Review

Chronic Positive Mass Balance is the Actual Etiology of Obesity: Time for A Paradigm Shift?

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Abstract

According to known laws of physics, chronic positive mass balance is the actual etiology of obesity, not positive energy balance. The relevant physical law in terms of body mass regulation is the Law of Conservation of Mass, not the Law of Conservation of Energy. A recently proposed mass balance model (MBM) describes the temporal evolution of body weight and body composition under a wide variety of feeding experiments, and it seems to provide a highly accurate description of the very best human experimental feeding data. By shifting to a mass balance paradigm of obesity, a deeper understanding of this disease may follow in the near future. The purpose of this article is to present the core issues of the upcoming paradigm shift as well as some practical applications related to the topic.

Keywords: macronutrients; body weight regulation; energy balance theory; mass balance model

Introduction

"*People are able to break any laws made by humans, but none made by physics*." – Elon Musk

Recently, Arencibia-Albite published an exceptionally clever article entitled "The energy balance theory is an inconsistent paradigm" in the *Journal of Theoretical Biology* [1]. My own article deals with exactly the same topic, but focuses on *practical applications*. So, the purpose is to explain in plain language what this large-scale paradigm shift will

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mean on a practical level. Therefore, in this article you will not find complex equations and formulas; rather, I have tried to summarize the core issues in such a way that every university-educated healthcare professional can reasonably understand them.

The energy balance theory is a flawed paradigm

It is widely assumed that the fundamental cause of obesity is an energy imbalance between calories consumed and calories expended (i.e., the energy balance theory; EBT: ”Calories In, Calories Out”). According to known laws of physics, however, this century-old obesity paradigm must be fallacious. **The relevant physical law in terms of body mass regulation is the Law of Conservation of Mass, not the Law of Conservation of Energy (i.e., the First Law of Thermodynamics).**

This is not a matter of opinion; rather, it is based on *exact* natural sciences. If matter (mass) can be exchanged between system and surroundings, then the system is an *open* one. So, all living organisms are open systems and such systems can be at mass balance while the system experiences a persistent energy imbalance. That is, energy balance may be positive ($\Delta E > 0$) or negative ($\Delta E < 0$) yet the *mass* change that may occur during energy flux is not required by the Law of Conservation of Energy to mirror the energy balance *direction* [1]. In practice, this means that an energy imbalance does not always lead to a change in body mass. It leads to a change in the body's mass only in the situation when one is simultaneously in a mass imbalance. *Body mass decreases in negative mass balance and increases in positive mass balance.*

The Law of Conservation of Mass

The Law of Conservation of Mass states that the mass can neither be created nor destroyed by chemical or physical changes. In other words, *total mass is always conserved*. This law dates from Antoine Lavoisier’s 1789 discovery *par excellence* that **mass is neither created nor destroyed in any chemical reaction** [2]. Clever Frenchman heated mercuric oxide (HgO) and demonstrated that the amount the chemical's mass decreased was equal to the mass of the oxygen gas

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released in the chemical reaction. Lavoisier proved that mass must be conserved in chemical reactions, meaning the total amount of mass on each side of a chemical equation is always the same. That is, **the total number of atoms in the reactants must equal the amount in the products**, regardless of the nature of the chemical change. This forms the basis of *stoichiometry*, i.e., the accounting process by which chemical reactions and equations are mathematically balanced in terms of both mass and number of atoms on each side.

As an example, the oxidation of one generic triglyceride molecule:

$C_{55}H_{104}O + 78O_2 \rightarrow 55CO_2 + 52H_2O$ + HEAT 8,084 kcal

Reactants:		*Products:*	
$C_{55}H_{104}O$	860 g	$55CO_2$	2,420 g
$78O_2$	2,496 g	$52H_2O$	936 g
+		+	
	3,356 g		3,356 g

Note that there is mass only in reactants and products, but not in energy (calories).

The mass-energy equivalence principle

The mass-energy equivalence principle implies that when energy is lost in chemical reactions, the system will also lose a corresponding amount of mass. As far as the regulation of body mass is concerned, however, this equivalence principle has been misunderstood. This **global misconception** requires a detailed clarification.

Here is a very good question from one of my colleagues:

”How is energy intake and expenditure not the governing factors that determines if the body store the food we eat as fat or not? How could one change that? How can the mass of the food change that? If the eventual weight loss is from water, urea, or whatever [it] is still determined by if the body replace it or not, or even store more than was used. **Where is the gap where energy expenditure is not representative of substrate [i.e., mass] being used?**"

In order to see why nutrient mass, not nutritional energy, is the quantity that determines body mass fluctuations one has to unavoidably think in terms of arithmetic and analytical chemistry as shown next. The caloric values of macronutrients are rounded.

Weight gain is the result of mass accumulation, not the result of energy accumulation

Consider two individuals that gain 1 kg of non-water body mass as they accumulate within body cells 1000 g of absorbed macronutrients. The macronutrient distribution of the first subject is as follows:

- 200 g of protein = 200 g x 4 kcal/g = 800 kcal
- 300 g of carbohydrate = 300 g x 4 kcal/g = 1200 kcal
- 500 g of fat = 500 g x 9 kcal/g = 4500 kcal

Thus, the total stored nutritional energy is 800 kcal + 1200 kcal + 4500 kcal = 6500 kcal.

Suppose, next, that the macronutrient distribution of the second subject is as follows:

- 400 g of protein = 400 g x 4 kcal/g =1600 kcal
- 400 g of carbohydrate = 400 g x 4 kcal/g =1600 kcal
- 200 g of fat = 200g x 9 kcal/g =1800 kcal

Thus, the total stored nutritional energy is 1600 kcal + 1600 kcal + 1800 kcal = 5000 kcal.

This example illustrates, therefore, that the property of food related to mass gain is its mass, not energy. The first subject, in effect, has accumulated substantially more nutritional energy than the second one yet both have experienced the same degree of weight gain.

Weight loss is the result of mass elimination, not the result of energy expenditure

Consider the oxidation of 100 g of glucose:

- $C_6H_{12}O_6 + 6O_2 \rightarrow 6H_2O + 6CO_2$ + HEAT (720 kcal/mol of $C_6H_{12}O_6$)

This requires the uptake of 107 g of O_2 as 100 g $C_6H_{12}O_6$ x (192 g O_2/180 g $C_6H_{12}O_6$) ≈ 107 g O_2. The Law of Conservation of Mass implies that mass of the products = mass of the reactants. The amount of water and carbon dioxide formed is 207 g as mass of the products = mass of the reactants = 100 g $C_6H_{12}O_6$ + 107 g O_2 = 207 g.

Now, assume that all the produced water and carbon dioxide are used in the following way:

1. Water becomes intracellular water in newborn cells

2. Hydrolysis reactions (i.e., the cleavage of a chemical bond by adding a water molecule which becomes part of the reaction products): for example, the release of thyroid hormones thyroxine (T4) and triiodothyronine (T3) requires a hydrolysis reaction.

3. Carboxylation reactions (i.e., the addition of carbon dioxide to a molecule): for example, carboxylation of acetyl-CoA during fatty acid synthesis.

Notice that in the aforementioned situation 400 kcal has been expended by oxidizing 100 g of glucose yet body mass will not decrease when heat is dissipated but when the 207 g of reaction products are eliminated which in the described case are not since, as illustrated, oxidation products become part of the body mass.

Energy balance cannot occur at body mass stability

The Law of Conservation of Mass guarantees that body mass stability (i.e., mass balance) can occur ONLY when the mean absorbed mass of each macronutrient equals its respective mean oxidized mass. Otherwise, body mass is increasing (i.e., absorbed mass > oxidized mass) or decreasing (i.e., absorbed mass < oxidized mass).

More specifically, energy balance can occur at body mass stability ONLY if the following three conditions are simultaneously satisfied:

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1. Average absorbed fat mass = average oxidized fat mass

2. Avarage absorbed carbohydrate mass = average oxidized carbohydrate mass

3. Average absorbed protein mass = average oxidized protein mass

Obviously, this can never happen. If, for example, all the absorbed protein mass (amino acids) is oxidized, where would the body get building blocks? Thus, *energy balance is unattainable at body mass stability*. This fact refutes the core idea of the EBT, i.e., that body mass remains constant in energy balance.

The regulation of body mass

By now it should be clear that the regulation of body *mass* is all about detailed *mass* balances ("Mass In, Mass Out"), not about energy conservation ("Calories In, Calories Out"). After all, we are talking about body *mass*. A recently proposed **mass balance model** (**MBM**) describes the temporal evolution of body weight and body composition under a wide variety of feeding experiments, and it seems to provide a highly accurate description of the very best human experimental feeding data [e.g., 1,3,4,5]. For example, we have compared head-to-head the predictions given by the MBM with the EBT-based model of Hall and coworkers, and the MBM seems to be superior to the EBT-based model [3]. And the ranking of such models is determined by their predictive accuracy; this is the reason why such models are developed in the first place. *I would like to emphasize that the MBM not only predicts the change in total body mass but also the change in fat mass*.

The Law of Conservation of Mass guarantees that *1)* the O_2 mass that enters cellular respiration plus *2)* the mass of macronutrients that served as energy fuel absolutely must equal the mass of the excreted oxidation products. *This is not a matter of opinion*. Daily weight loss must, therefore, be the result of daily elimination of oxidation products (CO_2, water, urea, SO_3; "Mass Out"), not a consequence of the heat release upon nutrient combustion (i.e., daily energy expenditure) [6]. And it is macronutrient mass intake ("Mass In") that augments body mass; the absorption of 1 g of glucose, protein

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or fat increases body mass by exactly 1 g independent of the substrate's Calories, as dictated by the Law of Conservation of Mass. The absorbed nutrient mass cannot be destroyed and, thus, it will contribute to total body mass as long as it remains within the body. Such a contribution ends, however, when the nutrients are eliminated from the body either as products of metabolic oxidation or in other forms (e.g., shedding of dead skin cells).

Animals, including humans, ingest food to get both energy and mass. While energy refers to capacity to do work, mass is used to build all bodily structures. Not a single gram of body mass is gained due to the energy intake. Calories represent the *heat* release upon food oxidation, and as such, Calories have no impact on body mass. Heat does not produce mass. Consequently, the *only* food property that can augment body mass is its nutrient mass, not its energy content (i.e., Calories).

It follows that any anti-obesity intervention must

1) ***Decrease intake of energy-providing mass*** (EPM) ("Mass In"), i.e., satiating effect. EPM is the daily intake of carbohydrate, fat, protein, soluble fiber and alcohol.

2) ***Increase elimination of oxidation products*** ("Mass Out"). Each day we experience a weight loss given by the weight of the energy expenditure-dependent mass loss (EEDML) plus the weight of the energy expenditure-independent mass loss (EEIML) [3]. EEDML refers to the daily excretion of EPM oxidation byproducts (CO_2, water, urea, SO_3), whereas EEIML represents the daily weight loss that results from *i)* the daily elimination of non-metabolically produced water; *ii)* minerals lost in sweat and urine; *iii)* fecal matter elimination; and *iv)* mass lost from renewal of skin, hair and nails [3]. Or

3) ***Both***.

A low-carbohydrate diet *vs.* an isocaloric high-carbohydrate diet

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A highly significant practical application of a mass balance approach is that **a low-carbohydrate/high-fat diet leads to a greater body mass and fat mass loss than an isocaloric high-carbohydrate/low-fat diet because it provides less nutrient mass** [1,3,4,5]. When the energy fraction from dietary fat increases, while energy intake is clamped (i.e., fixed), mass intake decreases due to the significantly higher energy density of fat compared with other energy substrates. Such a difference in mass intake translates into greater body mass and fat loss in a low-carbohydrate diet *vs.* an isocaloric high-carbohydrate diet. If such a feeding response is not observed, then it is simply not a well-controlled study, as alternative results would indicate a violation of the Law of Conversation of Mass.

If two persons eliminate body mass at the same daily rate, then the one ingesting less nutrient mass will express a greater daily body mass and fat loss. For example, daily energy intake of 2,500 kcal distributed as 30% fat (9.4 kcal/g), 55% carbohydrate (4.2 kcal/g) and 15% protein (4.7 kcal/g) corresponds to a mass intake of ~487g, whereas the same energy intake sorted as 60% fat, 30% carbohydrate, and 10% protein reduces mass ingestion by ~96g. This is not a small difference in the long run.

It has been suggested that a low-carbohydrate diet is more effective in losing body mass and fat mass than an isocaloric high-carbohydrate diet because the former lowers insulin levels [9]. However, it is worth noting that insulin – or any other hormone – cannot create any kind of mass out of thin air. Similarly, a lowered insulin level cannot magically destroy any mass (See **The Law of Conservation of Mass**). Although insulin levels decrease with a low-carbohydrate diet, it is not a causal factor in body mass and fat mass loss. It just happens simultaneously with a decrease in nutrient mass intake.

However, the insulin level can be important in terms of *where* body fat is reduced. It seems reasonable that during a high-carbohydrate diet, the reduction of body fat occurs mainly through a reduction in dietary fat intake, since high insulin levels favor fat synthesis and inhibit lipolysis. In contrast, a low-carbohydrate diet lowers insulin levels,

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reducing fat synthesis and stimulating lipolysis, which nullifies the effects of high dietary fat intake. These factors may explain why low-carbohydrate diets tend to work well for visceral fat reduction [e.g., 15].

In **Figure 1**, I present two hypothetical overweight individuals whose body composition and total energy intake are identical, but the distribution of macronutrients is clearly different.

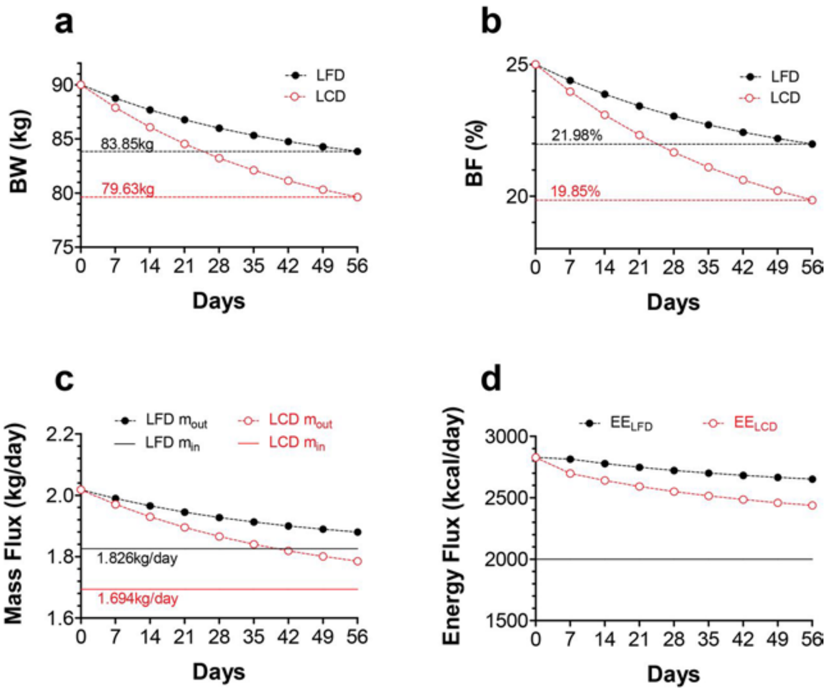

Figure 1. *MBM-based simulation of two hypothetical overweight (90 kg) individuals whose body composition and total energy intake are identical, but macronutrient distribution is clearly different*. In the initial situation, the nutrient intake is as follows: energy intake 2 750 kcal/day; 35% fat (F), 50% carbohydrate (C), 15% protein (P). Next, these individuals start following either a 2 000 kcal high-carbohydrate/low-fat diet (LFD) or a 2 000 kcal low-carbohydrate/high-fat diet (LCD), whose macronutrient distribution is as follows: LFD = 20% F, 65% C, 15% P or LCD = 70% F, 15% C, 15% P. According to the EBT, these diets should lead to almost identical effects in terms of body mass and fat mass. However, the MBM predicts that the LCD results in greater body mass and fat mass loss compared with the LFD. As demonstrated, the nutrient mass intake (m_{in}) is smaller compared with the eliminated mass (m_{out}); and thus the net daily mass loss is larger (i.e., $m_{in} – m_{out}$). BW = body weight; BF = body fat.

Epidemiological data supporting the mass balance approach

As recently pointed out by Mozaffarian [8], **the National Health and Nutrition Examination Survey (NHANES) data do NOT show any increase in energy consumption or availability over ≥20 years,** a time period when obesity has steadily risen (See Figure 1 in [8]). In fact, NHANES data suggest small but statistically significant *declines* in energy intake over this period [8]. What about the other side of the coin, i.e., energy expenditure? According to my understanding, similar epidemiological data on the matter is not available; however, high-quality studies utilizing double-labeled water (DLW) method indicate that **modern day total energy expenditure do not differ from modern-day hunter-gatherers** [12]. Despite of high physical activity level, the total energy expenditure of Hadza hunter-gatherers was similar to Westerners and others in market economies [12]. Thus, it seems clear that the main factor causing the obesity epidemic is increased food intake rather than declined expenditure.

If there has been no change in energy intake and energy consumption, what on earth is causing the obesity epidemic? If we follow the EBT paradigm, this seems paradoxical, but from the point of view of the mass balance approach, there is nothing surprising about it. According to nutritional recommendations, citizens should increase their intake of carbohydrates at the expense of fat. If such recommendations are followed (i.e., carbohydrates ↑; fats ↓), the intake of nutrient mass increases while the calorie intake remains the same. NHANES data indicates that, for men, the percentage of calories from carbohydrates increased between 1971 - 1974 and 1999 - 2000, from 42.4% to 49.0%, and for women, from 45.4% to 51.6% [13]. The percentage of calories from total fat decreased from 36.9% to 32.8% for men and from 36.1% to 32.8% for women [13].

Although self-reported dietary intake is subject to recall bias, there is every reason to assume that strongly marketed nutritional recommendations produced results in line with the goals at the population level.

The Nutrition Facts label

The Nutrition Facts label on packaged foods was updated in 2016 ”to reflect updated scientific information, including information about the link between diet and chronic diseases, such as obesity and heart disease.” [7]. One of the most prominent updates of the new food labeling regulations released by the Food and Drug Administration (FDA) is found on the calorie line; the font for calories has been significantly enlarged as well as emboldened for first-glance reference. The idea behind this well-meaning update was that Caloric values can be very simply understood without having to look very deeply into the food label. Humans need, of course, energy (i.e., the capacity to do work) but Calories have no impact on body mass. Thus, **the calorie line should be replaced, or complemented, with the mass line** (e.g., “Nutrient Mass” or just “Mass”).

It is also worth noting that the concept of ”light product” is very misleading. In reality, these products are often ”heavy products”. When the energy fraction from dietary fat increases, while energy content remains the same, mass intake decreases due to the significantly higher energy density of fat compared with other energy substrates. Thus, ***a high-carbohydrate ”light product” containing 200 kcal provides more mass than a high-fat product containing 200 kcal***. This fact should have a significant impact on the prevailing legislation and the operation of the food industry.

A flawed paradigm leads to misinterpretation of research data

In the research literature, it is easy to find plenty of feeding trial reports that seem to support the EBT. A flawed paradigm, however, almost always leads to incorrect interpretations and conclusions. There are many research reports in which the more effective weight loss effect of a low-carbohydrate diet compared to an isocaloric high-carbohydrate diet is attributed to a methodological error (e.g., underreporting of food consumption, low sensitivity of research equipment). The assumption is that such results would violate the Law of Conservation of Energy (i.e., the First Law of Thermodynamics). As has been shown before, this is not the case. In fact, the EBT does not comply with the Law of Conservation of Energy. In studies where a low-carbohydrate diet has not been more effective in terms of fat loss, EBT-

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based calculation formulas have been used, which give incorrect results (e.g., 10; see reanalysis in [14]). Such points are very important to consider when reading these reports.

The real "acid test" of every theory is how good results can be obtained in practice based on it. How effective have EBT-based obesity treatment interventions been? According to 2017–2018 data from the NHANES, nearly 1 in 3 adults (30.7%) are overweight [11]. Thus, it is clearly not possible to talk about effective interventions.

Conclusions

I would like to propose a new paradigm that paints a more accurate picture of the evolution of body weight: **Chronic positive mass balance is the actual etiology of obesity, not positive energy balance**, possibly opening up a completely new era in obesity research. By shifting to a mass balance paradigm of obesity, a deeper understanding of this disease may follow in the near future. The immediate consequence of such a shift is that feeding studies will become much more accurate and significantly less expensive as mass measurements are cheaper and do not suffer from all the problems that energy measurements do.

For further details, please see the key publications mentioned in the reference list. I intentionally kept the reference list short, as other references can be found in these key publications. I especially recommend reading the recent paper by Arencibia-Albite [1]. It must be clear as day that the paradigm shift must finally begin. The researchers' own honor cannot go above the importance of treating obesity. If the mistake has been great, so must the sacrifice.

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List of abbreviations

MBM = mass balance model; EBT = energy balance theory; EPM = energy-providing mass; EEDML = energy expenditure-dependent mass loss; EEIML = energy expenditure-independent mass loss; NHANES = National Health and Nutrition Examination Survey; DLW = double-labeled water; FDA = Food and Drug Administration.

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