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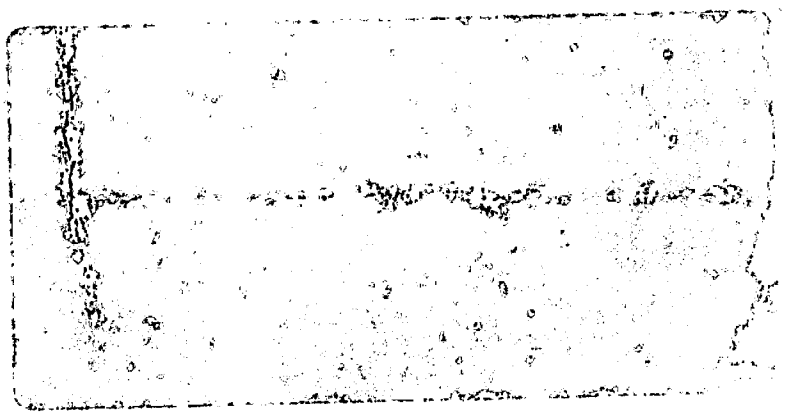

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INTRODUCTION

The critical role of thyroid function in lipid metabolism and transport is attested to by the wealth of significant clinical and experimental literature on this subject. In a series of classic reports, Hurxthal and his associates have pointed out the general trend toward elevation of serum cholesterol levels in hypothyroidism and myxedema and the trend toward low cholesterol levels in hyperthyroidism.[1,2,3,4,5] In these same studies the removal of the thyroid gland surgically in hyperthyroidism was shown to result in a significant rise in serum cholesterol level. The Hurxthal findings have been , in the main, confirmed by other investigators.[6] Recently the ablation of the thyroid gland in man by use of radioiodine (I^{131}) has been shown to result, on the average, in an elevation of the serum cholesterol level even in individuals not originally hyperthyroid.[7] The therapy of myxedema with thyroid extract has been demonstrated to produce a fall in serum cholesterol levels in general.[4] Further it has been pointed out by several observers that even in persons not clinically hypothyroid the administration of thyroid extract in adequate doses results in a lowering of the serum cholesterol level.[4,8,9,10] The mechanism by which thyroid function is related to control of serum lipid levels is by no means clear at this time.

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It is now known that the total serum cholesterol level is made up of contributions from a host of lipoproteins, differing from each other both in physicochemical and chemical structure.[11,12,13] The grossly differing lipoprotein patterns which give rise to identical total serum cholesterol levels undoubtedly bespeak significant metabolic differences. In one disease state the lipoproteins responsible for cholesterol elevation may be of an entirely different chemical structure from those producing an equivalent cholesterol elevation in another disease. Thus, xanthoma tendinosum is characterized by extreme elevations in Standard S_f 0-12 and usually Standard S_f 12-20 lipoproteins with unusually low Standard S_f 20-400 levels, whereas xanthoma tuberosum is characterized by gross elevations in Standard S_f 12-400 lipoproteins with unusually low Standard S_f 0-12 lipoproteins.[14]

It seems clear, therefore, that a more intimate understanding of the role of the thyroid in lipid metabolism might be aided by a determination of the influence of thyroid extract upon the various defined lipoprotein classes. The present study is concerned with the effect of thyroid extract upon all the low-density lipoprotein classes from Standard S_f 0 to Standard S_f 400.[16]

Experimental

Part of this study is based upon the responses to thyroid extract observed in nineteen schizophrenic patients, ranging in age from 19-49 years, and showing no evident physical deviations from normality. In addition, a separate series of four young clinically normal individuals was studied. In the group of schizophrenic patients an initial blood sample was obtained prior to the institution of thyroid administration. Subsequent blood sampling was done at regular intervals during the period of thyroid administration and at the same intervals over the two-month period following the cessation of administration of thyroid extract. Of the nineteen patients, eleven completed the entire course of thyroid administration, which involved one week on a dose of 3-1/2 grains of desiccated U.S.P. thyroid extract daily, an additional week on 7 grains daily, and then nine weeks on 10 grains daily. This group of eleven patients will be identified as Group A. The remaining

eight schizophrenic patients were studied on some modified dosage schedule, involving the use of less thyroid extract, because it was felt that there was some evidence of intolerance to the higher dosage of thyroid. This group will be designated as Group B.

In the group of four young normals a relatively short-term experiment was performed involving the use of 3 grains of thyroid extract daily for two to three weeks. In this group, designated as Group C, blood sampling was performed at three-to four-day intervals before, during, and after thyroid administration. This schedule allowed observation of more acute responses than was possible in the other groups.

Serum cholesterol determinations were performed on all samples by the method of Colman[15] and the lipoprotein analyses by the ultracentrifugal method of Gofman et al.[11,16] The lipoproteins were segregated into four classes, Standard S_f 0-12, Standard S_f 12-20, Standard S_f 20-100, and Standard S_f 100-400. Records of pulse rate, blood pressure, and body weight were obtained throughout the study. For Group A and Group B a protein-bound iodine determination on each patient determined six months after the course of thyroid administration was available to us. For Group C a protein-bound iodine determination was made before thyroid was given.

The analytical results of the serum cholesterol and lipoprotein measurements are presented in Tables I, II, and III for each of the individuals studied. A summary plot for Group A (patients completing the entire course of 10 grains of thyroid daily) averaging the individual cholesterol values, lipoprotein values, and body weights is given in Fig. 1. A similar summary plot for Group C is given in Fig. 2.

Group A Case 1

TABLE I

MB 25 yr. Male Schizophrenic PBI = 5.3μg

Date	8/8	9/13	9/20	9/22	9/27	10/2	10/12	10/23	11/3	11/13	11/24	Mean of all samples on 10 gr/day of thyroid	12/4	12/14	12/26	1/5	1/16	1/26
Thyroid gr/day	0	3.5	7	7	10	10	10	10	10	10	10		0	0	0	0	0	0
Cholesterol mg%	167			116		131	--	153	--	152	148	146	173	205	228	180	183	195
Standard S_f 0-12 mg%	272			218		174	170	203	199	227	188	194	291	257	347	426	280	347
Standard S_f 12-20 mg%	56			22		25	32	27	34	37	23	30	38	26	37	56	49	49
Standard S_f 20-100 mg%	101			59		102	114	100	87	98	77	96	72	49	71	60	49	74
Standard S_f 100-400 mg%	65			35		43	40	35	11	37	16	30	27	16	35	11	13	29
A.I	66			42		47	50	49	43	53	39	47	53	42	60	63	47	61
Weight, lbs.	144			--		142	140	141	139	136	133		143	143	143	140	--	144
Basal BP mm Hg	100/60		101/49*	105/48	108/58*	113/44*	113/51*	110/47*	110/48*	116/41*	108/16*		111/35*	98/50	104/64	104/60	120/64	118/70
Basal pulse rate			72*	72	68*	80*	87*	86*	87*	88*	91*		82*	68	84	80	88	72

* Mean of 2 or more measurements at 2-3 day intervals.

UCRL-2374

Group A Case 2 TABLE I - (Contd. . .)

AK 43 yr. Male Schizophrenic PBI = 5.1 μg

Date	8/3	9/13	9/20	9/22	9/27	10/2	10/12	10/23	11/3	11/13	11/24	Mean of all samples on 10 gr/day of thyroid	12/4	12/14	12/26	1/5	1/16	1/26
Thyroid gr/day	0	3.5	7	7	10	10	10	10	10	10	10		0	0	0	0	0	0
Cholesterol mg%	231			158		187	122	158	187	182	220	176	198	275	275	267	292	238
Standard S_f 0-12 mg%	299			180		172	140	216	267	250	206	209	208	412	430	407	469	370
Standard S_f 12-20 mg%	65			22		25	19	24	47	26	22	27	25	79	70	131	45	60
Standard S_f 20-100 mg%	91			53		52	31	45	69	43	55	49	65	46	72	55	45	78
Standard S_f 100-400 mg%	84			20		19	4	9	49	6	12	17	34	27	49	30	30	43
A.I	72			35		34	23	35	56	38	36	37	43	68	76	79	68	69
Weight, lbs.	130			--		129	119	119	113	111	114		115	125	130	134	134	132
Basal BP mm Hg	120/70		120/78*	110/60	118/83*	120/60	128/79*	129/80*	140/79*	127/71*	108/65*		109/68*	116/68	120/60	130/72	134/70	120/78
Basal pulse rate			89*	92	99*	102	102*	99*	99*	89*	88*		85*	86	92	80	84	80

* Mean of 2 or more measurements made at 2-3 day intervals.

Group A Case 3

TABLE I - (Contd. . .)

FG 33 yr. Male Schizophrenic PBI = 5.7 μg

Date	8/8	9/13	9/20	9/22	9/27	10/2	10/12	10/23	11/3	11/13	11/24	Mean of all samples on 10 gr/day of thyroid	12/4	12/14	12/26	1/5	1/16	1/26
Thyroid gr/day	0	3.5	7	7	10	10	10	10	10	10	10		0	0	0	0	0	0
Cholesterol mg%	225			167		164	204	144	162	154	148	163	198	208	210	215	213	210
Standard S_f 0-12 mg%	371			260		231	225	233	217	232	240	230	293	344	326	354	450	347
Standard S_f 12-20 mg%	68			29		31	36	43	36	24	47	36	43	29	26	43	47	40
Standard S_f 20-100 mg%	54			63		78	107	70	90	94	77	86	76	95	62	60	74	76
Standard S_f 100-400 mg%	39			54		27	35	27	54	26	32	34	25	48	46	16	36	34
A.I	65			52		47	54	48	53	48	51	50	55	65	56	53	72	61
Weight, lbs.	166			--		160	159	164	159	158	157		151	157	158	157	156	158
Basal BP mm Hg	118/78		93/57*	98/58*	94/50*	98/59*	99/57*	97/50*	98/46*	99/50*	94/34*		106/32*	100/30	104/60	100/50	98/40	104/60
Basal pulse rate			59*	64*	64*	69*	75*	81*	79*	80*	83*		86*	88	78	78	80	78

* Mean of 2 or more measurements made at 2-3 day intervals.

Group A Case 4 — TABLE I - (Contd...)

CE 37 yr. Male Schizophrenic PBI = 6.1 μg

Date	8/3	9/13	9/20	9/22	9/27	10/2	10/12	10/23	11/3	11/13	11/24	Mean of all samples on 10 gr/day of thyroid	12/4	12/14	12/26	1/5	1/16	1/26
Thyroid gr/day	0	3.5	7	7	10	10	10	10	10	10	10		0	0	0	0	0	0
Cholesterol mg%	201			170		148	124	136	155	130	146	140	190	275	260	205	250	200
Standard S_f 0-12 mg%	249			229		199	172	225	222	211	186	203	280	365	422	315	479	363
Standard S_f 12-20 mg%	57			24		24	19	27	27	31	17	24	29	42	63	32	63	49
Standard S_f 20-100 mg%	83			75		62	57	60	81	70	53	64	83	77	86	61	94	94
Standard S_f 100-400 mg%	50			29		56	6	12	29	6	22	22	36	34	75	26	52	38
A.I	58			45		45	32	40	46	40	35	40	54	63	81	52	84	68
Weight, lbs.	168			--		175	170	163	166	166	161		173	170	180	183	186	191
Basal BP mm Hg	100/60		130/75*	120/80	119/64*	128/70*	130/65*	123/68*	122/60*	128/72*	119/57*		125/70*	128/68	120/74	140/80	--/--	108/70
Basal pulse rate			69*	62	80*	80*	88*	89*	79*	86*	79*		73*	78	78	80	--	78

* Mean of 2 or more measurements made at 2-3 day intervals

Group A Case 5 TABLE I - (Contd...)

LH 29 yr. Male Schizophrenic PBI = 6.5 μg

Date	8/3	9/13	9/20	9/22	9/27	10/2	10/12	10/23	11/3	11/13	11/24	Mean of all samples on 10 gr/day of thyroid	12/4	12/14	12/26	1/5	1/16	1/26
Thyroid gr/day	0	3.5	7	7	10	10	10	10	10	10	10		0	0	0	0	0	0
Cholesterol mg%	199			148		138	107	110	--	128	138	124	190	257	257	275	266	260
Standard S_f 0-12 mg%	241			258		224	146	177	228	201	177	192	233	528	404	394	553	390
Standard S_f 12-20 mg%	73			21		21	20	12	38	24	20	23	27	64	42	55	80	43
Standard S_f 20-100 mg%	42			29		62	47	31	85	46	29	50	40	42	39	30	59	61
Standard S_f 100-400 mg%	10			4		14	16	17	36	22	7	19	11	29	15	10	29	6
A.I	46			35		39	29	28	51	36	28	35	37	76	57	56	85	58
Weight, lbs.	125			---		131	126	122	122	121	119		118	122	122	132	131	126
Basal BP mm Hg	108/70		103/71*	90/56	106/75*	103/54*	106/66*	99/57*	94/45*	105/65*	102/63*		120/68	120/76	110/80	112/70	118/70	94/70
Basal pulse rate			85*	88	92*	92*	97*	91*	93*	92*	87*		120	84	92	88	88	88

* Mean of 2 or more measurements made at 2-3 day intervals

Group A Case 6 TABLE I - (Contd...)

SR 26 yr. Male Schizophrenic PBI = 5.4 μg

Date	8/1	9/13	9/20	9/22	9/27	10/2	10/12	10/23	11/3	11/13	11/24	Mean of all samples on 10 gr/day of thyroid	12/4	12/14	12/26	1/5	1/16	1/26
Thyroid gr/day	0	3.5	7	7	10	10	10	10	10	10	10		0	0	0	0	0	0
Cholesterol mg%	388			450		318	218	198	185	216	216	225	307	388	330	408	353	318
Standard S_f 0-12 mg%	467			477		286	248	245	220	240	237	246	401	371	436	443	495	385
Standard S_f 12-20 mg%	178			115		74	74	60	78	63	57	68	92	92	114	120	204	101
Standard S_f 20-100 mg%	318			176		118	104	103	81	104	80	98	96	82	98	120	116	74
Standard S_f 100-400 mg%	86			56		33	49	62	18	39	18	37	31	34	41	36	13	16
A.I	149			108		68	65	64	53	60	51	60	78	74	88	93	108	72
Weight, lbs.	153			---		151	146	142	142	140	136		141	142	146	142	145	144
Basal BP mm Hg	110/70		108/59*	110/56	102/50*	104/63*	111/55*	104/53*	99/38*	110/55*	107/39*		115/30*	98/35	120/70	118/64	124/80	104/58
Basal pulse rate			59*	68	62*	70*	71*	72*	72*	73*	68*		80*	68	88	80	88	68

* Mean of 2 or more measurements made at 2-3 day intervals

Group A Case 7

TABLE I (Contd. . .)

OD 46 yr. Male Schizophrenic PBI= 6.6 μg

Date	8/3	9/13	9/20	9/22	9/27	10/2	10/12	10/23	11/3	11/13	11/24	Mean of all samples on 10 gr/day of thyroid	12/4	12/14	12/26	1/5	1/16	1/26
Thyroid gr/day	0	3.5	7	7	10	10	10	10	10	10	10		0	0	0	0	0	0
Cholesterol mg %	279			199		176	132	157	182	177	240	177	290	336	305	240	290	278
Standard S_f 0-12 mg %	412			261		180	179	223	273	252	341	241	470	522	431	406	347	426
Standard S_f 12-20 mg %	123			41		46	49	49	58	52	66	53	119	144	101	102	123	103
Standard S_f 20-100 mg %	170			105		97	94	101	166	112	86	109	224	134	131	130	130	148
Standard S_f 100-400 mg %	170			52		32	30	33	45	70	52	44	99	104	73	69	83	76
A.I	122			61		49	48	54	74	66	70	60	124	119	96	93	94	100
Weight, lbs.	131			--		137	131	121	123	120	124		130	129	129	138	136	142
Basal BP mm Hg	150/70		109/61*	112/70	113/64*	110/65**	115/63*	115/61*	107/59*	114/61*	111/53*		114/54*	108/40	118/60	104/60	110/64	110/60
Basal Pulse rate			69*	76	82*	86*	98*	97*	90*	87*	78*		86*	84	78	78	74	74

* Mean of 2 or more measurements made at 2-3 day intervals

Group A Case 8 TABLE I - (Contd. . .)

EF 38 yr. Male Schizophrenic PBI=9.3 μg

Date	8/3	9/13	9/20	9/22	9/27	10/2	10/12	10/23	11/3	11/13	11/24	Mean of all samples on 10 gr/day of thyroid	12/4	12/14	12/26	1/5	1/16	1/26
Thyroid gr/day	0	3.5	7	7	10	10	10	10	10	10	10		0	0	0	0	0	0
Cholesterol mg%	286			210		195	175	193	205	221	185	196	240	283	283	253	254	234
Standard S_f 0-12 mg%	374			305		338	286	423	278	411	302	340	464	516	497	444	473	420
Standard S_f 12-20 mg%	116			40		54	38	70	55	84	43	57	67	146	81	136	47	69
Standard S_f 20-100 mg%	117			85		114	80	123	71	132	84	101	141	97	67	74	54	86
Standard S_f 100-400 mg%	63			57		34	23	32	12	32	27	27	101	27	36	24	9	47
A.I	89			62		69	53	82	52	85	57	66	100	99	82	85	67	77
Weight, lbs	161			--		163	154	154	148	147	142		144	140	146	146	142	126
Basal BP mm Hg	120/70		123/73*	128/70	132/78*	121/69*	126/74*	112/55*	115/60*	113/63*	116/47*		--	122/68	125/42	122/64	125/78	118/68
Basal pulse rate			75*	88	87*	92*	97*	93*	93*	85*	95*		--	78	78	84	84	88

* Mean of 2 or more measurements made at 2-3 day intervals

Group A Case 9 TABLE I - (Contd...)

CC 36 yr. Male Schizophrenic PBI = 6.4 μg

Date	8/8	9/13	9/20	9/22	9/27	10/2	10/12	10/23	11/3	11/13	11/24	Mean of all samples on 10 gr/day of thyroid	12/4	12/14	12/26	1/5	1/16	1/26
Thyroid gr/day	0	3.5	7	7	10	10	10	10	10	10	10		0	0	0	0	0	0
Cholesterol mg%	267			204		192	186	152	193	--	192	183	213	298	244	278	271	287
Standard S_f 0-12 mg%	355			316		--	213	196	211	265	--	221	282	461	362	477	390	408
Standard S_f 12-20 mg%	92			40		--	43	49	31	40	--	41	31	56	29	45	47	58
Standard S_f 20-100 mg%	96			77		--	90	67	81	48	--	72	58	84	63	56	73	94
Standard S_f 100-400 mg%	51			35		--	25	14	31	11	--	20	25	25	15	29	27	29
A.I	77			58		--	49	42	46	44	--	45	48	75	55	71	66	72
Weight, lbs.	140			--		140	138	133	133	130	129		136	132	138	140	139	139
Basal BP mm Hg	118/70		105/46*	98/48	99/50*	106/44*	107/55*	120/55*	119/32*	115/50*	115/36*		112/48*	110/20	90/30	114/20	112/20	112/64
Basal pulse rate			67*	68	79*	84*	92*	95*	93*	93*	89*		88*	76	78	76	76	80

*Mean of 2 or more measurements made at 2-3 day intervals

Group A Case 10 TABLE I - (Contd...)

LB 29 yr. Male Schizophrenic PBI=6.5 μg

Date	8/1	9/13	9/20	9/22	9/27	10/2	10/12	10/23	11/3	11/13	11/24	Mean of all samples on 10 gr/day of thyroid	12/4	12/14	12/26	1/5	1/16	1/26
Thyroid gr/day	0	3.5	7	7	10	10	10	10	10	10	10		0	0	0	0	0	0
Cholesterol mg%	219			217		190	153	153	167	167	172	167	188	243	228	207	208	212
Standard S_f 0-12 mg%	364			283		290	229	254	231	272	331	268	311	405	359	395	367	332
Standard S_f 12-20 mg%	77			57		52	40	46	47	43	60	48	56	67	64	76	54	62
Standard S_f 20-100 mg%	89			75		99	104	112	110	129	110	111	146	114	102	98	65	69
Standard S_f 100-400 mg%	68			66		54	93	47	94	85	63	73	60	107	110	48	31	18
A.I	77			63		65	64	61	67	72	74	67	87	91	84	78	63	59
Weight, lbs.	243					251	243	239	237	233	234		235	234	239	236	235	233
Basal BP mm Hg	100/65		103/67*	102/62	105/56*	101/55*	111/60*	108/54*	106/55*	114/45*	104/36*		102/25*	105/40	132/50	120/60	--	180/70
Basal pulse rate			75*	72	76*	84*	86*	82*	84*	83*	82*		84*	92	88	80	--	88

*Mean of 2 or more measurements at 2-3 day intervals

Group A Case 11 TABLE I - (Contd. . .)

SGC 41 yr. Male Schizophrenic PBI = 7.8 μg

Date	8/3	9/13	9/20	9/22	9/27	10/2	10/12	10/23	11/3	11/13	11/24	Mean of all samples on 10 gr/day of thyroid	12/4	12/14	12/26	1/5	1/16	1/26
Thyroid gr/day	0	3.5	7	7	10	10	10	10	10	10	10		0	0	0	0	0	0
Cholesterol mg%	257			169		169	139	150	212	144	167	164	246	315	288	222	210	276
Standard S_f 0-12 mg%	365			282		154	178	215	193	252	213	201	325	391	370	452	468	448
Standard S_f 12-20 mg%	45			31		23	18	23	34	45	24	28	40	35	51	43	52	123
Standard S_f 20-100 mg%	73			60		33	44	16	43	63	46	41	69	78	79	74	83	108
Standard S_f 100-400 mg%	32			29		13	22	4	18	42	37	23	16	23	30	34	25	47
A.I	63			49		27	33	29	36	51	40	36	54	63	65	72	75	93
Weight, lbs.	120			--		126	121	112	113	108	106		116	123	119	124	130	130
Basal BP mm Hg	110/70		107/51*	100/60	107/65	108/60*	108/67*	115/59*	123/71*	121/46*	117/42*		107/52*	105/45	102/60	88/54	126/68	108/68
Basal pulse rate			75*	80	88	96*	96*	92*	89*	90*	83*		90*	84	80	84	80	80

*Mean of 2 or more measurements made at 2-3 day intervals

Group B Case 1

TABLE II

MK 32 yr. Male Schizophrenic PBI = 6.0 μg

Date	8/3	9/13	9/20	9/22	9/26	10/2	10/12	10/23	11/2	11/13	11/24	12/4	12/14	12/26	1/5	1/16	1/26
Thyroid gr/day	0	3.5	7	7	3.5	3.5	3.5	3.5	3.5	3.5	3.5	0	0	0	0	0	0
Cholesterol mg%	238			161		181	177	211	227	216	197	215	228	204	213	227	218
Standard S_f0-12 mg%	256			199		236	246	303	246	370	--	298	353	329	334	--	338
Standard S_f12-20 mg%	112			21		18	16	23	22	40	--	22	24	21	18	--	31
Standard S_f20-100 mg%	86			53		37	35	39	52	58	--	47	42	36	11	--	40
Standard S_f100-400 mg%	40			14		22	11	8	40	13	--	22	15	6	4	--	13
A.I	67			35		37	35	43	45	56	--	46	49	44	39	--	49
Weight, lbs.	132			--		---	132	141	--	--	133	131	133	129	---	121	128
Basal BP mm Hg	120/60			--	--	130/70	123/71*	118/72*	123/63*	114/60*	117/45*	122/62*	160/95	128/80	--	128/80	124/80
Basal pulse rate				--	--	80	87*	96*	84*	74*	82*	93*	100	100	--	120	100

*Mean of 2 or more measurements at 2-3 day intervals

Group B Case 2

TABLE II - (Contd. . .)

JG 34 yr. Male Schizophrenic PBI = 5.7 μg

Date	8/3	9/13	9/20	9/22	9/26	10/2	10/12	10/13	10/23	11/2	11/13	11/24	12/4	12/14	12/26	1/5	1/16	1/26
Thyroid gr/day	0	3.5	7	7	10	10	10	7	7	7	7	7	0	0	0	0	0	0
Cholesterol mg%	144			110		111	103		109	112	120	118	128	153	178	130	204	163
Standard S_f 0-12 mg%	200			153		166	139		195	181	155	160	186	239	288	330	410	287
Standard S_f 12-20 mg%	42			28		36	23		29	40	33	25	40	19	26	25	36	29
Standard S_f 20-100 mg%	71			51		82	66		66	49	47	56	52	66	82	50	81	60
Standard S_f 100-400 mg%	53			22		32	26		38	7	6	10	27	13	45	35	25	36
A.I	49			33		43	34		43	35	31	32	39	41	56	52	66	51
Weight, lbs.	134			--		132	125		120	--	110	108	106	114	111	120	118	117
Basal BP mm Hg	110/70	—	110/68*	106/46	106/60	116/63*	114/62*		114/67*	107/46*	111/56*	110/44*	112/58	108/40	120/45	108/62	104/55	110/70
Basal pulse rate			77*	88	84	88*	92*		93*	91*	92*	84*	118	82	100	92	72	100

*Mean of 2 or more measurements made at 2-3 day intervals.

Group B Case 3

TABLE II - (Contd...)

MD 22 yr. Male Schizophrenic PBI = 6.7 μg

Date	8/8	9/13	9/20	9/22	9/26	10/2	10/11	10/12	10/23	11/3	11/13	11/16	11/24	12/4	12/14	12/26	1/5	1/16	1/26
Thyroid gr/day	0	3.5	7	7	10	10	7	7	7	7	7	7	0	0	0	0	0	0	0
Cholesterol mg%	261			165		153		113	158	173	187		216	257	292	275	250	234	212
Standard S_f 0-12 mg%	300			220		191		136	223	214	243		320	426	417	412	442	383	298
Standard S_f 12-20 mg%	99			26		47		27	45	40	41		30	67	60	84	99	101	49
Standard S_f 20-100 mg%	128			61		82		48	67	86	58		56	101	65	80	72	85	105
Standard S_f 100-400 mg%	74			22		27		23	19	14	11		29	34	34	57	33	34	38
A.I	83			41		46		31	45	46	44		52	78	70	80	80	77	63
Weight, lbs.	140							130				124							
Basal BP mm Hg	100/60																		
Basal pulse rate																			

Group B Case 4

TABLE II - (Contd. . .)

AS 33 yr. Male Schizophrenic PBI = 6.2 μg

Date	8/1	9/13	9/20	9/22	9/28	10/2	10/12	10/23	11/2	11/13	11/24	12/4	12/14	12/26	1/5	1/16	1/26
Thyroid gr/day	0	3.5	7	7	3.5	3.5	3.5	3.5	3.5	3.5	3.5	0	0	0	0	0	0
Cholesterol mg%	316			260		307	283	302	262	271	280	328	385	372	334	338	320
Standard S_f0-12 mg%	304			559		430	310	479	360	408	425	544	436	548	551	560	542
Standard S_f12-20 mg%	67			84		103	49	128	82	107	65	121	95	105	110	116	112
Standard S_f20-100 mg%	87			104		129	97	128	118	125	98	168	127	81	96	103	146
Standard S_f100-400 mg%	62			98		107	94	148	163	116	96	134	129	91	81	108	164
A.I	68			106		102	73	119	100	102	88	128	105	103	105	113	128
Weight, lbs.	216						220				202						
Basal BP mm Hg	150/80																
Basal pulse rate																	

Group B Case 5

TABLE II - (Contd. . .)

DC 31 yr. Male Schizophrenic PBI = 8.4 μg

Date	8/8	9/13	9/20	9/22	9/26	10/2	10/12	10/13	10/23	11/3	11/13	11/22	12/4	12/14	12/26	1/5	1/16	1/26
Thyroid gr/day	0	3.5	7	7	10	10	10	7	7	7	7	7	0	0	0	0	0	0
Cholesterol mg%	336			170		201	195		187	212	206		295	356	--	275	254	254
Standard S_f0-12 mg%	483			204		282	260		255	255	273		500	475	--	462	352	403
Standard S_f12-20 mg%	149			45		97	72		80	60	89		87	175	--	108	69	58
Standard S_f20-100 mg%	157			69		125	132		157	81	95		116	152	--	132	69	34
Standard S_f100-400 mg%	65			40		53	41		57	16	32		58	103	--	33	11	20
A.I	113			47		76	69		77	53	65		96	123	--	94	61	60
Weight, lbs.	196			---		196	190		188	188	185	185	190	187	--	188	190	190
Basal BP mm Hg	130/80		114/55*	112/60	115/60	120/46*	118/42*		131/57*	118/30*	125/46*	127/23*	106/58	118/46	--	124/70	145/72	128/80
Basal pulse rate			76*	72	80	84*	93*		93*	82*	89*	92*	76	80	--	72	76	78

* Mean of 2 or more measurements made at 2-3 day intervals.

Group B Case 6

TABLE II - (Contd. . .)

TB 19 yr. Male Schizophrenic

Date	8/8	9/13	9/20	9/22	9/26	10/2	10/12	10/14	10/23	11/3	11/13	11/24	12/4	12/14	12/26	1/5	1/16
Thyroid gr/day	0	3.5	7	7	10	10	10	7	7	7	7	7	0	0	0	0	0
Cholesterol mg%	187			141		119	115		127	163	163	148	178	215	200	172	198
Standard S_f0-12 mg%	358			219		189	143		201	204	287	275	276	428	304	---	340
Standard S_f12-20 mg%	107			48		47	36		25	44	48	36	56	68	68	---	49
Standard S_f20-100 mg%	89			59		46	30		32	62	67	74	78	74	56	---	29
Standard S_f100-400 mg%	20			26		12	9		13	8	15	21	25	25	39	---	9
A.I	74			45		37	27		32	40	51	50	55	72	59	---	49
Weight, lbs.	143			---		136	132		136	137	138	136	140	138	141	142	139
Basal BP mm Hg	112/80		114/64*	104/48	100/40	113/53*	105/62*		104/62*	101/59*	106/69*	97/45*	105/64*	100/62	115/60	100/52	100/70
Basal pulse rate			83*	82	82	87*	87*		86*	86*	85*	84*	82*	84	72	72	80

* Mean of 2 or more measurements made at 2-3 day intervals.

Group B Case 7

TABLE II - (Contd. . .)

CB 49 yr. Male Schizophrenic PBI = 8.0 μg

Date	8/8	9/13	9/20	9/22	9/26	10/2	10/4	10/12	10/23	11/2	11/13	11/24	12/4	12/14	12/26	1/5	1/16	1/26
Thyroid gr/day	0	3.5	7	7	10	10	3.5	3.5	3.5	3.5	3.5	3.5	0	0	0	0	0	0
Cholesterol mg%	318			242		206		201	215	234	237	221	253	278	303	298	292	320
Standard S_f0-12 mg%	420			289		353		304	408	403	416	352	457	504	471	---	569	507
Standard S_f12-20 mg%	104			44		64		51	72	95	94	48	60	87	147	---	65	88
Standard S_f20-100 mg%	114			58		94		89	101	108	99	65	72	66	114	---	52	56
Standard S_f100-400 mg%	58			32		38		27	36	51	38	14	18	10	48	---	22	19
A. I	90			52		70		60	77	85	82	57	72	79	101	---	81	79
Weight, lbs.	202			---		191		187	184	185	180	181	186	186	185	186	183	185
Basal BP mm Hg	136/96		115/57*	115/60	112/65	118/72*	132/42	117/65*	109/59*	113/63*	105/62*	105/60*	101/59*	100/50	125/50	110/68	130/70	100/60
Basal pulse rate			65*	84	80	85*	88	84*	78*	73*	79*	79*	78*	70	80	76	78	74

* Mean of 2 or more measurements made at 2-3 day intervals.

Group B Case 8 TABLE II - (Contd. . .)

WDM 27 yr. Male Schizophreniic PBI = 6.2 μg

Date	8/8	9/13	9/20	9/22	9/26	10/2	10/5	10/12	10/23	11/2	11/13	11/24	12/4	12/14	12/26	1/5	1/16	1/26
Thyroid gr/day	0	3.5	7	7	10	10	3.5	3.5	3.5	3.5	3.5	3.5	0	0	0	0	0	0
Cholesterol mg%	176			123		---		103	124	144	150	153	183	223	198	163	210	227
Standard S_f0-12 mg%	249			160		80		155	147	181	198	164	253	308	291	255	316	358
Standard S_f12-20 mg%	42			26		19		32	14	27	23	28	52	38	24	20	27	43
Standard S_f20-100 mg%	55			86		46		63	42	74	38	50	63	74	35	58	69	38
Standard S_f100-400mg%	10			30		12		23	15	27	21	15	40	38	22	22	27	22
A.I	44			41		21		36	27	41	34	33	52	57	43	43	53	54
Weight, lbs.	114			---		108		102	96	101	111	111	124	120	121	121	119	122
Basal BP mm Hg	110/70		100/55*	115/68	98/58	109/47*	109/54*	113/60*	102/59*	111/64*	113/54*	102/46*	105/60*	110/40	110/70	130/78	110/78	148/80
Basal pulse rate			65*	84	76	79*	84	78*	65*	64*	72*	75*	78*	80	84	88	88	88

* Mean of 2 or more measurements made at 2-3 day intervals.

Group C Case 1

TABLE III

FG 25 yr. Male Normal PBI = 6.3 μg

Date	5/4	5/7	5/7	5/11	5/14	5/18	5/21	5/25	6/2	6/8
Thyroid gr/day	0	0	3	3	3	3	3	0	0	0
Cholesterol mg%	173	179		163	146	123	125	136	163	162
Standard S_f 0-12 mg%	215	213		188	175	159	164	193	233	242
Standard S_f 12-20 mg%	31	34		47	31	38	31	36	38	60
Standard S_f 20-100 mg%	90	38		63	63	36	60	81	43	103
Standard S_f 100-400 mg%	18	11		22	27	13	7	31	2	43
A.I	46	36		42	39	31	34	45	38	60
Weight, lbs.	157	156		156	156	156	154	155	---	156
Basal BP mm Hg	130/80	120/75		140/80	132/78	128/66	120/75	126/82	114/74	
Basal pulse rate	86	72		94	72	88	80	96	80	

Group C Case 2

TABLE III - (Contd...)

BS 29 yr. Female Normal PBI = 6.7 μg

Date	5/4	5/7	5/7	5/11	5/14	5/18	5/21	5/25	5/28	6/1	6/8	6/15	6/25
Thyroid gr/day	0	0	3	3	3	3	3	3	3	0	0	0	0
Cholesterol mg%	236	249		240	212	218	182	173	193	187	237	233	233
Standard S_f0-12 mg%	345	358		334	269	291	291	287	298	316	356	361	327
Standard S_f12-20 mg%	54	72		47	29	54	34	40	38	43	99	141	54
Standard S_f20-100 mg%	25	45		16	22	47	11	16	38	34	20	60	49
Standard S_f100-400 mg%	9	13		4	13	13	2	4	7	11	4	20	18
A.I	50	59		45	38	49	37	39	44	47	57	75	54
Weight, lbs.	126	126		126	124	125	123	125	123	126	125		
Basal BP mm Hg	105/88	115/72		112/70	118/62	108/56	105/60	100/60	104/58	112/60			
Basal pulse rate	88	78		70	72	68	88	70	70	106			

Group C Case 3

TABLE III - (Contd. . .)

DP 34 yr. Female Normal PBI = 6.2 μg

Date	5/4	5/7	5/7	5/11	5/14	5/18	5/21	5/25	6/1	6/8	6/15	6/22	6/30
Thyroid gr/day	0	0	3	3	3	3	3	0	0	0	0	0	0
Cholesterol mg%	153	154		132	146	118	123	132	147	115	140	160	---
Standard S_f 0-12 mg%	213	235		190	175	168	175	224	231	217	220	224	226
Standard S_f 12-20 mg%	20	27		18	18	20	27	25	16	16	25	29	29
Standard S_f 20-100 mg%	18	22		22	36	22	54	27	27	38	29	40	40
Standard S_f 100-400 mg%	4	4		9	13	9	16	7	2	7	13	18	13
A.I	29	33		28	29	26	34	33	31	32	34	38	37
Weight, lbs.	174	172		173	173	173	170	172	173	---	---	176	
Basal BP mm Hg	110/70	110/70		130/80	115/72	120/68	100/75	110/72	112/72				
Basal pulse rate	70	66		78	79	90	78	68	70				

Group C Case 4 TABLE III - (Contd. . .)

AT 26 yr. Male Normal PBI = 6.2 μg

Date	5/4	5/7	5/7	5/11	5/14	5/18	5/21	5/25	6/1	6/8	6/17	6/30
Thyroid gr/day	0	0	3	3	3	3	3	0	0	0	0	0
Cholesterol mg%	135	137		126	112	106	102	119	127	137	135	---
Standard S_f 0-12 mg%	172	186		132	132	134	137	155	166	186	208	159
Standard S_f 12-20 mg%	58	18		34	31	36	27	18	40	47	49	43
Standard S_f 20-100 mg%	47	29		63	36	72	34	43	74	36	45	69
Standard S_f 100-400mg%	4	11		20	11	29	9	4	11	2	20	40
A.I	36	29		34	29	37	26	27	38	33	41	43
Weight, lbs.	163	165		163	164	163	164	165	165	164	---	
Basal BP mm Hg	115/65	120/75		130/80	142/68	130/68	110/73	124/74	126/62			
Basal pulse rate	90	69		74	79	98	78	98	80			

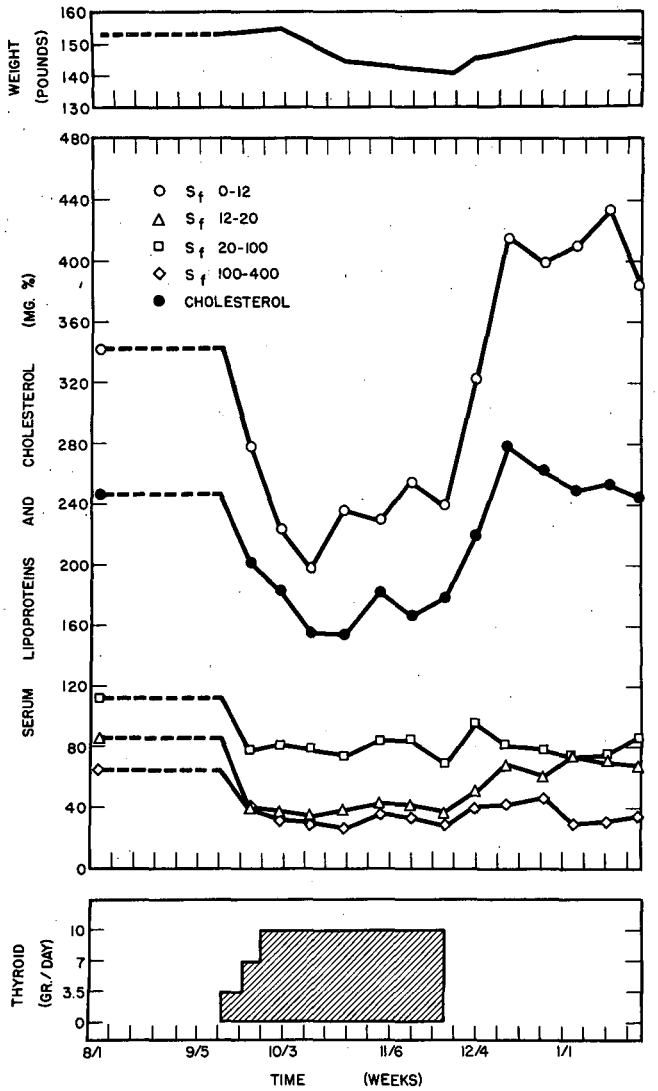

Figure 1

Weight, Standard S_f 0-12, Standard S_f 12-20, Standard S_f 20-100, Standard S_f 100-400 lipoproteins and Cholesterol curves are plotted for Group A Patients (those who completed the full course of thyroid administration).

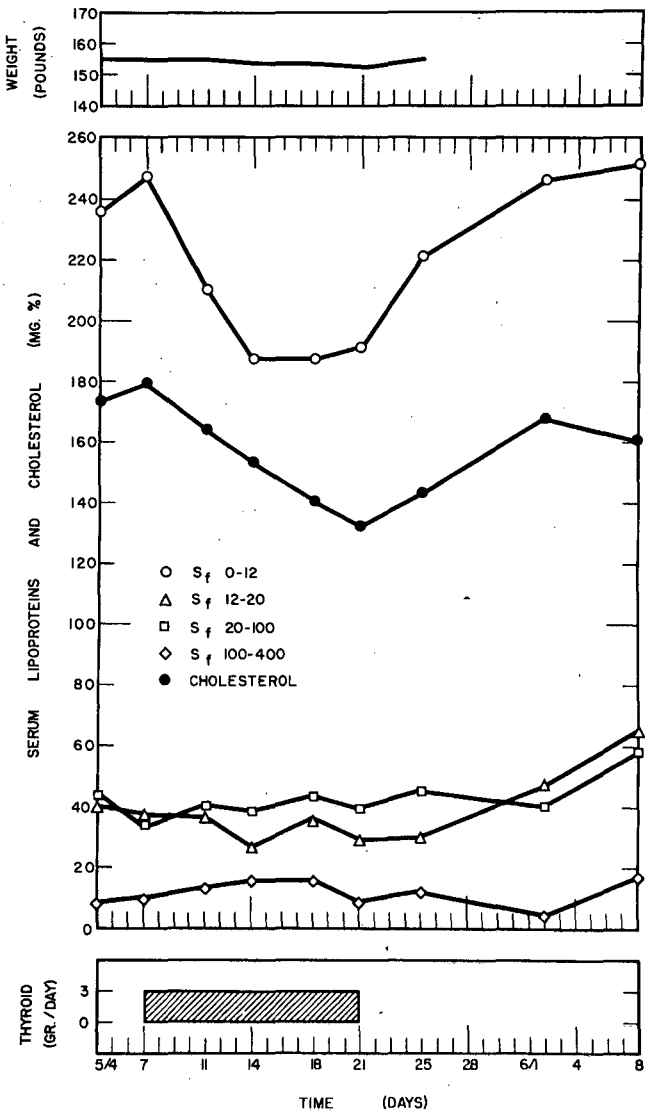

Figure 2

Weight, Standard S_f 0-12, Standard S_f 12-20, Standard S_f 20-100, Standard S_f 100-400 lipoproteins and Cholesterol curves are plotted for the individuals in Group C.

Results

In Group A, the mean serum cholesterol level, mean Standard S_f0-12 and mean Standard S_f12-20 all fell significantly ($p < 0.01$ in each case) during the period of thyroid administration, and then all three means rose significantly ($p < 0.01$ in each case) when the exogenous thyroid was withdrawn. Further, every individual patient showed a drop in each of these three measures when on thyroid extract. The responses in the Standard S_f20-400 (Standard S_f20-100 plus Standard S_f100-400) lipoproteins were not as uniform. The change in Standard S_f20-400 lipoprotein level on thyroid extract is of borderline significance (p approximately 0.05). Eight of the eleven cases showed apparent decreases in Standard S_f20-400 level on thyroid administration.

It may be noted in Fig. 1 that there was a mean weight loss in the Group A patients amounting to twelve pounds for the entire eleven-week period on thyroid extract, or, approximately one pound weight loss per week. Every individual patient showed a decrease in body weight during thyroid administration. The mean weight of the group returned to the original mean weight within six weeks after the cessation of thyroid administration.

In the additional eight schizophrenic patients (Group B) the full dose of thyroid extract (10 grains daily) was not given for the entire nine-week period because there was some indication (pulse rate increase, irritability, or excessive weight loss) that intolerance to the large dose of thyroid was being encountered. These eight patients completed the experiment on either 3-1/2 or 7 grains of thyroid extract daily. The trends in serum cholesterol levels and lipoprotein levels in this group did not differ from those observed for Group A. However in Group B the reduction of daily thyroid dosage resulted in a rise of the serum lipoprotein and cholesterol values toward the prethyroid value.

In Group C, consisting of four young normal adults, there was in every case a significant fall in serum cholesterol level and Standard S_f0-12 lipoprotein level evident in the two-week period on the dosage schedule of 3 grains of thyroid extract daily.

Discussion

In the group of schizophrenic patients receiving 10 grains of thyroid extract daily and in the group of normal laboratory workers receiving 3 grains of thyroid daily, it has been possible to confirm the effect of thyroid extract in depression of serum cholesterol levels. The lowering of serum cholesterol level is paralleled

by significant lowering of the Standard S_f 0-12 and Standard S_f 12-20 lipoproteins. The response in the Standard S_f 20-400 lipoproteins is less uniform and is only of borderline significance from these data. In exploring the mechanism by which exogenous thyroid extract produces such lipoprotein and cholesterol alterations the alterations in weight found in Group A patients deserve consideration. During the period of administration of 10 grains of thyroid extract this group lost, on the average, one pound of weight per week. From our own previous work[17] and that of Walker et al.[18, 19], it is known that lipoprotein and cholesterol levels will, on the average, fall during a period of negative caloric balance (i.e. weight loss) induced by restriction of dietary caloric intake (using low-fat, low calorie diets). It is possible that part, at least, of the lipoprotein and cholesterol drops observed in the present experiment with thyroid extract is related to the concomitant negative caloric balance. If this be the case, the present data would indicate that negative caloric balance induced by the calorigenic action of thyroid extract may affect lipoprotein and cholesterol levels in a manner analogous to that observed with negative caloric balance induced by food calorie restriction. However, it is also possible that the presently observed cholesterol and lipoprotein lowering are related to some action of administered thyroid extract wholly separate from it calorigenic its calorigenic action. Clarification of this issue could be obtained by maintaining a group of patients on thyroid extract over a sufficiently long period of time to stabilize body weights. If the lipoprotein and cholesterol lowering is maintained in spite of a steady body weight, it would then appear that the thyroid effect is not primarily related to the negative caloric balance. Such a long-term experiment is now in progress, utilizing a daily dose of 3 grains of thyroid extract, which dose is adequate to produce significant lipoprotein lowering.

The serum lipoproteins of the Standard S_f 0-400 band are of especial interest because of evidence which has been developed showing that these lipoproteins are strongly related to human coronary atherosclerosis and clinical coronary heart disease[16]. In that work it was shown that the best statistical combination of the lipoprotein information is obtained as a single value, which has been designated as the atherogenic index value (A.I value). The A.I value is determined by the following equation:

$$A.I = (\text{mg percent Standard } S_f 0\text{-}12) + (1.75 \times \text{Standard } S_f 12\text{-}400)$$

To obtain A.I values from the present data, the sum of Standard S_f12-20, Standard S_f20-100, and Standard S_f100-400 lipoproteins is first obtained to provide the Standard S_f12-400 value and then the above equation is applied. The A.I values have been calculated for all points during this experiment of thyroid administration (Table I) and the average values are plotted for Group A patients in Fig. 3. This plot demonstrates that a marked reduction in atherogenic index value is observed during the period of thyroid administration. Whether this marked reduction is maintained once the negative caloric balance disappears will be determined in the long-term experiment now in progress.

Protein-bound iodine values were within the so-called normal range (4-8 micrograms %) for all cases studied, except for one case with a value of 9.3 μg %. Thus with this criterion no case could be regarded as demonstrating thyroid hypofunction. Yet in every case a marked effect of thyroid administration upon lipoproteins was observed. There appears to be an impression current that exogenous thyroid extract is without effect in clinically euthyroid individuals. This impression is at variance with Greer's demonstration[20] of the suppression of radioiodine uptake in clinically euthyroid persons produced by thyroid extract and is at variance with the results on cholesterol and lipoproteins herein reported. Possibly part of the difficulty resides in the fact that there is considerable disagreement as to criteria for optimal thyroid function. Clinical features, caloric expenditure, radioiodine uptake, protein-bound iodine level, and cholesterol level have all been considered as criteria. In frank myxedema or overt hyperthyroidism the diagnosis is generally not contested. However between these extremes exists a region where the criteria for adequacy of thyroid function are at best equivocal. Hurxthal suggested that hypercholesteremia, when not explainable on any other basis, may be considered as possibly of thyroid origin, and is a rational indication for thyroid administration.[4] In the present study it is shown that exogenous thyroid extract is capable of reducing cholesterol and lipoprotein levels over a wide range of initial values of both measures. Further in Table IV it is demonstrated for the Group A and Group B patients that thyroid produces significantly greater reduction in cholesterol and Standard S_f0-20 lipoproteins, as measured in milligrams percent reduction, in individuals starting with high cholesterol and lipoprotein levels than in those patients with initially low values. The question may be raised as to the existence of optimal thyroid function in a person with elevated lipoprotein levels and who responds to thyroid administration with a lowering in level.[21] From the point of view of development of atherosclerosis,

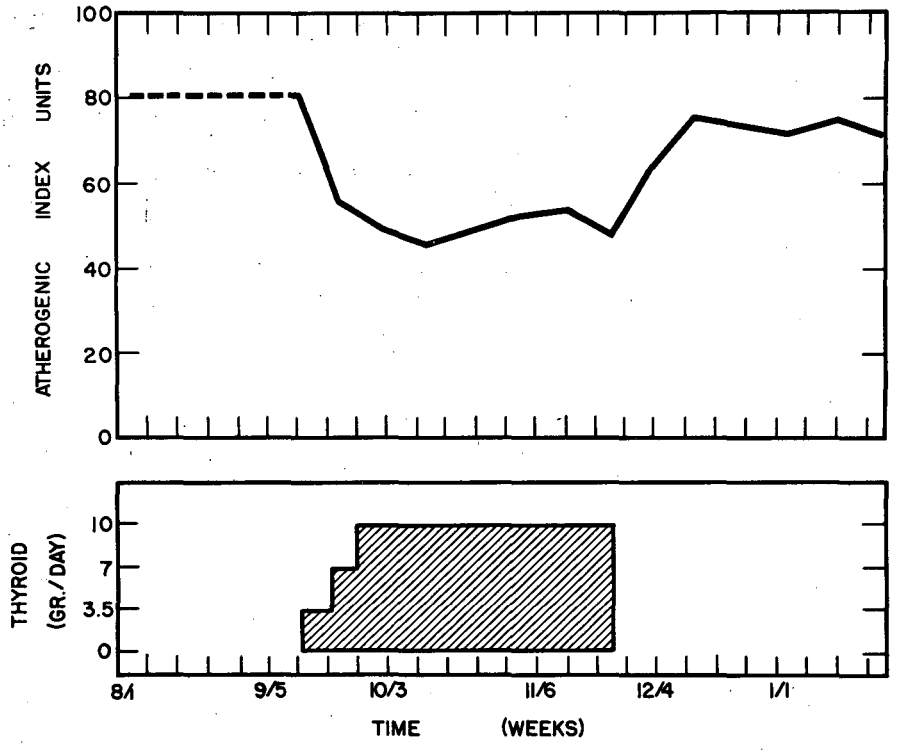

Figure 3

Atherogenic Index values are plotted for Group A Patients.

TABLE IV

Correlations of Thyroid-Induced Drop in Serum Cholesterol and Standard S_f0-20 Lipoprotein Levels with Initial Levels

(a) For Serum Cholesterol

Correlation coefficient (Pearson r) = + 0.70

95% Confidence limits; 0.44 r 0.96

99% Confidence limits; 0.36 r 1.0

(b) For Standard S_f 0-20 Lipoproteins

Correlation coefficient (Pearson r) = + 0.72

95% Confidence limits; 0.48 r 0.96

99% Confidence limits; 0.41 r 1.0

In this calculation, comparison was made for the sixteen group A and Group B patients who received the full 10-grain dose for at least one week of the experimental period. The drop in levels was measured either as milligrams percent cholesterol or lipoproteins, comparing initial values with those obtained in the first blood sampling in each case after institution of 10 grains of thyroid.

we would not regard elevated lipoprotein levels as optimal. On this basis individuals in this study who had initially elevated lipoprotein levels and whose levels dropped during thyroid administration may possibly have actually been hypothyroid with respect to the lipid metabolic function of the thyroid. Inasmuch as there has been no clearcut demonstration that all functions influenced by the thyroid need parallel each other, apparent clinical euthyroidism or protein-bound iodine levels within a so-called normal range could still be consistent with thyroid inadequacy with respect to serum lipid regulation. If, ultimately, one regards thyroid function as inadequate in an individual with elevated lipoprotein levels and who responds to thyroid extract by a lowering of these lipoproteins, it would be of primary interest to determine the basis for such inadequacy. The administration of thyroid extract in all likelihood would in many cases suppress thyroid function in ostensibly euthyroid individuals, as Greer has shown. The probable reason for the observed lipoprotein and cholesterol reduction is that in spite of decreased output of thyroid hormone, there is still available from the exogenous supply enough hormone to provide a greater than usual circulating hormone level. A more fundamental approach would be directed toward the basis for the thyroid inadequacy. Such simple possibilities as a relative lack of precursors in the synthesis of thyroid hormone deserve investigation. Current estimates of daily iodine requirements, for example, are based upon the crude criterion of an intake estimated to be adequate for the prevention of palpable goiter formation. Whether such an amount is sufficient to provide for optimal thyroid function has not been adequately demonstrated. Iodide administration is currently being studied in a fraction of the individuals we have shown to respond to thyroid extract by lipoprotein and cholesterol lowering. Other possible precursor deficiencies may be considered, or alternatively consideration may need to be given to an inadequacy in the thyroid gland itself. On the other hand, the observed findings with thyroid extract may represent a pharmacologic effect, unrelated to any real inadequacy of thyroid function. Further investigations of the mechanism of the lipoprotein and cholesterol lowering in apparently euthyroid individuals should help answer some of these questions.

Summary

1) The administration of thyroid extract in doses of 10 grains daily resulted uniformly in significant lowering of serum cholesterol, Standard S_f0-12 lipoproteins, and Standard S_f12-20 lipoproteins in nineteen schizophrenic patients. Lowering of serum cholesterol and Standard S_f 0-12 lipoproteins was observed in all of four normals given 3 grains of thyroid daily. Responses were of borderline significance

in the lipoproteins of the Standard S_f 20-400 band.

2) Protein-bound iodine determinations were above 4 μg % in all cases studied, so that for this criterion, at least, thyroid hypofunction was not present in any of the subjects.

3) The lipoprotein and cholesterol lowering was accompanied by a state of negative caloric balance in these experiments.

4) The magnitude of the drop in serum cholesterol or Standard S_f 0-20 lipoproteins was positively correlated with the initial levels of both measures. The question is raised as to whether this suggests that inadequate thyroid function, at least with respect to lipid metabolism, is present in individuals with elevated lipoprotein and cholesterol values, where other overt causes for the elevation are absent.

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BIBLIOGRAPHY

1. R. L. Mason, H. M. Hunt, and L. M. Hurxthal, Blood Cholesterol Values in Hyperthyroidism and Hypothyroidism; Their Significance. New England J. Med. 203, 1273 (1930)

2. L. M. Hurxthal, Blood Cholesterol in Thyroid Disease (I), Archives of Internal Medicine 51, 22, (1933)

3. L. M. Hurxthal, Blood Cholesterol in Thyroid Disease (II), Arch. Int. Med. 52, 86, (1933)

4. L. M. Hurxthal, Blood Cholesterol in Thyroid Disease (III), Arch. Int. Med. 53, 762, (1934)

5. L. M. Hurxthal, Blood Cholesterol and Hypometabolism, Arch. Int. Med. 53, 825, (1934)

6. J. P. Peters, and Evelyn B. Man, The Interrelations of Serum Lipids in Patients with Thyroid Disease, J. Clin. Invest. 22, 715, (1943)

7. H. L. Blumgart, A. S. Freedberg, and G. S. Kurland, Hypercholesterolemia, Myxedema and Atherosclerosis, Am. J. Med. 14, 665, (1953)

8. M. Levy and E. Levy, Thyroxin Therapy of Hypercholesteremia, Presse Med. 40, 240, Feb. 13, (1932)

9. C. I. Parhon, and I. Ornstein, Influence of Thyroxin on Cholesterol and Lipemia, Compt. Rend. Soc. de biol. 108, 303 Oct. 16, (1931)

10. A. G. Duncan, Effect of Thyroid Administration on the Blood Cholesterol, J. Mental Sc. 77, 332, April, (1931)

11. J. W. Gofman, F. T. Lindgren, H. Elliott, W. Mantz, J. Hewitt, B. Strisower, V. Herrying, and T. P. Lyon, The Role of Lipids and Lipoproteins in Atherosclerosis, Science, 111, 166, (1950)

12. F. T. Lindgren, H. A. Elliott, and J. W. Gofman, The Ultracentrifugal Characterization and Isolation of Human Blood Lipids and Lipoproteins with Applications to the Study of Atherosclerosis, J. Phys. and Colloid Chem. 55, 80, (1951)

13. H. B. Jones, J. W. Gofman, F. T. Lindgren, T. P. Lyon, D. M. Graham, B. Strisower, and A. V. Nichols, Lipoproteins in Atherosclerosis, Am. J. Med. 11, 358, (1951)

14. J. McGinley, H. Jones, and J. Gofman, Lipoproteins and Xanthamatous Diseases, J. of Invest. Derm. 19, 71, (1952)

15. D. Colman, An Improved Method for Determination of Total Cholesterol in Serum. To be published.

16. J. W. Gofman, B. Strisower, O. deLalla, A. Tamplin, H. B. Jones, and F. Lindgren, Index of Coronary Artery Atherogenesis, Modern Medicine, 119-140, June 15, (1953)

17. J. W. Gofman, Diet and Lipotropic Agents in Atherosclerosis, Bull. New York Acad. Med. 28, 279, (1952)

18. W. J. Walker, and J. A. Wier, Plasma Cholesterol Levels During Rapid Weight Reduction, Circulation 3, 864, (1951)

19. W. J. Walker, E. L. Lawry, D. E. Love, G. B. Mann, S. B. Levine, and F. J. Stare, Effect of Weight Reduction and Caloric Balance on Serum Lipoproteins and Cholesterol Levels, Am. J. Med. 14, 654, (1953)

20. M. A. Greer, The Effect on Endogenous Thyroid Activity of Feeding Desiccated Thyroid to Normal Human Subject, New England J. Med. 244, 385, Mar. 15, (1951)

21. P. Menof, The Thyroid Treatment of Essential Hypertension, So. African Medical Journal, 26, 967, Dec. 6, (1952)