

OBSERVATIONS ON THE SERUM CHOLESTEROL IN ACUTE INFECTIONS AS RECORDED DURING AND AFTER PNEUMONIA¹

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In a previous report (1) the relative stability of the serum cholesterol level was demonstrated in normal subjects over long periods of time. The cholesterol values were not altered significantly by the feeding of diets high or low in fat or cholesterol, or by the ingestion of potassium iodide. However, the administration of thyroid extract produced a sharp fall in serum cholesterol which was followed by a rise above normal when thyroid feeding was discontinued.

Acute infection is also known to produce a hypocholesterolemia. This was shown a number of years ago by Denis (2) and Kipp (3) and by numerous workers since. The behavior of the serum cholesterol during convalescence has received little attention. Stoesser and McQuarrie (4) and more recently Stoesser (5) reported that a plasma cholesterol determination made in infants or children convalescent from an acute infection was higher than one obtained at the height of the febrile episode. However, there have been no reports in which repeated determinations were made on the same individual during and for a protracted period after the acute infection. Accordingly, the present study was undertaken in an attempt to demonstrate what happens to the serum cholesterol of individuals who develop an acute infection—an infection which was, in these instances, pneumonia.

PLAN OF STUDY

Observations were made on 19 patients, varying in age between 12 and 52 years, who were admitted to the hospital with a diagnosis of pneumonia. There were 12 males and 7 females of whom 16 were white and 3 were colored. In the sputum studies on the 19 patients the pneumo-

coccus type was identified in 9, and the hemolytic streptococcus was found in 3. Five patients were treated with specific serum, 4 with sulfanilamide, and 1 with optochin. An initial serum cholesterol was determined using the method of Bloor, Pelkan and Allen (6) from blood obtained within 48 hours of the patient's entry to the hospital. Serum cholesterol determinations were made twice weekly thereafter while the patients remained in the hospital. After discharge, the patients were seen at weekly, bi-weekly or monthly intervals for periods ranging from 96 to 520 days. The total number of tests performed was 418, averaging 22 for each patient.

Basal metabolism estimations were made at frequent intervals after the fever subsided. In addition to the usual laboratory procedures, serum protein and bromsulphalein dye retention determinations were made on most of the patients.

Serum cholesterol level during febrile period

During the febrile period of pneumonia there is a hypocholesterolemia. At the lowest point of each individual curve, which was observed usually on the second to sixth day of the disease, the total serum cholesterol ranged between 86 and 206 mgm. per 100 cc. (Table I). At this time a reduction in cholesterol ester was apparent in the 6 patients in whom this fraction was determined. In 1 case the lowest value for the total serum cholesterol was not reached until the twenty-second day. The course of this patient was complicated by the development of active rheumatic carditis subsequent to pneumonia due to a hemolytic streptococcus.

Serum cholesterol level during convalescence

As soon as the fever subsided the serum cholesterol value in each patient rose, and for a variable

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TABLE I
Serum cholesterol values during and after pneumonia

Name	Sex	Age	Pneumonia		Days of fever over 102°	Treatment	Total days observed	Number of cholesterol determinations	Serum cholesterol									Elevation of serum cholesterol		
			Type	Location					Low			High			"Normal"			Ex-tent	Duration	
									Total	Ester	Day	Total	Ester	Day	Total	Ester	Day			
mgm.	per cent		mgm.	per cent		mgm.	per cent		per cent	days										
J. M.	F	17	Pneumococcus IV	L. L. L.	5	Sulfanilamide	168	31	167		1	312		21	210		130	53	40	
M. G.	M	25		R. M. L.	9		210	31	91		10	320		72	230		91	39	60	
G. S.	M	24	Pneumococcus IV	L. L. L.	6		192	18	140		5	274		39	225		60	23	39	
J. A.	M	28		R. L. L.	3		112	21	121		2	297		50	210		69	41	50	
L. I.	F	38	Pneumococcus I	L. L. L.	4	Serum	120	23	182	36	4	332	84	37	274		82	85	25	30
R. D.	F	20		L. L. L.	2		117	26	101		2	285		25	200		87	42	63	
J. S.	M	16		Bronchi	3		125	9	158		3	293		46	185		76	58	60	
M. B.	M	12	Hemolytic streptococcus	Bronchi	5		96	17	206		4	270		27	200		70	35	35	
D. C.	F	15		R. U. L.	4	Serum	506	42	123	48	6	450	68	76	200		83	170	125	110
A. N.	M	52	Pneumococcus II	L. L. L.	7		187	26	132	54	3	344	86	33	235	70	83	42	61	
C. P.	F	28	Pneumococcus IV	R. U. L.	5		336	26	166	42	5	299	78	44	210		79	78	42	55
L. B.	M	17		L. L. L.	5		Sulfanilamide	124	16	157		3	277		31	180		47	53	20
V. I.	F	33		L. L. L.	6	Serum	119	12	161		5	263		44	220		65	20	31	
W. M.	M	24	Pneumococcus VII	R. L. L.	2	Serum	156	22	176		4	316		38	266		63	20	32	
J. S.	M	34	Pneumococcus I	R. U. L.	5	Serum	112	20	86		3	261		30	235		90	11	30	
M. D. a.	M	21	Pneumococcus VII	L. U. L.	6		330	29	125	20	7	358	73	56	235	76	140	52	57	
M. H.	M	15	Hemolytic streptococcus	L. L. L.	14		510	39	96		22	239	87	58	200	84	150	20	80	
M. D. b.	F	44	Hemolytic streptococcus	L. L. L.	12	Sulfanilamide	105	12	125		4	295		10	255		85	17	47	
C. R.	M	52	Pneumococcus IV	R. U. L.	7	Optochin	520	36	136		10	255		28	225		140	13	92	
						Average	217	22						40			92	38	52	

time during convalescence strikingly wide fluctuations occurred in the cholesterol level (Figure 1). In general, there was a hypercholesterolemia due to an increase in both the ester and free fractions. The serum cholesterol of each of the 19 patients reached a peak during convalescence between the tenth and seventy-sixth days, usually about the fortieth day. The increase in serum cholesterol over the level that was subsequently found to be "normal" for each of the patients varied from 26 to 250 mgm. per 100 cc., with an average rise of 82 mgm. per 100 cc. The percentage of increase over the normal value varied from 11 to 125 per cent, with an average rise of 38 per cent. The elevation of the serum cholesterol persisted from 20 to 110 days, with an average of 52 days (Table I). Although the serum cholesterol fluctuated considerably during this period, the general pattern of response was characterized by a rise to a peak, with a subsequent fall toward normal (Figure 1).

Normal serum cholesterol level

The serum cholesterol reached the level designated as normal from 47 to 170 days after the onset of the illness (Table I). At this point fluctuations in the cholesterol level disappeared and

repeated determinations revealed values which were constant for the individual. Previous work by the authors (1) has shown the serum cholesterol to be remarkably constant in normal subjects over long periods of time. The results obtained in this study during the "normal" period which varied from 30 to 380 days, averaging 123 days, confirm this finding. Figure 1 demonstrates this observation in 6 of the patients. In patient D. C. during the 336 days of the normal period the serum cholesterol deviated only 7 mgm. from the mean. In patient C. P. the serum cholesterol varied only 8 mgm. from the mean during the normal period of 258 days.

DISCUSSION

From the foregoing it is evident that during pneumonia there is a decrease in the serum cholesterol level. After the infection subsides and the fever disappears there follows characteristically a rise above the level later found to be normal for the individual, with a marked instability of the serum cholesterol values which may persist for weeks or months before the stabilized level assumed to be normal is reached.

The mechanism producing this alteration in serum cholesterol is not clear. Because of the simi-

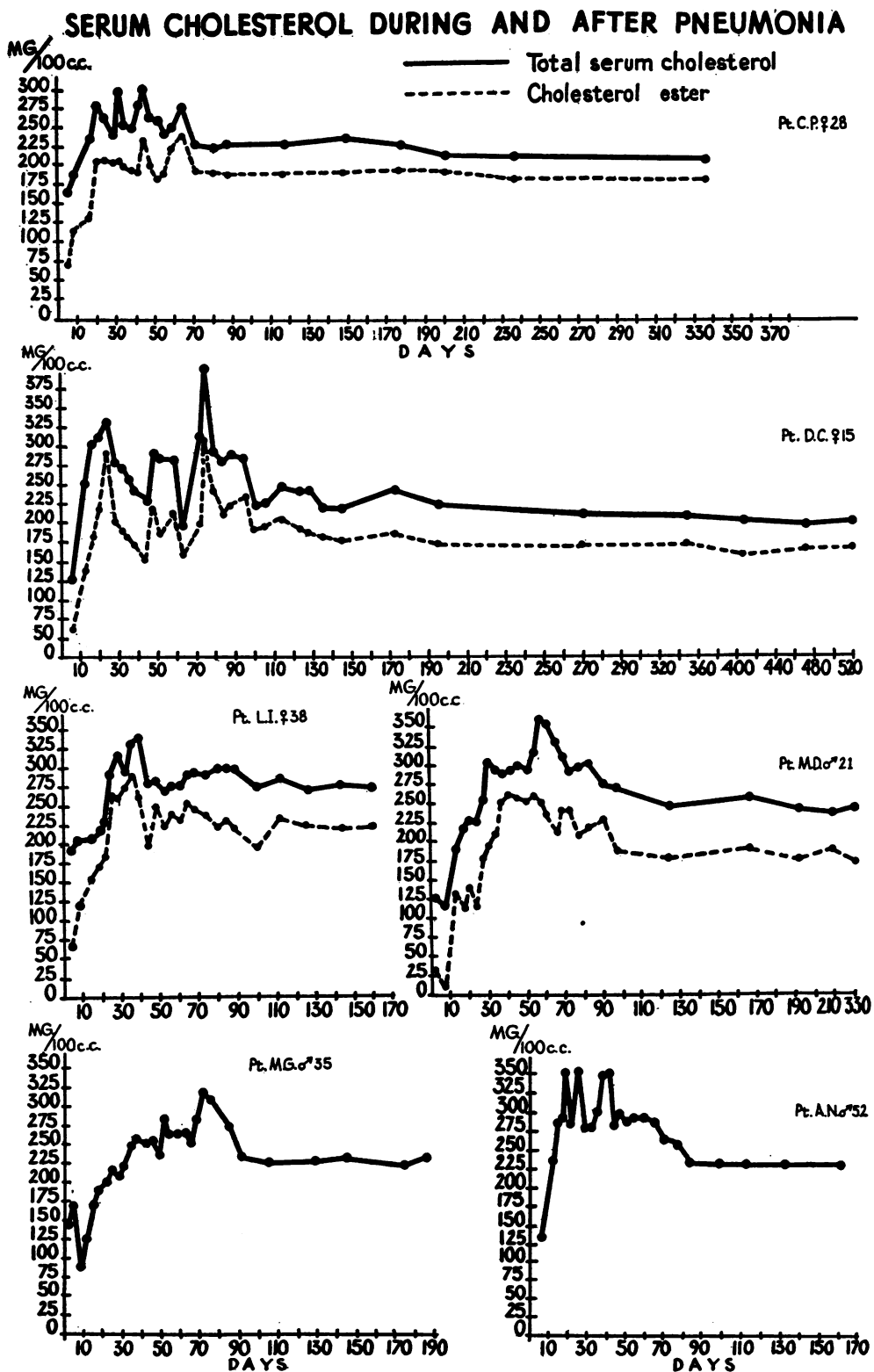


FIG. 1. ILLUSTRATIVE CURVES SHOWING THE DEPRESSION OF THE SERUM CHOLESTEROL DURING PNEUMONIA, THE RISE TO ABNORMALLY HIGH LEVELS ASSOCIATED WITH MARKED FLUCTUATIONS DURING CONVALESCENCE, AND THE STABILITY CHARACTERISTIC OF NORMAL WELL-BEING

TABLE II

Relation of basal metabolic rate and serum cholesterol

Patient	Basal metabolic rate	
	With highest cholesterol	With normal cholesterol
	<i>per cent</i>	<i>per cent</i>
C. P.	-16	- 8
C. R.	0	- 5
D. C.	+16	+ 8
L. I.	+ 3	+ 1
M. D. a.	-16	-10
M. H.	-26	-14

larity of the effect of thyroid administration and of acute infection on the serum cholesterol level and because hypothyroidism may be associated with an elevated serum cholesterol, determinations of the basal metabolic rate were made at frequent intervals after the fever subsided. No constant correlation between the basal metabolic rate and cholesterol level could be demonstrated (Table II). It is of interest, however, that following the lowering effect of thyroid extract administration on the serum cholesterol in humans (1) and in rabbits (7) the serum cholesterol overshot previous values and remained abnormally elevated for several weeks.

The marked fall in the cholesterol ester fraction during the febrile period suggested the possibility of an alteration in hepatic function and it was also considered that the hypercholesterolemia during convalescence might be another expression of the same cause. With this in mind, determinations of the serum protein were made in 10 cases, of which 7 also had bromsulphalein dye retention studies. In 3 instances the observations were made during the febrile period and in the remaining 7 at variable times during convalescence (Table III). Only 2 of the 10 patients showed any evidence of depression of liver function.

Therefore, it must be concluded that the mechanism producing these changes in the serum cholesterol level is unknown; nor is the significance of this response of serum cholesterol to infection at all clear. Numerous observers have attached importance to an elevation in serum cholesterol because of its possible rôle in the development of atherosclerosis. The hypercholesterolemia of improperly regulated diabetes mellitus, of myxedema, and of chronic glomerulonephritis has been felt

to be a responsible factor for the frequent premature and widespread atherosclerosis associated with these conditions.

It is a common observation that cholesterol deposits (atheromata) in arteries frequently show marked variation and gradation in extent and age. The process of deposition appears to be discontinuous. It is possible that such deposits of cholesterol are related to corresponding periods of hypercholesterolemia. Infection can now be added to the list of conditions resulting in or associated with hypercholesterolemia.

TABLE III

Observations on liver function during and after fever

Patient	Interval fever free	Serum		Brom-sulphalein retention
		Albumin	Globulin	
	<i>days</i>	<i>grams</i>	<i>grams</i>	<i>per cent</i>
G. S.	(during fever)	3.4	2.6	0
L. B.	(during fever)	4.3	2.7	0
M. B.	(during fever)	4.3	2.7	
M. D. b. .	3	4.0	2.7	
J. A.	6	4.5	2.5	
J. M.	6	4.1	3.7	0
A. N.	8	2.9	2.6	0
	18	3.1	3.4	
	33	3.7	3.1	
M. G.	10	3.9	3.0	0
L. I.	11	3.8	3.8	60
	19	3.7	3.9	10
	26	3.9	3.8	0
J. S.	21	3.8	2.3	0

SUMMARY

1. The serum cholesterol of 19 patients with pneumonia was followed at frequent intervals for 96 to 520 days after the onset of the disease.
2. Hypocholesterolemia occurred during the febrile stage of the illness and was largely due to a decrease in the ester fraction.
3. Hypercholesterolemia frequently associated with wide fluctuations occurred during convalescence from pneumonia for periods varying from 20 to 110 days, with an average of 52 days.
4. During convalescence the increase in serum cholesterol above that which was subsequently found to be normal for each patient varied from 26 to 250 mgm., averaging 82 mgm. The percentage of rise above normal averaged 38 per cent for the group of 19 patients.
5. Implication of the thyroid or liver as a factor

in the alteration of serum cholesterol level subsequent to infection was not demonstrated.

6. Additional evidence confirming the constancy of serum cholesterol in normal individuals was presented.

BIBLIOGRAPHY

1. Turner, K. B., and Steiner, A., A long term study of the variation of serum cholesterol in man. *J. Clin. Invest.*, 1939, **18**, 45.
2. Denis, W., Cholesterol in human blood under pathological conditions. *J. Biol. Chem.*, 1917, **29**, 93.
3. Kipp, H. A., Variation in the cholesterol content of the serum in pneumonia. *J. Biol. Chem.*, 1920, **44**, 215.
4. Stoesser, A. V., and McQuarrie, I., Influence of acute infection and artificial fever on the plasma lipids. *Am. J. Dis. Child.*, 1935, **49**, 658.
5. Stoesser, A. V., Altered lipid metabolism in acute infections of infants and older children. *Am. J. Dis. Child.*, 1938, **56**, 1215.
6. Bloor, W. R., Pelkan, K. F., and Allen, D. M., Determination of fatty acids (and cholesterol) in small amounts of blood plasma. *J. Biol. Chem.*, 1922, **52**, 191.
7. Turner, K. B., Present, C. H., and Bidwell, E. H., The rôle of the thyroid in the regulation of the blood cholesterol of rabbits. *J. Exper. Med.*, 1938, **67**, 111.