

# Lawrence Berkeley National Laboratory

## Recent Work

### Title

LONG-TERM EFFECT OF DESICCATED THYROID SUBSTANCE UPON SERUM LIPOPROTEINS AND SERUM CHOLESTEROL

### Permalink

<https://escholarship.org/uc/item/78n9d15h>

### Authors

Strisower, Beverly  
Gofman, John W.  
Galioni, Elmer F.  
et al.

### Publication Date

1956-09-28

TCP

UCRL 3534  
c.2

UNIVERSITY OF  
CALIFORNIA

*Radiation  
Laboratory*

LONG-TERM EFFECT OF DESICCATED THYROID  
SUBSTANCE UPON SERUM LIPOPROTEINS  
AND SERUM CHOLESTEROL

BERKELEY, CALIFORNIA

TWO-WEEK LOAN COPY

*This is a Library Circulating Copy  
which may be borrowed for two weeks.  
For a personal retention copy, call  
Tech. Info. Division, Ext. 5545*

## **DISCLAIMER**

This document was prepared as an account of work sponsored by the United States Government. While this document is believed to contain correct information, neither the United States Government nor any agency thereof, nor the Regents of the University of California, nor any of their employees, makes any warranty, express or implied, or assumes any legal responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by its trade name, trademark, manufacturer, or otherwise, does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof, or the Regents of the University of California. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof or the Regents of the University of California.

UCRL-3534  
Distribution:  
Health and Biology

UNIVERSITY OF CALIFORNIA

Radiation Laboratory  
Berkeley, California

Contract No. W-7405-eng-48

LONG-TERM EFFECT OF DESICCATED THYROID SUBSTANCE  
UPON SERUM LIPOPROTEINS AND SERUM CHOLESTEROL

Beverly Strisower and John W. Gofman

and

Elmer F. Galioni, Joshua H. Rubinger, Jean Pouteau, and Peter Guzvich

Stockton State Hospital  
of the  
Department of Mental Hygiene  
Stockton, California

September 28, 1956

Printed for the U.S. Atomic Energy Commission

LONG-TERM EFFECT OF DESICCATED THYROID SUBSTANCE  
UPON SERUM LIPOPROTEINS AND SERUM CHOLESTEROL

Beverly Strisower and John W. Gofman

Division of Medical Physics  
of the  
Donner Laboratory of Biophysics and Medical Physics  
University of California, Berkeley, California

and

Elmer F. Galioni, Joshua H. Rübinger, Jean Pouteau, and Peter Guzvich

Stockton State Hospital  
of the  
Department of Mental Hygiene  
Stockton, California

September 28, 1956

ABSTRACT

Desiccated thyroid substance in doses of 260 mg (4 grains) and 325 mg (5 grains) per day produces a sustained fall in serum lipoproteins of the  $S_f^0$  0-12,  $S_f^0$  12-20,  $S_f^0$  20-100, and  $S_f^0$  100-400 classes and in serum cholesterol.

The absolute magnitude of the drop in level of any lipoprotein class is, on the average, greater at higher initial lipoprotein levels.

"Escape" phenomena previously observed on a dosage of 195 mg per day of thyroid are not observed with the higher dosage schedule.

The large drops in Atherogenic Index for subjects characterized by high initial values of atherogenic index suggest that desiccated thyroid substance is worthy of consideration as a prophylactic agent with respect to coronary heart disease.

LONG-TERM EFFECT OF DESICCATED THYROID SUBSTANCE  
UPON SERUM LIPOPROTEINS AND SERUM CHOLESTEROL

Beverly Strisower and John W. Gofman

Division of Medical Physics  
of the  
Donner Laboratory of Biophysics and Medical Physics  
University of California, Berkeley, California

and

Elmer F. Galioni, Joshua H. Rubinger, Jean Pouteau, and Peter Guzvich

Stockton State Hospital  
of the  
Department of Mental Hygiene  
Stockton, California

September 28, 1956

Introduction

It has previously been reported by Strisower and co-workers<sup>1, 2</sup> that desiccated thyroid substance exerts a profound influence upon low-density serum lipoprotein and serum cholesterol levels. The earliest study reported the effect of 650 mg of desiccated thyroid substance administered daily over a period of approximately 10 weeks. In each of 11 cases on this dose of thyroid there was observed marked depression of the blood levels of cholesterol,  $S_f^0$  0-12, and  $S_f^0$  12-20 lipoproteins, during the entire period of administration of the thyroid.  $S_f^0$  20-100 and  $S_f^0$  100-400 lipoproteins showed less uniform depression when thyroid was administered. That study was to test response to thyroid on a very high dosage schedule. As it had been determined that all patients on a high dose of thyroid do respond with a fall in serum lipoproteins and cholesterol, the practical considerations of use as well as the need to understand mechanism dictated study of the response to lower doses of thyroid substance. A long-term study was therefore initiated, starting with a dosage schedule of 195 mg (3 grains) per day. The results of 30 weeks of administration of this dosage of thyroid have already been reported.<sup>2</sup> A marked drop in mean level of  $S_f^0$  0-12 and  $S_f^0$  12-20 lipoproteins and of serum cholesterol was observed initially on this dosage in a series of 50 patients. However, in spite of continued administration of the thyroid, the great majority of patients showed an apparent "escape" phenomenon in that the lipoprotein and cholesterol levels, maximally depressed at 3 weeks after starting the thyroid, gradually returned toward the control levels. At 30 weeks of continued administration of the same dose of thyroid the lipoprotein and cholesterol levels were not much below the control levels. The hypothesis was advanced that the "escape" phenomenon was in all likelihood the result of gradual shut-down of endogenous thyroid hormone production, with the end result that the daily available thyroid to the patient at 30 weeks of administration of 195 mg per day was not appreciably above that available during the pretherapy control period. It was expected that if the dosage of thyroid were increased, a point should possibly be reached at which the sum of endogenously plus exogenously avail-

able thyroid should leave the patient with a greater available daily supply of hormone than had characterized him before the experiment, and that the lipoprotein and cholesterol levels should then remain depressed. This concept has been tested now by extension of the original 30-week administration of 195 mg of thyroid to include two additional periods, the first at 260 mg (4 grains) per day for 39 weeks and the second at 325 mg (5 grains) per day for 36 weeks. These studies are reported here.

### Materials and Methods

Sixty schizophrenic patients at Stockton State Hospital were chosen as the experimental subjects. So far as could be determined these patients were physically and metabolically normal. The group of 60 patients was composed of 30 females ranging in age from 27 to 56 years (mean age 39.6 years) and 30 males ranging in age from 25 to 57 years (mean age 40.3 years). The only basis of selection used in constituting the group was that in each case the patient's mental status made leave or discharge from the hospital very unlikely for a long time.\*

Two important requirements of an experiment to test the efficacy of a drug such as desiccated thyroid in lowering lipoproteins are met by using patients in chronic mental wards. One consideration is a stable diet, approximated by an institutional diet, since it is well known that dietary alterations have profound effects on lipoprotein concentrations and distributions.<sup>3,4,5</sup> The second consideration is assurance that the medication is actually taken consistently by each patient. Interested nursing and technical personnel on the wards help to give this assurance.

Two control blood samples for lipoprotein and cholesterol analyses were drawn before the administration of desiccated thyroid substance was begun. At the same time weight, blood pressure, and pulse measurements were made.

Desiccated thyroid administration was begun in 20 patients (10 male and 10 female) in each of three succeeding weeks. Blood samples were drawn on the same staggered schedule at 3-week intervals during the first two periods of the experiment and later at 6-week intervals. Weight, blood pressure, and pulse measurements were made at the time of each blood sample. Lipoprotein and cholesterol measurements were made by techniques previously described.<sup>6,7</sup> The patients were started on desiccated thyroid at different times so that blood sampling would also be done in different weeks, in order to minimize the effect of any small technical variations in the analyses of serum lipoproteins and cholesterol.

The dosage of desiccated thyroid was maintained at 195 mg (3 grains) per day for an initial period of 30 weeks, followed by a period of 39 weeks on 260 mg (4 grains) per day and finally by a period of 36 weeks on 325 mg (5 grains) per day.

---

\* This experiment was begun in June 1953, before the common use of such therapeutic agents as reserpine and chlorpromazine. At no time in the course of this entire study were such agents administered to any of the patients in this group.

The patients were followed for an additional 27 weeks after the administration of desiccated thyroid had been stopped. Blood samples were drawn at 3, 6, 12, and 27 weeks off the desiccated thyroid. As during the period of thyroid administration, weight, blood pressure, and pulse measurements were made at the time of each blood sample.

Of the original group of 60 patients, 39 completed the entire course of thyroid administration, whereas for a variety of reasons 21 were lost to the study at some point. The 21 cases lost to the experiment and the reasons were:

- (a) 6 cases were transferred to a different ward for active psychiatric therapy (there was no indication on the part of attending physicians that thyroid administration was involved as a factor leading to such transfer);
- (b) 1 case was transferred to surgical ward for a hemorrhoidectomy;
- (c) 2 cases refused to cooperate further in the blood sampling;
- (d) 6 cases left the hospital;
- (e) 4 cases experienced weight loss of sufficient degree to lead the staff to consider possible thyrotoxic effects and to remove the subjects from the study;
- (f) 2 cases showed some increase in agitation, which, although probably not associated with thyroid administration, led the attending physicians to remove the subjects from the study.

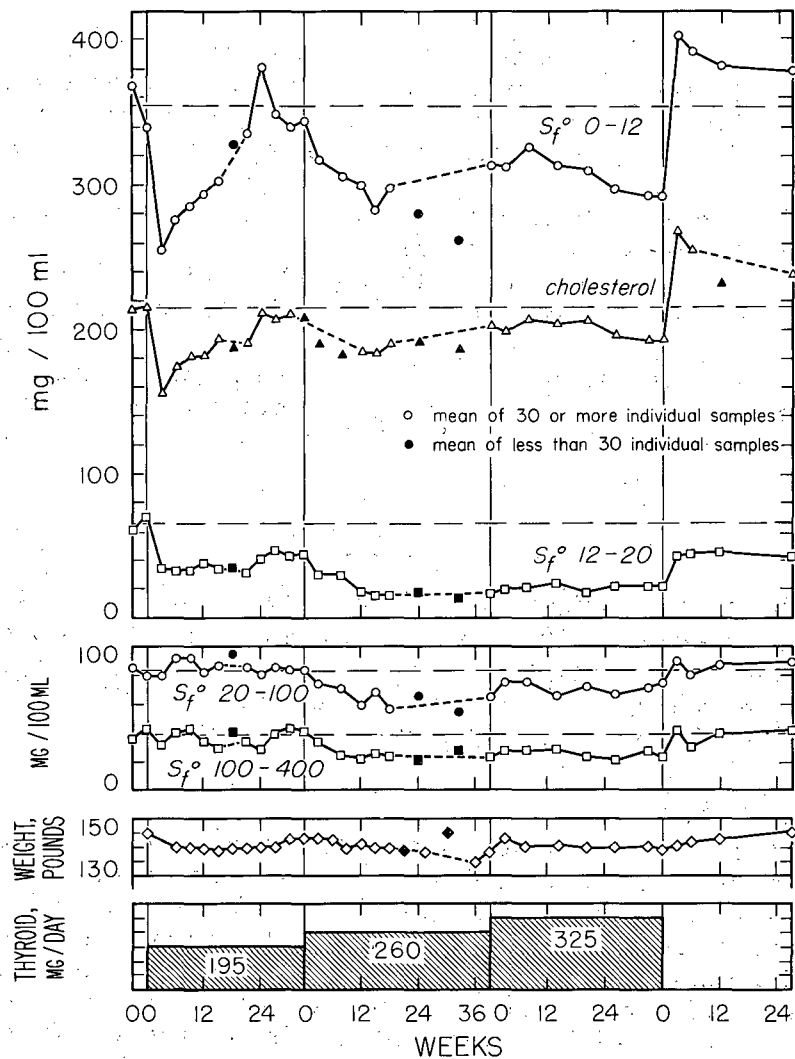
### Results

The mean changes in the four classes of low-density lipoproteins,  $S_f^0-12$ ,  $S_f^0 12-20$ ,  $S_f^0 20-100$ ,  $S_f^0 100-400$ , and the serum cholesterol for the 39 subjects who completed the entire course of thyroid administration are presented in Fig. 1. From the data plotted in Fig. 1 and from significance tests the following results can be described.

#### a. Serum Cholesterol

Initially, after 3 weeks on 195 mg of thyroid per day, there was a marked and significant ( $p < 0.01$ ) fall in the mean level of serum cholesterol from an initial level of 216 mg/100 ml to 157 mg/100 ml. Thereafter the mean serum cholesterol rose progressively toward the pretherapy levels. At 24 to 30 weeks of maintained dosage of 195 mg of thyroid per day, the cholesterol level had reached a value of 210 mg/100 ml, which cannot be proved significantly different from the initial values. With the increase in daily dose of thyroid to 260 mg per day a progressive and significant fall in serum cholesterol level to lower mean values was observed, with means being maintained between 184 mg/100 ml and 200 mg/100 ml throughout most of the 260-mg/day period. Toward the end of the 39 weeks on 260 mg/day and in the first 14 weeks of the 325-mg/day period the cholesterol levels showed evidence of a rising trend. While this part of the experiment was in progress the question was considered whether there was real evidence for some "escape" from the effect of the thyroid, or whether the patients were receiving less than the full dosage of 325 mg per day. The ward attendants were then re-impressed with the need for very careful attention to administration of the full dosage of the thyroid each day to every patient and





MU-12237

Fig. 1. The response curves of serum cholesterol,  $S_f^0$  0-12,  $S_f^0$  12-20,  $S_f^0$  20-100, and  $S_f^0$  100-400 classes of serum lipoproteins, and body weight during the periods on 195 mg, 260 mg, and 325 mg/day of desiccated thyroid and during the posttherapy period. Note: The light line superimposed on the response curve for each of the above measures represents the mean of two pretherapy control values.

were constantly reminded of this throughout the remainder of the experiment. It is of interest to note that following these discussions with the ward personnel, there was a progressive fall in serum cholesterol, which then remained lowered, at a mean level of 195 mg/100 ml, throughout the remaining 22 weeks of the administration of 325 mg/day of thyroid. Thus, during the period of administration of 325 mg/day of thyroid, when there was reasonable assurance that the patients received essentially the full dose of medication, no evidence of an "escape" phenomenon from the effect of thyroid upon the serum cholesterol levels was noted.

At 3 weeks after the cessation of administration of 325 mg per day of thyroid a marked rebound in serum cholesterol level occurred, reaching a mean of 269 mg/100 ml. Thereafter the mean cholesterol declined progressively to a level of 235 mg/100 ml, where it leveled out for the remaining 15 weeks of the 27-week posttherapy observation period.

#### b. The $S_f^0$ 0-12 Lipoproteins

In essentially all major features the  $S_f^0$  0-12 lipoproteins showed a response analogous to that observed for serum cholesterol levels. On a dose of 195 mg of thyroid/day a marked fall in mean  $S_f^0$  0-12 level occurred (maximal at 3 weeks from the initial value of 354 mg/100 ml to 256 mg/100 ml), followed by a gradual return to control levels at the end of the 30-week 195-mg/day period. With 260 mg of thyroid per day the mean  $S_f^0$  0-12 level fell progressively to a mean level of approximately 306 mg/100 ml. The rising trend in the last part of the 260-mg period and the first part of the 325-mg period corresponded to that observed for serum cholesterol levels. As with the serum cholesterol levels, following indoctrination of ward personnel for assurance that full medication be taken by all patients, the  $S_f^0$  0-12 levels fell and remained low, at a mean level of 294 mg/100 ml, throughout the remainder of the 325-mg/day period. No evidence for an "escape" phenomenon was noted.

The postthyroid period showed a marked rebound in  $S_f^0$  0-12 level to 403 mg/100 ml at 3 weeks off medication, followed by a gradual drop and leveling out at 378 mg/100 ml at 27 weeks after cessation of the thyroid.

#### c. The $S_f^0$ 12-20 Lipoproteins

The  $S_f^0$  12-20 lipoproteins showed a marked fall, from 76 mg/100ml to 44 mg/100 ml, with the administration of 195 mg per day of thyroid. In contrast to the  $S_f^0$  0-12 and serum cholesterol levels, the level of  $S_f^0$  12-20 did not show a tendency to rise throughout most of the 195-mg-per-day period, although in the final 9 weeks there was some increase. Even with this increase, however, the levels remained significantly below the pretherapy levels. With increase to 260 mg/day the  $S_f^0$  12-20 levels showed a marked further drop to a mean of approximately 25 to 30 mg/100 ml, where the levels remained for the rest of the 260-mg/day period and throughout the entire 325-mg/day period.

After cessation of thyroid administration there was a significant rise to 52 mg/100 ml, but no rebound above control levels. During the remainder of the 27-week postthyroid period  $S_f^0$  12-20 remained unchanged at 52 mg/100 ml.

d. The  $S_f^0$  20-100 and  $S_f^0$  100-400 Lipoproteins

In contrast with the findings for serum cholesterol,  $S_f^0$  0-12, and  $S_f^0$  12-20 lipoproteins, neither the  $S_f^0$  20-100 nor  $S_f^0$  100-400 classes of lipoproteins showed any significant change in mean level for the group of patients during the period of administration of 195 mg of thyroid/day. When the dose was raised to 260 mg/day, mean levels of both  $S_f^0$  20-100 and  $S_f^0$  100-400 showed gradual decreases to lowered levels which were thereafter maintained throughout the remainder of the 260-mg period and the entire 325-mg period. The  $S_f^0$  20-100 lipoproteins dropped from an initial mean value of 83 mg/100 ml to a mean value of 60 to 70 mg/100 ml during the 260-mg and 325-mg periods. The  $S_f^0$  100-400 lipoprotein value was 39 mg/100 ml initially. The mean value for the  $S_f^0$  100-400 lipoproteins dropped to approximately 25 mg/100 ml during the 260-mg and 325-mg periods.

When thyroid administration was stopped, both the  $S_f^0$  20-100 and  $S_f^0$  100-400 lipoproteins rose within 3 weeks to the prethyroid levels and remained at those levels for the entire 27-week posttherapy period.

e. Body Weight

During the first 6 weeks of administration of 195 mg/day the mean body weight fell from a mean value of 145 pounds to 140 pounds. Thereafter, during the 195-mg, 260-mg, and 325-mg periods the mean weight remained at 140 pounds except for some oscillations of 3 pounds above or below this level. Inspection of Fig. 1 for weight trends certainly does not lead to the suggestion that continued negative caloric balance (and hence, continued weight loss) is necessary in order to produce and maintain lipoprotein and cholesterol reduction. After cessation of thyroid there was a gradual return of the weight to the pretherapy weight of 145 pounds over the 27-week post-medication period.

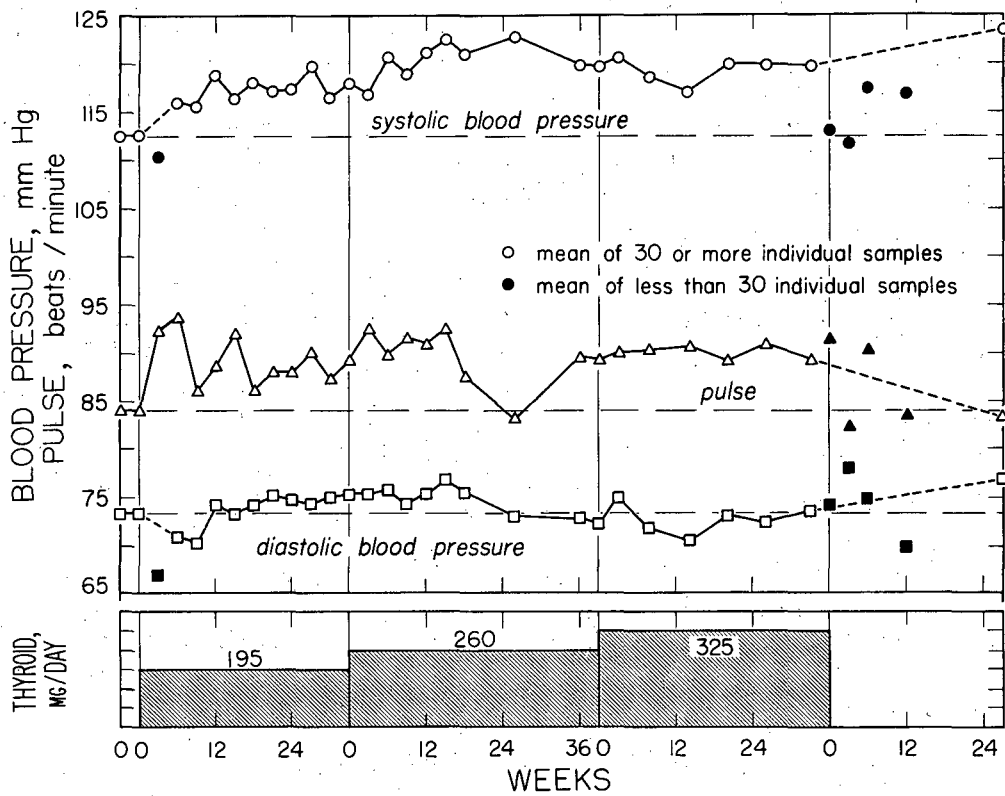
f. Blood Pressure and Pulse

The mean changes in pulse and in systolic and diastolic blood pressure for the various dosage schedules are presented in Fig. 2.

The pulse rate increased from an initial mean value of 84 beats per minute to an average of approximately 90 beats per minute during the entire period on desiccated thyroid at the three dosage levels of 195 mg, 260 mg, and 325 mg per day. With cessation of thyroid administration the pulse rate returned to the pretherapy level.

The systolic blood pressure rose gradually from a mean pretherapy level of 112 mm mercury to an average of approximately 120 mm mercury during the 260-mg/day and 325-mg/day thyroid periods. The systolic blood pressure remained at 120 mm mercury during the posttherapy period.

The diastolic blood pressure was characterized by no shift in the mean value of 74 mm mercury during the entire period on thyroid and the posttherapy period. The greatest changes observed are  $\pm 4$  mm mercury.



MU-12238

Fig. 2. The response curves of pulse and systolic and diastolic blood pressures during the periods on 195 mg, 260 mg, and 325 mg/day of desiccated thyroid and during the posttherapy period. Note: The light line superimposed on the response curve for each of the above measures represents the mean of two pretherapy control values.

### Discussion

The long-term study of the administration of desiccated thyroid substance at successive dosage levels of 195 mg, 260 mg, and 325 mg per day shows that it is possible to produce and maintain depression of the serum levels of cholesterol and  $S_f^0$  0-12,  $S_f^0$  12-20,  $S_f^0$  20-100, and  $S_f^0$  100-400 lipoproteins. The "escape" phenomenon, expressed in the form of a rise in lipoprotein and cholesterol levels, in spite of the continued administration of 195 mg of thyroid per day, was previously attributed by us to a shutdown on endogenous thyroid production. As a corollary it was predicted that the "escape" phenomenon should be preventable by an increase in thyroid dosage. The periods of administration of 260 mg and 325 mg of thyroid respectively show no "escape" phenomenon, and hence the results in these periods support the concept that thyroid shutdown was indeed the basis for the escape phenomenon that had been observed on a dosage of 195 mg. The rebound in levels--to levels above the control values--observed upon cessation of thyroid administration provides further evidence of the thyroid shutdown. During the immediate postthyroid period the exogenous supply of thyroid has been withdrawn, and if thyroid shutdown has existed during therapy the immediately available thyroid hormone supply is even lower than in the pretherapy control period. Hence a rebound in levels above those of the pretherapy control period may have been expected. As the endogenous supply increases with returning production of the thyroid gland, the lipoprotein levels may be expected to gradually decrease toward the pretherapy control levels. As has been noted, this was precisely the effect on lipoprotein levels observed during the later part of the postthyroid period.

In three cases out of the 39 the  $S_f^0$  0-12 level in the posttherapy period still remained more than 25% above the pretherapy level, even at 27 weeks following cessation of thyroid. In the absence of other reasons for such an elevation the possibility must be considered that reversal of the thyroid inhibition is extremely slow or will not occur at all. Such slowly reversible or irreversible thyroid inhibition would not appear to be of any serious consequence, since replacement therapy is readily available in the form of desiccated thyroid substance.

As one aspect of the effort to understand metabolic factors that might influence the response of thyroid substance, an evaluation was made of the extent of lipoprotein lowering in relation to the pretherapy lipoprotein levels in the subjects studied.

For the purpose the subjects studied were ranked upon their initial levels of the several lipoprotein classes, and then evaluated for the magnitude of drop in the corresponding classes that had resulted by the end of the 36-week 325-mg period. The findings are presented in Table I. It is quite clear from these data that whatever lipoprotein class is used to rank the patients, the higher the initial level of lipoproteins the greater the absolute magnitude of the fall in lipoprotein level. The net effect of therapy with thyroid is to decrease the variability, or range of values for each lipoprotein class, within the group under study. One possible interpretation of this observation is that for individuals showing high lipoprotein levels there is a relative thyroid deficiency, at least with respect to that aspect of thyroid function involved in lipoprotein control.

Table I

Lipoprotein response to thyroid substance as a function of pretherapy levels			
<u>Initial level</u>	n	Level at end of 325-mg period (mg/100 ml)	Change in level (mg/100 ml)
<u>Range</u> (mg/100 ml)			
<u>Ranked upon <math>S_f^0</math> 0-400</u>			
over 650	10	480	-241
500-650	16	458	-128
below 500	13	333	- 47
<u>Ranked upon <math>S_f^0</math> 0-12</u>			
over 400	16	340	- 87
300-400	15	295	- 55
below 300	8	184	- 34
<u>Ranked upon <math>S_f^0</math> 12-20</u>			
over 100	8	47	- 98
50-100	17	29	- 47
below 50	14	23	- 14
<u>Ranked upon <math>S_f^0</math> 20-100</u>			
over 100	13	94	- 26
70-100	10	73	- 8
below 70	16	54	0
<u>Ranked upon <math>S_f^0</math> 100-400</u>			
over 50	10	45	- 43
25-50	10	21	- 15
below 25	19	13	- 3

There has been interest in the possibility that the metabolic aspects of thyroid hormonal activity might be separable from the lipid aspects. From the observations by Goolden<sup>8</sup> with tetraiodothyroacetic acid, in a single euthyroid subject lowering of plasma cholesterol was observed without any lowering of body weight. Also in the observations by Trotter<sup>9</sup> with triiodothyroacetic acid, a lowering of blood cholesterol in three euthyroid patients was noted without significant alterations in basal metabolic rate. In an editorial in Lancet<sup>10</sup> the work of these two observers was commented upon with the statement that these newer compounds show promise of being able to lower blood cholesterol without causing unwanted side effects.

Our own observations indicate that considerable reservation should be used in setting apart these new thyroid-active substances, since we find that desiccated thyroid substance produces a marked effect upon the serum lipids in many patients without significant alterations in body weight, too. Thus in the series described here there were 18 patients who lost no more than 5 pounds in body weight over the entire 102 weeks of study. Of these, 8 actually gained weight. All these cases showed significant lipoprotein lowering as a result of administration of desiccated thyroid substance. The mean changes for this group were as follows:

n	mean weight change	mean $S_f^0$ 0-400 change
18	+ 3.1 pounds	- 41.0 mg/100 ml

Furthermore, as shown by reference to Fig. 1, from the last part of the 195-mg/day period through the entire 260-mg and 325-mg/day periods there was practically no alteration in weight for the entire group of subjects, and yet there was a fall in serum lipoproteins and serum cholesterol during these periods. In addition, in a separate study of patients with the  $S_f^0$  0-12 hyperlipoproteinemia characteristic of xanthoma tendinosum it has commonly been observed that marked lipoprotein reduction occurs without weight loss and indeed, often with a weight increase.<sup>11</sup> We would consider, therefore, that such possibly unwanted side effects as weight loss need not occur with desiccated thyroid substance itself. Thus, if any of the thyroid-active compounds recently studied does indeed show a greater dissociation of lipid effects from metabolic effects than does desiccated thyroid itself, the demonstration of this point would require a carefully controlled comparison of the various substances.

One area where the effect of thyroid substance upon lipoprotein and cholesterol levels is of especial interest is arteriosclerosis, and in particular coronary arteriosclerosis and its sequel, coronary heart disease. It has been shown that there exists a positive association of the serum levels of the  $S_f^0$  0-12,  $S_f^0$  12-20,  $S_f^0$  20-100, and  $S_f^0$  100-400 lipoproteins with clinical coronary heart disease.<sup>12</sup> A composite measure, designated as the Atherogenic Index value,\* or A. I. value, represents the best combination of the lipoprotein data in the segregation of cases of overt coronary disease from clinically healthy persons. Since elevated A. I. values are associated with increased risk of clinical coronary heart disease, one reasonable approach to prophylaxis of coronary heart disease is via efforts to reduce elevated

\* Atherogenic Index, or A. I. =  $0.1 (S_f^0 0-12) + 0.175 (S_f^0 12-400)$

A.I. values. The effect of thyroid substance in lowering lipoprotein levels and maintaining lowered levels suggests its possible application for this purpose. The data of Fig. 1 can be calculated on the basis of A.I. response to desiccated thyroid substance. These results are presented in Table II.

The reduction in A.I. value for either the 260-mg or 325-mg thyroid period is quite sizable. As was shown in Table I, the higher the initial lipoprotein level, the greater the absolute magnitude of the fall in lipoprotein level in response to thyroid administration. The comparison of A.I. response in the 10 cases with the highest initial  $S_f^{0-400}$  lipoprotein level with the 10 cases showing the lowest initial  $S_f^{0-400}$  lipoprotein level is of considerable interest. These data are presented in Table III.

It is clear that the initially high group shows a marked reduction in A.I. value in response to thyroid administration, which reduction should correspond to a materially lower risk of clinical coronary heart disease. The initially low group shows a much smaller response in absolute A.I. reduction as well as in percentage reduction. The initially low group is already characterized by a low risk of clinical coronary heart disease and is only slightly further lowered by thyroid administration. From the point of view of possible prophylaxis of coronary heart disease, the much greater effect of thyroid upon elevated A.I. values than upon low ones is especially useful, since it is precisely the group with the highly elevated A.I. values that is in greatest need of prophylaxis in terms of A.I. lowering.

Table II

Effect of desiccated thyroid substance upon Atherogenic Index values  
(39 cases)

Time	Mean A. I. value (A. I. units)
Initially	70.0
At 30 weeks on 195 mg of thyroid	65.7
At 39 weeks on 260 mg of thyroid	51.0
At 36 weeks on 325 mg of thyroid	52.0



Table III

Atherogenic Index response to thyroid administration as a function of initial lipoprotein level

Time	Mean A.I. value (A.I. units)	
	For the 10 cases with the highest $S_f^0$ 0-400 lipoprotein level	For the 10 cases with the lowest $S_f^0$ 0-400 lipoprotein level
Initially	94.1	43.0
At 30 weeks on 195 mg	84.6	46.5
At 39 weeks on 260 mg	62.0	39.9
At 36 weeks on 325 mg	64.0	37.1

### ACKNOWLEDGMENTS

The authors gratefully acknowledge the assistance of Minnie Adams, Ellen Davis, John Sanders, and the other ward personnel of Stockton State Hospital for administering the desiccated thyroid, for measuring blood pressures, pulse rates, and weights, and for drawing the blood samples. We also wish to express our appreciation for the assistance of the technical group at Donner Laboratory in making the ultracentrifugal analyses and to Alice McPhee of the Donner Laboratory for all the serum cholesterol analyses.

The desiccated thyroid substance for this experiment was supplied by the Armour Laboratories, Kankakee, Illinois.

This work was supported (in part) by the United States Atomic Energy Commission, the Albert and Mary Lasker Foundation, Inc., and Wyeth Laboratories, Inc., Philadelphia, Pennsylvania.

BIBLIOGRAPHY

1. Strisower, Gofman, Galioni, Almada, and Simon, Effect of Thyroid Extract on Serum Lipoproteins and Serum Cholesterol, *Metabolism* 3, 218 (1954).
2. Strisower, Gofman, Galioni, Rubinger, O'Brien, and Simon, Effect of Long-Term Administration of Desiccated Thyroid on Serum Lipoprotein and Cholesterol Levels. *J. Clin. Endocrinol. and Metabolism* 15, 73 (1955).
3. Gofman, Tamplin, and Strisower, Relation of Fat and Caloric Intake to Atherosclerosis, *J. Am. Dietet. Assoc.* 30, 317 (1954).
4. Glazier, Tamplin, Strisower, deLalla, Gofman, Dawber, and Phillips, Human Serum Lipoprotein Concentrations, *J. Gerontol.* 9, 395 (1954).
5. Nickols, Dobbin, and Gofman, The Influence of Dietary Factors upon Human Serum Lipoprotein Concentrations, UCRL-3407, May 1956.
6. Oliver deLalla, and J. Gofman, Ultracentrifugal Analysis of Human Serum Lipoproteins, in Methods of Biochemical Analysis, D. Glick, ed., Vol. 1, Interscience, New York, 1954.
7. David M. Colman and Alice F. McPhee, An Improved Method for Determination of Total Serum Cholesterol, *Am. J. Clin. Pathol.* 26, 181 (1956).
8. Goolden, A. W. G., The Physiological Activity of Tetraiodothyroacetic Acid, *Lancet* 170, 890 (June 9, 1956).
9. W. R. Trotter, Effect of Triiodothyroacetic Acid on Blood-Cholesterol Levels, *Lancet* 170, 885 (June 9, 1956).
10. Editorial: Thyroid Hormones and Coronary Disease, *Lancet* 170, 896 (June 9, 1956).
11. Gofman, Nichols, Strisower, Tamplin, and Tandy, Lipid Metabolism and Arteriosclerosis (in press).
12. Gofman, Strisower, deLalla, Tamplin, Jones, and Lindgren, Index of Coronary Artery Atherogenesis, *Modern Medicine* 21, 119 (June 15, 1953).