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Editorial

Accountability and the Decision to Publish New Findings

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In my first insights, the hot hospital environment was harmful for diarrheic infants. I showed the possibility of slowdowns in nutrient absorption/progression in correlation with metabolic slowdowns and high BG [1-3]. For these demonstrations, I studied xylose absorption in animals and humans in a hot environment in comparison with a cold environment.

Further studies explained the damage mechanism: intestinal slowdown in progression/absorption implied long nutrient permanence in the intestine. Every meal raises a conflictual process between the absorption of energy rich nutrients (Nutrition) and the nutrient exploitation by bacterial growth (decomposition). This competition is similar to that in the outside world: food requires accurate storage and has to be consumed before decomposition. Bacteria double every 10 - 20 minutes in the warm, humid, oxygen poor intestinal environment. The growth of bacteria on intestinal mucosa elicits an immune response and the ensuing inflammation eliminates the immune stimulants with damages to the host's tissues [4,5]. Suppression of any decomposition inside the alimentary canal would much advantage diarrheic infants. Here, we had an important achievement. Mothers and adults in general can learn and recognize hunger sensations after adequate teaching and training [6] and an Initial Hunger Meal Pattern can be constructed (IHMP = Three IH arousals per day). The three arousals were giving a precise, subjective indication for daily energy intake as well as for adaptations to expenditure. The precise indication on limits and the experiencing small delays eliminated any anxiety about becoming weak and fading for hypoglycemia hours before the next mealtime. Although this view changed the way to treat patients like the Semmelweiss's views on sterility changed surgical interventions, I encountered only opposition at any report. The application of these views in hospital required scientific support by published demonstrations. At last, a friend (!) published my first international paper on Initial Hunger" (IH) [7]. At this point science revealed its obscure site. Scientific Journals have different readership volumes and this means different power (impact factor). The truth of a notice depends on the Journal. This means that Science is directed by the principle of Authority. The criticisms persisted much the same: We do not understand, the paper requires the editing by an English professor of Medicine. The paper edited by Professor Garza (Cornell University) was at last published [8,9]. I directed a third level Gastroenterology Unit in a Pediatric Hospital and brought to conclusions my early insights: The appearance in Scientific Journals of insulin resistance and of the associated overall sterile inflammation allowed an extension of intestinal prevention to the prevention of all body risks [10-13]. The mucosal tolerance by Brandtzaeg explained the vascular and tissue damages in all body in absence of intestinal involvement [14]. In the subsequent 15 years, my huge accumulation of lab data allowed the elaboration of findings and concepts that I never had imagined in the previous decades.

IHMP decreased energy intake, mean preprandial BG, HbA1c, body weight, insulin resistance, functional disorders and fecal energy loss. In all studies, we found a consistent minority (30%) that already at recruitment showed low BG and did not respond with decreases during IHMP [15-18]. The sequence of 21 preprandial BG measurements in a week (Mean BG) was stable through months and characterized the safety (health) degree of individual meal pattern. Low preprandial Mean BG (76.6 ± 3.7 mg/dL) was associated to an even energy balance in blood (insulin sensitivity) as well as in the body (BMI). Mean BG assessed the degree of an individual meal pattern in a scale of human risks from a null extreme by an even balance (homeostasis, insulin sensitivity) up to an overall sterile inflammation, and full development of vascular and many malignant diseases at the other extreme [19]. Broadly speaking, meals during high BG (and high RMR)

elicit negative feedbacks. First of all, a depression of nutrient progression and absorption [1-3, 20,21], bacterial growth on mucosa, no hunger sensations and functional disorders. The consistency of the findings and their initial reproductions by independent AA [22,23] may abate any doubt about Truth.

Differences between Conditioned Hunger and Hunger after Meal Suspension. Assessment of the Individual Error in BG Estimation.

The training consisted in BG measurements at hunger arousal, lasted two weeks, and one month later 64 trained and 72 control, untrained subjects attended the hospital lab before breakfast after an overnight fasting [17,18,24]. All subjects declared current presence or absence of hunger, and estimated BG (Figure 1). A glucose auto analyzer measured actual BG. All hungry subjects described hunger sensations as gastric emptiness or gastric pangs. In the hungry trained group, the mean estimated BG was 78.1 ± 6.7 and the mean measured value was 80.1 ± 6.3 mg/dL. This measured BG was significantly lower than the measurements in hungry control subjects (89.2 ± 10.2 mg/dL) and in not-hungry subjects of both trained (90.0 ± 6.6 mg/dL) and control (90.6 ± 10.9 mg/dL) groups. The absolute value of the difference between

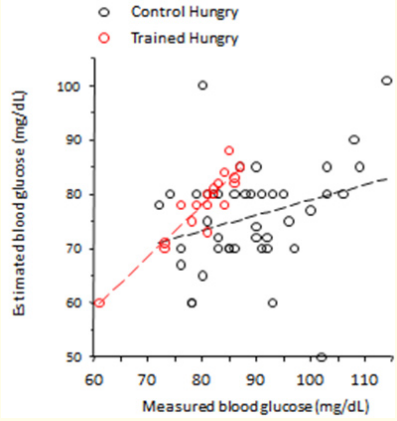

Figure 1: *Subjects reporting hunger at the laboratory final investigative session. 42 untrained controls (black circles, r = 0.29, NS) vs. 18 trained subjects (red circles), r = 0.93, P = 0.0001). Copyright © 2006, Dove Medical Press Ltd. Image courtesy of Ciampolini M., et al. [25].*

Estimated and measured glucose (estimation error) in the hungry trained group (3.2% ± 2.4% of the measured value) was significantly lower than the one in the hungry control group (16.7% ± 11.0%). These findings prove that control (untrained) subjects do not reflect their biochemical condition when stating to be hungry and estimating BG. Trained subjects instead, show a low BG condition when hungry and estimate accurately their current energy availability. In the hospital lab, at the question on hunger, control, untrained subjects focused on food and developed gastro duodenal Pavlovian reflexes that are weaker and shorter than the sensations after eating suspension. The main difference is at the sensation onset: either before focusing on food (after meal suspension) or after focusing on food (conditioned). Low BG confirmed the distinction much more often than expected. We repeated an uncontrolled study in children younger than three years of age. In the hospital laboratory the auto analyzer measured BG in 16 toddlers not demanding food before breakfast in comparison with 54 toddlers who were demanding food, all after training with 42 measurements at hunger arousal [16]. No demand was associated with a significantly higher BG than the condition of food demand (96.3 ± 10.5 mg/dL versus 74.6 ± 7.7 mg/dL; P = 0.0001). Based on these studies, the initial demand (ID or IH) was conceived as a threshold phenomenon triggered by low energy availability in blood, indicated by low BG; normal activity is not inhibited by low energy. The intervention may be conceived as an abrupt weaning of the mother and child from the automatic, scheduled feeding to implement a habitual evaluation of time and amount of meal.

Validity of a Portable Device for BG Measurements

The training was accomplished by home BG preprandial measurements, with a portable device (a portable potentiometer for whole BG measurement with the hexokinase method: Glucocard Memory; Menarini Diagnostics; Florence, Italy). The subject had to personally measure BG with the portable instrument against the auto analyzer in the lab as he/she did at home. At blood sampling, we supervised the performance of the comparison. The auto analyzer was checked every morning in comparison with the other 50 laboratories in Tuscany. A difference in BG from the mean had to remain within 1% every day. The heparinized blood sample for the auto analyzer was immediately centrifuged and measured with the hexokinase method. In the meantime, the patient performed his/her measurements on the same blood sample by glucometer. The auto analyzer obtained a mean ± SD of 89.9 ± 11.3 mg/dL (N = 85). Subjects measured 89.0 ± 12.5 mg/dL. The mean difference (0.9 ± 7.1) was not significant. On absolute values, the mean difference was: 5.7 ± 4.3 mg/dL with no bias. This error is within the spontaneous BG wavering of 10% every 12 minutes and is too low (6.0%) to confound results.

The Resting Metabolic Rate and the Total Daily Energy Expenditure at recruitment and during IHMP

In 24 infants, we measured their Resting Metabolic Rate by indirect Calorimetry and the Total Energy Expenditure by doubly labeled water. Energy intake decreased from 85.7 ± 15.3 to 70.3 ± 15.8 kcal/kg/d ($P < 0.001$). TEE decreased from 80.1 ± 6.9 to 67.8 ± 10.0 kcal/kg/d ($P < 0.001$). These figures confirmed a 15, 5% decrease of both expenditures under IHMP in comparison with values at recruitment. These findings validated the energy intake reports by diary. The passage from insulin resistance at recruitment to insulin sensitivity during IHMP is associated with a significant decrease in RMR and in total daily expenditure. Referees surfing my manuscripts often missed these figures.

IHMP for malnourished infants

We studied IHMP in 9 malnourished infants [26]. Six subjects under intervention and three controls were followed for 2 years. Energy intake decreased from 126 ± 21 kcal/kg/d to 85 ± 6 kcal/ kg/d in treated infants and from 111 ± 53 kcal/kg/d to 107 ± 37 kcal/kg/d in controls during the first 2 months of study ($P < 0.01$ on longitudinal differences). Days with vomiting became null after 2 months of treatment, whereas in control subjects, 4 or 5 events every 60 days persisted for all follow-ups. The difference in the Chi square for trend was significant on energy intake and in the numbers of days with vomiting or diarrhea ($P<0.002$). Further longitudinal differences were significant on days with diarrhea after three months, and on plasma triglycerides at the two sampled times during treatment. Serum triglycerides decreased from 148 ± 27 mg/dL to 70 ± 10 mg/dL under intervention, and increased from 119 ± 47mg/dL to 139 ± 59mg/dL in controls ($P<0.002$ on the longitudinal difference). Values after two years of follow-ups were respectively: 73.2 ± 12.3 mg/dL and 89 ± 37 mg/dL ($P<0.05$). Toward the end of the study, anthropometric measurements increased per age from recruitment in treated infants with differences from control subjects that were not significant in the longitudinal comparisons between groups. Weight per age reached 88.8 ± 8.7% under intervention, and 79.7 ± 10.2% in control subjects. We reported these findings to explain the expectation for IHMP that not solely concerns weight loss. The population requires to know the harmful mechanisms involved in the acquisition of energy availability and to know their consequences. People may then either use the physiological knowledge to prevent disorders and diseases or refuse them as immediately useless [27]. The direction of the American Society for Nutrition has unfortunately surfed my findings taking into consideration only BG measurements and home diaries. The construction of Nutrition and Immune damages by the rotten Meal is founded on doubly labeled water that was measured outside my Institute, on indirect calorimetry, on many blood measurements by auto analyzer including GTTs, on microbiology, on body weight. Big information canals give power in Medicine and the powerful information has become harmful. Science is damaged by any power not only by money conflicts. General consensus does not coincide with catching the truth. There will always be mass errors that are induced by wishful thinking and are powerfully reinforced and enlarged by commercial success, even though we cannot speak of true conflicts of interests. Merchants rely on consensus but humans and scientists absolutely cannot. Then, how can humans distinguish true from false reports? How can the referee rely on a report on new findings, outside the referee's experience? Going beyond experience, Science might be better based on the rationality of inserting the novel findings in a past logical construction. By reading reports and reports (also as a referee) and observing patients and eventual developments, we can add thousands and thousands of small facts and observations in a logical construction. The construction implies uniting together visive imagines by their coincident portions, like in a construction of the mental map of a unknown city. The resulting movie of events

may perfectly predict the subsequent events around the corner. Objectivity and verifications (accountability) seem as a prerequisite for democracy, for a benevolent attitude toward other humans, and Science is part of Democracy. Authority in Medical Sciences is currently harmful, at least unable to solve Fattening/insulin resistance and associated illnesses [28]. Ignoring Initial Hunger may contribute to the increase in children asthma, autism, congenital malformations, dyslexia, attention deficit, hyperactivity, schizophrenia, obesity and diabetes [29]. A new formulation of the National Children's Study (NCS, US) should both highlight the current ignorance between a subjective sensation of hunger and current BG and plan a new awareness of the relationship between hunger sensation and meals. ASN authorities are the gate keepers for scientific journals with high impact factor. They dictate common wisdom and general consensus around conservative, fattening choices, and their power ought to be limited. The Florentine "priori" remained in charge two months at the initial explosion of a successful capitalism [30].

The hardness of the scientific conflict suggests similar difficulties in IHMP implementation. In the first days of life, scheduled and demanded meals are equivalent, and either choice is dictated by familial and medical customs, current local fashion, convenience, and also by a null hypothesis on their difference of effects that was shown to be wrong [18]. Given the fact that part of the population maintains low preprandial blood glucose by free choice, given the demonstrated maintenance of demanded meals up to 12 years of age [5,27], given the equivalence of early instructions for new mothers, given the habitual, persistent nature of Mean blood glucose due to associated organic changes, and emphasizing better health in children and adults who maintain preprandial low blood glucose [18], a change in instructions on rearing seems obvious and mandatory from the neonatal days. Implementation in adults has the difficulties of beginning a new play: within three to four days, many subjects understand the difference between hunger that arises after meal suspension (IH) and conditioned hunger. At hunger arousal, the surprise for guessing BG may take a similar interval of exercising with the portable instrument.

We taught how to recognize the correspondence between the subjective sensation of hunger (trend with hunger at meals, IHMP) and the BG. The aim was both to obtain, meal by meal, a low pre-prandial BG concentration that means an even balance of energy in blood (homeostasis) and to curb fattening/insulin resistance. The optimal energy intake corresponded to a low BG level before meals that turned out to be the same in several studies carried out on different subjects (about 76.6 ± 3.7 mg/dL in sedentary people) [17-19]. Such level can be easily maintained after a two-week training of BG measurements at arousal of Initial Hunger. Developing such awareness is within the population's reach. At recruitment a remarkable minority of (untrained) children [18] showed pre-prandial BG concentrations alike those of children whose mothers had been trained not to offer food. Studies in adults confirmed the coincidence [17].

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Volume 3 Issue 4 February 2016