Steroid balance studies after cholesterol feeding

To the Editor:

In a recent paper, Maranhão and Quintão (1) reported data on steroid balance after long-term cholesterol feeding in five normal and eight hypercholesterolemic subjects. The latter group included two subjects who were presumably genetically homozygous hypercholesterolemics, whereas the six other subjects should rather be classified as "clinically hypercholesterolemic," their blood concentration of cholesterol exceeding the "normal" value of 260 mg/dl. These authors concluded that "changes in serum cholesterol subsequent to cholesterol feeding were unrelated to the amount absorbed and to the steroid balance" during that period and also "that serum cholesterol concentration is independent of the parameters of cholesterol body metabolism measured." This conclusion can be questioned because lack of discrimination between subsets of hypercholesterolemics may have misled the authors into an incorrect statistical interpretation of their data. Indeed, after exclusion of the two genetically hypercholesterolemic subjects, there are highly significant correlations between steroid balance and either basal cholesterolemia or its variations after a dietary cholesterol load.

Table 1 presents the data of Maranhão and Quintão (1) in a slightly different manner and **Table 2** reports the correlation coefficients between the variables for 11 of the 13 subjects, the two genetically hypercholesterolemics being excluded. The steroid balance data obtained by Maranhão and Quintão are quite similar to those obtained previously by Nestel and Poyser (2). However, their subjects exhibited a much wider range of basal cholesterolemia and their capacity to absorb dietary cholesterol varies widely, leading to positive cholesterol balance in some individuals, whereas intestinal cholesterol absorption was almost constant in subjects of Nestel and Poyser. Taking as a group only the 11 subjects with a normal or a clinically abnormal blood cholesterol concentration, the variations in cholesterolemia (as well as cholesterolemia during cholesterol feeding) are significantly and inversely related with both intestinal dietary cholesterol absorption and steroid balance during cholesterol feeding ($r = -0.73$ in both cases). Thus statistical evaluation of the data leads to the paradoxical conclusion that the better the capacity to absorb cholesterol, the smaller the variations of cholesterolemia due to cholesterol feeding. The subjects showing small increases, or even decreases of cholesterolemia after a cholesterol load, tend to exhibit a positive steroid balance (e.g., accumulation of cholesterol within the body) whereas those subjects who respond by large increases in blood cholesterol maintain a negative steroid balance. Furthermore, the statistical analyses can be extended and the following multivariate regression equation computed.

1) Variation in cholesterolemia

$$= 31.6 - 12.8\ (\text{intestinal cholesterol absorption during PII})$$

$$F = 18.1;\ P < 0.005$$

$$+ 13.4\ (\text{endogenous cholesterol excretion during PIII})$$

$$F = 7.8;\quad P < 0.025$$

$$\text{overall}\quad r = 0.88,\quad N = 11.$$

However, utilization of the steroid balance in PII instead of intestinal cholesterol absorption does not lead to a multivariate regression equation that exhibits any significant improvement over balance alone.

Basal cholesterolemia during PI seems to be related itself to the subjects' capacity to adapt to cholesterol feeding. Indeed, subjects who exhibit a lesser endogenous steroid excretion under the cholesterol load than during the following recovery period (PIII) have a low cholesterolemia. On the contrary, the basal cholesterolemia values of individuals with increased endogenous steroid excretion relative to the recovery period are situated in the upper range. This relationship is expressed by the positive correlation coefficient ($r = 0.72$) between basal cholesterolemia and the difference between endogenous steroid excretion during periods PIII and PII. Once again, a multivariate regression equation can be computed show-

TABLE 1. Data from Maranhão and Quintão (1) reevaluated in present paper[a]

Subjects	1	2	3	4	5	6	7	8	9	10	11	12	13
						mg/dl							
1. Cholesterolemia in PI	168	189	227	252	257	268	293	301	312	318	358	523	717
2. Cholesterolemia in PII	178	410	199	235	271	342	405	301	344	300	402	588	808
3. Variation (PII–PI)	10	221	−28	−17	14	74	112	0	32	−18	44	65	91
						mg/kg body weight							
4. Dietary cholesterol absorption in PII	7.35	2.16	15.57	12.34	7.71	3.15	8.19	11.12	8.69	13.05	2.56	5.68	14.30
5. Steroid balance in PII	2.66	−7.43	7.47	3.85	−3.37	−1.58	−5.43	−2.33	2.73	7.56	−6.75	−5.53	10.50
6. Endogenous steroid excretion in PI	8.07	10.61	13.55	5.74	11.15		9.49	9.89	14.11	15.20	5.32	16.79	4.20
7. Endogenous steroid excretion in PII	4.69	9.59	8.10	8.49	11.08	4.73	13.62	13.45	5.96	5.49	9.31	11.21	3.80
8. Endogenous steroid excretion in PIII	7.33	12.06	9.72	8.10	10.31	7.73	12.08	10.94	4.59	7.35	4.72	16.74	4.28
9. Endogenous steroid balance relative to PIII in PII	−2.64	−2.47	−1.62	0.39	0.77	−3.00	1.54	2.51	1.37	−1.86	4.59	−5.53	−0.48
10. Endogenous steroid balance relative to PIII in PI	0.74	−1.45	3.83	−2.36	0.84		2.59	−1.05	9.52	7.85	0.60	0.05	−0.08

[a] PI, PII, PIII: periods before, during, and after cholesterol supplementation (1350 mg/day) to a baseline diet devoid of cholesterol. Dietary cholesterol absorption in PII: dietary cholesterol − (fecal neutral steroids − endogenous cholesterol secretion) during PII. Steroid balance in PII: dietary cholesterol − total fecal steroids during PII. Endogenous steroid excretion in PI or PIII: total fecal steroids during PI or PIII. Endogenous steroid excretion in PII: steroid balance in PII − dietary cholesterol absorption in PII.

ing that the relative steroid balance during PI is related, though marginally, to basal cholesterolemia.

2) Cholesterolemia in PI

$$= 252 + 21.7\ (\text{endogenous steroid excretion in PII} - \text{endogenous steroid excretion in PIII})$$

$$F = 26.5;\ P < 0.005$$

$$+\ 6.3\ (\text{endogenous steroid excretion in PI} - \text{endogenous steroid excretion in PIII})$$

$$F = 7.0;\quad P < 0.05$$

$$\text{overall } r = 0.90,\quad N = 10.$$

Thus statistical evaluation of the results, excluding genetically hypercholesterolemic patients, shows that there is no essential difference between the way subjects with "normal" or "elevated" concentrations of blood cholesterol handle cholesterol. Multivariate regression equations, which account for about 80% of individual variations in cholesterolemia, either before or during cholesterol feeding, can be computed for the whole group, notwithstanding the clinical classification of each subject. However, there may be minor differences in the factors controlling cholesterol homeostasis. For example, the second variables which have been introduced into both regression equations gain most of their significance from their ability to accommodate the six subjects with the highest cholesterolemia.

The regression equations for basal cholesterolemia as well as for its variation after cholesterol feeding includes the steroid balance in PIII as one of the significant factors that permits the best fit to the data. This is a surprising result. Indeed, the value for endogenous steroid excretion during PIII, i.e., 2 weeks after the end of the dietary cholesterol load, may be considered as the reference value to which the values during PI and PII should be compared. On the contrary, one would have expected that the value in PI, before cholesterol feeding, would have been the baseline value. Steroid excretion during PI is not correlated at all with that during PII ($r = -0.27$) or PIII ($r = 0.07$). This observation cannot be readily explained but it is potentially important for the experimental design of future steroid balance studies.

The results can best be explained by considering the steroid balances as the correlate of the measure of cholesterol synthesis. Thus basal cholesterolemia is inversely related to the capacity of individuals to downregulate their cholesterol synthesis, as evidenced by its relation to the endogenous steroid balance, relative to PIII, in PI and PII. As for variations in cholesterolemia after cholesterol supplementation to the diet, it is positively related to residual cholesterol synthesis during PIII, and more significantly, to the amount of cholesterol being effectively absorbed; which is, of course, an important determinant of the dose–response relationship in the down-regulation

TABLE 2. Correlation matrix between variables for normocholesterolemic and "clinically" hypercholesterolemic subjects[a]

1. Cholesterolemia in PI									
2. Cholesterolemia in PII	0.49								
3. Variation in cholesterolemia	−0.23	0.73[b]							
4. Cholesterol absorption in PII	0.02	−0.64[c]	−0.73[b]						
5. Steroid balance in PII	−0.11	−0.73[b]	−0.73[b]	0.80[d]					
6. Endogenous steroid excretion in PI[a]	0.03	−0.07	−0.10	0.44	0.48				
7. Endogenous steroid excretion in PII	0.21	0.34	0.22	0.04	−0.57	−0.27			
8. Endogenous steroid excretion in PIII	−0.42	0.08	0.41	0.09	−0.32	0.07	0.66[c]		
9. Relative endogenous steroid balance in PII	0.72[b]	0.37	−0.15	−0.05	−0.40	−0.42	0.60	−0.20	
10. Relative endogenous steroid balance in PI	0.38	−0.05	−0.25	0.31	0.50	0.77[b]	−0.48	−0.47	0.09
Variables	1	2	3	4	5	6	7	8	9

[a] Number of subjects (N) = 11, except for variables computed with steroid excretion in PI where N = 10.
[b] $P < 0.025$.
[c] $P < 0.05$.
[d] $P < 0.005$.

of cholesterol synthesis by HMG-CoA reductase, as suggested by the results of Mistry et al. (3).

However, steroid balance can only be an inadequate measure of cholesterol synthesis. The subjects with the smallest increment in blood cholesterol during PII actually accumulate cholesterol according to the steroid balance. Mistry et al. (3) have shown that blood mononuclear cells are enriched in cholesterol after cholesterol feeding. Thus the minimal rise or the decrease in cholesterolemia can be explained, at least partially, by the immobilization of the sterol in peripheral cells, whose capacity to degrade LDL is impaired. Therefore, these results cast doubts about the validity of considering the steroid balance as a measure of cholesterol synthesis by the body, as this would lead to negative cholesterol synthesis. Even in cases when the steroid balance is negative, it is not known what role immobilization of sterol could play. However, accumulation of cholesterol by tissues raises the problem of the eventual fate of the immobilized cholesterol, when and if a steady-state is reached. It should be noticed in this respect that endogenous steroid excretion during PIII is not correlated with intestinal cholesterol absorption ($r = 0.09$), indicating that any accumulated cholesterol is not eliminated in the second week after the end of cholesterol supplementation.

Whatever the explanation for the observed structure in the data of Maranhão and Quintão (1), it remains that the same parameters expressed by steroid balance measurements seem to govern plasma cholesterol levels in all individuals; they can be classified clinically as normocholesterolemic or as hypercholesterolemic, as long as they are not monogenetic hypercholesterolemic.

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Authors' Response

In the accompanying letter addressed to the *Journal of Lipid Research,* Dr. Morazain argues that the authors were misled into an incorrect statistical interpretation of the data when all 13 patients included in the study had been analyzed. Yet he agrees with the major conclusion of our paper when he states: "Thus statistical evaluation of the results, excluding genetically hypercholesterolemic patients, shows that there is no essential difference between the way subjects with "normal" or "elevated" concentrations of blood cholesterol handle cholesterol." Our data support this conclusion, either with the exclusion or inclusion of the two most severe hypercholesterolemic subjects (Patients 12 and 13). Correlation matrices between variables were calculated with additional data (bile acids) not available in the tables of our original paper. Considering the level of significance as above 0.707, it is evident from **Table 1,** where Patients 12 and 13 were included, as well as from **Table 2** (11 patients), that basal serum cholesterol (PI) is independent of the parameters of cholesterol metabolism measured in our study, namely, variation in cholesterolemia, absorption of dietary cholesterol, fecal steroid balance (PII), and endogenous steroid excretion in the three study periods.

However, in spite of Morazain's interesting analysis, the inclusion of the two most severe hypercholesterolemics ought to strengthen the significant inverse correlation between variation of serum cholesterol elicited by cholesterol feeding and steroid balance, in order to conform to the model proposed by Mistry et al. (1), since the LDL high affinity receptor activity measured in the basal diet is supposed to be markedly diminished in the familial hypercholesterolemics. Also, we were puzzled by the behavior of two correlations that should be directly dependent on the presence of a wide range of serum cholesterol values: the correlation between the variation of cholesterolemia (PII–PI) and cholesterolemia in PII is present in Table 2 (11 patients) but not in Table 1 (13 patients), and yet correlation between cholesterolemia in PI and PII found in Table 1 is absent from the 11-patient matrix (Table 2). Furthermore, on trying to interpret some significant steroid balance correlations between the three diet periods (Table 2, items 9 and 10), Morazain states that the lack of correlation between steroid excretion in PI and PII or PIII "cannot be readily explained but is potentially important for the experimental design of future steroid balance studies." We contend that several statistical correlations bear no relationship whatsoever to the exclusion or inclusion of the two most severe hypercholesterolemics, but are biologically meaningful because of the unique response of the individuals towards cholesterol feeding, either in maintaining a negative steroid balance during PII (Patients 2, 5, 6, 7, 8, 11, and 12) as shown in **Table 3,** or in accumulating body cholesterol (positive balance: Patients 1, 3, 4, 9, 10, and 13) as shown in **Table 4.** It is important to emphasize that it was possible to demonstrate in six out of seven cases (Table 3) that the mass of cholesterol absorbed was perfectly matched by an increased endogenous cholesterol excretion and an interrupted body synthesis. Accordingly, fecal steroid balance while on cholesterol feeding reliably measured body synthesis, which did not happen in the cases reported in Table 4.

Multiple correlation analyses of our original data maintain our published conclusions that compensatory mechanisms were equally efficient in normal and hypercholesterolemic individuals. Nevertheless, such statistical treatment of the data disclosed meaningful metabolic

TABLE 1. Multiple regression analysis (13 patients); significant values (>0.707) underlined

1. Cholesterolemia in PI											
2. Cholesterolemia in PII	0.<u>918</u>										
3. Variation (PII–PI)	0.141	0.520									
4. Dietary cholesterol absorption in PII	0.211	−0.054	−0.591								
5. Steroid balance in PII	0.260	0.022	−0.505	0.<u>868</u>							
6. Endogenous steroid excretion in PI	−0.154	−0.182	−0.122	0.016	−0.064						
7. Endogenous steroid excretion in PII	−0.241	−0.130	0.193	−0.345	−0.<u>765</u>	0.143					
8. Endogenous steroid excretion in PIII	−0.125	−0.000	0.270	−0.254	−0.546	0.510	0.<u>710</u>				
9. Endogenous steroid balance relative to PIII in PII	−0.090	−0.138	−0.151	−0.050	−0.165	−0.520	0.237	−0.514			
10. Endogenous steroid balance relative to PIII in PI	−0.072	−0.176	−0.286	0.250	0.362	0.563	−0.368	−0.341	0.032		
11. Bile acid excreted in PI	−0.107	−0.024	0.169	0.072	0.067	0.263	−0.041	−0.038	0.012	0.269	
12. Bile acid excreted in PII	−0.012	−0.034	−0.057	−0.181	−0.325	−0.184	0.375	−0.122	0.622	−0.073	−0.053
Variables	1	2	3	4	5	6	7	8	9	10	11

TABLE 2. Multiple regression analysis (11 patients); significant values (>0.707) are underlined

1. Cholesterolemia in PI											
2. Cholesterolemia in PII	0.494										
3. Variation (PII–PI)	−0.236	0.728									
4. Dietary cholesterol absorption in PII	0.023	−0.645	−0.740								
5. Steroid balance in PII	−0.108	−0.732	−0.733	0.839							
6. Endogenous steroid excretion in PI	0.032	−0.068	−0.102	0.437	0.479						
7. Endogenous steroid excretion in PII	0.201	0.438	0.331	−0.158	−0.669	0.273					
8. Endogenous steroid excretion in PIII	−0.420	0.092	0.435	0.050	−0.333	0.065	0.696				
9. Endogenous steroid balance relative to PIII in PII	0.788	0.466	−0.100	0.240	−0.472	−0.422	0.503	−0.269			
10. Endogenous steroid balance relative to PIII in PI	0.384	0.049	−0.247	0.314	0.504	0.771	−0.499	−0.465	−0.091		
11. Bile acid excreted in PI	−0.035	0.153	0.200	0.095	0.107	0.351	−0.075	−0.034	−0.043	0.253	
12. Bile acid excreted in PII	0.667	0.473	0.002	−0.199	−0.386	−0.209	0.419	−0.058	0.624	−0.146	−0.086
Variables	1	2	3	4	5	6	7	8	9	10	11

correlations elicited by cholesterol feeding whenever "non-accumulators" and "accumulators" of body cholesterol are studied as separate groups. We cannot agree at all with Morazain for including in the same correlation matrix patients who responded towards cholesterol feeding in utterly opposite ways.

"Non-accumulators" did conform to the metabolic model proposed by Morazain, namely, there was observed the paradoxical increase of serum cholesterol as fecal balance data became more negative (Table 3, footnote b). In other words, the better the capacity to excrete steroids, the greater the variation of serum cholesterol elicited by cholesterol feeding.

Fecal endogenous steroids include newly made body

TABLE 3. Multiple regression analyses of data from seven patients on negative steroid balance (while on cholesterol feeding) in PII (patients 2, 5, 6, 7, 8, 11, 12); significant values (>0.707) are underlined

1. Cholesterolemia in PI											
2. Cholesterolemia in PII	0.739[a]										
3. Variation (PII–PI)	−0.389	0.332									
4. Dietary cholesterol absorption in PII	0.021	−0.423	−0.608								
5. Steroid balance in PII	0.002	−0.558	−0.767[b]	0.920[c]							
6. Endogenous steroid excretion in PI	0.505	0.557	0.054	0.173	0.148						
7. Endogenous steroid excretion in PII	−0.010	−0.216	0.281	0.897[d]	0.654	0.161					
8. Endogenous steroid excretion in PIII	0.364	0.548	0.239	0.243	0.098	0.939[e]	0.362				
9. Endogenous steroid balance relative to PIII in PII	−0.366	−0.684	−0.421	0.200	0.234	−0.911[f]	0.120	−0.881[f]			
10. Endogenous steroid balance relative to PIII in PI	0.144	0.013	−0.184	0.192	0.008	−0.165	0.330	−0.105	0.292		
11. Bile acid excreted in PI	−0.268	0.293	0.776[g]	−0.649	−0.683	−0.104	−0.456	0.004	−0.257	−0.649	
12. Bile acid excreted in PII	−0.087	−0.355	−0.362	0.062	0.122	−0.763[h]	−0.010	−0.748[h]	0.792[h]	−0.173	0.130
Variables	1	2	3	4	5	6	7	8	9	10	11

[a] Serum cholesterol levels in PI and PII (0.7391), a rather expected finding.
[b] Variation in serum cholesterol (PII–PI) inversely related to steroid balance in PII (−0.767). That is, as the excretion approaches the intake level, serum cholesterol variation is bound to decrease. This is an apparent paradoxical response towards cholesterol feeding.
[c] A larger cholesterol absorption is associated with a less negative balance (0.920).
[d] Absorption and endogenous steroid excretion in PII (0.897).
[e] Endogenous steroid excretions in PI and PIII represent similar events (0.939) since the body has not stored cholesterol in PII.
[f] Endogenous steroid excretion in PI and PIII is negatively related to endogenous excretion difference (PII–PIII), respectively, −0.911 and −0.881.
[g] Bile acids in PI and increment of serum cholesterol (PII–PI), 0.776.
[h] The increment of bile acid excretion in PII correlates negatively with endogenous steroid excretion in PI (−0.763) and PIII (−0.748), and positively with endogenous steroid difference PII–PIII (0.792).

TABLE 4. Multiple regression analyses of data from six patients who accumulated cholesterol (positive balance) in PII (patients 1, 3, 4, 9, 10, 13); significant values (>0.707) are underlined

1. Cholesterolemia in PI											
2. Cholesterolemia in PII	0.995[a]										
3. Variation (PII–PI)	0.849[b]	0.897[b]									
4. Dietary cholesterol absorption in PII	0.410	0.326	−0.082								
5. Steroid balance in PII	0.745[c]	0.689	0.354	0.831[c]							
6. Endogenous steroid excretion in PI	−0.452	−0.475	−0.516	−0.015	−0.137						
7. Endogenous steroid excretion in PII	−0.626	−0.671	−0.786[d]	0.255	−0.324	0.211					
8. Endogenous steroid excretion in PIII	−0.694	−0.747[d]	−0.886[d]	0.313	−0.101	0.244	0.750[e]				
9. Endogenous steroid balance relative to PIII in PII	0.260	0.275	0.303	−0.063	−0.204	−0.080	0.188	−0.505			
10. Endogenous steroid balance relative to PIII in PI	−0.146	−0.145	−0.125	−0.155	−0.093	0.900[f]	−0.122	−0.200	0.145		
11. Bile acid excreted in PI[g]	−0.067	−0.077	−0.109	0.322	0.037	0.432	0.451	0.119	0.441	0.383	
12. Bile acid excreted in PII[g]	0.120	0.044	−0.296	0.513	0.538	0.538	−0.053	0.174	−0.286	0.465	−0.116
Variables	1	2	3	4	5	6	7	8	9	10	11

[a] Serum cholesterol levels in PI and PII (0.995), a rather expected finding.
[b] Variation in serum cholesterol (PII–PI) with basal cholesterolemia (PI) and with serum cholesterol in PII (respectively, 0.849 and 0.897).
[c] PI serum cholesterol and positive balance (0.745); absorption and positive balance (0.831).
[d] Endogenous steroid excretion in PII and PIII negatively related to the PII–PI variation of serum cholesterol (respectively, −0.786 and −0.886). Also, endogenous steroid excretion in PIII is inversely related to serum cholesterol in PII (−0.747).
[e] Endogenous steroid excretion in PII and PIII (0.750).
[f] Endogenous excretion in PI and endogenous steroid difference PI–PIII (0.900).
[g] No correlations with bile acids are apparent.

cholesterol, re-excreted absorbed dietary cholesterol, and bile acids. Endogenous steroids in PI are not related to the variation PII–PI of serum cholesterol, but bile excretion is (Table 3, footnote g). Also, the greater the excretion of bile acids during cholesterol intake, the less the excretion of endogenous steroids in PI and PIII (Table 3, footnote h). Thus, the increments of serum cholesterol and bile acid excretion on cholesterol feeding are closely coupled and probably reflect a diminished efficiency to excrete endogenous steroids on cholesterol-free diets.

Absorption of dietary cholesterol equals intake − (total fecal neutral steroids − endogenous neutral sterols). Accordingly, absorption is greater as endogenous neutral sterols increase (Table 3, footnote d) and also as the balance is less negative (Table 3, footnote c).

The efficiency with which endogenous steroid excretion is enhanced among patients on cholesterol feeding is inversely related to the excretion of endogenous steroids in patients on a cholesterol-free diet. Accordingly, the greater the efficiency in eliciting endogenous steroid excretion by cholesterol feeding, the less the endogenous steroid output when cholesterol is absent from the diet (Table 3, footnote f: −0.911 and −0.881). In other words, individuals who are good excretors of endogenous steroids on a cholesterol-free diet cannot further enhance this excretion when fed cholesterol.

Basal hypercholesterolemia is an aggravating factor only in patients who accumulate body cholesterol (Table 4, footnotes a, b, and c). The paradoxical response of serum cholesterol to cholesterol feeding, observed in Table 3, does not hold for this group. In addition, cholesterolemia in PII correlates with PI, as should have been expected both for those that store body cholesterol and for individuals that have efficient compensatory mechanisms.

Body cholesterol accumulators are unable to enhance the endogenous steroid excretion when fed cholesterol (Table 4, footnote d). Furthermore, since they might eliminate in PIII cholesterol stored in PII, it is expected that endogenous excretions in PIII and PI are not related to each other, as opposed to the "non-accumulators" (Table 3, footnote e), and also that PII and PIII are correlated (Table 4, footnote e). Excellent correlation of endogenous steroid excretion in PI and its difference PI − PIII must result from the complex combination of interruption of body synthesis and re-excretion of cholesterol that had been stored in PII and is still present in the short-lasting PIII (Table 4, footnote f). The events in PIII shown in Table 4 cannot simply be defined by residual synthesis as suggested by Morazain.

Finally, and most interestingly, in "accumulators" bile acid excretion in PI and PII does not correspond with other parameters, whereas in "non-accumulators" bile acid excretion and serum cholesterol rise simultaneously. In "accumulators" fecal bile acids are not related to PI and PIII endogenous steroids as they are in "non-accu-

mulators." Conceivably a combined partial deficiency in endogenous and bile acid excretion leads to indiscriminate cholesterol storage in the body. It is worth noticing that bile acid correlations are absent from both the 13-patient and 11-patient correlation tables (Tables 1 and 2, respectively). Certainly more adequate mathematical models could be drawn from present data, especially if the latter were analyzed in combination with other reports on human balance cholesterol that might fully explain the intricacies of human body cholesterol dynamics on cholesterol feeding. Nevertheless, the question remains why in some individuals the efficiency to deal with absorbed cholesterol is completely unrelated to the basal serum cholesterol, whereas hypercholesterolemia and accumulation are correlated in other cases. Conceivably the level of serum HDL could be a factor distinguishing between these two types of responses. This possibility accords with the finding of Schwartz et al. (2) that free cholesterol from HDL is more rapidly incorporated into biliary cholesterol than free cholesterol from LDL.

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