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A new method for studying gut transit times using radioopaque markers

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SUMMARY A simple technique for measuring gastrointestinal transit times using radioopaque pellets of barium-impregnated polythene has been developed and validated. A normal range has been established by studying 25 normal subjects; all passed the first marker within three days and most passed 80% of the markers within five days.

No simple quantitative method for measuring gastrointestinal transit times is currently available. The quantitative methods used at present tend to be complex or time-consuming; the simple methods give information only about the rate of passage of the first or the final parts, but not the main bulk, of the marker. The quantitative method described here, in which radioopaque pellets are used as markers, has the advantage that the passage of the markers may be simply observed either by taking serial radiographs of the abdomen or of the stools.

METHOD

THE MARKERS Initial studies were made using solid cylindrical pellets, 2, 3, or 5 mm in diameter, punched from sheets of polythene, 3 mm thick, containing 20% (w/w) of barium sulphate. The specific gravity of the material was 1·05 so that the weights of the pellets were 12, 21, and 55 mg respectively for the three sizes. The two larger pellets proved the most useful.

The material from which these solid pellets were made is not generally available so a second type of marker was prepared by cutting 3 mm segments from radioopaque polythene tubing[1] of 2·7, 3·7, and 4·5 mm external diameter. The specific gravity of the material was 1·19 and the weights of these hollow pellets was 14, 20, and 20 mg for the three sizes.

STOOL COLLECTION If the stools are to be radiographed a method is required by which the stools may be collected simply and completely, without direct handling, and such that they may be transported to the *X*-ray Department in a convenient container free from smell. This has been achieved by collecting the stools in a 10 × 10 in. PVC or polythene bag suspended over the lavatory pan by means of a metal frame (Fig. 1a). The

[1]Portex Radiopaque Polythene Tubing pp 202, pp 290, pp 355. Lengths of the tubing or the prepared pellets may be obtained from Portland Plastics Ltd, Hythe, Kent.

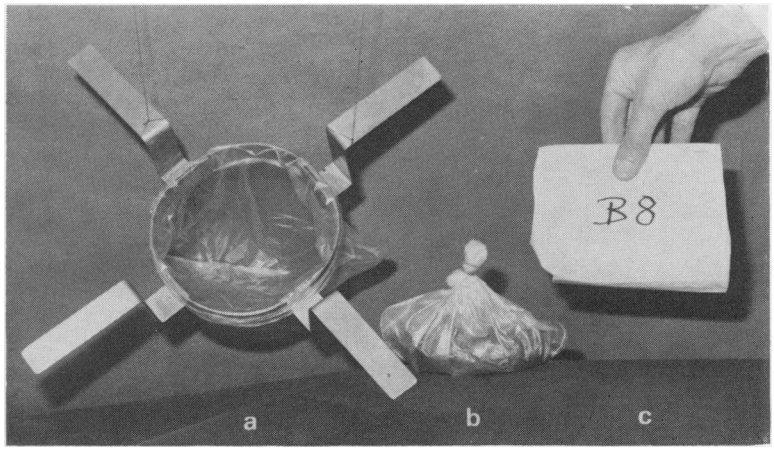

FIG. 1. *Illustration of the method of stool collection (a) and preparation of the specimen (b and c) for radiological examination.*

frame consists of a ring, 6 in. in diameter, supported by four detachable arms, the flanged upper edge of the ring being 1½ in. below the top of the pan. Using this device urine and faeces can be completely separated. The bag is attached to the ring by an elastic band placed below the flange and after defaecation the subject detaches the bag and seals the neck with another rubber band (Fig. 1b). The bag is labelled and stored in an airtight tin. For transport to the Radiographic Department the problem of smell is avoided by enclosing the bag in a second polythene bag and the nature of the specimen is concealed by enclosing this in a non-transparent paper bag (Fig. 1c).

MEASUREMENT OF TRANSIT TIMES The pellets are easy to swallow if taken with a drink. A known number of pellets, usually 20, is administered and the disappearance of the pellets from the gut or the appearance of the pellets in the stool is observed by serial radiographs. The time taken to pass the first pellet, a proportion of the pellets, or all the pellets may be noted. In practice the last one or two pellets tend to be disproportionately delayed and the most satisfactory way of expressing the results was found to be as the times taken for the passage of the first and of 80% of the markers.

When radiographs are taken of the stools it is important to flatten the stool so that one pellet does not obscure another. For the abdomen, a fast film and high KV may be used as detail is not required. It is important that the film should include the whole abdomen and the pelvis (Fig. 2). The gonads are shielded in men.

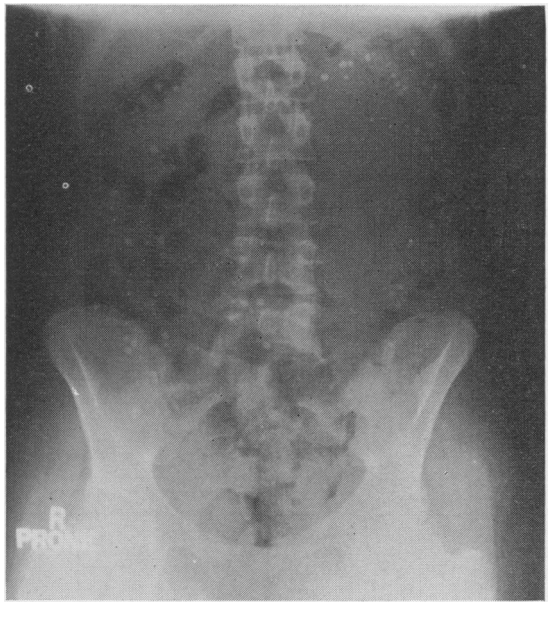

FIG. 2. *Radiograph illustrating the distribution of pellets in the colon. The use of different sizes of pellet enables the transit rate and mixing of pellets administered at the same or different times to be studied.*

VALIDATION OF METHOD

COMPLETENESS OF RECOVERY Of 1,200 markers administered during 30 studies divided equally between three normal subjects, all but eight markers were counted on subsequent stool radiographs giving a recovery rate of 99·3%. Of 1,340 markers administered during 55 studies on 20 patients, all but 21 were counted on stool radiographs giving a recovery rate of 98·5%.

REPLICATE STUDIES The reproducibility of transit times in one person was investigated by doing five separate studies on each of six normal subjects. Markers were always given immediately before breakfast and the subjects continued their usual activities and took a normal diet. The results are shown in Table I. It can be seen that for all subjects and for both the first and 80% of markers two studies could give identical results or results differing by only one hour. At the other extreme, variation between two studies ranging from 14 to 51 hours were obtained; the greatest differences occurred in the times for passage of 80% of markers. These variations were less than the range of variation for normal subjects shown below.

TABLE I

TRANSIT TIMES OF MARKERS IN REPLICATE STUDIES

Subject	*Time for Passage of Markers (hr)*						
	Study					*Least Variation*	*Greatest Variation*
	1	*2*	*3*	*4*	*5*		
First marker							
A	25	37	24	23	24	0	14
B	25	47	47	26	24	1	23
C	29	52	28	54	28	0	26
D	25	25	7	6	25	0	19
E	14	16	50	26	26	0	36
F	12	13	16	37	9	1	28
80% markers							
A	49	37	26	25	24	1	25
B	48	49	47	73	26	1	47
C	79	52	52	54	28	0	51
D	25	73	49	30	25	0	48
E	26	42	50	26	26	0	24
F	37	62	38	37	36	0	26

COMPARISON BETWEEN DIFFERENT SIZES AND THE TWO TYPES OF MARKER Two or three types of marker were given simultaneously in tests on both patients and normal subjects and the transit rates of the different types of marker compared. The results shown in Table II demonstrate that there is a close correspondence between the different sizes and types of marker.

COMPARISONS BETWEEN MARKERS GIVEN BEFORE AND MARKERS GIVEN WITH A MEAL A series of com-

TABLE II

COMPARISON OF TRANSIT TIMES OF DIFFERENT SIZES AND TYPES OF MARKER

Size and Type of Markers Compared	*No. of Comparisons*	*Comparison*	*Times for Passage of Markers (hr)*			
			First	*20%*	*50%*	*80%*
5 mm solid	30	Same	29	28	25	26
with		Slower	—	1	—	3
3 mm solid		Faster	1	1	5	1
Solid with	10	Same	8	10	9	8
hollow		Slower	1	—	1	1
		Faster	1	—	—	1
4·5 hollow	10	Same	7	7	6	6
with		Slower	2	2	2	3
3·7 hollow		Faster	1	1	2	1
2·7 hollow	10	Same	8	8	6	5
with		Slower	—	1	3	4
3·7 hollow		Faster	2	1	1	1
4·5 hollow	10	Same	7	8	8	7
with		Slower	2	1	1	2
2·7 hollow		Faster	1	1	2	1

parisons was made between the transit rate of 20 markers given together just before a meal and 20 markers of a different size spread through the meal. In 10 comparisons, the times for first markers were the same on nine occasions, and on one occasion the markers given before the meal were faster. For 80% of the markers the times were the same on eight occasions, the markers given before the meal in the other two tests being slower. Markers given all at once before a meal, a method which is both convenient and easy to supervise, are thus representative of the food residue from that meal.

COMPARISONS WITH OTHER TYPES OF MARKER A comparison was made between the transit time of the pellets and of a simultaneously administered dose of ^{51}Cr-labelled sodium chromate. A dose of 3 to 6 μc of the isotope in 5 to 10 ml of the solution was given. The stools were counted in a large-volume, well-type scintillation counter and the proportion of the administered dose in each stool was calculated with reference to a standard solution. The comparisons were made in two groups: normals and patients with an intact gut, and patients with ileostomies to make the comparison through the upper gut. The results are shown in Table IIIa and IIIb. This shows that while in both groups the

TABLE IIIa

COMPARISON BETWEEN TRANSIT TIMES (HOURS) FOR PELLETS AND ^{51}CR SODIUM CHROMATE SOLUTION THROUGH THE WHOLE GUT

	Subject No.											
	1		*2*		*3*		*4*		*5*		*6*	
Marker	*Pellets*	*^{51}Cr*	*Pellets*	*^{51}Cr*	*Pellets*	*^{51}Cr*	*Pellets*	*^{51}Cr*	*Pellets*	*^{51}Cr*	*Pellets*	*^{51}Cr*
First	2	2	10	10	24	24	23	23	49 (S)	28	22	22
20%	22	22	10 (F)	14	57	57	25	25	49	49	22	22
50%	22	22	10	33[1]	59 (F)	85	25	25	49	49	22 (F)	46
80%	22	22	22	—	95	95	25 (F)	26	49 (F)	53	46	93[1]
Last	22 (F)	26	22	—	95 (F)	129+	26 (F)	26+	97 (F)	100+	69	—
Recovery (%)	100	98·1	100	51·0	100	97·8	100	90·0	100	93·0	100	81·8

[1]Indicates last counted specimen contained < 0·5% of the administered ^{51}Cr; (F) = pellets faster than sodium chromate; (S) = pellets slower than sodium chromate

TABLE IIIb

COMPARISON BETWEEN TRANSIT TIMES (HOURS) FOR PELLETS AND ^{51}CR SODIUM CHROMATE SOLUTION IN ILEOSTOMY SUBJECTS

	Subject							
	1		*2*		*3*		*4*	
Marker	*Pellets*	*^{51}Cr*	*Pellets*	*^{51}Cr*	*Pellets*	*^{51}Cr*	*Pellets*	*^{51}Cr*
First	0·75	0·75	3·25	1·75	3·0 (F)	4·25	4·75	4·75
20%	0·75	0·75	3·25	3·25	4·25 (F)	5·75	4·75 (F)	6·25
50%	3·5 (S)	1·25	5·75	4·25	4·25 (F)	5·75	4·75 (F)	7·75
80%	9·5 (S)	5	8·25	—	4·25 (F)	6·75	6·25	9·25
Last	> 31 ? < 22	> 31 < 22	> 13 < 22	—	5·75 (F)	30[1]	6·25 (F)	11·25
Recovery (%)	100	91	100	70·7	100	90	100	98

Mean recovery pellets 100%
Mean recovery ^{51}Cr 93·4%

transit times for the first markers are similar, the times for the later pellets are less than the times for the corresponding proportions of sodium chromate in the majority of subjects. The ileostomy studies indicate that at least part of this delay can be in the upper gut.

A comparison was also made between the transit rates of the pellets and of two simultaneously administered gelatin capsules of powdered carmine. It was only possible to compare the transit times for the first and last red colour as there is no simple method available for measuring carmine in the stool. In 30 comparisons the times for the first markers and the first apperance of the carmine were the same on 25 occasions, the markers being slower on four occasions and faster once. For 100% of markers and the last visible carmine the times were the same on 16 occasions, the markers being slower in eight instances and faster in six.

SIDE EFFECTS In all, approximately 13,000 solid pellets and 1,000 hollow pellets were given to 30 normal subjects and 129 patients. One normal subject and three patients (all ileostomists) complained of abdominal pain during a study. In the three patients there was no radiological evidence of obstruction. The normal subjects did not consider that taking the markers altered their bowel habit.

RESULTS IN NORMAL SUBJECTS

Transit times were measured by taking radiographs of the stools in 25 normal male subjects, members of the hospital staff and medical students. They all considered themselves to be free of bowel symptoms. The age distribution of the subjects was < 20 years, two; 20-29 years, eight; 30-39 years, 14, and > 40 years, one. Markers were taken immediately before breakfast. The results are shown in Table IV. It will be seen that all subjects passed the first marker within 66 hours (three days) and that all except one passed 80% of the markers within 114 hours (five days). The distribution of the transit times in the 25 subjects is shown in Table V.

TABLE IIIa—*continued*

COMPARISON BETWEEN TRANSIT TIMES (HOURS) FOR PELLETS AND ^{51}CR SODIUM CHROMATE SOLUTION THROUGH THE WHOLE GUT

Subject No.													
7		*8*		*9*		*10*		*11*		*12*		*13*	
Pellets	*^{51}Cr*	*Pellets*	*^{51}Cr*	*Pellets*	*^{51}Cr*	*Pellets*	*^{51}Cr*	*Pellets*	*^{51}Cr*	*Pellets*	*^{51}Cr*	*Pellets*	*^{51}Cr*
24	24	12	12	28	28	24	24	26	26	47	47	20	20
24	24	12 (F)	24	28	28	24	24	26	26	47	47	20	20
24	28	24	24	28	28	24	24	52 (S)	26	47 (F)	76	20	20
49 (F)	72	24	24	28	28	24 (F)	39	52	52	76 (F)	94	43	43
72[a]	72+	50 (F)	98	68	68	39 (F)	144[1]	52	52	76 (F)	104	43 (F)	91
96	88·0	100	94·8	100	94·6	100	111·0	100	101·0	100	90·2	100	91·4

[a]Only 24 of 25 pellets collected indicating incomplete collection

TABLE IIIb—*continued*

COMPARISON BETWEEN TRANSIT TIMES (HOURS) FOR PELLETS AND ^{51}CR SODIUM CHROMATE SOLUTION IN ILEOSTOMY SUBJECTS

Subject											
5		*6*		*7*		*8*		*9*		*10*	
Pellets	*^{51}Cr*	*Pellets*	*^{51}Cr*	*Pellets*	*^{51}Cr*	*Pellets*	*^{51}Cr*	*Pellets*	*^{51}Cr*	*Pellets*	*^{51}Cr*
1·00	2·25	3·75 (S)	3·25	1·25	1·25	2·25 (S)	1·25	2·75 (S)	1·25	3·00 (S)	3·50
1·00	2·25	4·25 (F)	5·75	1·75	1·75	3·00 (S)	2·25	2·75 (F)	3·75	3·50 (F)	4·00
2·25	2.25	5·75	5·75	2·75	2·75	8·00 (S)	2·25	5·00 (S)	3·75	6·00 (S)	4·00
3·00	—	10·5	10·5	2·75 (F)	3·75	8·00 (S)	4	5·75	5·75	6·75	6·75
4·00	—	10·5 (F)	24[1]	3·75 (F)	24[1]	11·00 (F)	> 13	> 13	> 13 ?	7·75 (F)	13
							< 19	< 21	< 21		
100	76·3	100	102	100	100	100	102	100	99	100	105

TABLE IV

TRANSIT TIMES OF MARKERS IN NORMAL MALE SUBJECTS

Subject	Time Taken (hr) to Pass Different Proportions of Markers					Percentage Recovery
	First	20%	50%	80%	Last	
1	25	25	49	49	49	100
2	25	25	48	48	95	100
3	29	29	29	29	76	100
4	25	25	25	25	25	100
5	14	14	26	26	38	100
6	12	12	37	37	37	100
7	25	25	25	25	49	100
8	9	9	26	26	72	100
9	25	25	25	25	60	100
10	30	30	30	30	73	100
11	24	24	24	48	72	100
12	46	46	46	84	106	100
13	59	59	59	150	169	100
14	27	27	27	27	47	100
15	28	28	28	53	53	100
16	51	51	51	51	100[1]	96[1]
17	26	26	26	30	80	100
18	53	62	82	82	99	100
19	23	25	25	32	58	100
20	23	23	23	47	71	100
21	61	61	61	61	120[1]	96[1]
22	17	17	28	28	48	96
23	10	10	28	28	48	96
24	33	33	33	33	33	100
25	48	63	63	63	74	100

[1]Stool collection incomplete

TABLE V

DISTRIBUTION OF TRANSIT TIMES IN 25 NORMAL SUBJECTS

	Day					
	1	2	3	4	5	5+
First marker	2	14	6	—	—	—
80%	0	13	8	2	1	1

DISCUSSION

Methods that have been used to measure gut transit may be classified as radiological, colorimetric, particulate, chemical, and isotopic.

For the radiological technique bismuth subnitrate and barium sulphate have been used as markers (Hurst, 1919; Wallace, Ehrenfeld, Cowett, Joliffe, Shapiro, and Sturtevant, 1938; Lönnerblad, 1951; Manousos, Truelove, and Lumsden, 1967). This technique has the merit of simplicity but the disadvantage that only the head and tail of the column of marker can be timed and the end point of the tail is indefinite. Alvarez and Freedlander (1924) have questioned the validity of the method, stating that amounts of 60 g of barium sulphate increase the transit rate above normal, whereas others (Barclay, 1936) have not found this to be the case.

The usefulness of insoluble coloured powders such as carmine and charcoal is also limited by the fact that only the first and last of the marker to be passed can be observed, with the further disadvantage that direct observations on the stool are required.

Coloured glass beads were used by Alvarez and Freedlander (1924) in their classical studies on transit times. However, the method required that the stools should be sieved to recover the beads. Furthermore, Hoelzel (1930) later showed that an increase in average transit time from 25 to 30 to 40 hours occurred in the same subject when glass beads of specific gravity 2·6 were used instead of particles with a specific gravity of 1 to 1·5 such as tomato, millett, and grape seeds, and knots of cotton. Unfortunately these latter markers, though physiological, also require that the stools should be sieved for their quantification.

Barium sulphate (Alvarez and Freedlander, 1924; Dick, 1967), chromium sesquioxide (Whitby and Lang, 1960), and copper thiocyanate (Dick, 1969) have been estimated chemically and used as markers. They are useful research tools and valuable in metabolic studies, but are too complex for the routine clinical measurement of transit rate.

Likewise ^{51}Cr-labelled sodium chromate and chromium sesquioxide (Hansky and Connell, 1962; Davignon, Simmonds, and Ahrens, 1968) and ^{140} lanthanum (Hayes, Carlton, and Nelson, 1964) have been used as markers for research purposes both in balance studies and to measure transit times.

Reference to Table IIIa and IIIb shows that in five studies (two ileostomy and three whole gut) the recovery of sodium chromate was less than 85%. This was also the case in six of the 10 studies of Hansky and Connell (1962) using sodium chromate and chromium sesquioxide. Roche and his colleagues (1957) found in four subjects given ^{51}Cr sodium chromate that 1·0 to 9·0% of the isotope was recoverable in the urine. More recently it has been shown (Donaldson and Barreras, 1966) that if ^{51}Cr sodium chromate is given directly into the duodenum or by mouth to patients with a histamine-fast achlorhydria 25 to 50% of it is recoverable in the urine. In contrast absorption of chromic chloride or of sodium chromate used to label red cells does not occur. From this work it is now clear that ^{51}Cr sodium chromate is not an ideal marker.

A marker that is to give a physiologically meaningful measurement of gut transit rate must not be absorbed but measurable and completely recoverable in the stool, must travel at a similar rate to the normal contents, and must not alter the activity of the gut. The radioopaque pellets described here are clearly not absorbed and recovery rates in excess of 98% have been obtained in clinical use. Direct proof that markers are travelling at the same rate as

food residues is difficult and has not been obtained for any marker. However, the observations that these markers have similar specific gravity to the gut content, and that the pellets travelled at similar rates to a liquid and a finely powdered marker, are good indirect evidence. The pellets are quite inert and there was nothing to suggest any alteration in gut activity. Quantitation is simple as the transit of the markers through the gut can be followed with serial radiographs of the subject, with or without radiographs of the stool.

A difficulty arises when expressing the results in the conversion from hours to days. The best dividing line between one day and the next is the period of sleep. Since defaecation may occur soon after the end of the sleeping period the actual dividing line is made at the beginning of sleep. Since the markers are given at breakfast time the length of the first day is not likely to be more than 18 hours. Day 1 is therefore taken as the first 18 hours after taking the markers, subsequent days being 24-hour increments on this figure. Thus day 2 ends at 42 hours, day 3 at 66 hours, day 4 at 90 hours, and so forth.

The results on the 25 normal male subjects in Table IV show that all subjects had passed their first markers by the end of the third day and all but one had passed 80% by the end of the fifth day. This provides an upper limit of normal for transit time. Likewise at the lower limit, no normal subject had passed 80% of the markers at the end of the first day.

It is difficult to compare our results for normal male subjects with those obtained by others because their results are expressed in several different ways and some workers have allowed the markers to be ingested at different times of the day. Only Alvarez and Freedlander (1924) used a technique where the time for the passage of both first and 80% of markers could be estimated. Of their eight subjects all had passed their first markers by the end of the third day but only six had passed 80% by the end of the fifth day, the other two taking more than nine days. This longer time for passage of 80% of markers as compared with our results is probably due to the slower transit rate of the beads which had a specific gravity of approximately 2·0.

The technique described here has both clinical and research applications. It may be used to determine whether patients complaining of diarrhoea or constipation have transit times outside the normal range. A simple technique for investigating constipation using only two plain abdominal radiographic films has been devised, and is discussed elsewhere (Hinton and Lennard-Jones, 1968). As a research tool it may be used in the assessment of the effect of drugs upon the colon (Hinton, 1967).

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