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Diabesity: Palliating, curing or preventing the dysmetabolic diathesis



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ABSTRACT

This opinionated evidence-based selective review addresses flawed concepts related to "obesity", bariatric surgery and approaches to treatment and prevention of a dysmetabolic syndrome of overnutrition and underactivity from the perspective of developmental origins of diseases prevalent in mid-life and beyond. Innovations focus on methods affecting appetite regulation and energy expenditure applicable throughout the life-cycle on the individual level but with transgenerational population-wide implications. Readers can expect new knowledge and enhanced understanding of a global health problem: "diabesity".

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1. Preamble

"Obesity" has caught on, both as a global pandemic and as an object of attention of politicians, the media and even scientists and physicians. It is ironic that the re-rediscovery of "obesity" as a disease recognized by Hippocrates, highlighted in the early 19th century [1], affirmed by the NIH in 1985 [2] and now discovered by the American Medical Association [3], appears when the term, appropriately, is under attack as conceptually limited if not flawed, and the medical profession must profess that it has grossly failed in its mission to palliate, cure, or prevent "obesity".

The noun *obesitas* was derived from *ob* (over) and *edere* (to eat) but its adjective *obesus*: corpulent, plump or very fat (conflating lipid and adipose tissue) conclusively camouflaged the perceived mechanism (overeating). Why this pedantic lesson in semantics? "Obesity" has become a catchall for incongruent concepts, although explained by recent advances in integrative physiology with studies of body composition, metabolism, neuroscience and molecular biology [4].

The nub of the problem lies in fixation on body **weight**, a continuous, mostly normally distributed, second-order phenotype of size which, like height is not a disease, unlike hypertension, anemia, dyslipidemia and hyperglycemia. The remedy is either to qualify "obesity", as in "metabolic" vs. "physical" or combined obesity (Fig. 1), or abandon it in favor of the mechanistic

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"overnutrition", analogous to the readily accepted "undernutrition". Sedentism is "underactivity", a neglected term in the energy equation. Unfortunately more exact descriptives such as "chronic, inflammatory, insulin-resistant overnutrition syndrome" (CIIRO) or "dysmetabolic diathesis" are incongruous and opaque. Could CIIRO become the new "obesity"? Because of the close relationship between obesity and diabetes the term "diabesity" was coined 25 years ago; being used increasingly it might suffice. The following text will use **diabesity**.

A corollary of abandoning weight (as in "overweight" or "obese") as the global descriptor of a metabolic syndrome is replacing **body** mass index (BMI) after it has almost become a household word, recommended by the Public Health community instead of "ideal" or "desirable" weight standards in Eurocentric societies. Although BMI is highly correlated with body fat it is an insufficient surrogate for defining disease [5] as is body fat per se, by not reflecting the more important differential distribution and qualitative aspects of adipose tissues function. The most serious flaw of BMI is its use to define threshold action levels for treatment imposed by governments and other insurers creating perverse incentives for sick people to gain weight or excluding them from necessary treatment [6,7]. The status of BMI as prime indicator of a dysmetabolic state has been challenged for more than 3 decades, starting with the other anthropometric: the waist:hip ratio (WHR; the ratio between standardized measurement of "waist" and "hip" circumferences, corrected for sex), superseded by "waist" alone [8], subsequently complemented by blood pressure and by blood and/or urine biomarkers [9-11]. The advantage of BMI is its utility for defining 'obese' on a population level, compared to the 2-dimensional weight-for-height, adjusted for 'frame' and sex. Just the same, weighing and measuring require staff, given the gross

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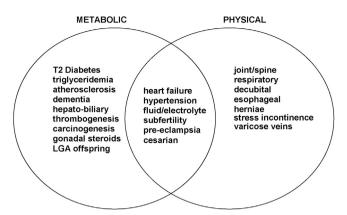


Fig. 1. Metabolic and physical (weight-related) obesity-related conditions with combined forms

inadequacy of self-report [12,13] especially among the severely obese with limited access to high-capacity scales in poor communities where diabesity is rapidly proliferating [6,14]. Population studies are important for ambitious governments but are of less value for clinicians and are even detrimental when they determine reimbursement policies and practice guidelines.

Another flawed concept extant in the fields of nutrition and metabolic disease is embodied in "bariatric", as in Bariatric Medicine, Bariatric Surgery or Bariatrics. The word was happily adopted by practitioners willing to take money for regularly weighing people and giving largely useless advice about "weight management", enhancing their self-importance with a contrived foreign term. Much-maligned surgeons (for) operating on "morbidly (as if 'obesity' itself was not a disease) obese" patients saw the term 'bariatric' as a portal to legitimacy, devoting years to quibbling about expressions of excess weight, willingly following the bariatricians. Thus the term bariatric surgery became established. But there are two problems: "bariatric" focuses on weight (baros) and treatment (iatros: physician and iasthai: heal), whereas body weight is not a disease, thus not requiring healing, and "bariatric surgery" erroneously implies that all anti-obesity operations are mechanistically similar and are devised to treat (excess) weight, as in "weight-loss surgery". In fact, "bariatrics", "bariatric medicine" and "bariatric procedures" are conflated, including anything from life-style modification (for weight loss) to endoscopically placed gastric balloons, natural orifice trans-endoscopic surgery (NOTES) and gastrointestinal restrictive, resective or diversionary operations.

"Bariatric surgery" is commonly used to lump together purely gastric restrictive (e.g. banding) operations, imposing a "gastroplasty diet" [15], with combined, diversionary, gastrointestinal (bypass) operations transiently restricting intake but more significantly durably altering the sequence and kinetics of nutrient absorption eliciting neuro-hormonal reflexes affecting ingestive behavior and energy balance, i.e. metabolism. To remedy this confound, much to the displeasure of the purveyors of bands, it is necessary to distinguish between metabolically inferior banding and gastrointestinal bypass operations [16]. After banding the resultant weight loss intrinsically has beneficial metabolic effects, at least transiently, whereas bypass instantly and independent of weight loss has clinically significant enduring metabolic effects [17].

2. Background

"Midlife and beyond" covers ages with the highest morbidity and mortality; ranking lists of causes change over time and differ globally. In aggregate "obesity" has recently become the leading cause of death in most nations, whether or not it is considered 'preventable', competing with smoking. At least 7 among the top 10 worldwide leading causes of death are associated with diabesity, the exceptions being diarrheal disease and HIV/AIDS. In high-income countries where dementias (rank 3rd) and cancers are prevalent, 9 of the 10 causes of death are attributable to diabesity, the exception being airway-lung cancers; the diabesity-related breast and colorectal cancers rank 5th and 7th. The difference is attributable to increased longevity with higher income. Dementia in particular has only recently been identified as a substantial midlife co-morbidity associated with severe impairment of quality of life of patients and their families and leading to premature death [18].

With the recognition of developmental origins of adult disease (DOAD) has come the realization that the lead-time preceding appearance of numerous conditions above the clinical horizon is very long. This was previously considered to be due to cumulative effects or insults, as with 'pack-years' of cigarettes for emphysema and lung cancer, and bottles of whisky for cirrhosis and pancreas cancer, prompting physicians' exhortations to engage in healthier life-styles, although it has always been convenient to blame "bad genes".

The peak incidence of clinical manifestations of the dysmetabolic diathesis is in mid-life, although many cancers and weight-related diseases are skewed to the right on the time-line. The trend toward earlier, pediatric, manifestations of diabesity comorbidities is dramatic, and too steep to attribute solely to underactivity and overnutrition, even though body weight increases are accelerating in the upper ranges [6,14].

There is always controversy over whether to allocate limited resources to treatment (palliation or cure) of the suffering with a bias favoring the young, or to invest in prevention, avowed to be cost-effective with an advantageous risk-benefit. The argument is more complex when comparing primary to secondary prevention, whether strictly considering economic metrics or a nebulously defined 'greater good', so scarce in real politics. The following is intended to introduce recent and novel bio-medical findings that might add perspective to long-running controversies such as 'nature vs. nuture' and treatment vs. prevention. How can potentially dangerous, heavily rationed surgery inform these debates?

3. Metabolic surgery

3.1. History

The first operations for corpulence simply excised large aprons of skin and adipose tissue in the early days of Plastic Surgery. Regardless of its detrimental metabolic effects lipectomy, removal of large amounts of adipocytes, is not a method for treating diabesity [18]. Resection of several meters of small bowel, an irreversible operation, was performed successfully in Sweden 1951-1952 in 3 middle-aged women who went on to live long healthy lives with minimal physician contact, but this drastic procedure was soon replaced by **intestinal bypass** operations consisting of short-cuts through the small bowel intended to reduce absorption [19-21]. Intestinal bypass dominated obesity surgery from the early 60ies to early 80ies, although gastric bypass for obesity was invented by Mason in 1965 based on his experience with gastric resection for cancer [22]. Since Mason and other surgeons were convinced that the mechanism for weight loss was the small stomach restricting food intake, they developed gastroplasty – an operation that simply diminishes the size of the proximal stomach through stapling and rigid bands, prevalent during the 80ies. It was replaced by adjustable circumgastric (inflatable) banding which has become predominant with the advent of laparoscopic

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