Experience with a gastrointestinal marker ($^{51}\text{CrCl}_3$) in a combined study of ileal function using $^{75}\text{SeHClAT}$ and $^{58}\text{CoB}_{12}$ measured by whole body counting

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Abstract

Introduction of a radioactive gastrointestinal marker ($^{51}\text{CrCl}_3$) into a combined study ($^{75}\text{SeHClAT} + ^{58}\text{CoB}_{12}$) of ileal function by whole body counting has been undertaken. The technique was assessed in 23 subjects (15 patients with inflammatory bowel disease, six on non-steroidal anti-inflammatory drugs for rheumatoid arthritis, and two normal subjects). Mean (SD) $^{51}\text{CrCl}_3$ retention was only 4.1 (6.0)% on day 4, and was similar on day 7 in subjects given a second dose of $^{51}\text{CrCl}_3$ on day 4. Only one subject had more than 20% of $^{51}\text{CrCl}_3$ retention after four days. A $^{51}\text{CrCl}_3$ correction method adequately corrected for colonic hold up of $^{58}\text{CoB}_{12}$, when compared with final equilibrium values of $^{58}\text{CoB}_{12}$ retention. Use of the non-absorbed $^{58}\text{CoB}_{12}$ fraction as a gastrointestinal marker gave good agreement with the $^{51}\text{CrCl}_3$ method in correcting $^{75}\text{SeHClAT}$ values. In all subjects studied, corrections for colonic retention of $^{75}\text{SeHClAT}$ on day 4, were small (<7% of dose) and did not affect the assessment of any subject. In conclusion, an additional gastrointestinal marker such as $^{51}\text{CrCl}_3$ is unnecessary in our combined study since that role can be effected, when indicated, by the non-absorbed $^{58}\text{CoB}_{12}$ fraction.

The synthetic bile acid 23- ^{75}Se seleno-25-homotaurocholate ($^{75}\text{SeHClAT}$) has been shown to be a specific test substance for investigation of ileal function.^{1,2} Total body retention of orally administered $^{75}\text{SeHClAT}$ has been used as a simple indicator of abnormal bile acid turnover in a variety of gastrointestinal disorders.³⁻⁸ Methods that avoid the need for faecal radioassay⁹ have involved the use of whole body counters,^{4,5,8,10,11} probe NaI detectors,¹² and uncollimated gamma cameras,^{3,11-13} and $^{75}\text{SeHClAT}$ retention measured seven days after administration has been the criterion most commonly applied. Sensitive whole body counting has the advantage of reducing the patient's absorbed dose of radiation compared with the other systems. All these methods which directly measure total body or abdominal retention of $^{75}\text{SeHClAT}$, however, permit only an empirical assessment of bile acid turnover because the measurements also include the effects of radioactivity outside the enterohepatic bile acid pool, in particular that which resides in the colon before elimination. Thus, an abnormally long and variable colonic retention could potentially impair these determinations. Because of this, Ferraris *et al*¹⁴ used a gastrointestinal transit

marker, $^{51}\text{CrCl}_3$,¹⁵ to monitor and correct for colonic retention of $^{75}\text{SeHClAT}$ measured by abdominal counting using a gamma camera.

Vitamin B_{12} is also absorbed predominantly at the terminal ileum, but by a different mechanism to that for $^{75}\text{SeHClAT}$, and the combined use of radiolabelled B_{12} and $^{75}\text{SeHClAT}$ has been successfully exploited by whole body counting.^{5,6,10} In our combined study of $^{75}\text{SeHClAT}$ and $^{58}\text{CoB}_{12}$,¹⁶ it was suggested that analysis of the relative patterns of retention of the two test substances could be used to check for evidence of colonic retention. It was considered prudent, however, to attempt to apply the $^{51}\text{CrCl}_3$ gastrointestinal marker technique in our whole body counting protocol to substantiate this claim and furthermore to assess and quantify the influence of colonic retention on the overall results. We therefore incorporated $^{51}\text{CrCl}_3$, administered orally and together with $^{75}\text{SeHClAT}$ and $^{58}\text{CoB}_{12}$ (plus intrinsic factor), in our combined test of ileal function¹⁶ to assess the efficiency of colonic emptying on three study days (days 4, 7, and 10), and to consider the prospects for correcting the $^{75}\text{SeHClAT}$ and $^{58}\text{CoB}_{12}$ retention values in patients with inflammatory bowel disease and non-steroidal anti-inflammatory drug enteropathy.

Subjects and methods

SUBJECTS

Twenty three subjects were investigated. Fifteen had inflammatory bowel disease – four had pan-ulcerative colitis, four had extensive Crohn's colitis, and seven had ileal or ileocaecal Crohn's disease. Their mean age was 38 years (range 17–62), none had undergone intestinal resection, and their disease was quiescent (Harvey and Bradshaw¹⁷ score <3). Six elderly patients (mean age 63 years, range 56–77) had classic or definitive rheumatoid arthritis and had been treated with non-steroidal anti-inflammatory drugs for more than six months. Two normal volunteers were studied in order to obtain retention values more frequently than was possible with patients. The normal ranges of $^{75}\text{SeHClAT}$ and $^{58}\text{CoB}_{12}$ retention values had been established in a previous study.⁸ These studies were carried out with the approval of the Harrow Health Authority Ethical Committee.

METHODS

Each subject was given orally a combination of three substances, $^{75}\text{SeHClAT}$, ^{58}Co vitamin B_{12} (with intrinsic factor), and $^{51}\text{CrCl}_3$, the latter

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Figure 1: Whole body gamma-ray spectra obtained from subjects containing the three radiopharmaceuticals $^{75}\text{SeHCAT}$, $^{58}\text{CoB12}$, and $^{51}\text{CrCl}_3$ separately and from one containing all three. The chosen counting channels for the three radionuclides are indicated.

acting as a non-absorbed gut marker. The subsequent retention of these substances was monitored by whole body counting using a multidetector system (8 NaI crystals 10.1 cm dia $\times$ 7.5 cm) in a 15 cm thick steel room.¹⁸ After an initial background measurement, $^{75}\text{SeHCAT}$ (37 kBq) was administered in a gelatin capsule to fasting subjects and whole body counting was repeated at one hour, immediately before administration of a drink containing both $^{58}\text{CoB12}$ (18.5 kBq) with intrinsic factor and $^{51}\text{CrCl}_3$ (260 kBq). A further whole body measurement was made one hour later and the net counts in the three counting channels (Fig 1) obtained one hour after administration of each substance were used as the 100% retention values. Subsequent whole body counting was performed at four and seven days in all subjects, and also at 10 days in 10 subjects. These are the times chosen for our standard test protocol, as previously described.¹⁶ Additional measurements earlier than four days were made in five subjects, especially for the purposes of this study. In 17 subjects, a second oral dose of $^{51}\text{CrCl}_3$ (260 kBq) was administered immediately after the whole body count on day 4: prior counting of the two $^{51}\text{CrCl}_3$ doses under standard conditions allowed determination of the 100% whole body retention value of the second dose in relation to that of the first.

CROSSOVER OF WHOLE BODY GAMMA RAY SPECTRA

Considering the combined use of ^{75}Se (0.12–0.40 MeV), ^{51}Cr (0.32 MeV), and ^{58}Co (0.51, 0.81 MeV) in individual subjects, it was necessary to obtain estimates of spectral crossover factors for ^{58}Co in the ^{51}Cr and ^{75}Se channels, for ^{51}Cr in the ^{75}Se channel, and also for ^{75}Se in the ^{51}Cr channel because of overlap of the channels selected for ^{51}Cr and ^{75}Se (Fig 1). Crossover of one radionuclide (A) with another (B) is defined as the ratio (net counts/second in channel B)/(net counts/second in channel A).

(a) *Crossover of ^{58}Co into ^{51}Cr and ^{75}Se channels.* These data were obtained retrospectively from whole body measurements on 15 patients who had undergone diagnostic assessment of B_{12} absorption using $^{58}\text{CoB12}$ alone. Crossover factors were obtained at between five and 14 days after $^{58}\text{CoB12}$ administration and, additionally, crossover into the ^{51}Cr channel was measured at one hour. Crossover factors were plotted against body weight, and linear regression lines together with 95% confidence limits about regression were calculated.

(b) *Crossover of ^{51}Cr into ^{75}Se channel.* Data were obtained retrospectively from whole body counting studies on seven subjects given oral ^{51}Cr ethylenediaminetetra acetic acid for investigation of intestinal permeability.¹⁹ For each subject the average crossover factor obtained from three to four measurements over two days was calculated and plotted against body weight. As above, linear regression and 95% confidence limits were calculated.

(c) *Crossover of ^{75}Se into ^{51}Cr channel.* Data were obtained individually for subjects in the present study, one hour after oral administration of $^{75}\text{SeHCAT}$. In view of the fact that $^{58}\text{CoB12}$ and $^{51}\text{CrCl}_3$ were administered immediately after this measurement, later observations of this crossover could not be made and consequently the one hour crossover served for analysis of measurements made at all times. Tests were conducted to establish that this was a sufficiently accurate procedure.

CALCULATIONS

Crossover factors (a) and (b) above were interpolated from curves using the subject's weight. Count rates, net of background, in the ^{75}Se and ^{51}Cr channels were corrected firstly for crossover of the ^{58}Co spectrum. The corrected counts were then used in simultaneous equations, incorporating the respective crossover factors for these two channels, to obtain count rates due to $^{75}\text{SeHCAT}$ and $^{51}\text{CrCl}_3$ alone. These, together with the net count rate in the ^{58}Co channel, were decay corrected to day 0 and expressed as a percentage of the appropriate 100% (one hour) count rates. In all cases, 95% confidence limits on these values, resulting from the uncertainty in crossover corrections, were also calculated.

Results

CROSSOVER OF GAMMA-RAY SPECTRA

The crossover data are shown in Figure 2 plotted against body weight. Best fitting straight lines were calculated and used to interpolate appropriate crossover factors for subjects in the present study. The average 95% confidence limits on these crossover factors were $\pm 8.8\%$ and $\pm 7.5\%$ for ^{58}Co in the ^{51}Cr channel at early (one hour) and later (five to 14 days) times respectively; $\pm 2.7\%$ for ^{58}Co in the ^{75}Se channel; and $\pm 5.9\%$ for ^{51}Cr in the ^{75}Se channel. The effects of these limits on measured and corrected $^{75}\text{SeHCAT}$ retention values are shown later. Only the crossover of ^{75}Se in the ^{51}Cr channel was obtained directly in the present studies, as measured one

Figure 2: Relation between crossover factors and body weight: (A) $^{58}\text{CoB12}$ into $^{75}\text{SeHCAT}$; (B) $^{58}\text{CoB12}$ into $^{51}\text{CrCl}_3$; and (C) $^{51}\text{CrCl}_3$ into $^{75}\text{SeHCAT}$. In (B) both early (1 hour; $\circ$) and late (5–14 days; $\bullet$) crossovers are shown. The 95% confidence limits are shown but, for the sake of clarity, the limits on the 1 hour data in (B) have been omitted.

hour after administration of $^{75}\text{SeHCAT}$. The validity of using this and other crossover factors was examined in seven patients from previous studies who were given $^{75}\text{SeHCAT}$ and $^{58}\text{CoB12}$ without $^{51}\text{CrCl}_3$: using crossovers as described above, the residual whole body counts estimated in the ^{51}Cr channel at four and seven days were equivalent, on average, to less than 0.5% of the mean $^{51}\text{CrCl}_3$ activity administered in the present studies.

Absorbed $^{58}\text{CoB12}$ is eliminated slowly from the body and consequently whole body retention becomes effectively constant after complete excretion of the non-absorbed fraction. Thus, by observation of this true absorption value, the accuracy of the correction method can be assessed. The observed $^{58}\text{CoB12}$ retention curve and the corrected early values are shown in Figure 3 for a normal subject measured on several occasions. The $^{51}\text{CrCl}_3$ corrected values

WHOLE-BODY RETENTION OF $^{51}\text{CrCl}_3$

In all 23 subjects, the average whole body retention on day 4 was 4.1 mean (SD) (6.0)% of the first administration of oral $^{51}\text{CrCl}_3$ and exceeded 5% in only five. Seventeen subjects, who were given a second $^{51}\text{CrCl}_3$ administration on day 4, showed average retention of the first administration, 4.8 (6.6)% (day 4) and, of the second administration, 4.4 (6.8)% (day 7) and 0.4 (1.0)% (day 10; $n=8$). Only one subject, a patient with ileal Crohn's disease, had a $^{51}\text{CrCl}_3$ retention greater than 20% – that is 22.0% of the first administration (day 4) and 28.5% of the second (day 7).

CORRECTION OF WHOLE-BODY RETENTION VALUES USING $^{51}\text{CrCl}_3$

In the following methods for correcting retention values of $^{58}\text{CoB12}$ and $^{75}\text{SeHCAT}$ for colonic hold up, it is assumed that the non-absorbed fractions of these substances have a gastrointestinal transit identical to that of the gastrointestinal marker $^{51}\text{CrCl}_3$.

(a) $^{58}\text{CoB12}$. Values of whole body retention of $^{58}\text{CoB12}$ were corrected using the formula:

$$B_{12}(\%) = 100(C_o - C_r) / (100 - C_r)$$

where B_{12} is the corrected retention and C_o and C_r are the observed whole body retentions (%) of $^{58}\text{CoB12}$ and $^{51}\text{CrCl}_3$ respectively at time t .

Figure 3: Total body retention curves of $^{58}\text{CoB12}$ and $^{75}\text{SeHCAT}$ from a normal subject given all three radiopharmaceuticals ($\circ$). In both figures the $^{51}\text{CrCl}_3$ retention is illustrated ($\bullet$) and the early retention values of $^{58}\text{CoB12}$ and $^{75}\text{SeHCAT}$ have been corrected using the $^{51}\text{CrCl}_3$ retention values. The 95% confidence limits shown for the corrected values ($\bullet$) are based on crossover errors.

Figure 4: Early $^{58}\text{CoB12}$ retention values, before (○) and after (●) correction by the $^{51}\text{CrCl}_3$ technique, compared with final equilibrium $^{58}\text{CoB12}$ values. The 95% confidence limits due to crossover errors are indicated for the corrected values. Points indicated by (■) represent values for 15 subjects who retained less than 5% of $^{51}\text{CrCl}_3$ at the early measurement.

show good agreement with the equilibrium retention value. Similar comparisons were made for all the measured subjects and the data are shown in Figure 4, where early $^{58}\text{CoB12}$ retention values (up to day 4) are plotted against the final (equilibrium) values (days seven–10). Fifteen subjects had less than 5% $^{51}\text{CrCl}_3$ retention at the early measurements, and in these there was good agreement between early and final $^{58}\text{CoB12}$ estimates. In the remainder, who had more than 5% $^{51}\text{CrCl}_3$ retention at the early measurements, $^{58}\text{CoB12}$ retention values were displaced from the line of identity to a variable extent. These values, however, were corrected by use of the above formula with reasonable accuracy in all cases. The 95% confidence limits shown for the corrected values are due to inaccuracy of the $^{51}\text{CrCl}_3$ retentions resulting from errors on crossover values. Uncorrected $^{58}\text{CoB12}$ values are, of course, unaffected by crossover.

(b) $^{75}\text{SeHCAT}$. Whole body $^{75}\text{SeHCAT}$ retention values were corrected for $^{51}\text{CrCl}_3$ retention using a similar formula to that given above for $^{58}\text{CoB12}$. Since $^{75}\text{SeHCAT}$ undergoes a sequence of recycling by the enterohepatic system with partial elimination via the gastrointestinal tract at each cycle, there is no equilibrium retention value (Fig 3) equivalent to that of $^{58}\text{CoB12}$ with which to compare the corrected values. In view of the fact that the non-absorbed fraction of $^{58}\text{CoB12}$ also acts as an effective gut marker, however, the early $^{75}\text{SeHCAT}$ retention data were additionally corrected using $^{58}\text{CoB12}$ retention values by means of the formula:

$$\text{SeHCAT (\%)} = 100 - \left[\frac{100 - \text{Se}_t}{100 - \text{Co}_t} \right] (100 - \text{Co}_\infty)$$

where Co_∞ represents the equilibrium $^{58}\text{CoB12}$ retention value.

Figure 5: Comparison of $^{75}\text{SeHCAT}$ retention values corrected by the $^{51}\text{CrCl}_3$ technique and by unabsorbed $^{58}\text{CoB12}$. Five comparisons of day 4 values are indicated as (●) while other symbols represent paired values for 3 subjects measured earlier than day 4. Point A is the result of variation in geometrical counting efficiency in the absence of excretion. After significant excretion in this subject the corrected $^{75}\text{SeHCAT}$ value is shown as point B. 95% confidence limits are based on crossover errors.

Values of $^{75}\text{SeHCAT}$ retention corrected in this way were compared with values corrected by $^{51}\text{CrCl}_3$ retention as shown in Figure 5 for the eight subjects who had $^{51}\text{CrCl}_3$ retentions in excess of 5% at one or more of the whole body measurements. There are five single values (day 4) and three pairs of data from three subjects measured on two separate earlier days. In general, there is good agreement between the two methods of correction. However, point A (Fig 5) illustrates the potential error that can arise as a result of variations in whole body counting geometry which led to an apparent small change in retention initially, before any excretion had in fact occurred (day 2). After subsequent excretion in this patient, this anomaly was rectified (point B). The confidence limits shown on the corrected values in Figure 5 indicate the possible errors that could result from the extremes of the ranges of the 95% confidence limits on the various crossover factors used. As expected, largest potential errors exist when crossover corrections are large, particularly in the early days after administration. In this study, however, confidence limits on $^{51}\text{CrCl}_3$ -corrected values of retentions on day 4 did not exceed $\pm 11\%$ of administered $^{75}\text{SeHCAT}$, with an average of $\pm 5.0\%$ ($n=5$).

(c) *Whole body retention patterns: observed and corrected.* Whole body retention values of $^{58}\text{CoB12}$ and $^{75}\text{SeHCAT}$ are shown in Figure 3 for a normal subject measured on nine separate occasions. Each figure includes the retention curve of the $^{51}\text{CrCl}_3$ marker, and the early $^{75}\text{SeHCAT}$ and $^{58}\text{CoB12}$ values corrected for $^{51}\text{CrCl}_3$ retention.

(d) *Radiation dose.* Using data from ICRP Publication 53,²⁰ the effective dose equivalents (EDE) resulting from the three radioactive substances, administered to a normal subject are 0.041 millisieverts (mSv) from 37 kBq $^{75}\text{SeHCAT}$, 0.139 mSv from 18.5 kBq $^{58}\text{CoB12}$, and 0.009 mSv from 260 kBq $^{51}\text{CrCl}_3$. Thus the highest effective dose equivalents, in a normal subject given two $^{51}\text{CrCl}_3$ administrations, is 0.2 mSv.

Discussion

Our results show that, with appropriate attention to technical details, the use of a $^{51}\text{CrCl}_3$ non-absorbed gastrointestinal marker can be applied successfully in a combined test with $^{75}\text{SeHCAT}$ and $^{58}\text{CoB12}$ measured by whole body counting. Application of specific crossover corrections for individual subjects is facilitated by the observed relations between crossover and body weight. The accuracy of the crossover factors interpolated from these relations was verified by the finding that net counts in the ^{51}Cr channel were practically zero in patients given both $^{75}\text{SeHCAT}$ and $^{58}\text{CoB12}$ but no $^{51}\text{CrCl}_3$. The 95% confidence limits on all crossover factors have been taken into account in calculating the range of error in individual retention values resulting from the most adverse combination of these errors. In this study, the ranges for retention values on and after day 4 were acceptable, mainly because we found low retention of $^{51}\text{CrCl}_3$ at these times. It is clear, however, from Figures 3 and 5 that

Figure 6: Whole body retention of $^{75}\text{SeHCAT}$ on day 4 in the different patient categories. Values are shown before and after correction by $^{51}\text{CrCl}_3$ marker. The 95% confidence limits due to crossover errors are shown for all values before and after correction. The normal mean (2 SD) value and range, obtained in a previous study,⁸ are indicated.

considerably larger potential errors are associated with earlier retention measurements. We conclude from these observations that the addition of the $^{51}\text{CrCl}_3$ marker has not seriously compromised the estimates of $^{75}\text{SeHCAT}$ retention or marker corrected values for days 4, 7, and 10, which was the main objective of this study. Our results suggest, however, that if earlier retention values were required, using the $^{51}\text{CrCl}_3$ marker, the details of the present protocol would require modification.

In this study of 23 subjects there was satisfactory gut clearance as indicated by a mean retention of less than 5% of the $^{51}\text{CrCl}_3$ marker on day 4, which is the first measurement day in our protocol for the combined $^{75}\text{SeHCAT}$ and $^{58}\text{CoB}_{12}$ test. Figure 6 shows the values of whole body retention of $^{75}\text{SeHCAT}$ on day 4, before and after correction by $^{51}\text{CrCl}_3$ marker, for all the subjects studied. The normal range was established in a previous study⁸ based on uncorrected data. In the present study, all the 12 subjects whose retention at four days fell within the normal range, had normal retentions at day 7. With only one marginal exception, retention values remained in the normal range after correction by $^{51}\text{CrCl}_3$. Of the remaining 11 subjects whose retentions on day 4 were subnormal, 10 remained subnormal on day 7. Further evidence of continued gut clearance at later stages in the study was observed in 17 subjects who were given a second administration of $^{51}\text{CrCl}_3$ on day 4. Only one measurement showed a raised retention of marker greater than 20%, and this was in a patient with Crohn's disease. Six patients with rheumatoid arthritis showed a mean (SD) retention of $^{51}\text{CrCl}_3$ at four days of only 4.6 (5.8)%. In our earlier studies,⁸ we found significant reductions in the mean four and seven day retentions of $^{75}\text{SeHCAT}$ by patients with rheumatoid arthritis treated with non-steroidal anti-inflammatory drugs compared with normal subjects, but this effect was much less than that seen

in patients with Crohn's disease. There was a wide range in retention values for the patients with rheumatoid arthritis but the present results suggest this finding may be due to variable effects of administered drugs on bowel function rather than artefacts resulting from colonic retention. Examination of the patterns of $^{58}\text{CoB}_{12}$ retention in the earlier studies⁸ also supports this conclusion.

These results show that the use of $^{51}\text{CrCl}_3$ gastrointestinal marker administered as a bolus together with $^{58}\text{CoB}_{12}$ corrects for colonic retention of the latter with reasonable accuracy, suggesting that the $^{51}\text{CrCl}_3$ marker and non-absorbed $^{58}\text{CoB}_{12}$ are handled in a similar manner by the gastrointestinal tract. Thus since B_{12} absorption is a non-cycling event, the estimation of non-absorbed $^{58}\text{CoB}_{12}$ using the $^{51}\text{CrCl}_3$ marker, administered simultaneously, accurately predicts the absorbed fraction of $^{58}\text{CoB}_{12}$ (Fig 4). Similarly, there is no reason to believe that colonic transit of $^{75}\text{SeHCAT}$ differs from that of the $^{51}\text{CrCl}_3$ marker. Because $^{75}\text{SeHCAT}$ is constantly recycled in the entero-hepatic system, however, its elimination from the gastrointestinal tract is a continuous process, unlike that of B_{12} , and an accurate correction for the colonic content of $^{75}\text{SeHCAT}$ cannot be achieved by a single administered bolus of $^{51}\text{CrCl}_3$. This is illustrated by the whole body retention curve (Fig 3). The colon is likely to contain $^{75}\text{SeHCAT}$ as long as any remains in the body, and this could only be accurately corrected for by constant infusion of a gastrointestinal marker. Nevertheless, the use of a $^{51}\text{CrCl}_3$ bolus does allow a correction based on a 'first pass' of $^{51}\text{CrCl}_3$, as indicated by the plateau in Fig 3 and which can be deduced up until the $^{51}\text{CrCl}_3$ marker is totally eliminated. Whether the application of such a correction in a modified test of $^{75}\text{SeHCAT}$ retention by whole body counting would increase the sensitivity of the test is uncertain but our results suggest that a correc-

tion based on non-absorbed $^{58}\text{CoB}_{12}$ is a valid and feasible alternative, effectively eliminating the need for administration of a $^{51}\text{CrCl}_3$ marker in the combined $^{75}\text{SeHCAT}$ and $^{58}\text{CoB}_{12}$ protocol.

Ferraris *et al*¹⁴ described a method of abdominal counting of $^{75}\text{SeHCAT}$ by collimated gamma camera in which an administered bolus of $^{51}\text{CrCl}_3$ was used to correct for colonic retention of $^{75}\text{SeHCAT}$, assuming exponential clearance of both substances. Colonic $^{75}\text{SeHCAT}$ retentions of up to 68% were reported and, after correction, the retention slope of $^{75}\text{SeHCAT}$ was similar to that obtained for the gall bladder region alone. We have not investigated this technique in our studies because, with one exception, we have not seen colonic retentions of such magnitude on days 4, 7, or 10, either in the present studies using $^{51}\text{CrCl}_3$ or in our previous studies as judged from $^{58}\text{CoB}_{12}$ retentions. In our previous studies only one patient, who had a psychiatric illness, showed excessive retention; all the administered $^{75}\text{SeHCAT}$ and $^{58}\text{CoB}_{12}$ being measurable in the body up to 10 days.

Although the measurement of $^{75}\text{SeHCAT}$ retention in the gall bladder, using a collimated gamma camera, provides a method of measuring bile acid turnover free from artefacts due to colonic retention, it has required the administration of 925 kBq of $^{75}\text{Se}^{14}$. Abdominal counting by uncollimated gamma camera requires less $^{75}\text{SeHCAT}$ activity (185–370 kBq^{3,11,12}) but is unsuitable for this type of multiple radionuclide study, for which whole body counting is the most practical technique. The latter requires only 18.5–37 kBq $^{75}\text{SeHCAT}^{4,6,16}$ and, although it is subject to errors arising from colonic retention, the results of the present study indicate that colonic retention of $^{75}\text{SeHCAT}$ at seven days is unlikely to be a serious problem, and that in the combined test ($^{75}\text{SeHCAT} + ^{58}\text{CoB}_{12}$) any hold up would be apparent from the differing patterns of retention of the two substances. Moreover, the principal use of $^{75}\text{SeHCAT}$ is in the investigation of diarrhoea, in which colonic hold up is not a feature.

In conclusion, the incorporation of a non-absorbed gastrointestinal marker such as $^{51}\text{CrCl}_3$ into the protocol of a combined test of ileal function using $^{75}\text{SeHCAT}$ and $^{58}\text{CoB}_{12}$ ¹⁶ is not recommended for the following reasons:

(a) It complicates the test, requiring extra calibration and, in particular, estimates of additional crossover factors which reduce the accuracy of measurement.

(b) A single bolus marker is not ideal for

monitoring the continuously emptying pool of $^{75}\text{SeHCAT}$.

(c) Any significant colonic hold up of $^{75}\text{SeHCAT}$ would be evident and correctable from the pattern of $^{58}\text{CoB}_{12}$ retention.

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