APPLICATION FOR RESEARCH GRANT

February 10, 1955

Application is hereby made for a grant in the amount of $9,106.00
for a period of one year for the purpose of conducting a research
project on the following subject: NAV1.941208.080

A STUDY OF THE PREVALENCE AND SEVERITY OF THYROID
DEFICIENCY IN YOUNG AND MATURE ADULT MALES

Name of principal investigator: Paul Starr, M.D.
Professor of Medicine
(Head) Department of Medicine
School of Medicine
University of Southern California

Address of principal investigator: Box 138, 1200 N. State Street
Los Angeles 33, California

Name of financial officer to whom check should be mailed:

Robert Fisher
Financial Vice-President

Address of financial officer: University of Southern California
3518 University Avenue
Los Angeles 7, California

Name of institution: University of Southern California

Name and title of official authorized to sign for institution:

[Signature]
Robert Fisher
Financial Vice-president

[Signature]
Paul Starr, M.D.
(Head) Department of Medicine

Enclosure (1) to ONR/Fac. Ltr
Serial 30109 dated FEB 25 1955
Personnel
Paul Starr, M.D., F.A.C.P., Principal Investigator
Arnold G. Ware, Ph.D., Consultant in Chemistry
Statistical Secretary & Social Worker (Part time) 1800.00
Chemical Technician (Full time) 3600.00

Permanent Equipment
Furnace, electric - Braun Muffle Multiple Unit with Rheostat 320.00
Centrifuge, International Equipment Co., Model SBV-R complete with Head, Metal shields, Trunnion carrier and cushions 780.00

Consumable Supplies
Chemicals and Glassware 500.00

Total 7000.00
39% Provisional Overhead 2106.00
Total 9106.00

Estimate of future requirements: Two years @ $8,006.00 per year
Reason for the investigation:

(1) No information is available because former determinations were made with the basal metabolic rate test which has been found to conceal hypothyroidism. The test is made to appear normal by nervousness and other factors even in individuals having no thyroid gland function (Hoskins, R.G. The thyroid pituitary apparatus as a servo (feed-back) mechanism. J. Clin. End. 9: 1429, 1949).

(2) Hypothyroidism is a prime cause of mental sluggishness, poor memory, fatigability, feeble response to stress, and of prolonged production of vascular and parenchymatous degeneration (Kimble, S.T. and Steiglitz, E.J. Geriatrics 7: 20, 1952).

(3) A reliable biochemical method is available for the direct determination of the thyroid hormone in the blood (Barker, S.B. et al., J. Clin. Inv. 30: 55, 1951).

(4) Hypothyroidism is not recognized in routine physical examinations.

(5) The condition is completely correctible by thyroxine medication with dosage adjusted by serum protein bound iodine tests.

Research Plan

A. Specific Aims: The general incidence of hypothyroidism, defined as the condition usually associated with a serum protein bound iodine of less than 4 micrograms percent, is to be found by blood chemistry tests in young adult males (college students, medical school students, hospital employees, young veterans) and men from 30 to 40 years of age giving blood at the hospital blood bank and in veterans of this age. Life history and physical examination, EKG, routine clinical laboratory tests will be done in all positive cases. The purpose is not to establish the serum protein bound iodine in "normals" but to discover the occurrence of low values in a general population of people leading their usual lives. The pathogenic mechanism of the hypothyroid state will be analyzed when possible by radioactive iodine and thyrotropic hormone tests. The associated systemic pathology will also be determined and studies carried out to determine the possible causal relationship between the hypothyroid state and the pathology found.

The question may be raised as to the volume of serum protein bound iodine determinations that can be done. In this regard it may be stated that a competent chemical technician can perform fifty determinations per week, 2500 a year. The reliability of this work is under the supervision of Dr. Arnold Ware, Head Chemist, L.A.C.G.H., and Assistant Professor of Biochemistry and Nutrition, University of Southern California. Inter and intra-laboratory controls are in operation. (Henry, R.J., and Segalove, M. Running of standards in clinical chemistry and the use of the control chart. J. Clin. Path. 5: 305, 1952).
A study of clinical experience with the serum protein bound iodine method was reported in 1950. In this study 572 reports of patients of the Los Angeles County Hospital were analyzed by clinical diagnosis. (J. Clin. Endo. 10: 1237, 1950). A review of hypothyroidism (Paul Starr, Hypothyroidism: an essay in modern medicine, American Lecture Series, Charles Thomas Publisher, 1954) has been made, in which a tabulation is made of 5061 reports of serum PBI submitted by private physicians to the Bio-Science Laboratories, Director, Richard Henry, University of Southern California, Assistant Clinical Professor of Medicine.

As an example, results of blood chemistry tests for serum protein bound iodine are shown below in a tabulation.

Tabulation of PBI Values Determined in Patients Suspected of Thyroid Disease
Los Angeles County Hospital June 1950 - June 1951

<table>
<thead>
<tr>
<th>Category</th>
<th>Range</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very Low</td>
<td>0.0 - 2.0</td>
<td>181</td>
</tr>
<tr>
<td>Low</td>
<td>2.0 - 3.0</td>
<td>336</td>
</tr>
<tr>
<td>Subnormal</td>
<td>3.0 - 4.0</td>
<td>505</td>
</tr>
<tr>
<td>Low Normal</td>
<td>4.0 - 5.0</td>
<td>525</td>
</tr>
<tr>
<td>Normal</td>
<td>5.0 - 6.0</td>
<td>356</td>
</tr>
<tr>
<td>Normal</td>
<td>6.0 - 7.0</td>
<td>145</td>
</tr>
<tr>
<td>High normal</td>
<td>7.0 - 8.0</td>
<td>75</td>
</tr>
<tr>
<td>Total cases</td>
<td></td>
<td>2123</td>
</tr>
</tbody>
</table>

Note that this clinical material is made up of the aged, malnourished, and severely sick charity patients suspected of thyroid disease. Possible incidence in young American males may be only one percent, possibly five percent, or, if very prevalent, ten percent.

B. Facilities Available:
1. Thyroid and Endocrine Clinics of the University of Southern California and the Los Angeles County Hospital.
2. The chemistry laboratory of the Thyroid Clinic supported by private commercial funds.
3. The Bio-assay Laboratory of Doctor Boris Catz, supported by U.S. Public Health Service.
4. University of Southern California isotope laboratory supported by the American Cancer Society.
5. Los Angeles County Hospital Steroid Laboratory
6. Basal Metabolism Laboratory of the Thyroid Clinic
Curriculum Vitae - Paul Starr, M.D., F.A.C.P.

Born: April 24, 1893, Winnetka, Illinois
Harvard College, A.B., 1916
Pre-Med: University of Chicago, B.S., 1919
Medical Schools: Rush Medical College, 1921, Degree: M.D.
Internship: Cook County Hospital, Chicago, Illinois, 1921-23
Licensure: Illinois 1922, California 1945
Fellowship: Massachusetts General Hospital, 1923-24
Teaching Appointments: Instructor and Assistant Professor of Medicine,
Northwestern University, 1924-42; Clinical Professor of Medicine,
University of Southern California, 1945-48; Professor and Chairman,
Dept. of Medicine, University of Southern California, 1948.
Voluntary Assistant, Peter Bent Brigham Hospital, 1923
Post Graduate education: Berne, Switzerland, 1931
Hospital Staffs: Huntington Memorial, Pasadena, California; St. Luke's
Pasadena; Los Angeles County General Hospital, Los Angeles; Hospital
of the Good Samaritan, Los Angeles.
Memberships: American Society for Clinical Investigation; Central Society
for Clinical Research; Endocrine Society; Fellow, American College of
Physicians, 1946; Western Society for Clinical Research; Society for
Experimental Biology and Medicine (Chairman, Southern Calif., 1954-55);
American Goiter Society; and Sigma Xi.
Specialty: Internal Medicine (American Board of Internal Medicine, 1937)
Military experience: 1917-18 Camp Mead Base Hospital, Corporal Medical
Chief of the Medical Service.

Curriculum Vitae - Arnold O. Ware, Ph.D.

Born: June 1, 1915, Butler, Illinois
B.A. Carthage College 1933-37
M.S. University of Colorado 1939
Ph.D. University of Colorado 1942
Fellowship: University of Colorado 1937-38 Blood Chemistry
Fellowship: Colorado General Hospital, Chemistry Laboratory 1938-40
Teaching Assistant, University of Colorado 1940-42
Military Service: Captain, Nutrition Officer, Sanitary Corps, 1942-45.
Research Associate: Department of Physiology, Wayne University 1946-49
Assistant Professor of Biochemistry and Nutrition, University of Southern
California 1949-1952
Associate Professor of Biochemistry and Nutrition, University of Southern
California 1953--

Memberships: Sigma Xi; American Association for Adv. of Science; American
Society of Biolog. Chemists; International Society for Hematology.
Effect of iodine in exophthalmic goiter.
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Rapid response of guinea pig thyroid to a single injection of thyrotropic hormone.


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Endocrine studies of patients after subtotal hypophysectomy.

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Starr, Paul and Pomerene, Herman

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Clinical and biochemical observations on the use of large doses of
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