DIRECT QUANTITATION OF HEAT LOSS
IN HUMAN SUBJECTS
USING INFRARED THERMOGRAPHY

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CHAPTER 1

INTRODUCTION

Conceptually

The regulation of body weight is simplistic, on both a theoretical and

mathematical basis:

Change in Energy Stores = Energy Intake - Energy Output.

The problem occurs when scientists attempt to apply this simple idea to the

human body, which is a system operating unsteadily, not only from day to day,

but also hour to hour. During the span of a year, the caloric intake and

output of an individual differs by several thousand kilocalories (kcal), yet in

a normally lean individual, body weight remains stable (1).

On the other end of the scale is the obese individual, who appears to eat

no more than the normal weight person, yet has grossly enlarged adipose tissue

stores. Previous studies have suggested that the obese may suffer from a

thermogenic defect, which results in a more efficient utilization of energy,

but this theory remains controversial (2,3).

Historically, investigators have used direct calorimeters to quantitate

heat loss, which is the end product of energy expenditure. The classic

investigations of Benedict and Carpenter (4) focused attention on the use of a

simpler method, indirect calorimetry (IC), which measures heat loss as a

function of oxygen consumption. Their studies demonstrated a close correlation

between these two methods. Subsequent investigators have used these findings

to justify applying only the IC method in the study of energy metabolism, often

ignoring the fact that these studies were performed on normal, healthy people

with reported values representing a minimum of 24 hours.

The naiveté of this view is reflected by current scientific publications

which remark on the difficulty of predicting changes in body weight even when

energy intake and energy expenditure are known (5,6). In 1983, one publication cited the case of an obese woman, who failed to lose the amount of weight predicted for the hypocaloric regimen on which she had been placed (7). In addition, clinical situations exist in which the discrepancy between the amount of energy needed to achieve caloric balance and that which was predicted is often large. An illustration of this phenomenon is the patient with carcinoma, who requires more energy than predicted or measured by indirect calorimetry to attain a positive caloric balance (8). Thus, it would appear that measuring only oxygen consumption provides insufficient data for accurately determining energy needs in all individuals. One possible explanation for these results is that although all oxidative processes are thermogenic, as the body is not 100% efficient at energy conversion, all thermogenic processes are not oxidative. Therefore, IC would not detect the inefficient energy transfer of futile cycling or the uncoupled oxidative phosphorylation of brown adipose tissue.

Thus, it is apparent that both indirect and direct calorimetry must be used if these findings are to be explained and to determine if a change in metabolic efficiency does indeed occur. The indirect calorimetric method is easily adapted for use in a variety of clinical and non-hospital environments. However, direct calorimetry lacks this flexibility, as it is expensive and requires subject confinement, which precludes its use in any setting other than a research laboratory.

For the past five years, our laboratory has been developing infrared thermography (IRT) as a means of directly quantitating heat loss. The IRT system is portable, non-invasive and does not require contact with or confinement of the subject. Thus, it offers tremendous potential for investigating efficiency of human metabolism in settings outside of the

research environment. Using this method, mean body surface temperature can be measured. This value, when used in conjunction with theory permits computation of radiant, convective, evaporative and total heat losses.

The initial methodologic research on the IRT system was completed by Kathleen Golos in partial fulfillment of the requirements for her Master of Science degree from the University of Illinois. Her investigations centered on the feasibility of quantitating heat loss using the infrared thermographic system, determination of the appropriate heat loss equations and finally, initial studies with the system. The present investigations validated the IRT technique by comparing heat loss data to heat production data obtained with indirect calorimetry under fasting conditions. Subsequently, the ability of the system to detect the following were evaluated: [1] fasting thermogenesis; [2] postprandial thermogenesis in subjects consuming a meal of known energy, protein, carbohydrate and fat content; and [3] intraprandial thermogenesis in patients receiving intravenous nutritional support as total parenteral nutrition (TPN).

The present investigations did not include evaluation of the effects of exercise in potentiating diet-induced thermogenesis, nor did they address the possible existence of a blunted thermogenic response in obesity. However, it was necessary to discuss the results of these studies as it was only in this context that the topic of thermogenesis was covered in the literature. This information was particularly pertinent to the present investigations as few have used either infrared thermography or direct calorimetry to evaluate heat loss. Currently, most studies use indirect calorimetry to measure energy expenditure. Although a few direct calorimeters still exist, they are seldom used for quantitation of heat loss. Instead, this equipment functions as a

respiration chamber for the measurement of gas exchange. To provide further background, discussions of techniques for measuring energy expenditure, energy balance, the components of energy expenditure, fasting thermogenesis and total parenteral nutrition and its influence on thermogenesis.

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CHAPTER 2

LITERATURE REVIEW

Despite the number of studies investigating energy metabolism, little is known of the efficiency of substrate utilization or energy requirements of normal, healthy humans. Even less information is available concerning the effects of intravenously administered nutrients on energy expenditure in malnourished or critically ill patients.

In the clinical setting, energy requirements are estimated using the Harris-Benedict equations, which predict resting metabolic rate (RMR) based on the subject's age, sex, height and weight (1). Daly and Heymsfield et al (2) have shown that these formulae tend to overestimate caloric needs of healthy men and women by as much as 10 to 15%, on the average. This finding is not unexpected as these equations represent statistical summaries of measurements collected on large numbers of healthy individuals. This finding is further supported by Owen et al (3) who have reported that currently available tables and regression equations overestimate the RMR of healthy women by 7 to 14%. Most likely, the Harris-Benedict formulae are being inappropriately applied when used to predict precisely the energy needs of a single individual, particularly a hospitalized patient. Thus, to collect accurate data on energy balance in healthy subjects and sick patients, caloric expenditure must be directly measured and not based on prediction equations.

There are numerous techniques available for determining human energy expenditure, each with its advantages and disadvantages. They vary in terms of accuracy, versatility, complexity, availability and cost.

TECHNIQUES FOR MEASUREMENT OF ENERGY EXPENDITURE

Direct Calorimetry

Although still considered the definitive method or "gold standard" for determining energy expenditure, direct calorimetry is seldom used today as less than ten direct calorimeters exist world-wide. The expense involved in construction and maintenance of the calorimeter and the complexity of its operation produce experiments which are tedious (4). To retain the sensitivity and responsiveness of the calorimeter and the reliability of the data collected, subjects must be confined in a small, chamber-like room (5) for several days, which precludes its use in long-term studies of energy balance in normal subjects or critically ill patients. Adaptation to environmental conditions in the calorimeter requires a great deal of time thus, subjects must enter the room several hours before the scheduled start of the investigation.

Indirect Calorimetry

Attempting to overcome the limitations of direct calorimetry, early investigators focused attention on developing alternate techniques for measuring energy expenditure. In the early 1900's, the classic studies of Benedict and Carpenter (6) demonstrated an almost perfect correlation between direct and indirect calorimetry. Subsequently, investigators have justified using only the latter method for studies of energy metabolism based on the Benedict and Carpenter findings, while apparently overlooking that this relationship was demonstrated to exist only for 24 hour data.

IC, the most popular technique in use today, indirectly assesses heat production or metabolic rate using O_2 consumption and CO_2 production data. If urinary nitrogen excretion is known, the type of substrate oxidation within the body can be calculated using the non-protein respiratory quotient (RQ). In

a fasting individual, an RQ greater than 1.00 typically indicates hyperventilation, which reflects a lack of steady state conditions and an inaccurate test. An RQ less than 0.70 is associated with the oxidation of ketones or the synthesis of carbohydrate from fat, i.e., the glycerol moiety, but usually low values indicate a methodological error.

RQ	Substrate Oxidized
> 1.00	Fat Synthesis
1.00	Carbohydrate
0.85	Mixed Diet
0.80	Protein
0.71	Fat

Although requiring less sophisticated equipment than the direct method, IC has its disadvantages. The open circuit technique uses cumbersome collection devices connected to large bore tubing through which expired air is collected in a meteorologic balloon. Subjects should be trained in the use of the equipment as unfamiliarity with the apparatus can adversely affect data collection. Apprehension, anxiety or hypo- and hyperventilation result in marked variations of the RQ, which are not related to fuel oxidation (7). In the clinical setting, Damask and Askanazi et al (8), using the rigid lucite head canopy method, demonstrated that a relatively minor procedure, such as a muscle biopsy, can induce temporary, but major increases in respiratory gas exchange. VCO_2 showed an average increase of 93% with a rise of 103% for VO_2. This resulted in an overestimation of the RMR.

Methods Combining Direct and Indirect Calorimetry

The mobile suit calorimeter, designed by Webb et al (9), combines the direct and indirect methods. The "suit" is a clothing assembly consisting of a

water-cooled undergarment and a heavily insulated overlying garment. The face is covered by a plastic mask attached to the indirect calorimetry equipment. Unfortunately, the face, a site of high heat loss, is not covered by the water-cooled system. This situation injects a potential source of error into determinations. While wearing the suit calorimeter, the subject is connected to an elaborate system of computers, flow sensors and a water cooler/heater unit. Because of the amount of equipment involved and the need for the subject to remain attached to it, the number of studies which can be performed outside of the research setting is limited. Also, the suit effectively isolates the individual from the environment, such that during the performance of physical tasks, energy expenditure measurements might not be accurate due to loss of environmental stimuli. With the current design of the suit, it is of little to no value in the study of energy expenditure in the clinical setting.

Infrared Thermography

Recently, investigators have turned to infrared thermography (IRT) for evaluating both quantitative and qualitative data on heat loss. There is a paucity of data on visualization of heat changes in the body by infrared thermography. To date, studies have centered on quantitative changes in surface temperature over areas of skin covering suspected sites of brown adipose tissue (BAT) in obese and lean subjects (10,11). Although these studies have demonstrated statistically significant increases in skin surface temperature after eating, it is unknown if these changes were due to activation of BAT or to cutaneous vascular changes causing heat emission from the skin.

ENERGY BALANCE

Body energy stores are a function of the interaction of nutrient intake and

energy expenditure. The basic tenets of energy balance are simplistic:

    Energy Intake > Energy Output   Result: Weight Gain

    Energy Intake < Energy Output   Result: Weight Loss

    Energy Intake = Energy Output   Result: Weight Maintenance

However, problems ensue when scientists attempt to apply these concepts. It then becomes apparent that each component of the energy balance equation is composed of several others. Energy intake refers to the metabolizable energy of foods ingested, not total energy consumed. However, energy output is far more complex, consisting of: [1] metabolizable energy excreted from the body in the urine and stools; and [2] the thermogenic process, or heat production. This heat, produced as a consequence of metabolism, should not be viewed as a waste product. Man, as a homeotherm, requires this internal "furnace" for maintaining a relatively constant body core temperature of 37°C. Another postulated use of this added heat is to signal that feeding has occurred. When exposed to high or low ambient temperatures, higher animals will decrease or increase their food intake respectively, proving an interrelationship between control of body temperature and feeding (12). Moreover, during undernutrition, Keys et al (13) reported that subjects complained of being cold or having cold hands and feet. Even during the hot summer months of the study, individuals slept under heavy blankets and wore extra clothing.

COMPONENTS OF ENERGY EXPENDITURE

Daily total energy expenditure can be accounted for by the summation of four moieties: [1] resting metabolic rate (RMR) which is a by-product of cellular and body maintenance; [2] the thermic effect of physical exercise (TEE); [3] adaptive thermogenesis (AT); and [4] the thermic effect of food

(TEF) or diet-induced thermogenesis (DIT), the more commonly used term (14).

1. Resting Metabolic Rate

The RMR accounts for approximately 60-75% of the total daily energy expenditure, which is required for maintenance of normal body functions and homeostasis, plus a small component related to sympathetic nervous system activity. To measure the RMR, the subject should have rested for 30 minutes, eaten a meal two to four hours prior to the test and have not participated in significant physical activity. These criteria are more readily fulfilled than those of the basal metabolic rate which require that [1] data be collected with the subject at rest in bed, shortly after awakening in the morning; [2] 12-18 hours after a meal; and [3] in a thermoneutral environment (15). Factors influencing RMR include: age, sex, genetics, preceding diet, body composition, temperature (ambient and core), hormones, drugs and stress (14).

2. Thermic Effect of Exercise

The TEE is the energy required for muscular activity. Its contribution to daily caloric expenditure is dependent on the duration and intensity of the physical activity, but generally accounts for approximately 30% of total energy output. However, it is the most variable of the components of thermogenesis, with a rate of caloric expenditure that can be as great as 10 to 15 times the RMR. Although alterations of an individual's nutritional state do not appear to affect TEE, interest has arisen concerning a possible potentiation of DIT by exercise (16).

3. Adaptive Thermogenesis

This component appears to account for no greater than ± 10-15% of daily energy requirements, but might be a major determinant of long-term weight

changes. However, its role in humans has yet to be defined. AT is
primarily a change in RMR resulting from adaptation to environmental
stresses, such as changes in ambient temperature, food intake and emotional
stress. With undernutrition, the decline in RMR is initially greater than
that which can be accounted for by loss of body mass alone. During
overnutrition, a 10-15% rise in RMR may occur. Biochemical changes, such
as activation or suppression of futile cycles and changes in the efficiency
of oxidative phosphorylation and activity of the sodium-potassium pump are
also possible mechanisms of adaptation (14).

4. Diet-Induced Thermogenesis

DIT is one of a number of expressions used to describe the increase in heat
production specifically related to feeding. Other terms include:
postprandial thermogenesis, specific dynamic action (SDA) and
luxusconsumption. Currently, DIT is the term of choice as it includes both
immediate and long-term increases in heat production, which are related to
feeding. It consists of two separate components: [1] a putative
regulatory or energy dissipative process and [2] an obligatory or basal
process, which consists of the energy costs of digesting, absorbing and
utilizing or storing substrates (17). It is this last component which has
been the subject of a number of investigations in recent times.

HEAT PRODUCTION AND LOSS IN THE ABSENCE OF THERMOGENIC STIMULI

The classic investigations of Benedict (1,6,18) revealed the almost perfect
correlation existing between direct and indirect calorimetric methods, when
data were considered on a 24-hour basis (Figure 1). However, today's
investigators tend to overlook that Benedict's data also demonstrate that in

13

Figure 1. Three day values for indirect and direct
calorimetry expressed on a 24 hour basis. These data were
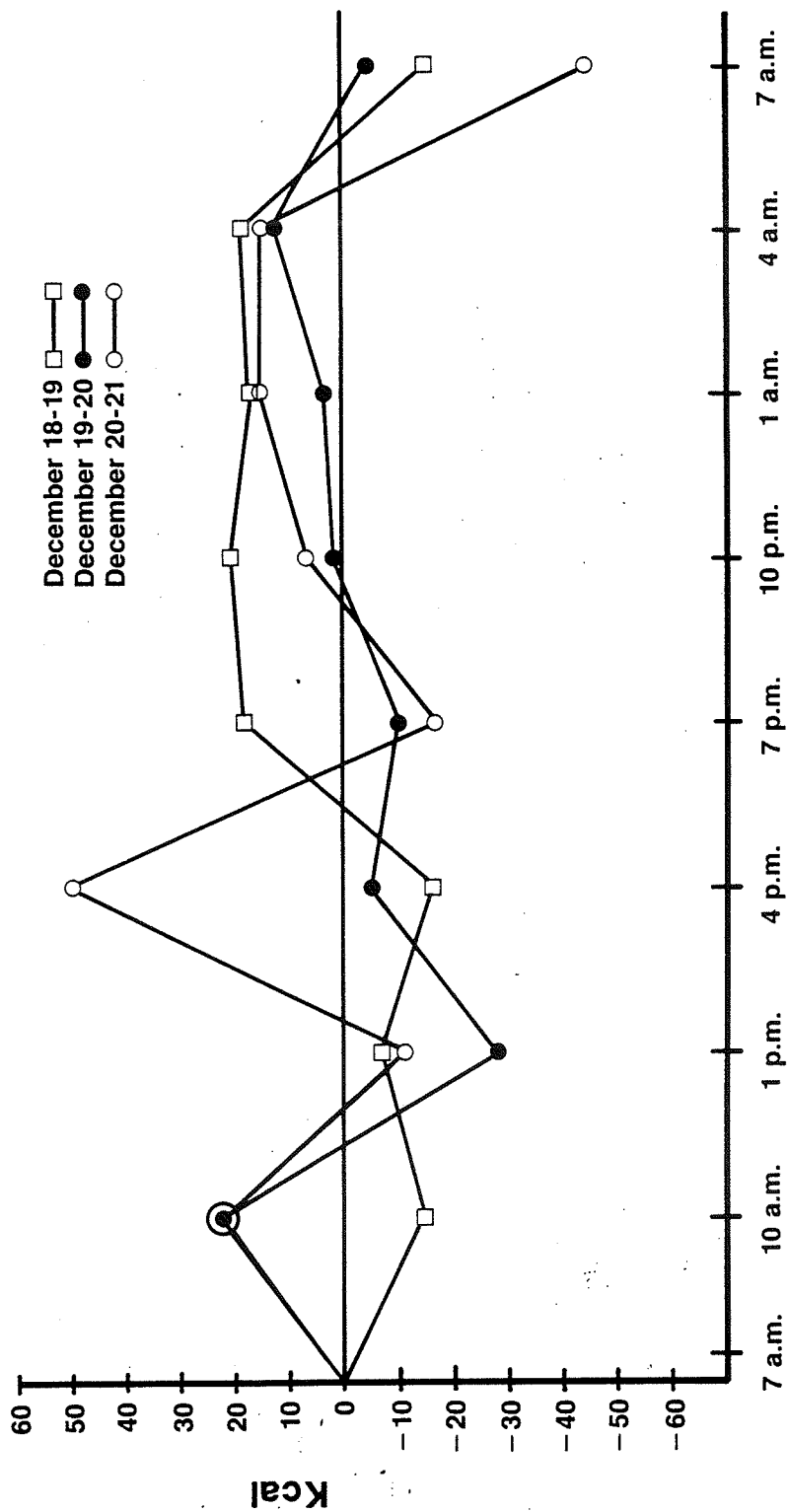collected on one fasting individual. Data adapted from FG
Benedict, 1907.
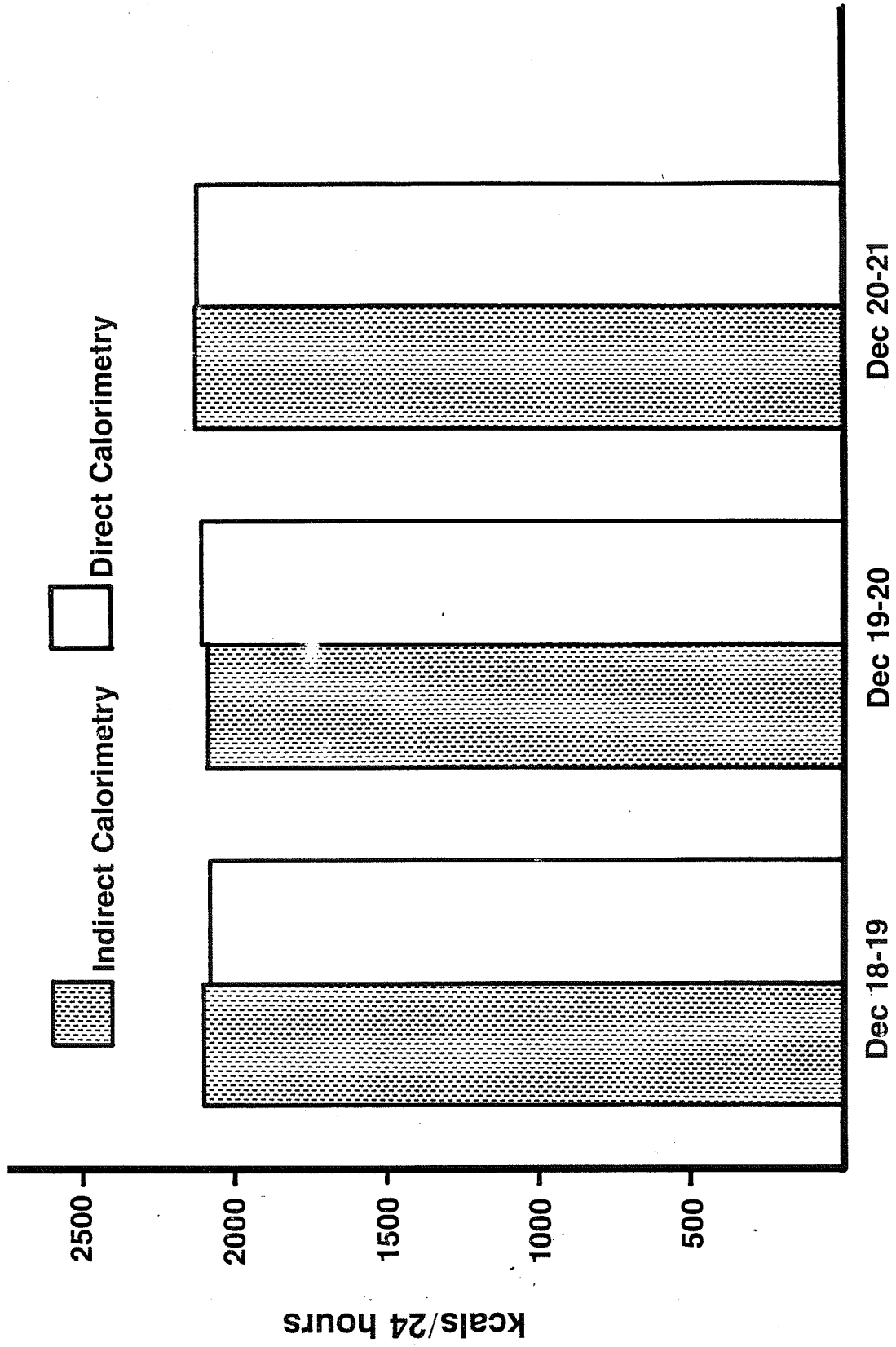
*Data from FG Benedict, Carnegie Institute, 1907

the absence of thermogenic stimuli, energy metabolism, measured over two to three hour time periods, shows great variability when heat production (IC) and heat loss data (direct calorimetry) are compared. Figure 2 illustrates the breakdown of the 24 hour day into three hour time periods. As is apparent from visual inspection of the graph, direct and indirect calorimetry do not always agree as well over time frames shorter than 24 hours. Moreover, the differences between the two methods varied on both sides of zero, i.e., at times indirect calorimetry (IC) exceeded heat loss, while the reverse was true at other times producing a cyclic pattern. Unfortunately, Benedict did not discuss the reasons for this variability in his publications. However, he did report in his book Vital Energetics (19) that "far greater progress will be made by discarding all thoughts of a uniformity in heat loss and emphasizing the non-uniformity in heat production".

Other investigations have also reported findings demonstrating this inequality between heat production and heat loss. Durnin (20) stated that with the shorter time periods of today's studies which measure metabolic rate, heat loss may not be absolutely identical to energy expenditure determined by O_2 consumption. Using a direct gradient layer calorimeter to measure heat loss and IC for metabolic rate, considerable differences between the results obtained by these two methods were shown to exist.

Using the mobile suit calorimeter, Webb (21) studied two male subjects over 24 hours and determined their heat balances were +14 kcal and +7 kcal. Thus, it appeared that significant heat storage had not occurred. However, evaluating the data on an hourly basis revealed the same discrepancies between IC and heat loss as previously reported by Benedict and Durnin. Despite storage or loss of 20 and 30 kcal per hour with a concomitant heat production

December 18-19 □
December 19-20 ●
December 20-21 ○

Kcal

60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60

7 a.m.   10 a.m.   1 p.m.   4 p.m.   7 p.m.   10 p.m.   1 a.m.   4 a.m.   7 a.m.

*Data From F.G. Benedict, Carnegie Institute, 1907

of 30 and 90 kcal, the subjects were comfortable. Grouping the heat loss values into three hour segments showed the possible existence of a human circadian rhythm of heat storage for 12 hours and heat loss for 12 hours, which was reflected in the diurnal curve of rectal temperature. In this situation, heat production leads heat loss by approximately an hour, which results in net heat storage and a rise in rectal temperature. Later in the day, heat production falls sooner than heat loss causing a decrease in rectal temperature. Since these initial studies, Webb has completed several others with essentially the same results (22,23).

Pittet et al (22) used direct and indirect calorimetry to evaluate the thermic effect of a glucose load on 10 control and 11 obese female subjects. These investigators demonstrated a negative thermal balance in the control group during the fasting period prior to glucose ingestion, i.e., mean heat production measured by IC was exceeded by mean heat loss (177.8 vs 192.0 $kJ/m^2/hr$). The obese women were in zero thermal balance with mean values of 164.0 (IC) and 163.0 (direct) $kJ/m^2/hr$. However, the differences between the two techniques were apparent in both groups of women (Table 1).

DIET-INDUCED THERMOGENESIS

Not only is diet-induced thermogenesis (DIT) an area of current research interest, but it has been the subject of investigations for decades. By definition it refers to the increase in energy expenditure above resting metabolic rate that can be measured for several hours after a meal. The thermogenic properties of protein, carbohydrate and fat have been well-established and are well-accepted by the nutrition community. Although it can vary between individuals, DIT is generally assumed to account for

Table 1. Indirect and direct calorimetry values for obese and normal weight
women during a short-term fast*

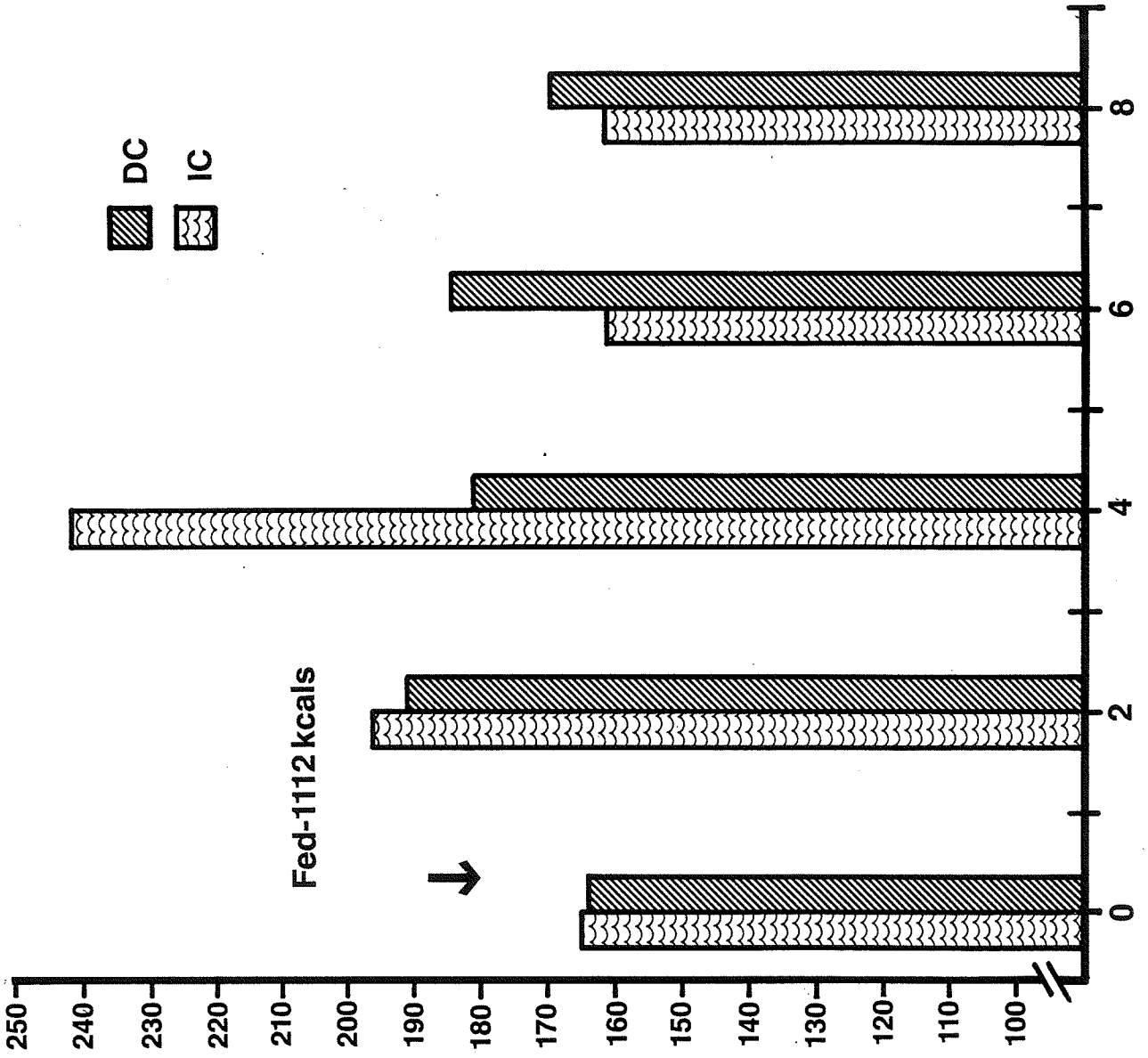| Subject	NORMAL		OBESE	
	Indirect	Direct	Indirect	Direct
1	195.1 ± 2.9	226.1 ± 5.1	145.0 ± 2.9	145.0 ± 2.5
2	149.4 ± 5.8	198.4 ± 0.4	180.0 ± 2.9	187.0 ± 7.6
3	174.3 ± 2.4	174.5 ± 1.1	165.0 ± 4.7	154.0 ± 3.2
4	162.4 ± 4.7	165.7 ± 1.1	186.0 ± 1.8	160.0 ± 2.2
5	189.3 ± 3.4	188.8 ± 1.6	158.0 ± 2.5	184.0 ± 1.1
6	172.8 ± 1.9	182.0 ± 0.7	166.0 ± 6.1	166.0 ± 1.8
7	197.3 ± 3.2	205.9 ± 0.9	144.0 ± 1.1	153.0 ± 0.7
8	190.5 ± 4.4	197.1 ± 1.5	167.0 ± 16.6	156.0 ± 3.2
9	182.4 ± 2.5	193.8 ± 2.5	157.0 ± 1.4	167.0 ± 3.2
10	164.0 ± 3.9	187.6 ± 1.3	148.0 ± 2.9	152.0 ± 2.5
11			189.0 ± 1.8	164.0 ± 1.1
MEANS	177.8 ± 5.0	192.0 ± 5.3	164.0 ± 4.8	163.0 ± 4.0

* Values represent means ± SEM for a 40 minute control period.

approximately 10% of daily energy output and most likely is determined by the caloric requirements for storing energy as glycogen, protein and triglycerides (25). DIT consists of two separate components: a putative regulatory or energy dissipative process and a basal or obligatory process which was originally referred to as the SDA (specific dynamic action of food).

As cited in an article by Rothwell and Stock (26), Rubner was most likely the first investigator who noticed that food ingestion stimulated heat production resulting in the loss of potentially useful food energy. Feeding only single nutrients, he demonstrated a greater effect for protein than either carbohydrate or fat. However, in subsequent studies using complete diets, Forbes and Swift (27) discovered that the effects of food on thermogenesis were related to the nutrient ratio in the diet and not solely to the protein content.

In 1918, Benedict and Carpenter (6) evaluated the effects of food ingestion on O_2 consumption and heat loss. As depicted in Figure 3, after consuming a meal, both O_2 consumption and heat loss rose significantly with IC data exceeding the direct calorimetric values for several hours postprandially. These investigators summarized much of the older literature on DIT and concluded that heat production due to food ingestion comprised 6% of the metabolizable energy of carbohydrate, 2% for fat and 12% for protein-rich diets.

Since reports in the literature have questioned the length of time for observation of the metabolic effects of a meal, Glickman et al (28) measured heat production for six to seven hours postprandially. Through extrapolation, they concluded that equilibrium was reached 15 to 16 hours after food intake. The thermogenic effect of a high protein diet was calculated to be 17% and that

DC
IC

250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100

Fed-1112 kcals

0   2   4   6   8

*Data from F.G. Benedict and T.M. Carpenter, Carnegie Institute, 1918

of a high carbohydrate diet as 11%, which were much higher values than those reported by Benedict and Carpenter.

If the thermogenic effects of a meal persist for at least 15 hours - and Dauncey and Ingram (29) have published evidence that the effects of a previous meal persist for over 20 hours in pigs and for 14 hours in humans (30) - then basal metabolism is affected by previous meals and this effect may be unintentionally superimposed on the one under consideration. This situation can be overcome if the 24 hour metabolism of subjects who have subsisted on the same amounts of food for several days is measured (31).

An offshoot of research on diet-induced thermogenesis centers on the potentiation of the thermic effects of food by physical exercise. However, a majority of the current literature has demonstrated a general lack of effect of postprandial exercise on the thermogenic response to a meal. Thus, it would appear that exercise after meal ingestion offers no greater benefit to obese individuals who are dieting than does preprandial exercise (32).

Diet-induced thermogenesis and its possible relationship with obesity has been the topic of numerous investigations. Interest in this field has been spurred on by evidence supporting the presence of a reduced thermogenic response to food ingestion as a causative factor in obesity (24,33,34,35). However, other studies have either failed to support this treatise (36) or investigators do not believe that a blunted thermogenic response plays an important role in causing or maintaining obesity in human subjects (37).

The thermic response of eight obese and eight nonobese subjects to a high carbohydrate and high fat meal were studied by Schwartz et al (38). These investigators demonstrated a greater thermic effect with the high carbohydrate meal as compared to the high fat meal. Although no statistical differences

between groups were noted for either diet, the trend toward a diminished response to the high carbohydrate diet was evident in the obese. The overall thermic effect of the meal was 8-13% of the 800 kcal provided.

Using continuous measurement of energy expenditure in a respiration chamber, Schutz et al (39) assessed the overall thermogenic response to food intake in 20 young non-diabetic obese women. The integrated DIT was computed as the difference between energy expended minus the quantities of the physical activity plus basal metabolic rate. These investigators found a blunted thermogenic response in the obese (8.7 ± 0.8%) as compared to the controls (14.8 ± 1.1%) and the DIT was negatively correlated to body weight.

Pittet and coworkers (24) have utilized both indirect and direct calorimetry in their studies, although recently, they have switched to the exclusive use of a respiration chamber. In their 1975 study of the thermic response to a 50 gram glucose load by obese and lean women, they reported that total heat losses were not significantly altered in either group after eating. However, total heat losses ($kJ/m^2/hr$) of the obese group were significantly lower than the control group throughout the experimental period. The obese women also oxidized less carbohydrate than the control group. After glucose consumption, heat production (IC) exceeded heat losses (direct calorimetry) resulting in a positive thermal balance. The mean skin temperatures of the obese subjects were significantly lower than in the controls and remained so throughout the postprandial period. When looking at O_2 consumption versus heat loss, IC values exceeded heat loss after eating, which is the opposite of that which occurs during an overnight fast.

Webb et al (9) reiterated that calorimetric energy balance, i.e., IC minus heat losses, is irregular from hour to hour. In 1980, they reported that the

amount of food ingested in comparison with energy expenditure for the day dramatically affects the measurement of energy balance. During these experiments, it was again demonstrated that heat loss and heat production are not always equal. With food intake almost matching energy expenditure in their subjects, the two methods gave similar results over 24 hours, but hourly differences were apparent.

TOTAL PARENTERAL NUTRITION AND THERMOGENESIS

Energy Expenditure: Measured and Predicted

Despite the number of studies investigating energy metabolism, little is known of the effect of intravenous administration of nutrients on energy expenditure in malnourished or critically ill patients. This is particularly disconcerting when one considers that total parenteral nutrition (TPN) has been an accepted treatment modality in the clinical setting for over 15 years. An accurate assessment of the caloric expenditure of hospitalized patients is necessary if adequate energy to meet requirements is to be provided while avoiding complications associated with administration of excessive energy.

Using indirect calorimetry, Paauw et al (40) measured the actual energy expenditure of 119 hospitalized patients and compared them to the results obtained using methods commonly employed, i.e., the Harris-Benedict equations (HBE), HBE plus stress factors, Wilmore's nomogram and estimates based on 25 and 35 kcal/kg. Of all the methods, the most accurate in predicting energy needs were the HBE and 25 kcal/kg. When compared to O_2 consumption data, the other techniques overestimated energy requirements.

Extending these studies, Mann et al (41) compared predicted energy expenditures which had been calculated using the HBE equations (ideal or actual

body weights) and the recommended caloric allowances to indirect calorimetric values. They demonstrated that in 50 acutely ill surgical patients, predicted energy expenditure based on actual and ideal weights exceeded measured values by 59% and 52%, respectively, while those based on the recommended allowances averaged 39% greater. However, Chan et al (42) examined predicted energy expenditure versus that measured by IC in 54 patients with radiographic evidence of Crohn's disease. These investigators were unable to demonstrate any statistically significant differences between the values obtained via the two methods.

Kinney et al (43) have investigated the effects of injury, sepsis and nutritional depletion on energy needs. They demonstrated that resting energy expenditure ranged between -30 (partial starvation) to +110% (third-degree burns) of normal under these conditions. However, variability in caloric needs was great, even with patients sustaining comparable injuries or similar degrees of infection or depletion.

MacFie (44) evaluated the active metabolic expenditure of 30 patients who had undergone gastrointestinal surgery and were receiving TPN. He concluded that few uncomplicated cases would ever require more than 2000 kcal/day to achieve a positive energy balance as evidenced by the caloric expenditures of the two groups (Preoperative: 1865 kcal/d vs postoperative: 1583 kcal/d).

Effects of Intravenous Nutrient Administration

Changes in whole-body energy metabolism of depleted cancer and non-cancer patients were reported by Edén et al (45) in 1983. Energy expenditure measurements were performed before and after TPN consisting of 30% glucose and 70% lipids providing 200 kcal/g nitrogen. During intravenous nutrient infusion, resting energy expenditure was increased substantially by 55-85% in

both the malnourished cancer and non-cancer patients measured under identical conditions. This occurred concomitantly with a proportional rise of in vitro muscle protein synthesis. From this, the authors speculated that the TPN-induced increased energy expenditure is partially due to the elevated muscle protein turnover.

Shaw et al (46) published findings similar to those of Edén et al. Ten nutritionally depleted patients received, in random order, TPN containing 180 mg/kg/d or 364 mg/kg/d of nitrogen with equicaloric amounts of glucose and lipid which provided 33.0 kcal/kg/d. Resting energy expenditure (REE) increased significantly with time during administration of the high nitrogen solutions. However, this did not occur with the low nitrogen diet. In terms of REE, the difference between the two diets increased sharply for the first three days, but did not change significantly after that, achieving an apparent steady state. With both diets, REE was significantly higher than during dextrose infusion alone. Moreover, the results of this study showed a distinct thermic effect equivalent to 9% of REE from amino acids, when added to an intravenous diet already containing adequate nitrogen.

The metabolic consequences of hypercaloric glucose infusions in nutritionally depleted and hypermetabolic patients was the topic of articles by Robin et al (47,48). They reported that nutritionally depleted patients demonstrated a moderate rise in CO_2 production and a minor rise in O_2 consumption, when glucose was infused above energy requirements. RQs often rose above 1.00. Patients with trauma or sepsis demonstrated a marked rise in CO_2 production and O_2 consumption, but in contrast to depleted patients, RQs usually remained below 1.00. This finding was probably due to the inability of the high carbohydrate infusion to inhibit net fat oxidation and/or

its failure to trigger net lipogenesis to the same degree as that which occurred in the nutritionally depleted patients. Since endogenous fat oxidation continued to supply a substantial portion of energy needs, RQs remain below 1.00 (49,50).

In an earlier study examining the effects of intravenous fat emulsion on depleted patients, Elwyn et al (51) administered different TPN regimens to two groups, one with glucose as the sole energy source and the other with 10% lipid emulsion substituted for one-third of the glucose calories. Each treatment was given alternately to every patient for one week at a time. Nitrogen balance was positive with both regimens. Amino acid and glucose infusions were kept constant over 24 hours, while fat emulsion was infused over six to eight hours. During this latter time period, fat was oxidized significantly faster, while RQ and carbohydrate oxidation were significantly lower than during the remainder of the day. This suggested that these changes were the direct result of fat infusion and were not due to diurnal variation. Immediate effects of fat infusion were increased fatty acid oxidation, decreased glucose oxidation and increased glycogen deposition rate, with no change in the rate of resting energy expenditure.

MacFie et al (52) reported findings similar to those of Elwyn et al and Robin et al in two groups of surgical patients who received either glucose alone or glucose and 60% of their energy needs as fat emulsion. The amount of amino acids provided were similar for both groups. The patients receiving glucose alone displayed a persistent elevation of RQ greater than 1.00 with a significant increase in energy expenditure. Those patients receiving the additional fat emulsion never had an RQ exceed 1.00 and displayed a mean energy expenditure significantly lower than the glucose group.

Thiebaud et al (53) employed the euglycemic insulin clamp technique in combination with IC to determine the effect of graded levels of hyperinsulinemia on energy expenditure. They found that glucose storage represented over 60-70% of total glucose uptake. The net increment in energy expenditure increased with increasing blood insulin concentrations and showed a significant relationship. However, at each level of hyperinsulinemia, the theoretical value for the energetic cost of storing glucose only accounted for 45-63% of the actual increase in energy output measured by IC. The authors concluded that other factors, in addition to glucose storage as glycogen, must be responsible for the increase in energy expenditure during glucose infusion.

As further support of this treatise, Gil et al (54) reported that infusion of glucose in excess of requirements produced a non-protein RQ greater than 1.00 and increased resting energy expenditure due, in part, to the storage of glucose as glycogen and fat. Patients with protein-energy malnutrition received six days of TPN with a low (Group I) or high (Group II) level of glucose intake. REE increased by 10% in Group I and 28% in Group II. The theoretical cost of glucose storage as fat and glycogen accounted for approximately 50% of the actual increase in REE in Group II patients which compares favorably to the values of Thiebaud and coworkers. Gil et al concluded that most of the remaining increase in REE was due to the thermic effect of amino acids.

Expanding on these studies, Jéquier (55) reported that in normal subjects, the thermogenic response to lipid infusion was 2 to 3% of infused energy and glucose-induced thermogenesis was 6%. The energy cost of nutrient storage for the amount of energy stored was 12% for glucose and 4% for lipid. The author concluded that lipid induced a lower thermogenic response and required less

energy for storage making it a more efficient means of providing energy to patients than glucose.

In summary, the literature points to and supports the need for actual measurement of energy expenditure in obese subjects, normal weight individuals and critically ill patients as prediction equations can overestimate caloric requirements. It would also appear that both O_2 consumption and heat loss should be measured to accurately determine the effects of nutrient administration on metabolism and more appropriately define nutritional regimens.

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CHAPTER 3

DIRECT QUANTITATION OF FASTING AND POSTPRANDIAL THERMOGENESIS BY INFRARED THERMOGRAPHY

ABSTRACT

This study describes the adaptation of infrared thermography (IRT) to the investigation of human energy metabolism. Nineteen control subjects were studied on two separate days, during a prolonged overnight fast and then after consuming a meal. IRT, a non-confining, non-contact and non-invasive method, accurately and rapidly measures body surface temperature. In the 10°C range of surface temperature, the camera is capable of detecting temperature differentials as small as 0.07°C. Using mean temperature in conjunction with theory, radiant, convective, evaporative and total heat losses were calculated. To validate the IRT method, heat loss data were compared to those obtained by indirect calorimetry (IC). No significant differences were demonstrated between the data collected by the two methods. However, trends in IC and IRT values were noted. During the short-term fast, IRT values exceeded those of IC, while the reverse was true of the postprandial studies. Both IC and IRT results displayed significant increases after eating, with IC values increasing by 30 minutes postprandial and remaining elevated. A lag period was demonstrated for IRT values, which were not significantly increased until 60 minutes after eating. It was concluded that IRT can be used to quantitate heat loss and study postprandial thermogenesis in human subjects. Further, it is apparent from this investigation that measurement of O_2 consumption alone does not adequately delineate changes occurring in energy metabolism after eating.

INTRODUCTION

Nutritional scientists have long endeavored to explain the mechanisms by which the energy stores of the body are regulated. The basic tenet of this control is simplistic: energy stores = caloric intake minus energy expenditure. Unfortunately, application of this principle to the human subject fails to explain why caloric intakes and energy expenditures can vary by hundreds to thousands of calories per day, yet body weight remains stable (1).

To understand why the above occurs, nutritionists must measure energy expenditures of individuals in an accurate and efficient manner. The classic investigations of Benedict (2,3) revealed almost perfect agreement between direct and indirect calorimetry (IC) in the fasting state. In light of these findings and in an attempt to simplify data collection, IC alone has since been used for measuring energy expenditure. Using this technique, investigators have demonstrated that food intake increases oxygen consumption and energy expenditure in a process referred to today as diet-induced thermogenesis, or DIT (4,5). In obese individuals, DIT appears to be blunted (6,7).

Although direct and indirect calorimetry data are similar on a 24 hour basis during fasting, when data are evaluated for shorter time periods of two to three hours, variability has been demonstrated (Figure 4) (2,8). These differences become even greater with exercise or food ingestion (5). Study of these discrepancies may begin to explain the mechanisms behind regulation of body energy stores in the normal weight individual as well as in the obese and in other metabolic states such as anorexia nervosa, hyperthyroidism, cancer cachexia, burns, trauma, etc. In order to achieve this goal, both heat production, measured by IC, and heat loss, measured by direct calorimetry must be quantitated. However, with a limited number of direct calorimeters available worldwide, the expense of purchase and maintenance of this

Two-hour Time Periods

□ Direct + Indirect ◇ Difference
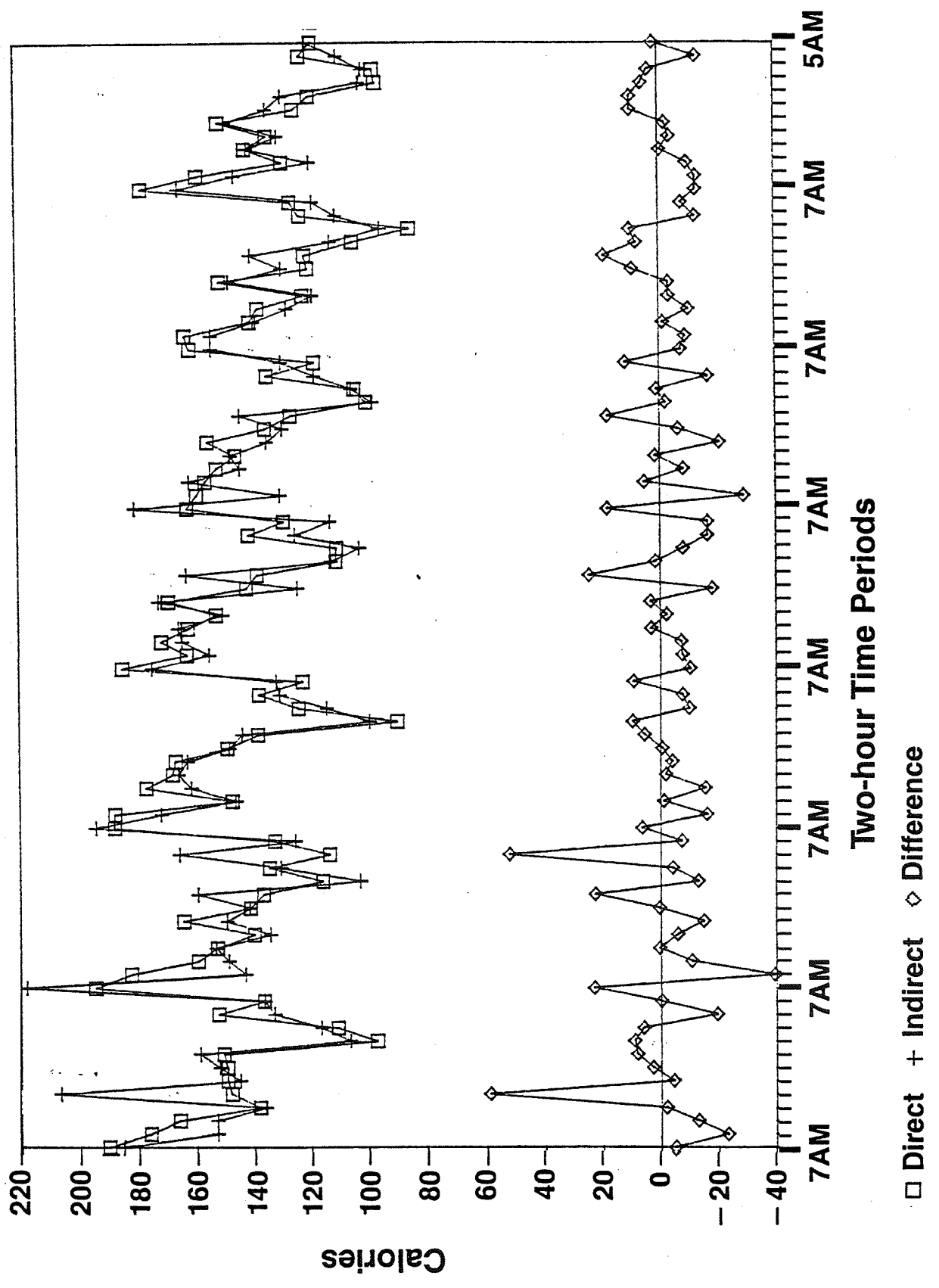
From F.G. Benedict (1907)

equipment and the need to confine the subject for prolonged periods to collect data, the use of this method is impractical. Even the availability of IC in the research and clinical settings is declining. Therefore, instead of measuring energy expenditure directly, the most universally employed technique for determining caloric requirements is to estimate them using the prediction equations developed by Harris and Benedict (2). These investigators used multiple regression analysis to relate basal energy expenditure to height, weight, age and sex. However, these equations can yield results which exceed caloric needs of healthy individuals by an average of 7-15% (9,10).

Therefore, to measure caloric expenditure of an individual, new and accurate techniques must be developed which can be used outside of the research environment for the study of subjects in their natural environments. To this end, researchers have used infrared thermography (IRT) to quantitate changes occurring in skin surface temperature with food ingestion (11,12).

Ongoing work in our laboratory has reconfirmed the ability of IRT to quantitate mean skin surface temperature in human subjects. This value is used in conjunction with equations for radiant, convective and evaporative heat loss the results of which can be summed to quantitate total heat losses of an individual. Preliminary studies have demonstrated the feasibility of using the IRT system for this purpose. The present investigation sought to to validate the ability of the IRT system to quantitate heat loss by comparing its results to those of indirect calorimetry, the current "gold standard" for determination of energy expenditure. Subsequently, fasting and postprandial thermogenesis were evaluated on two separate days for 2.5 hours in 19 control subjects.

MATERIALS AND METHODS

Subjects

Study participants resided in Champaign-Urbana, Illinois. They were
recruited from the employees of the Department of Medical Research at Carle
Foundation, medical and graduate students of the University of Illinois and
outpatients of the Carle Clinic in Urbana, Illinois. This investigation had
the approval of the Institutional Review Boards of the University of Illinois
and Carle Foundation Hospital. Written informed consent was obtained from each
subject. After initial expression of interest, each subject was contacted by
one of the investigators, the study protocol was briefly explained and
willingness of each individual to participate was confirmed. Subject
eligibility was based on the following criteria: [1] $\geq$ 18 years of age; [2]
normotensive; [3] normothermic ($\leq$ 37.7°C); and [4] lack of acute infectious
processes.

Subject Attire

To facilitate data collection, it was considered desirable to have as much
skin exposed as possible without embarrassing the subject. Thus, participants
wore shorts, a t-shirt, appropriate undergarments and ankle socks (if desired).

Anthropometrics

Weight was measured to the nearest quarter pound on a balance beam Detecto
scale (Detecto-medic, Brooklyn, NY). Height, measured by meter sticks, was
recorded to the nearest 0.1 cm. Ideal body weight (IBW) was obtained from the
1983 Metropolitan Life Insurance Company tables (13). Wrist circumference, for
computation of body frame size (14), was measured to the nearest 0.1 cm using a
fiberglass tape. Bicep, tricep, subscapular, suprailiac and mid-thigh
skinfolds were obtained using Lange skinfold calipers (Cambridge Scientific

Industries, Inc, Cambridge, MD). From these values, percent body fat and
kilograms of body fat and lean body mass (LBM) were estimated (15,16). To
ascertain body surface area (BSA), the 19 circumference and length
determinations of DuBois (17) were measured to the nearest 0.1 cm.

Dietary Intake Record

Study participants were mailed dietary record forms with detailed
instructions for completion. Using standard units of measure, food intakes
were recorded by the subjects for the 24 hours immediately preceding the days
of the study. During the first day of the study, subjects chose the types and
amounts of food they wished to consume on the second day for the postprandial
investigations. The meal was obtained from the Carle Foundation Hospital by
one of the investigators. Food portions were weighed or measured as
appropriate. The only stipulations place on food selections were: [1] no
caffeinated beverages and [2] women were to consume at least 500 kcal and men,
800 for the meal. Food intakes were analyzed for kcal, protein, carbohydrate
and fat content using a microcomputer nutrient analysis software program,
Nutritionist III (N-squared[R] Computing, Silverton, OR).

Infrared Thermography (IRT) System

The model 525 infrared imaging radiometer (Inframetrics, Bedford, MA) is a
small, lightweight field instrument which produces a television compatible
video output signal. The subject's naturally emitted infrared radiation
(8-12 μm) is converted by a liquid nitrogen-cooled Hg-Cd-Te detector to an
electrical signal that is processed into a television picture of the
temperature patterns in the scene which the camera is viewing. These "infrared
images" are recorded on VHS videotapes and saved for later data analysis. A
calibrated grey scale with 256 divisions, from white to black, is presented

across the bottom of the image in normal scanning mode, which provides a means for indicating the relationship between the contrast in the display and the temperature differential. Video processing is set such that for the 10°C surface temperature range of these studies, the central portion of the calibrated scale represents 160 levels, each with an associated discrete temperature (18). Although the camera is calibrated internally on a continuous basis, a direct temperature readout cannot be obtained. Therefore, temperature data from three independent standards, the black bodies, were used to generate a calibration curve comparing grey scale values from the camera system to known temperatures recorded at the time of scanning. The temperatures chosen for the black bodies covered a span from 23-33°C, which is comparable to the 10°C range of surface temperatures detected on human subjects. Black body temperatures were measured with surface thermistors (YSI series 400, model 409A), telethermometer (YSI series 400, model 42SC, Yellow Springs Instruments, Inc, Yellow Springs, OH) and YSI model 4002 twelve channel switch box. Ambient temperature was monitored with a YSI model 405 air temperature thermistor. Oral temperature was also obtained by using a thermistor from the same YSI series. A full-range mercurial barometer (Princo Instruments, Inc, Southampton, PA) was used to measure barometric pressure and relative humidity was obtained via a motor-driven psychrometer (Vista Scientific Corporation, Ivyland, PA).

Calibration of Thermistors and Thermometers

Due to the dependence of IRT heat loss data on ambient and black body temperature measurements, it was necessary to calibrate the air and surface thermistors and the psychrometer thermometers and determine their ability to accurately measure temperature. Each thermistor or thermometer was suspended

in water contained in a wide-mouthed dewar. Along with it, a certified
thermometer which had been calibrated to those from the National Bureau of
Standards was also suspended. Temperature varied according to the range in
which the instrument typically functioned. From the studies, regression
equations were generated which corrected thermistor and thermometer readings by
no more than 0.1°C. The correlation coefficients for these equations were 0.98
to 0.99.

Temperature Differentials in the Study Room

To account for the temperature differential between the floor and ceiling
that existed in the study room, a regression equation relating the recorded
ambient temperature to the average of three thermistors located at varying
heights between the ceiling and floor. As the heat loss equations permit
inclusion of only one value for ambient temperature, a weighted mean air
temperature was used. It was calculated by taking 75% of the value obtained
from the regression equation as the area between the chest and feet of each
subject fell within the range of the three thermistors. The remaining 25% was
based on the actual air thermistor reading which was representative of the
temperature surrounding the subject's head and shoulders (Appendix 1).

Computer Analyses of IRT Data

Infrared patterns of each subject's heat loss were recorded on videotape
using a VHS video player/recorder (Canon, Lake Success, NY). For purposes of
data analyses, the tape was played from the video cassette player into a video
frame store (Colorado Video, Inc, Boulder, CO), which digitized the entire
infrared image from each frame and simultaneously displayed the image on a
black and white television monitor (Panasonic, Secaucus, NJ). With the aid of
a VT240 microcomputer system, PDP-11 microprocessor and RX02 dual disk drive

(Digital Equipment Corporation, Champaign, IL), the frame chosen for analysis was frozen and stored on an eight-inch floppy disk. Upon retrieval of the image from the disk, computer software programs were used to remove the background thermal patterns from the frame, leaving only the digitized front or back view of the subject. Another facet of the software tallied the number of pixels contained in 0.5°C divisions of the 10°C study range over the total body surface area. From this information, mean surface temperature was calculated. This value was one variable used in equations for computing radiative and convective heat losses as well as evaporative heat losses due to diffusion through the skin and from the respiratory tract (Table 2) (19). As subjects stood during scanning, heat loss by conduction was ignored since only the soles of the feet, minor parts of total body surface area, contacted another surface. Convective heat losses were assumed to represent free rather than forced convection, since air flow measured by hot wire anemometer (series 100VT, Datametrics, Dresser Industries, Inc, Wilmington, MA) was less than 0.002 m/sec. For human subjects, transition between free and forced convection is thought to occur at an air flow velocity of 0.2 to 0.3 m/sec.

Indirect Calorimetry Measurements

The indirect calorimetric procedure was explained to each subject prior to initiation of expired air collection into a meteorological balloon. Open-circuit indirect calorimetry with a mouthpiece, noseclamps and a non-rebreathing valve was completed after the IRT scanning procedure and while the subject stood. Air collection lasted for three to five minutes, after which the minute volume was determined using a chain-compressed Tissot gasometer (Warren E. Collins, Inc, Boston, MA). Respiratory gases were analyzed by a Beckman LB-2 CO_2 infrared analyzer and a Beckman OM-14 O_2

Table 2. Radiant, convective and evaporative heat loss equations[1]

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1. Radiant Heat Loss: $R = A_D h_r (\overline{T}_{cl} - T_a)$
    Where: A_D = DuBois surface area

    h_r = linearized radiant heat loss coefficient

    $\overline{T}_{cl}$ = mean surface temperature

    T_a = ambient temperature

2. Convective Heat Loss: $C = A_D \overline{h}_c (\overline{T}_{cl} - T_a)$

    Where: $\overline{h}_c$ = convective heat exchange coefficient

3. Evaporative Heat Loss: $E_{dif} = A_D f_{pcl} w h_e (P_s - \varphi_a P_a)$

    Where: f_{pcl} = Nishi moisture permeation factor for clothing

    w = wettedness factor

    h_e = evaporative heat transfer coefficient

    P_s = saturated vapor pressure over water at $\overline{T}_{cl}$

    φ_a = relative humidity

    P_a = saturated vapor pressure over water at T_a

    E_{re} = V_E in kg/hr $(0.029 - 0.00066\varphi_a P_a)$ kg H_2O (kg dry air $^{-1}$)

    (575 kcal/kg)

    Where: V_E = ventilation volume at STPD

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[1]Equations originally published in the Master's thesis of Kathleen Golos (19).

polarographic analyzer (Beckman Instruments, Inc., Fullerton, CA). Routine calibration of the instruments was performed prior to each measurement, using a gas mixture composed of 15.72% O_2, 3.95% CO_2 and the remainder as nitrogen. The caloric value for each liter of O_2 consumed by the subject was based on the respiratory quotient, using the method of Consolazio et al (20).

Study Protocol

Subjects arrived at the Medical Research Center at Carle Foundation Hospital at 8:00 a.m. the morning of the study after an overnight fast of at least 10.5 hours. They were instructed not to have participated in strenuous physical activity (running, biking, etc.) the mornings of the study to eliminate the possibility of heat storage. To avoid affecting metabolism, stimulants, such as caffeinated beverages, were not allowed the morning of the study. If necessary, clothing was changed to meet the criteria previously described. Participants were escorted to the study room, where they reclined for 20 minutes prior to measurement of resting energy expenditure by IC. After that determination, subjects sat for at least 10 minutes before the initiation of the study. During this 30 minute period, individuals were adapting to the environmental conditions of the room (ambient temperature: 22.0-23.0°C). Thermal comfort perception questionnaires were completed for both days. Baseline IC and IRT measurements were performed after which a 10-15 minute simulated meal period (Day 1-fasting) or the 500-800 kcal meal was consumed (Day 2-postprandial). At the end of this time, another baseline IRT scanning took place followed by one every 15 minutes up to 90 minutes after the "meal" on day 1 and to 105 minutes on day 2. Each IRT measurement consisted of scanning the subject's front and back, three times. IC measurements were performed every 30 minutes. Surface area measurements were obtained at the end of the study.

Statistical Analyses

Descriptive statistics were used to evaluate the data on the protein, carbohydrate and fat percentage of the test meal and its energy content, age, height, weight, percent IBW and body surface area of the subjects. All other data were analyzed by the student's $\underline{t}$-test and one-way analyses of variance. A value of $p < 0.05$ was chosen as the level of significance (22). Data were analyzed statistically using a microcomputer statistical software package, Abstat (Anderson-Bell, Parker, CO). Due to unequal sex distributions, data were not analyzed for sex-related differences.

RESULTS

Nineteen subjects participated in the fasting and postprandial studies. Mean descriptive subject data (mean ± SEM) include the following: age: 33.8 ± 2.8 years; height: 169.4 ± 2.2 cm; weight: 70.5 ± 5.6 kg; % IBW: 112.0 ± 6.9; and body surface area: 1.81 ± 0.08 m². The composition of the test meal for day 2 (postprandial) of the study was as follows: caloric content: 630.9 ± 64.8 kcal; % protein: 16.6 ± 2.0; % carbohydrate: 45.9 ± 3.4; and % fat: 37.4 ± 2.6. The percentage composition of the test meal was similar to the average of the two day dietary records which was: % protein: 17.2 ± 1.3; % carbohydrate: 50.0 ± 3.0; and % fat: 33.8 ± 2.1.

Indirect Calorimetry Studies

A total of 76 indirect calorimetric measurements were completed during the prolonged overnight fast (day 1) on the 19 control subjects. The mean IC data were statistically similar for the 90 minute study period (Table 3). This finding was also evident in the small percentage change in IC values as compared to baseline, which were calculated at 5.6 ± 2.7% (30 minutes), 4.0 ± 2.5% (60 minutes) and 6.2 ± 3.0% (90 minutes).

Table 3. Fasting (Day 1) and postprandial (Day 2) mean indirect calorimetry , minute volume, CO_2 production, O_2 consumption and respiratory quotient data for the 19 control subjects*

TIME (min)	IC (kcal/hr)	MINUTE VOLUME (l/min)	CO_2 PRODUCTION (l/min)	O_2 CONSUMPTION (l/min)	RESPIRATORY QUOTIENT
FASTING VALUES					
0	76.1 ± 6.2[a]	8.10 ± 0.83[c]	0.249 ± 0.025	0.255 ± 0.019[c]	0.88 ± 0.02[c]
30	79.2 ± 5.7[a] [e]	7.96 ± 0.60[c]	0.249 ± 0.020	0.269 ± 0.018[d]	0.86 ± 0.02[de]
60	77.6 ± 5.3[a] [e]	7.78 ± 0.70[c]	0.237 ± 0.022	0.262 ± 0.016	0.83 ± 0.02[de]
90	78.5 ± 5.3[ace]	7.60 ± 0.52[ce]	0.236 ± 0.019	0.268 ± 0.018	0.83 ± 0.02[de]
POSTPRANDIAL VALUES					
0	77.1 ± 4.2[a]	7.66 ± 0.50[c]	0.235 ± 0.015[a]	0.261 ± 0.014[a]	0.89 ± 0.02
30	88.5 ± 5.3[b] [x]	8.38 ± 0.57[d]	0.276 ± 0.017[b]	0.298 ± 0.018[b]	0.93 ± 0.02[f]
60	88.2 ± 4.7[b] [Q]	8.52 ± 0.57[d]	0.274 ± 0.015[b]	0.297 ± 0.016[b]	0.92 ± 0.02[f]
90	86.8 ± 4.5[bf] [f]	8.06 ± 0.45[cf]	0.265 ± 0.014[b]	0.293 ± 0.015[b]	0.83 ± 0.02[f]

*Values represent means ± SEM. Means with unlike superscripts differ significantly at: a,b,p < 0.001; c,d,p < 0.05; Day 1 vs Day 2: e,f,p < 0.05.

[handwritten notes: "SPSS", "ANOVA rank clone", "No analysis in fasting... Confirm sex", "0.91", "0.01"]

Seventy six IC measurements were completed on Day 2. The first measurement served as the baseline and was obtained during fasting. The subsequent values represented postprandial measurements at 30, 60 and 90 minutes. The mean IC data for these latter three time periods were significantly higher than the fasting value ($p < 0.0000$) (Table 3). The percentage change in IC measurements from Day 2 was also greater than Day 1 with values of $14.9 \pm 2.5\%$ (30 minutes), $15.1 \pm 2.7\%$ (60 minutes) and $13.3 \pm 2.6\%$ (90 minutes).

When data were compared across study days, there were no significant differences between the two baseline values (Time = 0'). However, the Day 2 data from 30, 60 ($p < 0.0000$) and 90 minutes ($p < 0.001$) were significantly greater than those of Day 1 which were collected at approximately the same time.

On Day 1, neither initial minute volumes nor initial CO_2 production differed significantly from subsequent values (Table 3). In general, values tended to decrease for both parameters as the study period progressed through the course of the morning. Oxygen consumption was significantly elevated ($p < 0.03$) over baseline readings at 30 minutes. Although it remained higher than initial values for the remainder of the experimental period, it was not statistically significant. Respiratory quotient (RQ) data are also presented in Table 3. Values at 30, 60 and 90 minutes were significantly lower than the initial reading of 0.88. The lowest RQ, 0.83, occurred at 60 minutes and remained stable at this level throughout the remainder of the experiment.

In contrast to the fasting values, Day 2 minute volumes at 30 and 60 minutes were significantly ($p < 0.03$) higher than baseline (Table 3). Although no longer significant at 90 minutes, the mean value was still elevated above fasting levels. After eating, CO_2 production and O_2 consumption were

statistically greater than fasting values (p < 0.001). Although the values for

RQ increased from the fasting value and remained elevated, no statistical

significance was demonstrated.

The mean initial minute volumes from Days 1 and 2 were compared for the

same time periods and were demonstrated to be statistically similar. However,

the postprandial values were higher than the fasting values at 30, 60 and 90

minutes. Baseline CO_2 production and O_2 consumption values for Days 1 and

2 were also similar. At 30, 60 and 90 minutes, the postprandial levels of

CO_2 production and O_2 consumption were statistically significant

(p < 0.001). When the initial fasting RQ from Day 1 was compared to that from

Day 2, no significant differences were noted. Values at 30, 60 and 90 minutes

were significantly higher on Day 2 versus Day 1 readings (p < 0.03).

For 13 of the 19 subjects, indirect calorimetric measurements obtained

after a 20 minutes of reclining were compared to those from the same subjects

after they had stood for at least five minutes (Table 4). The reclining values

were significantly less than the standing IC measurements (p < 0.02).

Statistically significant increases were evident in minute volume, CO_2

production and O_2 consumption with standing exceeding reclining values.

Although the RQ of the standing subjects exceeded that measured while they

reclined, the difference was not significant.

Infrared Thermography Studies

A total of 322 scannings were completed on the 19 control subjects over the

course of the two day period. For the fasting studies on Day 1, no

statistically significant differences were noted when comparing the baseline

heat loss value (scanning 1) to the subsequent IRT scannings. This was also

true if scanning 2 was used as the baseline (Table 5). Using the paired

Table 4. Indirect calorimetry, minute volume, CO_2 production, O_2 consumption and respiratory quotient values for 13 fasting control subjects who had expired air measurements completed while reclining and standing*

PARAMETER	RECLINING VALUE	STANDING VALUE
Indirect calorimetry (kcal/hr)	61.9 ± 3.9^a	75.9 ± 6.6^b
Minute volume (1/min)	5.45 ± 0.44^a	7.54 ± 0.76^b
CO_2 production (1/min)	0.189 ± 0.015^a	0.244 ± 0.020^b
O_2 consumption (1/min)	0.210 ± 0.013^a	0.255 ± 0.020^b
Respiratory quotient	0.89 ± 0.03	0.94 ± 0.03

* Values are means ± SEM. Means with unlike superscripts differ significantly at: a,b, $p < 0.02$.

Table 5. Fasting and postprandial mean radiant, convective, evaporative and total heat loss data (kcal/hr) for 19 control subjects*

TIME (min)	RADIANT HEAT LOSS	CONVECTIVE HEAT LOSS	EVAPORATIVE HEAT LOSS	TOTAL HEAT LOSS
FASTING				
-15 (1)[1]	42.9 ± 2.2^c	22.3 ± 1.1	15.6 ± 1.0	80.8 ± 4.2
1 (2)	43.6 ± 2.2^c	22.7 ± 1.1^c	15.6 ± 1.0	81.9 ± 4.2
15 (3)	43.8 ± 2.3	22.7 ± 1.1	15.7 ± 1.0	82.2 ± 4.3
30 (4)	44.0 ± 2.3^d	22.8 ± 1.2	15.7 ± 0.8	82.5 ± 4.2
45 (5)	42.6 ± 2.2	22.0 ± 1.1	15.8 ± 0.8	80.3 ± 4.1
60 (6)	42.9 ± 2.2^g	22.1 ± 1.1^g	15.5 ± 1.0	80.6 ± 4.2^a
75 (7)	42.1 ± 2.1^d	21.8 ± 1.0^{di}	15.6 ± 0.9	79.4 ± 3.9^a
90 (8)	43.2 ± 2.2	22.3 ± 1.1^k	15.5 ± 0.8	$81.0 \pm 4.1^{**a}$
POSTPRANDIAL				
-15 (9)	44.5 ± 2.6	23.0 ± 1.3^c	15.7 ± 0.7^e	83.3 ± 4.5
1 (10)	43.7 ± 2.6^c	22.6 ± 1.3	15.6 ± 0.7^{cf}	81.9 ± 4.5^a
15 (11)	43.6 ± 2.7	22.6 ± 1.3	15.5 ± 0.7^f	81.7 ± 4.6
30 (12)	43.5 ± 2.5	22.4 ± 1.2^d	16.2 ± 0.8^d	82.2 ± 4.3
45 (13)	43.8 ± 2.5	22.6 ± 1.2	16.1 ± 0.8	82.5 ± 4.3
60 (14)	44.9 ± 2.5^{dh}	23.2 ± 1.3^h	16.5 ± 0.8^{df}	84.5 ± 4.3^b
75 (15)	44.0 ± 2.5	22.7 ± 1.2^j	16.5 ± 0.8^{df}	83.3 ± 4.3^b
90 (16)	44.6 ± 2.3	23.0 ± 1.2^l	16.2 ± 0.7	83.7 ± 4.1^b
105 (17)	44.4 ± 2.4	22.9 ± 1.2^l	16.1 ± 0.7	83.5 ± 4.2^b

* Values represent means ± SEM. Means with unlike superscripts differ significantly at: a,b,p < 0.01; c,d,p < 0.05; e,f,p < 0.02; and Day 1 vs Day 2: g,h,p < 0.03; i,j,p < 0.05; k,l,p < 0.01.

** N = 18.

[1] Values in parentheses indicate IRT scanning numbers.

t-test, scannings 9 and 10 on Day 2 were compared to the subsequent IRT measurements. No significant differences were noted with scanning 9. When scanning 10, measured immediately after eating, was used as the baseline value, a significant rise in heat loss occurred at scanning 14, which was the 60 minute postprandial reading.

Comparing values across days failed to demonstrate significant differences between the first five scannings on each day. However, postprandial heat loss was significantly higher than fasting values at 60, 75, 90 and 105 minutes ($p < 0.01$). These changes are best illustrated when the mean differences in total heat loss between the second scanning on each day were compared to their subsequent scannings (Figure 5).

Total heat loss is the summation of radiant, convective and evaporative losses. The latter form is composed of heat which is lost due to diffusion of water vapor through the skin and the heat loss associated with water vapor expired from the lungs. For purposes of the present investigation, only the total evaporative heat losses are of consequence and will be considered in subsequent calculations.

Radiant, convective and evaporative heat losses are presented in Table 5. During the fasting studies on Day 1, significant differences were noted between scannings 1 and 4 and 2 and 7 ($p < 0.05$) for radiant heat loss and between scannings 2 and 7 for convective loss. On Day 2, radiant heat loss from scanning 10 (immediately after eating) was significantly less than that from scanning 14 (60 minutes postprandial). Convective heat loss values for scanning 12 were significantly greater than those for scanning 9 ($p < 0.05$). When scanning 10 was used as the baseline, no significant differences were noted. The greatest changes in heat loss were demonstrated in the evaporative
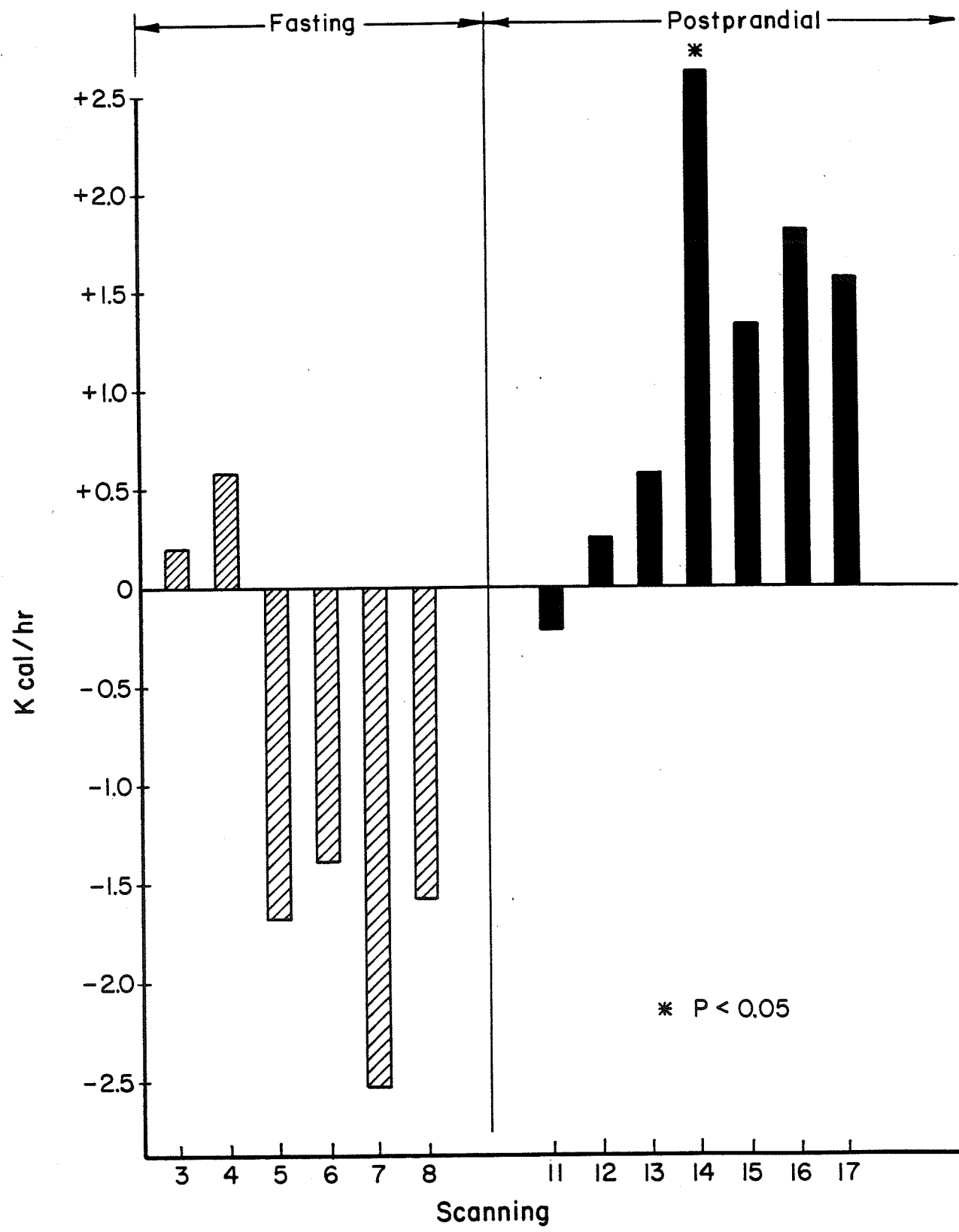
component. Statistically significant changes (p < 0.02) over baseline (scanning 9) occurred at 1 minute, 15 minutes, 60 minutes and 75 minutes after eating. Using scanning 10 as the initial value, significant differences at 30, 60 and 75 minutes were demonstrated.

Comparing component heat losses from Day 1 to those of Day 2 for the same time periods showed significant elevations in radiant and convective losses (p < 0.03) at 60 minutes postprandial as opposed to the 60 minute fasting value. Although evaporative heat loss at this time was also elevated over fasting levels, the difference was not significant. Radiant and convective losses on Day 2 were also significantly elevated over fasting Day 1 levels at 75 (p < 0.05), 90 and 105 minutes (p < 0.01) after eating. As was true at the 60 minute reading, Day 2 evaporative heat loss was elevated over the Day 1 values, but the increase was not statistically significant. Figure 6 depicts the mean differences in radiant, convective and evaporative heat losses between the second scanning on each day and those subsequent.

Although considered an insensitive indicator of body core temperature, oral temperature varied during the course of the data collection. The lowest mean temperature on Day 1 was recorded at the first scanning (mean ± SEM: 35.9°C ± 0.1) and the highest at the second (36.3°C ± 0.1). The values for the remaining scannings fell between 36.0 to 36.1°C. Statistical significance was demonstrated when the initial oral temperature was compared to those following (p < 0.05). The lowest mean oral temperature (35.9°C ± 0.2) on Day 2 of the study was noted at scanning 10 (immediately after eating), while the highest (36.2°C ± 0.1) was recorded from 30-105 minutes postprandial. The only statistically significant differences occurred between scanning 9 and 10 and 10 versus 12 (p < 0.05). Comparing oral temperatures across days showed a
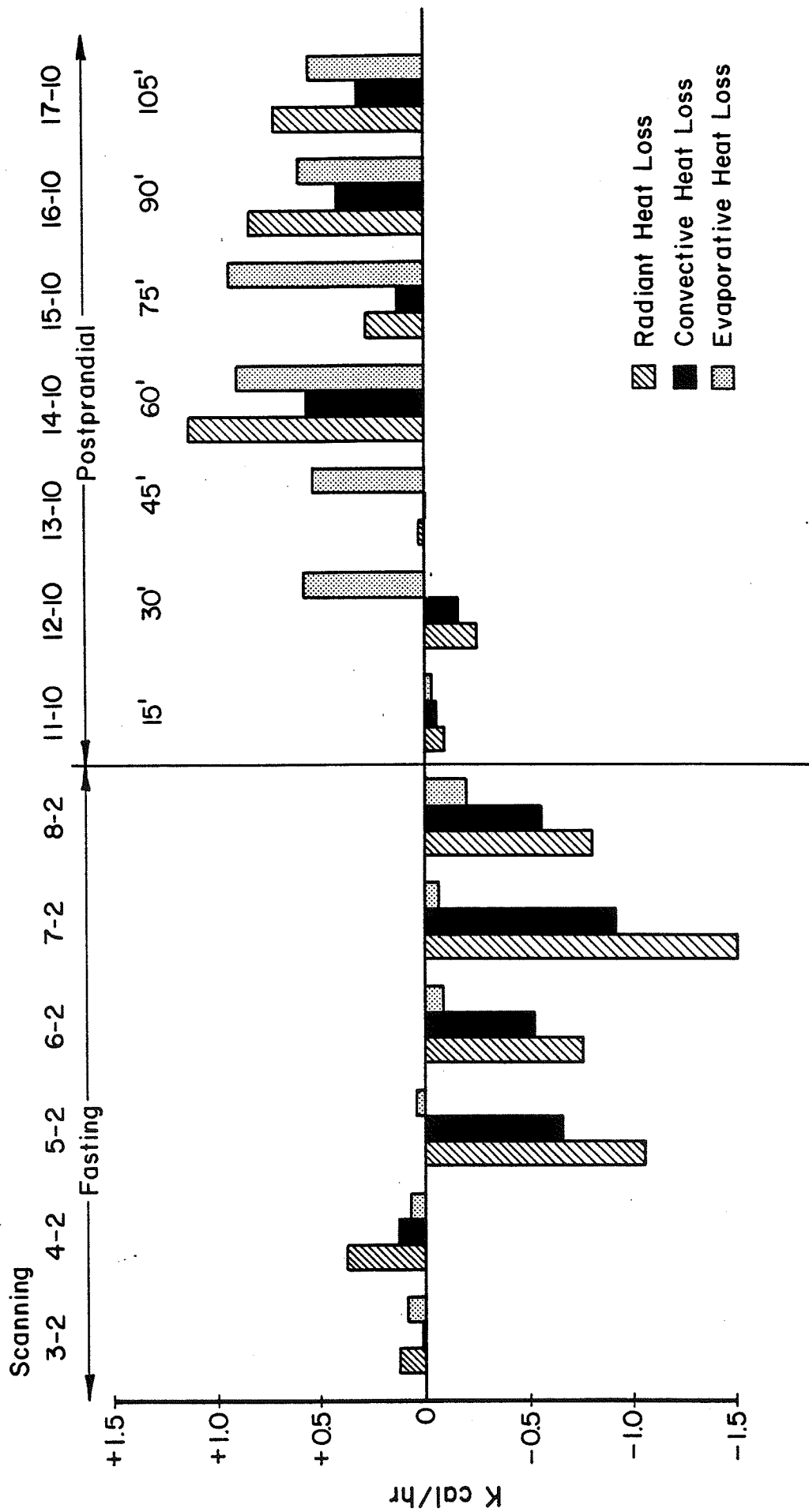
significant difference between the initial scanning on each day (p < 0.02). The scanning 2 value was higher than that of scanning 10 (p < 0.05) and the reading from scanning 8 was lower than that of scanning 16 (p < 0.01).

As determined by computer analysis of the infrared thermogram, mean body surface temperatures of the subjects varied during the 2.5 hour experimental period (Table 6). From Day 1 data, it was evident that mean surface temperature rose as the study progressed through the morning. Irregardless of which mean body surface temperature was chosen as the baseline (scanning 1 or 2), subsequent scannings were shown to be significantly elevated (p < 0.05) with the exception of scanning 1 versus 2. Postprandial mean surface temperatures increased when scanning 10 was compared to subsequent scannings. Significant differences were noted at 30, 60, 90 and 105 minutes (p < 0.02). When scanning 9 was used as the baseline, no significant differences were noted. Data compared across days demonstrated no significant differences.

As a corollary to surface temperature measurements, subjects were asked to qualitatively indicate perceptions of thermal comfort for their head, arms, hands, trunk, thighs, legs, feet and an overall evaluation. The questionnaire was scaled form a value of -3 (cold) to +3 (hot) with 0 indicating neutrality. For purposes of data analysis, the groups were collapsed into three categories: [1] cold; [2] neutral; and [3] hot. The areas of the body most often cited as feeling cold were the arms (40.5%), the hands (51.4%) and the feet (70.3%). Despite this finding, the majority individuals (64.9%) perceived their overall thermal comfort as neutral. Visual inspection of the infrared thermogram by one of the investigators demonstrated that the hands and feet were typically cooler than the remainder of the body, while the head, face and neck were the warmest surface areas. This was substantiated by subjects, who

Table 6. Fasting and postprandial mean body surface temperatures (°C) in 19 control subjects*

TIME (min)	FASTING SURFACE TEMPERATURE	POSTPRANDIAL SURFACE TEMPERATURE
-15	28.2 ± 0.2[a]	28.5 ± 0.2
1	28.3 ± 0.2[a]	28.4 ± 0.2[c]
15	28.4 ± 0.2[b]	28.5 ± 0.2
30	28.5 ± 0.2[b]	28.6 ± 0.2[d]
45	28.6 ± 0.1[b]	28.5 ± 0.2
60	28.7 ± 0.2[b]	28.6 ± 0.2[d]
75	28.6 ± 0.2[b]	28.5 ± 0.2
90	28.7 ± 0.2[b]	28.7 ± 0.2[d]
105	----	28.7 ± 0.2[d]

* Values represent means ± SEM. Means with unlike superscripts differ significantly at: a,b,p < 0.05; c,d,p < 0.02.

reported thermal perceptions of the head to be neutral (97.3%) and the trunk to be neutral (81.1%) or hot (10.8%).

Comparison of Indirect Calorimetry to Infrared Thermography

Figure 7 depicts the indirect calorimetric data compared to that obtained using the infrared thermography system. There were no statistically significant differences demonstrated between the two methods on either day. However, it should be noted that during the fasting studies on Day 1, IRT measurements tended to exceed IC values, while after eating these findings were reversed.

DISCUSSION

For decades, direct and indirect calorimetry were considered the "gold standards" of research in the field of energy metabolism. Unfortunately, the expense and complexity involved with use of the equipment for the direct method has lead to the disassembling of many of the calorimeters so that today less than 10 exist worldwide. However, with the almost perfect agreement between the two methods demonstrated by the classic studies of Benedict (2,3), researchers have almost totally abandoned direct measurement of heat loss for the more convenient determination of oxygen consumption (IC). But, not all thermogenic processes are oxidative and lack of data on actual heat loss from an individual injects a potential source of error into analyses. That this information deficit is of practical import is reflected by the literature which reports on the inability of the scientific community to explain why some individuals appear to gain weight more readily and lose it more slowly than those who are normally lean or other obese individuals (22); or patients who lose weight despite the provision of apparently adequate calories (23).
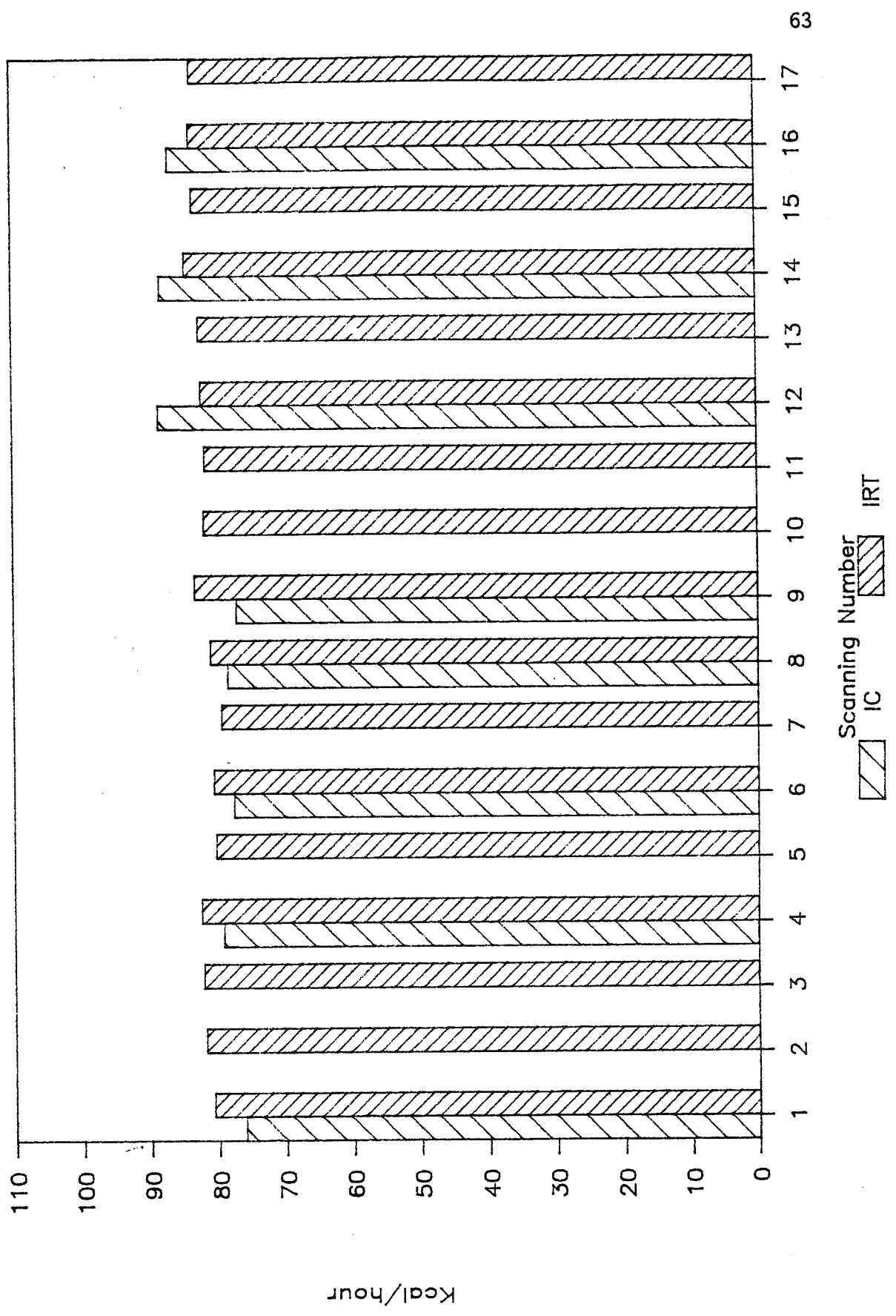
In an attempt to develop alternate methods of quantitating heat loss, the present investigation focused on adapting infrared thermography to the study of human energy metabolism. The system is composed of the infrared imaging radiometer and a microcomputer system. The former generates a mean body surface temperature which is input into a series of equations for computation of radiant, convective, evaporative and total heat losses by the latter component.

To validate the ability of thermography to assess energy expenditure in human subjects, IRT data, collected during the fasting state, were compared with the currently established and accepted research methodology for measuring caloric expenditure, indirect calorimetry. The protocol of the present investigation required subjects to stand during both IRT and IC data collection for two reasons. First, standing minimized conductive heat loss, as only the soles of the subjects' feet, a very minor component of total body surface area, were contacting another surface. Also, the floor was carpeted, which served an insulatory function and aided in limiting heat loss via this route. Based on this reasoning, conductive heat losses were deemed minimal and eliminated from all calculations of total heat losses. Standing for the scanning and expired air collection maintained consistency of data collection. When standing IC values were compared to IRT results, there was a failure to demonstrate significant differences between the two methods, which the investigators feel confirmed the ability of the IRT system to quantitate caloric expenditure. Validation studies were completed during fasting as it was assumed that in the absence of thermogenic stimuli, heat production and heat loss should be equal, since energy storage is not occurring. This assumption is supported by data from Benedict (2) and Webb (5). Based on the findings of the present

investigation, it appears that the thermographic system functions as a portable, non-confining calorimeter which measures energy expenditure by quantitating heat loss directly.

A second study objective was to evaluate the ability of the IRT system to detect changes in heat loss associated with food ingestion, i.e., diet-induced thermogenesis. To assess this appropriately, the protocol was expanded to include a second day of fasting measurements. Data were collected on fasting thermogenesis over essentially the same time frame as the postprandial studies, usually on two consecutive mornings. In the comparison of fasting and postprandial data, each subject served as his or her own control. This protocol design eliminated a potential source of error which can occur if the results from an initial baseline fasting measurement are extrapolated to cover the entire morning of the investigation. In this situation, it would not be known if the changes occurring in metabolism with food ingestion were due to the stimulus of food or to fluctuations in metabolism, which would have normally taken place during that time period. Lack of significant differences between the four IC measurements and between the eight IRT scannings on Day 1 indicated that no significant changes in metabolism had occurred in these subjects between 8:00 and 10:30 a.m.

Although no statistically significant differences were noted for IC or IRT measurements on Day 1, the data from this investigation justify the inclusion of fasting control studies using the same protocol and occurring over the same period of time as postprandial studies, if small changes in heat loss or IC data are to be detected. That this is true is supported by the following: IC measurements, compared across days, demonstrated the significant increase that occurred with eating. Comparing values for minute volume, O_2 consumption,

CO_2 production and RQ across days, no statistical difference was demonstrated for the initial measurements. However, significance was demonstrated at 30, 60 and 90 minutes for all parameters. If only Day 2 values were considered and the initial values were taken as representative of the morning, the significant elevation in the minute volume at 90 minutes and the significant rise in RQ at 30, 60 and 90 minutes would have gone undetected. In this same vain, IRT measurements for Day 2 only achieved statistical significance at 60 minutes (scanning 14). But if data are compared across days, significant elevations in heat loss were also apparent at 75, 90 and 105 minutes postprandial. Significant differences were noted for radiant and convective heat losses at these same time periods, when data were compared across days.

To determine the variability of metabolism from Day 1 to Day 2, the baseline IC (including minute volume, O_2 consumption and CO_2 production) and IRT measurements were compared. As noted in Table 3, no significant differences were demonstrated between any of the parameters, which indicated that subjects appeared to be at the same metabolic baseline on both study days. Therefore, it was assumed that any changes occurring during postprandial studies were the result of food ingestion rather than normal variation in metabolism.

Statistical analyses were completed using scannings 1 and 2 on Day 1 and scannings 9 and 10 on Day 2 as the baseline values. As the length of time subjects required to adapt to the thermal conditions present in the study room was unknown, 30 minutes was arbitrarily chosen. In analyzing the data from Day 2, it was demonstrated that total heat losses, mean surface temperatures and oral temperatures decreased from scanning 9 to scanning 10 with the decrease in oral temperature achieving significance ($p < 0.05$). In contrast, Day 1 values

for these same parameters increased, with changes in oral and mean surface temperatures being significant at $p < 0.05$ and $p < 0.02$, respectively. One possible explanation for the Day 2 findings is that meal ingestion resulted in a shunting of blood from the skin surface, decreasing mean body surface temperature and total heat loss. However, this explanation seems unlikely. The most reasonable interpretation for these findings is that the 30 minute thermal adaptation period was inadequate. It is likely that although the physical activity associated with subjects transporting themselves to the Research Center was not intense, it was enough to cause heat storage to occur which had to be dissipated. This finding is in agreement with that of Webb (24), who has stated that heat loss lags behind heat production by approximately one hour. Therefore, the findings from the present investigation and those of Webb, indicate that a 60 minute thermal adaptation period is more likely to be adequate. Based on this conclusion, only the data comparing the second scanning to those subsequent will be discussed.

For the IRT system to be useful in studies of energy metabolism within and outside of a research setting, its sensitivity must be such that small changes in surface temperature or energy expenditure can be detected, especially when studying alterations in metabolic efficiency. If these investigations are to be of any practical significance in understanding the mechanisms behind the causation of obesity, cancer cachexia or other disease processes, the IRT system must be able to evaluate the metabolic response which occurs when a subject ingests a meal reflecting what he normally eats. For example, many of Benedict's postprandial studies were completed on normal weight individuals consuming unusual food combinations such as 1000 kcal of bananas and cream or butter and potato chips (4). Taking this into consideration, participants were

permitted to select foods characteristic of the type and amount they typically ingested. The average caloric intake and the percentage composition of protein, carbohydrate and fat content of the two day food records compared favorably to those of the test meal.

Comparing data across days, it is evident that the postprandial thermogenesis stimulated by meal consumption was detected by the IRT system. This conclusion was supported by the significant elevation which occurred in total heat losses at 60, 75, 90 and 105 minutes after eating. The increase in postprandial heat loss occurred because of the rise in evaporative heat loss brought about the the elevation in minute volume. Radiant and convective heat loss increased postprandially as a result of the significant rise in mean surface temperature. Detection, by IRT, of the elevation in mean surface temperature after eating has been previously reported (11,12).

When IC and IRT data were compared to each other, no statistical differences were demonstrated, yet some interesting trends were noted. First, in the fasting state, mean heat loss measured by IRT exceeded heat production, measured by IC. However, this situation was reversed in the postprandial studies. These findings were similar to those of Benedict (4), Webb (5,24) and Pittet et al (6). Possible explanations for these results follow. After eating energy storage occurs, since humans ingest more energy than required at the time of meal consumption. This accumulation of energy provides a caloric reserve which can be drawn upon during periods of short- or long-term fasting. However, this process requires that a portion of that energy, equivalent to approximately 10% of daily energy expenditure, be expended to absorb, transport, transform and store the ingested energy, i.e., diet-induced thermogenesis. Conversion of carbohydrate, fat or protein into ATP, is not

100% efficient so that a portion of this energy is ultimately lost from the body as heat (25). However, as stated by Webb (24) and confirmed by this study, there is a lag period between a significant change in heat production and when that heat is lost. Because of this, heat storage occurs, which causes a rise in body core temperature of approximately 0.1-0.2°C. This increase was significant in the present study, but not in those by other investigators (4,5,6). After the processes of energy absorption, conversion and storage are completed, O_2 consumption and heat production decline and heat loss increases. But the heat produced as a consequence of metabolism is not a waste product. It is used for the regulation of body core temperature through a negative feedback mechanism as so beautifully depicted in the graph of Benedict's data found in Figure 4. It also appears that this heat functions as an indicator that feeding has occurred (26). With feeding, heat production increases as a result of increased O_2 consumption. Body core temperature rises and heat dissipating mechanisms, such as vasodilation are activated. Greater blood flow to the surface of the body elevates skin surface temperature as heat from the body core is brought to the surface. This elevation was demonstrated in this and previous studies (6,11,12). Radiant and convective heat losses increase because the greatest determining factor for the magnitude of loss in these forms of thermal energy is the difference between surface and ambient temperatures. As the heat is dissipated to the environment, core temperature falls until it reaches a point below the thermostatic set, at which time heat dissipation ceases and heat production begins, once again cycling. thus, a representation of core temperature fluctuation in the fasting state would be similar to the graph of the differences between IC and direct calorimetry at the bottom of Figure 4.

In conclusion, with the similarities between our data and those of previous investigators, it is apparent that the infrared thermographic system can be used to detect changes in mean surface temperature and heat loss in individuals who are fasting or have eaten. Due to its portable, non-confining and non-invasive nature, it holds great potential for the study of energy expenditure in the research and clinical settings.

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APPENDIX 1

o Normal position for air thermistor.

o Thermistor #1

o Thermistor #2
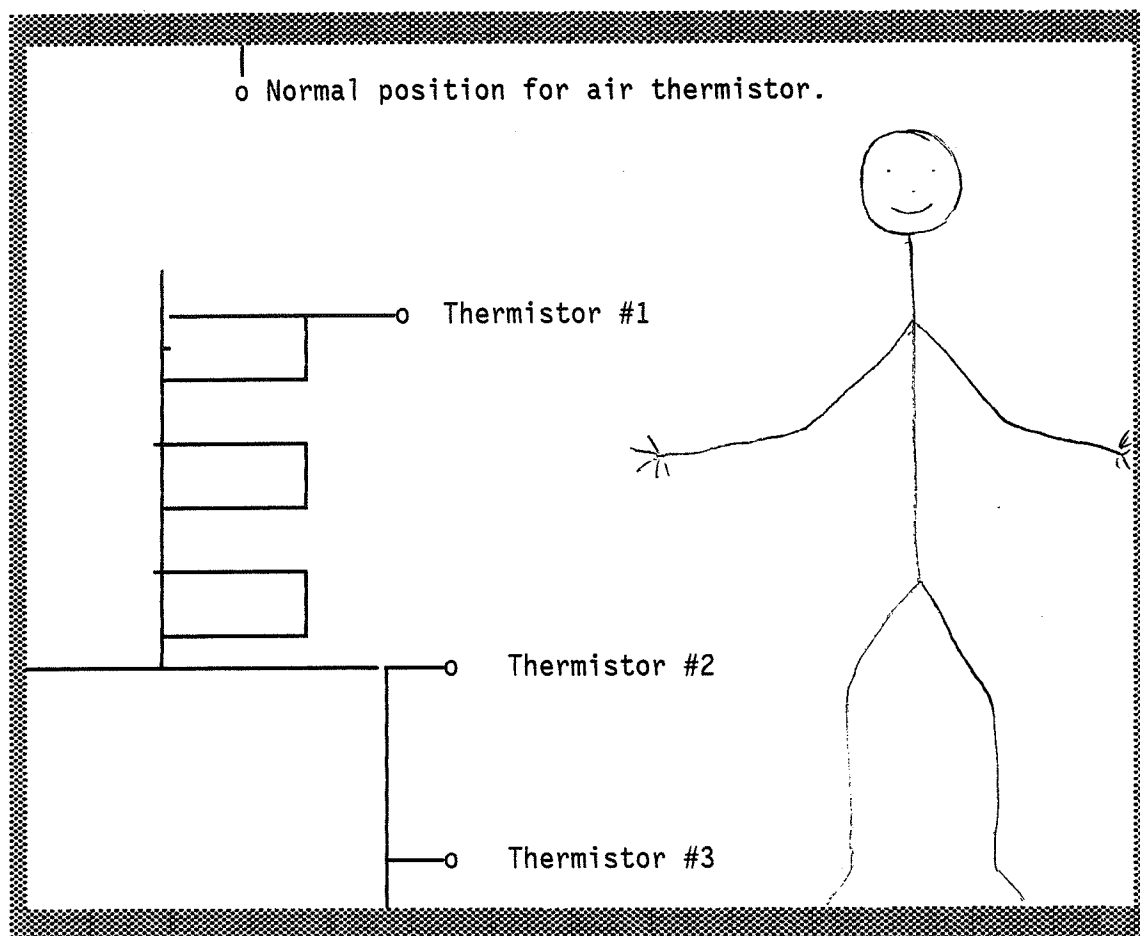
o Thermistor #3

The data collected confirmed that a 2°C temperature difference existed in the room, with air thermistor temperature at the ceiling being the highest. A regression equation was developed to account for this difference:

$$Y = 0.41X + 11.86.$$

X = air thermistor reading; Y = corrected ambient reading.

CHAPTER 4

HEAT LOSS FROM PATIENTS RECEIVING TOTAL PARENTERAL NUTRITION:
DIRECT QUANTITATION WITH INFRARED THERMOGRAPHY

ABSTRACT

Previous investigators have used infrared thermography (IRT) to measure surface temperature changes, which occur after eating, in lean and obese individuals. The current study describes the adaptation of the infrared thermography system to the investigation of human energy metabolism in the clinical setting. Twenty patients were studied, while they were receiving total parenteral nutrition (TPN) by constant infusion. Under these conditions a steady state in energy metabolism was achieved. IRT is a non-invasive, non-contact and non-confining means of rapidly and accurately measuring mean body surface temperature. This value, used in conjunction with theory, permits calculation of radiant, convective, evaporative and total heat losses. To valid this method for use in hospitalized patients, the results from IRT were compared with those of indirect calorimetry (IC). No significant differences were apparent between the two techniques. Data was analyzed based on the type of nutritional support the patient received (TPN with or without intravenous (IV) fat emulsion) and type of malnutrition (kwashiorkor or marasmus-kwashiorkor). Patients receiving IV fat emulsion demonstrated a positive energy balance by both IC and IRT, while those not receiving fat were in a negative balance as assessed by both methods. The patients receiving fat and those with marasmus-kwashiorkor evolved more heat/kg and had a higher mean skin surface temperature than the other two groups. In patients not receiving fat, there were times when IRT exceeded both energy intake and IC. Use of the IRT system may begin to explain why some patients continue to lose weight despite apparently adequate nutrient intakes.

INTRODUCTION

In the clinical setting, a limited number of studies have investigated substrate utilization by patients receiving intravenous nutritional support, i.e., total parenteral nutrition (TPN). Also, little is known of the effects of a constant infusion of intravenous nutrients on energy expenditure in humans, who typically ingest food on an intermittent basis. This situation is disconcerting, as TPN has been used in hospitals for over 15 years and the complications associated with its use are well-known (1,2,3,4).

With the advent of the DRGs (diagnosis-related groups), both the length of hospitalization and financial reimbursement to health care institutions have been decreased. Thus, the importance of providing efficacious, yet cost-effective nutritional support regimens is apparent. In order to achieve these goals, energy expenditures of hospitalized patients must be measured and not estimated, allowing nutritional therapy to be tailored to the patient's requirements. Until the 1950s, this was not a problem, as hospitals possessed indirect calorimetric equipment for determining O_2 consumption, CO_2 production and energy expenditures of patients with suspected thyroid dysfunction. However, with the development of radioimmunoassays for evaluation of thyroid function, this equipment is no longer readily available in most institutions. As a result, health care professionals are now in a position of treating many clinical conditions based on an assumed knowledge of energy expenditure and energy balance. Today, in most hospitals, energy expenditures of patients, if reported at all, are only estimations obtained from application of the Harris-Benedict equations (HBE). These regression formulae calculate resting metabolic rate (RMR) as a function of an individual's height, weight, age and sex (5). However, Mann et al (6) have reported that the HBEs tended to

overestimate caloric needs of acutely ill surgical patients by as much as 50%, a figure far greater than the 7-15% overestimation demonstrated for healthy men and women (7,8).

Therefore, actual measurement of energy expenditure in hospitalized patients is preferred to the use of prediction equations for estimating caloric needs. The classic investigations of Benedict (5,9,10) have shown conclusively that measurement of respiratory gas exchange, over 24 hours, is equivalent to quantitating heat loss in a direct calorimeter and that both methods measure energy expenditure. A previous study (Chapter 3) described the infrared thermography (IRT) system, its adaptation for use in the measurement of human energy expenditure and the favorable statistical comparison of the results from IRT to those of IC. The present investigation represents the first trial with the IRT system in the clinical setting. As such, the investigators deliberately chose to study patients with differing diagnoses and surgical procedures. Energy intakes were not standardized on a per kilogram body weight basis, but all patients received the solutions continuously over 24 hours for at least five consecutive days. Under these steady state conditions, the results from IRT and IC measurements should be statistically similar, if the following two assumptions are correct: [1] the thermographic system is indeed measuring energy expenditure; and [2] the findings of Benedict and all subsequent investigators regarding the correlation between IC and direct calorimetry are true. Thus, the goals of the present investigation were to answer the following: [1] What is the feasibility of using IRT for the instantaneous determination of heat loss from postsurgical patients in the clinical setting? [2] Do patients receiving TPN with intravenous fat emulsion produce and evolve more or less heat than those receiving TPN without fat? and

[3] Does the type of malnutrition influence the amount of heat that patients produce and lose?

MATERIALS AND METHODS

Subjects

Study participants were patients recruited from the services of Colon and Rectal Surgery and Internal Medicine at Carle Foundation Hospital in Urbana, Illinois. This investigation had the prior approval of the Institutional Review Boards of the University of Illinois and Carle Foundation Hospital. Written informed consent was obtained from each patient and verbal consent for study participation was obtained from each patient's attending physician. After initial expression of interest, patients were contacted by one of the investigators, the study protocol was briefly explained and willingness to participate was confirmed. The criteria for patient selection included the following: [1] no oral intake of food for at least five consecutive days; [2] receiving TPN with or without intravenous (IV) fat emulsion; [3] afebrile (oral temperature $\leq$ 37.7°C or 99.9°F); and [4] able to stand unassisted.

Patient Attire

To facilitate data collection, skin exposure was maximized without disrupting routine postoperative nursing care or unduly embarrassing the patient. Thus, subjects wore a hospital gown with or without undergarments. Because of their medical conditions, some patients wore antiembolism stockings.

Intravenous Nutritional Support Solutions

Total parenteral nutrition solutions were prescribed by the patients' attending physicians based on their nutritional status, medical conditions and

estimated caloric needs as dictated by the results of the nutritional
assessment. The nutritional support regimens on which the patients were placed
on one of the following: [1] 3.5 or 5.0% crystalline amino acid solution
(Aminosyn[R]: Abbott Laboratories, Abbott Park, IL) and 5-35% dextrose
solution (Dextrose monohydrate: 3.4 kcal/g; Abbott Laboratories, Abbott Park,
IL); or [2] 3.5 or 5.0% crystalline amino acid solution, 5-35% dextrose and 10
or 20% intravenous fat emulsion (Liposyn[R]: Abbott Laboratories, Abbott Park,
IL). All therapies included appropriate levels of trace elements, electrolytes
and vitamins.

Nutritional Assessment

As part of the routine protocol for patients receiving TPN, a nutritional
assessment was performed. This information was collected from the patient's
medical record. To evaluate the type and severity of nutritional compromise,
the criteria and nomenclature of Blackburn et al (11) were used. Kwashiorkor
was the diagnosis of patients with visceral protein depletion, but who were of
normal to excessive body weights; marasmus-kwashiorkor was the designation for
patients who had experienced loss of body fat and muscle with concomitant
visceral protein depletion. Weight was measured to the nearest one-quarter
pound on a balance beam Detecto scale (Detecto-medic, Brooklyn, NY). Height
was measured to the nearest 0.1 cm. Ideal body weight (IBW) was obtained from
the 1983 Metropolitan Life Insurance Company tables (12). Wrist circumference,
for computation of body frame size (13), was measured to the nearest 0.1 cm
using a fiberglass tape. Bicep, tricep, subscapular and suprailiac skinfolds
were obtained using Lange skinfold calipers (Cambridge Scientific Industries,
Inc, Cambridge, MD). From these values, percent body fat and kilograms of body
fat and lean body mass (LBM) were estimated (14). To ascertain body surface

area (BSA), the 19 circumference and length determinations of DuBois (15) were measured to the nearest 0.1 cm.

Infrared Thermography (IRT) System

The model 525 infrared imaging radiometer (Inframetrics, Bedford, MA) is a small, lightweight field instrument which produces a television compatible video output signal. The subject's naturally emitted infrared radiation (8-12 μm) was converted by a liquid nitrogen-cooled Hg-Cd-Te detector to an electrical signal that was processed into a television picture of the temperature patterns in the scene which the camera was viewing. That image was recorded on VHS videotapes for later data analyses A calibrated grey scale with 256 divisions was presented across the bottom of the picture in normal image mode, which indicated the relationship between the contrast in the display and the actual surface temperature. Video processing was set such that for the 10°C temperature range of the body surface, the central portion of the calibrated scale represented 160 levels, each with an associated discrete temperature. The smallest temperature differential which was detectable by the camera was 0.07°C (16). Although the camera was internally calibrated on a continuous basis, a direct temperature readout was not possible. Therefore, three black bodies, acting as independent temperature standards, were used to generate a calibration curve for comparison of grey scale values from the camera to known temperatures recorded at the time of IRT scanning. The temperatures chosen for the black bodies covered a span from 23-33°C, which was comparable to the 10°C range of surface temperatures detected on human subjects. Black body temperatures were measured with surface thermistors (YSI series 400, model 409A). Ambient and oral temperatures were monitored with thermistors from the same YSI series. A full-range mercurial barometer (Princo

Instruments, Inc, Southampton, PA) was used to measure barometric pressure and relative humidity was obtained via a motor-driven psychrometer (Vista Scientific Corporation, Ivyland, PA).

IRT Data Analyses By Computer

Each frame of the thermal patterns of subjects recorded on videotape is digitized by a video frame store. With the aid of a microcomputer system, all background from the chosen frame is removed, leaving only the digitized front or back view of the individual. These thermal images are analyzed by computer which generates a weighted mean surface temperature. This value is then used with theory to compute radiant, convective, evaporative and total heat losses in kcal/hour (17). Normally, conduction, the fourth route of heat loss, must also be considered. However, as patients stood during the IRT scanning procedure, only the soles of their feet, a minor component of total body surface area, were conducting heat to the floor. This amount of heat was judged as negligible and thus was ignored.

Indirect Calorimetry

The indirect calorimetric procedure was explained to each patient prior to initiation of expired air collection using a meteorological balloon. Open-circuit indirect calorimetry with a mouthpiece, noseclamps and a non-rebreathing valve took place after the IRT scanning procedure, while the patient sat. Although the ideal situation would have been to have the patients stand during IC, this was not possible. The initial scanning occurred after only one or two days had elapsed from the time of surgery and patients could not stand for prolonged periods. Thus, to maintain consistency in data collection, all IC measurements were performed with patients seated. Expired air collection lasted for three to five minutes, after which the minute volume

was determined using a chain-compressed Tissot gasometer (Warren E. Collins, Inc, Boston, MA). Respiratory gases were analyzed by a Beckman LB-2 CO_2 infrared analyzer and a Beckman OM-14 O_2 polarographic analyzer (Beckman Instruments, Schiller Park, IL). Routine calibration of the instruments was performed prior to each measurement using a gas mixture composed of 15.72% O_2, 3.95% CO_2 and the remainder as nitrogen. As 24-hour urinary nitrogen excretion was known, IC values were adjusted accordingly. The caloric value for each liter of O_2 consumed by the subject was based on the respiratory quotient using the method of Consolazio et al (18).

Nitrogen Balance Studies

When possible, a 24-hour urine specimen to evaluate nitrogen balance was collected for each patient. The collection was started on the day of the IRT scanning and was completed the following day. Urine specimens, in containers with 1 ml of 6N HCl added as a preservative, were kept on ice for the 24-hour collection. At the end of this time period, urine volume was measured and recorded and a representative sample was obtained and frozen for later analysis. Specimens were analyzed for total nitrogen content using Kjeldahl digestion and automatic colorimetric determination of the ammonia released (19,20).

Nitrogen intake was determined by multiplying the amount of TPN fluids infused, during the period of the 24-hour urine collection, by the percentage of crystalline amino acids in the solution. This calculation yielded the number of grams of amino acids infused. Dividing this result by 6.34 grams of protein/gram of nitrogen yielded grams of nitrogen intake. The value of 6.34 was used in calculations rather than the standard 6.25 since the actual nitrogen content of the solution was known (Source: Abbott Laboratories,

Abbott Park, IL). Nitrogen output was also corrected for integumental and
fecal losses (21).

Study Protocol

The original study protocol called for IRT scannings to be completed on the
second and fifth postoperative days. However, this was not always possible so
data were collected on any day between days one and five after surgery. With
two exceptions, all IRT scannings and IC measurements took place in the same
conference room in Carle Foundation Hospital. On the other two occasions, the
studies were completed in either a patient's room or a conference room located
on another floor in the hospital. Patients were brought by one of the
investigators to the study room approximately 45 minutes before the beginning
of data collection to allow an adequate period for thermal adaptation to
environmental conditions. Once in the room, patients removed their robes and
slippers, if worn, and sat down. During the adaptation period, thermal comfort
questionnaires were completed by the patients and composition and rate of
infusion of TPN solutions were recorded by the investigators.

Patients were in steady state in terms of adaptation to the continuous
nutrient infusions and environmental conditions prior to the initiation of the
studies. Patients stood for the IRT scanning procedure, which included front
and back views. Three scannings were completed on each patient and the middle
one was chosen for later data analyses. Afterwards, IC data were collected,
while the patient sat. In 11 cases, IRT data were also collected after the IC
measurement was done.

Statistical Analyses

Descriptive statistics and the student's t-test were used to evaluate the
patient data. All other data were analyzed by the student's t-test and one-way

statistical software package, Abstat (Anderson-Bell, Parker, CO). When patients were categorized based on both type and severity of malnutrition, the resultant groups were too small to permit statistical analyses. The decision was made to separate the patients into groups based only on type of malnutrition. Also, since the IRT scannings were not always completed on the same postoperative days, each of the scannings was counted independently.

RESULTS

Twenty patients, nine men and eleven women, were recruited for participation in the study. Mean descriptive patient data are presented in Table 7. Patients diagnosed with kwashiorkor (K) weighed significantly more than those with marasmus-kwashiorkor (M-K) (p < 0.002). Based on % IBW, the K group was overweight (between 115%-120% of IBW), while the M-K group was judged as moderately underweight (70-85% of IBW). For body surface area (BSA), the only significant difference was the presence of a smaller body surface area for the patients with marasmus-kwashiorkor. The diagnoses and surgical or medical procedures for each patient are listed in Table 8.

Indirect Calorimetry Studies

Patient data from the indirect calorimetry measurements are presented in Table 9. Values for IC per kg were significantly (p < 0.05) higher in the patients receiving IV fat emulsion than those who were not. This parameter was also significantly higher in the patients with marasmus-kwashiorkor than those with kwashiorkor (p < 0.005). However, this finding was reversed, when the absolute values for IC were compared for the types of malnutrition even though this difference was not significant. There were also no significant differences between groups when the absolute values for IC were compared for

Table 7. Mean height, weight, percent ideal body weight (%IBW), body surface area (BSA) and age of patients receiving TPN with or without intravenous fat emulsion and by nutritional diagnosis*

GROUP	HEIGHT (cm)	WEIGHT (kg)	% IBW	BSA (m^2)	AGE (yr)
Overall (20)**	169.7 ± 2.3	66 7 ± 4.3	104 ± 5	1.79 ± 0.07	44.8 ± 4.2
IV Fat (9)	168.3 ± 3.8	61.8 ± 6.1	98 ± 8	1.73 ± 0.10	42.3 ± 5.1
No IV Fat (12)	170.8 ± 2.8	70.7 ± 6.1	109 ± 7	1 84 ± 0.09	46.8 ± 6.6
Kwashiorkor (13)	172.0 ± 2.7	76.2 ± 4.7[a]	116 ± 5[a]	1.94 ± 0.07[a]	52.2 ± 4.6
Marasmus- Kwashiorkor (5)	169.4 ± 3.3	46.1 ± 3.6[b]	74 ± 4[b]	1.49 ± 0.07[b]	25.6 ± 5.3

* Values are means ± SEM. Means with unlike superscripts differ significantly at: a,b,p < 0.002.

** Values in parentheses represent the number of patients in each group.

Table 8. Medical diagnoses and surgical or medical procedures for the 20 patients receiving TPN

PATIENT ID	DIAGNOSIS	PROCEDURE
2	Mid-rectal carcinoma	Low anterior resection
3	Right colon carcinoma	Right hemicolectomy
4	Polyposis coli with dysplasia	Abdominal colectomy, ileorectostomy with reservoir
5	Crohn's colitis with anal involvement	Total colectomy with ileostomy
6	Sigmoid carcinoma	Sigmoid resection
7	Duodenal ulcer, gastritis cholestasis, fatty liver, pancreatitis	Bilateral vagotomy, pyloroplasty
8	Hemorrhagic pancreatitis	Exploratory laparotomy, gastrostomy, cholecystectomy, feeding jejunostomy
9	Short bowel syndrome local recurrent rectal cancer, bowel obstruction due to adhesions	Small bowel resection
10	Small bowel obstruction	Laparotomy with lysis of adhesions
11	Crohn's disease, small bowel obstruction	Exploratory laparotomy, lysis of adhesions, ileal resection, ileal-colonic anastomosis
12	Chronic ulcerative colitis	Subtotal colectomy, ileostomy
14	Peri-rectal abscess Severe anal Crohn's disease	Medical treatment with bowel rest
15	Crohn's disease in small bowel, malnutrition	Pre-operative TPN
16	Multiple enterocutaneous fistulae, adhesions, infarcted bowel	Small bowel resection, ileocolostomy bypass
17	Invasive carcinoma in sigmoid polyp, s/p polypectomy	Sigmoid colectomy with anastomosis
18	Pelvic fibrosis	Lysis of adhesions, abdominal perineal resection, prostatectomy, cystectomy, creation of ileal conduit
19	Crohn's disease with strictures and fistulae	Small bowel resection
20	Crohn's disease with strictures, malnutrition anemia	Lysis of adhesions, exploratory laparotomy, small bowel resection, ileorectostomy
21	Crohn's disease with intestinal obstruction, Anal Crohn's disease	Right hemicolectomy, sigmoid resection
22	Crohn's colitis with stricture	Right hemicolectomy

Table 9. Mean indirect calorimetry data for patients receiving TPN, grouped by nutritional diagnosis and if receiving or not receiving infusion of intravenous fat emulsion*

GROUP	IC DATA (kcal/hr)	IC PER KG (kcal/hr)
Overall (28)**	72.5 ± 4.1	1.21 ± 0.08
IV Fat (14)	74.7 ± 5.8	1.38 ± 0.12[a]
No IV Fat (14)	70.3 ± 5.9	1.05 ± 0.08[b]
Kwashiorkor (18)	75.7 ± 5.7	1.07 ± 0.08[c]
Marasmus- Kwashiorkor (8)	69.0 ± 5.0	1.58 ± 0.11[d]

* Values are means ± SEM. Means with unlike superscripts differ significantly at: a,b,$p < 0.05$; c,d,$p < 0.005$.

** Values in parentheses represent the number of scannings for each grouping.

the fat/no fat groups. However, the trend was for heat loss in the group receiving IV fat to exceed that of the group not receiving the fat infusion.

Separating the indirect calorimetric data into component parts, no significant differences were noted for minute volume, O_2 consumption, CO_2 production and respiratory quotient (RQ), when patients receiving fat emulsion were compared to those not receiving it or when the group with kwashiorkor was compared to that with marasmus-kwashiorkor (Table 10). However, trends were apparent for the four groups of patients. Values for the four parameters in the group receiving IV fat emulsion and in the patients with kwashiorkor exceeded those of the group not receiving fat and the patients with marasmus-kwashiorkor, respectively.

As the nitrogen excretions of patients were known, the non-protein respiratory quotients were calculated for the various groups and are presented in Table 11. Although no significant differences were noted between groups, protein utilization was highest in the group not receiving IV fat as compared to patients who were receiving it. Protein utilization was greatest in the group with kwashiorkor as compared to the M-K group. The group receiving the IV fat emulsion had a higher non-protein RQ than the group not receiving fat, while the non-protein RQ of the K group exceeded that of the M-K group.

Infrared Thermography Studies

Comparing across groups, the patients with kwashiorkor demonstrated a significantly higher ($p < 0.001$) heat loss than those with M-K. Patients receiving IV fat evolved less heat than those who were not getting the fat infusion, but this difference was not significant (Table 12). Expressing these data on a per kilogram of body weight basis still failed to demonstrate any differences between the fat/no fat groups. However, expressing the data in

Table 10. Mean data on minute volume, O_2 consumption, CO_2 production and respiratory quotient from patients receiving TPN grouped by nutritional diagnosis and with or without infusion of intravenous fat emulsion*

GROUP	MINUTE VOLUME (l/min)	O_2 CONSUMPTION (l/min)	CO_2 PRODUCTION (l/min)	RESPIRATORY QUOTIENT
Overall (28)**	9.22 ± 0.84	0.241 ± 0.014	0.255 ± 0.018	1.05 ± 0.03
IV Fat (14)	10.19 ± 1.54	0.251 ± 0.021	0.277 ± 0.031	1.08 ± 0.04
No IV Fat (14)	8.31 ± 0.72	0.232 ± 0.017	0.234 ± 0.019	1.01 ± 0.03
Kwashiorkor (18)	10.30 ± 1.19	0.257 ± 0.019	0.274 ± 0.025	1.05 ± 0.03
Marasmus-Kwashiorkor (8)	7.56 ± 0.76	0.217 ± 0.015	0.228 ± 0.023	1.04 ± 0.05

* Values are means ± SEM.

** Values in parentheses represent number of scannings from which data were generated.

Table 11. Mean protein utilization and non-protein respiratory quotient data for patients receiving TPN with or without intravenous fat emulsion who have been diagnosed as suffering from kwashiorkor or marasmus-kwashiorkor*

GROUP	PROTEIN (kcal/hour)	NONPROTEIN RQ
Overall (28)**	10.7 ± 0.6	1.11 ± 0.03
IV Fat (14)	10.0 ± 0.8	1.16 ± 0.05
No IV Fat (14)	11.4 ± 1.0	1.06 ± 0.04
Kwashiorkor (18)	11.4 ± 0.8	1.12 ± 0.05
Marasmus- Kwashiorkor (8)	9.3 ± 0.9	1.10 ± 0.06

* Values are means ± SEM.

** Values in parentheses represent number of scannings from which data were generated.

Table 12. Mean infrared thermography data for TPN patients expressed as actual values and on a per kilogram body weight basis grouped by nutritional diagnosis and if receiving or not receiving intravenous fat emulsion*

GROUP	IRT (kcal/hr)	IRT/KG (kcal/hr)
Overall (28)**	68.8 ± 3.6	1.12 ± 0.05
IV Fat (14)	65.2 ± 5.6	1.17 ± 0.08
No IV Fat (14)	72.5 ± 4.6	1.07 ± 0.05
Kwashiorkor (18)	77.7 ± 3.9^{a}	1.08 ± 0.04^{c}
Marasmus-Kwashiorkor (8)	55.7 ± 4.2^{b}	1.29 ± 0.10^{d}

* Values are means ± SEM. Means with unlike superscripts differ significantly at: a,b,$p < 0.001$; c,d,$p < 0.05$.

** Values in parentheses represent the number of scannings from which data were generated.

this way reversed the findings for the patients with malnutrition. The K group displayed a lower heat loss per kilogram weight than the group with M-K ($p < 0.05$).

When radiant, convective and evaporative heat losses were compared across groups, no statistically significant differences were noted between the fat/no fat groups (Table 13). Comparing these data for the kwashiorkor/marasmus-kwashiorkor groups revealed significant differences were demonstrated for radiant ($p < 0.003$), convective ($p < 0.01$) and evaporative ($p < 0.02$) with the kwashiorkor group displaying increased values over those of the M-K group. Analyzing these data on a per kilogram of body weight basis still failed to demonstrate any significant differences for the fat/no fat group, while the differences for radiant ($p < 0.02$) and convective ($p < 0.02$), but not evaporative heat losses, remained statistically significant, when nutritional diagnosis was used as the grouping parameter.

Mean skin surface temperature for the fat group was 28.5 ± 0.2°C (mean ± SEM) versus 28.3 ± 0.2°C for the no fat group. Comparing mean surface temperatures, with data grouped by nutritional diagnosis, revealed that the group with kwashiorkor had a slightly lower skin temperature (28.4 ± 0.2°C) than the group with marasmus-kwashiorkor (28.6 ± 0.3°C). However, none of these findings were significant.

As a corollary to mean surface temperature, patients were asked to assess their levels of thermal comfort by recording if their heads, arms, hands, trunk, thighs, legs and feet felt cool, normal temperature or warm. Over 70% responded that these body segments were either normal temperature or warm. The sections of the body most often judged as feeling cool were the legs (29.0%), the arms (25.8%) and the feet (22.6%).

Table 13. Mean radiant, convective and evaporative heat loss data (kcal/hr) for patients receiving TPN grouped by nutritional diagnosis and if receiving or not receiving intravenous fat emulsion*

GROUP	RADIANT HEAT LOSS	CONVECTIVE HEAT LOSS	EVAPORATIVE HEAT LOSS
IV Fat (14)**	33.3 ± 3.2	17.5 ± 1.7	18.1 ± 2.2
No IV Fat (14)	36.4 ± 2.1	18.9 ± 1.1	17.3 ± 1.2
Kwashiorkor (20)	39.5 ± 2.1^a	20.4 ± 1.1^c	20.0 ± 1.6^e
Marasmus-Kwashiorkor (8)	28.1 ± 2.2^b	15.1 ± 1.4^d	13.8 ± 0.9^f

GROUP	RADIANT HEAT LOSS (kcal/kg)	CONVECTIVE HEAT LOSS (kcal/kg)	EVAPORATIVE HEAT LOSS (kcal/kg)
IV Fat (14)	0.57 ± 0.04	0.30 ± 0.03	0.31 ± 0.036
No IV Fat (14)	0.54 ± 0.03	0.28 ± 0.02	0.26 ± 0.02
Kwashiorkor (20)	0.54 ± 0.02^e	0.28 ± 0.01^e	0.28 ± 0.02
Marasmus-Kwashiorkor (8)	0.66 ± 0.06^f	0.35 ± 0.04^f	0.31 ± 0.01

* Values are means ± SEM. Means with unlike superscripts differ significantly at: a,b,$p < 0.003$; c,d,$p < 0.01$; e,f,$p < 0.02$.

** Values in parentheses represent the number of IRT scannings used to generate the mean data.

When IC values were compared to IRT values across groups (Table 14), no significant differences were noted between the two methods, if data were analyzed by nutritional diagnosis or by fat/no fat groups. Generally, IC values tended to exceed those of IRT when all patients were considered together as a group. In the IV fat group, IC measurements were greater than those of IRT, but this was reversed in the group that was not receiving IV fat. The IC values exceeded those of IRT in the marasmus-kwashiorkor group, while heat loss was greater than IC measurements in those with kwashiorkor.

When the IRT data (59.7 ± 4.2 kcal/hr) collected before the IC measurement were compared to those obtained after IC (58.5 ± 4.2 kcal/hr), no significant differences were noted. This was also true when these values were compared to the IC data (68.0 ± 2.8 kcal/hr).

Balance Studies

Considering mean data from all patients together, a slightly positive nitrogen balance of $+0.5 \pm 0.9$ g/day (mean $\pm$ SEM) was demonstrated (Table 15). Nitrogen balance in the IV fat group was greater than that in the group not receiving fat, but this difference was not significant. However, the patients with marasmus-kwashiorkor displayed a significantly higher ($p < 0.005$) nitrogen balance than those in the kwashiorkor group, which was slightly negative (-0.6 ± 1.0). In terms of nitrogen intake, nitrogen output and protein per kilogram of body weight, no significant differences were noted between the group receiving IV fat emulsion and the patients not receiving it. On the other hand, the M-K group had a significantly greater intake of nitrogen in grams per day ($p < 0.03$) than the patients with kwashiorkor. Further, the M-K group also had a greater intake of protein per kilogram of body weight ($p < 0.0000$) than the K group. Nitrogen losses were demonstrated to be statistically similar in all groups.

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Table 14. Mean data comparing indirect calorimetry and IRT results for TPN patients, grouped by nutritional diagnosis and if receiving or not receiving intravenous fat emulsion*

GROUP	IRT (kcal/hr)	IC (kcal/hr)
Overall (28)**	68.8 ± 3.6	72.5 ± 4.1
IV Fat (14)	65.2 ± 5.6	74.7 ± 5.8
No IV Fat (14)	72.5 ± 4.6	70.3 ± 5.9
Kwashiorkor (18)	77.7 ± 3.9	75.7 ± 5.7
Marasmus-Kwashiorkor (8)	55.7 ± 4.2	69.0 ± 5.0

* Values are means ± SEM.

** Values in parentheses represent the number of scannings from which data were generated.

Table 15. Mean nitrogen intake, nitrogen loss, nitrogen balance and protein intake per kilogram of body weight for TPN patients, grouped by nutritional diagnosis and if receiving or not receiving intravenous fat emulsion*

GROUP	NITROGEN INTAKE (g/day)	NITROGEN OUTPUT (g/day)	NITROGEN BALANCE (g/day)	PROTEIN PER KILOGRAM (g/day)
Overall (28)**	11.3 ± 0.7	10.7 ± 0.6	0.5 ± 0.9	1.4 ± 0.1
IV Fat (14)	12.4 ± 0.6	10.2 ± 0.8	2.2 ± 0.9	1.5 ± 0.2
No IV Fat (14)	10.2 ± 1.2	11.2 ± 0.9	-0.9 ± 1.3	1.1 ± 0.2
Kwashiorkor (18)	10.8 ± 0.8[c]	11.4 ± 0.8	-0.6 ± 1.0[a]	1.0 ± 0.1[e]
Marasmus-Kwashiorkor (8)	13.8 ± 0.7[d]	9.4 ± 0.9	4.4 ± 0.8[b]	2.1 ± 0.6[f]

* Values are means ± SEM. Means with unlike superscripts differ significantly at: a,b,$p < 0.005$; c,d,$p < 0.03$; e,f,$p < 0.0000$

** Values in parentheses represent the number of scannings from which data were generated.

Finally, the energy balances of the patients were computed by subtracting the IC and IRT measurements from the energy intakes. The results of these data analyses are presented in Table 16. As is readily apparent from the table and Figure 8, patients receiving the IV fat emulsion had the greatest energy intakes per hour. The patients in the M-K group also had a high caloric intake. In looking at the differences between energy intake, IC and IRT, the group receiving IV fat emulsion displayed a positive energy balance irregardless of which method for determining energy expenditure was utilized. However, a more positive balance was determined by the IRT method. For the group not receiving IV fat, energy balance was negative, when energy intake was compared to IC and IRT measurements (Figure 9). When data were grouped by nutritional diagnosis, positive energy balance was demonstrated with either method. As is readily apparent from Figures 8 and 9, at times IC exceeded IRT and vice versa. In other instances, IC and IRT were both greater than energy intake. Finally, cases exist where IC was greater than both IRT and energy intake and at other times IRT was greater than both IC and energy intake.

DISCUSSION

Since the advent of TPN in the early 1970's, health care professionals have possessed the capability of nutritionally supporting hospitalized patients who are incapable of eating sufficient calories to meet their energy requirements or who, because of gastrointestinal contraindications, cannot ingest oral nutrients. With its use in the clinical and home environments, deficiency syndromes and other complications associated with overzealous administration of these solutions have been reported.

In severely depleted patients, metabolic rate, levels of digestive enzymes,

Table 16. Mean data on energy intake and energy balance for TPN patients as determined by indirect calorimetry and infrared thermography, grouped by nutritional diagnosis and if receiving or not receiving intravenous fat emulsion*

GROUP	ENERGY INTAKE (kcal/hr)	ENERGY INTAKE MINUS IC (kcal/hr)	ENERGY INTAKE MINUS IRT (kcal/hr)
IV Fat (14)**	149.3 ± 11.6	75.4 ± 12.6	84.1 ± 13.8
No IV Fat (14)	63.7 ± 6.2	-5.3 ± 9.5	-8.8 ± 8.5
Kwashiorkor (18)	93.9 ± 11.2	19.3 ± 11.9	16.2 ± 11.7
Marasmus-Kwashiorkor (8)	134.1 ± 20.6	65.8 ± 22.2	78.5 ± 23.6

* Values are means ± SEM.

** Values in parentheses represent the number of scannings from which data were generated.
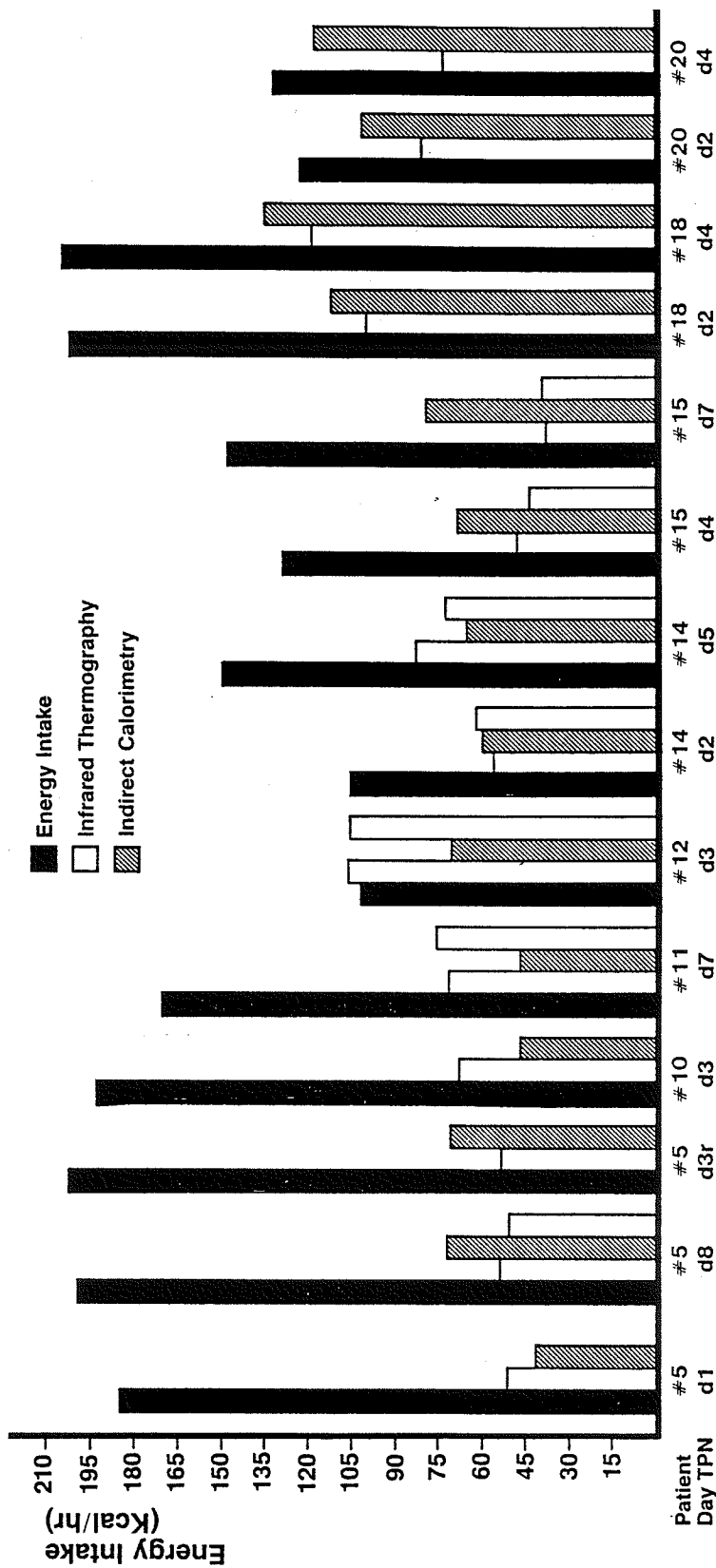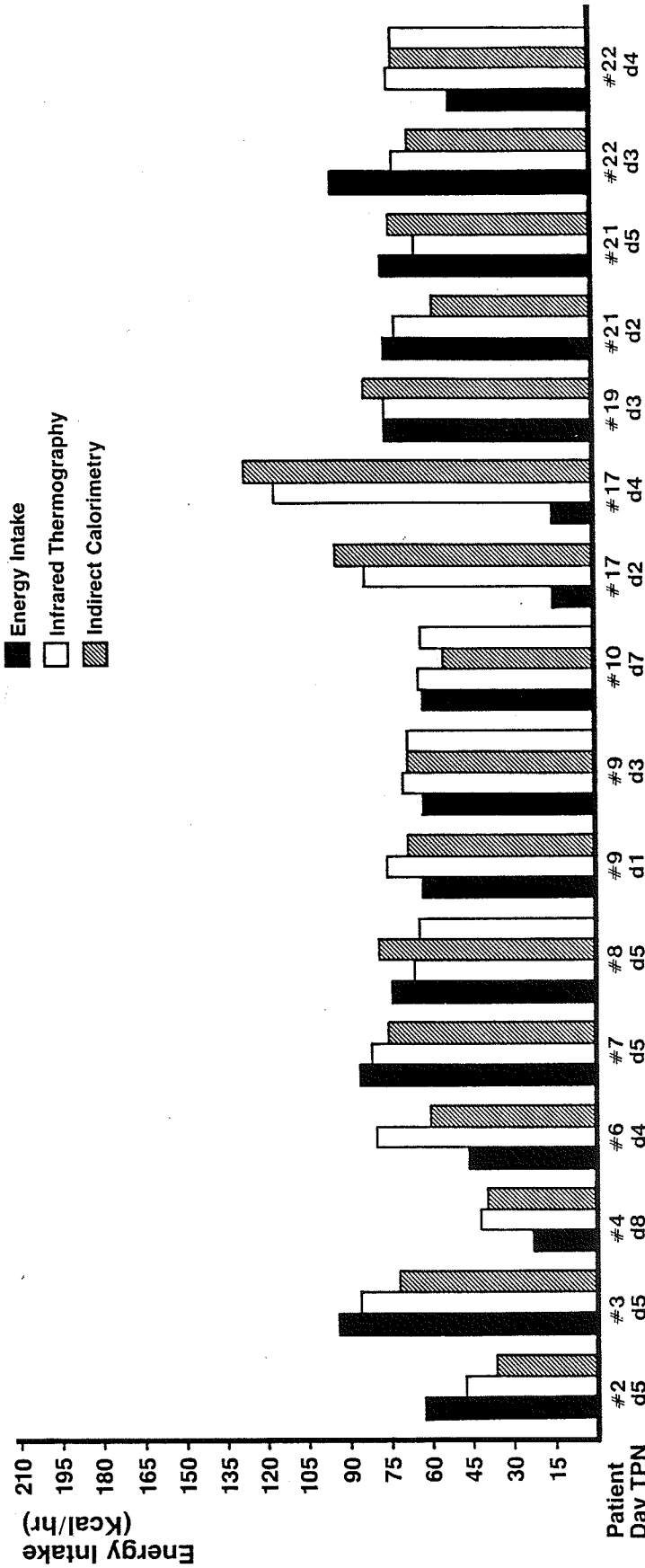
body core temperature and heart rate are significantly depressed. As reported
by Keys et al (23) in their classic studies of the effects of starvation on
human metabolism, the heart muscle atrophies in proportion to the amount of
weight lost. Upon refeeding, especially when calories are provided well in
excess of requirements, metabolism increases, which stresses organ systems
adapted to lower levels of functioning can potentiate organ failure. This
metabolic decompensation can be avoided if patients are refed gradually, but
this requires that energy expenditures be measured rather than estimated.
Unfortunately, in most hospitals, energy requirements are estimated by
prediction equations, which have been shown to overestimate caloric needs in
healthy individuals (7,8) as well as in patients (6). This finding was
substantiated by the data from eight patients in the present study. In these
cases, the HBEs overestimated resting energy expenditure (REE), as measured by
IC, by an average of 16.6%. For the remaining cases, the HBEs underestimated
REE by an average of 28.0%. Paauw et al (24) demonstrated that predicting
caloric requirements using 25 kcal/kg body weight gave a better average
estimate of actual energy needs than did the HBEs. Data from the present
investigation also supported this contention. The average caloric expenditure
based on 25 kcal/kg was 1667.3 ± 108.4 kcal/d versus 1714.6 ± 100.2 and 1461 ±
52.9 kcal/day for the HBEs. One possible explanation for IC measurements
exceeding the HBE results in our study is that our data were collected with TPN
solutions infusing continuously, while the others were completed on fasting
subjects. However, it is unlikely that the thermogenic effects of nutrient
infusion were of a magnitude sufficient to account for the differences,
especially when the measured versus predicted values differed by over 40%.
With further analysis of our data, IC values exceeded 2000 kcal/day in only

four of 28 measurements, which agreed with the findings of MacFie (25).
Therefore, the importance of measuring energy expenditure of patients is
evident.

The data from this investigation clearly demonstrate that the infrared
thermography system is a valid method for measuring energy expenditure and can
be used in the clinical setting under conditions of steady state during a
constant nutrient infusion. Our studies, which involved 38 scannings for
instantaneous quantitation of heat loss from patients receiving TPN, did not
demonstrate any statistical differences between IC and IRT. This result was
further substantiated, when heat loss obtained after the O_2 consumption data
were compared to those before IC and to the IC values themselves. Lack of
statistical significance can be interpreted as implying that the IRT system
yielded reproducible data. Another likely explanation for these data is that
the IRT studies confirmed the existence of a steady state of energy metabolism
in these patients. The significance of these findings is increased by the
manner in which the data were collected, i.e., in a conference room located at
the hospital; from patients who were chosen at random and differed in body
weight, type and degree of malnutrition, type of surgery, diagnosis, age,
amount and type of nutritional support solutions. In other words, use of this
method is not restricted to a research environment.

For purposes of comparison, data were expressed as kcal/kg/hr. This
manner of expressing the data was suggested by Durnin (26), who stated that the
surface laws do not apply to mammals in general, a view shared by Kleiber,
Harris and Benedict, Brody, Keys and Brozek and that there is no reason why
they should be used for metabolic data from humans. An alternative is to
express data on a fat-free mass basis. However, this quantity is not easily

measured by all investigators nor does it remain constant, particularly in pathologic states. When compared to lean body mass, adipose tissue is considered relatively inert, metabolically. However, expressing data on a fat-free mass basis, as opposed to body weight, implies that the physical work involved in transporting the additional weight does not influence O_2 consumption. Finally, body weight is readily measured in all laboratories.

On a per kilogram basis, IC data and IRT data were higher in the IV fat and the marasmus-kwashiorkor groups than in the other two groups. These results were supported by the elevated radiant, convective and evaporative heat loss data (kcal/kg) for the IV fat and M-K groups. The slightly increased values for mean surface temperatures supported the elevated radiant and convective heat losses for these two groups. These findings differed from that of MacFie et al (27), who demonstrated a significant rise in REE in the group receiving glucose only. Their patients, receiving 60% of daily kcal as fat emulsion with the remainder as glucose, showed an increase in REE, but it was significantly less than that of glucose alone. These differences were noted after nine days of TPN, whereas the data from the present investigation were collected over only five days. The most plausible explanation for these discrepancies reported in the present study were the greater energy (fat: 49.5 ± 4.8 versus no fat: 25.1 ± 3.1 kcal/kg/hr) and protein (Table 15) intakes per kilogram of the IV fat group. These findings were also true in the M-K group as well. The higher protein intakes of these two groups were of particular significance in light of the report of Jéquier (28), who stated that the thermogenic response to amino acid infusion in depleted patients amounts to 30 to 40% of the amino acid energy infused. Continuing in this line of research, Shaw et al (29) reported on the significant increase in REE, over time,

associated with infusion of high nitrogen solutions, which did not occur on low nitrogen intakes. The results from the present study (Figures 8 and 9) demonstrated an increase in IC measurements with continued infusion of TPN over days (70.5 ± 24.4 versus 77.1 ± 17.9 kcal/hr). Although this increase was not significant, this finding does support that of Shaw et al. Given the supporting data from other investigators, heat loss and O_2 consumption would be expected to be greater.

Of great interest were the nitrogen and energy balances, which were strongly positive in the IV fat and M-K groups, but not in the group with kwashiorkor or in the patients who were not receiving fat. That nitrogen balance was not positive in the last group might be explained by the negative energy balance which was demonstrated. With an inadequate energy intake, the infused protein was used to meet energy requirements rather than to replete body proteins. Also, the amount of protein provided by the TPN solutions was below 1.4 g/kg, which is considered to be an amount sufficient to achieve an anabolic state. The negative nitrogen balance in the patients with kwashiorkor was most likely the result of inadequate provision of protein to a moderately stressed postoperative patient.

In evaluating the differences in energy balance from Figure 9, it was noted that four distinct states occurred, when carbohydrate was the sole source of energy provided in TPN solutions. When energy balance was positive, several patients displayed IC values that exceeded energy expenditure as measured by IRT. One plausible interpretation of this finding is that substrate sufficient to exceed metabolic needs is being provided. Energy is being used to meet the body's energy requirements at that moment and captured for later use as stores of ATP, fat and glycogen are repleted. That O_2 consumption exceeds heat loss

in this situation is not unexpected when energy storage is occurring.

The second situation depicted in Figure 9 is that of energy intake exceeding IRT which is greater than IC. This finding is probably best explained by discussing the possible interaction of three factors: the thermoregulatory processes of the body, the instantaneous quantitation of heat losses by the IRT method and futile substrate cycles. With further metabolism of ingested nutrients occurring at the cellular level, heat is generated and released as biochemical reactions in the body are not 100% efficient in conversions of substrates from one form to another. If this heat were not continuously dissipated, body core temperature would increase to potentially lethal levels in a relatively short period of time. As the heat is transferred to the periphery, skin surface temperature increases, which in the case of our patients, created a large differential between skin surface and ambient temperatures, facilitating heat loss to the environment. These phenomena coupled with the instantaneous heat loss measurement with the IRT system resulted in the findings presented. Futile cycling has been postulated as a possible mechanism explaining patients who lose weight in the face of apparently adequate energy intakes as determined by IC. It is unlikely that this would explain the results from the present study as our patients were in positive energy balance and gaining weight. These results are similar to the postprandial data of Benedict (9), Pittet and Jéquier et al (30) and Webb et al (31), whose results for O_2 consumption and heat loss demonstrated the same variability with food ingestion.

When IRT and IC exceed energy intake, the patient is in negative energy balance and weight loss occurs, a very straightforward concept. The most interesting situation is the one in which IRT exceeds energy intake which, in

turn, exceeds IC. It is in the elucidation of the mechanisms responsible for this phenomenon that the IRT system holds its greatest research potential.

In the clinical setting, there are patients who continue to lose weight even with provision of adequate energy intakes. However, if energy expenditure is measured at all, it is through the use of indirect calorimetry. Although use of this method is far better than estimating needs using prediction equations, there are situations where IC does not completely reflect caloric expenditure. The explanation for this inadequacy is found in the method itself. By definition, IC measures heat production indirectly as a function of O_2 consumption. The caloric equivalent of a liter of O_2 is based on respiratory gas exchange, from which the RQ is determined. Thus it is assumed that all processes in the body are aerobic and measurement of O_2 consumption will reflect energy expenditure. However, although all aerobic processes are thermogenic, the reverse is not true. Possible sources of heat production in the absence of O_2 consumption include the inefficient energy transfer of futile substrate cycling and brown adipose tissue thermogenesis. These pathways of energy dissipation may have enhanced function in patients with cancer cachexia, cardiac cachexia, severe chronic obstructive pulmonary disease, diabetes mellitus, burns and other conditions characterized by substantial weight loss despite a 'normal' dietary intake.

In summary, the IRT system can be used in the clinical setting to quantitate heat loss of patients receiving continuous nutrient infusions. Use of the infrared thermography system in patients who continue to lose weight in the face of an adequate nutritional intake can potentially provide clinicians and researchers with insight into the mechanisms regulating energy metabolism in disease.

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CHAPTER 5

SUMMARY

Infrared thermography has been used by other investigators to quantitate changes in mean surface temperature, after eating, in lean and obese subjects. The possibility of adapting this method to the quantitation of heat loss from human subjects during a prolonged overnight fast, after eating and during a continuous infusion of nutrients were investigated. To determine the validity of the measurements obtained by the IRT system, heat loss values from scannings were compared to energy expenditure data calculated from O_2 consumption, i.e., indirect calorimetry.

The first set of experiments was designed to evaluate the ability of IRT to detect postprandial thermogenesis and to validate the method. Comparing the initial IC and IRT measurements across study days failed to show any statistical differences. In addition, when the initial IRT scanning and IC measurements were compared to those subsequent, no differences were demonstrated. Based on this information, it was assumed that any changes occurring after eating were due to the ingestion of food and not to changes in metabolism. When data obtained during fasting were compared to those measured postprandially, significant increases in O_2 consumption (IC) and heat losses (IRT) were noted, with the increase in O_2 consumption preceding that of heat loss by approximately 30 minutes. To validate the IRT method, data obtained by IRT were compared to those from IC. There were no significant differences demonstrated. It was concluded that IRT was a valid method for quantitating postprandial thermogenesis.

Adaptation of the infrared thermography system for use in the clinical setting was the objective of the final experiment. Twenty patients receiving

total parenteral nutrition with or without intravenous fat emulsion were studied. This condition was chosen to evaluate the effects of continuous nutrient infusion on heat loss and to determine if the type of nutrient solutions infused or type and severity of malnutrition influenced heat loss. To validate the IRT method in the clinical setting, IC and IRT data were compared. No statistically significant differences were noted between the results of the two methods. Heat losses (kcal/kg) were higher in the group receiving IV fat emulsion and in patients with the nutritional diagnosis of marasmus-kwashiorkor than in the group not receiving fat or in patients with kwashiorkor. The former two groups also displayed a more positive energy balance as assessed by both IC and IRT than did the latter groups. It was concluded that IRT can be used in the clinical environment to determine energy expenditures of patients with varying nutritional intakes and body weights. Further, these data indicate that determination of energy expenditure using the IRT system need not be restricted to only the research setting.

As with any new methodology, an analysis of probable error associated with the technique must be completed. For the thermographic method, the approach taken involved a determination of the best guess for each factor of the heat loss equations for which data needed to be input. Once these were determined, the corresponding values were input into the equations in a manner that would result in calculation of the lowest and highest heat losses around the reported IRT value, if all parameters varyed in the same direction at the same time. The results of this analysis demonstrated that the confidence interval for the IRT data was ± 20%, which means that for a reported heat loss of 96 kcal/hr, the true value can fall anywhere between 77 and 118 kcal/hr.

Given this error, interpretation of heat loss data must be completed

carefully. In studies on large numbers of individuals, this error is not as great a problem, since trends in the data will most likely be apparent. It would be difficult to believe that the IRT method was consistently off in the same direction and to the same degree during 50 different data collection periods.

The major problem with an error of this size is similar to that with which nutritionists deal on a daily basis, i.e., how to adapt data collected on a large population to use on an individual basis, particularly in the clinical setting, where IRT would be an invaluable tool for assessing the efficacy of a nutritional support regimen. One way in which to deal with this is to decrease the error associated with the method. Analyzing the input parameters for the heat loss equations one at a time demonstrated that the greatest sources of error were the average convective heat loss coefficient (7.81%) and mean surface temperature (6.95%). Improvements in these values would substantially decrease the percentage error of the method. If this was not possible, the next option would be interpretation of the data in light of the patient's clinical condition. Using the previous example of 96 kcal/hr with a range of 77 to 118 kcal/hr as a guide, a physician could begin therapy at the lower end of the scale and monitor the patient's progress clinically. If weight gain did not occur then therapy is inadequate and the levels of intake should be increased to the determined value with continuation of monitoring and any further adjustments made as needed. If IRT is used in a patient already receiving therapy, demonstration of a highly positive energy balance could be the basis to justify decreasing energy intake, which would reduce patient costs as well as lower the metabolic stress on the body. These goals could be achieved without compromising nutritional repletion. Again, careful monitoring

would be necessary to avoid inadequate levels of energy.

In general, the IRT system can provide investigators with information on heat loss in a variety of clinical and research settings, and under varying conditions. Use of this technique will provide scientists with information necessary to unravel the mechanisms by which the body regulates energy metabolism under conditions of varying energy intakes.