1. Interruption of automatic feeding of fattening and associated immune deficiency

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Abstract. Vascular risks, allergy, joint pain and loss of functional efficiency in sight, hearing, memory etc. develop in proportion to immune stimulation, i.e. on growing inflammatory responses throughout the body that are persistent and subclinical most times. Every inflammation destroys antigens and nearby tissue. We here assume that multiple antigenic invasions sum their stimulation. Genetic and epigenetic factors influence localization of lesions in the joints, skin, liver, bronchial mucosa or elsewhere, whereas extension and intensity of inflammation depend on the incoming antigen burden. In Tuscany, the inflammatory state depends on positive energy balance in blood (fattening) for about two thirds of population. Other pro-inflammatory causes are persisting infections and long convalescence periods. The positive energy balance in blood (“abundant intake” or fattening) is measured by high blood glucose (BG) before meals or by insulin-resistance, the two measures are associated, and the state of positive balance (fattening) may become conscious at mealtimes after training by coupling BG measurements at arousal of hunger sensations. The state of fattening that we are describing has been mentioned as Subclinical Inflammation and Proinflammatory State. We want to
use another synonymous, Reversible Immune Deficiency (RID), in order to evoke its effective role to clinicians and patients. The state reverts easily to null balance in trained people who become conscious on complete or incomplete exhaustion of previous meal after learning “hunger recognition”.

**Energy balance in blood and reversible immune deficiency (RID)**

The bloodstream may be seen as the result of incessant influx and efflux of nutrients. The resulting dynamic (instant) balance of energy indicates instant energy availability and is approximately measured by BG [1]. The lowering level is correlated with the arousal of Initial Hunger (IH) that we have scientifically defined from what people name with this word [2-7]. Before any meal, energy availability (dynamic balance, BG) indicates if the energy of previous meal is exhausted or not. A high BG indicates incomplete exhaustion and positive balance between meals (abundant intake in the previous meal). A low BG and/or IH arousal indicates null balance, and a very low BG indicates negative balance. Studies on overweight (OW) subjects confirmed no body weight decrease when BG was maintained high before meals ($91.4 \pm 7.7$ mg/dL) and a body weight decrease after regular exhaustion of previous meal energy and low pre-prandial BG achievement ($76.5 \pm 3.9$ mg/dL) [3]. Trained subjects recognize this level by IH arousal [1-4]. Null balance in blood produced body weight decrease in OW people because of a high release of fatty acids from stores in blood after the end of intestinal absorption. In OW people, the high post-absorptive fatty acid delivery is three times as large as in normal-weight people [8]. The copious fatty acid influx into blood may thus be associated with negative total body energy balance for decrease of fatty stores. Also intense physical exercise and the associated modest muscle mass loss produce abundant influx of small molecular weight nutrients into blood. Lean subjects maintained steady body weight and ate 100 kcal more per meal than overweight subjects who lost weight [3] because they missed the high fatty acid influx (mean = 100 kcal) associated with body weight decrease [3]. In our extensive studies, normal-weight (NW) people had some kind of immediate, functional feedback after sustained abundant intake, whereas OW people silently, and easily, fattened. Although showing different intake and different body weight, all people have to equally reach $76.5 \pm 3.9$ mg/dL of BG before any meal to maintain null energy balance in blood (homeostasis, Table 1) [3, 5, 6]. Thus, maintenance of null balance in blood is equally difficult or equally easy in NW as well as in OW subjects.

The high fatty acid loss from fatty stores is not limited to those who have body mass index over 25. A subject may have accumulated a modest amount
of fat (2 – 3 kg body weight) and remain lean, but his/her fatty stores deliver abundant fatty acids to blood, and maintain high post-absorptive BG and insulin resistance [5 – 10 ]. The post-absorptive delivery of fatty acids depends more on the abundance of replenishment of fatty cells than on their number, i.e. depends more on replenishment of storage space than on its extension [12]. A lean body may unfortunately be composed by a poor lean body mass associated with thick (3 cm) arm skinfold, and may thus maintain insulin resistance for long periods of time.

Table 1. Prevalence of low mean blood glucose (LBG) either by free, spontaneous choice at recruitment (Before) or after training (After) Hunger Recognition in 8 different groups.

<table>
<thead>
<tr>
<th>Subgroups and training</th>
<th>% within subgr.</th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 9 out of 24 NW ctrl adults,</td>
<td>38</td>
<td>77.3 ± 3.92</td>
<td>No training</td>
</tr>
<tr>
<td>26 out of 66 trained NW adults,</td>
<td>39</td>
<td>76.5 ± 3.9</td>
<td>76.7 ± 4.1</td>
</tr>
<tr>
<td>40 HBG out of 66 trained NW adults</td>
<td></td>
<td>91.4 ± 7.7</td>
<td>80.1 ± 6.67</td>
</tr>
<tr>
<td>8 out of 21 OW ctrl adults,</td>
<td>38</td>
<td>77.4 ± 3.6</td>
<td>No training</td>
</tr>
<tr>
<td>12 out of 38 trained OW adults</td>
<td></td>
<td>77.1 ± 3.1</td>
<td>77.2 ± 4.8</td>
</tr>
<tr>
<td>26 HBG out of 38 OW adults</td>
<td></td>
<td>91.3 ± 6.5</td>
<td>79.6 ± 7.57</td>
</tr>
<tr>
<td>49 HBG out of 70 infants</td>
<td></td>
<td>91.3 ± 7.2</td>
<td>76.9 ± 6.7</td>
</tr>
<tr>
<td>21 out of 70 infants</td>
<td></td>
<td>76.4 ± 4.5</td>
<td>75.2 ± 6.6</td>
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1 90 normal-weight (NW), 59 overweight (OW) adults and 70 infants in the second year of life at recruitment and after 5 months. These three groups are each divided in two subgroups, trained and control (ctrl). The subgroups are divided in subjects beyond and below 81.8 mg/dL, and are named HBG, high blood glucose and LBG, low blood glucose. Six adult groups and two infant groups are presented. HBG ctrl subjects (NW and OW) are excluded because useless for this table. From Table 2 of reference 3, and from 6 2 Mean ± SD of 21 pre-prandial BG from week-diary in mg/dL. 3 No training refers to subjects kept as control (ctrl).

The etiology: Infections, abundant intake

The powerful immune stimulation during acute infection may promptly subside, although leaving abnormal inflammatory low grade stimulation throughout the body for weeks and months. The endurance depends on the
gravity of the passed acute inflammation. In this state, ‘healthy’ people may suffer functional complaints like diarrhea, abdominal pain, allergies, headaches, weakness, increase of vascular risks and infection worsening although they actively feel well on their working and recreational hours. We are describing the “convalescent state” that allows effective gym activity and even athletic performances in association with diminished resistance to supervened infections. This reversible immune deficiency (RID) is the most important character in proinflammatory state or subclinical inflammation for clinicians, and for this reason we propose Reversible Immune Deficiency (RID) as a valuable synonymous [12–19]. After one–two months the susceptibility fades away. In addition to these remitting events of convalescence, there is an unremitting entry of bacterial antigens from small intestinal mucosa, which stimulates inflammation and RID throughout the body in a sort of either low or high grade ground stimulation [20, 21]. Mucosa of small intestine is the largest immune organ and produces half immunoglobulin of the total production in humans [22]. The correspondent antigenic stimulation is the largest in the body and never stops [22]. The healthy mucosa maintains low grade inflammation in temperate climate, but bacteria and inflammation are more copious in tropical countries [23, 24]. The inflammation is locally tolerant, i.e., traps and kills bacteria but destroys poorly antigenic components, producing few damages in the mucosa and discharging most antigens in blood and lymph [20–22]. The consequent body subclinical inflammation produces destructions of antigens and nearby structures and is incessant either low or high in blood and organs, and represents the biological basis for risks and deterioration [12–27]. The level of this permanent antigenic stimulation (antigenic burden) depends on established intake customs, i.e., on habitual provision of energy to body cells [25–27].

The etiology: Measuring meal patterns

Energy intake does neither classify errors in eating nor evaluate their gravity. We found differences of ten times in intake of general population, and those who ate less were the fattest. Instead, energy availability in blood is useful to evaluate abundance and insufficiency of eating. Energy availability directly influences all tissues: it is correlated to either insulin resistance or sensitivity, to either positive or negative balance of energy, to either fattening or fat decrease and to associated changes in body weight [1–11]. Energy availability is the aim of meals and meal energy amounts may be judged by the energy availability that meals produce. A direct measuring of energy
availability does not exist now. We assume that BG is representative (a measure) of all nutrients in blood [1 - 11]. Healthy people on a mixed diet oxidize blood glucose before other nutrients [9 –14]. Abundance of other nutrients spares blood glucose, but does not stop its decline because glucose reserves are exhaustible [9 - 11]. On the contrary, parasympathetic nervous system promptly releases free fatty acids from fat stores at every abrupt increase in expenditure [28]. BG shows the level of the current dynamic balance of energy in blood: i.e., the function of instant provision of energy to body tissues [1, 5]. A high pre-meal level is indicative of inter-meal positive balance, fattening and increase of insulin resistance. Insulin resistance consists of high blood energy provision so that cells are replete, BG entry into cells is impaired, pathophysiological reflexes emerge, intestinal absorption slows down, microflora overgrows and damages begin to emerge (= RID). This association is strongly documented [1 – 6, 12 - 22]. “Mean BG” consists of the mean of 21 preprandial measurements of blood glucose in a week, a variable that measures the habitual accomplishment of eating aim: abundant, balanced or scarce. Mean BG was distributed among ten significantly different strata in adults and remained constant over 5 months [5]. Mean preprandial BG is a metabolic characterization of individual, energy meal pattern, because measured at a standard metabolic time, at the lowest levels during subsequent days, just before main meals, and thus allows comparisons and classifications better than mean daily energy intake [5]. Mean BG shows customary intake/balance of energy, is associated with insulin sensitivity/resistance, and consequently indicates the amount of ground antigenic stimulation from intestinal mucosa. The large differences in individual mean BG explain huge differences in intestinal antigen burden entry, risks, functional losses year after year, and health.

The pathogenesis: Conflict between intestinal bacteria growth and nutrients absorption

The mucosa of small intestine hosts a moderate local inflammation, consisting of IgA and phagocytic responses [22]. This “tolerant” inflammation discharges antigens in circulation and stimulates a subclinical inflammation throughout the body. Colon mucosa may participate to this stimulation although the demonstration is poorer. Subclinical inflammation in intestinal mucosa and throughout the body and Reversible Immune Deficiency (RID) are consequent to the increase in bacterial number on the mucosa. We have shown increases of at least 11 times on normal mucosa of
healthy children during the interval between meals [27]. Reversing RID requires the reduction of the bacterial growth between meals, or better, the reduction of the persistence of a bacterial film on intestinal mucosa. Bacteria grow rapidly on liquid food at 37 – 38 °C, a doubling every ten – fifteen minutes. Given this possibility, the expectation for a maximal health means meal consumption at the lowest number of bacteria on small intestine mucosa. Health means least persistence of food inside the lumen. This state means absence of food before intake and rapid return to an empty intestine.

Insulin resistance and RID derive from positive energy balance in blood for about two thirds of times and from viral/bacterial infections for one third. Vicious circles tend to maintain the pathologic condition. Monocytes/macrophages contact bacteria and viruses during an infection to capture them in a vacuole. This action is associated with release of cytokines that are active on hypothalamic centers [29]. The subsequent events are symptoms of illness with inter-individual (genetic) differences in their full development. The subject develops fatigue, hypotension, anorexia, sleepiness, increase in body temperature (fever) and all the events of insulin resistance: high fatty acid release from adipose tissues and high BG. BG remains sufficient up to the end of illness despite poor or no intake. Fever is always associated with decrease of intestinal absorption, which may develop in absence of fever [29]. Food may be consumed in spite of anorexia and high BG [30], and arrives in the small intestine that functions poorly. Nutrients slowdown in small intestine may occur also in health. Researchers infused glucose IV in opposition to saline infusion in healthy adults. During infusion, they administered a meal at usual mealtime. Subjects receiving glucose consumed the offered meal despite high BG [31]. Under glucose infusion, digestion and absorption slowed down in comparison with saline solution. The emission of pancreatic enzymes and bile salts, the small intestine motility and absorption rate decrease as BG increases [32 - 37]. Also a moderate meal slowed down progression of intestinal content. One meal taken when BG was 150 mg/dL was sufficient to produce relapse in children with recurrent diarrhea or malabsorption [38, 39]. In normal condition, transit time in small intestine depends on meal energy content. In dogs, transit time is positively associated with the square root of energy content [40, 41]. Absorption rate by surface unit is constant [41], and thus global absorption rate increases when transit time is rapid. In humans, whole (100%) meal transit time is 168±14 min (SEM) after 220 kcal and 368±36 min after 880 kcal [40, 41].

Microflora takes advantage from prolonged persistence of nutrients inside the lumen [27]. Most of many hundreds of species isolated from
human intestine are innocuous. About one hundred are incapable of giving illness in healthy subjects, but stimulate local and bodily inflammation [20 - 26]. Spots of bacteria expand on mucosa. Mucosal invasion is rapidly stopped by prompt killing of invaders. Bacterial antigens and endotoxins invade the circulatory system and raise RID (subclinical inflammatory state) that slows and aggravates the main infection in a vicious circle [1, 25, 26].

**The physiological feedback for abundant intake: Hunger sensations**

Food remaining in small intestine is poor and rapidly eliminated in concomitance with phase 3 movements, the functional basis for epigastric hunger sensation [32, 42 - 46]. We assumed that epigastric sensations of hunger marked the food absence from jejunum [32 – 38, 42 - 48], and minimal growth of microflora on mucosa [27]. The expectation of maximal health implies a rather short interval between two subsequent events of hunger that coincide with phase 3 movements. Internal cues are necessary for deciding intake start, amount and cessation, and have been therapeutically used, although ineffectively, considering current obesity epidemic [49]. Strong habits establish adult’s meals at mealtimes and some kind of hunger follows the decision of eating [1 - 6]. This internal, habitual cue is poorly effective in intake regulation. The spontaneous arousal of hunger must be searched. Adults require (first) meal suspension to interrupt the habitual pattern in the first training day, and (second) learning the identification of “initial hunger” (IH) by BG pre-meal checking. We have defined the concept of Initial Hunger (IH), the cornerstone of this elaboration on human eating [1, 2]. Adults learn the recognition of spontaneous arousal of IH and validate the recognition by BG. Instructions for the first training day interrupted automatic, habitual food intake at mealtimes and implemented habitual evaluation of either a arousal or not of IH. Figure 1 demonstrates that hunger sensations may become reliable in the assessment of the current energy availability (instant balance) in blood that we assumed to be measured by BG. IH is identified as the first arousal of hunger after meal suspension. After this initial sample arousal, IH is recognized at subsequent mealtimes and recognition is validated by the identity of the associated blood glucose (BG) measurement [1, 2]. The meaning of this validation is that subjects can recognize IH as manifestations that arise at a constant (low) BG, ie corresponding to a physiological identifiable condition. The arousal of the learned sensation allows estimation of current BG (Figure 1 and ref 2). IH
consists of epigastric sensations of gastrointestinal constriction, emptiness or movements. Sensations of mind or physical weakness must be included in IH, because arousing about the same BG like epigastric sensations. Weakness sensations are not specific of low energy availability in blood, although at mealtimes, allow BG estimation of current BG with the same error like the epigastric sensations [2]. The estimation error is the difference between estimated and measured BG. Based on these studies, epigastric hunger (IH) was conceived as a threshold phenomenon triggered by low energy availability in blood indicated by low BG; prior to IH normal activity is not inhibited by low energy availability.

![Figure 1. Estimated vs. measured blood glucose of subjects reporting to be hungry at the final laboratory investigative session. Hollow red circles, trained hungry subjects (n = 18); hollow black circles, control (untrained) hungry subjects (n = 42). Linear correlation was significant for the trained data (dashed red line; r = 0.92; p = 0.0001) but not for the control data (dashed black line; r = 0.29, p = 0.06). (By courtesy of the Authors: Ciampolini and Bianchi, 2006 [2]).](image-url)
Children are often habituated to scheduled feeding since the first days of life. Scheduled-feeding is defined as the initiation of meals when based on time of day or external events, whereas in demand-feeding, meals are initiated only upon request of the infant or toddler for food. In toddlers, we interrupted habitual feeding by asking mothers to suspend food intake for a few hours, and make note of the specific manifestations of the child’s first food demand [6, 7]. Crying, mood changes like loss of enthusiasm for playing, gestural or verbal demand and searching for food without any ‘external’ stimulus all were considered to be signs of demand (Initial demand, ID or Initial Hunger, IH). Mothers learned ID manifestations. The principal investigator accurately phoned every end of the first training day to ascertain the actual change made by the mother. First adherence to this protocol resulted in a mean meal consumption after a delay of two hours (0 - 48 hours range). At subsequent mealtimes, mothers evaluated arousals according to their first experience to assess if the demands were due to hunger. Absence of IH manifestation before meals was treated in subsequent meals by alternations in behavior that would enhance hunger, such as a decrease in energy-dense food in subsequent meals. Our previous studies [1 - 6] show that BG is significantly lower in children that demand food than those who do not after training. We reported the validation of demand recognition previously [6]. After training with 42 measurements at hunger arousal, we investigated 16 toddlers not demanding food in comparison with 54 who were demanding in the hospital laboratory before breakfast [6]. No demand was associated with a significantly higher mean BG than the condition of food demand (96.3 ± 10.5 mg/dL vs. 74.6 ± 7.7 mg/dL; P = 0.0001). Based on these studies, IH was conceived as a threshold phenomenon triggered by low energy availability in blood indicated by low BG [1 - 7]; prior to IH normal activity is not inhibited by low energy. The intervention may be resumed as a stop of automatic feeding before every meal and practicing a judgment on the amount to be eaten (initially 150 kcal for infants and 300 kcal for adults). The interaction between subject (mother) and expert (couching) is necessary to interrupt the automatic feeding and to stop any dependence on fullness sensations (manifestations) toward meal end. Fullness sensations tend to deceive toward an excessive intake and long inter-meal interval. Scheduled feeding appears to be insufficiently established as a habit in toddlers at recruitment to the point that infant’s demand for food is still reliable. We trained mothers to rely on recognition of IH manifestations (Initial Demand, ID in infants) to administer meals, but did not require BG measurements [7]. We checked administration changes by measuring changes in resting metabolic rate (RMR) by indirect calorimetry in 14 infants and total energy expenditure in 10 infants by doubly labeled water [7]. Energy
intake decreased from 86.0±17.3 kcal/kg/d to 70.7±18.8 and from 87.8±13.9 to 71.1±14.6 in the two groups and showed no difference at recruitment from local population of same age [7]. Afternoon RMR (sleeping MR) fell by -9.6 ± 8.6 kcal/kg/d (-15.4 % of value at recruitment), i.e. from 58.6 ± 7.8 to 49.0 ± 9.1 kcal/kg/d. Daily energy expenditure fell by -12.3 ± 7.2 kcal/kg/d (-15.5%), i.e. from 80.1 ± 6.9 kcal/kg/d at recruitment to 67.8 ± 10.0 kcal/kg/d at follow-up (Table 2). Parents educate their infants to scheduled feeding and excess intake since the early days of life!

Mothers received information on food energy contents, on balance factors, on recommended vegetable intake and physical activity amount per day. Half kg per day was the recommended fruit and vegetable amount for infants, one kg for adults. The investigators discussed, and promoted energy expenditure by decrease in over-heating and over-clothing, and fostering outdoor and gym activities. Avoiding snacks was suggested, though earlier than optimal IH was satisfied with fruit and adequate energy-dense food if needed. Social obligations like parties and school catering were included in planning the intake amount and timing of the previous and subsequent meals.

The physiological feedback for RID: Initial Hunger Meal Pattern (IHMP, Hunger Recognition)

As mentioned already, BG is significantly lower in children that demand food than those who do not after training [1 - 7]. The meaning of the validations in toddlers is that trained mothers can recognize food request as manifestations that arise at a constant (low) BG in their infants. After couching, mothers recognize a condition of low energy availability in blood, and validation by BG measurement is unnecessary. The intervention in adults and children may be summarized as 1) Stop of automatic start of eating that adds unnecessary energy to the previously unexhausted intake. 2) Stop on dependence on fullness sensations at end of the meal that tend to deceive toward a prolongation of the satiety interval.

The decreases in mean BG and RMR were significantly larger when recruitment values were high. In animals, decreases in BG and in RMR precede meal consumption [48]. RMR increases when energy availability in blood is high and decreases when the availability is low. Summarizing, BG measures energy provision to body tissues, and determinates ± 15% of RMR value, the sign depends on energy balance in blood that may be either positive, null or negative. The decreases in energy provision and production may constitute the biological bases for reporting weakness as IH sensation in humans. Table 1 suggests that we can find 20% - 30% of untrained infants
and untrained adults who maintain the mean BG that we found after adoption of IHMP. This finding suggests that IHMP is a “normal” eating pattern. Moreover, the association of LBG with insulin sensitivity [5] suggests that IHMP is “healthy”.

We generally opted for three daily meals although overweight people have high capacity of energy storage, and might take two daily meals and even one. OW people have the same difficulty of lean people in achieving IH before meals. Four – five hours might be appropriate, but night needs a different computation because it is associated with rest, thermal neutrality and sleeping, and all together these decrease metabolic expenditures and intestinal movements in comparison to the day [1, 42 - 46]. Night may count for only one - two additional hours when epigastric hunger arises on waking up, but may count for a number of hours higher than 12 if the subject does not recognize Initial Hunger just after getting up. Last meal of the day is the most risky in temperate regions.

**Figure 2. Difference after training versus value in mean blood glucose for each trained subject at recruitment.** Column height shows 5-month mean blood glucose difference (post less pre) from 7d-diary in each trained subject. Significant increases in blue, significant decreases in red and not significant changes in black. Mean blood glucose reported in sequentially increasing order at recruitment, not in linear correlation with segment length on the x-axis scale. The dashed division indicates the most significant division between subjects who showed no mean blood glucose decrease after training (LBG group, n = 34 subjects) and those who showed significant decrease of mean blood glucose (HBG group, n = 55 subjects; $\chi^2$ analysis: P = 0.00001). This threshold blood glucose at recruitment (demarcation point) is 81.8 mg/dl (4.5 mmol.l) at recruitment [5]. (By courtesy of the Authors: Ciampolini et al., 2010 [5]).
The main problem for all is an intake amount that allows IH arousal after the desired number of hours. IH is associated with BG about 76 mg/dL (Table 1). In the first meals during training, subjects may choose an insufficient portion (150 - 200 kcal for toddlers and 300 for adults) that has to be increased at verification of early IH that means insufficiency. When IH arises approximately at the planned mealtime, the amount of consumed energy should remain constant. Any increase in energy intake prolongs absorption and delays IH in proportion to the root square of the amount of increased energy [40, 41]. In the present review, we intend to show a variety of factors that sometimes determine a positive balance in blood raising insulin resistance and the associated immune stimulation (RID).

**Balance in blood: Fattening**

An absence of symptom feedback during abundant intake is characteristic of people who are able of further fattening. Inborn hormonal conditions (high insulin and cortisol production) allow fattening for months and years. These people may have only esthetical feedback in progressive fattening. Yet, the esthetical deterioration is part of a larger deterioration than a simple impairment of sexual appeal. Immune stimulation up to formation of subclinical inflammation is associated to fattening. Young people may guess this condition from skin desquamation, dissemination of erythematous points and development of acnes. Adolescents may spend attention to improve sex appeal more than to decrease risks and functional deterioration. We found 2 kg of body weight decrease after use of IHMP and a recovery of low preprandial BG (LBG) and insulin sensitivity in adults who were insulin resistant, normal-weight (NW) and in reversible immune deficiency (RID) at recruitment (hidden OW). Insulin resistance and RID are positively associated in subjects with thick skinfold thickness as well as in subjects with thin skinfold thickness. Intake abundance is more prevalent than OW and obesity that are about 40% worldwide [49]. Given this wide prevalence, people seriously need improvement in knowing development and consequences of diabetes and fattening that together form the metabolic syndrome [49]. Multiple factors raise this derangement. Being fully aware of this suggests self-promotion of increase in daily expenditure as a lifestyle. This goal has diffuse consensus. People easily perceive personal improvements by physical activity, they need increasing awareness about the major role of thermo-dispersion on expenditure, about changes in environmental temperature, ventilation and humidity (thermo-dispersion) from one hour to another, and about need for promoting thermo-dispersion by multiple ways in our indoor living that is thermally moderate. IHMP reduced
energy intake and mean BG in controlled studies on 88 infants after seven months [38], 114 infants after 4 years [50], on 311, 244, 125 and 88 infants during a sequential follow-up with assessments after 5 months, 4, 8 and 12 years [Table 1 in reference 51], on 143 infants after 4 months [6] and in 107 normal-weight adults and 74 overweight adults after five months [3]. In adults, the decrease in energy intake and mean BG was associated with decrease in insulin resistance and body weight except for adults who were normal-weight and insulin sensitive [3 - 5]. Moreover, the skill of IH recognition was long lasting [3 - 5]. Yet, the validity of energy intake reports has been questioned. We found no significant difference between diary energy intake and total daily expenditure by doubly labeled water either at recruitment, on the pre/post longitudinal differences or after training [7].

**Balance in blood: Physical exercise**

Muscles contain an important nutrient reserve, about 6000 kcal [8]. The exercising muscle breaks down a larger amount of glucose than that which is completely oxidized. During anaerobic physical activity, production of lactic acid is abundant, and lactate, the small molecule, escapes from muscles into blood to be recovered by liver, reconstituted to glucose and released into blood. BG availability increases in blood and the increase is in proportion to intensity and time length of activity. Housework and sedentary activity is poorly effective on expenditure, 1.3 - 1.5 times as much as resting metabolic rate [52]. Walking or cycling for half an hour elevates BG and delays hunger arousal for half an hour or more. Hunger delays for three quarters of an hour after running for half an hour [53]. In our Gastroenterology Unit, we examined young subjects who practiced three hours of intense activity like cycling or running in cold environment without having breakfast. They had no perception of hunger during activity. After three hours, hunger sometimes occurred even in trained subjects. After no consumption of breakfast or other snack in the morning, deep and persistent weakness ensued without being alleviated by a meal. In general, physical exercise lightly increases subsequent meal consumption. During meals, absorbed nutrients are taken up by depleted muscles, and this increased uptake represents an increase in insulin sensitivity. Muscle refilling by glucose and fatty acids is more intense during the first two hours of nocturnal sleep.

**Balance in blood: Thermodynamics**

Mammals have intake and expenditure as high as ten times those of reptiles to maintain constant body temperature against a variable climate and
lower environmental temperature than skin temperature [47]. When animals run, the rate between mammals and reptiles decreases to about 7 times. Before feeding, Burma python shows this difference from a mammal. After ingestion of a lamb, the reptile increases its energy emission almost to the level of mammals, and returns to the pre-meal value after about a month without food [54]. BG was a measure of energy availability in blood in past investigations [5, 6]. In infants, we recently showed that BG was positively correlated to resting metabolic rate (RMR), and both showed a difference of \( \pm 15\% \) between scheduled meals and demanded meals (IHMP, in infants initial demand meal pattern) [7]. The difference between reptiles and mammals shows us that energy expenditure in mammals is mainly devoted to maintain body temperature at 37\( ^{\circ} \)C against a variable gradient. The human body loses four times energy at 8 \( ^{\circ} \)C compared to 27 \( ^{\circ} \)C [47]. Insulin resistance and emission of body energy ceases at 30 \( ^{\circ} \)C, at humidity saturation [56 - 58]. In opposite circumstances, immersion in cold water increases thermo-dispersion 25 times compared to the same gradient in air [59]. Thermo-dispersion in a cold climate increases energy expenditure, energy absorption, intake, and anticipates hunger [52 - 59]. Thus, a cold environment tends to be protective against intestinal microflora growth by increasing absorption and flow rate of nutrients [60 - 62]. Rapid increases and decreases in temperature are more effective than the subsequent maintenance.

Risky moments: warm/humid climate.

We report suggestions for home environment by the Meteo Center in Florence: Relative humidity of 40\%, movement of air between 0.1 e 0.2 m s\(^{-1}\) (= 0.36 – 0.72 km/h), temperature between 19 and 22 \( ^{\circ} \)C. Higher relative humidity is associated with poor ventilation, depresses metabolism in warm environment and increases cold sensations in a cold environment inducing ambient heating. Over 60\%, humidity promotes molds and bacteria growth, as well as risk increase (RID or subclinical inflammation) [56 - 58]. In Florence, monthly means in the year 2009 were between 65\% e 78\%. Separately or in an addictive combination, the warm, humid and stagnant air provokes decrease in energy metabolism and intestinal absorption (Figure 3). We compared absorption in a warm environment (30 \( ^{\circ} \)C) with absorption in cold environment (18 \( ^{\circ} \)C for humans and 6 \( ^{\circ} \)C for animals) [60, 62]. In rats, we found an absorption decrease of xylose of 50\%. We published the following figure 3 and related data in Italian [62]. The figure 3 adds an important finding: a decrease in intestinal absorption is progressive by increasing environmental temperatures and absorption decrease accelerates beyond 28 \( ^{\circ} \)C [62].
Figure 3. Negative, significant correlation between environmental temperature and xylose absorption in man. The article reporting this figure included subjects and data that we reported in the paper on man in I.R.C.S. 1975 and data from 5 additional adults [60 - 62]. The 5 subjects performed the experiment at 33 °C at the high environmental temperature and at 18 °C at the low one. The whole protocol followed the report on I.R.C.S. 1976 [61]. (By courtesy of the Authors: Ciampolini et al., 1977 [62]).

Each thermic factor (insulation, ventilation, irradiation and humidity) is able separately or additively to increase insulin resistance. Indulging for years in insulation and abstinence from physical activity gives raise to low energy expenditure in the meantime. Sedentary life is risky currently and by reducing lean body mass, a permanently poor outlook. Dressing increases the thickness of insulating air and convection decreases the thickness. Large rooms and high ceilings have more air movement than small rooms. Outdoors staying and windy weather are effective by thinning the immobile thickness of air over skin, thus potentiating conduction and evaporation. A ventilated, dry environment may allow better health. Briefly, people (we should better say hours) differ in expenditure for different lifestyles, for amount of walking
and outdoor hours, for dressing, habituation to indoor air movement (either open or closed window), home exposition to either sun or wind, living in either a coastal oceanic or continental climate, and either in mountain or at the sea level. Differences in lifestyle may allow over ten times inter-individual differences in daily intake, and are much more effective on expenditure than inborn factors.

An environmental temperature higher than 18°C – 19 °C, a humidity higher than 60%, a ventilation lower than 0.36 km/h, or excessive dressing suggest a decrease in intake. An acute climate change toward high heat and humidity is risky. The abrupt decrease in metabolic expenditure might slow nutrient absorption and provoke long permanence of nutrients in the small intestine and consequently provoke immune stimulation. Reducing intake to compensate environmental insulation and maintain rapid digestion is advisable. At meals, we suggest to plan intake on predictable expenditure before subsequent arousal of Initial Hunger: two apples for dinner before a night in overheated hospital as opposed to one thousand calories before swimming in cold water.

**Risky moments: Experimental acute infection**

A useful experiment shows the negative effect of maintaining usual intake during illness [63]. A number of mice received 50% of a lethal dose of bacteria. Part of the mice consumed poor amounts and lost weight. These survived. The others maintained their weight and died [63]. During infections, negative -body balance is associated with meal by meal BG positive balance in blood for large provision of fatty acids from deposits, and this paradoxical association is useful for recovery. During fever, blood requires Na, Cl, K and water: vegetal broth, i.e. filtered water of cooked carrots, celery and a spoon of rice. Abstinence from food for two days is easy and without untoward consequences. The patient may not ask for food: complete abstinence from food may be fruitful even for a few days until BG remains over 80 mg/dL and systolic pressure over 85 mm Hg. These points are the feedback references during starvation, which suggest administration of energy or higher energy amounts. We suggest this procedure or a modest decrease in intake in association with rigorous attention to IH arousal also in local inflammation, like torticollis, knee or lumbar ache, headache, abdominal pain, which we consider as a local expression of subclinical inflammatory state. During acute respiratory illness, we encourage rest and endurance of excess warming from the early hours of infection, when the patient may only perceive a little reddening of eyes and modest nose inflammation, before the development of local pain, cough, and general
Reversible immune deficiency

symptoms like weakness. Immune defenses depend on blood supply and thermoregulation move blood supply from a body region to another. Occasionally, we observed recovery from cold by intense physical activity like two hours running.

**Risky moments: Acute inflammation**

Animal experiments suggest that anorexia, by reducing energy intake, has a significant protective role in the host [63]. On the other hand, maintaining or replenishing body protein is extremely difficult during inflammatory catabolism. This is illustrated in a study by Streat and associates of eight patients with sepsis in an intensive care unit who received an average of 2716 kcal per day and 22.6 g of amino acid—derived nitrogen per day (141 g of amino acids) intravenously [64]. The body composition was determined before and 10 days after the nutritional program had begun. Despite what was presumed to be an adequate diet, the patients lost an average of 6.2 kg in body weight over a period of 10 days together with a 6.8-kg loss of body water. Body fat increased 2.2 kg, but 1.5 kg of body protein was lost — 12.5 percent of the body cell mass. Our Unit faced this nutritional dilemma of either losing body cells or increasing insulin resistance by treating 53 infants, five months old, with acute diarrhea, arm skinfold thickness of about 7 mm, about the 15th percentile of normal distribution. Our aim was maintaining an empty and active small intestine by exclusion of any period of time with a positive energy balance in blood [65]. We accepted a loss of 3 or 4 mm of thickness to have a prompt recovery. We used TPN in these infants in the hope of maintaining empty the small intestine [65]. We measured energy intake and body weight.

**Risky moments: Severe illness**

Energy administration may be more effectively regulated on BG. We consider BG as a measure of instant provision of energy to body cells [1]. The New England Journal Medicine recently updated attempts of tight glycemic control in Intensive Care Units. The incidence of hyperglycemia (BG > 126 mg/dL) after cardiac surgery in infants and young children is uniformly high, reaching more than 90% in some series [66]. A Belgian study of 2001 [67] reported a decrease in mortality from 8.0% to 4.6% by intensive insulin therapy (maintenance of blood glucose at a level between 80 and 110 mg per deciliter) on adults in comparison with conventional treatment (infusion of insulin only if the blood glucose level exceeded 215 mg per deciliter and maintenance of glucose at a level between 180 and 200 mg per deciliter).
Recently The NICE SUGAR study involved over 6000 critically ill adults [68]. Intensive glucose control led to moderate (blood glucose, 41 to 70 mg per deciliter i.e., 2.3 to 3.9 mmol per liter) and severe hypoglycemia and ≤40 mg per deciliter i.e., 2.2 mmol per liter, both of which are associated with an increased risk of death. The time-weighted BG was 115 ± 18 mg/dL in the intensive control group (3013 patients), and the absolute increase in the risk of death at 90 days was 2.6% as compared with the conventional-control group (144 ± 23 mg/dL). The association exhibits a dose–response relationship and is stronger for death from vasodilated shock. However, these data cannot prove a causal relationship. Agus studied 980 children 0 – 36 months of age, undergoing surgery for cardiopulmonary bypass [69]. He administered insulin targeting a BG of 80 to 110 mg/dL. Only 3% of the patients assigned to tight glycemic control had severe hypoglycemia (BG < 40 mg/dL), but the tight control did not significantly change the infection rate, mortality, length of stay, or signs of organ failure in comparison with standard therapy (variable). Further AA used a BG target that was similar to the BG associated with Initial Hunger (IH): 70 – 100 mg/dL, but had numerous events of hypoglycemia [70].

We studied 53 infants (mean age 5 months) with persistent diarrhea, and treated them by total parenteral nutrition for 12 days in 1976 [65]. We had fully developed the nutritional project that we displayed subsequently in later papers and books [1 - 6]. We administered 42.5 kcal/kg/d of energy as glucose 10% (50 ml), hydrolyzed casein (Amigen, 50 ml) and 20 ml of Ringer Lactate. This i.v. administration of 42.5 kcal/kg/d can be compared with the oral requirement of 70 kcal/kg/d suggested by Butte [71], with 70.3 ± 15.8 kcal/kg/d intake during IHMP at the age of two, and with a RMR during IHMP of 49.0±9.1 kcal/kg/d at the age of two. Butte reports 10% lower measures for RMR and intake in the second three months of life than at the age of two years. Thus, 42.5 kcal/kg/d approximately covered the RMR of the 5 month infants if the physicians had the intake aims of IHMP (hunger recognition).

Consistently, the infants maintained the mean body weight of recruitment during the 12 days of exclusive TPN (Figure 4). A decrease of 10% body weight was seen after addition of oral food (20 kcal/kg/d). Two infants out of 53 died after the controversial addition of this oral food amount to TPN; substitution would have been better. The results in weight and outcome of exclusive TPN in diarrheic infants was much better than the NICE study. Of course, the studied population was different. This is the same conclusion of the related editorial [66]. The difference in population may not consist in the gravity of the illness. The diarrheic infants who appeared better had an addictive food *per os* that was unfortunately fatal in two. We regulated energy
Figure 4. Body weight (kg) during total parenteral nutrition by 42.5 kcal/kg body weight/day in 53 five month old infants with persistent diarrhea. Upper line: body weight of infants exclusively fed by TPN. Lower line: body weight of infants who had additional oral food [65]. Number of subjects examined each day, reported on the top. (By courtesy of the Authors: Bartolozzi, Ciampolini et al., 1977 [65]).

administration by the TPN infusion that was constantly near or a little less than the presumed RMR for the same subjects in health. Because of the night suspension, we may guess a morning BG of 76.5 ± 3.9 mg/dL or a little more for continuing inflammation persistence.

TPN is carried out in complex and different conditions that may require different procedures. We wonder why this use of insulin. During inflammatory condition, cells are replenished by fatty acids and glucose, their membranes refuse inside transport of blood glucose that is abundant inside
cells. On the reports mentioned above, high energy intake seems useless because it does not spare body protein depletion. On the contrary, maintenance of usual intake proved to increase mortality in experimental animals [63]. We did not use insulin that is an uneasy additional variable in the context. There is not any advantage by the increase of 10 or 20% of the energy availability inside the cells when it is already high. High availability provokes inefficient intestinal activity. This is untoward in some subjects who have already a high number of bacteria on the intestinal mucosa. Our reasoning is that the main difference between our subjects and other investigations on TPN consists of the background illness. We investigated diarrheic infants and they were quite sensitive to the energy administration amount. The oral addition of 20 kcal/day to the infusion brought administration to 62.5 kcal/kg/d, and this amount is higher than RMR during IHMP that is lower than 49 kcal/kg/d at 5 months of age. We have repeatedly shown that IHMP is effective (necessary?) to rapidly overcome a diarrheic condition [1 - 6]. We clearly considered that diarrhea produces a condition of intense conflict between intestinal bacteria and immune cells in mucosa, even when it was forwarded by a viral infection. The first objective was to escape from RID and recuperate normal immune stimulation on intestinal mucosa that also meant normally functioning and absorbing. Infants and adults reported by NEJM had no such necessity.

We suspect that other variables may be important during TPN and the NICE investigation suggests that patients are different from one another. Some patients may have higher RMR and may have low bacteria number in small intestine than those in the investigation performed by us. Avoidance of the insulin variable would simplify the treatment and avoid hypoglycemia events. Capillary BG might be measured every three hours to increase glucose administration when BG decreases below 90 mg/dL. The administered amount might be adjusted accordingly during the night. During IHMP, meals are taken at 76.5 mg/dL. During inflammatory illness, BG requires a higher maintenance, over 80 – 90mg/dL, between 80 and 110 [29]. A BG of 80mg/dL, a blood pressure of 80/40 and sensations of hunger suggest administration or administration increase of energy. These guidelines are similar to those of van den Berghe on adults and Agus on children and also the NICE SUGAR study [66 - 70]. All three however used insulin administration, the first with positive results and the third with negative results. Recruitment of thousands of patients may be associated with heterogeneity and detailed overlooking. Patients with diarrheal diseases are sensitive to hypoglycemia. We had good results in our series when TPN was exclusive, but we did not use insulin. A continuous efflux of serum solutes is maintained in health and during diarrhea may be deranged. These patients may require periodical lowering glucose concentration, and transient,
complete emptying of intestine. We obtained these conditions by night suspension of TPN. Critically ill patients for many other diseases may not require such BG decreases, or may better tolerate constant high BG.

**Risky moments: Chronic inflammation, insulin resistance and malnutrition**

On the other hand, infection may persist for months and suspension or reduction of meals may become unsustainable. The physician may break this vicious circle by specific therapy. Chronic infections are frequent in old people. Elderly people have little pain in the throat, modest cough and little complaints like fatigue, and do not stop usual activity to rapidly recover from a flu-like illness. Sometimes, conditions become worse after weeks. The supervened infection worsens a subclinical inflammatory state that already pre-existed at lower intensity before infection. If intake and activity have not been promptly reduced [29], the inflammatory state worsens further. People lose weight, especially fat-free mass, bone and muscle. Experimentally, feverish subjects received IV 2000 kcal/day. After a week, skin-fold thickness showed a significant increase without avoiding loss of muscle and bone mass in comparison to control subjects who received a saline solution [64]. A tuberculosis patient represents a typical person who is affected by malnutrition, even by eating as much as possible. Unfortunately, increase in fat tissues is associated with gradual development of insulin resistance that increases risks (Reversible Immune Deficiency, subclinical inflammation or pro-inflammatory state). The infection does not subside. This patient needs first immune improvement and only after this immune improvement, the patient needs weight recovery. During summer, spending some time in the mountains and long walks have been useful. Outdoor moderate physical exercise is essential. An accurate adaptation of intake to variable expenditure is the solution (with antibiotics).

Because of these infective and inflammatory mechanisms, about one billion people are currently affected by malnutrition in present world because of malaria, parasites, chronic hepatitis, tuberculosis, AIDS, celiac disease, urinary diseases, respiratory obstructive diseases. Thus, malnutrition usually requires treatment of these illnesses, which is much more difficult than food provision.

**Risky moments: Old age**

Metabolism declines in old age: IV. infusion of triolein and measurement of breath carbon dioxide for 8 hours showed oxidation decline by 23%
between 17 and 65 years, and 25% between 65 and 87 years [72]. The decline may depend on decrease of oxidative metabolism in all tissues. Uncoupling proteins 1, 2 and 3 decrease in mitochondria, in association with decrease of energy destination to dissipation [73]. The production of ATP and of energy for cell functions have no change. Elderly people reverse their own metabolism toward that one of reptiles, and feel cold at higher temperatures than young people do, due to decrease in production of metabolic energy. At the same time elderly people need to lower energy intake, but may have no information or do not notice the metabolic change. No adaptation of intake to lower expenditure means developing diabetes. We can contrast metabolic regression by physical activity. Heavy physical activity for half an hour every day increases about 250 grams lean body mass per year. Muscles, bones, arterial diameter, capillary network increase at the same time. These improvements may fail after the age of 80 [74]. These observations imply that country people in Tuscany who worked on land without motor utensils, gained over 10 kg lean body mass over the amount that may be gained by an informatics worker who worked indoor all lifelong. Long endurance of physical activity in outdoor, ventilated, cool environment promotes meal by meal achievement of null energy balance in blood. Regular achievement of null balance contrasts development of autoimmune markers, a basic mechanism of aging through RID [75].

Risky moments: Menstrual cycle

At the end of the menstrual cycle women may frequently reach a pathological functional disorder (dysmenorrhea). Non recognition of the changing hormonal condition and no adaptation in intake produce a transient diffuse inflammation. In women, energy expenditure has a minimum on the 7th day after the onset of last menses [76 - 79]. On the 14th day, progesterone increases, and so does energy expenditure and energy intake. The difficult days recur toward the end of the cycle. Women confusedly perceive initial hunger. BG and insulin resistance increases by 15% of the value at cycle onset [76 - 79].

Risky moments: Stressful states

Acute stress is unexpected, external and almost instantaneous, and is elaborated with different, subjective intensity toward depression or anger. The stress state elevates adrenalin, cortisol and BG for a few hours or longer, and during this time the stressed subject presents anorexia or increased eating, although gastric motility always decreases [80]. The stressful
Reversible immune deficiency

Condition implies polarized attention to the anxiety factor and automatic responses to problems that do not depend on the stressing factor. It implies no perception of personal dynamic balance and of high BG at mealtimes, implies no recognition of personal sensations. In this psychological sequence consists the *primus movens* of a vicious circle. Stressed people may eat as usually, and even more. Automatic eating means weight increase in subjects capable of fattening [81], and rapid development of insulin resistance and of associated diseases in people genetically or epigenetically incapable of further weight increase [82]. The balance in blood becomes positive and this condition produces feedback consequences. Automatic eating implies slow absorption, pro-inflammatory state, RID, vascular disease and infarction, schizophrenic or depressive recurrences and relapses of intestinal disorders. We interpret psychosomatic illnesses as a consequence of eating in a stressed state.

After Selye’s findings in the sixties, functional disorders have been considered and treated more and more year after year as psychosomatic. There is no doubt about the association between stressful events and intestinal and circulation events [82, 83]. This point of view is incomplete. The psychological stress elevates BG for hours or days, and meals become unsafe until BG decreases toward 76.5 mg/dL. The stressful condition may often last only hours. Being conscious allows to stop eating and rapid overcoming the difficult moment. On the contrary, a person may have no stop or even have abundant intake. The energy balance becomes positive in blood. During stressful states, any food is addictive to energy in blood that is largely provided by fatty acid influx from fatty stores. Muscles may contribute both by increased activity and by decreased activity. The stressful condition does not differ from that of experimental studies on intestinal absorption of xylose at high environmental temperature in animals and humans [53 - 62]. In stressful and feverish states, energy balance in blood may be positive when body energy balance and body weight are negative [29], although the two balances are highly correlated in the long period [1 - 3]. High energy availability to body cells is well known as insulin resistance and alimentary diabetes, and is associated with increased immune stimulation and RID throughout all the body. Any intake in stressful condition may be abundant for high BG and no IH at meal onset, and the condition of abundance slows absorption, increases availability of nutrients to intestinal bacteria, let microflora overgrow. One or two species of immunogenic bacteria may rapidly grow. The overgrowth produces high immune stimulation to intestinal mucosa and from here through blood to all body [85]. Ineffective inflammatory processes develop everywhere in the body: subclinical inflammation, a face of RID. A common example may be an infant with
fever. He may even eat abundantly but fever goes up. The sequence is demonstrated in our recent book: “Meal by meal dynamic energy balance in blood” [1].

Man has currently an excessively intense emotional life, hence a wide evidence about the association between these states and altered activity of nervous endings plus the increase in corticotrophin releasing factor (CRF) and derangement of mucosal permeability. Here is the core of our research: the association is not *primum movens*. Modern man is not a victim of his furious activity. Man is a victim of nutritional abundance, a blessed achievement *per se*. Large scientific consensus consider insulin resistance as the measure of a personal harmful abundance in eating and in nutrient provision to body [12 - 27]. Similar consensus considers overweight as harmful [49]. At stressful moments, CRF and nervous endings only multiply and magnify intake errors and risks in an environment of nutritional abundance [82 - 84]. Man needs to get aware of this dilemma and either fight stress or positive energy balance. Findings here collected point out that eating may be safely stopped for up to 48 hours recovering insulin sensitivity and Initial Hunger! A stressful event is innocuous if insulin sensitivity is recovered as soon as possible.

**Risky moments: A big meal and failure of exhausting previous meal**

In experimental animals, a test meal by gastric probes has been investigated for an hour in a comparison between starved rats for three hours and fed rats. At the end of the experiment, i.e. after one hour from administration, starved rats had almost completed absorption, whereas fed rats still presented half meal in small intestine [86]. In human experiments, emptying of jejunum coincides with perception of hunger [42 - 46]. The reality is that food choices are often automatic and made without full conscious awareness [87]. When the meal is too big, Initial Hunger arousal is delayed, and sufficient time has to elapse before another meal.

Health depends for two thirds on decrease of immune conflicts in small intestine. We have this abatement by rapid absorption, low bacterial growth on mucosa, null or modest immune stimulation in mucosa and finally poor systemic immune stimulation and reversion of RID. Absorption rapidity depends on high degree of exhaustion of previous meal, on adequate meal energy intake and low insulin resistance that means low recent fat accumulation. The meal onset that we propose is a metabolic time, checked by BG decrease that is associated with many physiological changes, for
example, emptying of small intestine, start of peristaltic waves in duodenum, decrease of insulin in blood….and hunger. We showed that initial hunger although being subjective, was identifiable by BG and reliable as a sign for meal onset and for maintaining null energy balance. Would I have been informed earlier [88]!

**Deceiving BG measurements**

In hospital, the laboratory measured BG just after patients’ BG estimation. The estimation error was the difference between estimation and measurement. During training, we observed an increase in this estimation error during 30 – 90 minutes after physical exercise, after food tasting, after intake of one – two grams of food, after indoor entry, after stop in ventilation in a closed ambient, after increase in wearing or after a stressful event, or during a feverish or not feverish infection. The listed events elevate BG from about one hour, two hours or few days, but subjects in training fail the elevation at estimation. Subjects must omit BG measurement in all these circumstances and busy people must postpone training. A significant increase in error was unfortunately permanent despite of any training after 60 years of age in comparison with younger ages (unpublished findings).

**Conclusion**

Current limits on body weight or energy intake are arbitrary. We may instead learn and validate the recognition of subjective, instinctive sensations of hunger (IH) to signal meal start. We may learn the approximate calculation of variable (starting with 300? kcal in adults) need for happy activity in inter-meal interval, and learn the self-imposition of meal stop when intake covers the calculated amount. This Initial Hunger Meal Pattern produced Low Blood Glucose (LBG) before meals, prevented covered fattening below IBM of 25 (insulin resistance) and overt fattening beyond 25, prevented the associated Reversible Immune Deficiency (pro-inflammatory state and subclinical inflammation are synonymous) and even prevented negative energy balance within the day and over years. Part of population (20% - 40%) maintains LBG before every meal, suggesting an easy acquisition of the described, long lasting skills.

Many governments are deeply indebted and in shortage of money in these days. USA, UE and also UK need to decrease expenses for National Assistance Insurances. My Country is deeply indebted. Present report is proposing: Fighting Reversible Immune Deficiency instead of fighting each consequent illness. A recent book has emphasized the powerful role of habit
changes [89]. Diffuse consciousness in population on personal energy balance by "Hunger Recognition" instead of single delivery of treatment for every single illness. The school (middle - high school) ought to work on this goal for all people, and physicians should transform their working from less medicine delivery to counseling and coaching IHMP. National Assistance Organizations can contrast reversible immune deficiency and “hidden and overt fattening” by creation of a market. Insurance companies may discount the payment to those who have low HbA1c and CRP. In other Organizations, a higher income may be given to physicians for every patient with low HbA1c and CRP.

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