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Studies on the Transport of Small Bowel Contents

An Experimental Study in the Rat with Special Reference to the Evaluation of Non-propulsive Intestinal Movements

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ABSTRACT

An earlier study (4) of chyme propagation through the small bowel in conscious rats has revealed that the luminal contents are transported in separate portions, which exchange material only to a limited extent. In the present study this transport pattern was confirmed also after the following changes in the standardized experimental conditions used previously: (*a*) replacement of the standard radioactive labels (^{125}I-PVP and ^{131}I-PVP) with $Na_2{}^{51}CrO_4$ and $^{99}Tc^m$-sulphur colloid, (*b*) replacement of the test meal with saline and (*c*) investigation of animals without a preceding starvation period. It was also found that the small bowel propulsion was enhanced when the test substance was infused at a higher rate, and that this change did not affect the exchange of material between the portions. The small mixing was further confirmed in experiments in which shifts of label were made repeatedly at constant intervals throughout the infusion period. Distinct regions in which one of the labels predominated could be demonstrated along the entire small bowel when the time interval was diminished to 30 but not to 20 min.

INTRODUCTION

Apart from propulsion of intestinal contents the small bowel musculature should also assure adequate mixture of food with digestive juices and allow close contact of all parts of the chyme and the surface epithelium. Despite the obvious importance of such a mixing action it has been studied very little, probably because of a lack of appropriate and quantitative methods.

To this end a method was worked out in our laboratory for quantitative measurement of the mixing of small bowel contents in conscious rats (4). Two differently labelled test substances are infused continuously, one after the other, into the duodenum via a permanent catheter. A border zone is thus created between the two radiolabels and the propagation of this zone along small bowel can be followed. The degree of overlap between the labels in the border zone is measured after excision of the GI tract and is taken as a measure of intestinal mixing.

It was shown that the transport during a basal, inter-digestive state occurred in separate portions, which exchanged material only to a limited extent. Thus the quantitative estimate of the mixing was found to be much less than that which had been reported from intubation studied in man (6) and from that which can be deduced from other descriptions of small bowel muscular activities (1, 2).

It was stressed that the conclusions reached in our earlier study were pertinent only to the experimental situation selected, which possibly reflected an unphysiological state. In the present study the rate of infusion of the test substance and its physical and chemical composition were varied. Also freely fed animals were investigated in order to better simulate physiological conditions.

In order to further elucidate the mixing of the intestinal contents shifts between the differently labelled test substances were made repeatedly at equal intervals during the entire infusion period. The time interval between the shifts was diminished until distinct borders between labels no longer occurred along the small bowel.

It was found that these modifications of the experimental conditions did not appreciably affect the conclusions reached in an earlier study (4) and a wider applicability of the findings seems therefore justified.

MATERIAL AND METHODS

Animals

Male Sprague-Dawley rats weighing about 275 g each were used. The rats were maintained under standardized conditions (9).

Test substances

Polyvinylpyrrolidone (PVP), labelled with ^{125}I or ^{131}I (Radiochemical Center, Amersham, UK) was used rou-

Table I. *Data on the main part of the series*

Numbers of animals in different experimental groups and numerical values for each animal regarding degree of mixing (M) and the localisation of the transition point (TP). Data (mean ± S.D.) concerning M and TP values for two groups of animals investigated under identical experimental conditions and described earlier (4) are also included (within parentheses)

	Shift between the labels *one hour* before the end of the infusion			Shift between the labels *two hours* before the end of the infusion		
	n	M	TP	*n*	M	TP
^{125}I-PVP and ^{131}I-PVP, standardized test meal, infusion rate 0.2 ml/h, fasted rats	1 (13	0.20 0.16 ±0.05	73 69.7 ±4.6)	1 (12	0.26 0.25 ±0.07	88 83.3 ±4.7)
^{51}Chromate and ^{99}Tc^{m}-sulphur colloid, standardized test meal, infusion rate 0.2 ml/h, fasted rats	1 1 1	0.15 0.19 0.20	64 70 62			
^{125}I-PVP and ^{131}I-PVP, saline as test meal, infusion rate 0.2 ml/h, fasted rats	1 1 1	0.18 0.10 0.16	62 78 80			
^{125}I-PVP and ^{131}I-PVP, standardized test meal, infusion rate 0.2 ml/h, freely fed rats	1 1 1	0.14 0.13 0.10	68 62 74			
^{125}I-PVP and ^{131}I-PVP, standardized test meal, infusion rate 0.6 ml/h, fasted rats	1 1 1	0.15 0.13 0.15	81 72 83	1 1 1	0.23 0.35 0.31	91 95 94

tinely but in three animals $Na^{51}CrO_4$ (Radiochemical Center, Amersham, UK) and ^{99}Tc-^{m}-tagged sulphur colloid were given instead of ^{131}I-PVP and ^{125}I-PVP, respectively. The radiolabelled compounds were generally incorporated in a test meal of given composition, viscosity and pH (3). In three animals the standardized test meal was replaced by physiological saline (Table I).

Surgical procedures

The rats were starved but had free access to water for 18 hours before operation. Under ether anaesthesia the abdominal cavity was opened through an upper midline incision. A catheter (PE 50) was introduced into the duodenum through a stab wound in the bowel wall. The free end of the catheter was tunnelled subcutaneously to the animal's neck and protected by a plastic cap. After operation the rats were kept isolated.

Experimental procedures

The propulsion and mixing were measured seven days post-operatively. Routinely the animals were starved for 18 hours but were allowed to drink freely. Three animals were investigated with free access also to food until the experiments. The animals were placed fully conscious in cylindrical glass jars. The duodenal catheter was connected to an infusion pump. The extracorporeal part of the catheter was protected in a springy wire tube, which emerged through the cover of the jar. The tube was so long (20 cm) that the rats were subjected to minimum restraint. The test solution was generally infused at a rate of 0.2 ml/hour for totally 5 hours. In six animals the rate of infusion of test substance was 0.6 ml/hour. The interchange between the two test substances was made at one (*A* in Fig. 1) and in some animals at two (*B* in Fig. 1) hours before the end of the total infusion period. In six animals interchanges were made several times. In three rats interchanges were made every 30 min (*C* in Fig. 1), in three animals every 20 min (*D* in Fig. 1). At the end of the total infusion period the animals were killed by decapitation in ether anaesthesia. The stomach, small and large intestine were removed in continuity and placed on perspex plates. The activity density of each isotope was recorded digitally by passing the specimen over a slit collimated NaI (Tl) crystal (8).

Data reduction

Analyses of the raw data were performed on a calculator (Model 9821, Hewlett-Packard, USA). The activity density of the two isotopes in every fifth per cent of small bowel and colon length were obtained. Figs. 3 and 4 are original plotter outputs of the activity density along the GI specimen. The two isotopes can be distinguished by the appearance of the plot: one is of histogram character and the area under this curve is hatched.

The first step in the calculation of the quantitative overlap between adjacent activity densities was the determination of the transition point (TP). This was defined as that point along the small bowel which, at the end of the entire infusion period, had been passed by the same amount of the second test substance as was left behind by the first.

The degree of mixing (M) was defined as the time taken to infuse the amount of the first test substance that was found proximal to TP and which, by definition, was equal

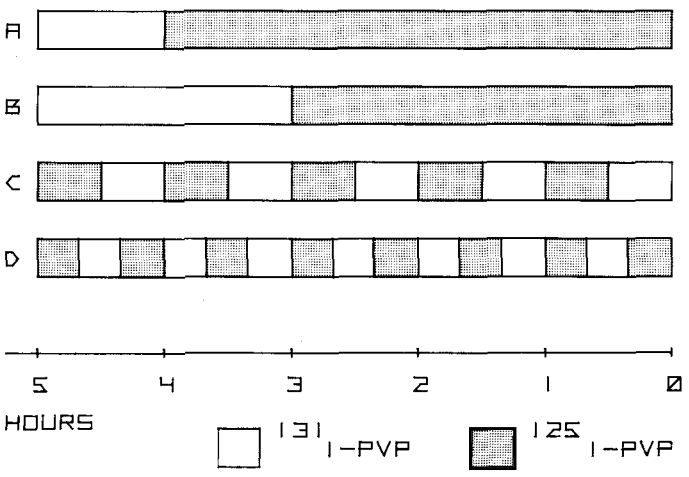


Fig. 1. Infusion periods of each test substance. The single interchanges between the labels were made 1 (*A*) and 2 (*B*) hours before the end of the infusion. Repeated interchanges were made every 30 (*C*) and 20 (*D*) min.

to the infusion time for the amount of the second test substance that was found distal to TP.

The illustrative cases given in Fig. 2 should serve to explain the calculation process, which is described in detail elsewhere (4). The examples are simplified by assuming a constant activity density all over the bowel specimen and the same infusion time for both isotopes. F, the activity distribution (accumulated activity) for the first (1) and second (2) test substance, is normalized so that it reaches its maximum value (100) at the end of the bowel specimen. In the first example (*A*) the two isotopes are completely separated. F_2 reaches 100 at the transition point, where F_1 starts. There is no overlap and, consequently, M×0.

In *B* there is a considerable overlap between the labels. The mixing (M) is given by the value of F_1 at TP ($F_{1(TP)}$) which is equal to $(100-F_{2(TP)})$.

In the highly theoretical case in *C*, there is a complete mixing of the two isotopes. Therefore F_1 is identical to F_2. The upper limit of M is 50% of the infusion time for each test substance.

RESULTS

The activity densities given in Fig. 3*a* were recorded from an animal investigated under the routinely used experimental conditions. The activity density is "peaky" with a few heavy accumulations of activity, separated by regions containing virtually no activity. Both isotopes are present together only in one of the peaks (between 65 and 80% of the bowel length). Hence the overlap between adjacent activity densities is minute.

The activity densities also have a similar appearance after replacement of the commonly used isotopes with radiochromate and Technetium sulphur colloid, respectively (Fig. 3*b*). The single difference is that the radiochromate accumulated at the entrance of the catheter in the duodenum.

Data from an animal representative of the three animals in which the standardized test meal was replaced by saline are given in Fig. 3*c*. The curves are similar to those seen in Fig. 3*a*, i.e. a change of the physical and chemical composition of the test meal does not seem to be followed by an appreciable change in the mixing of intestinal contents.

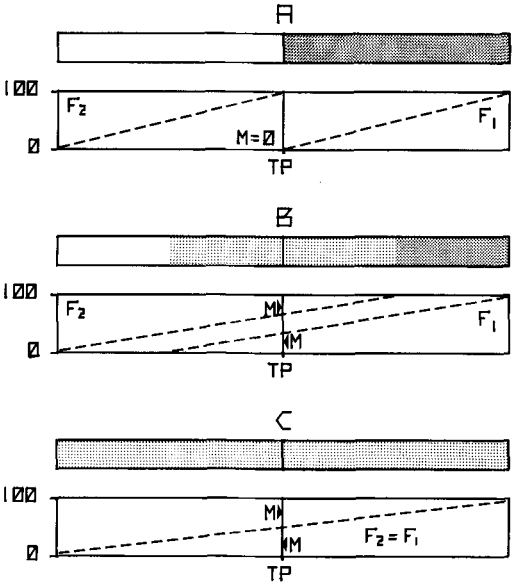


Fig. 2. Illustrative examples of the calculation of intestinal mixing. The cases are simplified by assuming a constant activity density along the entire small blowel and equal infusion periods for the two test substances. In practice, the two isotopes overlap each other to a varying degree (*B*). The hypothetical situations with no (*A*) or total (*C*) mixing are also given. F is the activity distribution (accumulated activity) for each test substance (1 and 2) along the excised bowel specimen. For definition of TP and M, see text!

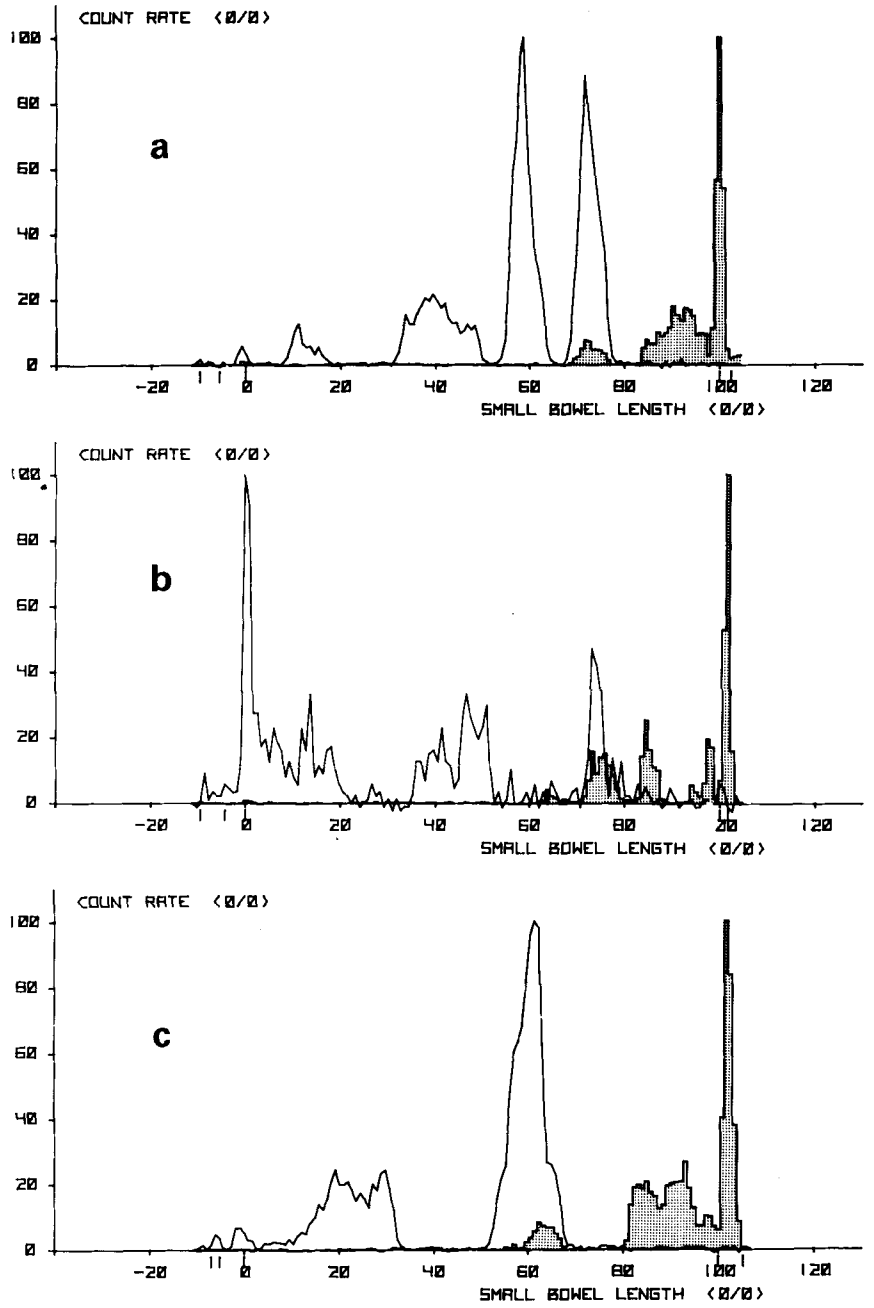
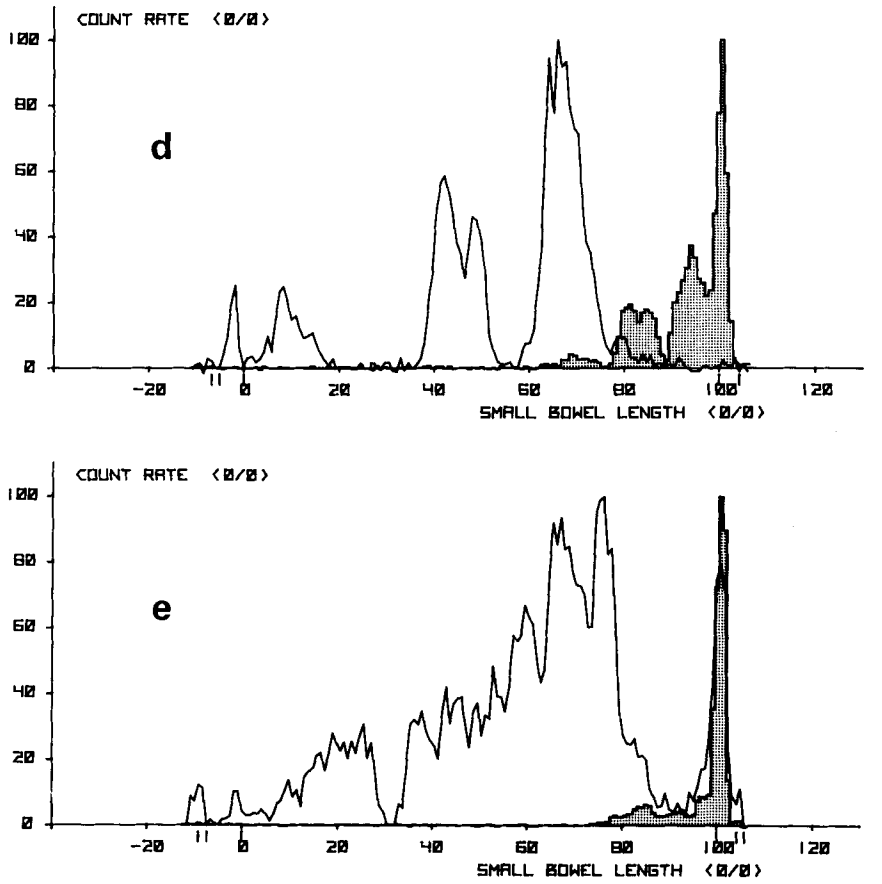


Fig. 3. Original plotter outputs of the activity density of each isotope along the GI specimen. The entrance of the duodenal catheter and the ileo-cecal valve are located at 0 and 100% of the bowel length, respectively. The two isotopes can be distinguished by the appearance of the plot: one is of histogram character and the area under this curve is hatched for increased clarity. The first test substance was infused for 4 hours, the second for the remaining one hour. In Fig. 3*a* the activity densities are given representative of animals investigated under the standard experimental conditions (^{125}I-PVP and ^{131}I-PVP, standardized test meal, 18 h starvation period, infusion of the test substance at the rate of 0.2 ml/h). Fig. 3*b* is representative of animals, in which the routinely used labels were replaced by $Na_2{}^{51}CrO_4$ and $^{99}Tc^{m}$-sulphur colloid. Note the chromium peak at the infusion site. Fig. 3*c* illustrates the case when the standardized test meal was replaced by saline. The activity density in Fig. 3*d* belongs to an animal investigated without the usual preceding starvation period. Fig. 3*e* illustrates the activity density along the GI specimen in an animal in which the test substance was infused at the higher rate (0.6 ml/h).



The activity densities in Fig. 3*d* are representative of the three animals which were investigated without a preceding starvation period. The presence of food in the stomach and small bowel does not, in a significant way, change the activity density along the small bowel.

In Fig. 3*e* data from an animal representative of the six animals in which the test substance was infused at an increased rate (0.6 ml/h) are given. The activity density was still peaky but there were no regions completely without activity, as were observed with infusion of the test substance at a rate of 0.2 ml/h (Fig. 3*a*). Apparently the increase in propagation velocity induced by infusion of the test substance at the higher rate was not coupled to an increase in the mixing.

According to Table I the variation of the experimental conditions did not appreciably affect the M values. The animals in which the test substance was infused at the higher rate seemed to have the transition point located further distally. In the other groups the numerical values of TP were closely similar.

The results of the experiments with multiple shifts of the test substances are given in Fig. 4. When the label of the test substance was changed every 20 min (Fig. 4*b*) the activity density of both labels were similar. When the time interval between the shifts was increased to 30 min, the activity densities could be distinguished better (Fig. 4*a*). Now distinct borders between regions in which one of the isotopes predominated could be demonstrated.

DISCUSSION

The similar appearance of the activity densities along the small bowel measured either with ^{125}I-PVP and ^{131}I-PVP or with ^{99}Tc^{m}-sulphur colloid, showed that all these compounds should be appropriate radiolables in the study of the propulsion and mixing of small bowel contents. Radiochro-

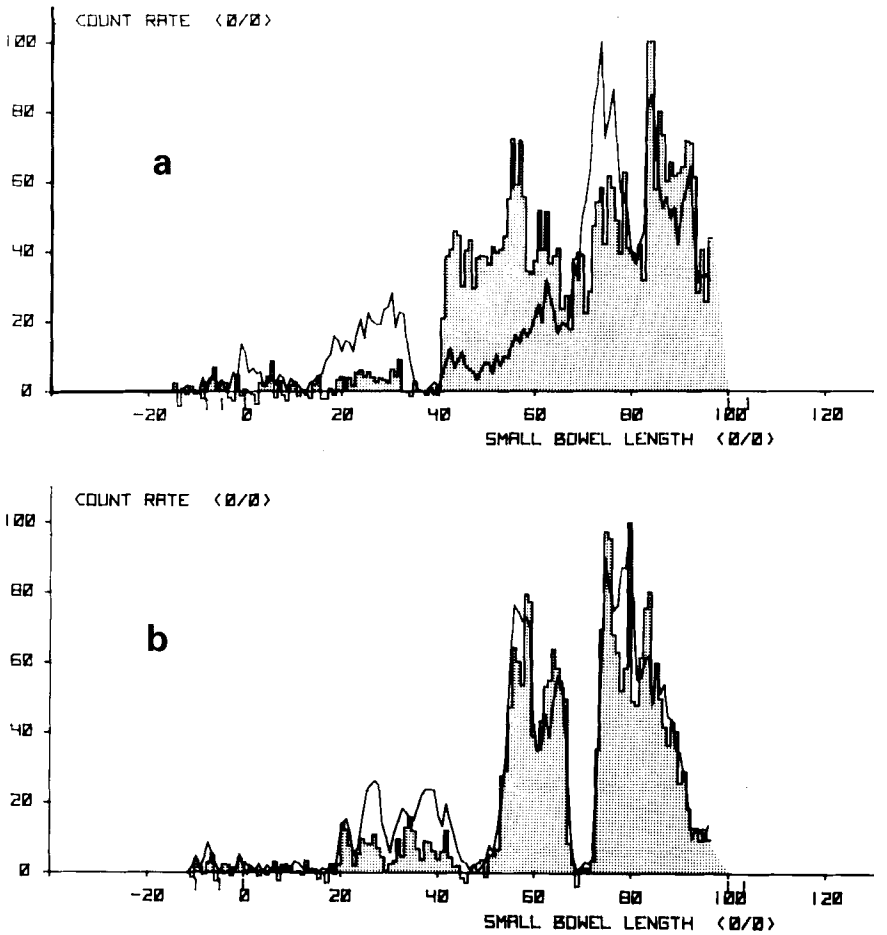


Fig. 4. Original plotter outputs of the activity density of each isotope along the GI specimen. The test substances were interchanged every 30 (*a*) and 20 (*b*) min. The rate of infusion of test substance was 0.6 ml/h.

mate, however, was found to be less suitable for studies of intestinal mixing, since a varying amount of activity was retained at the entrace of the catheter into the duodenum. When this was compensated for in the calculations it was found that the choice of nuclide did not influence the quantitative estimate of the intestinal mixing.

Replacement of the standardized test meal with saline meant a reduction in the osmolarity and a change in the chemical and physical properties of the administered test solution. The quantitative estimate of intestinal mixing was not influenced, however, as indicated by similar activity densities and similar numerical values of M and TP as compared with results obtained with the standardized test meal.

In dogs the myoelectrical pattern of the small bowel differs between "fasted" and "fed" state (10 7). As measured in the present study the quantitative estimates of intestinal mixing did not differ between fasted and fed states. Thus the presence of food in the stomach and in the small bowel does not change the motility pattern as measured by this method. It is thus difficult to correlate myoelectrical data from dog with findings concerning the net result of small bowel muscular activities in rat.

The load on the transport capacity of the small bowel was increased by infusion of the test substances at a higher rate. This was met by a faster transport of the contents and the regions completely without activity disappeared. A more thorough mixing of contents could then be expected. The minute mixing also found when the test substances were infused at the higher rate support the hypothesis that the transport of small bowel contents during physiological conditions also occurs in separate

portions which exchange material only to a limited extent.

The high rate of test substance infusion was also used in the multiple shift experiments. Distinct borders between regions in which one of the labels predominated were found when the time interval between shifts was diminished to 30 but not to 20 min.

It may be speculated that portions of small bowel contents are formed in the duodenum, at a rate of about one every 25 min. After their creation, the portions are transported isolated and the small bowel contents are not exchanged continuously between adjacent portions. Thus, the results of the multiple shift experiments support earlier conclusions regarding small bowel transport.

In conclusion I cannot resist drawing attention to the analogue between the transport of small bowel contents and the carriages in a train. The outcome of the present experiments demonstrate that this transport model is not restricted to an unphysiological experimental situation.

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