

ANALYSIS

ESSAY

The science of obesity: what do we really know about what makes us fat? An essay by Gary Taubes

The history of obesity research is a history of two competing hypotheses. **Gary Taubes** argues that the wrong hypothesis won out and that it is this hypothesis, along with substandard science, that has exacerbated the obesity crisis and the related chronic diseases. If we are to make any progress, he says, we have to look again at what really makes us fat

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Since the 1950s, the conventional wisdom on obesity has been simple: it is fundamentally caused by or results from a net positive energy balance—another way of saying that we get fat because we overeat. We consume more energy than we expend. The conventional wisdom has also held, however, that efforts to cure the problem by inducing undereating or a negative energy balance—either by counselling patients to eat less or exercise more—are remarkably ineffective.

Put these two notions together and the result should be a palpable sense of cognitive dissonance. Take, for instance, *The Handbook of Obesity*, published in 1998 and edited by three of the most influential authorities in the field. “Dietary therapy,” it says, “remains the cornerstone of treatment and the reduction of energy intake continues to be the basis of successful weight reduction programs.” And yet it simultaneously describes the results of such dietary therapy as “poor and not long-lasting.”¹

Rather than resolve this dissonance by questioning our beliefs about the cause of obesity, the tendency is to blame the public (and obese patients implicitly) for not faithfully following our advice. And we embrace the relatively new assumption that obesity must be a multifactorial and complex disorder. This makes our failures to either treat the disorder or rein in the burgeoning epidemics of obesity worldwide somehow understandable, acceptable.

Another possibility, though, is that our fundamental understanding of the aetiology of the disorder is indeed incorrect, and this is the reason for the lack of progress. If this is true, and it certainly could be, then rectifying this aetiological misconception is absolutely critical to future progress.

Energy balance hypothesis

Despite its treatment as a gospel truth, as preordained by physical law, the energy balance or overeating hypothesis of

obesity is only that, a hypothesis. It’s largely the product of the influential thinking of two physicians—the German diabetes specialist Carl von Noorden at the beginning of the 20th century, and the American internist and clinical investigator Louis Newburgh, a quarter century later. Its acceptance as dogma came about largely because its competing hypothesis—that obesity is a hormonal, regulatory disorder—was a German and Austrian hypothesis that was lost with the anti-German sentiment after the second world war and the subsequent embracing of English, rather than German, as the lingua franca of science.

Medicine today is often taught untethered from its history—unlike physics, for instance—which explains why the provenance of the energy balance hypothesis is little known, even by those physicians and researchers who are its diehard proponents. Nor is it widely known that a competing hypothesis ever existed, and that this hypothesis may have done a better job of explaining the data and the observations. Knowing this history is crucial to understanding how we got into the current situation and, indeed, how we might solve it.

The applicability of the laws of thermodynamics to living organisms dates from the 1880s and the research of the German physiologist Max Rubner. By the end of the 19th century, the American scientists Wilbur Atwater and Francis Benedict had confirmed that these laws held for humans as well: that the calories we consumed would be burned as fuel, stored, or excreted.² This revelation then led von Noorden to propose that “the ingestion of a quantity of food greater than that required by the body, leads to an accumulation of fat, and to obesity, should the disproportion be continued over a considerable period.”³

By the late 1920s, Newburgh had taken up the energy balance banner at the University of Michigan and was promoting it based on what he believed to be a fundamental truth: “All obese

persons are alike in one fundamental respect—they literally overeat.” As such, he blamed obesity on either a “perverted appetite” (excessive energy consumption) or a “lessened outflow of energy” (insufficient expenditure).⁴ If the obese person’s metabolism was normal, he argued, and they still refused to rein in their intake, that was sufficient evidence to assume that they were guilty of “various human weaknesses such as overindulgence and ignorance.”⁵

By 1939, Newburgh’s biography at the University of Michigan was crediting him with the discovery that “the whole problem of weight lies in regulation of the inflow and outflow of calories” and for having “undermined conclusively the generally held theory that obesity is the result of some fundamental fault.”⁶

As sceptics pointed out at the time, though, the energy balance notion has an obvious flaw: it is tautological. If we get fatter (more massive), we have to take in more calories than we expend—that’s what the laws of thermodynamics dictate—and so we must be overeating during this fattening process. But this tells us nothing about cause. Here’s the circular logic:

Why do we get fat? Because we overeat.

How do we know we’re overeating? Because we’re getting fatter.

And why are we getting fatter? Because we’re overeating.

And so it goes, round and round.

“The statement that primary increase of appetite may be a cause of obesity does not lead us very far,” wrote the Northwestern University School of Medicine endocrinologist Hugo Rony in 1940 in *Obesity and Leanness*, “unless it is supplemented with some information concerning the origin of the primarily increased appetite. What is wrong with the mechanism that normally adjusts appetite to caloric output? What part of this mechanism is primarily disturbed?” Any regulatory defect that drove people to gain weight, Rony noted, would induce them to take in more calories than they expend. “Positive caloric balance would be, then, a result rather than a cause of the condition.”⁷

Endocrinological hypothesis

The alternative hypothesis that Newburgh’s work had allegedly undermined was the idea that some “intrinsic abnormality”—Rony’s words—was at the root of the disorder. This was an endocrinological hypothesis. It took the laws of physics as a given; it rejected aberrant behaviour or ignorance as causal. It existed at the time as two distinct hypotheses.

One was the brainchild of Wilhelm Falta, a student of von Noorden and a pioneer of the science of endocrinology. Falta believed that the hormone insulin must be driving obesity on the basis, as he noted as early as 1923, that “a functionally intact pancreas is necessary for fattening.”⁸ Once insulin was discovered, Falta considered it the prime suspect in obesity. “We can conceive,” he wrote, “that the origin of obesity may receive an impetus through a primarily strengthened function of the insular apparatus, in that the assimilation of larger amounts of food goes on abnormally easily, and hence there does not occur the setting free of the reactions that in normal individuals work against an ingestion of food which for a long time supersedes the need.”⁹

The other version of the hypothesis was bound up in a concept known as lipophilia. It was initially proposed in 1908 by Gustav Von Bergmann, a German authority on internal medicine, and then taken up by Julius Bauer, who did pioneering work on

endocrinology, genetics, and chronic disease at the University of Vienna.

Von Bergmann initially evoked the term lipophilia (“love of fat”) to explain why fat deposition was not uniform throughout the body. Just as we grow hair in some places and not others, according to this thinking, we fatten in some areas and not others and biological factors must regulate this. People who are constitutionally predisposed to fatten, Von Bergmann proposed, had adipose tissue that was more lipophilic than that of constitutionally lean individuals. And if fat cells were accumulating excessive calories as fat, this would deprive other organs and cells of the energy they needed to thrive, leading to hunger or lethargy. These would be compensatory effects of the fattening process, not causes.

“Like a malignant tumor or like the fetus, the uterus or the breasts of a pregnant woman,” explained Bauer, “the abnormal lipophilic tissue seizes on foodstuffs, even in the case of undernutrition. It maintains its stock, and may increase it independent of the requirements of the organism. A sort of anarchy exists; the adipose tissue lives for itself and does not fit into the precisely regulated management of the whole organism.”¹⁰

Erich Grafe, director of the Clinic of Medicine and Neurology at the University of Würzburg, discussed these competing hypotheses in his seminal textbook *Metabolic Diseases and Their Treatment*, which was published in an English translation in 1933. Grafe said he favoured the energy balance model of obesity, but acknowledged that this model failed to explain key observations—why fat accumulates in certain regions of the body. “The energy conception certainly cannot be applied to this realm,” Grafe wrote. The lipophilia hypothesis could.

Grafe described lipophilia as “a condition of abnormally facilitated fat production and impeded fat destruction . . . a sort of *lipomatosis universalis*, in the sense that the lipophilia in certain tissues is primary and the sparing in the energy expended is secondary.” But he found the hypothesis troubling “so far as it presupposes overnutrition.” He acknowledged, nonetheless, that it was “a good working hypothesis.” As for Falta’s notions, Grafe wrote, “the fact that insulin is an excellent fattening substance has been observed.”¹¹

By 1938, Russell Wilder of the Mayo Clinic (later to become director of the National Institute of Arthritis and Metabolic Diseases) was writing that the lipophilia hypothesis “deserves attentive consideration,” and that “the effect after meals of withdrawing from the circulation even a little more fat than usual might well account both for the delayed sense of satiety and for the frequently abnormal taste for carbohydrate encountered in obese persons . . . A slight tendency in this direction would have a profound effect in the course of time.”¹²

Two years later, Rony wrote in *Obesity and Leanness* that the hypothesis was “more or less fully accepted” in Europe.

Language barrier

Maybe so. But it was lost with the second world war and the embracing of English as the lingua franca of science afterwards. In Grafe’s chapters on obesity, over 90% of the 235 references are from the German language literature. In Rony’s *Obesity and Leanness*, this is true for a third of the almost 600 references. But post-war, the German language references fall away quickly. In *Obesity...*, published in 1949 by two Mayo Clinic physicians—Edward Rynearson and Clifford Gastineau—only 14 of its 422 references are from the German language literature, compared with a dozen from Louis Newburgh alone. By the

late 1960s and 1970s, when the next generation of textbooks were written, German language references were absent almost entirely, as were the clinical observations, experience, and intuitions that went with them.

By then, obesity had evolved into an eating disorder, to be treated and studied by psychologists and psychiatrists, while laboratory researchers focused (as they still do) on identifying the physiological determinants of hunger, satiety, and appetite: why do we eat too much, rather than why do we store too much fat? Two entirely different questions.

What makes this transition so jarring in retrospect is that it coincided with the identification of the hormone insulin in the early 1960s as the primary regulator of fat accumulation in fat cells.¹³ Had Falta's ideas and the lipophilia hypothesis survived the second world war, this discovery would have served to bring these two hypotheses together. And because serum insulin levels are effectively driven by the carbohydrate content of the diet, this hypothesis would implicate refined, high glycaemic grains and sugars (sucrose and high fructose corn syrup, in particular) as the environmental triggers of obesity. They would be considered uniquely fattening, just as Falta had suggested, not because we overeat them—whatever that means—but because they trigger a hormonal response that drives the partitioning of the fuel consumed into storage as fat.

This might have been perceived, although it was not, as a medical triumph: the elucidation of both the biological underpinnings of obesity as well as an explanation for what was until then the conventional wisdom on the cause. "Every woman knows that carbohydrate is fattening," as Reginald Passmore and Yola Swindells wrote in the *British Journal of Nutrition* in 1963: "this is a piece of common knowledge, which few nutritionists would dispute."¹⁴

Academic backlash

That this insulin-carbohydrate hypothesis never gained traction can be explained, paradoxically, by the fact that it was embraced by practising physicians, who read the physiology and biochemistry literature and then designed carbohydrate restricted diet plans that seemed to work remarkably well. Indeed, the sessions on dietary therapy for obesity in the scattering of obesity conferences held from the end of the second world war through the mid-1970s invariably focused on the surprising efficacy of carbohydrate restricted diets to reduce excess adiposity.

When those physicians then wrote diet books based on their regimens, and these books then sold exceedingly well—*Dr Atkins' Diet Revolution* (1972) most notably—the result was a backlash from academic nutritionists and obesity researchers. Fred Stare, for instance, head of the Harvard nutrition department, testified in 1972 Congressional hearings that physicians prescribing such diets were "guilty of malpractice," on the basis that these diets were rich in saturated fat at a time when the medical community was coming to believe that high fat diets were the cause of heart disease. Exacerbating the dietary fat issue was the fact that these diet plans encouraged obese individuals to eat to satiety, effectively as much as they wanted (so long as they avoided carbohydrates), when the conventional wisdom had it that they got fat to begin with precisely because they ate as much as they wanted.

By the mid-1970s, the diets had been successfully tarred as dangerous fads (despite a history of common use in hospitals, including the Harvard Medical School,¹⁵ and a provenance going back at least to the 1820s) and the physician authors as quacks and confidence men. The notion that obesity is not an eating

disorder or an energy balance disorder, but a fat accumulation disorder—a hormonal, regulatory disorder—triggered not by energy imbalance but the quality and quantity of the carbohydrates in the diet, has been routinely dismissed ever since as unworthy of serious attention.

In a 21st century of genomics, proteomics, and high tech medicine, it's hard to imagine that the obesity problem might have been effectively solved by 1960s era endocrinology. Rather we assume that these competing hypotheses must have been rigorously tested, and the energy balance hypothesis must have won out. We know that it's excess calories, not carbohydrates—eating too much rather than "abnormal lipophilic tissue"—that make us fat because that's what the science has told us.

But this is not the case. One problem has been an almost ubiquitous misunderstanding of the alternative hypothesis and, indeed, of energy imbalance itself. The existence of an energy imbalance in people who are getting fatter is treated, as Newburgh did, as evidence that the energy balance hypothesis is correct. The same can be said for observations that obese people eat more than lean or are more sedentary, or even that per capita food availability has increased over the course of the obesity epidemic or that leisure time physical activity has decreased. All these observations, though, are consistent with both hypotheses.

Calories or carbohydrates

Attempts to blame the obesity epidemics worldwide on increased availability of calories typically ignore the fact that these increases are largely carbohydrates and those carbohydrates are largely sugars—sucrose or high fructose corn syrup. And so these observations shed no light on whether it's total calories to blame or the carbohydrate calories. Nor do they shed light on the more fundamental question of whether people or populations get fat because they're eating more, or eat more because the macronutrient composition of their diets is promoting fat accumulation—increased lipogenesis or decreased lipolysis, in effect, driving an increase in appetite.

The same is true for bariatric surgery, which is now acknowledged to be a remarkably effective means of inducing long term weight loss. But does weight loss occur after surgery because of the rearrangement of the gastrointestinal tract resulting in hormonal effects that minimise appetite or directly minimise fat accumulation? Does it occur because the patient reduces total calories consumed after surgery or reduces carbohydrate calories and, specifically, refined grains and sugars? The observation that bariatric surgery works doesn't answer these questions.

As Erich Grafe noted about the lipophilia hypothesis 80 years ago, it "presupposes overnutrition." If a patient is getting heavier, they must be taking in more energy than they expend. With the energy balance hypothesis, overnutrition is causal; with lipophilia, it's compensatory, a response to the hormonally driven fat accumulation. Either way, it has to exist while an individual is gaining weight. And, by the same token, undernutrition or negative energy balance has to exist if an individual is losing weight.

Sugary beverages are another example of how these different hypotheses lead to different conclusions that are relevant to solving the obesity epidemics worldwide. The conventional wisdom has it that sugary beverages are merely empty calories that we consume in excess, although it is possible that the metabolism of fructose (a key carbohydrate component that makes these sugars sweet) in the liver somehow circumvents

leptin signalling, leading us to consume these beverages and their calories even when we're not and shouldn't be hungry. The hormonal or regulatory hypothesis also focuses on the metabolism of fructose in the liver, but rather than leptin it uses evidence suggesting that fructose metabolism can induce insulin resistance, leading in turn to raised insulin levels and trapping fat in fat cells—increasing, in effect, lipophilia.

Shortcomings of obesity and nutrition research

Another problem endemic to obesity and nutrition research since the second world war has been the assumption that poorly controlled experiments and observational studies are sufficient basis on which to form beliefs and promulgate public health guidelines. This is rationalised by the fact that it's exceedingly difficult (and inordinately expensive) to do better science when dealing with humans and long term chronic diseases. This may be true, but it doesn't negate the fact the evidence generated from this research is inherently incapable of establishing reliable knowledge.

The shortcomings of observational studies are obvious and should not be controversial. These studies, regardless of their size or number, only indicate associations—providing hypothesis generating data—not causal relations. These hypotheses then have to be rigorously tested. This is the core of the scientific process. Without rigorous experimental tests, we know nothing meaningful about the cause of the disease states we're studying or about the therapies that might work to ameliorate them. All we have are speculations.

As for the experimental trials, these too have been flawed. Most conspicuous is the failure to control variables, particularly in free-living trials. Researchers counsel participants to eat diets of different macronutrient composition—a low fat, a low carbohydrate, and a Mediterranean diet, for instance—and then send them off about their lives to do so. In these trials, carbohydrate restricted diets almost invariably show significantly better short term weight loss, despite allowing participants to eat as much as they want and being compared with calorie restricted diets that also reduce the quantity of carbohydrates consumed and improve the quality. In these trials, the ad libitum carbohydrate restricted diets have also improved heart disease and diabetes risk factors better than the diets to which they've been compared. But after a year or two, the results converge towards non-significance, while attempts to quantify what participants actually eat consistently conclude that there is little long term compliance with any of the diets.¹⁶⁻¹⁸

Rather than acknowledge that these trials are incapable of answering the question of what causes obesity (assumed to be obvious, in any case), this research is still treated as relevant, at least, to the question of what diet works best to resolve it—and that in turn as relevant to the causality question. Should we restrict calories or carbohydrates to lose weight? If the answer is that it doesn't seem to matter because the participants eventually fail to adhere to any of the diets, this is perceived as somehow a confirmation that the only way to lose weight is to reduce calories, and so the energy balance hypothesis is the correct one.¹⁹

Imagine drawing conclusions about the cause of lung cancer or the reduction in risk that can be achieved by quitting cigarettes based on success rates in experimental trials of smoking cessation techniques—going cold turkey, for instance, versus using the patch or nicotine gum. The logic is similar if not identical.

Ultimately what we want to know is what causes weight gain. That's an entirely different question from whether advising someone to follow a Mediterranean diet is more or less efficacious than a low fat or a carbohydrate restricted diet or some variation thereof.

In metabolic ward studies, in which the diets of the participants have been well controlled, researchers typically restricted the calories in both arms of the trials—feeding participants, say, 800 calories of a low fat versus a low carbohydrate diet—and so building into the study design one of the hypotheses that is ultimately being tested. What we want to know, again, is what causes us to gain weight, not whether weight loss can be induced under different conditions of both semistarvation and carbohydrate restriction.

What can we do about this? It seems we have two choices. We can continue to examine and debate the past, or we can look forward and start anew.

A year ago, working with Peter Attia, a physician, and with support from the Laura and John Arnold Foundation in Houston Texas, I cofounded a not-for-profit organisation called the Nutrition Science Initiative (NuSI.org). Our strategy is to fund and facilitate rigorously well controlled experimental trials, carried out by independent, sceptical researchers. The Arnold Foundation has now committed \$40m over the next three years to this research programme. Our hope is that these experiments will be the first steps in answering definitively the question of what causes obesity and help us finally make meaningful progress against it.

We believe that ultimately three conditions are necessary to make progress in the struggle against obesity and its related chronic diseases—type 2 diabetes, most notably. First is the acceptance of the existence of an alternative hypothesis of obesity, or even multiple alternative hypotheses, with the understanding that these, too, adhere to the laws of physics and must be tested rigorously.

Second is a refusal to accept substandard science as sufficient to establish reliable knowledge, let alone for public health guidelines. When the results of studies are published, the authors must be brutally honest about the possible shortcomings and all reasonable alternative explanations for what they observed. "If science is to progress," as the Nobel prize winning physicist Richard Feynman said half a century ago, "what we need is the ability to experiment, honesty in reporting results—the results must be reported without somebody saying what they would like the results to have been—and finally—an important thing—the intelligence to interpret the results. An important point about this intelligence is that it should not be sure ahead of time what must be."²⁰

Finally, if the best we've done so far isn't good enough—if uncontrolled experiments and observational studies are unreliable, which should be undeniable—then we have to find the willingness and the resources to do better. With the burden of obesity now estimated at greater than \$150bn (£100bn; €118bn) a year in the US alone, virtually any amount of money spent on getting nutrition research right can be defended on the basis that the long term savings to the healthcare system and to the health of individuals will offset the costs of the research by orders of magnitude.

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Biography

Gary Taubes is cofounder of the Nutrition Science Initiative (NuSI.org), and an award-winning science and health journalist. He is the recipient of a Robert Wood Johnson Foundation Investigator Award in Health Policy Research and the author of *Why We Get Fat and What to Do About It* (Knopf, 2011) and *Good Calories, Bad Calories: Fats, Carbs, and the Controversial Science of Diet and Health* (Knopf, 2007), published in the UK as *The Diet Delusion* (see *BMJ* 2009;339:b5604). He lives in Oakland, California.

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