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The effect of fibre on gastrointestinal transit times in vegetarians and omnivores

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Summary

A pilot study has been carried out to investigate the effect of fibre on the gastrointestinal transit of a single unit and a multiple unit dosage form in vegetarians and omnivores, using the technique of gamma scintigraphy. Eight healthy male volunteers (four vegetarians and four omnivores) were studied after consuming a strict diet containing either 15 or 40 g dietary fibre per day. Gastric emptying of both types of dosage form was found to be unaffected by fibre content of the diet, however, small intestinal transit appeared to be longer in vegetarians than omnivores, irrespective of fibre intake. Transit time of the dosage forms within each region of the colon was highly variable, however, overall transit time in the vegetarians was slower than in the omnivores. The addition of supplementary fibre to the diet appeared to exert a 'normalising' effect on colonic transit, whereby initially rapid transit was retarded and initially slow transit accelerated. There appeared to be no definite relationship between transit time and laxation.

Introduction

It has been suggested that diseases such as colonic cancer, irritable bowel syndrome and diverticular disease, all of which are prevalent in the West, are a direct result of the consumption of highly refined diets containing little fibre (Gear et al., 1979, 1981). As a result, a number of studies have been carried out to characterise the effect of fibre on gastrointestinal (GI) transit. Contradictory evidence exists about the effect of fibre on transit time. The addition of, for example, 13.2, 20 and 8–10 g bran per day was found to lead to a decrease in transit time (Connell and Smith, 1974; Payler et al., 1975; Spiller et al., 1986). However, in contrast to the above, fibre has also been shown to increase colonic transit times (Krevsky et al., 1987), especially when subject colonic transit times were originally rapid (Payler et al., 1975).

Vegetarianism is becoming more popular as a consequence of the healthy eating campaign. Recent studies have shown that transit times in vegetarians are significantly shorter than in non-vegetarians (omnivores) (Gear et al., 1981). However, the dietary fibre intake of the subjects was not strictly controlled, and so it is not known

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whether rapid transit was solely due to high fibre consumption or other dietary factors.

Previous investigations in this field have used either radio-opaque markers or non-absorbable dyes to measure transit times (Connell and Smith, 1974; Payler et al., 1975; Gear et al., 1981; Spiller et al., 1986; Stevens et al., 1988). Dual isotope gamma scintigraphy permits the simultaneous assessment of the behaviour of two different formulations in vivo, i.e single unit (tablets) and multiple unit (pellets) (Davis et al., 1984a,b).

The behaviour of oral dosage forms in each region of the colon is poorly understood (Christensen, 1985; Krevsky et al., 1986). Knowing the site at which dosage form stagnation and absorption of colonic contents takes place could have important implications in the targeting of drugs to the colon. The aim of this pilot study was to characterise GI transit in vegetarians and omnivores, and to establish whether there are any significant differences between the two groups which would require further evaluation.

Materials and Methods

Labelled pellets

Labelled pellets were prepared and labelled with ^{99m}Tc in a similar manner to that described by O'Reilly et al. (1987). They were filled into size 2 hard gelatin capsules to a notional fill weight of 330 mg to give an activity of approx. 4 MBq ^{99m}Tc at the time of administration. Previous work has shown the tenacious nature of isotope binding to resins when this method of labelling is used (Khosla, 1987).

Labelled tablets

Non-disintegrating tablets (11 mm diameter) were prepared from ethyl cellulose (BDH Poole, Dorset) containing a small quantity of Amberlite resin (IRA 120 (BDH Poole, Dorset), density 1.2 g/cm^3) and radiolabelled with 1 MBq ^{111}In per tablet. A more detailed description of the preparation of similar tablets can be found elsewhere (Coupe et al., 1991a).

The tablets were coated with ethyl cellulose and then cellulose acetate in order to prevent their disintegration. The integrity of the film coats was assessed in vitro over a period of 24 h, after which there were no signs of tablet disintegration. The in vivo integrity of the tablets was later shown not to be compromised in the scintigraphic study.

Subjects

The study was carried out in eight healthy male volunteers (age 20–24 years). All the subjects were considered normal after having undergone a medical examination, which included a haematological and a biochemical screen. Four of the volunteers had been vegetarian for a period of at least 6 months prior to the study, and the other four were considered to eat an average diet which included meat (omnivores).

All volunteers were non-smokers and none were on any medication at the time of the study. Also, none of the volunteers had a history of suffering from any GI disturbances.

The experimental protocol was approved by the Ethics Committee of the University of Nottingham and the study was conducted in accordance with the Declaration of Helsinki Guidelines for Ethics in Research. Approval to administer the radiolabelled formulations was obtained from the Department of Health, London.

Diets

The study took place on two days separated by 1 week. The dietary fibre intake of all volunteers was strictly controlled for a period of at least 6 days prior to each study day, so as to allow the GI tract to become accustomed to the new diet. This equilibration time is approximately twice the mean transit time for males in the U.K., which is believed to be adequate to eliminate the effects of any previous diets on the bowels (Cummings, J.H., personal communication).

All diets were carefully planned in conjunction with the Dietetics Department, Queen's Medical Centre, Nottingham. During the first study period, the vegetarians consumed a high-fibre diet, and the omnivores consumed a low-fibre diet, and during the second study period, the fibre content of the diets was reversed. On the actual study days, the volunteers continued to eat the

TABLE 1

Composition of each study day diet

	Vegetarians		Omnivores	
	High fibre	Low fibre	High fibre	Low fibre
Dietary fibre (g)	40.7	16.5	40.0	15.0
NSP (g)	20.3	7.1	20.6	8.4
Energy (kJ)	8625.5	8600.0	8614.0	8618.2
Protein (g)	68.2	74.9	111.0	114.4
Fat (g)	79.2	94.0	80.2	79.4
Carbohydrate (g)	287.4	243.1	231.9	230.1

same diet that they had been eating for the previous 6 days.

The high-fibre diets contained approx. 40 g fibre (20 g non-starch polysaccharides, NSP), and the low-fibre diets contained approx. 15 g fibre (9–10 g NSP). The average dietary fibre content in the U.K. is in the order of 20 g per day (Bingham et al., 1981) and figures of 15 and 40 g of fibre represent extremes of the usual daily range.

Dietary intakes were calculated using values in McCance & Widdowson's Food Tables (Paul and Southgate, 1978), except for NSP intakes which were calculated using additional food tables (Englyst et al., 1988, 1989).

The diet for all the subjects consisted of three evening meal menus and two lunch menus which were used in rotation. Breakfast remained the same throughout each of the study periods. A summary of the diet composition is given in Table 1. All meals consumed on the study days had approximately the same calorific values (breakfast, 1200 kJ; lunch, 3500 kJ; dinner, 4000 kJ) so as to minimise the variables.

Dosage instructions, imaging procedure and analysis

On the study day, each volunteer swallowed the pellets and tablet with 100 ml of water approx. 30 min after breakfast. 4 h after administration, the volunteers were given lunch, and dinner was provided $9\frac{1}{2}$ h post-dose. Tea and coffee was available ad libitum throughout the day.

External ^{111}In-labelled anatomical reference markers were taped to the skin anteriorly and posteriorly over the right lobe of the liver. Simultaneous imaging of both radionuclides was undertaken immediately after dosing, with the subjects standing in front of a gamma camera (General Electric Maxicamera, type II) having a medium-energy (300 keV) parallel-hole collimator with a 40 cm field of view.

Both anterior and posterior images were taken, each of 60 s duration at intervals of approx. 15–20 min over a period of 14 h. The data were recorded by computer and stored on magnetic tape for later analysis.

Regions of interest were constructed around the stomach, ascending, transverse and descending colon of each volunteer, and the activity in these areas quantified. The boundary between the ascending and transverse colon was defined as a diagonal line which bisected the hepatic flexure, and the boundary between the transverse and descending colon was defined as a similar line bisecting the splenic flexure. The boundaries were constructed on an anatomical basis rather than linear measurement, since the human colon can vary considerably in shape between individuals.

Activity in the caecum was combined with ascending colon data, and any activity within the sigmoid and rectal regions was included in descending colon data. All the results were corrected for background radioactivity, loss of activity due to defaecation, decay of the radioisotope and 'scatter down' of the ^{111}In activity into the ^{99m}Tc channel (Davis et al., 1984a). The geometric mean of the anterior and posterior counts was used to give a result which is independent of depth of source (Tothill et al., 1978).

Gastric emptying (GE) profiles of the pellets were constructed and $T_{50\%}$ values calculated, which represent the time taken for 50% of the activity within the stomach, due to the pellets, to empty. Colonic transit profiles were also constructed in a similar manner.

The pellet small intestinal transit (SIT) times were calculated by subtracting the time taken for 50% of the pellets to empty from the stomach from that for 50% to enter the colon. The SIT time of the tablet was calculated by subtracting GE times from the colon arrival times.

Bowel habits during the study

During the study periods and on each of the study days, the volunteers recorded details of their bowel habits. This was to establish whether there is any relationship between frequency of bowel movements, transit time and levels of fibre in the diet.

Results and Discussion

Gastric emptying

GE times for the pellets are listed in Table 2. There was no statistical difference between mean emptying values for each group of individuals, which was expected. GE has been shown to be dependent upon the calorific density, volume (Hunt et al., 1985) and viscosity of the stomach contents (Russell and Bass, 1985), these parameters being virtually identical for each group of individuals in this study.

The effect of fibre on gastric residence time of the tablet is shown in Table 3. GE of the tablet was a discrete 'all-or-nothing' process, and in many cases it was observed that the tablet emptied from the stomach with or even before the pellets. This observation is in agreement with previous studies and the mechanism for emptying is discussed elsewhere (Coupe et al., 1991a,b). No specific trends were noted in the tablet emptying data and the spread of the results was in accord with previous studies on the variation in GI transit (Coupe et al., 1991a).

TABLE 3

Gastric emptying times (min) of the tablet after a high-fibre and a low-fibre diet in vegetarians and omnivores

	Vegetarians		Omnivores	
	High fibre	Low fibre	High fibre	Low fibre
	33.0	166.5	125.0	102.5
	11.5	33.5	78.0	57.5
	35.0	34.0	78.5	34.5
	148.0	56.0	56.0	34.5
Mean	56.9	72.5	84.4	57.3
SE	30.8	31.8	14.5	16.0

Small intestinal transit

Pellet SIT time results are shown in Table 4. The transit times for the omnivores in this study are in good agreement with the results reported previously by Davis et al. (1986) (approx. 180 ± 60 min), however, the transit times in vegetarians appeared generally to be longer. This is partly due to volunteer 4 who, for example, had an exceptionally long SIT time of 479.4 min after a high-fibre diet. This was mainly due to stagnation of the pellets at the ileo-caecal junction (ICJ).

A larger degree of variation was also apparent with the vegetarians, and it is interesting to note that a high-fibre diet appeared to reduce SIT time in omnivores, whereas in the vegetarians

TABLE 2

$T_{50\%}$ gastric emptying values (min) of the pellets after a high-fibre and a low-fibre diet in vegetarians and omnivores

	Vegetarians		Omnivores	
	High fibre	Low fibre	High fibre	Low fibre
	100.2	139.8	121.8	98.4
	123.0	75.0	78.6	118.2
	73.2	78.6	78.6	60.0
	109.8	76.8	75.0	105.0
Mean	101.6	92.6	88.5	95.4
SE	10.5	15.8	11.1	12.5

TABLE 4

$T_{50\%}$ small intestinal transit time (min) of the pellets after a high-fibre and a low-fibre diet in vegetarians and omnivores

	Vegetarians		Omnivores	
	High fibre	Low fibre	High fibre	Low fibre
	281.4	301.2	112.0	294.6
	357.0	399.6	161.4	152.4
	205.2	156.0	188.4	185.4
	479.4	283.2	159.6	108.0
Mean	330.8	285.0	155.4	185.1
SE	58.4	50.0	15.9	39.8

TABLE 5

Small intestinal transit time (min) of the tablet after a high-fibre and a low-fibre diet in vegetarians and omnivores

	Vegetarians		Omnivores	
	High fibre	Low fibre	High fibre	Low fibre
	203.0	268.5	89.5	112.0
	262.0	204.5	69.0	90.5
	274.0	111.5	80.0	113.0
	432.0	102.5	90.0	180.5
Mean	292.8	171.8	82.1	124.0
SE	48.9	39.7	5.0	19.5

SIT appeared to be increased after a high-fibre diet. The difference in transit times between the vegetarians and omnivores after the high-fibre diet is considered significant. It is possible that vegetarians, in general, have longer SIT times, however, no studies have been carried out comparing the transit characteristics of vegetarians and omnivores. High dietary fibre intakes have been shown to delay the breakdown and absorption of digestible solid material, for example, starch (Hamberg et al., 1989), and so it is possible that the small intestines of people consuming high-fibre diets, e.g., vegetarians, have adjusted to accommodate these dietary changes. However, it would be necessary to study a larger sample size to confirm this hypothesis.

SIT times of the tablet formulation are shown in Table 5 where it can be seen that the transit of the tablets was in general faster than that of the pellets. This is in conflict with others, since it has previously been shown that transit through the small intestine does not appear to be influenced by the physical state or size of the dosage form (Christensen et al., 1985a; Davis et al., 1986). It was noted that the tablets tended to arrive at the ICJ before the pellets and then enter the ascending colon, whilst the pellets re-grouped at the junction and entered the ascending colon as a bolus later. This may therefore account for the above discrepancy.

The phenomenon of pellet re-grouping and tablet stagnation at the ICJ has been observed previously (Christensen et al., 1985b; Khosla and Davis, 1989), and is thought to be due to the regulatory function of this region of the GI tract. The ICJ determines how intestinal contents move between the ileum and the colon, but the mechanisms by which it functions as yet remain unknown.

Colonic transit

Representative colonic transit profiles are shown in Figs 1 and 2, and colonic filling results, expressed in terms of $T_{50\%}$ values are listed in Table 6. In many of the volunteers the pellets tended to re-group at the ICJ before entering the colon. The pellets would then enter as a bolus

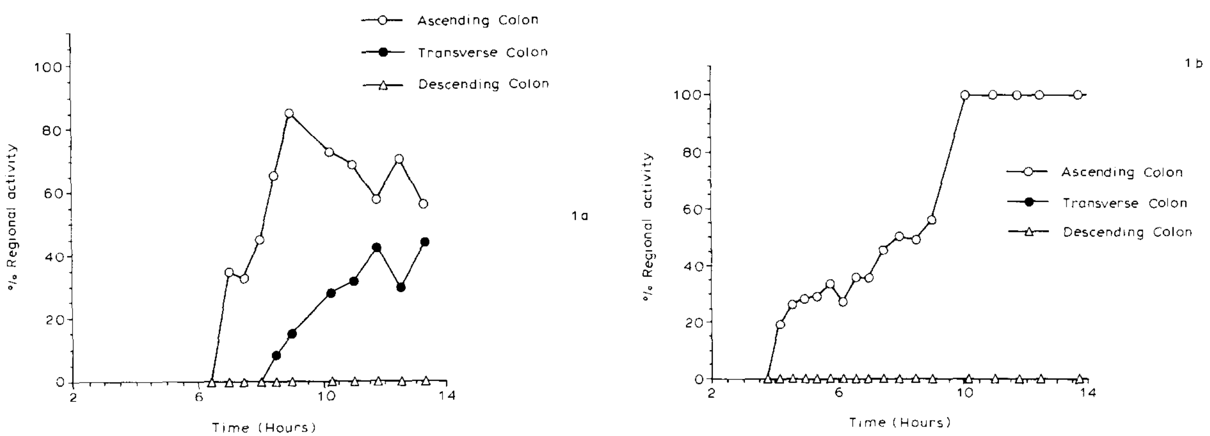

Fig. 1. (a) Colon profile after a high-fibre vegetarian diet: volunteer 2. (b) Colon profile after a low-fibre vegetarian diet: volunteer 2.

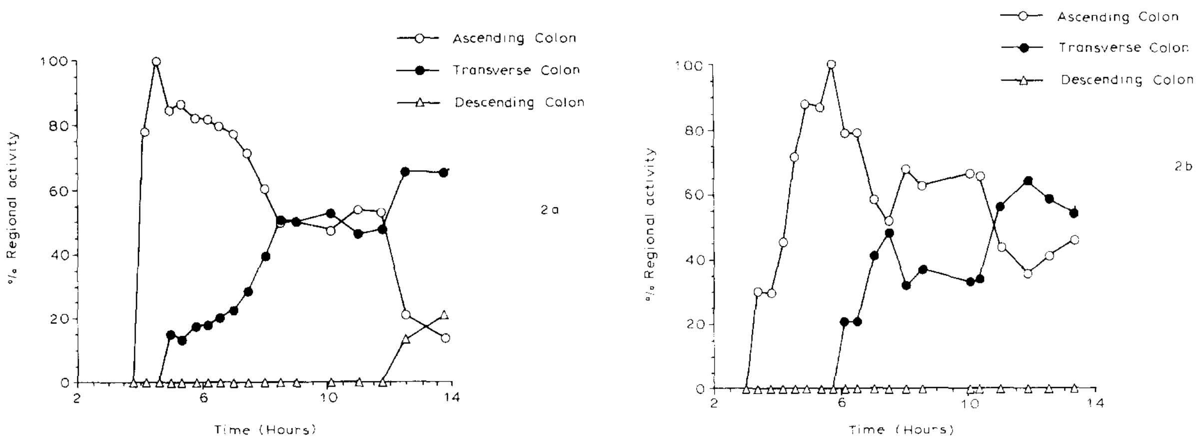

Fig. 2. (a) Colon profile after a high-fibre omnivorous diet: volunteer 6. (b) Colon profile after a low-fibre omnivorous diet: volunteer 6.

followed by the gradual progression of the remainder into the ascending colon.

In general, the pellets filled more rapidly in subjects on the high-fibre diet (especially the omnivores), however, this conflicts with reports that high-residue diets tend to fill and empty from the caecum and ascending colon less rapidly than more liquid diets (Kaufman et al., 1990). From the latter, it may be postulated that the pellets would take longer to enter the caecum after a high-fibre diet, since a greater amount of dietary residue would increase the viscosity of the intestinal contents, thus slowing their movement.

The degree of reproducibility in the results was highest in the 'high-fibre' volunteers, especially the omnivores. This may suggest that the fibre was exerting a 'normalising' effect on the behaviour of the colon and that this was more pronounced in the omnivores. In general, vegetarians tend to consume higher levels of dietary fibre than omnivores (Gear et al., 1981). The normalising effect of the fibre therefore could have been more pronounced in the omnivores because they were less used to high dietary fibre intakes than the vegetarians, whose colons may have become accustomed to this type of diet.

The pellets spread out as they gradually moved up the ascending colon towards the hepatic flexure. In several volunteers, stagnation and a degree of re-grouping of the pellets was seen at the

TABLE 6

$T_{50\%}$ ascending and transverse colon arrival values (min) of the pellets after a high-fibre and a low-fibre diet in vegetarians and omnivores

	Vegetarians				Omnivores			
	High fibre		Low fibre		High fibre		Low fibre	
	AC	TC	AC	TC	AC	TC	AC	TC
	37.8	169.2	21.6	60.0	22.2	436.2	191.4	–
	93.0	–	250.8	–	16.2	223.2	70.8	294.6
	11.4	–	10.8	–	16.2	–	21.6	–
	49.2	–	10.8	–	10.8	125.4	11.4	16.2
Mean	47.9	–	73.5	–	16.4	261.6	73.8	155.4
SE	17.0	–	59.2	–	2.3	79.5	41.3	98.4

flexure, before they progressed into the transverse colon, where a greater degree of spreading was observed. This observation is in agreement with the theory that the ascending part of the colon is the main site of fermentation and stagnation of colon contents (Kerlin et al., 1983; Christensen, 1985). However, others have found the opposite in their investigations (Krevsky et al., 1986; Karaus and Wienbeck, 1988).

The transit of the pellets in the transverse colon was slower in the vegetarians than in the omnivores, especially since a $T_{50\%}$ filling value was reached in one vegetarian only during the imaging period (Table 6). Although there were wide variations in the data for the omnivores, on examination of the filling curves, it was found that filling rates were either unaffected by dietary fibre or slightly decreased by a high-fibre diet.

In those volunteers in which the pellets progressed to the descending colon during the imaging period, re-grouping of the pellets at the splenic flexure in a similar manner to that observed at the hepatic flexure was noted. Activity in this region of the colon was recorded in all the omnivores after a high-fibre diet, but only in two (volunteers 5 and 8) after the low-fibre diet. The pellets reached the descending colon in only one vegetarian during the imaging period.

In all volunteers, the tablets reached the ascending colon before any of the pellets, and in the majority, a period of stagnation was noted in the caecum (Table 7). Stagnation was also observed at the flexures in some volunteers, but this may have been due to retrograde movement.

No definite trends were observed in relation to transit time through any region of the colon with either the pellets or tablets. There were wide variations between individual results in each section of the colon, this having also been observed by others (Wyman et al., 1978; Hardy et al., 1985; Khosla and Davis, 1989). However, the vegetarians appeared to have longer periods of tablet stagnation than the omnivores, which is partly illustrated by the fact that the tablet progressed further in the omnivores than in the vegetarians during the imaging period.

It is interesting to note that volunteer 8 had very fast tablet transit times after both diets which is believed to be due to a phenomenon known as 'streaming', whereby solids and liquids move at different rates within the colon. In this case the pellets behaved as a liquid, and the tablet behaved as a non-digestible solid and was thus passed more rapidly through the colonic contents. Others have noted the process of streaming occurring after the addition of bran to the diet (Findlay et al., 1973).

In order to draw any definite conclusions with respect to residence time in the distal colon, a longer imaging period would be required. However, the total imaging time was restricted due to the half-life of the ^{99m}Tc label. Alternatively, the method of direct instillation of solutions into the caecum could be utilised (Krevsky et al., 1986),

TABLE 7

Residence time (min) of the tablet within each region of the colon after a high-fibre and a low-fibre diet in vegetarians and omnivores

	Vegetarians						Omnivores					
	High fibre			Low fibre			High fibre			Low fibre		
	AC	TC	DC	AC	TC	DC	AC	TC	DC	AC	TC	DC
	23.5	379.0	157.5	199.0	515.5	263.5	421.0	152.5	625.0	23.5	95.5	208.5
	524.5	–	–	1175.0	–	–	318.0	263.0	685.0	258.5	756.5	278.0
	490.0	–	–	1005.0	263.5	–	249.5	27.5	173.5	676.5	43.0	574.0
	582.5	279.5	–	129.0	1126.5	–	81.0	–	–	23.5	168.0	135.5
Mean	405.1	329.3	157.5	627.0	635.2	263.5	267.4	147.7	494.5	245.5	265.8	299.0
SE	128.6	35.2	–	269.9	221.9	–	71.4	58.9	139.8	154.0	165.6	96.2

TABLE 8

Number of bowel movements in 24 h in vegetarians and omnivores on high- and low-fibre diets

	Mean	SE
High-fibre vegetarians	1.29	0.12
Low-fibre vegetarians	0.81	0.15
High-fibre omnivores	1.38	0.16
Low-fibre omnivores	0.96	0.16

but this would prevent the investigation of GE and SIT, and the procedure is believed to alter the normal physiological behaviour of the large bowel.

Bowel habits

The frequency of defaecation of the volunteers is shown in Table 8 and is expressed in terms of the number of bowel movements in 24 h. All volunteers experienced an increase in bowel movements when on the high-fibre diet, and some also noted an increase in stool size. The increase in frequency of defaecation is thought to be due to the bulking action of fibre which increases colonic intraluminal pressure (Ornstein and McLean Baird, 1987). The bulking action is a result of the water-absorbing capacity of fibre and an increase in the number of bacteria within the large intestine (Stephen and Cummings, 1980; Ornstein and McLean Baird, 1987).

Conclusions

The GE of single and multiple unit dosage forms is unaffected by fibre intake or a vegetarian or omnivorous diet. However, diet does appear to modify SIT time, since the transit of both the pellets and the tablet was always found to be slower in the vegetarians than the omnivores.

There were no large differences in colonic transit between the two groups of volunteers. Transit time in each region of the colon was highly variable.

It appears, however, that fibre exerts a normalising effect upon colonic transit, whereby the addition of supplementary fibre to the diet accelerates the transit of pellets and tablets through the colon of those with initially slow colonic transit times (i.e. the omnivores), but has the opposite effect upon the transit times of those with initially rapid colonic transit (i.e. the vegetarians).

High-fibre diets result in an increase in the frequency of defaecation and stool volume, but there appears to be no definite relationship between transit time and laxation.

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