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# Oro-cecal transit time: influence of a subsequent meal

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**Abstract**

**Background** Small intestinal and oro-cecal transit time (OCTT) is determined for clinical diagnostics and research purposes. Experimental protocols used vary with respect to the inclusion of a subsequent meal during the test period. This study was conducted to elucidate whether the ingestion of a subsequent meal during the test period influences the OCTT of the test meal.

**Materials and methods** The OCTT of a liquid test meal, measured with the lactose-[$^{13}$C]ureide breath test, was compared between four groups of healthy volunteers ($n$ = 36) who consumed the subsequent meal at different time points. Also, the OCTT was determined twice in eight subjects; a subsequent meal was ingested after 180 min (test A) and after 360 min (test B).

**Results** An apparently meal-related increase in median OCTT was observed. The OCTT of the eight volunteers measured in test A (210; 210–349 median; quartiles) was significantly shorter than that found in test B (345; 300–375 min, $P$ = 0·016). As result of the ingestion of the subsequent meal at 180 min the OCTT was shortened by 90; 64–116 min in 7/8 subjects.

**Conclusion** These data indicate that the ingestion of a subsequent meal affects the OCTT of a liquid test meal. This phenomenon could be explained by the increased intestinal motility in response to a meal, and should be taken into account when designing protocols for measurements of the OCTT and in the interpretation of small intestinal absorption studies.

**Keywords** Breath test, lactose-[$^{13}$C]ureide, oro-cecal transit time, small intestinal transit time.
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## Introduction

Small intestinal transit time is measured to investigate the cause of gastrointestinal symptoms like nausea, vomiting, pain and alterations in bowel movements as well as to evaluate therapeutic interventions [1]. Also, in absorption studies the small intestinal transit time is determined, as there is evidence that the extent of digestion and absorption of nutrients, especially of carbohydrates, is influenced by the period of time they are exposed to the digestive enzymes and absorbing surface of the small intestine [2–6].

One widely applied technique to assess small intestinal transit is gamma scintigraphy. Also, breath tests are available to measure the period of time needed by the head of the meal to reach the cecum (oro-cecal transit time: OCTT), which is frequently used as an indicator of small intestinal transit time. There are several extra-intestinal factors thought to influence small intestinal transit time such as the follicular and luteal phases of the menstrual cycle [7], exercise [8,9] and smoking [8], and generally the design of intestinal transit studies tries to eliminate these influences. Experimental protocols for the measurement of the small bowel transit or OCTT vary with respect to the inclusion of a second meal. During the study period no intake of food is allowed in some studies [10,11], whereas in others a subsequent meal is permitted at a certain time point (mostly at 240 min) after ingestion of the test meal [12–15]. Consumption of a meal results in increased bowel motility [16] and we hypothesized that this might affect the rate of transit of a previously ingested meal through the gut. To examine this hypothesis, the OCTT of four groups of healthy volunteers who consumed the subsequent meal at different time points was compared. To assess the observed meal-related effect at an individual level, the OCTT of eight volunteers was then measured on a second occasion under the same conditions with only the time of ingestion of the subsequent meal varied. For measurement of the OCTT, the lactose-[$^{13}$C]ureide

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breath test was applied in this study – a test that has been shown to be a less invasive and valid alternative to scintigraphy techniques [15].

## Methods

### Subjects

Thirty-six (30 female and six male) apparently healthy volunteers (mean age 21 years, range 20–31; BMI 22·1 kg $m^{-2}$, range 15·6–28·4) with no history of gastrointestinal disorders participated in the study. They had not taken any antibiotics or laxatives during the 3 months before the test. Six females of this group, who were taking oral contraceptives, and two males were tested twice. Verbal informed consent was obtained from all subjects. The protocol of the study was approved by the Ethics Committee of the University Hospital Groningen.

### Lactose-[$^{13}$C]ureide breath test

Lactose-[$^{13}$C]ureide resists enzymatic degradation in the small intestine but is cleaved by colonic bacteria [17]. As result of the bacterial fermentation of labelled urea, $^{13}CO_2$ is released and can be measured in breath [15,18]. A rise of $^{13}CO_2$ in breath thus indicates the arrival of the head of the test meal in the cecum. To induce the enzyme activity of colonic bacteria that is necessary to cleave the sugar-ureide bond, unlabelled lactose-ureide is administered the evening before the test.

### Experimental protocol

The evening before the test 1·0 g of unlabelled lactose-ureide in 150 mL of water was taken at 20·00 h by all subjects. After an overnight fast (> 10 h) the subjects ingested 25 g of glucose dissolved in 250 mL of water with 500 mg of lactose-[$^{13}$C]ureide. The volunteers did not consume any food during the whole test period except for the subsequent meal. Water and tea without milk and sugar were allowed to be taken from 2 h after intake of the test meal onwards. During the test period the volunteers remained seated and refrained from smoking.

Breath was sampled by breathing through a straw into 10-mL exetainers. Two breath samples were collected before ingestion of the test meal. During 9 h (7 h in the second test) after intake of the test meal breath samples were collected every 15 min.

The subsequent meal consisted of two bread rolls with ham or cheese and one glass of milk (415 kcal of which 52% were derived from carbohydrates, 22% from protein, 27% from fat) and was consumed within 15 min. In the first test 11 subjects ingested the subsequent meal 180 min, nine subjects 240 min, eight subjects 300 min and eight subjects 360 min after intake of the test meal.

From each group that received the subsequent meal at 180 min and at 360 min, four subjects took part in a second test. This test was conducted under the same conditions as the first one, only the time of intake of the subsequent meal was changed. Subjects who had first consumed the subsequent meal at 180 min received it at 360 min in the second test and vice versa.

### Analytical methods

$^{13}$C abundance in breath $CO_2$ was determined by gas isotope ratio mass spectrometry (IRMS) (Breath MAT, Finnigan MAT, Bremen Germany) measuring the $^{13}C/^{12}C$ ratio as $\delta^{13}C$ vs. Pee Dee Belemnite Limestone ($\delta^{13}C_{PDB}$) in per mill.

The OCTT was defined as time elapsed between ingestion of the test meal and a sustained (more than three time points) rise of $\delta^{13}C_{PDB}$ more than 2·0‰ above baseline.

### Statistics

Data are expressed as median with quartiles. The Kaplan-Meier log-rank test for linear trend was applied to test whether there was a linear trend in OCTT across the four groups who received the subsequent meal at increasing time intervals. Differences between the OCTT results of the group of volunteers tested twice were assessed with the Wilcoxon signed rank test. The analyses were performed with the statistical program SPSS 11·0 for Windows software (SPSS inc., Chicago, IL). $P < 0·05$ was considered to be significant.

## Results

### Effect of subsequent meals on different time points in four groups of volunteers

In all but two volunteers (group subsequent meal at 300 min) an increase in breath-$^{13}CO_2$ was measured during the study period. The median (quartiles) OCTT of the groups with a meal after 180, 240, 300 and 360 min was 225 [210–390], 270 [195–338], 323 [240–434] and 345 [259–432] min, respectively [Fig. 1, Table 1].

The OCTT tended to rise with increasing time interval between intake of the test meal and the subsequent meal: $P = 0·054$ for linear trend across the groups with an intake of the subsequent meal at 180, 240, 300 and 360 min and $P = 0·036$ for linear trend across the first three groups. These results were obtained on the assumption that the OCTT of the two nonresponders lay beyond the study period of 540 min and consequently their data were censored.

### Effect of subsequent meals on different time points in eight volunteers

The OCTT of the eight volunteers who ingested the subsequent meal after 180 min and on another occasion after

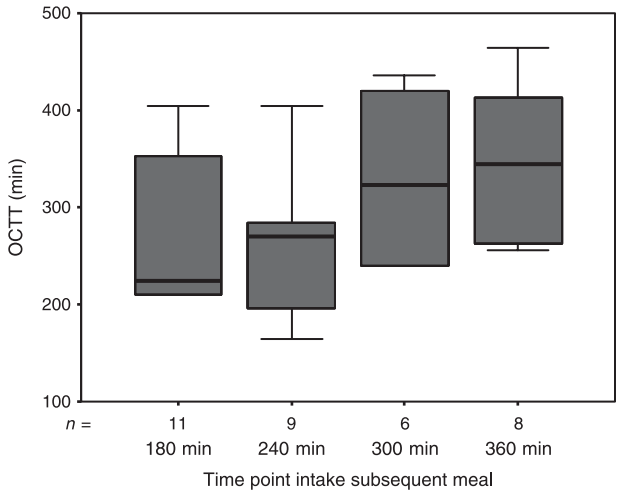


**Figure 1** Oro-cecal transit time (OCTT) of four groups of subjects who consumed a subsequent meal 180, 240, 300 and 360 min after intake of the test meal.

360 min were significantly different between both tests ($P = 0{\cdot}016$). The median (quartiles) OCTT in the test with the early meal (180 min) was 210 [210–349] min and 345 [300–375] min in the test with the late meal (360 min). In all but one volunteer the OCTT was shorter in the test with the meal at 180 min after intake of the test meal [Table 2, Fig. 2].

## Discussion

Measurement of the small intestinal transit time is of interest for clinical diagnostics and research purposes. It is determined for the diagnosis of gastrointestinal motility disorders and the evaluation of therapeutic interventions. Also, the small intestinal transit time is frequently examined in relation to the rate and extent of digestion and absorption of nutrients.

To obtain reliable results the influence of extra-intestinal factors that might affect small intestinal transit time should be minimized during tests. Various studies describe the inclusion of a subsequent meal during the test period of the measurement of small bowel transit time and OCTT. Despite indications that the consumption of a meal might affect the transit time of the test meal [13,19], this phenomenon has not, to our knowledge, been studied until now.

We observed an apparently meal-related increase in median OCTT across four ($P = 0{\cdot}054$) and three ($P = 0{\cdot}036$) groups of volunteers by using a censored data set. Our assumption that the absence of a rise in breath-$^{13}CO_2$ in two subjects

**Table 1** Oro-cecal transit time (OCTT) of four groups of subjects who consumed a subsequent meal 180, 240, 300 and 360 min after intake of the test meal

| Meal taken after | 180 min | 240 min | 300 min | 360 min |
|---|---|---|---|---|
| OCTT (min) | 210* | 165 | 240 | 255 |
| | 210* | 195 | 240 | 255 |
| | 210* | 195 | 300 | 270 |
| | 210 | 270 | 345 | 330* |
| | 210 | 270 | 420 | 360* |
| | 225 | 270 | 435 | 375* |
| | 300 | 285 | No response during 9 h of measurement | 450 |
| | 315* | 390 | No response during 9 h of measurement | 465* |
| | 390 | 405 | | |
| | 405 | | | |
| | 405 | | | |
| Median | 225 | 270 | 322·5 | 345 |

*OCTT of subjects who took part in the second test.

**Table 2** Oro-cecal transit time (OCTT) of eight subjects (A–H) who consumed a subsequent meal 180 and 360 min after intake of the test meal

| | OCTT (min) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Ingestion meal at | A | B | C | D | E | F | G | H | Median |
| 180 min | 210* | 210* | 210* | 210 | 210 | 315* | 360 | 375 | 210† |
| 360 min | 285 | 300 | 300 | 330* | 360* | 375 | 465* | 375* | 345† |
| Difference OCTT | 75 | 90 | 90 | 120 | 150 | 60 | 105 | 0 | 90 |

*Results of first test.
†Significantly different, $P = 0{\cdot}016$.

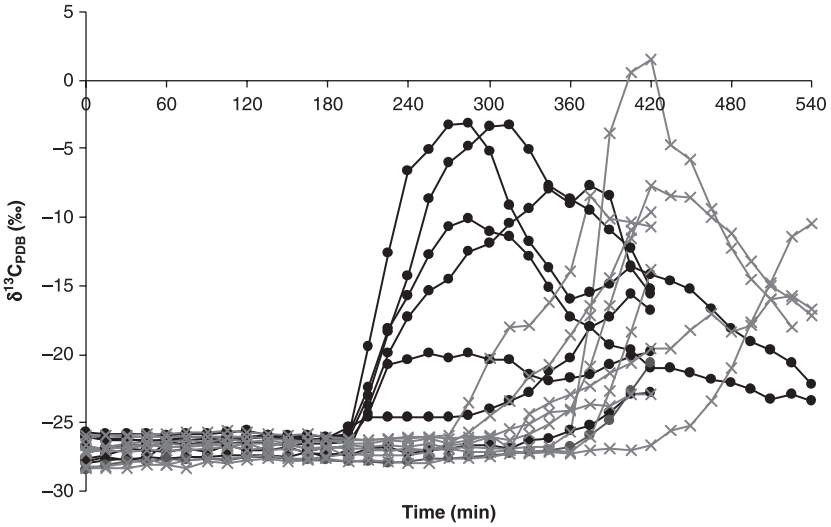


**Figure 2** Breath $^{13}C$ response in eight subjects with a subsequent meal consumed 180 min (—●—) and 360 min (—×—) after intake of the test meal.

was the result of our relatively short study period seems justified, as in the literature to date no $^{13}CO_2$ nonresponders have been reported in studies where the sampling period exceeds 9 h [15,20–22]. Evidence for a meal-dependent effect on the transit time is stronger, as the group receiving the subsequent meal after 360 min is excluded. This is plausible because it can be expected that as the subsequent meal is taken late, a meal-independent rise in breath-$^{13}CO_2$ is more likely to occur.

To confirm the observed meal-dependency, eight volunteers were tested on a second occasion. Their OCTT measurement in a test with an early subsequent meal (180 min after intake of the test meal) was compared with that found in a test with a late subsequent meal (at 360 min). Our results show that the OCTT of the test meal was shortened by ingestion of an early subsequent meal during the test period. This observation could be explained by the increased motility of the gastro-intestinal tract following the entrance of food into the stomach [16]. Scintigraphic studies have shown that dietary residues and liquid-phase markers accumulate in the ileum and are transferred into the cecum in bolus movements across the ileocolonic junction [13,19,23–25]. A study conducted by Camilleri *et al.* showed that out of a total of 46 bolus transfers observed during an 8-h test period in 20 subjects, 21 [46%] occurred within the first hour after ingestion of a meal (at 240 min) [19]. Similar results were reported by Bennink *et al.* who observed 13/24 [54%] bolus transfers ($n$ = 12) within the first hour after a meal [13]. However, it remained unclear in these studies whether the meal was indeed the cause of the bolus movements, as no control studies without administration of a subsequent meal were conducted.

In our study the arrival of the head of the meal in the cecum was indicated by the rise in breath-$^{13}CO_2$. Five out of eight volunteers tested twice responded with an increase of $^{13}CO_2$ in breath within 1 h after the meal taken 180 min after the test meal. After administration of the subsequent meal at 360 min the OCTT was prolonged by 60–150 min in 7/8 volunteers [Table 2]. The faster OCTT observed in the test with the early meal can thus be related to the ingestion of the subsequent meal in 5/8 volunteers. It could be speculated that in the remaining 2/7 cases of accelerated transit no marker was present in the ileum at the time the subsequent meal was consumed, explaining the absence of a direct (within 1 h) response to the meal. In the test with the late subsequent meal, $^{13}CO_2$ in breath increased before intake of the meal in 5/8 cases. These early and obvious meal-independent rises thus indicate spontaneous bolus transfers. The recordings of slow OCTT (360–465 min, Tables 1 and 2) in our study imply that administration of a subsequent meal even as late as 360 min after ingestion of the test meal might interfere with the transit measurements in some cases.

To summarize, our data show that consumption of a subsequent meal during the test period can influence the rate of transit of a previously ingested liquid meal through the gut. This should be taken into account when designing studies to measure the OCTT and in interpretation of small intestinal absorption studies.

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