Effect of 3,3',5-Triiodothyropropionic Acid (T_3P) on Serum Cholesterol Values of Old Female White Carneau Pigeons. (30455)

CHARLES H. EADES, JR.,* VICTORIA B. SOLBERG, IRENE C. HSU, CAROL A. EKHOLM AND GEORGE E. PHILLIPS (Introduced by W. M. Govier)

Biochemistry Department, Warner-Lambert Research Institute, Morris Plains, N. J.

3,3',5-Triiodothyropropionic acid (T_3P) has been shown to lower serum cholesterol in man (1,2) and rats(3). Since the White Carneau pigeon has a relatively high serum cholesterol, it was of interest to determine what effect, if any, this drug would have in lowering the serum cholesterol, in anticipation that the pigeon might serve as a living hypercholesterolemic system in which to test hypocholesterolemic drugs.

Procedure. Old (5-7 years) female White Carneau pigeons were obtained from Palmetto Pigeon Plant, Sumter, S. C. in May, 1961. The 48 pigeons used for our studies were divided into 4 groups of 12 birds each and housed 6 birds per cage and handled as described in our paper in which the control group was thoroughly discussed(4). The 3 experimental drug groups received 25, 75 or 200 μg per bird per day of T_3P in pill form by mouth for a period of 15 months. The control group received a placebo pill daily. Purina Pigeon Chow Checkers and water were available *ad libitum* to all groups. Blood, for serum, was drawn bi-weekly from alternate wings for about 6 months and then every 4 weeks for the remainder of the study. Cholesterol values were determined by the Abell *et al* method(5).

Results. While the pigeons were being studied the mean weight for each group remained remarkably steady even though there were fluctuations among the members of each group. Since T_3P is known to stimulate BMR in man and animals, some slight weight loss was anticipated at the start of the study. However, no great change was observed and the birds were a few grams heavier at the end of the study than at the start. Food consumption averaged approximately the same for each group—about 27-28 g per day per bird. The individual serum cholesterol values for each pigeon at each sample period are shown in Fig. 1, 2 and 3 for the 3 dose levels of T_3P. (The control data has been published(4)). These data illustrate the same wide variations among birds of the various groups as were observed in the control group. Among these T_3P dosed pigeons, the loss of the seasonal cyclic variation of serum cholesterol was observed to occur similarly to the control pigeons, obviously because all were housed and handled under identical conditions and T_3P would not be likely to restore the serum cholesterol level to a higher value than would be present if the drug were not given. However, as in the control group, in a few pigeons in each of the test groups serum cholesterol values tended to rise late

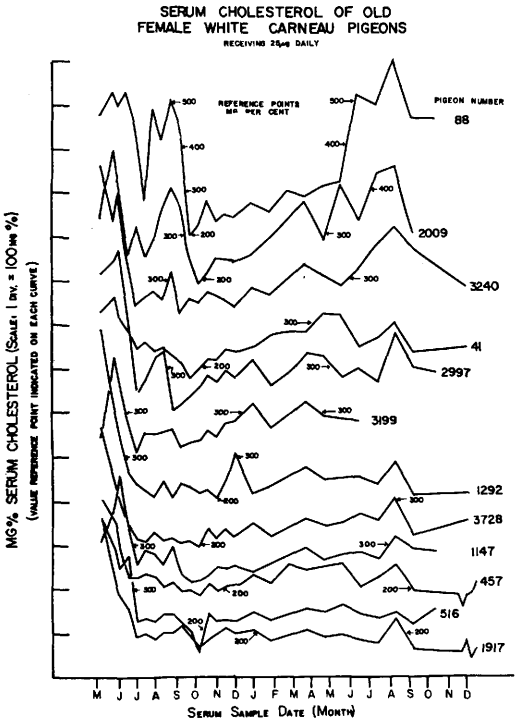

FIG. 1. Individual serum cholesterol values of old female White Carneau pigeons receiving 25 μg T_3P daily for 15 months. The drug was started 6/1/61.

* With technical assistance of Friedrich Harrsch.

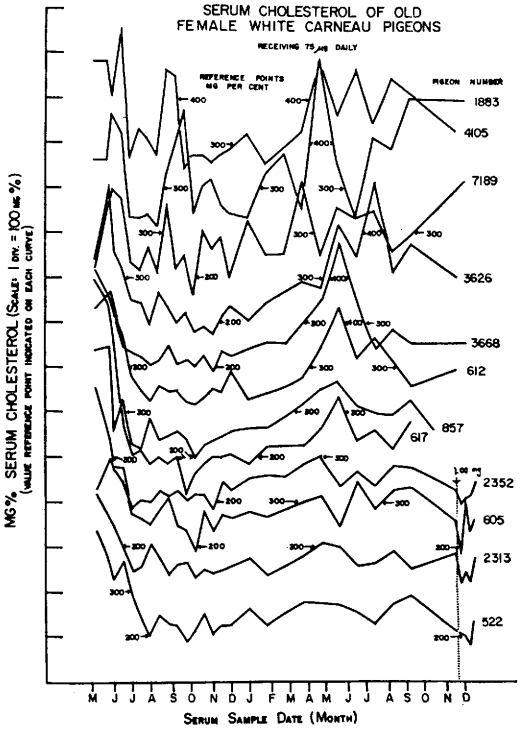

FIG. 2. Individual serum cholesterol values of old female White Carneau pigeons receiving 75 μg T_3P daily for 15 months. Drug was started 6/1/61.

in the study—July, August and Sept. of 1962. This rise occurred in more birds in the 75 μg group than in either of the other 2 groups. Mean values for the serum cholesterol at each sample date are shown in Table I. Values of the control group are repeated here for statistical comparison of the data. Mean values with standard errors are shown and the differences of the means listed. In almost all instances the drug-treated groups show values below control. When these differences of means are treated statistically, the effect of T_3P is highly significant ($P<0.001$) even though the absolute reduction of serum cholesterol at any one sample period may vary considerably and not be dramatically large. The mean serum cholesterol lowering for all of the groups combined (22%) was evaluated because there did not appear to be a dose-response relationship among these 3 dose levels. Apparently the 25 μg dose brought about the maximum effect and the higher doses did no better. Thus, the data reported here confirm in another species, the pigeon, the results obtained with the rat; T_3P lowers serum cholesterol significantly. Since the serum cholesterol of the pigeon varies so widely and fluctuates so capriciously, the number of experimental birds necessary to conduct studies with hypocholesterolemic agents in a screening program would be too great to warrant the use of the pigeon in a routine procedure. However, with enough members of a study group and adequate controls, sufficient data can be obtained to evaluate the effectiveness of a drug provided the experiment is carried out for a long enough period to overcome the statistical effect of the variability of the pigeon serum cholesterol values.

Summary. Old female White Carneau pigeons were given 3,3′,5-triiodothyropropionic acid at 25, 75 and 200 μg per day for a period of 15 months. Mean serum cholesterol lowerings for 23 sample periods for the 3 groups compared to controls were 26%, 14% and 25% for the respective dose levels

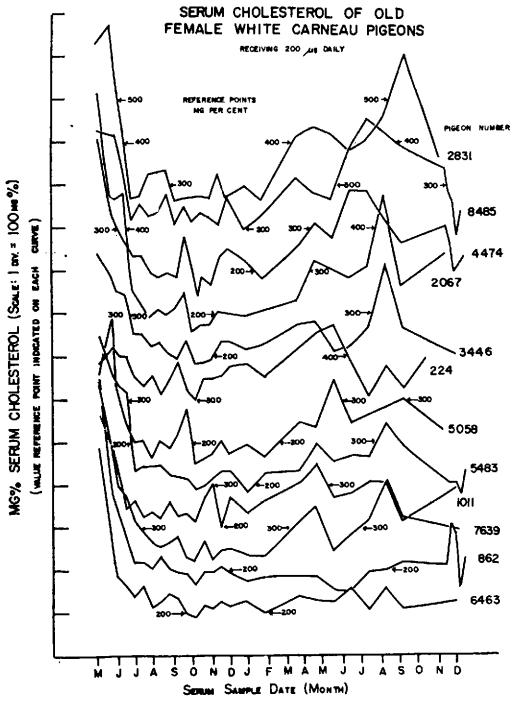

FIG. 3. Individual serum cholesterol values of old female White Carneau pigeons receiving 200 μg T_3P daily for 15 months. The drug was started 6/1/61.

TABLE I. Mean Serum Cholesterol Values for Groups of 12 White Carneau Pigeons Receiving 0, 25, 75 and 200 μg T_3P per Pigeon per Day for 15 Months.

Sample date	Serum cholesterol, mg % ± S.E.						
	Control	25 μg dose	mg % diff from control	75 μg dose	mg % diff from control	200 μg dose	mg % diff from control
6/ 1/61*	364 ± 21	389 ± 27	+25	372 ± 16	+ 8	389 ± 23	+25
6/19/61	337 ± 27	317 ± 25	—20	347 ± 25	+10	352 ± 22	+15
7/ 5/61	261 ± 13	260 ± 20	— 1	244 ± 9	—17	256 ± 13	— 5
7/18/61	266 ± 15	246 ± 8	—20	239 ± 10	—27	253 ± 10	—13
8/ 1/61	254 ± 17	267 ± 22	+13	239 ± 13	—15	239 ± 16	—15
8/15/61	283 ± 16	269 ± 19	—14	242 ± 9	—41	242 ± 12	—41
8/29/61	286 ± 20	275 ± 27	—11	275 ± 23	—11	246 ± 16	—40
9/12/61	276 ± 27	250 ± 22	—26	269 ± 23	— 7	237 ± 16	—39
9/26/61	237 ± 9	212 ± 9	—25	240 ± 24	+ 3	247 ± 11	+10
10/10/61	229 ± 10	208 ± 9	—21	204 ± 9	—25	201 ± 14	—28
10/24/61	271 ± 10	237 ± 9	—34	244 ± 11	—27	227 ± 16	—44
11/ 7/61	249 ± 12	230 ± 7	—19	230 ± 12	—19	226 ± 16	—23
11/21/61	267 ± 10	243 ± 7	—24	246 ± 8	—21	241 ± 14	—26
12/ 5/61	252 ± 10	234 ± 7†	—18	242 ± 8	—10	238 ± 17‡	—14
1/ 2/62	265 ± 9	251 ± 9	—14	256 ± 12	— 9	230 ± 17	—35
1/30/62	260 ± 11	244 ± 9	—16	256 ± 9	— 4	228 ± 15	—32
2/27/62	274 ± 7	244 ± 11	—30	264 ± 14	—10	245 ± 12	—29
3/28/62	301 ± 13	288 ± 13	—13	296 ± 13	— 5	277 ± 25	—24
4/24/62	315 ± 17	274 ± 11	—41	349 ± 31‡	+34	311 ± 23	— 4
5/22/62	342 ± 35	281 ± 15	—61	347 ± 22	+ 5	288 ± 25	—54
6/19/62	346 ± 27	286 ± 24	—60	310 ± 19	—36	295 ± 21	—51
7/17/62	344 ± 36	292 ± 27	—52	316 ± 24	—28	308 ± 22	—36
8/14/62	369 ± 28	338 ± 31	—31	308 ± 18	—61	356 ± 24	—13
9/11/62	332 ± 36	270 ± 26‡	—62	321 ± 22	—11	307 ± 31	—25
Mean (6/19–9/11/62)	288 ± 8	262 ± 6		273 ± 9		263 ± 9	
Mean of diff from control ± S.E.			—26±4		—14±4		—25±4
(N = 23, df = 22)	"t" = Mean/S.E.		6.5		3.5		6.3
	"p"		<.001		<.01		<.001

When all drug groups are combined at each sample date and means compared to control, the mean of differences from control = —22 ± 3; "t" = 7.3; "p" = <.001.

* Blood sample drawn before starting drug on this date.

† Mean of 10 birds only.

‡ Mean of 11 birds only.

with a grand mean of 22% for all groups combined (since no dose response-relationship was apparent at these levels). This lowering was highly significant and agrees with the results found with the rat. The use of the pigeon to screen hypocholesterolemic drugs would not be the one of choice because of the wide fluctuations in serum cholesterol values and therefore the need for rather large numbers of birds and long periods of study to obtain significant data.

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