What is the Meaning of Colorectal Transit Time Measurement?

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This study was done to understand the different available methods used to calculate colorectal transit times. A single abdominal radiograph is taken following six successive daily ingestions of the same number of identical radiopaque markers. This method correlates well ($P < 0.001$) with that using a single ingestion of markers with daily x-ray films until total expulsion. In techniques used to measure colorectal transit time with multiple ingestion of markers, the number of days of ingestion depends on the kinetics of marker defecation. This was found to differ markedly in various groups of control subjects and constipated patients ($P < 0.001$) and can be used to obtain reliable data, even in subjects with severe constipation. When they ingest 20 markers, constipated patients are found to retain eight or more markers three days after ingestion, and taking a plain film of the abdomen on that day is sufficient to make a diagnosis of constipation. Transit time studies are reproducible from month to month in patients with an irritable bowel syndrome. Control subjects who claim that their bowel habits are not modified by stress have shorter transit times, similar in both sexes, than those who say they are ($P < 0.001$). This may explain why a large percentage of constipated patients have been found by most authors to have "normal" colorectal transit times. The choice of control subjects is thus a key element in studies of functional bowel motor disorders. Stool frequency and consistency, in health, correlate only to rectosigmoid transit time. [Key words: Colon; Colonic transit time; Methodology; Modelization]

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The best information about colorectal function in constipation has been derived from ingested radiopaque marker studies.[1] These are counted in stools[2] or on plain films of the abdomen.[3–6] Calculating the mean transit time of a single radiopaque marker permits one to distinguish segmental activity in the different parts of the large bowel.[5] These studies have shown that stool frequency does not correlate to colorectal transit time,[7, 8] and this is because the latter also takes individual stool weight into account. Recent studies have focused on a practical goal: reducing the amount of radiation exposure. The basic principle has been to multiply the frequency of marker ingestion and concomitantly decrease the frequency of radiograph-taking, with the use of multiple films[9, 10] or a single film.[11, 12] These studies, even if they compare well with that using daily films,[5] are open to a number of criticisms. Steady-state conditions of marker intake and output after three days of ingestion only[9, 10] may not have been reached within such a short period of time. In those studies that did use a prolonged period of ingestion of markers in the hope of reaching these necessary steady-state conditions,[11, 12] segmental transit time was not always calculated,[12] and an empirical approximation was used to determine the number of days of ingestion; this may not be valid in all groups of patients. The use of different types of markers to evaluate retrograde movement is based on the major assumption that the transit time of a single radiopaque marker is reproducible from day to day.[9, 10] Because defecation frequency is not as autonomous as colorectal function, the correlation between the multiple markers and the multiple film techniques decreases as one progresses along the bowel and, for the same reason, is better in constipation than in health.[5, 9, 10] When a single film is taken it is impossible to evaluate the change in distribution of markers on a day-to-day basis. This may be pertinent, since reflux of markers from

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distal to more proximal colon is associated with differences in personality and psychophysiologic relationships[13] and probably with retrograde movement of propagating electrical activity in the large bowel.[14, 15] Finally, in the single[10] or triple[9] film-multiple marker ingestion techniques, the dispersion of data is noticeable and its significance has not been explored.

Many patients, who complain of constipation, have normal colorectal transit times.[1, 6, 14, 16-22] The transit studies identify patients who deny having a bowel movement.[6, 20] In the others, diagnosis of a "normal" transit time rests on the choice of "normal" subjects serving as controls. More than 50 percent of people in the general population respond to stress by a change in bowel habits and/or abdominal pain.[23] Moreover, some parameters of personality influence bowel habits[24]; this is not usually taken into account in the selection of healthy subjects and is important since constipated patients with "normal" transit times have more psychopathology than those with slow-transit constipation.[21] Thus, more refined studies of the colorectal transit times of control subjects are in order.

The aim of this study is to explore different aspects of the techniques used to measure segmental colorectal transit times, in order to better understand the meaning of these measurements.

First, is it possible to detect constipation in a simplistic way, using a single ingestion of markers and a single abdominal x-ray?

Second, is it possible to measure segmental and total colorectal transit times, with prolonged ingestion of a single type of radiopaque marker and taking of a single abdominal x-ray, during steady-state conditions between intake and output?

Third, is the measurement of colorectal transit times reproducible?

Fourth, does stress influence bowel function of healthy subjects, and how should normality be defined?

Finally, is there a correlation between colorectal function and stool characteristics?

MATERIALS AND METHODS

Population

Among the three institutions involved in the study, a total of 174 subjects (109 patients and 65 controls) have been investigated (Table 1). No statistically significant difference was found for any of the variables among the three medical centers; therefore, all data were pooled.

Table 1.
Population

	Type of Subjects	Males	Females	Total
Controls:	Healthy controls	15	17	32
	Stress-free controls	14	19	33
Patients:	Irritable bowel syndrome	10	44	54
	Colonic inertia	—	8	8
	Hindgut dysfunction	—	13	13
	Outlet obstruction	1	10	11
	Constipation with normal transit	5	18	23

Sixty-five control subjects were evaluated and recruited through a newspaper advertisement from the general population. Thirty-two subjects were asymptomatic, had a completely negative physical examination, and had always been in good health. Thirty-three other subjects were retained for the study, because, in addition to these same criteria, they also claimed that stress did not modify in any way their bowel habits (toward constipation or diarrhea) and did not trigger abdominal pain.

Fifty-four consecutive patients with an irritable bowel syndrome were evaluated. A full evaluation[1] failed to yield an organic cause to their complaint. By clinical scoring, they were all diagnosed as suffering from irritable bowel syndrome.[25]

Fifty-five consecutive patients with chronic idiopathic constipation were divided into four different groups according to published criteria[1]: colonic inertia: transit time is prolonged in the ascending colon; hindgut dysfunction: transit time is prolonged in the descending colon, but normal in the ascending colon; outlet obstruction: transit time is prolonged in the rectosigmoid area, but normal in the right and left colon; constipation with normal transit: colorectal transit times fall within "normal" limits.

This classification, of course, is heavily dependent on the criteria used to define normality. For the purpose of this part of the present study, "normal" values were set at 37, 26, 41, and 88 hours, respectively, for transit in the ascending, descending, rectosigmoid, and entire large bowel of adults. These values were obtained from the 32 healthy controls (Table 2).

The sex ratio distribution is different between those patients who claim to be constipated and have a delay in colorectal transit, as exemplified

Table 2.
Colorectal Transit Times in Stress-Free Controls and Healthy Controls (Mean ± SE; Calculated Range,* in Hours)

Site	Stress-Free Controls	Healthy Controls	*P* Value
Right colon	7.3 ± 1.2 (0–20)	12.3 ± 2.2 (0–37)	NS
Left colon	4.2 ± 0.8 (0–14)	9.1 ± 1.5 (0–26)	<0.02
Rectosigmoid segment	9.2 ± 1.4 (0–25)	13.3 ± 2.4 (0–41)	NS
Total	20.7 ± 1.9 (0–43)	34.7 ± 4.7 (0–88)	<0.01

* Values of range have been rounded up, from mean ± 2 SD.

by marker studies (practically all are females), and those patients who claim to be constipated but have "normal" transit time (22 percent of these subjects are males) ($P < 0.05$).

Measurement of Total and Segmental Colonic Transit Time with One Type of Marker and Daily Abdominal x-Ray Films

Twenty radiopaque markers within a gelatin capsule (M1) (SITZMARKS®, Konsyl Pharmaceuticals, Inc., Fort Worth, TX) were ingested on day 0 at 9 AM. Starting the next day, a plain film of the abdomen was taken every day, at 9 AM, until all markers were defecated, and never beyond seven days.[5]

Markers were localized and counted every day in the different segments of the large bowel according to bony landmarks, as previously described.[4–6] The spinal column served to separate the right from left colon; the pelvic inlet separated the rectosigmoid area from the left colon. In order to diagnose constipation without having to calculate transit time, a day-to-day comparison was done every day between constipated patients and controls. This was done with the hope of finding a discriminating number on a single x-ray.

Segmental and total colorectal transit times were calculated according to the distribution of the markers, in the different segments of bowel, over successive days. This was done with the formula we previously validated:

$$TT = 24 \times \Sigma n_i / 20 = 1.2 \times \Sigma n_i,$$

where n_i is the number of markers on day i in the studied zone and TT is the mean transit time of a single marker in a given site.[5]

All subjects had been eating, for at least two weeks prior to the study, a diet rich (30 g/day) in dietary fiber and remained on this diet during the marker study.

Control subjects counted their stools in a diary and indicated their consistency (hard; normal; soft) for a minimum of a month while remaining on the same diet. This evaluation was not done in constipated patients because of the wide spectrum of stool frequency in patients; it would have caused markedly different variances, difficult to compare unless the diary would have been prolonged for several months.

Validation of the Measurement of Total and Segmental Colonic Transit Time with One Type of Marker and One Abdominal X-ray Film

Twenty-six consecutive patients, aged 21 to 72, with an irritable bowel syndrome ingested 10 radiopaque markers of another kind (M2) at 9 AM on six consecutive days. The first day they also ingested 20 markers of the first type (M1), as used in the technique described above. An abdominal x-ray film was taken daily at 9 AM until the disappearance of M1 from the film and the day after the last ingestion of M2 (Fig. 1). No patient had any marker M1 on the last film.

For M1, segmental and total colonic transit time was calculated as previously described. For M2, segmental and total colonic transit time was calculated by:

$$TT = 24 \times n/10 = 2.4 \times n,$$

where n is the number of M2 markers on the studied zone, on the last film. The difference between 2.4 and 1.2 in the first method is due to the fact that here, only 10 M2 markers were ingested. This was done in order to diminish the number of markers in the abdomen and make analysis easier in severely constipated patients. The principle of the equivalence between the two methods of measure is indicated in Figure 2.

Reproducibility of the Measurement of Colorectal Transit Times

Twenty-eight other patients with irritable bowel syndrome underwent twice, a month apart, in random order, a study of colorectal transit time. One study was done, with the single marker ingestion, multiple-films technique, as described above.[5]

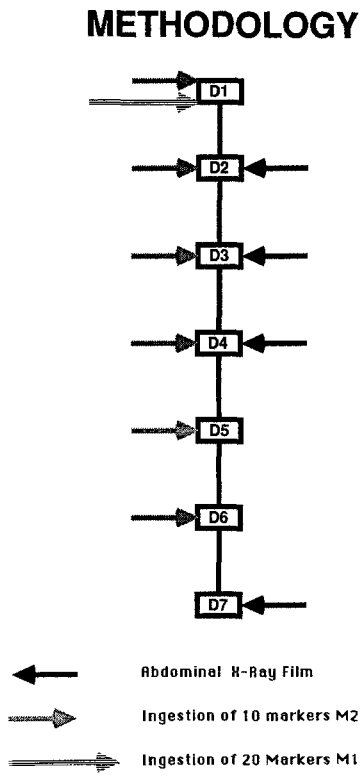

Figure 1. Comparison of two methods to measure colorectal transit time. Ten radiopaque M2 markers are ingested every day for six days, and 20 radiopaque M1 markers are ingested only once on the first day. A film of the abdomen taken on the seventh day allows calculation of the transit times from M2 marker distribution (see text). In this example, all M1 markers had been defecated by day 4 (D4), and, therefore, no films had to be taken on days 5 and 6. Calculation of transit time with the single ingestion-multiple films technique[5] is obtained from data on the film of days 2, 3, and 4.

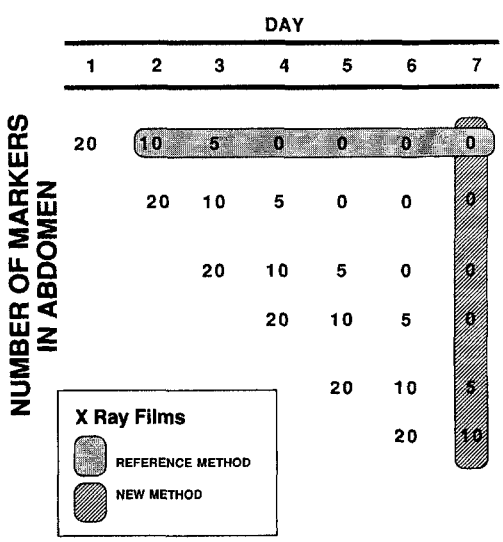

Figure 2. Equivalence of the methods of measurement. The reference method[5] uses a single ingestion of 20 markers followed by daily abdominal x-rays. The method described here uses a single film subsequent to repeated ingestion of markers.

The other one was done with the multiple marker ingestion, single-film technique also described above. The latter was also used in an ongoing study of evacuation patterns.

Data Analysis

Comparison of data was made, using analysis of variance (ANOVA) with repeated measurements.[26] The design of ANOVA included one subject factor and one within factor, time with multiple measures. Comparison between the two groups (normal *vs.* constipated patients) was made with another factor, the group. Day-to-day comparisons were made with the Student-Newman-Keuls test. This analysis was made under SAS 5.16 software (SAS Institute Inc., Cary, NC).

Regression was calculated between the number of markers on day i N(i) and the time between the ingestion (i) according to the law:

$$N(i) = 20 \times \exp(-(i/T)^k),$$

where T is the time constant of the decreasing curve and k the exponent coefficient of this decrease.

To determine the time necessary to reach steady-state conditions between ingestion and output of markers, a model of the decrease in number of markers was calculated with the Weibull law.[27]

Wilcoxon signed-rank was used for comparison of paired values; Spearman rank correlation coefficient was used for the correlation between quantitative variables; nonlinear regression and discriminant analysis were made under STATITCF 4.0 software (STATITCF, Boigneville, France).

The ethics committees of the involved institutions approved the protocol. Informed consent was obtained from all subjects.

RESULTS

Simple Discrimination Between Health and Constipation

A plain film of the abdomen taken three days after ingestion allows one to make a reliable diagnosis of constipation in 100 percent of cases. Constipated patients had eight or more markers on this day. Table 3 shows that it is on this day that the greatest difference in average is found as compared with healthy controls as well as stress-free controls, and that it is very significant.

Table 3.
Markers in the Abdomen in Healthy Subjects and Constipated Patients (Mean ± SD)

	Day After Ingestion of 20 Markers					
	1	2	3	4	5	6
Stress-free controls	12.9 ± 6.4	4.0 ± 4.3	0.4 ± 1.2	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Healthy controls	15.3 ± 6.2	8.0 ± 7.8	3.7 ± 6.3	1.7 ± 4.2	0.4 ± 1.9	0.3 ± 1.4
Constipated patients with delayed transit	19.8 ± 0.7	19.1 ± 2.1	18.2 ± 2.7	12.3 ± 7.9	9.8 ± 7.3	7.5 ± 7.6
Constipated patients with normal transit	16.0 ± 5.8	8.3 ± 7.2	1.7 ± 2.0	0.5 ± 0.9	0.2 ± 0.5	0.0 ± 0.2
	t Value Between Constipated Patients with Delayed Transit*					
Stress-free controls	6.01	17.80	34.10	8.85	7.60	5.60
Controls	4.10	7.86	11.99	6.74	7.03	5.31
	t and *P* Values Between Constipated Patients with Normal Transit					
Stress-free controls	1.84	2.58	2.77	2.79	2.01	1.00
	NS	$P < 0.02$	$P < 0.01$	$P < 0.01$	$P < 0.05$	NS
Controls	0.41	0.16	1.65	1.52	0.52	0.81
	NS	NS	NS	NS	NS	NS

* For this comparison, only constipated patients with delay in transit time of radiopaque markers are included. All values are significantly different at $P < 0.001$ from those obtained in stress-free and healthy controls.

Validation of the Measure of Total and Segmental Colonic Transit Time with One Type of Marker and One Abdominal X-ray Film

In the 26 subjects, who had simultaneously both types of measure, there was a very significant correlation between the two techniques used to measure segmental and total colonic transit time. Spearman's coefficient was r = 0.703 ($P < 0.001$) for the right colon, r = 0.700 ($P < 0.001$) for the left colon, r = 0.664 ($P < 0.001$) for the rectosigmoid area, and r = 0.688 ($P < 0.001$) for the total colonic transit time (Fig. 3). Individual values were compared two by two, and no significant difference was found between the two methods (t = 0.50 for the right colon, 1.13 for the left colon, 1.42 for the rectosigmoid segment, and 0.30 for the entire large bowel).

Modelization of the Decrease in Number of Markers

Parameters characteristic of the decreasing curves of markers appear in Table 4. Curves shown in Figure 4 are calculated (and not measured) from these parameters. The greatest variations are in the T parameter ranging from 1.55 in the stress-free group to 8.22 in the colonic inertia group. The spread in variance in the colonic inertia group is much greater than in the other groups and demonstrates more heterogeneity.

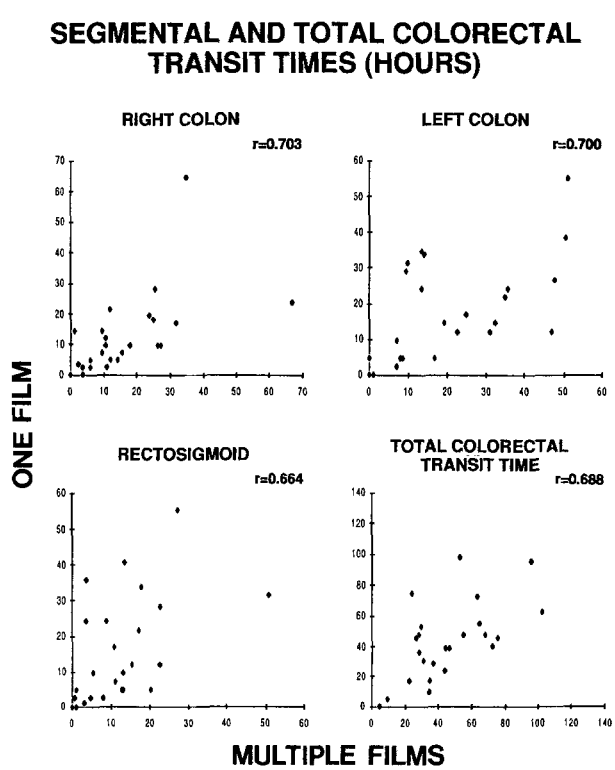

Figure 3. Relationship between the two methods used for the measurement of segmental and total colonic transit times.

Reproducibility of Colorectal Transit Times

In the 28 patients who had asynchronous measurements, transit times were similar at first and second examination. Differences between them

Table 4.
Model of Decrease in Number of Markers (Parameters)

Groups	k (Mean ± 2SD)	T (days) (Mean ± 2SD)
Stress-free controls	1.89 ± 0.43	1.55 ± 0.12
Healthy controls	2.09 ± 0.65	2.06 ± 0.20*
Constipation with normal transit	2.11 ± 0.56	2.08 ± 0.18*
Colonic inertia	1.78 ± 1.37	8.22 ± 3.68*
Hindgut dysfunction	2.61 ± 1.06	5.02 ± 0.57*
Outlet obstruction	3.58 ± 1.45	6.33 ± 0.59*

* $P < 0.05$ as compared with stress-free controls.

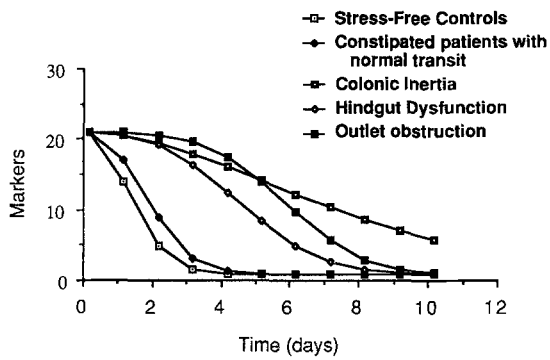

Figure 4. Decrease in the number of markers in control subjects and constipated patients, according to groups (curves are calculated from parameters obtained from real data).

were found to be (mean ± SEM) 2.1 ± 2.9, 0.34 ± 2.2, 1.54 ± 2, and 0.21 ± 5.5 hours, respectively, in the right colon, left colon, rectosigmoid area, and entire large bowel (P = NS). Thus, both the multiple marker-single x-ray and single marker-multiple x-ray studies provided similar results, and, because of the random order, the first transit study did not differ from that performed a month later. The correlation coefficients were of the same order as for the synchronous studies described above: r = 0.587 ($P < 0.001$) for the right colon, r = 0.773 ($P < 0.001$) for the left colon, r = 0.547 ($P < 0.01$) for the rectosigmoid area, and r = 0.657 ($P < 0.001$) for the colon and rectum.

Comparison of Healthy Subjects, Stress-Free Controls, and Constipated Patients with "Normal" Transit Time

Constipated subjects with "normal" transit time were compared with healthy subjects whose bowel habits are not changed by stress. Table 3 shows that they retain significantly more markers than stress-free controls from day 2 to day 5 after ingestion. The slopes of decrease in markers for both groups are significantly different ($P < 0.001$): the T parameter (time constant of the decreasing curve) is significantly different in the two groups ($P < 0.05$) (Table 4). In contrast, there was no difference between the group of healthy subjects who were not asked whether or not they were sensitive to stress and the group of constipated patients with "normal" transit (Table 3).

This conclusion from analysis of number of markers was confirmed when transit times were calculated. Table 2 provides values of upper range that can be used in clinical practice on single patients. The main difference between the two groups is in the left colon, where transit is significantly prolonged when subjects are not immune to stress.

Discriminant analysis was used, as done previously,[13] to sort our stress-free controls, "healthy" controls, and constipated subjects with "normal" transit, in order to subdivide "healthy" controls into two groups. This analysis classified 44 percent of "healthy" subjects as being "constipated," the other 56 percent being similar to the stress-free controls, and thus demonstrates the heterogeneity of the "healthy" control group.

There was no sex difference in transit time, either among subjects or among stress-free controls.

Relationship Among Stool Frequency, Stool Consistency, and Colorectal Transit Times in Healthy Subjects

There was a significant correlation between rectosigmoid transit time and the number of days without defecation (r = 0.531; $P < 0.01$), as well as with the number of days with at least one stool (r = −0.501; $P < 0.01$) or stool frequency (r = −0.366; $P < 0.05$). There was no correlation between defecation pattern and right or left colon transit time.

If subjects had often hard stools, they also recorded a greater number of days without defecation (r = 0.427; $P < 0.02$) and the occurrence of hard stools correlated to rectosigmoid transit time (r = 0.317; $P < 0.05$). Conversely, if subjects recorded more soft stools, they were less likely to skip a day without defecation (r = −0.372; $P < 0.05$). There was a negative correlation between frequency of normal stools and that of soft stools (r = −0.853; $P < 0.001$). It appears that "normality" is thus having "normal" to "hard" stools, but not "soft" stools.

DISCUSSION

This study provides some information about the usefulness and the meaning of counting radiopaque markers during gastrointestinal transit and of calculating colorectal transit times from their numbers.

A simplistic method to assess constipation is described: a single ingestion of markers is followed by the taking of a single film of the abdomen, the patient is constipated.

This study also describes a technique of measurement of colorectal transit times which minimizes radiation, is comparable to a previously validated technique, is reproducible, and is simple enough to obtain reliable data in subjects with severe constipation and prolonged transit times. X-raying stools after ingestion of radiopaque markers eliminates radiation to the patient but does not evaluate segmental colonic transit.[4, 28] Recent techniques,[9-12] and that described here, using multiple ingestions of markers, allow one to both minimize radiation and obtain segmental transit times. In contrast to previous studies,[9, 10] in the method proposed in this paper, steady-state conditions between intake and output of markers were looked for by having subjects injest a bolus of markers every day for a longer period of time, *i.e.*, for six days. Other authors have insisted on the importance of having such an equilibrium,[11, 28] but the determination of the duration of ingestion period was purely empirical. With the modelization of colonic transit time, the day t where the number of markers N is negligible, *i.e*, inferior to 1, can be calculated with the following formula:

$$N < 1 <=> t > T \times [\mathrm{Log}(10)]^{1/k},$$

where T is the time constant of the decreasing curve and k is the exponential coefficient of this decrease (Table 4). The mean value of time is 2.4 days for the stress-free controls, 3.1 days for the normal group and constipated subjects with "normal" transit, but 6.9 days for patients with hindgut dysfunction, 8.0 days for those with outlet obstruction, and 13.1 days for those with colonic inertia, if 10 markers are ingested. The value of ingesting markers for six days in this study thus only permits a good evaluation of subjects who do not have delayed colonic transit (colonic inertia, hindgut dysfunction, or outlet obstruction). In this group, the application of the Nyquist rate, used to measure the duration of a temporal phenomenon, is in order and requests that measurement of an event duration should be done over a period of time that is at least twice the duration of this event.[27] Thus, markers should be ingested for at least 14 days (2 × 6.9) in hindgut dysfunction, 16 days (2 × 8) in outlet obstruction, and 27 days (2 × 13.1) in colonic inertia. The number of markers to be counted on the single film may become considerable. If five markers are ingested every day, using the same formula, ingestion of markers may be reduced to three weeks (2 × 10.7) in colonic inertia and two weeks in hindgut dysfunction (2 × 6.0) and outlet obstruction (2 × 7.2). These transit times, up to now, could not be calculated and used for statistical analysis, because all that could be said was that they actually exceeded a given measured value.[8, 13, 19]

A comparison of the various available methods used to measure colorectal transit times is in order. The technique of single ingestion of a bolus of markers with multiple daily films[5] measures the mean transit time of one single marker. In contrast, all other techniques, including the present one, using multiple ingestions of markers with single film provide data on a mean transit time, made of successive mean transit times of one single marker already shown to vary from day to day.[10, 28] It is thus not surprising that the correlation coefficient is only 0.7, and this explains less than 50 percent of the variance of the measured values (0.7 × 0.7). This is rather constant and does not vary much from site to site, being maximum in the right colon and minimum in the rectosigmoid segment.[9, 10] This results from the imprecision of the measurement, which is amplified when a three-day study is performed.[9, 10] In the method proposed in the present study, correlation with the daily ingestion of markers is independent from the site of measurement. This results from the prolonged ingestion of markers, six days, which minimizes the influence of time of defecation, a voluntary act. Ingestion of pellets during three days only maximizes the importance of day 3, which is the more discriminant day, as proven in the present study. The technique of multiple daily films permits one to detect patients who deny defecation, by confronting a diary where no stool is reported, with clear evidence on the film of that day of a decrease in the number of markers. Similar information can be obtained with the techniques using multiple ingestions of markers and a single film: if patients claim they did not

defecate at all, all ingested markers should be present on the abdominal x-ray film. However, if patients claim they defecated only once, for instance, and the x-ray film confirms that some of the ingested markers have been defecated, it is impossible to know with the single-film technique whether they actually defecated more than once.

This study provides a demonstration that, although quite variable, colorectal transit times remain stable over a period of one month in untreated patients with an irritable bowel syndrome. This information is of paramount importance in order to appreciate the effects of treatment on the course of disease in patients with constipation. However, correlation coefficients are slightly less than in synchronous studies, and it indicates that colorectal transit of patients with an irritable bowel syndrome is likely to fluctuate with time. It must be noted, however, that the calculations of the confidence intervals of the correlation coefficients between the two types of methodology in this study, and the two previously published ones,[9, 10] are overlapping.

Healthy controls or stress-free controls? Constipated patients with "normal" transit do not differ from the former but do from the latter. This is ample demonstration that the question is not theoretic. Such patients are likely to be rejected as faking disease, and it is not surprising to learn that they consume psychotropic drugs, are involved in medicolegal litigation,[17] and have a lot of psychopathology.[21] In this study, half of the "healthy" subjects had a motor pattern which could not be differentiated from that of constipated patients with "normal" transit. This probably explains why, as a group, they had a delayed transit in the left colon only, as compared with stress-free controls. We know that a large percentage of subjects in the general population have symptoms of an irritable bowel syndrome and that the majority of them respond to stress by a change in bowel habits and/or abdominal pain.[23] Is this why some "healthy" controls were indistinguishable from constipated patients with "normal" transit? Is it "normal" to react to stress with changes in bowel habits and abdominal pain? At minimum, it may be concluded that, in studies dealing with bowel motor dysfunction, control subjects should be described more carefully, in positive terms, rather than simply as "not sick." In addition, this raises the critical issue of what constitutes a "normal" range of colorectal transit times. It can be readily seen from Table 5 that values of overall colorectal transit times obtained in our healthy controls (88–93 hours) appear superior to those obtained elsewhere (67–76 hours)[9, 29, 30] but that values obtained in our stress-free controls appear markedly inferior. Therefore, we have compared constipated patients with "normal" transit, healthy controls, and stress-free controls, taking 70 hours as the upper limit of the normal range. Table 6 shows that constipated patients with "normal" transit still have a slower transit than stress-free controls but also have a slower transit than healthy controls with transit time below 70 hours; yet the two groups of controls are now similar. This comparison permits us to conclude that differences in normal range from center to center probably result from the variable percentage of subjects with vulnerability to stress, in terms of bowel habits and abdominal pain, that are included among controls; one could argue from the present study that we have presented the extremes, *i.e.*, a group with a lot of subjects responding to stress, more so than in other institutions, and a group with none, in contrast to other authors.

No difference in transit time was found between

Table 5.
Maximal "Normal" Transit Time in the Colon and Rectum (Mean ± 2SD†, in Hours)

Site	Chaussade[9]	Metcalf[29]	Hinds[30]	Arhan[5]	Bouchoucha (present study)	
n	22	73	31	38	32	33
Right	24	32	24	38	37	20*
Left	30	39	32	37	26	14*
Rectosigmoid	44	36	45	34	41	25*
Colon and rectum (total)	67	68	76	93	88	43*
Technique	Multiple ingestion		Single ingestion			

* Stress-free controls (see text).

† Except for data from Arhan's study, which are not calculated from a Gaussian curve but are the maximal experimental values.

Table 6.
Comparison Between Constipated Patients with "Normal" Transit and Control Subjects (Upper Normal Value is 70 Hours)

Day	Number of Radiopaque Markers (Mean ± SE)						
	Constipated		Healthy		Stress-Free		Constipated
1	16.0 ± 1.2	$t = 1.13$ NS	14.2 ± 0.9	$t = -0.89$ NS	12.9 ± 1.1	$t = 1.84$ NS	16.0 ± 1.2
2	8.3 ± 1.5	$t = 1.99$ $P < 0.05$	4.9 ± 0.8	$t = 0.80$ NS	4.0 ± 0.8	$t = 2.58$ $P < 0.02$	8.3 ± 1.5
3	1.7 ± 0.5	$t = 1.40$ NS	0.9 ± 0.4	$t = 1.13$ NS	0.4 ± 0.2	$t = 2.77$ $P < 0.01$	1.7 ± 0.5
4	0.5 ± 0.2	$t = 2.51$	0	—	0	$t = 2.79$	0.5 ± 0.2
5	0.2 ± 0.1	$t = 2.01$ $P < 0.05$	0	—	0	$t = 2.01$ $P < 0.05$	0.2 ± 0.1
6	0		0		0		0
	Colorectal Transit Time (hours) (Mean ± SE)						
	32.1 ± 2.9	$t = 2.23$ $P < 0.02$	24.1 ± 2.9	$t = 1.16$ NS	20.7 ± 1.9	$t = 3.19$ $P < 0.005$	32.1 ± 2.9

male and female controls. This may reflect the care taken in choosing truly asymptomatic subjects, since it is known that many women suffer from an irritable bowel syndrome but do not consult for it, and it confirms a similar lack of difference in a previous study.[30]

Stool consistency and frequency, previously thought not to be influenced by colorectal transit duration[5, 7, 8, 10, 30]—a determinant of stool output that includes not only stool frequency but stool weight—were in fact found to be influenced by the segmental transit time in the rectosigmoid area.

At the completion of this study, we can make a number of recommendations: 1) A diagnosis of constipation can be made on a film taken three days after ingestion of 20 radiopaque markers if it contains over eight markers. 2) To investigate healthy or diseased subjects and quantify total and segmental transit time, one film should be taken after at least six successive daily ingestions of 10 or more markers. Repeat studies, used as quality control of treatment and to observe the normal course of disease, must be done that way to avoid unnecessary radiation. 3) If reflux of markers is essential information to be obtained, daily films are necessary, as well as to evaluate the kinetics of decrease of the number of pellets.

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