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# Effect of dietary fat on the small intestinal mucosa

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SUMMARY **The presence of food within the small intestinal lumen promotes mucosal cell proliferation. To define the trophic role of triglycerides, three groups of eight female Wistar rats were isocalorically fed for four weeks with either Vivonex, or Vivonex with 50% calorie substitution with an essential fatty acid mixture, or Vivonex with 50% calorie substitution with a saturated fatty acid mixture. Although Vivonex caused greater body weight gain, both essential fatty acids and saturated fatty acids increased small intestinal weight, mucosal weight, protein and DNA overall, and in each of three intestinal segments (proximal, middle and distal), compared with Vivonex. Mucosal indices were similar for essential fatty acids and saturated fatty acids. These results show that triglycerides, regardless of essential fatty acid content, are trophic to the rat small intestinal mucosa.**

Luminal nutrition, or the direct effect of food within the lumen on the intestinal mucosa, maintains normal small intestinal structure and causes it to adapt to altered luminal circumstances.[1-3] The relative roles of specific dietary constituents however, are unclear. Calorie for calorie, long chain triglycerides are more potent at inducing adaptation after intestinal resection than are medium chain triglycerides, protein or carbohydrate.[4] Free fatty acids are even more effective.[5] We have recently shown that supplementation of an elemental diet with essential fatty acids increases intestinal mucosal weight above that of animals fed either the diet alone or normal chow,[6] and so we compared the intestinal response with supplementation of an elemental diet with fat either high or low in essential fatty acids, to distinguish the effects of fat from those of its constituent fatty acids.

## Methods

### ANIMALS AND FEEDS

Twenty four adoloscent female Wistar rats weighing 240–250 g were divided into three equal groups and fed simultaneously. Group I received Vivonex liquid elemental diet (Norwich-Eaton Ltd Surrey) alone (100% of calorie requirements); group 2 Vivonex and an essential fatty acid mixture (Efamol Ltd, Surrey) in equicalorific amounts – that is, 50% of calorie requirements from the elemental diet and 50% from the essential fatty acid mixture; group 3 Vivonex and a saturated fatty acid mixture in similar equicalorific amounts. The composition of Vivonex is given in Table 1. Eighty four per cent of the fatty acids of the essential fatty acid mixture (75% linoleic acid; 9% gammalinolenic acid) are essential, and 16% non-essential (Table 2). The saturated fatty acid mixture was olive oil (Boots Ltd, Nottingham) and coconut oil (Sigma Chemical Company, Dorset), 3:7 w/w, giving 4·4% essential and 95·6% non-essential fatty acid content. Vivonex contains 1·3% fat, mainly of essential fatty acids (Table 1).

Animals were housed individually in wire bottomed cages to prevent coprophagia and all received 64 calories/day (1·0 g fat = 9 calories) for four weeks. This resulted in submaximal weight gain, but ensured that all daily feed was eaten so that the calorie intakes of the three groups were the same. All feeds were liquid, and animals were fed from non-spill valved containers, with tap water *ad libitum*. Body weights were measured weekly before the daily feed.

### EXPERIMENTAL PROTOCOL

Each animal was killed by a blow to the head. The abdomen was immediately opened and the entire

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Table 1 *Main composition of Vivonex liquid elemental diet*

| | *Calorific Contribution (%)* | *By weight* % |
|---|---|---|
| Carbohydrate type | 90·5 glucose solids | 86·3 |
| Amino acids type | 8·2 pure amino acids | 1·2 |
| Fat type | 1·3 safflower oil (80% triglyceride of linoleic acid) | 0·5 |

Osmolarity=550 mOsm/l. Vitamin, electrolyte and trace element content as manufacturer's data (Norwich-Eaton Ltd, Woking, Surrey, UK).

Table 2

*Composition of high essential fatty acid mixture*

| | | % |
|---|---|---|
| 18:2 | Linoleic acid | 75·0 |
| 18:3 | Gammalinolenic acid | 9·0 |
| 18:1 | Oleic acid | 8·5 |
| 16:0 | Palmitic acid | 5·5 |
| 18:0 | Stearic acid | 2·0 |
| | | 100·0 (84% essential) |

*Composition of saturated (low essential) fatty acid mixture*

| | | |
|---|---|---|
| 18:2 | Linoleic acid | 4·3 |
| 18:3 | Gammalinolenic acid | 0·1 |
| 18:1 | Oleic acid | 24·8 |
| 18:0 | Stearic acid | 2·1 |
| 16:0 | Palmitic acid | 9·5 |
| 14:0 | Myristic acid | 13·7 |
| 12:0 | Lauric acid | 34·7 |
| Other non-essential fatty acids | | 10·8 |
| | | 100·0 (4·4% essential) |

small intestine from the ligament of Treitz to the ileo-caecal valve excised.

The total small intestinal length was measured under a standard 10 g tension, and then the intestine divided into three segments of equal length: A, proximal; B, middle, and C, distal including terminal ileum.

Each segment was cannulated, and carefully flushed with cold isotonic saline and then air to remove intestinal contents. After dissection of fat and mesentery each segment was weighed. The mucosa was scraped off with glass slides, weighed and stored at −20°C. Mucosal deoxyribonucleic acid (DNA) and protein content were measured by standard methods.[7,8]

Results are expressed as means (SEM). Statistical comparisons between groups were made by one-way analyses of variance.

## Results

### WEIGHT GAIN

Initial body weights were similar in all three groups. Feeding of an elemental diet at 64 calories/day increased total body weight significantly ($p<0·001$) more than isocaloric feeding of the same elemental diet with either 50% essential or non-essential fatty acid substitution (Vivonex 33·9 (3·1), essential fatty acids 7·6 (5·9), saturated fatty acids 9·2 (3·2) g body weight gain over four weeks).

### TOTAL INTESTINAL AND MUCOSAL WEIGHTS

There was no difference in overall gut length between groups (Vivonex 110·0 (1·7), essential fatty acids 110·3 (2·7), saturated fatty acids 115·8 (1·5) cm).

Overall total intestinal weight/cm was significantly increased by essential fatty acids and saturated fatty acids compared with Vivonex (Vivonex 46·4 (1·45), essential fatty acids 56·5 (1·6), saturated fatty acids 62·0 (0·8) mg/cm gut, $p<0·001$). Overall mucosal weight/cm showed similar changes (Vivonex 16·5 (0·6), essential fatty acids 23·6 (1·3), saturated fatty acids 23·5 (0·7) mg/cm gut, $p<0·001$). The overall greater weights on the high fat diets were caused by weight increases in all three intestinal segments (Figs. 1, 2).

### MUCOSAL DNA AND PROTEIN

Overall mucosal DNA/cm was significantly increased by essential fatty acids and saturated fatty acids compared with Vivonex (Vivonex 107·2 (7·5), essential fatty acids 152 (11·3), saturated fatty acids 164·1 (17·6) μg/cm gut DNA, $p<0·02$). Overall mucosal protein/cm was also increased by essential fatty acids and saturated fatty acids (Vivonex 4·7 (0·1), essential fatty acids 5·8 (0·1), saturated fatty acids 6·4 (0·2) mg/cm gut, $p<0·001$). Again, these parameters were also increased in the segments by the high fat diets (Figs. 3, 4), although for DNA the increase was not statistically significant in segment A.

## Discussion

All animals ate all the food provided each day and although calories were restricted all increased their weight. The diets were isocaloric and so the intestinal effects were not the result of differing calorie intakes. This is important because hyperphagia causes mucosal hyperplasia.[9] The greater weight gain in Vivonex fed animals is interesting, particularly as in previous studies we have confirmed that Vivonex is calorie for calorie less nutritious than chow.[6] In the present experiment the higher weight gain may

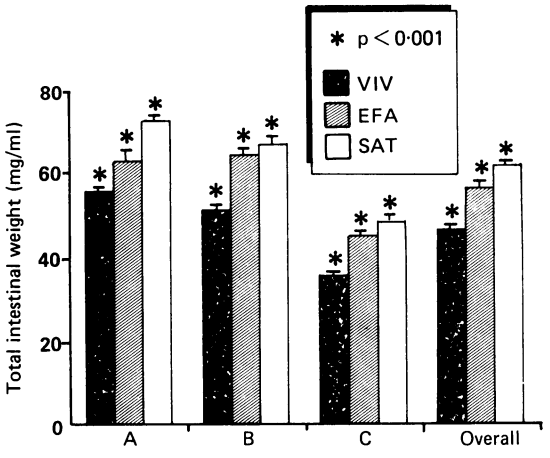


Fig. 1 *Effect of diet on segment and overall total small intestinal weight/cm.*

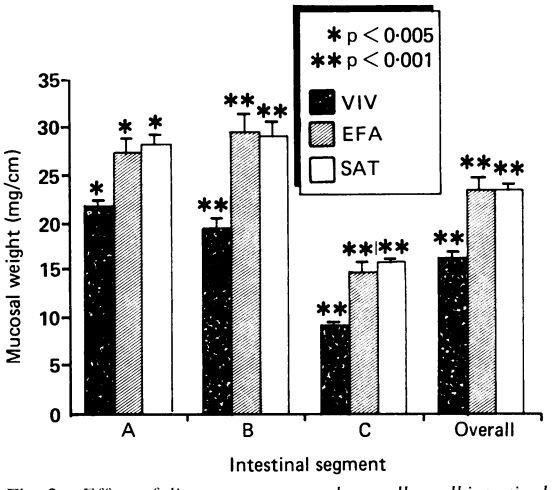


Fig. 2 *Effect of diet on segment and overall small intestinal mucosal weight/cm.*

reflect a greater intake of nitrogen or other nutrients in Vivonex than in the other two groups. We have given intestinal parameters as absolute numbers, but expressing them per 100 g/body weight would not alter the findings, other than to accentuate the differences found.

In spite of lesser weight gain, isocaloric oral feeding of an elemental diet with 50% of calories substituted with an 84% essential fatty acid mixture increased total gut weight and mucosal weight, DNA and protein throughout the small intestine compared with the same elemental diet alone. Fifty per cent substitution with a fat mixture containing only 4·4% essential fatty acids also did so, however, and to levels similar to those found with the essential fatty acid mixture.

The results suggest that intestinal hyperplasia is caused by fat regardless of its essential fatty acid content. Essential fatty acid deficient diets do impair the mucosal hyperplasia that follows partial small intestinal resection and even reduce mucosal mass in sham control rats.[10] It is therefore still possible that our results could be explained on the basis of essential fatty acid deficiency, if the essential fatty

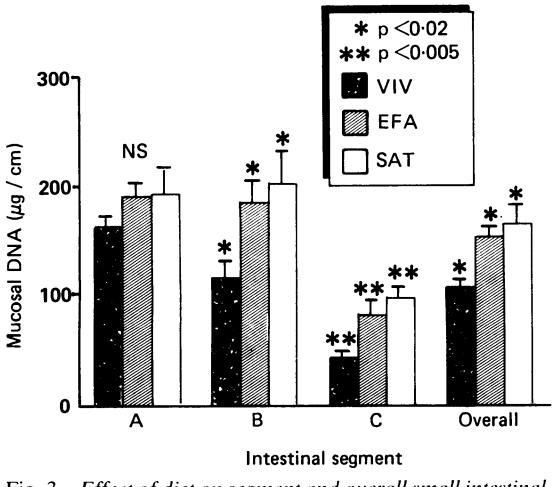


Fig. 3 *Effect of diet on segment and overall small intestinal mucosal DNA/cm.*

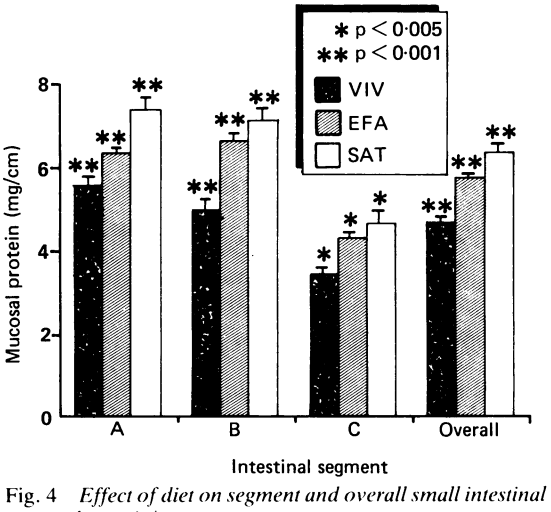


Fig. 4 *Effect of diet on segment and overall small intestinal mucosal protein/cm.*

acid content of Vivonex (1% of total calories) is suboptimal for maintaining mucosal mass. The critical difference for essential fatty acid content would then have to be between 1% and 2·7% total calories, the latter being the overall content of the saturated fatty acid – Vivonex mixture. Against this, the changes were almost always greater in the low than the high essential fatty acid group. Nevertheless, this possibility is under investigation.

Although replacing half the Vivonex with fat resulted in reduction of nitrogen, vitamin and mineral intake, and not only of carbohydrate, it is unlikely that this could account for the trophic changes unless any of these nutrients actually retard mucosal growth. It is therefore more likely that fat has a trophic action. Possible mechanisms include release of pancreaticobiliary secretions that may be trophic to the mucosa,[11] or of a trophic gut peptide, perhaps enteroglucagon,[12] which has been shown to be released by small intestinal infusion of fat in man.[13]

This study suggests that fat, regardless of essential fatty acid content, has a trophic action on the small intestinal mucosa. This may be important in formulating enteral feeds and in enhancing mucosal hyperplasia in the small intestine in the short bowel syndrome.

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