Measurement of 24 h energy expenditure in male tuberculosis patients

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Background & objectives: The total daily energy expenditure in patients with infectious disease is presumed to be high because of an increase in the basal metabolic rate (BMR), a reason for the weight loss observed in these patients. A reduction in daily physical activity, which may reduce the total daily energy expenditure. The aim of this study was to measure the free living total daily energy expenditure and physical activity of newly diagnosed hospitalized patients with tuberculosis using the labelled bicarbonate method.

Methods: In 6 healthy volunteers and 6 patients with newly diagnosed tuberculosis, 13C labelled bicarbonate method was used to measure free living total daily energy expenditure and physical activity. The 13C sodium bicarbonate (NaH13CO3) tracer was infused intravenously over a 48 h period and breath samples collected at regular intervals to estimate expired 13CO2.

Results: The patients had a 14 per cent increase in their BMR although they were not febrile at the time of measurement. However, their total daily energy expenditure was lower than that of the controls (mean value of 8.3 and 10.3 mJ/day respectively) and their physical activity level was also lower (mean 1.4 and 1.6 units respectively).

Interpretation & conclusion: The total daily energy expenditure of afebrile patients with newly diagnosed tuberculosis is not higher than that of sedentary controls, despite an increased basal metabolic rate. It is possible that the observed weight loss in patients with tuberculosis is due to a reduced energy intake linked to anorexia associated with the disease. These findings may have relevance in nutritional treatment of chronic infections.

Key words Energy expenditure - labelled bicarbonate method - NaH13CO3 - tuberculosis

The energy expenditure of man is presumed to be higher in disease states and this may be due to the hypermetabolic response to disease, which operates through a variety of processes1. Total daily energy expenditure (TEE) in an individual has three major components: the basal metabolic rate (BMR),
thermogenesis, and physical activity. It is known that the BMR of individuals with disease is increased by a factor that varies with the type of pathology, and this has led to the assumption that the energy requirement of such patients is higher than normal. Conversely, the physical activity component of energy expenditure in these individuals would naturally be reduced as a consequence of the disease, and an increase in the BMR could be offset or more than offset by the decrease in physical activity. Therefore, it is possible that patients with illness may not have an increased energy requirement, and their energy requirements may actually be reduced. This has been studied through careful measurements of TEE in studies done in developed countries in HIV infection where there have been reports of increased BMR but no change in TEE\textsuperscript{1-3}, and in one study on melioidosis in Thailand with the same result\textsuperscript{4}. In a similar chronic infection like tuberculosis, a disease associated with weight loss, it is possible that the weight loss is not only due to an increased catabolic rate and possibly increased daily energy expenditure, but also due to a reduced energy intake. The combination or the latter would lead to a negative energy balance and consequent weight loss.

In order to explore this possibility, one would need to measure the daily, free-living energy expenditure in health and disease. The evolution of tracer techniques has made it possible to measure energy expenditure in free living conditions. The labelled bicarbonate technique in man\textsuperscript{5,6} assesses CO\textsubscript{2} production, from which energy expenditure can be measured by using energy equivalents of CO\textsubscript{2}\textsuperscript{7-9}. The technique requires an infusion of \textsuperscript{13}C labelled bicarbonate, which can be achieved with a portable infusion pump, thereby allowing free voluntary movement. The measurement of the ratio of TEE to the BMR can also be measured as an index of physical activity that is independent of body size, and allows for comparisons of physical activity between groups. Therefore, the aim of the present study was to assess total energy expenditure and physical activity by the infusion of \textsuperscript{13}C-bicarbonate, in free-living Indian patients with pulmonary tuberculosis associated with weight loss and to compare these values with healthy control subjects. The principles and validity of the bicarbonate technique have been previously discussed in health and disease\textsuperscript{5,10,11}.

**Material & Methods**

The study was approved by the Institutional Ethics Review Board of St John’s Medical College, Bangalore, India. All subjects gave their informed consent to this study. The control subjects were healthy young males (age range 18-35 yr), had a BMI between 18.5 to 24.9 kg/m\textsuperscript{2} and were recruited through advertisement from the students and laboratory technicians in St. John’s Medical College Hospital. A brief medical history and examination was conducted on all subjects and those who were taking medications, or had a relevant past medical history, or who were smokers, were excluded from the study. All control subjects were weight stable and did not report a weight change of >2 per cent over the last two months and none had changed their normal dietary habits in the few days prior to the study. The patients (n=6) were all males (age range 18-35 yr) and recruited sequentially from the Pulmonary Division of the Department of Medicine, St. John’s Medical College Hospital. All had been diagnosed to have pulmonary TB by chest X-ray, clinical signs and elevated erythrocyte sedimentation rate (ESR) within the previous two weeks, and all had been started on multi-drug therapy within one week of the tracer experiment. Their renal and hepatic functions were within normal limits and their mean haemoglobin was 9.7 gm/dl. The patients were not febrile on the day of the experiment. There was no other significant past history of illness. The patients had lost about 10 per cent of their weight in the preceding two months, but this was not precisely quantifiable.
The controls (n=6) were admitted to the metabolic ward of the Division of Nutrition for the duration of the study (48 h). During this time they were allowed to continue their normal work and were free to go where they pleased, except that they were supervised during this time, and a 10 min interval time and motion diary of their activity was maintained. Patients who were recruited into this study, stayed in their respective hospital wards, with a person assigned to monitor their physical activity (by time and motion diary) and their dietary intakes. They were only brought to the Division of Nutrition’s metabolic laboratory for the measurement of their BMR in which, minute to minute oxygen consumption (VO₂) and carbon dioxide production (VCO₂) were determined with the aid of an open circuit indirect calorimeter with a ventilated hood. Whole system calibration was verified by combustion of pure ethanol, where the observed difference between measured and predicted total CO₂ production was <3 per cent and the average respiratory quotient (RQ) was between 0.64 and 0.68. The BMR of the controls and patients was also predicted using a weight based regression equation, which had been earlier developed for Indian subjects.

The controls were provided with a diet which consisted of chappatis (bread made from refined wheat flour) and oil, with egg albumen as the main source of protein. Wheat was chosen as the source of carbohydrate, in order to attain low ¹³C content in the diet and consequently, a relatively steady background in breath ¹³CO₂ enrichment over the experiment period. The total daily food intake had an energy content that was designed to keep the subjects weight stable at their habitual activity patterns and was consumed as three meals at the kitchen of the Nutrition Division, under supervision of the dietary staff. The patients also had similar meals provided thrice a day by the hospital dietary service, except that rice and lentils were also added.

On the day of the experiment, an intravenous 22-Gauge catheter (Jelco, Medex Medical Limited, Lancashire, UK) was placed in a forearm vein at a site that would allow free mobility of the arm. This was connected to the syringe of an infusion minipump (Graseby Medical Ltd, Watford, UK) by a connecting tube. The tracer solution of ¹³C labelled bicarbonate (99.9%, Mass Trace Ltd, Woburn, MA, USA) was prepared in 0.9 per cent normal saline under sterile conditions and thereafter sterilised with a 0.22 µ filter (Millipore, USA), had a pH of about 8, and an osmolality of about 600 mosmol/l. The labelled bicarbonate solution was loaded into the minipump syringe and then weighed on an electronic balance (sensitive to 0.0001g, Ohaus Corporation, New Jersey, USA). This was repeated when removing or changing the syringe, so that the exact volume of infused solution could be recorded. The infusion pump was placed in a holster that was attached to a belt placed around the waist of the subject. The tracer was administered in a dose of 3.9 µM/kg/h, and was primed with a bolus dose of 4.5 µM/kg. The infusion was started in the morning at about 1000 h, and continued for the next 48 h. The infusates were checked for their bicarbonate content immediately after the infusion ended by liberating the CO₂ in a known quantity of tracer bicarbonate solution, by the addition of phosphoric acid. The amount of CO₂ liberated was determined by isotope ratio mass spectrometry (IRMS, Europa Scientific Ltd, Crewe, UK) using sodium carbonate as a standard.

Three baseline breath samples were collected at 30, 15, and 5 min, before the tracer infusion started, in 10 ml plain glass tubes (Vacutainer, Becton & Dickinson, New Jersey, USA), to determine the background enrichment of ¹³CO₂. Breath samples were then serially collected during the second 24 h of infusion, starting in the fasted state at 0800 h on the second day of the infusion (the additional 2 h of sample collection between 0800 and 1000 h was to allow for measurement of bicarbonate recovery). For the purpose of calculation of TEE, breath enrichments
for the last 24 h (from about 1000 h on the second
day until the infusion ended at about 1000 h on the
last day), were used. Samples were then collected at
consecutive half-hourly intervals throughout the
second 24 h of the study. This necessitated waking
the subjects for breath samples, and therefore, at
night, samples were collected hourly. In the patients,
samples were only collected hourly throughout the
24 h. The samples were stored at room temperature
until analysed for their $^{13}$CO$_2$/$^{12}$CO$_2$ ratio by isotope
ratio mass spectrometry (IRMS) (Europa Scientific,
Crewe, UK), as described earlier$^{14}$. The increase in
breath enrichment in any sample was expressed as
atom per cent excess (APE), which was calculated
by taking the arithmetic difference between
enrichment of each breath sample and the pre-dose
basal breath sample.

The recovery of $^{13}$C bicarbonate through excretion
of the label in the breath was also measured, since it
is known that not all the generated $^{13}$CO$_2$ on the body
is immediately recovered in the breath. This can be
performed with an infusion of $^{13}$C bicarbonate, and
matching the rate of excretion of $^{13}$CO$_2$ in the breath
with the rate of infusion. Since it was required that
the subjects were free-living, and since the fasted
bicarbonate recoveries were similar to the fed state
recoveries in an earlier study in similar subjects$^{14}$, a
decision was taken not to measure the fasted state
recovery in the present study subjects, as this would
add a period of curtailment of activity to the day, and
reduce the free living nature of the study. In addition,
this measurement was only made in the control
subjects, as it would have been difficult for the patients
to stay fasted in the morning up to 1000 h. Therefore,
measurements of excretion of $^{13}$CO$_2$ were made during
the 48 h tracer experiment, in the last 2 h of the first
and second 24 h periods (between 0800 and 1000 h,
which would be early in the morning in the fasted
state). Total carbon dioxide production ($VCO_2$) was
determined by indirect calorimetry. The excretion of
$^{13}$C in the breath was calculated as the product of the
volume of CO$_2$ and its $^{13}$C enrichment. The recovery
of label in the breath was calculated as the ratio of the
rate of excretion of $^{13}$CO$_2$ in the breath to the rate of
infusion of $^{13}$C bicarbonate. The mean recovery factor
measured in this fashion, in the control subjects, was
then applied as a fixed factor for calculating the total
CO$_2$ output during the day in controls and patients as
shown below.

$$VCO_2 = \frac{^{13}\text{C bicarbonate infusion rate}}{\text{Breath enrichment of } ^{13}\text{CO}_2} \times 1/f$$

Where $f$ = recovery of label; in this case 0.75 (mean
of measured recoveries).

24 h $VCO_2$ = sum of all 30 min values over 24 h.

The RQ was assumed to be equivalent to the food
quotient (FQ) calculated from the diet according to
Black et al$^{15}$. The total energy expenditure of each
subject was calculated from the energy equivalent
of CO$_2$ ($E_{eq CO_2}$) that was appropriate for the
measured FQ of each subject according to the method
of Elia$^{9}$ and expressed in MJ/day.

The ratio of the TEE and BMR so measured were
used to estimate the physical activity level (PAL).
However, since the BMR is likely to be elevated in
patients, thereby giving a lower PAL, the energy
expenditure associated with physical activity (EEPA)
was also measured as the difference between the TEE
and the BMR. However, diet induced thermogenesis
could account for about 10 per cent of the TEE in
energy balance conditions; since the patients were
not weight stable, the thermogenic component of the
TEE was calculated as 10 per cent of the energy
intake (EI). Therefore, EEPA was calculated as the
difference between TEE and the sum of the BMR
and 10 per cent of the energy intake$^4$, and also
expressed as a percentage of the TEE.
Time and motion studies were also conducted on the controls and patients in order to assess if the bicarbonate tracer method gave reasonably similar values. Observers were assigned to each subject, and recorded their activities during the 48 h experimental period, in slots of 10 min each. Sleep was recorded as a block ranging from when the person went to bed to when he awoke. The activities were assigned values for energy cost of each activity from previously published tables in the literature; these were summed over each 24 h period, and averaged for daily physical activity level estimation. The PAL estimated by this method was also compared with the PAL measured by the tracer technique.

Differences between groups were assessed by the Student’s independent ‘t’ test. Differences were considered significant if \( P < 0.05 \). The measurement of PAL by the tracer method was compared with the PAL measured by the time and motion method using analysis of differences. Estimates obtained by the experimental methods were subtracted from the same estimate obtained from the prediction and the mean and ± SD of these differences (bias) were calculated. A positive bias indicated that the prediction estimates were greater than those obtained by the experimental methods. The differences were also regressed against the mean of the estimates being compared, in order to evaluate if the difference increased with the magnitude of the measurement.

**Results**

There were no significant differences in the age of the subjects. The weight of the patients was much lower than that of the controls (Table I), as was the BMI, however, their heights were similar (mean height 1.65 and 1.61 M in controls and patients respectively). There were also significant differences in the mid upper arm circumference (MUAC) as well as in the per cent fat between controls and patients (Table I).

The diet provided to the control subjects had an energy content of about 172 kJ/kg based on a physical activity level (PAL) of 1.6, which reflected their habitual activity levels, and a protein intake of about 1 g/kg/day. The intake of the patients was controlled by the availability of food through the hospital dietary service, and this included large amounts of lentils. Their protein intake was higher, at about 1.4 g/kg/day, as was the energy content of their diets (about 188 kJ/kg), which was about 1.8 times their normal BMR; however, the actual food intake was not

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<tr>
<th>Table I. Characteristics of healthy volunteers (controls) and patients studied for their energy expenditure</th>
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<td><strong>Characteristic</strong></td>
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<td>Age (yr)</td>
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<tr>
<td>Weight (kg)</td>
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<td>BMI (kg/m²)</td>
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<tr>
<td>MUAC (cm)</td>
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<td>Per cent body fat (%)</td>
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Values are mean ± SD
MUAC, mid upper arm circumference
Patients, n=5 for MUAC and per cent body fat (%)
*P<0.01 compared to controls

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<th>Table II. Measured and predicted energy expenditure over 24 h, in patients and controls</th>
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<td><strong>Parameter</strong></td>
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<tr>
<td>Measured BMR (MJ/day)</td>
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<tr>
<td>TEE (MJ/day)</td>
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<td>PAL measured</td>
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<td>PAL observed</td>
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<td>EEPA (MJ/day)</td>
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<td>EEPA/TEE (%)</td>
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Values are mean ± SD
Independent t test; *P<0.05 compared with controls
BMR, basal metabolic rate; TEE, total energy expenditure; PAL, physical activity level; EEPA, energy expenditure associated with physical activity
measured in the patients as leftovers were not weighed or recorded.

The recovery of infused bicarbonate in the control subjects, in the fasted state, in the present study was 75.4 ± 8.2 and 75.3 ± 8.4 per cent during the end of the first and second 24 h periods. The range of recoveries was from 63 to 89 per cent, and was stable within subjects. The pattern of enrichment of breath $^{13}$CO$_2$ was phasic, with lower enrichments observed during sleep and higher enrichments during the day with feeding (Fig. 1). The measured BMR of the subjects was 6.3 ± 0.7 MJ/day (Table II) which compared well with the subjects predicted BMR of 6.1 ± 0.3 MJ/day. In the patients, there was a higher measured BMR compared to the predicted BMR (5.9 ± 0.8 vs 5.2 ± 0.4 MJ/day, respectively). This meant that the BMR of the patients was increased by their tubercular disease, by about 14 per cent.

The measurement of TEE by the tracer method showed that the TEE was significantly higher in the controls (Table II), although this significance disappeared when the TEE was expressed per kg body weight. The measured TEE expressed per kg body weight was not significantly different between the groups (182.7 vs 195.4 KJ/kg/day in controls and patients, respectively) despite the patients having a 14 per cent mean increase in their BMR. The slightly higher (but non significant) TEE/kg body weight/day in the patients was possibly due to their low body weight in comparison to controls, but the general similarity of TEE in both groups meant that there was a compensation for the increased BMR through a reduction in voluntary physical activity (Fig. 2). This is relevant since the patients were free to move around and were not told to specifically reduce their activity beyond standard hospital instruction.

When the measured TEE was divided by the measured BMR to give an index of physical activity (PAL) that is independent of weight, the value was 1.6 ± 0.1 and 1.4 ± 0.2 in controls and patients, respectively. These values were just short of being
significantly different \((P=0.06)\), and implies that the patients tended to have a lower physical activity level when compared to the controls. The PAL values ranged from 1.4 to 1.8 in the controls and from 1.1 to 1.7 in the patients showing their heterogeneity. The estimates of EEPA (calculated using 10% of energy intake to represent thermogenesis in both groups) were significantly different \((P<0.05)\) between groups. When expressed per kg body weight, the values tended to be lower in the patients, although not significantly so \((53.1\pm17.8 \text{ and } 38.0\pm22.4 \text{ KJ/kg}, \text{ controls and patients respectively. The EEPA when expressed as a percentage of TEE tended to be higher in controls } (28.4\pm6.5) \text{ than in patients } (18.8\pm10.2\%), \text{ but this difference was not significant. The EEPA/TEE ratio also showed a non significant trend towards an inverse relationship with the factor by which the patients BMR was increased } (r=0.5, P=0.3). \text{ The estimates of EEPA as a percentage of TEE also correlated well with the PAL } (r=0.8, P<0.05).

The tracer based estimate of PAL was also compared with the estimate of PAL from the time and motion study. These showed a reasonably good approximation of each other, with mean differences between methods of 0.1 PAL units in both controls and patients; however, in the controls the variability of differences was less with an SD of 0.05 PAL units, while in the patients it was 3 times this value at 0.14 PAL units. The difference in PAL estimates was also plotted against the mean value of PAL by both methods (Fig. 3), and the differences were close to the zero value in the controls and in most of the patients, except in two, in whom the PAL was low in general, and in whom the time and motion study estimate of PAL was higher than the tracer estimate. In general, the tracer based TEE gave a good
approximation of the time and motion study based TEE. This is particularly relevant, as a major assumption made in the tracer experiment was the use of an assumed factor for the recovery of tracer in the patients.

Discussion

This study showed that the TEE in a chronic infectious disease was not increased beyond that of a normal person with a sedentary activity profile. The measurements were made in patients who were not pyrexic, but had a mean increase in their BMR of about 14 per cent. The BMR is known to be increased during injury or infection and this increase is dependent on the severity of the injury, ranging from 100 per cent with large burns of the body surface to about 10 per cent after surgery. If there is fever associated with the injury, the metabolic rate will increase concomitantly. The increase in the basal metabolic rate is driven by the inflammatory response, in particular due to the cytokine response to the infection. The overall BMR response to chronic infection will also depend on what effects the weight loss has on body composition. The loss of fat free mass for example, would lead to a reduction in BMR compared to a loss of less metabolically active tissues such as fat. Measurements of body composition in adults with TB have shown that they lose lean tissue and fat in approximately equal proportions, and that the lean tissue loss is appendicular (most likely muscle). In this case, the preservation of more metabolically active visceral tissue would probably also contribute to an increased BMR/kg body weight. However, measurements of TEE made in other chronic infections such as HIV, have been shown to be comparable to that of normal subjects, and similar to the present study, the physical activity level of HIV positive patients was compatible with that expected for people leading a sedentary lifestyle. This suggests that in general, the cause for a negative energy balance leading to weight loss, is unlikely to be due to a large energy expenditure, but more likely because of poor energy intake due to anorexia and associated social factors in these patients. Habitual

![Graph of differences in physical activity level (PAL) estimates by the ‘tracer method’ and the ‘time and motion’ method plotted against the mean value of these estimates. Solid and dashed lines represent the mean difference values for controls and patients respectively.](image)

Fig. 3.
energy intake in the months prior to admission was not measured in these patients since it was felt that a historical record under these circumstances would not be accurate. In general however, all patients admitted to eating less, but were unable to quantify precisely how much less they had eaten.

The bicarbonate infusion method allows for total daily energy expenditure to be measured over short periods like one to four days in free-living individuals. Since the recovery of bicarbonate is generally constant 1-4 days after the start of the infusion it is desirable that the actual measurement is performed 24 h after the start of the infusion. The enrichment of the blood pool of CO₂ is represented by the measurement of the enrichment of CO₂ in alveolar air, necessitating the collection of breath samples over frequent and regular intervals throughout the measurement period, which effectively reduces the true free living nature of the measurement. An alternative to this method of sampling, which is tedious for the subject or patient, is to collect urine over the measurement period (in this case, 24 h), and to measure the ¹³C enrichment in urinary urea. This value is expected to mirror (with a 15% systematic error) the changes in the enrichment of the blood bicarbonate/CO₂ pool, and therefore afford a relatively non-interfering method of sample collection; in one study there was no difference between the labelled bicarbonate method (using urinary urea based) and whole body calorimetric estimates of TEE using ¹⁴C-labelled bicarbonate. There are possible errors that can exist when converting CO₂ production rates to energy expenditure. The energy equivalents of CO₂ are much more variable than the energy equivalents of O₂, and attention needs to be paid to the use of the correct energy equivalents. Further errors may arise in the determination of the FQ, since the method used in this study assumed that the energy equivalents of oxygen are same for all macronutrients; however, this small error can be ignored. An additional source of error comes from the assumption that the RQ is equal to the FQ in weight losing patients. Ideally, this is addressed by accounting for the proportion of body fat or protein lost, in the calculation of the FQ, and as observed in the anthropometric profile (low body fat) of the patients, their weight loss was likely to be due to the oxidation of fat stores. However, first, it is very difficult to accurately measure body composition change over the short duration of the bicarbonate tracer experiment and second, the error in the measurement of TEE associated with ignoring the body compositional change are small and likely to be less than 5 per cent.

The measurement of PAL in the present study was made by the determination of the ratio of TEE and the measured BMR. It might be argued that the PAL should have been measured by the ratio of the TEE and the predicted (normative) BMR. However, the PAL should be reflective of the activity energy expenditure over the measured BMR, even when the BMR is increased or decreased. The estimates of EEPA as a percentage of TEE correlated well with the PAL but were not exactly concordant with each other, because the energy expended due to thermogenesis was measured as a function of the energy intake and then deducted from the TEE, before calculating the EEPA. However, when the PAL was calculated from the time and motion study data, based on literature values for the physical activity ratio of each activity, these values correlated well with estimates of PAL by the tracer method in both controls and patients, except in two patients with low PAL values. The physical activity ratios for different physical activities in the literature are based on healthy subjects, and it is not known whether the PAR is increased for different activities in patients with tuberculosis, and how much this is dependent on the severity of the disease, or presence of cough. This will insert a degree of variability into the estimate of PAL by the time and motion study. If the PAR values were truly higher, then the PAL estimated by the time and motion study would have been underestimated; however, the average PAL estimated by the time and
motion study was similar to that measured by the tracer method in both groups, and similar in most individuals.

The PAL was similar between the controls and patients, and both reflected the sedentary nature of their lifestyles. In the patients, who were admitted in hospital, movement was not restricted and they were free to walk around the ward. The only other tracer method to measure free living TEE is by the double labelled water technique, however, the labelled bicarbonate technique is much cheaper to perform than the double labelled water technique, and is easier to deploy over shorter term periods of a few days (as opposed to 10 days in the double labelled water method) and more particularly, has a definitive use in hospital bound or sick patients. In earlier validation studies against whole body indirect calorimetry, the bicarbonate method has been shown to differ from indirect calorimetric estimates of energy expenditure by a mean value of less than 2 per cent10.

The recovery factor for bicarbonate in the present study controls was lower than that documented previously in other studies10,25, but similar to those we have recorded in earlier 24 h experiments in similar subjects14. Further, the same lower recovery has also been observed with bolus experiments in Indian subjects with 13C-labelled bicarbonate26. One possible reason for the lower recovery was that it was not measured during the entire day, but only measured in the fasted state. The recovery was measured in this fashion because we have earlier found that fasted and fed state bicarbonate recoveries are reasonably similar in a very similar group of control subjects14, and recoveries remain quite stable after the first 24 h24. The reasons for the incomplete recovery of 13C-bicarbonate are well known and include CO2 fixation as well as equilibration and entry of the label into slowly turning over pools8,25. Methodological issues could also potentially contribute, such as the contribution of dietary 13C to the enrichment of breath 13CO2 and the preparation and delivery of the isotope solution. If the 13C contribution from the diet was significant, then higher recoveries should have been recorded; however, the dietary contribution of 13C is likely to have been low particularly in the controls, because of their low 13C-containing diets. The isotope solution was prepared in 0.9 per cent saline, with a pH of 8, and the solution of labelled bicarbonate infused was analyzed immediately before and after the infusion. It is not known, at present, whether Indian subjects have a relatively larger (for example, bone27) slowly turning over pool, which might account for the lower value for 13CO2 recovery recorded. The value of 75 per cent that was observed in the present study was also used as a fixed factor for the patients; the use of a higher value for recovery (for example, 80-90%) would have resulted in an even lower estimate of TEE in the patients. Further, in the controls, the measured TEE correlated reasonably well with the TEE estimated by the use of a time and motion diary, affording face validity to this measurement.

In conclusion, the present tracer based estimate of total daily energy expenditure showed no increase in spite of an increased BMR, due to a reduction in physical activity. The weight loss observed in these tuberculosis patients is more likely to be due to a negative energy balance induced by a lower energy intake, linked to the anorexia associated with disease. The nutritional requirement in chronic infections need not be beyond normal levels, and anorexia of illness and the sensory aspects of food presentation to patients should receive attention.

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