

Diet and cholesterol metabolism in the gut

– implications for coronary heart disease and large bowel cancer

By Henrik Andersson

Summary

The effects of the interactions between different dietary factors and the enterohepatic circulation of cholesterol and bile acids in the small bowel, could be studied in ileostomy subjects. Two different mechanisms of high-fibre products could be separated. 1) A specific bile acid-binding effect, resulting in an increased bile acid excretion from the small bowel and a reduction of serum cholesterol, caused by certain viscous components as β -glucanes in oat and citrus pectin. 2) An effect associated to high fibre food and products with increased cholesterol and reduced bile acid excretion from the small bowel. This effect is suggested to be due to plant sterols.

Such bioactive substances and substances to be metabolised by the colonic flora may reduce the risk of colonic cancer. Ileostomy studies have also been used in order to analyse and measure the amount of substances delivered to the colon.

Introduction

The circulation and metabolism of cholesterol are key factors in the development of atherosclerosis. The events which result in the incorporation of cholesterol in arterial vessels are preceded by complex regulations of lipoprotein transport in blood vessels and cellular metabolism in the liver and gut. Moreover, the amount of bile acids entering the colon and the substrate for bacterial degradation of these bile acids into secondary bile acids are associated with the development of colon cancer. In this report the cholesterol metabolism in the gut is discussed primarily based on our ileostomy studies, to elucidate possible mechanisms of action important in the prevention of coronary heart disease and colonic cancer.

Pathways of cholesterol metabolism

Most cholesterol in the body is synthesised from acetate, mainly in the liver, but a considerable part is also absorbed from the diet. Out of the cholesterol present daily within the intestinal lumen 250-350 mg comes from the diet (1) and 800-1200 mg from bile (2). An additional 250-400 mg originates from the intestinal mucosal epithelium (3).

Cholesterol within the intestinal lumen consists of a mixture of free and esterified cholesterol. In the presence of pancreatic cholesterol esterase and bile acids, cholesterol esters are hydrolysed to free cholesterol. Free cholesterol is also solubilized in mixed micelles together with bile acids, monoglycerides and fatty acids. There also exists a liquid crystalline phase separated from the micellar and oil phases in duodenal content (4). The mechanisms by which cholesterol is absorbed and how

bile acid facilitates cholesterol absorption are not fully understood (5).

About 50 percent of the intraluminal cholesterol is absorbed in the small bowel, passing in the chylomicron fraction through the thoracic lymph duct into the circulation. Cholesterol is partly returned to the liver as chylomicron remnants, where cholesterol is excreted to the bile as cholesterol or degraded to bile acids, forming an enterohepatic exogenous metabolic pathway.

In the endogenous metabolic pathway, cholesterol is secreted in VLDL particles by the liver and then transported via different lipoproteins in blood and tissues back to the liver. While the concentration of different fasting lipoprotein fractions (LDL, HDL) have been used as markers of coronary risk, events in the exogenous pathways beside postprandial hyperlipidaemia (6) seem to be mainly overlooked. The exogenous pathways i.e. the metabolism of cholesterol in the gut and liver, have, however, to be explained in order to understand the development of hypercholesterolemia and the interactions between dietary factors and cholesterol metabolism.

The importance of the exogenous cholesterol pathway was early considered and cholesterol balance studies have been performed during the last 40 years, based on the idea that changes in dietary fat intake induce alteration in faecal excretion of bile acids and neutral sterols. The equation for estimation of cholesterol synthesis in a steady state condition is expressed as a sterol balance: $\text{chol}_{\text{balance}} = (\text{chol}_{\text{excretion}} - \text{chol}_{\text{intake}}) + \text{bile acid}_{\text{excretion}}$.

This is still the only quantitative way to measure cholesterol synthesis sterol balances.

Sterol balances

The conventional sterol balance technique has a very low precision (7). Even in a carefully performed sterol balance study of twelve men studied for 5 weeks, only a mean change in cholesterol balance of more than 50% reached statistical significance (8). Such a change in excretion is difficult to obtain with a change in dietary intake and conflicting results have thus appeared in various studies.

While epidemiological and intervention studies have shown a direct relationship between the frequency of coronary heart disease and the serum cholesterol level, the mechanisms whereby a high serum cholesterol level is developed or reduced remain unclear. These mechanisms were, however, expected to be explained through sterol balance studies, and much effort has been made to study the effects of different serum-lipid-lowering diets in this way. The inconclusive results in sterol balance studies have not only left the mechanisms unexplained but also weakened the lipid hypothesis and the possibilities to understand and develop powerful serum-lipid-lowering diet therapies. The focus of interest has thus been changed from events in the gut and the liver to the serum lipid patterns and processes within the arterial wall. The methodological weaknesses of the conventional sterol balance technique have thus served as an obstacle to the understanding of serum-cholesterol-lowering mechanisms.

Many of the methodological problems inherent in conventional sterol balance

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studies could be overcome by using subjects without an intact colon (i.e. ileostomy subjects).

Method

The ileostomy model

Although studies in ileostomy subjects have been performed earlier (9), reliable results of specific analyses of the ileostomy contents could not be obtained until we introduced studies using a controlled diet in the late 70's, where efforts also were made to minimise bacterial degradation by frequent collection of ileostomy contents and immediate freezing: the ileostomy model (10).

The main advantage of the ileostomy model is that the intestinal transit time is so short, that the effluent corresponding to one day's intake is completely excreted before the next morning (11,12). The within-patient, within-diet and day-to-day variations are small, making short-term balance studies feasible. The standard error of the mean for nitrogen and calcium cumulative balances, was similar for a four-day balance period in ileostomy subjects (1.5 and 1.0 mmol/24 h, respectively) compared to that for 52 days of study in subjects with an intact large bowel (1.5 and 1.9 mmol/24 h, respectively) (13). The coefficient of variation between days for dry matter excretion in ileostomy subjects is about 5% (14).

Our first ileostomy studies used three to four days' balance periods on each diet with groups of 6-9 subjects (11,15). The order of the diets was randomised. In later studies, two-day periods were used (16). The diets were prepared in a metabolic ward kitchen and analysed by a double-portion technique. Collection of the ileostomy content was made by changing the bags every one to two hours during the day and once during the night, with immediate deep-freezing upon solid carbon dioxide in a portable Dewar vessel to avoid bacteriological degradation.

Collection of ileostomy contents is relatively easy to perform for ileostomy subjects, as handling of ileostomy excreta is a routine matter for these subjects. In contrast, constant supervision and encouragement are needed to obtain complete faecal collections from normal healthy persons.

Objections against the ileostomy model

The ileostomy model could be criticized because ileostomy subjects have lost the ileo-caecal valve together with a minimal part of the distal ileum. Furthermore, the bacterial flora differs from that of the normal distal ileum. The number of bacteria in the terminal ileum of ileostomy

subjects has been estimated to be 10^7 - 10^8 /g compared to 10^5 - 10^6 /g in the normal ileum (17).

A number of studies, however, support the idea that there is only a small microbial degradation in the ileostomy bags when properly handled. Thus, degradation of bile acids and neutral steroids is minimal (18,19). Furthermore, there is no or minimal degradation of non-starch polysaccharide (NSP) components from pectin, bran or starchy foods (16,20,21). Less than 5 mmol/l of short chain fatty acids are found in ileal samples (22). The pH of the ileostomy content is generally in the range of 7-8. Moreover, in order to determine whether significant fermentation occurs in the terminal ileum, two ileostomy subjects have been studied both with and without the antibiotic Metronidazole (20). No significant difference was observed in the recovery of non-starch polysaccharides (NSP), starch or resistant starch with or without the antibiotic. Consequently, the ileostomy model could be used for determination of small-intestinal digestion of carbohydrates without interference from any substantial bacteriological degradation.

It could also be questioned, whether the transit through the small bowel in the proctocolectomized subject differs from the normal one. However, transit-time through the stomach and small intestine of ileostomy subjects is similar to that observed in healthy subjects (23,24). Moreover, the so-called ileal brake, whereby fat in the terminal ileum may influence gastric emptying rate and the intestinal transit time, also seems to be operative in ileostomy subjects (25).

The function of the distal ileum seems to remain intact in patients where there is only a small resection of the distal ileum, as after proctocolectomy for ulcerative colitis. Ileal excretion from patients operated for Crohn's disease does not reflect the normal excretion to the large bowel. The excretion of bile acids from the ileostomy is seldom increased above 1 g/24 h, and was found to be 410 ± 72 (mean \pm S.E.M.) mg/24 h in a well controlled group of 9 ileostomy subjects studied recently (14) which equals faecal losses. These 9 subjects had a mean serum cholesterol level of 6.0 mmol/l, within the normal range of healthy subjects on a Western diet.

Two studies have also been performed to show that there is no difference between the immediate response on ileal excretion to a diet change and the excretion pattern after some weeks on the same diet (26,27). The immediate response to the diet appears thus to remain in long term studies. Moreover, the reduction in serum cholesterol induced by oat bran in ileostomy subjects was similar to that of normal persons (26).

Results and discussion

Excretion patterns

Ileal excretion of sterols has been measured at our laboratory in groups of 6 to 11 ileostomy subjects (18,19,26-33). The effect of a product on excretion is calculated as the difference between the excretions before and after addition of the product to a basic diet.

There is a correspondence between reported serum cholesterol-lowering (SCL) effects of different NSP products and the sterol excretion (net cholesterol plus bile acids) in the ileostomy. Wheat bran, with no SCL effects (34) does thus not influence ileal sterol excretion (18). Citrus pectin and oat bran, known to have evident SCL effects (34), increase the excretion of ileal bile acids as well as of total sterols (18,26), while the effects of Brewers' spent grain and beet fibre on serum cholesterol levels give discrepant results and sterol balances are not changed (27,29). Moreover, exchange of butter for margarine with high content of polyunsaturated fatty acids (PUFA) (19), as well as for olive oil (28) reduces serum cholesterol and increases small bowel sterol excretion.

Studies in the ileostomy model have thus shown various immediate sterol excretion patterns from the small bowel with different NSP sources added to a low-NSP diet. Different mechanisms are suggested based on these observations.

A cholesterol excreting mechanism

An increased cholesterol excretion and a reduced excretion of the same magnitude of bile acids was seen with beet fibre (Figure 1) (29) and Brewers' spent grain (27). This mechanism also seems to dominate when brown bread, vegetables and fruits are added to the diet of ileostomy subjects (14, Figure 2). Subsequently, increasing the amount of NSP from 13 to 28 g/day, with 50% of the dietary fibre increase derived from whole meal bread and 50% from fruits and vegetables, results in an increased ileal mean excretion of cholesterol (excretion minus intake) of 0.27 mmol/d, and a significant reduction of cholic acid excretion of 0.14 mmol/d, calculated from these figures (14). The reduced uptake of cholesterol (Figure 3) seems to be back-regulated by a reduced excretion of bile acids to the small bowel, the reverse of a mechanism which has been suggested as protective against hypercholesterolaemia (35). Whether this interchange is different in various phenotypes remains to be studied.

The increased cholesterol excretion seen with beet-fibre and Brewers' spent grain corresponds to a postprandial reduction in chylomicron cholesterol concentration

found in normolipidaemic men after addition of fibre products (6). Such a reduced uptake of cholesterol has earlier been found in the thoracic lymph of rats after addition of different dietary fibre products (36).

Studies in rats (37) and dogs (38) have also shown that an increase of dietary cholesterol increases the synthesis of bile acids. Are such mechanisms which protect from cholesterol accumulation also operative in man? It seems so, as *Lin* and *Conner* have shown that prolonged feeding of dietary cholesterol to normal subjects has resulted not only in a decreased cholesterol biosynthesis (feed back inhibition) but also in an increased synthesis of bile acids (39).

The reduced uptake of cholesterol seen with sugar beet and barley fibre in ileostomy subjects may therefore cause a lower bile acid synthesis in the liver and a decreased excretion of bile acids in bile (Figure 3).

A possible mechanism for reduced absorption of cholesterol

Plant sterols (sitosterols) in vegetable fats and NSP-diets are long since known to interfere with cholesterol absorption (40). There seems also to be a relationship between cholesterol excretion and the main plant sterol excretion in our ileostomy studies (Table 1), which could contribute to an explanation of the results.

Epidemiological data strongly supports a negative correlation between NSP intake and the incidence of colon cancer (41). The reduced bile acid excretion from the small bowel induced by such NSP-high diets could therefore be one explanation to a protective effect for colonic cancer since there is a positive correlation in population studies between faecal bile acid excretion and the incidence of colon cancer (42).

Mechanisms related to bile acids

In ileostomy subjects, pectin (18) and oat fibre (26) added to a low fibre diet result in an increased excretion of bile acids and cholesterol. Moreover, a recent study has shown that the bile acid binding capacity is related to the β -glucan in oats (30), while the cholesterol-binding effect is much less. Pancreatic lipase, colipase and bile acids acts synergistically in the hydrolysis of lipids (43) and a considerable increase of lipase activity in ileostomy contents has been found in our pectin studies as well (44). These findings support the hypothesis of whole micelles being entrapped or encapsulated and excreted from the small bowel with citrus pectin and oat fibre (Figure 4). The increased conversion to bile acids results in increased cholesterol synthesis and reduced LDL cholesterol in serum.

Figure 1. Effects of addition of 32 g of sugar-beet fibre to a basic low-fibre diet on sterol excretion in 9 ileostomy subjects (mean values(SE), calculated from (29)).

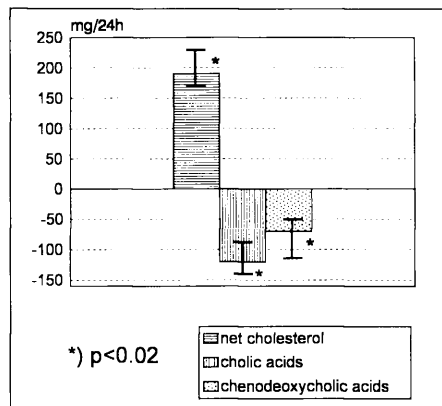
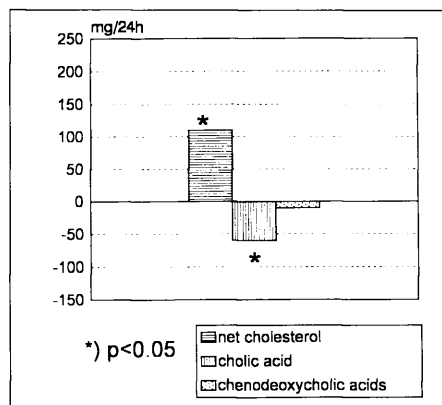


Figure 2. Effects of addition of 15 g of dietary fibre as whole wheat bread, broccoli, bananas, raisins and raspberries to a basic low-fibre diet (13 g) on sterol excretion in 9 ileostomy subjects (mean values), calculated from (14).



Sodium alginate (33) and autoclaved amylo maize (31) induce a reduced excretion of bile acids from the small bowel. These mechanisms remain also to be further elucidated and explained.

Propionate and cholesterol inhibition

Fermentable soluble carbohydrates not absorbed in the small bowel increase the concentration of short chain fatty acids in the colon, portal vein and hepatic blood (45). Studies in cholesterol-fed rats have shown that, out of these, propionate specifically inhibits hepatic cholesterol synthesis, which has been considered to explain the serum cholesterol-lowering effect of fermentable fibres (46).

The production of short chain fatty acids is very low in ileostomy subjects (22). In an ileostomy study (26) the serum cholesterol level decreased significantly after 17 days on oat fibre, while the bile acid excretion remained increased. Consequently, the ileostomy study does not support the hypothesis that inhibition of

Figure 3. Suggested mechanisms of cholesterol – bile acid interchange. Potential importance for cancer prevention.

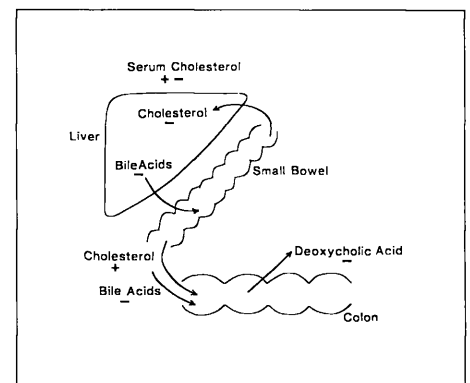


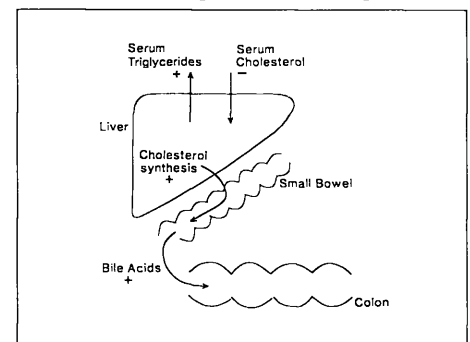
Table 1. Sterol excretion from the small bowel, average values (mg/day).

Diets	PSE ¹	NCE ²	Ref
1. Butter (100 g) Olive oil (100 g)	116 237	84 218	28
2. Basal diet + beet fibre (30 g)	167 196	297 451	29
3. Basal diet + Brewer's spent grain (62 g)	279 412	171 249	27
4. Low-fibre diet (12 g) High-fibre diet (27 g)	218 347	182 291	14

¹ Plant Sterols Excretion

² Net Cholesterol Excretion

Figure 4. Suggested mechanisms of increased bile acid excretion. Of importance for CHD prevention.



cholesterol synthesis by propionate is of considerable importance in man.

Diet and colonic cancer

Colon cancer is one of the most common forms of cancer. Through epidemiological migration studies, the importance of environmental factors on the occurrence of colon cancer in countries with a typical western food pattern (high fat intake and low fibre intake) has been made evident. These observations have resulted in many

Figure 5. Mean daily ileostomy excretion of non-fibre carbohydrates on a period with bean flakes (n=7), calculated from (16).

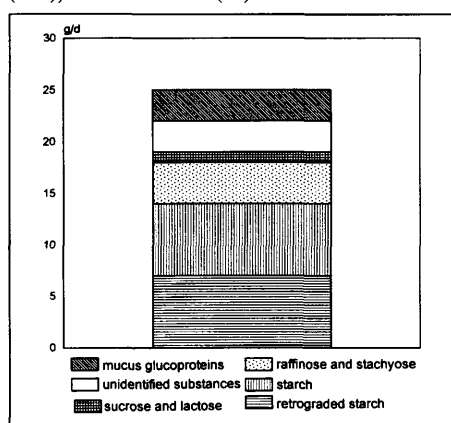


Table 2. Composition of substrates entering the colon (g/24 h). Two-days studies on 9 ileostomy subjects (mean figures, mainly estimated from (14)).

	Low-fibre diet	High-fibre diet
Dietary fibre	14	33
Protein	11	15
Starch	3	4
Other carbohydrates ¹ (oligosaccharides, sugars, etc.)	8	13
Fat	1	3
Ash weight ²	5	7
Sum	42	75
Mean dry weight	47	81

¹ By difference

² Estimated from (11).

epidemiological studies investigating the relationship between diets with different fibre contents and the incidence of colon cancer. A metaanalysis of 37 preventative epidemiological studies supports a preventive effect related to dietary fibre (42). A recently published summary on case-control studies of more than 15,000 cases showed an inverse relationship in 12 of 13 studies between dietary fibre intake and colon cancer but at the same time only a weak inverse relationship between vitamin C or β -carotene and colon cancer (47). A prospective study has also revealed a preventive effect of fruits and vegetables in colorectal cancer (48). Diets with a high content of starch have recently been found to have an even greater protective effect than diets with a high-fibre content (49).

Diets rich in undigestible carbohydrates give large faecal volumes. The factor which has the most obvious negative correlation to colon cancer is the weight of faeces

(50). The risk in a population is high when the weight of faeces is around 100 g/d but reduced by 80% when faecal weight reaches 200 g/d. These data cannot explain whether it is dietary fibre, resistant starch or associated bioactive factors that causes the decreased risk, while a protective effect of antioxidant vitamins seems less probable (51).

It has been suspected for a long period of time that a high content of bile acids, especially secondary ones, would have a cancer promoting effect in the colon (41). This hypothesis is built on comparisons between different populations, animal experiments and observations in cancer patients.

Carbohydrates and protein that reach the colon are metabolised by anaerobic bacteria. The final products are different short-chain fatty acids (acetate, propionate, and butyrate). Butyrate has been shown to have a protective effect against colon cancer. Diets high in resistant starch produce more butyrate as an end product in the colon compared with diets high in NSP. It may be this property of resistant starch that explains the epidemiological association between diets rich in starch and a low frequency of colon cancer (49).

In summary these observations show that dietary factors that increase the bacterial mass in the colon, increase butyrate as an end product of metabolism or decrease the amount of secondary bile acids could be protective against colon cancer. Ileostomy studies are a useful means to study the amount of energy and nutrients as well as bile acids leaving the small bowel.

Amount of substrates for colonic fermentation

When calculating the amount of substrates entering the colon from ileostomy contents, possible limitations with the technique must be taken into consideration. Does the flow of energy and nutrients into the ileostomy bags represent what is normally passing from the small to the large bowel? This question relates to a possible postoperative adaptation of energy and nutrients.

Our earlier experience (52,53) do not, however, favour this, as we have found no reduction in the amount of energy recovered in the ileostomy content from subjects on enteral feeds during the immediate postoperative course (6.4 per cent of the intake) compared to the situation several months later (7.0 per cent of the intake).

Bomb calorimetry is a simple and reliable method to estimate total energy of diets and ileostomy contents. A high-fibre diet of 174 g bean flakes/d was compared to a diet with 102 g potato flakes daily

added to the same basic diet in 7 ileostomy subjects (54,16). The total daily energy content in the ileostomy bags on the high-fibre diet was about 400 kcal/d and about 200 kcal/d on the low-fibre diet. Less than half of the energy was, however, derived from dietary fibre *per se*. The amount of carbohydrates of non-fibre origin was calculated by difference to 25 g/d. Almost all energy giving substances could be characterised by analyses (Figure 5). It is reasonable to assume that these unidentified carbohydrates consist of oligosaccharides and degraded products of carbohydrates. These diets, however, are not typical for a mixed diet in Europe.

In order to study the substances delivered to the colon from ordinary Western diets, the ileostomy content from a previous study with prudent diets have been further characterised.

In this study (14) two of the diets given to nine subjects were either a low-fat (30 E%)/low-NSP (15 g/d) or a low-fat (30 E%)/high-NSP (35 g/d) diet. Almost all dietary fibre was recovered from the diet and amounted only to 33 and 43 per cent of the total energy output. The difference between the total energy of ileostomy contents and the energy value of the known substances could be explained by endogenous losses, oligosaccharides and degraded products. Mucus carbohydrates are estimated from earlier studies (56,57). The total amount of nutrients is close to the mean dry weight of the effluent, including ash weight, which makes the given figures reliable (Table 2).

A calculation of the amount of energy metabolised in the large bowel could be made as an energy balance between the amount of energy in the ileostomy content and calculated figures from faecal losses. These hypothetical faecal losses could be estimated from equations presented by Livesey (58). The difference, which is an estimation of the amount of energy metabolised in the large bowel, amounted to 63 and 175 kcal/d, respectively (Table 3).

Conclusions

Ileostomy studies have shown that

A. Diets high in NSP and resistant starch influence cholesterol metabolism in the gut by different mechanisms:

1. A main mechanism causing an increased excretion of cholesterol suggested to be mediated by plant sterols. As a secondary effect, the excretion of bile acids from the liver is reduced, which is of possible importance for colon cancer prevention.
2. A specific mechanism, attributed to viscous NSP as β -glucan in oat and citrus pectin, by which structures including

bile acids as mixed micelles are encapsulated and excreted. The increased drain from the liver could induce a reduction in serum cholesterol.

3. A third mechanism with a reduced excretion of bile acids seen with alginates and a resistant starch product.

B. The fat content and the fat quality of the diet influences cholesterol metabolism in the liver and gut. In the gut, cholesterol absorption may be reduced by plant sterols related to different lipids.

The amount of substrate from the diet resistant to hydrolysis and absorption in the small bowel could be estimated by ileostomy studies. Our results show that:

1. NSP compose less than half of the energy substrate delivered daily to the colon.
2. Two to four per cent of the starch intake is made up by resistant starch, if for example the diet is not high in beans.
3. 15-40 g of carbohydrate and protein are metabolised and absorbed daily from the colon.

References

5. Wilson, R: Cholesterol absorption review. *J Lip Res* 1994;35:943-54.
6. Cara L, Dubois C, Borel P, Armand M, Senft M, Portugal H, Pauli A-M, Bernard P-M, Lairon D: Effects of oat bran, rice bran, wheat fiber, and wheat germ on postprandial lipemia in healthy adults. *Am J Clin Nutr* 1992;55:81-8.
7. Andersson H, Bosaeus I: Sterol balance studies in man. A critical review. *Eur J Clin Nutr* 1993; 47:153-9.
8. Kay RM, Jacobs M, Katan MB, Miller NE, Lewis B: Relationship between changes in plasma lipoprotein concentration and fecal sterol excretion in man during consumption of four experimental diets. *Atherosclerosis* 1985;55:15-23.
9. Werch SC, Ivy AC: On the fate of ingested pectin. *Am J Clin Nutr* 1940;8:101-5.
10. Andersson H, Sandberg A-S: En försöksmodell för kostfiberstudier. *Livsmiddelsteknik* 1979; 194-5.
11. Sandberg A-S, Andersson H, Hallgren B, Hasselblad K, Isaksson B: Experimental model for *in vivo* determination of dietary fibre and its effect on the absorption of nutrients in the small intestine. *Br J Nutr* 1981;45:283-94.
12. Englyst HN, Cummings JH: Digestion of the carbohydrates of banana (*Musa paradisiaca sapientum*) in the human small intestine. *Am J Clin Nutr* 1986;44:42-50.
13. Tornquist H, Rissanen A, Andersson H: Balance studies in patients with intestinal resection, how long is enough? *Br J Nutr* 1986;56:11-6.
14. Ellegård L, Bosaeus I: Sterol and nutrient excretion in ileostomists on prudent diets. *Eur J Clin Nutr* 1991;45:451-7.
15. Sandberg A-S, Ahderinne R, Andersson H, Hallgren B, Hultén L: The effect of citrus pectin in the absorption of nutrients in the small intestine. *Hum Nutr: Clin Nutr* 1983; 37C:171-83.
16. Schweizer TH, Andersson H, Langkilde AM, Reimann S, Torsdottir I: Nutrients excreted in ileostomy effluents after consumption of mixed diets with beans or potatoes. II. Starch, dietary fibre and sugars. *Eur J Clin Nutr* 1990; 44:567-75.
17. Bosaeus I, Carlsson N-G, Sandberg A-S, Andersson H: Effect of wheat bran and pectin on bile acid and cholesterol excretion in ileo-

Table 3. Mean small bowel excretion of energy and calculated faecal energy excretion from the intake of two diets eaten by nine ileostomy subjects.

	Ileostomy contents kcal/d	Faecal excretion calculated from intake of energy and fibre kcal/d	Difference kcal/d
Low-fat (30 E%), low-fibre (16 g) diet	192	129	63
Low-fat (30 E%), high-fibre (34 g) diet	343	168	175

(ref 14) (Eq 2, ref 58)

4. Considerable amounts of mucus, carbohydrates and protein are metabolised from the large bowel. These substances and their physiological effects remain to be characterized.

Hypotheses and generalisations

The diet modulates lipidaemia by processes in the liver and small bowel. The metabolic pathways are genetically influenced.

Plant sterols and viscous properties of

NSP influence cholesterol absorption and bile acid excretion and may act as protective substances against hypercholesterolaemia.

Bioactive substances such as plant sterols indirectly cause a reduced bile flow to the large bowel. Different carbohydrates resistant to small bowel absorption can be quantified in ileostomy studies and fermented to short chain fatty acids in the colon. These effects may be protective against the development of colon cancer.

19. Bosaeus I, Andersson H: Short-term effect of two cholesterol-lowering diets on sterol excretion in ileostomy patients. *Am J Clin Nutr* 1987;45:54-59.
26. Zhang J-X, Hallmans G, Andersson H, Bosaeus I, Åman P, Tidehag P, Stenling R, Lundén E, Dahlgren S: Effects of oat bran on plasma cholesterol and bile acid excretion in nine subjects with ileostomies. *Am J Clin Nutr* 1992; 56:99-105.
27. Zhang J-X, Lundin E, Andersson H, Bosaeus I, Dahlgren S, Hallmans G, Stenling R, Åman P: Brewers' spent grain, serum lipids and fecal sterol excretion in human subject with ileostomies. *J Nutr* 1991;121:778-84.
28. Bosaeus I, Belfrage L, Lindgren C, Andersson H. Olive oil instead of butter increases net cholesterol excretion from the small bowel. *Eur J Clin Nutr* 1992;46:111-5.
29. Langkilde A-M, Andersson H, Bosaeus I. Sugar-beet fibre increases cholesterol and reduces bile acid excretion from the small bowel. *Br J Nutr* 1993;70:757-66.
30. Lia Å, Hallmans G, Sandberg A-S, Sundberg B, Åman P, Andersson H. Oat (β -glucan) increases bile acid excretion and a fiber-rich barley fraction increases cholesterol excretion in ileostomy subjects. *Am J Clin Nutr* 1995; 62:1245-51.
31. Langkilde AM, Andersson H: Nutrients and sterols excreted in ileostomy effluents after a diet with autoclaved amylo maize or ordinary corn starch. *Eur J Clin Nutr* 1992;46, Suppl 2:S127.
32. Zhang J-X, Lundin E, Hallmans G, Adlercreutz H, Andersson H, Bosaeus I, Åman P, Stenling R, Dahlgren S. Effect of rye bran on excretion of bile acids, cholesterol, nitrogen, and fat in human subjects with ileostomies. *Am J Clin Nutr* 1994;59:389-94.
33. Sandberg A-S, Andersson H, Bosaeus I, Carlsson N-G, Hasselblad K, Härröd M. Alginate, small bowel sterol excretion, and absorption of nutrients in ileostomy subjects. *Am J Clin Nutr* 1994;60:751-6.
35. Grundy SM: Absorption and metabolism of dietary cholesterol. *Ann Rev Nutr* 1983;3:71-96.
39. Lin DS, Connor WE: The long term effects of

40. Mattson FM, Volpenkeim FA, Erickson BA: Effect of plant sterol esters on the absorption of dietary cholesterol. *J Nutr* 1977;109:139-46.
41. Trock B, Lanza E, Greenwald P. Dietary fiber, vegetables, and colon cancer: Critical review and meta-analyses of the epidemiologic evidence. *J Natl Cancer Inst* 1990;82:650-61.
44. Sandberg A-S, Andersson H, Hultén L, Isaksson G: Kostfibers effekt på enzymaktivitet i tunntarmsinnehåll. *Näringsforskning* 1984;28, Suppl 20:105.
46. Chen W-J L, Anderson JW, Jennings D : Propionate may mediate the hypocholesterolemic effects of certain soluble plant fibers in cholesterol-fed rats. *Proc Soc Exp Biol Med* 1984;175:215-18.
47. Howe GR, et al. Dietary intake of fiber and decreased risk of cancer of the colon and rectum. *J Natl Cancer Inst* 1992;84:1887-96.
49. Cassidy A, Bingham S, Cummings JH. Starch intake and colorectal cancer risk: an international comparison. *Br J Cancer* 1994;69:937-42.
52. Andersson H, Hultén L, Magnusson O, Sandström B: Energy and mineral utilization from a peptide-based elemental diet and a polymeric enteral diet given to ileostomists in the early postoperative course. *J Parent Ent Nutr* 1984; 8:497-500.
53. Andersson H, Bosaeus I, Ellegård L, Hallgren B, Hultén L, Magnusson O: Comparison of an elemental and two polymeric diets in colectomized patients with or without intestinal resection. *Clin Nutr* 1984;3:183-9.
54. Langkilde AM, Andersson H, Schweizer TF, Torsdottir I: Nutrients excreted in ileostomy effluents after consumption of mixed diets with beans or potatoes. I. Minerals, protein, fat and energy. *Eur J Clin Nutr* 1990;44:559-66.
58. Livesey G: Calculating the energy values of foods: Toward new imperial formulae based on diets with varied intakes of unavailable complex carbohydrates. *Eur J Clin Nutr* 1991; 45:1-12.

A complete list of the 58 references can be ordered either from the author or the office of the journal. □