: 31 October 1950

ANATOMY, PHYSIOLOGY, AND CHEMISTRY

NR-182-077 — Dietary and Other Factors Concerned in Mouth and Tooth Deterioration — (Unclassified)

Contractor: Cornell University, Ithaca, New York
Contract: N6-ori-91, Task VI, (6/1/46 to 6/30/51)
Investigator: C. M. McCay

In order to evaluate the many conditions in which oxalates of foods protect the teeth against etching, studies are in progress with various species of animals such as rats, hamsters, cotton rats, and dogs. Special attention is being given to the protection by oxalates against acid erosion of enamel and against "caries" produced by feeding cotton rats and hamsters diets rich in sugar. The nature of the oxalate coating and its wearing ability on teeth are being studied. Since the oxalate coatings which can be laid down from natural foodstuffs not only protect teeth but also resemble calculi, efforts are being made to analyze the deposits and define the mechanism of deposition.

Substantial use has been made of the test for the buffering capacity of the mouth against acids in studies with men and women. This buffering capacity is remarkably constant for a given individual but varies widely between individual persons.

It is planned to increase the studies with dogs to include research on the effect of maternal diets upon the teeth of the offspring and to initiate exploratory studies with cats in attempts to determine if dietary relationships with periodontal tissues can be established. (Pottenger's claims.)

Progress to 6/30/48: Investigations are being made to learn more about the effects of oxalate on teeth, and to devise methods to employ oxalate in some form such as rhubarb and at the same

ANATOMY, PHYSIOLOGY, AND CHEMISTRY, NR-182-077 (Cont.)

time not dissipate available dietary calcium. Rats and dogs are being tested to determine if the proper timing of ingestion of citrus fruits and rhubarb taken at one time of day and whole milk taken at another time will protect the teeth against acid etching, and at the same time acquire possible favorable effects from fruit juices utilizing dietary calcium to the optimum extent. Utilization of calcium in old age is being studied by use of radioactive calcium 45. Techniques in the study of calcium absorption in rats and dogs using this isotope are being established. Etching on the teeth of a rat that has drunk only 10 ml of an acid sucrose solution can now be detected. A single drink of 5 ml cannot be detected.

Since pineapple juice contains a small amount of oxalate it was tested and found to etch teeth although its pH ranges from 3.2 to 3.5. By adding .1% sodium oxalate in the pineapple juice the etching was prevented.

The origin, chemical composition, and lasting quality of the film produced by oxalate on teeth was studied. No deposit could be produced on the teeth of four steers fed powdered sodium oxalate at the rate of 7 gm per day for 33 days. In rats, deposits were irregular and appeared in scattered patches and in many instances only on the upper molars, or were heavier than on the lower molars.

In other experiments it was shown that when oxalate solutions were fed for preliminary periods prior to feeding the acid drink the deposit failed to prevent etching. It appears, therefore, that the oxalate must be incorporated in the acid beverage in order to be effective or protect against etching.

In connection with an exploratory study to determine whether the oxalates would prevent decay in the teeth of cotton rats fed sugar caries-producing diets, it was found that some differences were noted, namely; that there seemed to be some protection against caries by the oxalates. However, here the investigator refers to the work of Comdr. Carl Schlack at the Naval Medical Research Institute which showed that there was no relationship between the oxalates and dental caries in the white or cotton rat but does suggest that there might be some individual species differences as well as strain differences.

Further studies are under way to determine what effective mixtures of rhubarb with lemon juice for human consumption are possible, since rhubarb gathered at different seasons of the year may exert different protective action from that produced in hot houses or in the early spring.

Comparisons are being made of dog meal, used in the investigator's laboratory, as a stock diet with the diet of coarsely ground corn meal devised by Hoppert and associates for the production of tooth decay. Studies are under way to determine the effect of additional sucrose in the diet on decay, and to determine if sodium oxalate might check this decay. One hundred and fifty young hamsters four to five weeks old were divided into six groups and fed the following diets: (1) stock, (2) stock-2 parts, sucrose-1 part, (3) same as (2) but supplemented with 200 mg sodium oxalate per 100 gm of feed, (4) Hoppert's diet of corn meal-60 parts, powdered milk-30 parts, linseed meal-6 parts, alfalfa meal-3 and NaCl-1, (5) #4 diet-2 parts, sucrose-1 part, (6) #5 diet plus 200 mg sodium oxalate per 100 gm of feed. These diets are being supplemented with oak sprouts from the very beginning and after 125 days each diet is enriched by addition of 5% dry Brewer's yeast and 5% whole milk powder. This study was begun on January 8th 1947. At the end of 100 days five females from each group were killed and their teeth prepared for study. After 125 days 10 animals, 16 males and four females, from each group were killed and their teeth prepared. The remaining animals are now a year old and it is planned to continue the study until most of the animals have died in old age.

Estimated Completion: Indefinite

NR-182-407 Nutrition and Dental Supporting Structures (Unclassified)

Contractor: Columbia University, New York, New York
Contract: N6-onr-271, Task X, (11/1/47 to 10/31/48)
Investigator: D. E. Ziskin

ANATOMY, PHYSIOLOGY, AND CHEMISTRY, NR-182-407 (Cont.)

Studies will be made of: (1) The action of various collagen-stimulating substances (endocrine) on the supporting dental structures in animals being fed a diet deficient in vitamin C, and (2) the effect of vitamin D on tooth development and eruption in hypothyroid and normal animals.

Clinical and histological studies will be made on 14 groups of guinea pigs as to the effect on the dental supporting structures of dilantin, thyroid, dilantin and thyroid, male sex hormone, female sex hormone, supplementary vitamin C added to an adequate diet, and to a diet deficient in vitamin C.

An investigation will also be conducted on ten groups of weaning rats as to the effect on tooth development and eruption of supplementary vitamin D deficiency, and addition of vitamin D after D avitaminosis has been produced in normal thyrodectomyzed and hypothyroid animals.

Progress to 6/30/48: One hundred twenty guinea pigs each weighing 275 to 400 gm have been divided into 12 groups of 10 each and kept on the regimen shown above. In both groups receiving the alpha estradial benzoate a change in the texture of the subcutaneous tissue has been seen clinically. This tissue, originally loose and yielding, now appears hard and unyielding. It has become progressively more difficult to lift the skin, or to pierce it with a hypodermic needle. However this histological study must be made before a more definitive description can be given. The animals had been on this experiment eight weeks when the status report was received on 3 May 1948.

Estimated Completion: Indefinite

NR-182-434 Vitamin C in Gingivitis and Amylolytic Activity of Saliva and Dental Caries (Unclassified)

Contractor: Georgetown University, Washington, D. C.
Contract: N7-onr-461, (12/1/47 to 11/30/48)
Investigators: W. C. Hess, E. Everitt

Under this project a quantitative study will be made of the vitamin C content of the blood with a view of arriving at a correlation between the vitamin C content of the blood, and the degree of gingivitis present in patients. If there is a positive correlation, vitamin C therapy will be instituted, and the manner in which this therapy affects the patient will be studied.

Progress to 6/30/48: The studies on the amylolytic activity of saliva and dental caries have been completed and submitted for publication to the Journal of Dental Research. Conclusions reached on this phase of the study are: (1) Salivary anylase activity can be measured in serially diluted saliva by the quantitative estimation of total reducing sugar by the Folin-Wu method. Amylase activity is directly proportional to concentration when pH, temperature and time are constant. (2) Salivary amylase activity in the same individual does not vary significantly from day to day. (3) There was no significant difference between the salivary amylase activity of a series of 20 non-carious individuals, and a series of 36 individuals with caries of varying degrees.

No progress to report on Vitamin C studies.

Estimated Completion: December 1948

NR-182-459 Salivary Ammonia and Dental Caries and Parodontosis (Unclassified)

Contractor: Western Reserve University, Cleveland, Ohio
Contract: N7-onr-470, Task I, (11/1/47 to 6/30/50)
Investigators: J. A. Muntz, T. J. Hill

ANATOMY, PHYSIOLOGY, AND CHEMISTRY, NR-182-459 (Cont.)

Under this project a study will be made of the rate of formation of salivary ammonia and its influence as an etiological factor in resistance and susceptability to dental caries and periodontal disease.

A new method will be used whereby ammonia in the saliva can be determined accurately, conveniently, and rapidly. The correlation between rates of salivary ammonia production, periodontal disease, and dental caries will be investigated, as well as the correlation between rates of salivary ammonia production, Ph of saliva, buffering capacity of saliva and its ability to ferment glucose. A biochemical study will be made of the mechanism involved in producing salivary ammonia and of the nature of its inhibitory action upon oral lactobacilli and the manner in which it inactivates enzymatic processes. Human subjects will be studied.

Progress to 6/30/48: Work has been largely organizational in character. Experiments are under way to develop cultural media for the growth of L. Acidophilus in masses suitable for use in the Warburg apparatus with special regard for the glycolytic activity of the harvested organisms. It has been observed that an acetate medium favors the latter feature.
Estimated Completion: 30 June 1950

NR-182-485 Dietary Protein and Dental Caries (Unclassified)

Contractor: Massachusetts State College, Amherst, Massachusetts
Contract: N7-onr-460, Task I
Investigator: J. O. Holmes

Dietary factors involved in dental caries are not well known. Under this project an investigation will be made of proteins as possible factors in inhibiting or promoting dental caries.

A litter of male white rats will be fed, finely ground synthetic rations, for 14 weeks, rations containing various levels of (1) casein or other protein, (2) different amino acids and low casein, and (3) casein preparations free of contaminants. The caries incidence will be determined by the method used at the Naval Medical Research Institution.

Progress to 6/30/48: No progress has been reported.
Estimated Completion: Indefinite

NR-182-630 Changes in the Glycogen Metabolism of the Oral Mucous Membrane Associated with Pre-Cancerous Lesions (Unclassified)

Contractor: Harvard University, Cambridge, Massachusetts
Contract:
Investigator: D. Weisberger

The purpose of this project is to study lesions of the oral mucous membranes in individuals under a variety of circumstances. Their lesions may be called pre-cancerous because of the chemistry and also because of their potentiality for developing irreversible changes such as proliferative leukoplakia and not infrequently cancer. The local biological mechanism concerned with deposition of glycogen in normal mucous membranes and interference of such mechanism in abnormal mucous will be studied.

Progress to 6/30/48: No progress to report, project being negotiated.
Estimated Completion: July 1950

BACTERIOLOGY AND PATHOLOGY

NR-183-242 Use of Germ-Free Animals in the Study of Dental Caries (Unclassified)

Contractor: University of Chicago, Chicago, Illinois
Contract: N6-ori-20, Task XIII, (12/1/46 to 11/30/48)
Investigator: J. R. Blayney

Under this project rats are born and raised under completely aseptic conditions and fed a sterilized diet which is identical with (except for sterilization) a diet on which rats develop caries in about 100 days. The technique makes possible the inoculation of specific microorganisms into the oral cavities of these rats.

Three separate conditions were investigated in terms of dental decay: (1) nutrition without influence of bacterial action, (2) specific bacterial action, and (3) nutrition plus either specific or mixed bacterial action.

Progress to 6/30/48: Since 1 June 1947, 27 litters with an average of 10 to 12 fetuses per litter have been delivered by Caesarian section into the germ-free cages. The majority of these rats have been used for biochemical studies in order to improve the nutrition of future litters. From these litters five rats have been maintained on a dental caries-producing diet for 152 days in a bacterial free environment. Three pregnancies in germ-free rats, two of which occurred in animals on the caries-producing diet. None survived any length of time.

In dental caries studies the rodents have been kept on the caries diet 150 rather than 100 days in order to provide greater opportunity for tooth decay to appear. Since the beginning of the project 65 rats have been examined for dental caries. To date 29 remain to be examined. Only five of these animals were germ-free for the required time on the dental caries diet. Four of these were dental caries free. One rodent showed a badly broken down molar which will be prepared for microscopic examination to determine whether this was due to caries or fracture. Eight rats which were accidentally contaminated with various bacteria showed no caries. The microorganisms recovered from their mouths were not lactobacilli and none produced acid to the same degree as lactobacilli. Control animals revealed caries incidence of 60% during the 100 day dietary period. Those on the diet 150 days showed increase of caries incidence.

The skulls of the germ-free animals were 10 to 20% smaller at the time of their death than the skulls of the control animals.

Throughout the current year the possibility of rearing experimental animals on a low fluoride containing diet, and comparing the fluoride content of the femurs of such animals with those of animals fed the usual stock rations, has been investigated. The diet contained 2.6 to 4.68 parts per million of fluorine ion as compared to 37 to 58 parts per million found in Pruina of Rockland chows. The femurs of the animals on the low fluorine caries producing diet ranged from 50 to 90 parts per million fluorine in contrast to 250 to 280 parts per million in femurs of animals, on standard stock rations. This is taken to assure the worker that the absence of dental caries in the teeth of the animals cannot be attributed to the fluoride content of enamel.
Estimated Completion: Indefinite

NR-183-333 The Study of Oral Microorganisms (Unclassified)

Contractor: University of Pennsylvania, Philadelphia, Pennsylvania
Contract: N6-onr-249, Task V, (2/1/48 to 2/1/49)
Investigator: J. L. Appleton

The purpose of this project is to recognize and evaluate the factors influencing the types and quantity of microorganisms in the human mouth. Studies will be made of the inter-relations among the microbiotic populations of the oral, pharyngeal, and nasal cavities, and of the effects of saliva on microorganisms. Surveys will be made of oral microflora (seasonal, by age, etc.), and its correlation with oral pathology. The mechanism of the deleterious effects of the local use of chemotherapeutic and antibiotic agents will also be investigated.

BACTERIOLOGY AND PATHOLOGY, NR-183-333 (Cont.)

Progress to 6/30/48:

1. Extending the work of Bloomfield (Amer. Rev. Tuberc. 5:903-914, #11, Jan. 1922), lamp black, suspended in the subject's own saliva, was applied to the tip of the uvula. Inspection, immediately following the closing and opening of the mouth, showed areas of blackness on the posterior wall of the oropharynx and on the lingual dorsum in several subjects. This indicated a mechanism by which microorganisms could be exchanged between the oral cavity and the oropharynx.

   The next step was to apply Serratia marcescens (Bacterium prodigiosum) to the tip of the uvula and then to study (a) the frequency with which this organism could be recovered from various sites on the oral mucosa and (b) the duration of its survival at these sites. The data furnished by (a) might reveal if there were any relatively constant and individual pathways by which microorganisms were distributed within, and eliminated from, the mouth.

   Nine sites were chosen and observations were made on two groups of 10 girls in their late teens or early twenties, with better than average mouth conditions (dental hygienist students). Observations were collected until 10 sets were completed, the resulting data are now being statistically analyzed.

   It is proposed, on the basis of what is learned from the work described above, to extend the observations along the following lines:

   a. Use other sites of initial inoculation than the tip of the uvula.
   b. Use other bacteria than S. marcescens.
   c. Use bacteriophage, as a representative of a virus, in place of the bacteria.

2. The treatment of infected root canals in this school has revealed that in many instances penicillin therapy failed because of penicillin resistant bacteria. The bacteria were identified as belonging to the enterococci, thus it was decided to determine the prevalence of these microorganisms in the mouths of patients reporting at the school for dental treatment of all types. This survey will contribute to information on the kinds and types of bacteria found in the oral cavity.

   A total of 16 salivas have been collected and cultures completed. The identification of enterococci has been possible in six out of the 16 salivas. The study is being continued.

3. Reports in the literature have described observations which indicate that antibacterial substances are present in the mouth. Several authors have suggested that the principal activity may be due to an immunologic substance identical with, or analogous to, the classical antibodies of blood serum. Plans have been outlined and preliminary steps undertaken to investigate the proteins in saliva. It is proposed to determine (a) whether proteins are in saliva that may be related to antibodies, and (b) what effect they may have on bacteria.

Estimated Completion: Indefinite

NR-183-420 Bacteriemias Resulting from Tooth Extraction (Unclassified)

Contractor: Tufts Dental School, Medford, Massachusetts
Contract: N7-onr-463, Task I, (11/1/47 to 10/31/48)
Investigator: J. P. Lazansky

Under this project a comparison will be made of bacteriemias produced by tooth extraction and periodontal treatments, and an evaluation will be made of the methods of control.

Blood cultures of approximately 200 patients will be examined before, during, and after tooth extraction, and a comparison will be made between the groups premedicated with penicillin, or given local gingival penicillin injection, penicillin lozenges, or gingival diathermy. Suitable controls will be used in all groups.

BACTERIOLOGY AND PATHOLOGY, NR-183-420 (Cont.)

Progress to 6/30/48: Blood cultures of an increasing number of patients are being made immediately after and then five minutes after oral surgical interferences of minor and moderate variety. The organisms recovered have been identified but it appears that defense mechanisms of the majority of the patients studied have been sufficiently effective to give a negative blood culture five minutes after oral surgical interferences. Comparison of immediate blood culture after single and multiple tooth-extractions still reveals a trend toward positive culture in patients subjected to multiple tooth extractions. Bacteriemias produced after scaling of teeth are few to date. As yet no antibiotics have been administered prior to oral surgery in these studies
Estimated Completion: 31 October 1948