EFFECTS OF DIETARY COMPONENTS ON PLASMA CHOLESTEROL METABOLISM IN MAN

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ABSTRACT

Changes in diet have profound effects on plasma lipoprotein concentrations in man. Three examples are discussed including possible mechanisms of action.
Replacement of saturated by polyunsaturated fatty acids is the most potent single dietary intervention to lower total and LDL cholesterol concentrations. HDL cholesterol concentrations are less affected. The effect may be mediated by reduction of VLDL synthesis.
Dietary cholesterol has a small but definite effect on total, LDL and HDL cholesterol levels. Absorbed cholesterol probably adds to liver pools. Plasma concentrations may then go up either because lipoprotein cholesterol output is increased or because uptake of cholesterol with LDL via the LDL-receptor is depressed.
Pectin is a gel-forming dietary "fibre". Both isolated pectin and pectin-rich vegetables and fruits lower plasma cholesterol. As pectin is non-absorbable the effect must take place within the gut, possibly through enhanced excretion of bile acids.
Thus, different cholesterol-lowering food components have different mechanisms of action.

DIET IS A MAIN DETERMINANT OF PLASMA CHOLESTEROL LEVELS

Plasma cholesterol concentrations vary between species, and within Homo sapiens they vary from population to population. Much of this variation is caused not by nature but by nurture. Thus monkeys given "human" diets achieve "human" cholesterol levels (1). In man, feeding a Finnish-type diet to Italians reverses their cholesterol levels to those common in Finland, and vice versa.

POLYUNSATURATED AND SATURATED FATTY ACIDS

Replacement of saturated by polyunsaturated fatty acids is the single most powerful intervention to lower serum cholesterol levels. Table I gives the composition of the diets in a recent fatty acid experiment of ours. The polyunsaturate content of 21% of energy in the high-P/S diet is about the maximum that can be accommodated in a natural mixed solid diet, and it is at least twice the amount recommended nowadays to the general public. The low-P/S diet had 23% of energy as saturated fatty acids, which exceeds the present mean intake of 18 energy% in the Netherlands, but is similar to habitual intakes in Finland in the sixties. Such a level is easily achieved by the liberal use of butter and other products rich in dairy fat. This diet caused an increase of 25% in total cholesterol and of 10% in HDL cholesterol compared with the high P/S diet (Table II). Similar changes have been found by many other investigators.

Cholesterol Metabolism in Health and Disease: Studies in the Netherlands, edited by A. C. Beynen, M. J. H. Geelen, M. B. Katan, and J. A. Schouten. Ponsen & Looijen, Wageningen 1985

Table I. Composition of the diets in the fatty acid experiment.

Nutrient	Unit	High P/S[1] Diet	Low P/S[1] Diet
Protein	% of energy	13	14
Fat	% of energy	45	44
Saturated	% of energy	11	23
Poly-unsaturated	% of energy	21	5
Carbohydrates	% of energy	40	39
Alcohol	% of energy	2	2
Cholesterol[2]	mg/MJ	42	40

[1] P/S, Polyunsaturated/saturated fatty acid ratio.
[2] Mean daily intake was about 500 mg.

Table II. Effect of dietary fatty acid composition on total and HDL cholesterol (N = 23).

Fraction	High P/S diet	Low P/S diet	Change
	(mmol/l)		
Total cholesterol	4.43	5.53	+25%
HDL cholesterol (Mn-heparin soluble)	1.41	1.56	+10%

The excretion of bile acids and of cholesterol and its bacterial metabolites was not affected by the diets (Glatz et al., this Volume). By inference, cholesterol synthesis must have been unchanged also. Thus we must look elsewhere for an explanation of the effect of fatty acids on LDL concentrations. Beynen and Katan (2) have proposed that polyunsaturated fatty acids, instead of being incorporated by the liver into triglycerides and excreted into plasma as VLDL, are converted into ketone bodies. Catabolism of VLDL results in formation of LDL, which would then occur on diets rich in saturated fatty acids but not when polyunsaturates are consumed. This speculative proposal awaits confirmation in man. The alternative explanation, namely enhanced catabolism of LDL via LDL receptors, cannot be excluded. However, the classical LDL receptor theory (3) offers no satisfactory explanation for the effects of fatty acid saturation level on plasma LDL.

DIETARY CHOLESTEROL

Table III exemplifies the effect of dietary cholesterol on plasma cholesterol, again in a controlled trial employing mixed natural solid diets. The mean daily cholesterol intake was 130 mg in the first four weeks. This low level can be attained with normal foodstuffs if cholesterol-rich products are avoided. Addition of about 3 egg yolks per day increased the intake to 990 mg/day in the second four-week period; some protein and fat were left out to compensate for those in egg yolk.

Table III. Effect on serum total and HDL cholesterol concentration of adding egg yolk cholesterol as sole dietary variable in controlled diets (N = 32).

Fraction	Baseline concentration	Change
	mmol/l	%
Total cholesterol	5.14	+13
HDL cholesterol (Mn-heparin soluble)	1.42	+10

The observed rise in plasma cholesterol of 13% is typical of what is seen in properly designed dietary trials of egg yolk and cholesterol. Both LDL and HDL cholesterol concentrations increased. Thus the well established depression of endogenous cholesterol synthesis by exogenous cholesterol in man was not sufficient to keep plasma cholesterol levels constant. Some mechanisms by which increased cholesterol intake may increase plasma levels are depicted in Fig. 1.

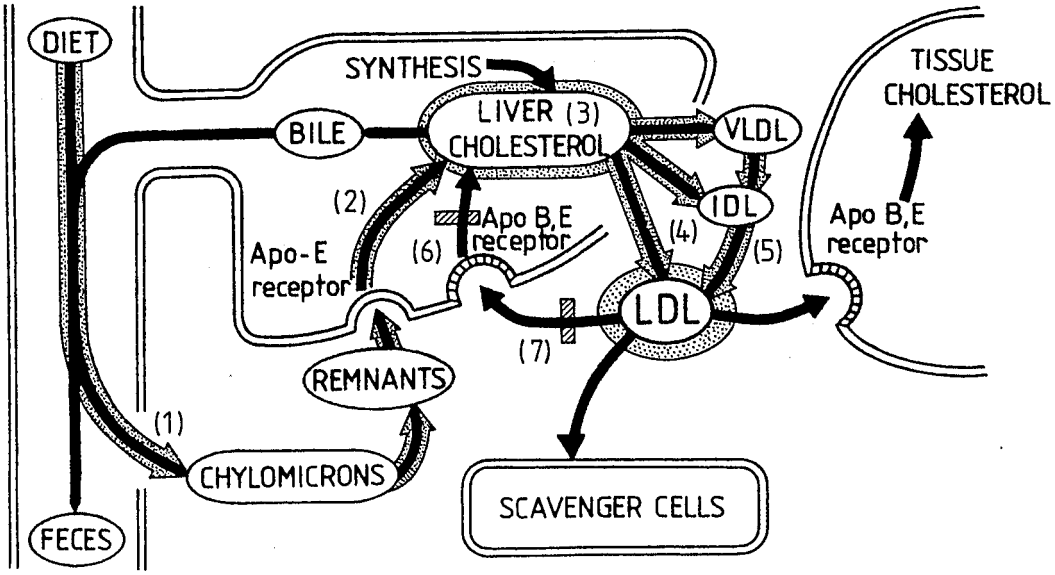

Fig. 1. Hypothetical pathways for the elevation of plasma lipoprotein cholesterol levels by dietary cholesterol.

Dietary cholesterol is incorporated by the mucosa cells of the gut into chylomicrons (step 1 in Fig. 1), and stays with the chylomicrons in the circulation while they are being relieved of their triglyceride load. The resulting chylomicron remnants are taken up by a liver receptor (step 2), and

the cholesterol adds to one or more of the liver cholesterol pools (step 3; cf. Wirtz, K., this Volume). The increase is sensed by the cholesterol synthesizing machinery, so that cholesterol production decreases. It may also lead to suppression of LDL receptors (steps 6 and 7), causing LDL to accumulate in plasma, and to excretion of cholesterol-rich lipoproteins into the plasma (steps 4 and 5). It remains to be established which of these mechanisms predominates in man.

PECTIN

Pectins are minor but essential components of cell walls in plants, to which they provide consistency and water-holding capacity. Pectins are large polymeric structures consisting of a polygalacturonic acid backbone with side chains of neutral sugars, e.g. arabinogalactans. Under suitable conditions, small amounts of pectin (< 1%) can bind large amounts of water, forming gels.

Fig. 2 shows the effect of pectin and other fibre sources on serum cholesterol.

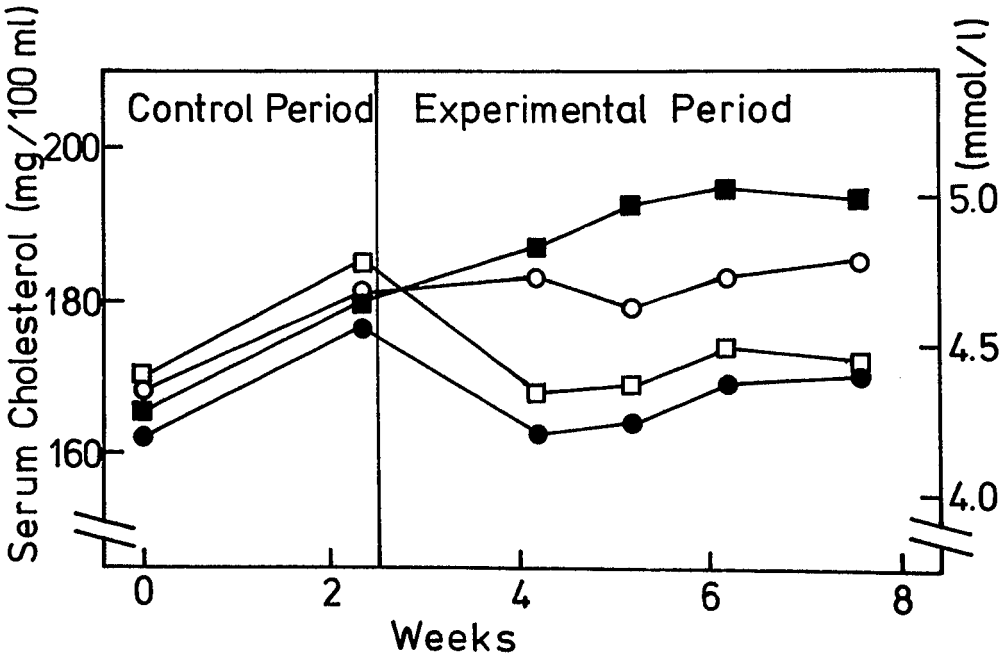

Fig. 2. Effect of various sources of dietary fibre on serum cholesterol. Four groups, each of 15 or 16 student volunteers, received a low-fibre diet containing 37% of energy as fat (4% polyunsaturated) for a control period of 2 1/2 weeks. One group (O———O) continued on this control diet for the ensueing 5-week experimental period; the other groups received added bran (■ - - ■), citrus pectin (□ - - □), or a diet high in vegetables and fruits (●———●).

Both isolated pectin and pectin-rich fruits and vegetables lowered cholesterol. Note that bran actually elevated serum cholesterol levels (4).

As dietary fibre components are by definition unabsorbable, these effects must be caused by things that happen in the gut. Pectin enhances the fecal excretion of bile acids, and thus its mechanism of action may resemble that of cholestyramine. Note, however, that pectin is acidic, which precludes direct ionic binding of bile acids.

VARIA

Like pectin, many other dietary components will cause small changes in plasma cholesterol levels; space forbids their discussion here, and the reader is referred to standard texts (5, 6).

CONCLUSION

Although the mechanism by which diet affects plasma lipoprotein concentrations has only begun to be explored, it is already obvious that different food components act via different pathways. This should result in the effects of different nutrients being additive. It is comforting that this prediction has been verified experimentally (7).

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