Lipid and lipoprotein concentrations in 1604 men and women in working populations in north-west London

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Summary

Serum lipid and lipoprotein concentrations in men and women vary with age, and so-called "normal" limits should take account of this. Serum cholesterol, triglyceride, and phospholipid concentrations were measured in 1027 men and 577 women in five working populations in north-west London, and lipoprotein electrophoresis and quantitative analyses of lipoprotein concentrations were also performed. In men the best fit between serum cholesterol, triglycerides, and phospholipids, on the one hand, and age, on the other, was given by a curvilinear relationship expressed as a quadratic regression. In women the best fit was given by a linear regression. White men had higher serum cholesterol and triglyceride concentrations than Black men, and these differences were reflected in the distributions of the lipoproteins. There were no differences between values in White and Black women. Young women on oral contraceptives had lipid concentrations similar to those of older women not on these preparations. These data suggest that the adoption of concentrations of serum cholesterol (275-300 mg/100 ml (7·1-7·8 mmol/l)) and triglycerides (175-200 mg/100 ml (2·0-2·3 mmol/l)) recommended by a recent report on the prevention of coronary disease as limits above which special attention should be given to the management of hyperlipidaemia could result in as few as 2% of younger men or as many as 31% of older men being selected for treatment.

Introduction

The interpretation of the serum lipid concentrations in individuals should be based on a sound knowledge of the concentrations within the population from which the subjects are drawn. Differences between the sexes, changes with age, social customs, and the racial structure of the population may have important effects; a normal range established in the United States,[1 2] in small control samples from the population,[3] or in a screened population[4] is unsatisfactory for general use in Britain.

A recent report, *Prevention of Coronary Heart Disease*,[5] recommends treatment for adults with raised lipid levels, particularly men aged 30 to 50 years with serum cholesterol concentrations of 275 to 300 mg/100 ml (7·1 to 7·8 mmol/l) or above and fasting triglyceride values of 175 to 200 mg/100 ml (2·0 to 2·3 mmol/l) or above. The size and practical implications of such an exercise in this country can be established only by a detailed knowledge of the lipid levels in the population at large. There is also an increasing need for population-based data on lipoproteins.

As part of a prospective study of coronary heart disease, primarily concerned with measures of haemostatic function,[6] fasting serum lipid concentrations were measured. We describe here the fasting lipid concentrations and lipoprotein distributions and concentrations in participants at entry to the study. Serum lipid concentrations were compared between Blacks and Whites and between women using and not using oral contraceptives. The distribution of lipoproteins by electrophoresis was also examined, and the concentration of lipoproteins throughout the S_f 0-400 range was measured in a randomly selected group of 338 people out of the total of 1604.

Methods

The study population was drawn in random order from nominal rolls of the employees of five industrial concerns in north-west London. About 80% of those invited to participate did so. Some two-thirds returned on a second day in a fasting state, apart from 50 g glucose taken orally one and a half to two hours before venous blood sampling; it is on these participants that this report is based. At recruitment the 1027 men were aged 18 to 64, and the 577 women 18 to 59. Of the men 996 were White and 31 Black. The women included 459 Whites and 45 Blacks not on oral contraceptives and 73 Whites on oral contraceptives. (Results on Asian participants and the few Black women on oral contraceptives were omitted because the numbers were too small.)

Serum cholesterol was measured by the Sperry-Webb[7] method, serum triglycerides by the method of Van Handel and Zilvermidt,[8] and serum phospholipid by the method of Allen.[9] Electrophoresis of lipoproteins was carried out on agarose gel using a Biorad electrophoretic kit adapted to the method of Noble,[10] and the results were analysed by densitometry. Quantitative analyses of lipoprotein concentration were carried out by the method of De Lalla and Goffman.[11] (Serum cholesterol and triglyceride concentrations were also measured by different methods from those described here on non-fasting samples from all participants, and triglyceride estimations were repeated on the fasting samples of those who returned on the second day. These non-fasting lipid estimations, augmented by fasting triglyceride estimations in most cases, provided the lipid data for the study population as a whole.[6] Thus, there were two independent sets of lipid analyses available for about two-thirds of the total population; they gave similar results.)

To indicate how lipid and lipoprotein concentrations varied with age lines of best fit were calculated for men and women separately. A linear relation was assumed unless the data showed a departure from linearity significant at the 5% level, in which case a quadratic curve was fitted. The ability to detect curvature depends on the sample size, and this may partly explain why a curvilinear regression was usually found necessary for the men but not for the women. Since the distributions of serum cholesterol and triglycerides were positively skewed, logarithmic transformations were used in deriving the regressions, although actual concentrations are shown in tables and figures. Logarithmic transformation of phospholipid values was also indicated by a probability plot as marginally preferable to the use of untransformed values, although the distribution of phospholipids is not as strongly skewed as those of cholesterol and triglycerides.

Results

The distributions of cholesterol, triglycerides, and phospholipids in White men and White women not on oral contraceptives are shown

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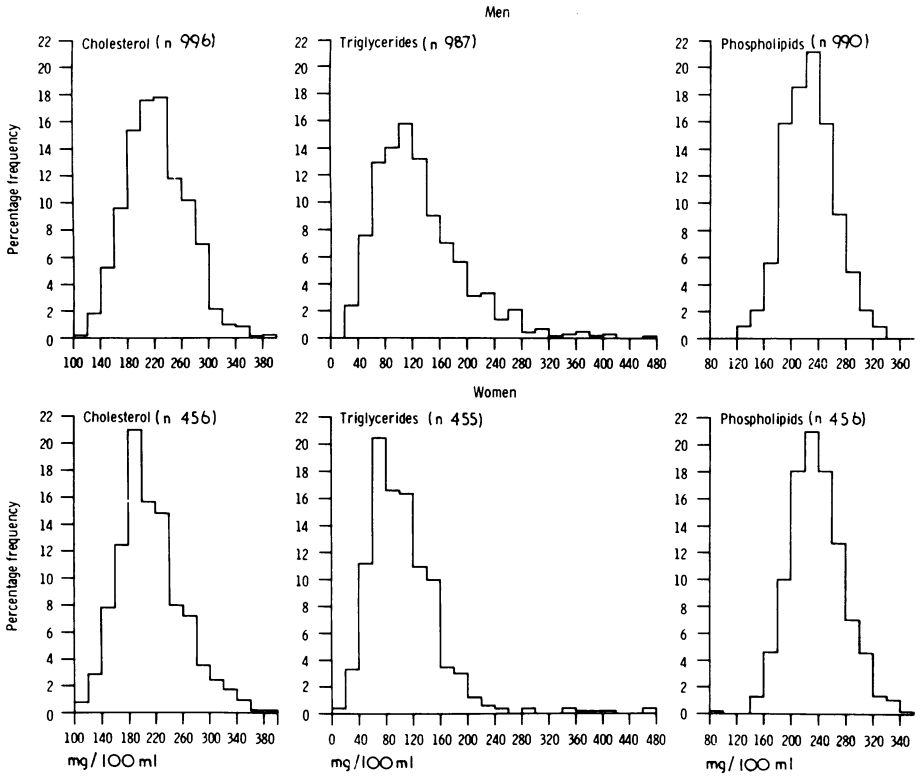

FIG 1—Distributions of serum cholesterol, triglycerides, and phospholipids in White men and in White women not on oral contraceptives.

Conversion: traditional to SI units: Cholesterol: 1 mg/100 ml ≈ 0·026 mmol/l. Triglycerides: 1 mg/100 ml ≈ 0·0113 mmol/l. [Owing to difficulties in conversion the values in all the figures and tables have been retained in traditional units.]

TABLE I—*Mean fasting serum cholesterol, triglyceride, and phospholipid levels (±1 SD) in White men and in White women not on oral contraceptives*

Age	Cholesterol (mg/100 ml)				Triglycerides (mg/100 ml)				Phospholipids (mg/100 ml)			
	Men		Women		Men		Women		Men		Women	
	No	Mean ± 1 SD	No	Mean ± 1 SD	No	Mean ± 1 SD	No	Mean ± 1 SD	No	Mean ± 1 SD	No	Mean ± 1 SD
18–29	213	191·7 ± 39·2	50	184·8 ± 28·7	211	96·2 ± 47·8	50	66·6 ± 29·3	213	203·4 ± 36·4	50	203·9 ± 34·6
30–39	182	213·6 ± 42·9	54	199·7 ± 35·9	182	110·5 ± 56·9	54	78·3 ± 39·4	181	218·8 ± 37·7	54	208·3 ± 34·9
40–49	267	232·5 ± 43·4	142	227·0 ± 38·5	264	133·7 ± 71·2	142	95·0 ± 42·5	264	233·2 ± 37·0	142	233·3 ± 32·6
50–59	237	230·7 ± 42·7	203	247·2 ± 43·8	235	115·9 ± 53·0	202	109·4 ± 49·8	235	234·2 ± 36·0	203	250·5 ± 38·7
60–64	97	236·0 ± 46·5			95	124·4 ± 67·5			97	233·0 ± 37·3		

Conversion: traditional to SI units—Cholesterol: 1 mg/100 ml ≈ 0·026 mmol/l. Triglycerides: 1 mg/100 ml ≈ 0·0113 mmol/l. [Owing to difficulties in conversion the values in all the figures and tables have been retained in traditional units.]

TABLE II—*Proportion of β-, pre-β-, and α-lipoproteins, expressed as percentages (±1 SD), in White men and in White women not on oral contraceptives*

Age (years)	β-lipoprotein (%)				Pre-β-lipoprotein (%)				α-lipoprotein (%)			
	Men		Women		Men		Women		Men		Women	
	No	Mean ± 1 SD	No	Mean ± 1 SD	No	Mean ± 1 SD	No	Mean ± 1 SD	No	Mean ± 1 SD	No	Mean ± 1 SD
18–29	195	49·0 ± 6·8	48	49·0 ± 5·1	195	20·3 ± 7·3	48	13·1 ± 5·6	195	30·5 ± 7·6	48	37·8 ± 6·2
30–39	173	50·8 ± 7·2	50	49·7 ± 6·5	173	20·6 ± 7·8	50	15·2 ± 5·5	173	28·4 ± 7·2	50	35·0 ± 6·6
40–49	249	50·0 ± 7·4	135	50·2 ± 6·1	249	23·0 ± 9·2	135	16·4 ± 6·6	249	26·8 ± 6·6	135	33·3 ± 7·6
50–59	227	51·5 ± 6·6	191	50·7 ± 7·5	227	19·9 ± 7·8	191	17·7 ± 7·6	227	28·5 ± 7·1	191	31·4 ± 7·2
60–64	93	52·6 ± 6·8			92	21·3 ± 9·0			93	26·4 ± 6·4		

in fig 1, and lipid levels by 10-year age groups are shown in table I. In men a curvilinear relationship, expressed as a quadratic regression, gave the best fit between serum cholesterol, triglycerides, and phospholipids, on the one hand, and age, on the other. In women the best fit was given by a linear regression. The fitted regressions, regression equations, and residual standard deviations (in parentheses) for serum cholesterol, triglycerides, and phospholipids in White men and White women not on oral contraceptives are shown in fig 2.

More detailed information about the distribution of lipoproteins in fasting serum was obtained by electrophoresis and quantitative analytical ultracentrifugation. Table II shows the distribution by age and sex of the proportions of β-, pre-β-, and α-lipoproteins in White men and White women not on oral contraceptives, and table III shows similar data for the concentrations of serum lipoproteins obtained by analytical ultracentrifugation. As before, the fitted regressions, regression equations, and residual standard deviations are shown in fig 2; lipoprotein in the flotation range S_f 100-400 showed no significant change with age in either men or women.

Table IV compares fasting serum concentrations and proportions of lipoproteins by electrophoresis in Blacks and Whites. All results were adjusted to age 40. Among men cholesterol and triglyceride levels and the proportion of pre-β-lipoproteins were significantly higher in Whites than in Blacks; the proportion of α-lipoprotein was higher in Blacks than in Whites. These differences were not found in the comparison of White and Black women. By contrast with Whites, lipid concentrations and proportions of different lipoproteins did not seem to vary with age in Blacks.

Mean lipid concentrations and proportions of lipoproteins in premenopausal women according to oral contraceptive use are shown in table V. Cholesterol levels (and possibly also those of triglycerides)

do not increase with age in women on oral contraceptives[12]; comparisons by oral contraceptive use were therefore influenced conconsiderably by the age at which these comparisons were made. Results in table V are adjusted to age 30, which was the mean age of the women on oral contraceptives. Triglyceride and phospholipid levels were higher in those on oral contraceptives than in those not on oral contraceptives, and the proportion of α-lipoproteins was lower.

Discussion

Serum concentrations of cholesterol, triglycerides, and phospholipids varied with age in both White men and White women not using oral contraceptives, in five working groups in northwest London. Each of these distributions was more or less skewed to the right, and for statistical purposes requiring a normal distribution there was some advantage in using a logarithmic transformation. This was particularly true of serum triglyceride concentrations in both sexes. The fitted regression lines summarise our cross-sectional data. We should emphasise that the regression equations give only approximate mean values at different ages after smoothing and that there was a large scatter about these means, as indicated by the residual standard deviations in fig 2.

In simple terms, in this population, serum cholesterol, triglyceride, and phospholipid concentrations increased in men until middle age and then levelled off. In women serum cholesterol, triglyceride, and phospholipid concentrations increased with age until 60 years of age, when the mean serum concentrations of cholesterol and phospholipids exceeded those of men of the same age. So far, however, we have no prospective data to confirm the apparent decline in serum lipid concentrations in men after middle age; longitudinal observations are needed to examine age-related changes in individuals.

It is important to recognise differences with age and sex, of the sort we have described, when arbitrary limits for lipid concentrations are used in, for example, giving advice about modifying lipid levels. Our data suggest that any serum cholesterol value suggested as an upper limit will have very different implications for the proportions of men and women exceeding the limit at different ages, and for individuals seeking advice about hyperlipidaemia.

The recent Royal College of Physicians-British Cardiac Society (RCP-BCS) report *Prevention of Coronary Heart Disease*[5] recommended that men aged 30 to 50 with cholesterol levels of 275 to 300 mg/100 ml (7·1 to 7·8 mmol/l) or more and triglyceride concentrations of 175 to 200 mg/100 ml (2·0 to 2·3 mmol/l) or more should be considered for treatment of hyperlipidaemia, these being the levels above which there is likely to be a substantially increased risk of coronary disease. The shaded bands in fig 3 indicate the raised serum cholesterol and triglyceride levels suggested by the RCP-BCS report in relation to the regressions with age from our data. At 30 years of age the recommended upper limit for cholesterol is more than two standard deviations above the mean, and so less than 2% of the male population would be eligible for treatment. At 50 years of age the recommended lower limit is less than one standard deviation above the mean, so as many as 21% of the male population at this age would be eligible. When serum triglyceride concentrations are considered 8% of the male population at age 30 and 31% at age 50 might be recommended for the specially strict treatment advised by the report. (Some people would, of

TABLE III—*Mean concentrations of lipoproteins (±1 SD) according to flotation rates in White men and in White women not on oral contraceptives*

Age	Men		Women	
	No	Mean ± 1 SD	No	Mean ± 1 SD
		Sf 0–12		
18–29	42	268·2 ± 73·8	12	250·8 ± 62·5
30–39	41	286·3 ± 82·9	9	300·1 ± 100·1
40–49	66	313·4 ± 79·0	23	292·5 ± 76·0
50–59	61	316·1 ± 95·2	48	336·8 ± 94·1
60–64	36	359·2 ± 100·8		
		Sf 12–20		
18–29	42	36·0 ± 23·1	12	37·1 ± 24·2
30–39	41	45·9 ± 19·0	9	35·4 ± 23·1
40–49	66	49·1 ± 23·6	23	55·1 ± 22·1
50–59	61	53·5 ± 29·0	48	63·1 ± 27·7
60–69	36	64·5 ± 35·2		
		Sf 20–100		
18–29	42	55·1 ± 44·2	12	36·2 ± 24·7
30–39	41	68·3 ± 42·4	9	51·1 ± 41·0
40–49	66	85·8 ± 66·5	23	60·1 ± 49·7
50–59	61	73·1 ± 47·5	48	72·6 ± 46·3
60–64	36	88·3 ± 48·2		
		Sf 100–400		
18–29	42	20·0 ± 36·7	12	7·4 ± 9·7
30–39	41	21·3 ± 35·6	9	10·6 ± 21·3
40–49	66	31·6 ± 46·3	23	13·7 ± 30·3
50–59	61	19·9 ± 21·7	48	14·7 ± 18·5
60–69	36	32·7 ± 43·4		

TABLE IV—*Mean fasting serum lipid concentrations and proportions of lipoproteins (by electrophoresis) in White and Black men and in White and Black women not on oral contraceptives*

	No of subjects	Cholesterol (mg/100 ml)	Triglycerides (mg/100 ml)	Phospholipids (mg/100 ml)	Lipoproteins (%)		
					β	Pre-β	α
			Men				
White	996	215·3	113·0	221·3	50·3	21·0	28·5
Black	31	196·8	72·8	215·8	50·1	14·7	34·7
P value		<0·01	<0·001	NS	NS	<0·001	<0·001
			Women				
White	459	214·3	87·1	223·8	49·8	15·7	34·3
Black	45	206·5	88·5	223·4	50·8	14·6	34·4
P value		NS	NS	NS	NS	NS	NS

NS = Not significant.

TABLE V—*Mean fasting serum lipid concentrations and proportions of lipoproteins (by electrophoresis) in premenopausal White women according to oral contraceptive use. Values are adjusted to age 30*

	No of women	Cholesterol (mg/100 ml)	Triglycerides (mg/100 ml)	Phospholipids (mg/100 ml)	Lipoproteins (%)		
					β	Pre-β	α
On oral contraceptives	73	203·7	92·0	224·4	50·7	15·3	33·8
Not on oral contraceptives	214	196·8	75·9	209·4	49·6	14·1	36·2
P value		NS	<0·01	<0·001	NS	NS	<0·02

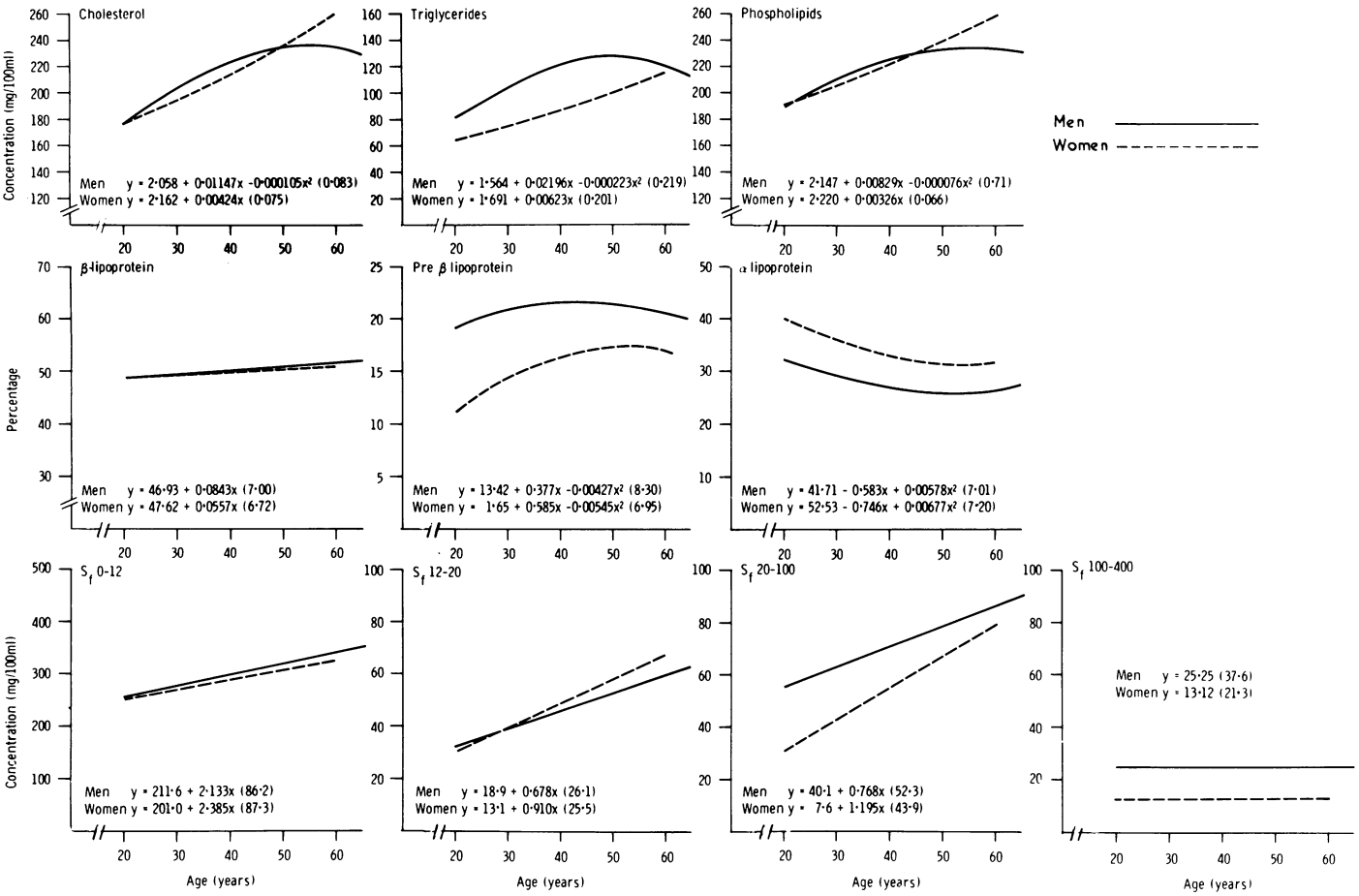

FIG 2—Fitted regressions with age and regression equations for lipid concentrations and lipoprotein proportions (by electrophoresis and ultracentrifugation) in White men and in White women not on oral contraceptives. y = Age-specific mean (log values for cholesterol, triglycerides, and phospholipids). x = Age. Residual standard deviations are shown in parentheses.

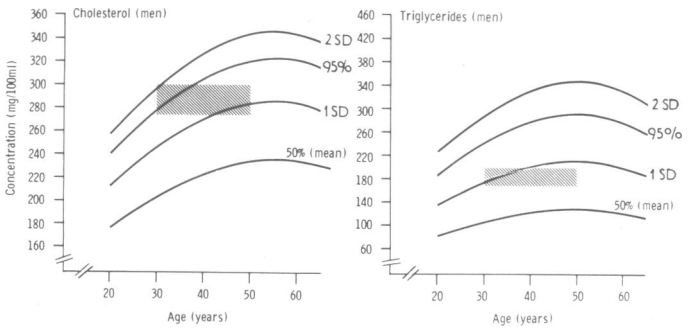

FIG 3—Age-specific values for serum cholesterol and triglycerides in White men at mean, at 1 SD above mean, at 95th percentile, and at 2 SD above mean. Shaded areas indicate definitions of hyperlipidaemia in *Prevention of Coronary Heart Disease*.[5]

course, be covered by the criteria for both cholesterol and triglycerides.) The feasibility of the community health programme implied by the report's criteria must be open to some doubt. Rather than be guided by uniform guidelines for all ages, it would be more appropriate to suggest age- and sex-specific criteria to select suitable candidates for treatment. Relatively stricter—that is, lower—limits could be set for younger men, in whom long-term measures aimed at preventing coronary heart disease might be more effective than in older men.

If raised lipid concentrations are considered as a risk factor for coronary heart disease the differences between White and Black men accord with the differences in their incidence of the disease in Britain.[13] Lipid levels are higher in White men than in Black men, and these levels rise with age in the Whites but not in the Blacks. Among men it is also of interest that a higher proportion of lipoprotein is carried as α-lipoprotein in Blacks than in Whites.

Recent reports have shown increased risks of coronary heart disease in women taking oral contraceptives.[14,15] It is not clear how these risks are mediated, though there is a positive association between plasma factor VII, on the one hand, and serum cholesterol and triglyceride concentrations, on the other, in women on oral contraceptives that is not found in women not using these preparations.[16] These and other findings[12] suggest that younger women on oral contraceptives may be adding to their later risk of coronary heart disease by virtue of having been exposed for several years to the high lipid concentrations characteristic of older women.

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Typhoid catatonia responsive to ECT

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Summary

Twelve patients with typhoid fever presented with a catatonic syndrome that persisted after other signs of the fever had disappeared. The syndrome was distinct from the delirium seen in typhoid fever and did not have the characteristics of an affective or schizophrenic illness. Electric convulsion therapy produced rapid and lasting improvement.

Introduction

Catatonia is often seen in schizophrenia, but it may also occur in the course of other diseases.[1-5] The many publications on typhoid fever, make only scant reference to its psychiatric manifestations. Thus Pathania and Sachar[6] described 340 cases of enteric fever in Punjab. They mentioned delirium in the acute stages of the disease but gave no details of any other psychiatric complications. Gadeholt and Madsen[7] described 2647 cases that occurred in Bergen over five decades, in which there was a 1% incidence of "psychosis," including paranoia, melancholia, hysteria, and delirium. Stuart and Pullen[8] in New Orleans during 1939-44 reported that stupor occurred in the acute phase of typhoid in 72·8% of cases and that a "psychosis" persisted in 1·9% after all other evidence of the disease had passed. Osuntokun *et al*[9] described the neurological complications of 959 Nigerian patients. Five had initially been diagnosed as schizophrenic and the diagnosis of typhoid was made later, either during their hospital stay or at necropsy, but there was no description of a catatonic syndrome persisting after the fever had subsided.

We cannot find any detailed description of persisting catatonia other than a single case described briefly by Bleuler.[10] The patient, a physician, had "neurasthenia" at 29. At 31, after typhoid fever, he became catatonic. At 47 he was apparently "cured" and resumed his practice. He was well for the next two years.

In our experience a persisting catatonic syndrome is a fairly common complication of typhoid fever, and we report 12 cases seen in India.

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Present series

During 1974-6, 238 patients were admitted to the Christian Medical College Hospital with typhoid fever. Of these, 45 showed gross behavioural disturbances, which in 32 cases necessitated psychiatric examination. Though most of these patients had typical delirium, 12 presented with a catatonic syndrome that persisted after the fever had resolved and their physical condition had returned to normal. These 12 patients are the subject of this report.

Of the 12 patients, 11 were aged 17-24 years, and one was a 7-year-old (table). The slight preponderance of men was typical of admissions to the hospital, and they came from various socioeconomic backgrounds. All the patients were brought to the hospital because of high fever and behavioural change, in many cases insomnia and restlessness or excitement, and in others withdrawal, muteness, strange movements of limbs, or posturing. The duration of fever before admission varied up to 12 days. In most cases there were few definite physical findings apart from the fever. Two patients had moderate splenomegaly. In some cases pathogens were grown in blood culture, and in every case the Widal test gave a positive result. One patient underwent electroencephalography (EEG), which showed excessive diffuse slow-wave activity.

In most cases psychiatric examination showed a typical catatonic picture of withdrawal and mutism, which in several progressed to stupor, the patients being apparently awake and aware of their surroundings but unable to respond to spoken or written communication. Some patients were excited rather than withdrawn and reacted irritably or aggressively. In two cases excitement alternated with mutism and withdrawal, and many patients exhibited catatonic posturing and waxy flexibility. Volitional symptoms such as negativism and automatic obedience, were apparent in some patients but ambivalence and ambitendency were not seen. Clinical features of delirium were not observed; so far as could be ascertained the patients were orientated and aware of their surroundings and did not experience the frightening delusions and hallucinations that occur in delirium. They also denied alteration of mood.

In the first two or three cases phenothiazine alone had little or no effect. Electric convulsion therapy (ECT), however, produced a rapid response in every case in which it was used. In some cases three or four sessions were enough to obtain a remission, and no patient received more than seven. All patients improved, and most were completely recovered after two or three weeks.

Seven patients were followed up 6-24 months after discharge. All had maintained their improvement and were functioning normally. There had been no recurrence of symptoms and there was no evidence of a persisting psychiatric disorder. The following two cases are described in detail.

CASE 1

This 20-year-old man was admitted to hospital with a history of moderately high, continuous fever for two weeks and withdrawal and abnormal behaviour