JOURNAL OF NUCLEAR MEDICINE 8:588-600, 1967

Medical Utility of a Total Body Counter—a Four-Year Assessment[1]

Norman S. MacDonald,[2] Michael Hayes,[2] and Wm. G. Figueroa[2]

Los Angeles, California

Within the last decade, numerous technological advances have made it relatively easy to measure exceedingly small quantities of gamma-emitting nuclides within the human body *in toto.*

Instrument systems capable of accomplishing such measurements can be assembled in a wide range of physical sizes, shapes and degrees of electronic sophistication. All, however, represent a considerable investment in initial monetary cost, space, personnel training and operating expense.

Of what value is such an installation to a hospital or medical center? This report presents an evaluation of the medical utility of the UCLA Total Body Counter (TBC) based on four years of operation as a clinically-oriented facility. The intent is to present information of a practical nature to any who may be contemplating acquisition of a total body counting system to enlarge the scope of their activities in nuclear medicine. No attempt is made to review the pertinent literature or to list the many uses to which total body counters have been put. Several recent symposia serve admirably to acquaint the interested reader with the many facets of whole-body counting (1-3). We shall illustrate how this growing technology can serve a medical center and provide unique assistance for certain of its needs.

EQUIPMENT

The TBC at UCLA consists of four uncollimated NaI scintillation detectors each 5 × 4 inches in diameter, arranged in pairs above and below a cot upon which the human subject rests in the supine position. The cot is placed in the center of a room (8′ × 8′ × 8′) having walls, ceiling, floor and doors all of six-inch steel, with a ⅛th-inch thick inner lining of lead. A fifth detector consisting of a 3″ × 3″ NaI crystal with a flat field collimator mounted

[1]This work was supported by Contract AT-04-GEN-12 between the United States Atomic Energy Commission and the University of California, Los Angeles.

[2]Laboratory of Nuclear Medicine and Radiation Biology, Department of Radiology and Department of Medicine, UCLA School of Medicine Los Angeles, and Wadsworth Hospital, Veterans Administration Center, Los Angeles.

on a movable extension arm is used when measurements over selected body areas are desired. Drapes, soft lighting, FM music and a two-way voice intercommunication system are provided for comfort of the subjects. The electronic equipment includes a conventional high voltage power supply, linear amplifiers and a multi-channel pulse height analyser. Date readout options are: Teletype printer, X-Y recorder and coded punched paper tape. The facility was installed on a basement level in the Medical Center with good access to elevators and wards.

TBC PROCEDURES OF FREQUENT PRACTICAL ASSISTANCE IN DIAGNOSTIC PROBLEMS

The number of TBC procedures which have become of practical assistance to the clinician in his day-to-day problems of diagnosis are disappointingly few. However, in a few instances, information pertinent to the patient's condition can be obtained with an ease and certainty that is not achievable by other means. Four of these procedures which are offered as routine services are discussed below:

I. *Iron Absorption and Retention:* A number of reports have shown how tracer doses of ^{59}Fe, ^{55}Fe and, more recently, ^{52}Fe can be used to elucidate the important features of iron metabolism in a patient (4-6). The distinctive value of the TBC in this field lies in its ability to estimate the efficiency of absorption of dietary iron and its overall retention in the body without the inconveniences and inaccuracies of repetitive stool collections and assays. The patient is counted for a period of five minutes before the test in order to establish his body background. He then ingests an aqueous solution of 25 mg of iron as ferrous ammonium citrate containing 5 or 10 μC of ^{59}Fe and is recounted four hours later for a period of two minutes. He returns at 4, 14 and 21 days thereafter for short 3-5 minute recounts. After corrections for background and decay, the counting rates are expressed as percentages of the four-hour counting rate.[1] The value of the test is greatly enhanced if two other parameters are also determined—liver and spleen uptake as measured with the collimated 3 × 3 inch detector; and amount of tracer incorporation into red cells as measured by assay of a blood sample taken at weekly intervals for three weeks. Therefore, the ^{59}Fe dose is 5 or 10 μC rather than 0.1 μC, which would otherwise be quite sufficient for measurement of oral absorption and total body retention.

Figure 1 illustrates the results with a normal male adult (WGF) and two cases showing high absorption (M R) and low absorption (J B). The range for absorption in normals is between 5-12% of the administered dose under our test conditions. Patient MR, a middle-aged woman, absorbed about 33% of an

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[1]During the first 12 hours following ingestion, redistribution of this iron in the stomach, gut, liver, blood, etc., causes unpredictable changes in the observed counting rate. However, intercomparison of the responses of each of the four individual detectors at 10 minutes, 2 hours, 4 hours and 8 hours has shown that the final distribution at 21 days is most closely matched by the detector responses at four hours post dose. Clearance of unabsorbed ^{59}Fe from the gastrointestinal tract is usually not complete until at least seven days post dose and sometimes later. Therefore, several observations should be made over a period of at least 21 days to permit extrapolation back to time zero.

oral dose of iron, well above our normal range. Her serum iron was 350 $\mu g/100ml$ with a total iron binding capacity (TIBC) of 492 $\mu g/100ml$ and a per cent saturation of 71 per cent. After 21 days, the counting rate observed with the wide field collimator and probe detector placed over the liver area was six times the rate observed over the heart. The ratio in normals is around 0.8 to 1.5. Intramuscular administration of 1 gm of CA DTPA (diethylene-triamine penta-acetic acid) caused urinary excretion of 10 mg of Fe in 24 hours—about three times the normal response. These findings suggested a diagnosis of hemochromatosis. Patient J B showed a body retention of ^{59}Fe of only 1.3% and none could be found in his red cells. His hematocrit was only 25; serum iron 228 $\mu g/100ml$; TIBC of 256 $\mu g/100ml$ and a saturation of 89%. These findings suggested a greatly reduced erythropoetic function in keeping with his refractory anemia.

Repeated TBC measurement of ^{59}Fe in the body following intravenous injection is also an excellent way to distinguish anemia due to chronic blood losses from anemia due to other causes (7).

II. *Calcium Absorption and Retention:* Determinations of calcium absorption and retention are carried out in a manner similar to that described above for ^{59}Fe, using an oral dose of 10 μC of ^{47}Ca as the tracer. Preliminary studies of 14 patients on calcium balance in the metabolic ward included radioassay of ^{47}Ca excreted in all urines and stools for at least three weeks following oral administration. Body retention of the tracer was also measured with the TBC and the results compared with retention calculated from the excreta collections. The TBC values were within eight per cent of the values based on excreta except for three instances, two of which could be attributed to accidental loss of samples. While this agreement was not spectacular, we feel justified in substituting the TBC method for the notoriously troublesome method of total excreta assay, which is often inaccurate because of incomplete stool collection. This substitution makes it possible to perform calcium absorption tests easily and cheaply on an outpatient basis. The subject makes only four short visits to the counter at intervals of about a week and no collections of excreta are required of him.

Figure 2 presents the results in two unusual cases and demonstrates the usefulness of the method. Subject I was under hospital observation during experimental treatment for obesity by starvation. His absorption of ^{47}Ca was about 35% of the dose, at the high end of the normal range and he avidly retained this dose of calcium. Retention half-time was about 55 days—higher than our range for normals. Subject II, on the other hand, absorbed a very large fraction of his oral dose, about 60%, but rapidly lost it from his body (half time about six days). This man had a portacaval shunt of about a year's duration which may have been responsible for this effect on his calcium metabolism.

Table I illustrates how repetitive tests can be helpful. Subject M A, a 51-year-old male with idiopathic osteoporosis and vertebral fractures, had two successive ^{47}Ca absorption tests, one month apart, while on a control diet with a normal calcium intake of about 900 mg per day. Both tests showed an absorption of about 35 per cent. However, when the dietary calcium was raised to 2600 mg/day, the absorption dropped to 23%, which is a normal response to such an increase. This patient apparently had no current abnormality in either gastrointestinal absorption or body retention of calcium.

The data on patient M I, a 30-year-old male, showed the effect of surgical removal of a parathyroid adenoma. Before operation, the patient had elevated values for serum and urinary calcium and a low value for serum phosphorus.

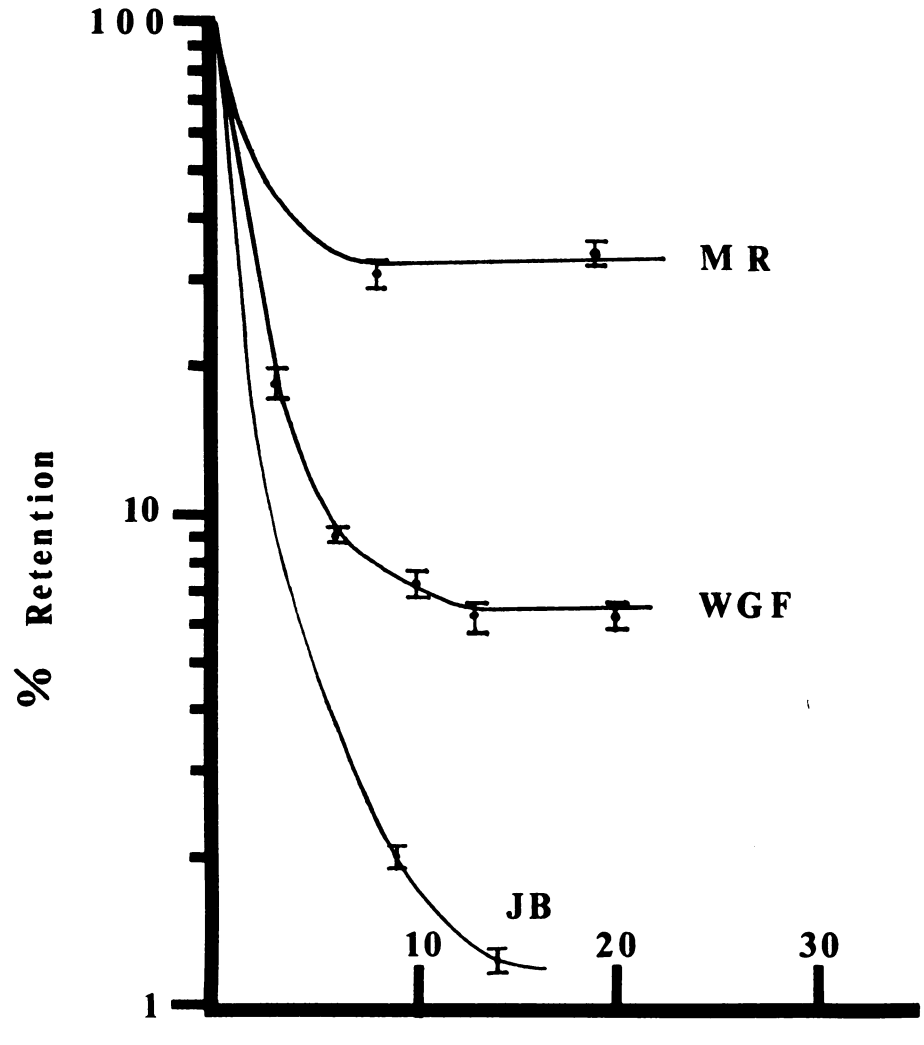

Fig. 1. Absorption and retention of an oral dose of 25 mg of iron as ferrous citrate, labeled with 10 μC of iron-59. The absorption is taken as the percentage in the body at 14 to 20 days post dose. The standard deviation of each measurement is about $\pm$0.07 of the value. Thus, for example, the estimated absorption for patient MR was 33% $\pm$ 2%.

Removal of the tumor returned these parameters to normal levels and the percentage of calcium absorbed orally was reduced by half, bringing it into the normal range. On the other hand, in the case of patient D D, a 52-year-old male, surgical removal of a parathyroid adenoma did *not* result in return of the abnormally high values for calcium absorption to the normal range. Two of eight serum calcium determinations have been elevated, (5.7 mEq/1), and the patient still has vague complaints. He is under observation to evaluate the possibility of another parathyroid adenoma or other illness.

III. *Serum Albumin Turnover:* The usual method for estimating the rate of turnover of serum proteins is to assay plasma samples taken at various times following injection of the radioactively-labeled protein of interest. By including

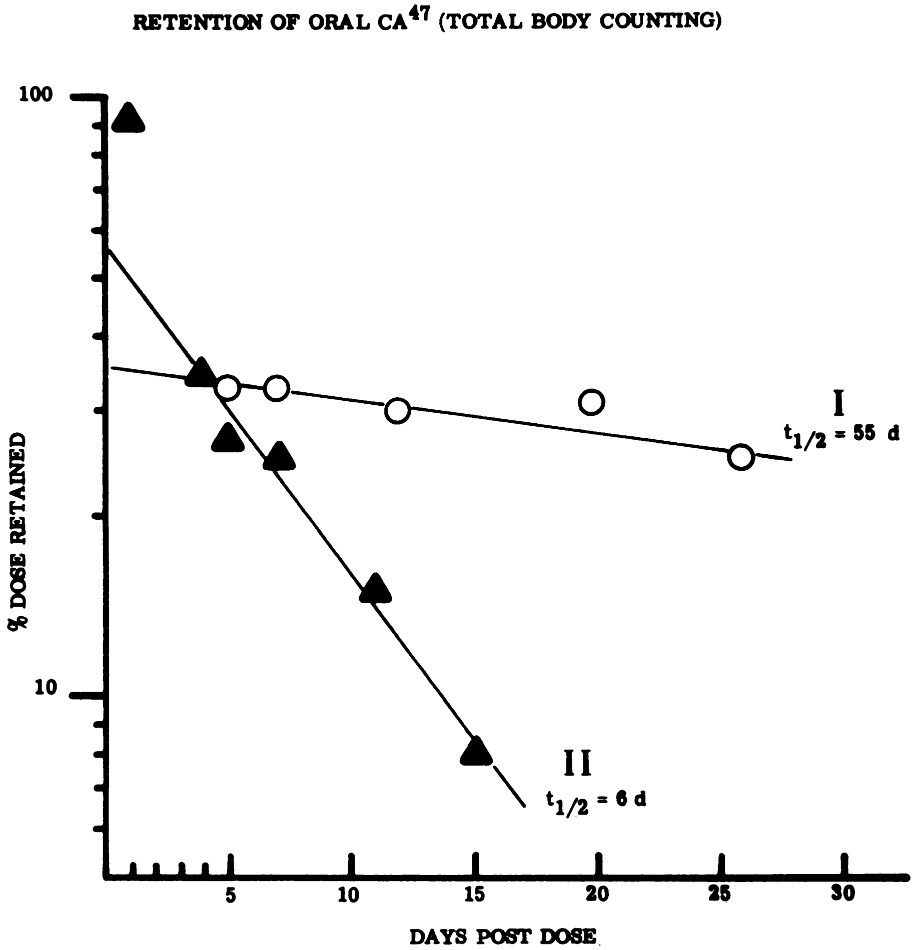

Fig. 2. Absorption and retention of an oral dose of 100 mg of calcium, as $CaCl_2$ labeled with 15 μC of calcium-47. The absorption is taken to be the value obtained by extrapolation of the line through the data for days 5-25 back to 6 hours, post dose. Each point has a standard deviation of about ±0.07 of its value. Thus, the absorption for patient I was 35% ± 2%.

assay of excreta samples, estimates of gastrointestinal loss of protein can also be made. The radioactive tag is commonly ^{131}I or ^{51}Cr (8, 9). The TBC offers the great advantage of making turnover measurements of these materials with a radiation dose to the subject which is only 1/100 or less than that delivered in plasma and excreta assay methods, a most desirable capability in the case of infants and young children. For example, figure three shows the retention data for ^{131}I-labeled serum albumin (0.05 μC dose I.V.) in a 10 month girl in mild distress from what appeared to be an allergic reaction to cows' milk. After removal of this item from her diet, a second test six weeks later showed a much longer retention half-time of 20 days. Unfortunately, we have only sparse data for this early age, but our half-time values for 9 normal children, 1 to 10 years, ranged from 8-13 days and for normal adults, 16-19 days.

It must be noted that this measurement of the retention of ^{131}I in the whole body with the TBC does not necessarily represent the turnover rate of the albumin in the circulating serum compartment. We are not measuring changes in serum concentration, but rather the changes in total body content of iodine-131. Thus, we cannot calculate the size of the exchangeable or circulating "albumin pool" from the TBC data alone. Furthermore, in our calculations we assume that this observed ^{131}I is still fixed on the albumin molecules as originally administered and that any major metabolic alterations of this albumin result in removal of the ^{131}I, followed by its rapid and complete excretion with no reabsorption in the gut. Uptake of freed iodine by the thyroid gland presumably is blocked by Lugol's drops given daily to the subject. The validity of all these assumptions has not been demonstrated rigorously as yet. Nevertheless, the TBC yields information on serum protein metabolism and/or gastrointestinal loss of protein which, though empirical in nature, can be useful to the physician. The information is obtained in a simple and safe manner, but at least four weeks' time is required before it is complete, since the curves from the plotted data can be described by at least two exponential functions. In spite of this complicated behavior, retention measurements over the first seven days often suffice to demonstrate abnormal conditions.

Excellent results in estimating the turnover of labeled serum globulins and albumin in patients by means of TBC measurements have been reported by Cohn *et al* (10) and Law *et al* (11).

IV. *Body Potassium:* The first developers of whole body counting systems soon realized that the great sensitivities of their equipment made possible the estimation of the amount of potassium in the human body by measurement of the gamma-emitting ^{40}K isotope naturally present in the chemical element and that such information is medically useful (12-15). Great effort has been expended by many investigators to calibrate their TBC systems for this purpose. By using ^{42}K, phantoms, and making various corrections for body shape and size, considerable success has been achieved in improving the accuracy of measuring body potassium-40. However, the problems of correcting for non-uniform tissue distribution of potassium and self absorption of the ^{40}K photons in overlying adipose tissue vary with each TBC system and are quite difficult to solve satisfactorily.

Blahd has studied the disease muscular dystrophy in detail, using a TBC and other techniques to elucidate the role of body potassium in this disorder. The exceptionally low body stores of potassium which occur in these patients and, indeed, oftentimes in unafflicted members of their families are readily demonstrable with the TBC (16).

However, we have found the accuracy of potassium measurement with the TBC to be insufficient for determination of day-to-day potassium balance. This accuracy is about ± 7-10% which corresponds to about 10-15 gms of potassium in the average adult. The serum potassium in a patient may have dropped to a seriously low level and the patient may be in critical condition without reduction of his total body stores of potassium below the range of our error in measuring it. Among the many patients with low serum potassium whom we have measured, only one has had a concurrent low value for total body potassium. Of course, depletion of body potassium can occur over a protracted period and can be demonstrated with the TBC. For example, 18 out of a group of 35 chronically ill patients, male and female, with renal disorders, cirrhosis and several additional diseases, had body potassium stores which were considerably below our normal range, based on measurement of over 200 healthy individuals.

The TBC has been helpful occasionally in following the progress of convalescence from illness accompanied by severe body wasting. Body potassium measurements with the TBC to assist in estimation of "lean body mass" have not been exploited sufficiently to make such estimations a routine service. Of course, this does not detract from their value in research projects, particularly when accompanied by measurements of total body water using dilution methods with tritiated water (17).

PROCEDURES OF OCCASIONAL OR BORDERLINE DIAGNOSTIC VALUE

There are a number of radioactively labeled materials of physiological interest whose behavior in the body can be followed accurately with the TBC. Many of these, however, are used only infrequently for diagnostic purposes and others can be utilized just as effectively by measurements of serum or urine specimens.

For example, exchangeable sodium can be determined easily by repeated TBC measurements of injected ^{22}Na over a period of several days. However, this offers no particular clinical advantage over the common dilution method of assaying blood or urine sample 24 hours after an I.V. dose of sodium-24 (18). The same may be said for TBC estimation of extra-cellular fluid space using bromine-82 (19).

Absorption of ^{60}Co-labeled Vitamin B_{12} can be determined with the TBC using only 0.02 μC of orally administered activity. However, we have found that the physician usually prefers the conventional Schilling test since he must wait only 24 hours for his answer, whereas the TBC method requires at least a week to permit clearance of unabsorbed labeled B_{12} from the gut. Furthermore, the most advantageous feature of the TBC method, namely its ability to yield results with a very low dose of ^{60}Co and thereby greatly reduce the radiation exposure to the patient, is largely discounted by using the shorter-lived ^{57}Co for the Schilling test.

We have been able to measure the rate of loss of ^{131}I-labeled thyroxine from the body after I.V. administration of 0.02 μC of activity for as long as two weeks. However, uncertainties as to what this information really means in terms of overall thyroid metabolism have hampered application to diagnostic problems.

UTILITY IN MEDICAL RESEARCH

The greatest long-term value of a TBC facility to a medical center lies in its unique capabilities as a tool for medical research, rather than as a diagnostic aid. These capabilities make possible the study of absorption and retention of a large number of labeled substances over time periods often of many weeks' and even months' duration. The amounts of radioactivity required can be so low as to permit such studies in infants and other subjects in whom the radiation exposure must be kept to an absolute minimum. Data are obtained with little or no discomfort to the subject, usually with few venipunctures and without the problems attendant upon stool and urine collection and assay. The excellent resolution of NaI detectors allows the simultaneous measurement of several different radioisotopes in the body, if nuclides with suitably different gamma emissions and appropriate half-lives are available. An evaluation of medical research carried out with TBC assistance will not be made in this report. Sampling of the sorts of problems taken under study by various investigators may be found in recent publications (3, 10).

ANCILLARY ACTIVITIES WITH THE TBC

As awareness of the existence and capabilities of the TBC increases among the staff at the medical center, more and more "odd jobs" are brought to the counter. For example, we have had several requests to ascertain whether or not certain patients had been given Thorotrast as a radiographic contrast agent a number of years earlier. The presence of thorium daughter activities was readily demonstrable. In another case, the presence of residual ^{90}Y activity (bremsstrahlung) was clearly apparent in a patient who had undergone partial ablation of the hypophysis by surgical implantation of ^{90}Y beads. It could be shown with the collimated detector that this activity was not generally distributed throughout the body and that the pellets had remained in place, rather than disintegrating and translocating.

The iron room of the TBC provides excellent shielding for performing radioisotope uptake tests in situations where very low doses are used and the background counting rates should therefore be as low as possible. Thus, we have measured the 24 hour uptakes of ^{131}I iodide in very young infants following injection of 0.05 μC. Though informative, these measurements are not fully satisfactory to the pediatrician because they do not define what fraction of the observed activity is in the thyroid gland itself. However, progress is being made toward correcting this fault. In any case, it is certain that tests of this sort require a low background environment and the iron room of the TBC is most

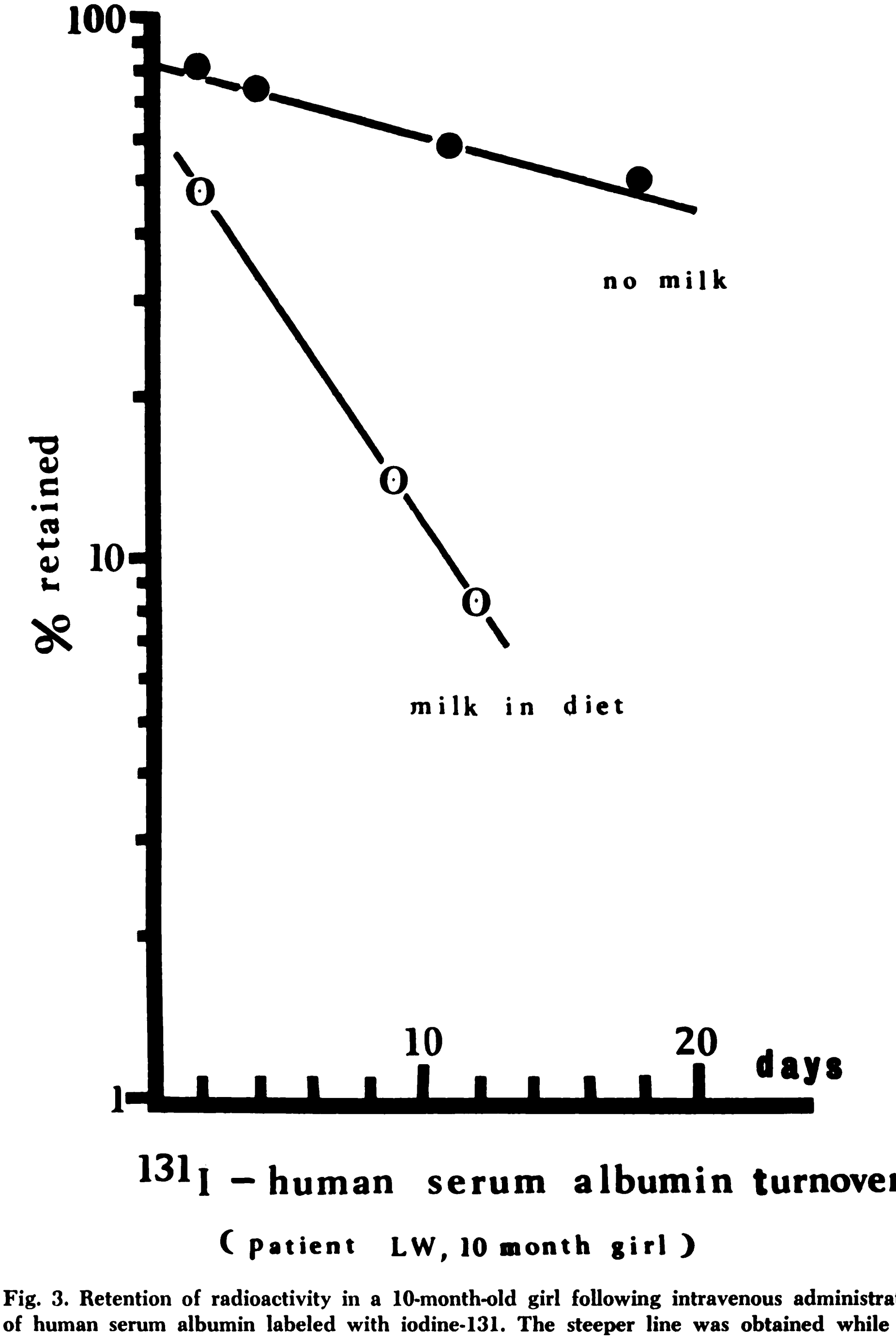

Fig. 3. Retention of radioactivity in a 10-month-old girl following intravenous administration of human serum albumin labeled with iodine-131. The steeper line was obtained while the patient was in a protein-losing phase probably associated with an acute allergic response to milk in her diet. The line with the shallower slope resulted from a second test one month later when the patient was on a milk-free diet. If loss of ^{131}I is assumed to correspond with albumin turnover and/or loss, then the "half times" during the first three-week period were about 4 days and 20 days, respectively.

convenient. The low background is also helpful in performing radioisotope osteograms for study of bone metabolism (20).

Of the more than one hundred TBC installations throughout the world, the greatest number are devoted primarily to monitoring radioactive contamination of persons in connection with health physics and radiation protection programs. This is also a legitimate and important activity for a TBC in a medical center. At UCLA, regularly scheduled TBC examinations are made of all personnel in the Center and in the whole University who use gamma-emitting isotopes in their work. These data provide evidence to the state radioisotope licensing authorities of continuing compliance with their regulatory procedures. Thus, among the technicians of the Radioisotope Service of the Radiology Department, no instances of internal contamination exceeding 2 μC have been found, though these people manipulate tens of curies of activity of many radionuclides during a year's time. Occasionally, an exceptionally interesting case is encountered. Figure 4 shows the spectrum of gamma activity normally observed in humans and the spectrum of a young man engaged in work at the Engineering Department Cyclotron. The unusual peak in his spectrum was identified as ^{7}Be, a nuclide with which he had never consciously worked. Inquiry revealed that he had recently entered the cyclotron area while the beam was on in order to adjust the target and that ^{7}Be was one of the products of the nuclear interactions occurring there. Though not a hazardous level of contamination, the amount detected clearly demonstrated the possible consequence of future careless actions.

Finally, the TBC serves a useful educational function in the medical center and indeed in the community, by providing information on the levels of radioactive contamination in members of the local population who are not exposed to radioisotopes for medical purposes. This information has been used on numerous occasions to demonstrate the ubiquitous nature of radioactivity in the human environment and thus to reduce the apprehension sometimes felt by uninformed patients encountering a radioisotope procedure in nuclear medicine for the first time. Figure 5 illustrates the trend of body burdens of radioactive cesium-137 in people living in the Los Angeles area. A peak was reached in 1964, but the mean body burden now is diminishing as a consequence of the cessation of large scale testing of nuclear devices in the atmosphere.
cillary services include routine monitoring of hospital staff, university faculty

SUMMARY

A total body counter can become a useful acquisition in a large hospital or medical center, providing unique assistance in the area of clinical diagnosis and medically oriented research, by applications of radioactive isotopes as tracers. Information of diagnostic value in problems involving the metabolism of iron, calcium, serum proteins and potassium can be obtained routinely and often solely by the TBC, without hospitalization of the patients or quantitative collections of excreta. The shielded enclosure of a TBC permits certain radioisotope uptake tests, such as measurement of the fixation of radioiodide by the thyroid gland, to be performed with greatly reduced radiation dosages. Valuable an-

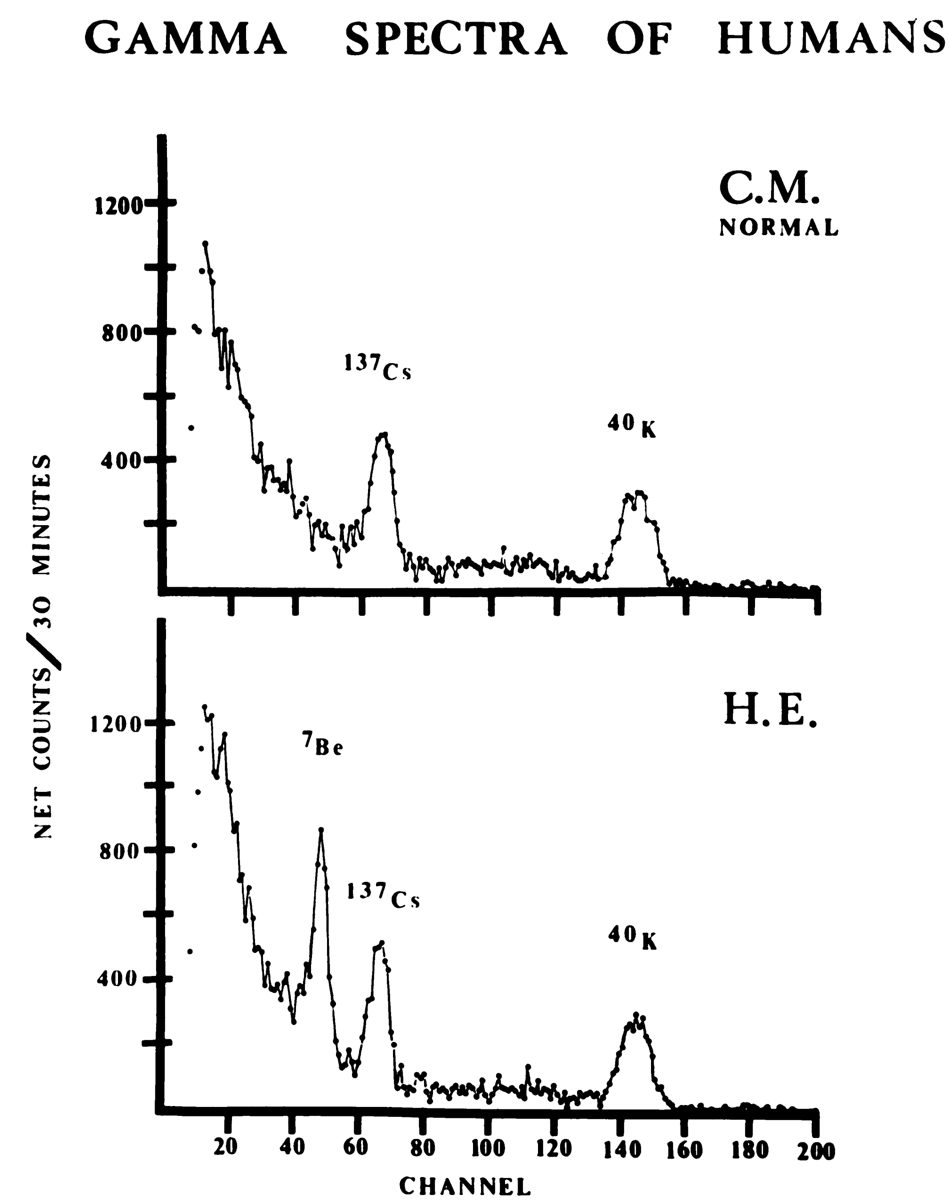

Fig. 4. Gamma spectra of a normal human (top) and a young man working in a cyclotron laboratory (H.E.). Potassium-40 and ^{137}Cs photopeaks appear at locations corresponding to photon energies of 1.46 MeV and 0.66 MeV, respectively. These nuclides are present in all humans now living. Subject H. E., however, has an additional peak at 0.48 MeV due to beryllium-7.

and students who work with radioactivity; emergency monitoring of personnel from nuclear industries in the community; and measurement of gamma activities in the local population-at-large, arising from environmental contamination.

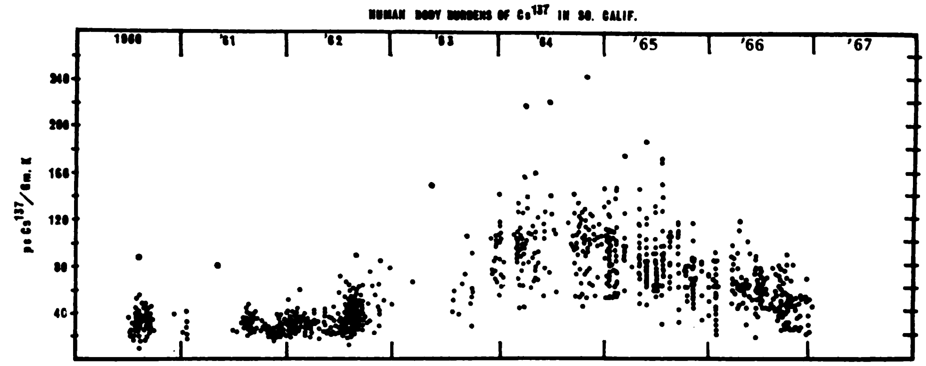

Fig. 5. Body burdens of Cesium-137 in residents of the Southern California area. The values are expressed as picocuries per gm of body potassium. (10^{-12}Ci/gm K).

TABLE I

CALCIUM-47 METABOLISM (ORAL)

Patient		*Absorption (% of dose)*	*t ½ Retention (days)*	*Remarks*
Osteoporosis				
MA	#1	37	20	922 mg Ca/day intake
	#2	36	20	922 mg Ca/day intake
	#3	23	21	2600 mg Ca/day intake
Hyperparathyroidism				
MI	#1	59	30	before surgery
	#2	32	35	after removal of parathyroid adenoma
DD	#1	58	26	before surgery
	#2	76	25	3 weeks after removal of parathyroid adenoma
	#3	68	28	11 weeks after removal of parathyroid adenoma

ACKNOWLEDGEMENTS

We wish to thank Dr. G. V. Taplin and Dr. L. R. Bennett for their aid and encouragement and Dr. W. Larson, L. Braden, R. Cassilas, E. Flynn, R. Hamel, M. Hepler, E. James and R. Van Deusen for their valuable technical assistance.

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