

REVIEW ARTICLE

MEDICAL HISTORY OF OBESITY

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Abstract

This paper contains the following sections, in approximate chronological order. Early years, Scientific research on energy metabolism, Clinical teaching, Evidence on health risks, Slow recognition of obesity in diabetes, Depression and war, some Obesity research continued in the 1950s and 1960s, New approaches to management, a Universal standard weight for height, Luxuskonsumption, Calories (incompletely) replaced by Joules, Food intakes of obese people, Genetics, unexpected Surge of obesity from 1980, Diabetes, Scarcity of effective, safe drugs for obesity, Leptin and Ghrelin stimulate basic research, Why has the obesity epidemic happened? What is the best weight-reducing diet? Bariatric surgery

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EARLY YEARS

Obesity has probably affected some humans since hunter gatherers evolved into agriculturalists, cities were built and a rich minority could eat as much as they wanted.

Hippocrates, in the 5th century BC [1] taught that fat people who want to reduce should take their exercise on an empty stomach and sit down to their food out of breath. Without recovering breath they should, before eating drink some diluted wine, and then meat should be dished up with sesame seeds seasoning. The meat should also be fat as the smallest quantity of this is filling. They should only take one meal a day, go without baths, sleep on hard beds and walk about with as little clothing as possible. These principles of management might still be acceptable today: exercise; only one meal a day based on fatty meat for satiety.

Hippocrates also included among his aphorisms that those who are naturally very

fat are apt to die earlier than those who are slender [2].

There are no statistics for the prevalence of obesity until the 20th century. Only one very fat man appears in the Bible, Eglon, king of Moab (Judges [3], [17]) (the first direct demonstration of abdominal obesity). Only one fat main character appears in Shakespeare's plays, Falstaff.

Three British kings were very fat late in their lives: William the Conqueror, Henry VIII and George IV. Trowell [3, 4] looked into the history of obesity, from literature and art and thought that obesity became common in the English upper classes in the late 18th century.

In that period Samuel Johnson, himself overweight, had this to say about a man much incommoded by corpulency (the precursor of our word "obesity"): "He eats too much, sir", to which Boswell replied: "I don't know, sir" You will see one man fat who eats moderately

and another lean who eats a great deal". Johnson again: "Nay, sir, whatever may be the quantity that a man eats, it is plain that if he is too fat, he has eaten more than he should have done" [5]. That conversation still continues.

The first dietary prescription for treatment of obesity was perhaps in a best-selling pamphlet self-published by Mr William Banting in 1863. He lost 35 pounds on a diet of meat or fish three times a day, a little fruit and leafy vegetables and several glasses of wines. This successful, low carbohydrate, high protein diet was prescribed by his ear surgeon, Dr William Harvey (not the discoverer of circulation of the blood), apparently for hearing loss because of fatty deposits obstructing his Eustachian tubes [6, 7]. Banting's luxurious diet reappeared in modern versions as the Atkins diet in 1972 [140, 142].

Charles Dickens in *Pickwick Papers* (1837) described a fat boy who kept falling asleep. Burwell (in 1956) [8] put this complication of obesity in the medical literature and demonstrated that the episodic somnolence is due to hypoventilation and hypercapnia. Osler had in the meantime described this "Pickwickian syndrome" in the 1916 edition of his textbook [9].

SCIENTIFIC RESEARCH ON ENERGY METABOLISM

Scientific understanding of energy metabolism started with Lavoisier, father of modern chemistry and the founder of nutritional science. Carbon dioxide had been discovered by Black in 1757, hydrogen by Cavendish in 1766, nitrogen by Rutherford in 1772 and oxygen by Priestley in 1774. They were not given these modern names and their functions were misunderstood. It required the brilliant mind of Lavoisier to meld these miscellaneous achievements into a harmonious whole around 1780 [10]. A monument to him in Paris bears this inscription:

"Analysis and synthesis of air – Composition of oxides and acids – composition of water – Theory of combustion – Respiration and animal heat – Permanence of weight of matter and simple substances – Imponderable nature of heat and its role in chemistry".

Lavoisier discovered oxidation and named the gas (that Priestley had called dephlogisted air) oxygen. Lavoisier and Laplace put a guinea pig in a very small closed chamber surrounded by ice. They measured the amount of ice melted over a 10 hour period and over the same time the amount of carbon dioxide (air fixe') given out by the animal. They also measured the heat produced when a known amount of carbon was burnt in their calorimeter [11].

They realised that the heat produced by the animal and the transformation of oxygen to carbon dioxide were similar processes. Respiration in animals is essentially the same as chemical combustion. Lavoisier even measured oxygen consumption in a human subject and showed it increased after food and after exercise.

Tragically, Lavoisier was guillotined in 1794 during the Terror that was part of the French revolution. He was a minor aristocrat and worked as a public servant as well as a part-time scientist. His execution has been called the most criminal act of the Revolution.

There was a directly transmitted intellectual inheritance from Lavoisier through his associate Berthollet to his pupil Gay-Lussac in Paris. Justus Liebig from Germany worked in Gay-Lussac's laboratory and then set up his own laboratory in the small German town of Giessen, where he was appointed professor of chemistry at the university in 1824 (when 21 years old) [11]. Liebig developed organic chemistry and became world famous. His contribution to agriculture was fundamental. Of relevance here, he asserted that (dietary) protein is consumed when muscles exercise. In 1852 he moved to be professor of chemistry at the University of Munich.

Carl von Voit was a student of Liebig's at Munich. Around 1860 he measured the urea excretion of dogs at rest and with exercise and was astonished to find no difference. Then in 1866 Fick and Wislicenus (professors of physiology and chemistry in Zurich) climbed a 1656m high mountain after going on a protein-free diet. They did not feel exhausted despite this diet and only excreted 5.5g nitrogen in the day. Late in his life Liebig admitted he had been wrong in asserting that protein is used for muscular work. In 1863 Voit was appointed professor of physiology at the University of Munich. He headed the leading research group investigating metabolism.

Voit and colleagues established the principles of nitrogen balance and found the effects of changing intake level, of different dietary proteins, of adding non-protein calories and of starvation. Amino nitrogen serves as a marker in following what happens to protein economy in the body. They already used faecal period markers. Voit built the first human metabolic chamber (1861), with money from King Maximilian II of Bavaria. It had a small room, to hold a bed or bicycle ergometer. Air coming in and out was continuously analysed for carbon dioxide. He had a smaller respiration apparatus for dog experiments. This complicated set of pumps, meters and bottles is illustrated in the front of Lusk's classic book [12].

Summarizing his work with Pettenkofer, Voit recalls "Imagine our sensations as the picture of the remarkable processes of the metabolism unrolled before our eyes... We found that in starvation protein and fat alone were burned, that during work more fat was burned and that less fat was consumed during rest, especially during sleep; that the carnivorous dog could maintain himself on an exclusive protein diet, and if to such a protein diet fat were added, the fat was almost entirely deposited in the body; that carbohydrates, on the contrary, were burned no

matter how much was given, and that they, like the fat of the food protect the body from fat loss..." [12].

Max Rubner was the most eminent of Voit's pupils. He worked out the principles of energy metabolism that we use today. In Munich, he showed that the energy value of protein is less when someone eats it than it is in a bomb calorimeter because of losses (urea and other substances) in urine. He was first to produce the energy values 4.1 Cal, 4.1 Cal and 9.3 Cal per gram for protein, carbohydrate and fat respectively (1879). He showed that the same calorie intake of any two of these give the same heat production in an animal – "the isodynamic law". He moved to be professor in Marburg in 1885 and there constructed the first reliable animal respiration calorimeter. He found that the energy production measured fasting and at rest, the Grundumsatz is constant for the individual and the fundamental base of energy expenditure. Increased energy output after food is due to additional biochemical reactions (Lusk in 1912 translated Grundumsatz as "basal metabolism"). A dog in the calorimeter for 45 days used 17,349 Cal calculated from respiration and produced 17,406 Cal as heat. This confirmed in an animal the first law of thermodynamics, the law of conservation of energy. In 1891 Rubner was invited to Berlin to take Robert Koch's place as professor of hygiene. He did more experiments confirming the law of conservation of energy. He collected data on basal metabolism of various animal species and propounded the surface area law – that the basal metabolism is proportional to a mammal's or person's surface area. He also discovered the specific dynamic action of foodstuffs, protein being most potent [10, 12, 13]. Rubner and Karl Thomas worked together to find the minimum amount of protein needed by man. Thomas went on in classic experiments to estimate the "biological values" of major dietary proteins in humans.

Compared with today Rubner was very economical in his use of animals and human subjects – all under $n=6$ [14]. “... a genius who drew correct conclusions from data inadequate for any other man.” [15].

When we calculate the energy value of foods or estimate energy requirements from height and weight (hence surface area) we are using Rubner’s principles of energy metabolism.

WO Atwater, an American who studied under Voit in Munich and was a friend of Rubner’s, built a functioning respiration calorimeter for human subjects at Wesleyan University, Connecticut in collaboration with EB Rosa, the professor of physics. The calorimeter was funded by the US government. Heat produced in the room was measured with circulating water, and CO₂ was collected over soda lime. It took 12 years to perfect and a team of assistants to work it. Garrow takes 2 pages to describe the equipment and its operation [16], Lusk takes four pages [12] and provides a table of results of subjects 5 to 10 in 1899. The differences between heat observed and estimated from respiration ranged between -4.1% and +1.4%: These and later experiments confirmed the law of conservation of energy in man.

“It is possible to make measurements (like Atwater’s) on a human subject over a period of several days with the precision customary in the physical sciences. It is possible but needed the skill, vigilance and dedication now reserved for exploits such as landing a man on the moon” [16].

Atwater’s work established the essential quantitative knowledge on which all assessments of human energy needs are based. Before concentrating on calorimetry, Atwater ran an extensive programme on the chemical composition of American foods, measuring also energy values in a bomb calorimeter and including 97 human digestibility experiments. The “Atwater factors” 4, 9 and 4 Kcal /gram for protein, fat and carbohydrate (by differ-

ence) were published in 1899 [17]. They are used when water, protein and fat have been analysed, to calculate the calorie value of a food. They are almost the same as the factors that Rubner had introduced.

The science and technology of human calorimetry had spread to the USA. Graham Lusk was one of Voit’s PhD students in Munich. He returned to the USA as professor of physiology at Cornell University Medical School, NYC. He did respiration calorimetry with dogs, confirming the constancy of basal metabolic rate (BMR) under standard conditions, and wrote the classic textbook, “The Elements of the Science of Nutrition” [12].

FG Benedict trained with Atwater. He set up a human calorimeter at the Carnegie Institute in Boston where he studied the changes in chemical and energy metabolism during undernutrition. In 1912 he made daily multiple measurements on a man who fasted for 31 days: heat production went down 28% after 3 weeks, more than body weight (16%) [18]. Later, during World War I, Benedict and colleagues had 22 subjects each eat a restricted diet for approximately 3 months (interrupted over Thanksgiving and Christmas). They lost 7 to 11% of body weight and had much larger reductions of basal metabolism per kg; so this fall in metabolism was not all due to loss of tissue [19].

During World War II another large and comprehensive study of underfeeding healthy men was made by Ancel Keys and colleagues at the University of Minnesota. 32 volunteers, conscientious objectors to military service, went through 24 weeks of carefully controlled semi-starvation and their average weight went from 69 to 53 kg (23% less). Again the basal metabolism went down more than would be expected from the reduced body size. Per man it declined to 63% of start value, per m² to 70% and per kg to 83%. Many other measurements were made, all

written up in a 2 volume report (1385 pages) [20].

During the 1920s research interest shifted away from energy metabolism and calorimetry. Biochemists became interested in enzyme function, and nutritionists were busy searching for new vitamins [21].

For Gowland Hopkins "These calorimeter studies, invaluable in themselves, were leading to doctrinal teaching that contained inherent errors... The assumption that carbohydrate and fats can replace each other indefinitely in a diet, so long as the total energy supplied remains the same has led to serious errors in practical dietetics... The newly discovered vitamins contribute little or nothing to the energy factor in nutrition." [22].

Measurement of BMR was still used clinically (with a portable spirometer to measure CO₂ production) for diagnosing over- or under- activity of the thyroid [23] until 1950, when less cumbersome chemical methods for thyroid hormones were available.

CLINICAL TEACHING

Clinical understanding of obesity in the early 20th century was in a far different world. Osler's major textbook in 1904 [24] had two pages on obesity (grouped under "Constitutional Diseases") of a total 1182 pages. "A condition for which we are consulted in three groups of cases. First, there are persons of both sexes who have a hereditary tendency to obesity. Secondly, in this country particularly, there is an increasing number of cases of obesity in children, associated with bad habits in eating, and usually carelessness and lack of control on the part of parents. Thirdly, and most frequently, we are consulted by women at the middle period of life, who are troubled with an overgrowth of fat... A great many stout persons enjoy unusual vigor. Nor is obesity always associated with over-

eating... Too much food and too little exercise are largely responsible in about half of the cases, but in the hereditary ones these factors do not prevail... Gout is an important agent in many cases". This seems to reflect Osler's private practice. On treatment Osler's advice was not very practical. He set out a detailed diet with prescribed food or drink at 8, 10, 12, 1, 3, 4, 6 and 8 o'clock (including 2 glasses of wine). These frequent feeds are "to obviate the tendency to weakness which these patients often experience". Then "in the treatment of extreme obesity it is very much better that the patient should be in hospital or under the care of a nurse, who will undertake the proper weighing and administration of the food".

A recurring problem with obesity is fat people who insist they eat less than average. Van Noorden [25] in 1907 classified obesity into exogenous due to overeating, or endogenous where the cause is internal. Engelbach (1932) [26] stated that endogenous obese people do not respond to diet and exercise, while those with the exogenous variety do.

Fröhlich in 1901 reported a single patient, a boy who became moderately fat in adolescence. He had headaches and left-sided blindness from optic atrophy. His penis was infantile and embedded in fat. Skull X-ray showed erosion of the back of the pituitary fossa. Operation in Vienna by the nasal route removed an adenoma the size of a hazelnut. The patient recovered from the operation but as an adult (at 26 y) continued to be of infantile habitus and still had deposits of fat [27]. Subsequent opinion is that the tumour was probably in the hypothalamus, not the pituitary.

A 1926 British book on obesity by Leonard Williams MD [28] starts: "There are only two kinds of obesity- the one is alimentary in origin, and is caused by surfeit; the other is endocrine in origin and is caused by underaction of an endocrine gland".

In the 1913 edition of Osler's textbook of Medicine [9], 20 of the 30 lines on etiology of obesity were about endocrine possibilities, including Fröhlich's syndrome. In Price's textbook (1930) 28 out of 48 lines on pathology were about likely endocrine gland involvement in obesity [29]. By 1952 the new Davidson's textbook of medicine [30] still had Exogenous and Endogenous causes of obesity, but "Endocrine factors are often blamed for obesity, though seldom on any good evidence. Obesity is NOT a characteristic feature of either hypothyroidism or anterior pituitary deficiency...Appetite is a primitive urge regulated by the hypothalamus: Damage to this area of the brain occasionally results in obesity (eg. In Fröhlich's syndrome)".

An editorial in the BMJ in the Christmas 1958 issue [31] remarked that "25 years ago obesity was generally held to derive from endocrine causes, known or unknown, so that any obese woman was suspected of Cushing's disease and too many fat boys were referred to consultants with a diagnosis of Fröhlich's syndrome".

EVIDENCE ON HEALTH RISKS

"Moderate obesity was considered a sign of health...until the 20th century, and some societies still consider it healthy. The positive attributes of body fat were extolled by early fertility symbols (eg. The Venus of Willendorf) from prehistoric times, by the ancient Greeks, and by Shakespeare" [32] ("Let me have men about me that are fat...").

Actuaries with large life insurance companies started to notice from around 1903 that people above average weight for height who applied for life insurance were more likely to die young, and hence less profitable to insure [33].

A large study of men with data from 1909 to 1928 from 32 life insurance companies reported in 1932 that men originally overweight had mortality well above average at

every age, and in general the greater the degree of overweight, the higher the mortality. The highest death rates were from degenerative cardiovascular and renal diseases, diabetes and cirrhosis of the liver [34].

Another study by the Union Central Life Insurance Company also reported in 1930 on men with substandard insurance because of overweight. Mortality from cardiovascular renal disease was 60% above and from diabetes it was 2.5 times above the rates for normal-weight men [35].

A study of insured women for the Life Insurance Medical Directors found that in overweight women, excess mortality from diabetes and gallbladder disease was three times as high as in normal-weight women; cardiovascular-renal deaths were also 50% higher in women who were obese [34].

Tables of ideal or desirable weight for height were first published by the Metropolitan Life Company of New York in 1942-3 [33]. The Society of Actuaries Build and Blood Pressure studies in 1959 and 1979 confirmed the earlier mortality risks of obesity and were used for new sets of desirable weights, complicated by 3 different frame sizes, in 1959 [36], which were revised in 1983 [37].

Epidemiologists regarded these statistics with suspicion because not everyone takes out life insurance and those that did have high socio-economic status and were mostly men. In the Seven Country study there was no clear relationship of relative weight or skinfolds with coronary heart disease (CHD). In most of the other 13 classic prospective studies of risk factors for CHD reporting 1963 to 1972 overweight (assessed in different ways) was not a risk factor or only under certain conditions [38]. Ancel Keys was critical of the life insurance companies biased samples and inadequate entry examination data [39]. Then, in the later prospective study in Gothenburg neither body mass index (BMI) nor sum of skinfolds predicted CHD, stroke or death in men, but waist/hip circumference

did [40]. Abdominal or central obesity is now one of the criteria for diagnosis of the “metabolic syndrome” [41].

SLOW RECOGNITION OF OBESITY IN DIABETES

When insulin became available for treatment of diabetes around 1923, physicians were preoccupied with insulin usage, hypoglycaemia and strict dietetic control of carbohydrate and sugar intake. The focus was on those diabetic patients prone to develop ketoacidosis. Joslin, however, as early as 1921 produced impressive evidence that “diabetes is largely a penalty of obesity” [42]. In his 1,000 cases, 10% were underweight (they were mostly young), 16% weighed within 5% of average normal weight and 74% were overweight (+6 to +71% over). But textbooks of medicine barely mentioned obesity in their chapters on Diabetes. Osler’s textbook gave obesity 2 lines in 1929 [43] and 5 lines (out of 18 pages) in 1942 [44]. Price’s textbook in 1930 [29] gave a line to obesity (as one of four exciting causes, another of which was anxiety).

In 1938 Newburgh drew attention to the common type of middle aged diabetic patient who, when able to lose weight lost all symptoms of diabetes, glucose in the urine and hyperglycaemia [45]. Sir Harold Hinsworth in 1939 hypothesized [46] that in diabetes the diminished ability of the tissues to utilise glucose could be either due to insufficient secretion of insulin OR to insensitivity to insulin. When Yalow (2) and Berson (1960) found how to assay plasma insulin with radioimmunoassay – that they had invented – [47] the two types of diabetes became much clearer. Type 2 is more common, due to insulin resistance and closely related to obesity.

By 1953 obesity was placed in the middle of the Diabetes chapter in Davidson’s new textbook of medicine: “The majority of patients who first develop diabetes in middle life are obese...In obese diabetics the essential principle is to impose a restriction of both carbohydrate and calories in order to bring the weight down to standard levels. This may be all that is needed to stop the glycosuria” [30]. Confirmation of the close association of obesity and diabetes came from Kelly West’s epidemiological study in 11 countries [48] and the American Cancer Society’s long-term prospective study of 750,000 men and women [49].

ECONOMIC DEPRESSION AND WAR

Obesity was replaced by under- and malnutrition in the concern of nutrition researchers in the 1930s when there was economic depression and widespread unemployment and the 1940s, the time of World War II with massive destruction in Europe and S.E. Asia and starvation over Europe [50].

In Britain, with well designed food rationing and widespread national nutritional advice the population was just adequately fed and nourished, and distribution was equalised. There were careful records of food moving into consumption; but measurements of body weight were rare. They were lower than in North America and there was little “middle aged spread” [51]. In continental Europe there was partial starvation in the 1940s [52]. This scarcity of calories had two health benefits: a dramatic decline in deaths from diabetes (in older people) in Britain that Hinsworth showed to relate to reduced fat consumption [53], and less dental caries in children. By 1946 exciting nutrition research was on malnourished children in Jamaica, Guatemala, Kampala, Cape Town etc. In Britain after the success of the rationing system and with (nearly all) the essential nutrients discovered it could have seemed

(2) Nobel prize, 1977

that most of the scientific problems with nutrition had been solved. Oxford University refused a grant to establish a department of human nutrition because its experts advised that all nutritional problems would be solved within 10 years and there would be nothing left to study [54]!

SOME OBESITY RESEARCH CONTINUED IN THE 1950s AND 1960s

Jean Mayer 1953 - 1955 proposed and developed the GLUCOSTATIC theory, that a fall of blood or tissue glucose stimulates appetite [55]. The sensitive tissue might be the ventro-medial nucleus (VMH) of the hypothalamus, which has an affinity for glucose. Injection of (toxic) gold thioglucose damages the VMH and leads to hyperphagia and obesity in mice.

Stunkard describes his own disappointments as a researcher doing human experiments to test the glucostatic theory [56]. The control of food intake is more complex.

Mellinkoff at about the same time proposed appetite signals from PROTEIN or amino acids [57]. Dietary protein induces satiety in the short term, and a diet of low protein foods leads to increased appetite for protein-containing foods [58] in subhuman species as well as humans [59]. This principle is used in some contemporary weight-reducing diets, such as the CSIRO Total Wellbeing Diet [60].

Kennedy (in Britain) in 1953 proposed a system whereby the amount of BODY FAT somehow signals the hypothalamus to control energy intake or expenditure and tends to maintain body fat and weight [61]. Forty years later, a mechanism for this system was provided by the discovery of leptin (see below).

A portable gas meter that takes small samples of expired air, the Max Planck respirometer was developed in Germany around 1950. It weighed only 3 kg, is worn as

a rucksack and could be used to measure energy expenditure of active moving people, which was not possible with the Douglas bag. Durnin and Passmore measured energy expenditure of industrial workers, coal miners, squash players and many other activities. They combined their results with literature findings in a 1967 book *Energy, Work and Leisure* [62]. Its information is valuable for people wanting to control weight with exercise, though the energy expenditures of blue collar workers are now much less than they were in the 1960s.

Stunkard appears to have been first to find a clear relationship between SOCIAL CLASS AND OBESITY [63] in a population sample of 1660 adults in Midtown Manhattan, NYC. Obesity occurred in 30% women of low socio-economic status, 16% of those in the middle status and only 5% of the upper status [64]. There were also differences in obesity by ethnic background. Trends in men were less marked in the same direction. In a smaller sample from two contrasting general practices in London, Silverstone et al [65] found low social class women had twice the prevalence of overweight (not obesity - the paper's title is misleading). In older men the highest weights were in the middle class, probably because of more physical activity at work in the lower SE group. In Tecumseh, Michigan sum of 4 skinfolds decreased with increasing education or income level in women but it increased with income level in men [66]. These and subsequent reports from different parts of the world are important for treating and preventing obesity, because they show where efforts and resources should be concentrated.

NEW APPROACHES TO MANAGEMENT

In 1959 Stunkard looked into the success of obesity clinics. In a large teaching hospital only 12% of very obese people were able to lose 20lb (or 10kg); 28% never returned after

the first visit and 2 years after the end of treatment only 2 patients had maintained their weight loss [67]. This was surely a stimulus to try and improve on the management at that time!

One approach was Therapeutic STARVATION. In the 1960s several groups reported this drastic treatment. Drenick et al starved 11 obese patients in hospital in Los Angeles [68] for 12 to 117 days. Thomson et al in Glasgow starved 13 patients in hospital for 25 to 249 days [69]. All they took by mouth was water and multivitamin tablets (containing 4 or 6 vitamins). Hunger was not as distressing as in partial starvation. There was some ketosis but no ketoacidosis. Plasma uric acid increased and blood pressure fell. But it was surprising how tolerable were the side effects and how large the losses of weight.

In 1969 a young woman (20y) fasted for 210 days and her weight declined from 118 to her ideal weight 60 kg. On the 8th day of refeeding she died of ventricular fibrillation [70]. Post mortem showed fragmentation of cardiac myofibrils. Correspondence opinions considered that too much lean body mass had been lost, that it was dangerous to lose more than 33-40% of the original body weight and monitoring of potassium status might have been inadequate. Instead of total starvation, requirement amounts of protein (about 30g protein or 120 Kcal) should be provided to slow loss of lean body mass.

Later a liquid protein very low calorie diet (VLCD), with the protein a collagen hydrolysate was publicised by a book "The last Chance Diet" and over 100,000 people in USA used this product in 1976. 17 people died from ventricular fibrillation and it was thought that the poor amino acid pattern of the protein (hence biological value), or potassium depletion were probably responsible [71, 72].

A British COMA subcommittee concluded, inter alia, that VLCDs are not suitable for people with heart disease, pregnancy or

lactation and should not be used beyond 4 weeks [73].

Meanwhile Baird and Alan Howard had tested different low calorie supplements with a starvation diet and found that addition of 30-45g carbohydrate would further increase the protection of nitrogen loss achieved by 30g per day good biological value protein [74]. With the addition of all required vitamin and inorganic micronutrients this was patented in the USA as the Cambridge diet (330 Kcal/day) and is still widely used today.

The second approach was to bring in the help of PSYCHOLOGISTS. RB Stuart introduced behaviour therapy for obesity in a paper in a specialised journal far from obesity doctors in 1967 [75]. The principles start: 1. Eat in one place, 2. Buy non fattening foods, 3. Look for and change times of your own weakness, 4. Train others to help you curb your eating, 5. Make small portions appear large and make second helpings hard to get, 6. Take steps to avoid loneliness, depression, hunger, 7. Always eat four regular, planned meals a day... 11. Build in some pay-off for following every step of this program [76].

In an early controlled trial Pennick compared weight reduction results between experienced obesity specialists and an inexperienced doctor using a behaviour modification (BM) script. BM was much more effective [77]. In another controlled comparison of an appetite suppressant drug and BM, weight fell faster on the medication, but by 12 months weight was lower in the BM group – and this treatment had cost less [78].

Stuart moved to be psychological director of Weight Watchers (which had started as a small organization in 1962) [79].

Behaviour modification is now incorporated in all orthodox management programmes for obesity and a recent article in Scientific American [80] concluded that programmes based on behavioural principles are more likely to help people take and keep the weight off than other approaches.

There have been three other approaches:

- Pop diets [81] come and go. At a 2010 exhibition at the Wellcome Institute in London there was a high bookcase with about 500 different books, each presenting their own reducing diet!
- Then there are commercial programmes, some with lecturers, some with products, some following a book. Published controlled trials are rare. The BBC, with nutrition and dietetic academics ran a comparison of four British programmes with a control group. The best of these, Weight Watchers clients lost (mean) 6.6 kg in 6 months [82].
- Surgery is obviously only indicated for people with severe obesity, but they have greater surgical risk than thin people. The first procedure used, from 1956 was jejunoileal bypass [83]. About 36 cm of the proximal jejunum was anastomosed to the last 10 cm of the terminal ileum (end to side). The distal part of the divided jejunum was closed, leaving most of the small intestine as a blind loop. The intended malabsorption and sustained loss of weight were achieved but there were serious side effects beyond expected diarrhoea: hypoalbuminaemia, many nutritional deficiencies, arthritis, even liver failure. Weight loss was due to reduced food intake as well as malabsorption [84]. For some patients the by-pass had to be reversed. Hocking et al reviewed 100 of their cases 5 years after surgery: only half had unquestionably benefited. They and other surgeons stopped performing this operation [85].

And there are also people who lose weight without any professional or commercial advisers. The US National Weight Control Registry was established in 1994 for those who have lost 30 kg and maintained at least half of it for 5 years. Of the 784 in the register (in 1997), 45% said they had done it on their

own [86]. By 2005 there were 4000 in the register [87].

A UNIVERSAL STANDARD WEIGHT FOR HEIGHT

After controversies over revision of desirable weights and (undefined) frame sizes, in the USA and relative weight and Broca's index, used in Europe, these and other measures were quietly replaced across the world by weight (kg)/height(in metres)², the rediscovered "Body Mass Index" (BMI), first proposed by the Belgian astronomer, Quetelet around 1871. Keys (1972) had concluded that, in the absence of skinfold measurements, BMI provided the most satisfactory index of obesity, based on height and weight [88]. The DHSS/MRC report on obesity research (1976) calculated that 120% of US "desirable" weight would be a W/H² of 27.5 to 29.9 for men of medium to large frame size, and 27.0, to 29.5 for women [89]. Garrow sensibly rounded the values in his practical 1981 book [90], so a W/H² above 30 is taken to mean obesity in men and women. The Australian NH&MRC adopted the BMI in 1985 and by 1990 it had been adopted by the WHO [91].

LUXUSKONSUMPTION

This is the hypothesis that some people can waste calories as heat and not put on body fat if they eat more than they require. Dr Reg Passmore was a possible example. A tail coal made for him at 21 still fitted at age 65 [92]. The term had been introduced by Neumann in 1902 [93]. In 1967 Miller and Mumford [94] reported experiments in which they and two sets of students ate excess calories for weeks and did not put on the expected weight gain. Reviewing this and other work, Garrow found it impossible to conclude either that thermogenesis, or luxus consumption, does occur in man, or that it does not [16].

Rats only eat to requirement, but when provided with “cafeteria food” instead of chow they overfed in Rothwell and Stock’s experiments [95] though they did not gain the body fat expected. They showed increased activity of brown adipose tissue (BAT). However it seems unlikely adult humans have enough BAT for this to make more than a small percentage change to overall energy balance [96]. Later detailed overfeeding human studies in Cambridge did not show diet-induced thermogenesis [97].

CALORIES (INCOMPLETELY) REPLACED BY JOULES

In 1972 the Royal Society in Britain and several other scientific academies agreed that the Calorie should be replaced by the Joule for measuring energy metabolism and energy

FOOD INTAKES OF OBESE PEOPLE

There have been repeated reports that obese people do not necessarily eat more than average (eg. ref [99]).

WPT James et al measured the resting metabolic rate (RMR) of 69 obese patients (mean BMI 37) with a ventilated hood system. Almost all of them had a rate, in MJ/24hrs. higher than that of age-matched normal weight subjects [100], but when expressed in the traditional way, per surface area most of the obese patients RMR/m² were in the normal range. The amount of RMR above expected normal was proportional to their excess body weight. When some of the patients successfully lost weight their absolute RMR fell to normal. Lean body mass, from 40K measured in a whole body counter was increased in the obese patients, in comparison to normal weight volunteers,

The doubly labelled water method is the only objective way to estimate energy expenditure over several days. The subject drinks water containing heavy hydrogen, ²H and heavy oxygen, ¹⁸O. The hydrogen mixes with body water; the oxygen goes into produced CO₂ as well as body water. The difference in the decline of ¹⁸O minus ²H in the urine samples indicates CO₂ production, and hence energy expenditure.

Neither isotope is radioactive. They have to be measured with a sensitive mass spectrometer. The ¹⁸O oxygen isotope is very expensive.

value of foods. Most countries followed suit. Scientists may have to use official SI units in the laboratory but it is unfortunate that the kilojoule and megajoule were imposed on ordinary people because, they are inconvenient sizes for foods, and there is bilingualism. Much nutritional information comes from the USA, where the public has held on to the Calorie. Thomas Moore’s reasoned objection [98] was largely ignored in Britain.

and this contributes to RMR.

The doubly labelled water (DLW) method [92] is one of the greatest recent discoveries in nutrition. With DLW a group in Cambridge reported in 1986 that [9] obese young women had energy expenditure of 10.2 MJ/day, while it was 8 MJ/day in [13] lean women [102]. Self recorded energy intakes were close to DLW energy expenditure in the lean subjects, but in the obese, they were only 66% of the DLW value. Since energy intake must balance energy expenditure in people at stable weight, it was at last clear that statements of food and energy intake – which

are essentially subjective – are likely to be under-reported by obese people [103].

CLINICAL GENETICS

It is a popular observation that overweight tends to run in families. From 1986 ingenious large human studies were published using Mendelian methods. Stunkard et al investigated 540 adults who had been adopted in Denmark (where there is a national adoption register). There was a strong relation between their weight class and the BMI of their BIOLOGICAL parents, but not with their adoptive parents who they grew up with [104]. Bouchard et al overfed 12 pairs of young adult male monozygotic twins for 84 days under controlled conditions. There was 3 times less variance in weight and fat gain within pairs than among pairs [105]. BMIs of middle-aged identical twins that had been reared apart had high interpair correlation, almost as high as those reared together [106]. Obese identical twin women lost weight on a very low calorie diet for 1 month in a hospital metabolic unit in Prague. Losses (ranging -5.9 to -12.4 kg) were highly correlated within the twin pairs [107]. There seem to be many genes responsible, working in different ways. They wait to be precisely implicated, by the new techniques of nutrigenomics [108]. The effect of genes identified so far is modest [109].

UNEXPECTED SURGE IN OBESITY FROM 1980

Unpredicted, unexplained and not noticed until the early 1990s, the prevalence of obese (BMI >30kg/m²) adults increased alarmingly in major countries in the 1980s & 1990s.

Long series of numbers from national measured samples were most adequate for the USA (Fig 1). In Australia an increase in obese adults in the late 1980s was captured by three surveys in major cities by the

National Heart Foundation. For men prevalence of obesity was 7.2% in 1980, 6.4% in 1983 and 9.3% in 1989. In women it was 7.0% in 1980, 8.7% in 1983 and 11.1% in 1989 [102, 103, 104]. The rate continued to increase to 17% in men and 20% in women by 2000 [115].

Figure 1: USA per cent Obese (BMI>30kg/m²)

	Men	Women
NHES, 1960	10	15
NHANES I, 1971-4	12	15.5
NHANES II, 1976-80	12.5	16
NHANES III, 1988-94	19	Almost 25
NHANES, 1999-2000	27	34
NHANES, 2007-8	32	35.5

Based on [110] and [111], numbers rounded.

In the UK obesity increased from 1980; comparable national sample measurements before this are not available. Between 1980 and 2000 the percentage of obese men increased from 6% to 22% and obese women from 8% to 23% [116].

Prevalence’s of obese children increased in the same period in some countries [116], [117] though there are fewer long-term national measurements, and the lack of a common standard for defining obese children makes this difficult [118].

Around the whole world data have accumulated that overweight and obesity have increased in almost all countries [118, 119, 120]. This must be due to environmental changes; genetic mutations could not occur so quickly and in so many places.

DIABETES

The immediate impact of this epidemic of overweight and obesity on disease risk is not as severe as it would have been in the 1950s. Hypertension and hypercholesterolaemia are now separately controllable by medications, and in the USA and Canada the relative risk of mortality is no longer increased in overweight people (BMI 25 to 30) [121, 122]. However death rates from diabetes increased by 33% from 1980 to 1996, while stroke and cardiovascular disease mortality were decreasing by about the same amount in the USA [123]. The prevalence of diabetes has increased worldwide [124].

Final proof of the causative association of type 2 diabetes with overweight came from two large important human trials of lifestyle intervention in Finland [125] and the USA [126, 127] in obese people with impaired glucose tolerance. The intervention groups in these randomised controlled trials received regular personal advice from a nutritionist and an exercise trainer. They lost around 5% of body weight, ate less saturated fat and more dietary fibre and increased regular physical exercise. Lifestyle intervention in both trials resulted in a 57% reduction in the incidence of diabetes in these high risk people. In the American Diabetes Prevention Program lifestyle intervention was significantly more effective in preventing diabetes than metformin [127].

SCARCITY OF EFFECTIVE, SAFE DRUGS FOR OBESITY

In 1998 George Bray, doyen of American obesity physicians, wrote a sad editorial [128]: “The history of drug treatment of obesity is indeed strewn with catastrophes”. The pharmacologic treatment of obesity was (probably still is) analogous to what was available for hypertension in 1958, before chlorothiazide.

Thyroid extract was first used in 1894 but it became clear that it could be harmful unless there was evidence of hypothyroidism. Amphetamine (benzedrine, dexedrine) was the first appetite suppressant, an indirect-acting sympathomimetic amine. It was the drug for obesity in the first (1953) edition of Davidson’s textbook of medicine [30], but by the mid 1970s concerns were increasing because of the risk of dependence and psychotic states, as well as insomnia and increased blood pressure. “Speed” is illegal today.

It was replaced by modified phenylethylamines, diethylpropion (Tenuate), phentermine (Duromine) and phenmetrazine (Preludin) in the 1960s, which had less cerebral stimulating activity. They were in turn replaced by fenfluramine. This still has the phenylethylamine skeleton but is modified by CF₃ on its benzene ring. It has serotonergic, not catecholnergic actions and is not a cerebral stimulant. In 1997 fenfluramine (Ponderax), dexfenfluramine (Adifax) and phentermine were the only appetite suppressants in the British National Formulary. They were recalled that year because of reports of primary pulmonary hypertension [129] and mitral valve disease [130] associated with their use. There is now no safe appetite suppressing drug on the market. Then sibutramine came and went [131].

With a different mode of action, Orlistat (Xenical) inhibits pancreatic lipase, so reduces fat absorption and acts outside the main body. Adverse effects include oily stools, faecal urgency, flatus.

LEPTIN AND GHRELIN STIMULATE BASIC RESEARCH

At about the time fenfluramine was withdrawn, obesity research was excited by announcement in quick succession of two new hormones that expand the already

complex knowledge of control of energy balance.

Discovery of **leptin** at the end of 1994 [132] stimulated more than 600 papers in four years, moving modern molecular biology into the field of obesity research [133].

Leptin is the protein expressed by the OB gene, the gene missing in OB obese mice. It is synthesized in white adipose tissue and suppresses food intake. This is the lipostatic hormone predicted in 1953 [61]. Injected leptin reduces weight and body fat in OB obese mice and had a modest weight reducing effect in humans. It was expected that most obese people would have reduced plasma leptin levels, but this proved incorrect; they appear to have resistance to leptin in the hypothalamus, where it normally inhibits NPY and AgRP synthesis.

Humans with very low leptin and obesity are very rare, having a recessive mutation in the leptin gene [134]. Their obesity is severe, starts in childhood and responds to continuing leptin injections.

In 1999 a new peptide that affects appetite was discovered in the stomach, Growth Hormone Releasing Endogenous Ligand – **Ghrelin** [135]. Very soon much more was found out about it. Ghrelin is produced by endocrine type cells in the submucosal layer of the stomach. It has 28 amino acids and the active form is acylated near one end with n-octanoic acid. It is secreted when animals and people are hungry and plasma levels go down after meals. In the hypothalamus it stimulates the synthesis of NPY and AgRP. Plasma ghrelin is very high in Prader-Willi syndrome [136].

It appears that ghrelin acts mainly as appetite stimulant in short term regulation of appetite, while leptin has a longer term controlling role. Three other gut hormones are secreted lower down the gastrointestinal tract and all act to slow or stop eating. **Cholecystokinin** (CCK) was discovered and named by Ivy and Oldberg in 1928 [137]. Its

satiating activity has been known since 1978 [138]. It is secreted in response to a meal by the upper small intestine. **Glucagon-like peptide 1** (GLP-1) secreted by the distal small intestine was first shown to reduce appetite in 1996. **Peptide YY3-36** (PYY) is secreted by the large intestine, triggered by fatty acids, fibre and bile acids. Its post-meal satiety effect has been studied since 2002. Plasma PYY levels may be lower in obese people.

In the last decade, along with these gastrointestinal hormones, research on the biochemistry and functions in the hypothalamic nuclei has intensified.

Peripheral hormones acting on the hypothalamus are insulin, adiponectin (from adipose tissue, discovered 1995), leptin, ghrelin, CCK, GLP-1, PYY and vagal efferents.

Inside the hypothalamus [139], neuropeptide Y (NPY) and agouti –related peptide (AgRP) stimulate appetite. POMC (pro-opiomelanocortin) and CART (cocaine and amphetamine-related transcript) are inhibitory. The arcuate, ventromedial and lateral nuclei and others are differently involved and beyond them the nucleus of the solitary tract, and the reward center, the nucleus accumbens.

Food intake is of course also influenced by the higher cortical centers. All the messenger proteins and neurotransmitters have multiple chemical forms and interact with one another and with the other endocrine systems. The comprehensive review by Katie Wynne et al. has 27 pages and 450 contemporary references [139]. John Blundell has specially studied eating regulation, satiation and satiety in humans in the last 20 years (3).

He reviews food intake behaviour from the peripheral side [140] As Time magazine put it “understanding a single biological unit – the heart, the lungs – is hard enough. Under-

(3) **Satiation** is the complex of factors that terminate an eating episode.

Satiety (or between meals satiety) is the processes that inhibit further eating in the postprandial period [140].

standing a process as complex as appetite – one that involves taste, smell, sight, texture, brain chemistry, gut chemistry, metabolism and most confounding of all, psychology – is exponentially harder – but science is trying” [141].

It will be difficult to find a drug to block one of the orexigenic (appetite stimulating) agents because NPY null mice have normal body weight and fat [142] and ghrelin knockout mice have similar body weight gain and food intake to wild-type mice [143].

WHY HAS THE OBESITY EPIDEMIC HAPPENED?

There are three possible immediate causes of the rising prevalence of obesity since 1980:

- a) Energy intakes exceeding expenditure,
- b) Less energy expenditure,
- c) Less smoking

The difficulty allocating blame is that we have to rely on national estimates and in each country there should have been a major increase of the population’s energy intake or decrease of energy expenditure related in time to the steepest increase in overweight and obesity.

a) Reports on national food consumption are based on crude figures and assumptions. There is even less accurate recording of the many types of food waste, so these estimates do not record what people actually eat. An example of this is the paper by Swinburn et al. [144] “Increased energy supply is more than sufficient to explain the US epidemic of obesity”. An alternative method uses individual intakes. Farouhi et al. report on 89,432 men and women in 6 combined west European EPIC cohort studies [145]. No significant association was found between fat intake (amount or type) and subsequent weight gain. But here the weakness is that fat people under-report; food frequencies are better for estimating quality rather than quantity of

diets and fat intake is the macronutrient most likely to be under-reported.

There have been many claims that some parts of the total food supply have contributed to overeating: fast food outlets (McDonalds and others), sugar-rich carbonated beverages (Coca cola and others), more advertising of foods dense in energy, cheaper energy-dense foods (high in fat, sugar and salt), increased portion size, increased plate size and loss of skills in domestic cookery. It is also very possible that anxieties in people with low socio-economic status lead to overeating. Probably all have contributed to some extent.

b) That energy expenditures have declined is more certain. The largest contribution must be the enormous increase in motorcars, hence reduced walking or cycling and carrying. In all aspects of domestic and professional life there are now labour/energy saving machines. A few examples: lifts, automatic doors, washing machines, mobile phones, power tools, chain saws, mechanical harvesters, cranes, milking machines, bar code scanners, robot machines in factories, diggers, even golf buggies.

Television viewing and computer use have replaced more active domestic and office activities. Hours per week of television viewing have been associated with weight gain [146].

An argument for reduced energy intake was well made by Andrew Prentice and Jebb [147]. Percentage of obese people in Britain increased steeply from 1950 to 1990 and cars (per household) went up in parallel, but energy intake appears to have declined slightly. Energy intake here was from the National Food Survey. This is a survey of household food intakes, unique to Britain, continuous from 1940. The weakest part of this survey is Eating Out which has been added from 1994 [148].

To increase energy expenditure is harder work than eating less as a way of losing

weight. Derek Miller used to upset people by his (reasonable) estimation that to lose 1lb of body fat (0.45kg) the activity equivalent is to walk from London to Brighton (52 miles; 83km) [149]. In weight reduction the time scale is much shorter and contrasts with the gradual process of putting on weight over a number of years. The American obesity epidemic, in absolute terms is caused by most people gaining small amounts of weight slowly: around 4kg over a generation [150]. If all the weight is fat this amounts to + 36,000 Kcal over 3,650 days or + 10 Kcal a day. The energy expenditure equivalent is 2.5 minutes walk per day. If the weight was doubled or the time halved, 5 minutes walk/day.

c) Tobacco smoking. The obesity epidemic coincided in time with the decline of smoking in Western countries. Smokers weigh 2 to 6 kg less than non smokers and if they manage to stop smoking they put on weight [151]. Nicotine, the active ingredient in tobacco smoke, suppresses appetite and also appears to increase metabolism. The percentages who have quit smoking have not been large enough to explain more than a part of the obesity epidemic.

WHAT IS THE BEST WEIGHT-REDUCING DIET?

The principle of a conventional reduced energy diet has been to target visible fats and sugar and retain the parts of the ordinary diet that supply most essential nutrients. Davidson's textbook (1953) recommended for obesity a diet of 1,000 calories with 100 g carbohydrate, 60 g protein and 40 g fat (C/D/F 40,24,36% energy) [30]. This continued through 16 successive editions. Though the fat is about half that in a usual diet it is not proportionately low, which makes possible a range of allowed foods. The WHO obesity report (2000) [109] recommended a reducing diet with 55-60% carbohydrate, 15% protein and 20-30% fat, which

is absolutely and proportionately low in fat. These two diet plans illustrate the range of conventional weight-reducing prescriptions.

There have been numerous named special diets for obesity. They have been ephemeral and not had major impact on the scientific and medical establishment. But **Dr. Atkins Diet Revolution** first published as a paperback in 1972 [152] became a best seller. The principle was a very low carbohydrate, consequently high fat and protein diet. Total carbohydrate should be only 20 to 40 g per day. This causes ketosis and loss of appetite. The Atkins diet was condemned by the American Medical association [153] and the Australian NH&MRC and a textbook of nutrition [92]. It would raise (LDL-) cholesterol and ketosis is not healthy. But many ordinary people in the USA and beyond found this diet plan helped them lose weight. The food industry reacted, Atkins wrote another book (1992) [154] and nutrition researchers were obliged to organise randomised controlled trials.

Five well conducted trials reported from 2003-9, with subjects ranging from overweight to severely obese. Atkins diets were compared with low fat and (in two trials) with other popular diets. Those taking Atkins diets lost more weight at first, but by 6 months [82] or by 1 year [155, 156] weight loss was not significantly different from the low fat diets. In a fourth trial there was less weight loss at 1 year with Atkins than with Weight Watchers, Zone or Ornish diets [157]. In these trials LDL-cholesterol fell less on Atkins than on conventional weight loss regimes but HDL-c was higher and triglycerides were lower on the very low carbohydrate diets.

A large trial (2009) in Boston and Baton Rouge (Louisiana) compared four weight loss diets - high or moderate protein, usual or low fat [158]. 811 people started and 80% completed 2 years. They were given diet plans, offered regular group sessions and

periodic individual sessions. Subjects looked after their own food. They were asked to keep daily diet diaries and had 3 telephone interviews at 6 and 24 months.

They lost an average of 6 kg at 6 months and then tended to regain weight. The completers lost (mean) 4kg over 2 years. There were no significant differences in weight loss between the four diet groups but many did not achieve or maintain their prescribed protein or fat intakes. Attendance at sessions had a strong association with weight loss: Participants who came to two-thirds of the sessions lost 9 kg of weight.

At about the same time another large trial [159] was carried out in 8 European countries, the Diogenes study (2010). Design, management and results were different from the American trial. Over 26 weeks, high protein and low glycaemic index diets reduced weight regain in 773 adult subjects who had first lost 8% of initial weight (with a 3.3 MJ (800 Kcal) diet in 8 weeks).

Here the high protein group had significantly higher urinary nitrogens. Diogenes showed that the satiating effects of increased protein (as in Atkins diets) could be effectively combined with moderate carbohydrate intake, avoiding disadvantages of high fat diets.

In these large weight loss trials that compared the efficiency of different diets most participants did not actually eat their prescribed diets and over time more subjects dropped out. Analysis by standard "intention to treat" can have little meaning, but those who persisted with close to their prescribed diet lost most weight. Astrup and Pedersen admit they would not personally like to be enrolled in a randomised controlled trial with the prospect of eating the same extreme diet every day for 12 months without any deviation [160].

Katan underlined the conclusion of Sacks et al [158] that "behavioural factors rather than macronutrient composition are the main

influences on weight loss". Even these highly motivated, intelligent participants who were coached by expert professionals could not achieve the weight loss needed to reverse the obesity epidemic... We do not need another diet trial; we need a change of paradigm".

As an example he points to the EPODE programme that started in two small French towns and is spreading. EPODE is Ensemble, *prévenons l'obésité des enfants* (together let's prevent obesity in children). Everyone in a town, from the mayor to shop owners, school teachers, doctors, pharmacists, caterers, restaurant owners, sports associations, the media, scientists and various branches of town government joined in an effort to encourage children to eat better and move around more [162].

The small weight losses with expert professional help have confirmed that for obesity prevention is much better than cure, and health professionals cannot do the prevention on their own [163]. We need the active cooperation of the whole community. In the Foresight report, commissioned by the UK Government [164] are Obesity System Maps. The full generic map has 104 variables in 7 groups: social psychology, food production, food consumption, individual psychology, physical activity environment, individual physical activity and physiology – all interacting ultimately with ENERGY BALANCE in the centre. The 104 individual variables include ambient temperature, convenience, cost of food ingredients, cost of physical exercise, force of (food) habits, food abundance, food literacy, lack of time, level of occupational activity, level of recreational activity, market price of food offering, NEAT (non-exercise activity), palatability of food offerings, parental control, perceived inconsistency of scientific messages, predisposition to activity, reliance on labour-saving devices, safety of unmotorised transport, societal pressure to consume, stress, walkability of the living environment, &c.

BARIATRIC SURGERY RETURNS FOR GROSS OBESITY

After decades in obscurity, bariatric surgery has emerged as an effective treatment for type 2 diabetes [169]. For someone with gross obesity and diabetes medical treatment is difficult and sufficient weight loss very slow and unlikely. Modern bariatric surgery is achieving weight loss of 20% or more with remission of the diabetes in many patients. The International Diabetes Federation considers it is a serious option if BMI is 35 kg/m² or more [166].

The Roux-en-Y gastric bypass was introduced by Mason in the 1960s [167]. A small fundal portion of the stomach is separated from the body of the stomach (which is closed) and anastomosed to a loop of jejunum. Alternatively the stomach can be reduced in volume by banding. These procedures can often be done nowadays using keyhole techniques. Operative mortality is only about 0.1 to 0.3 % [166] and over 6 years mortality in a large American series was lower than in controls with similar BMI and age [168]. With gastric bypass, ghrelin and GIP levels are reduced [169], the opposite of their increases with diet-induced weight loss. The UK National Bariatric Surgery Registry reports that costs of surgery are recouped in 3 years, by savings of treatment of diabetes and cardiovascular disease [170]. Of course the most cost effective policy is to make sure that people do not get to the stage of needing surgery in the first place.

COMMENTARY

The basic research behind obesity is Physics – energy balance, energy content of foods, the laws of thermodynamics, conversion of chemical energy to heat and movement. Yet people's intake and expenditure of energy happens in the fields of Psychology and Sociology. Overweight and underweight are routinely assessed by weighing a person, with

adjustment for height, usually kg/metres² (BMI) since 1985. But this doesn't tell how much of the weight is fat, how much are muscles.

It is remarkable that most adult people maintain an almost constant weight over long periods of time without calculating their energy balance. Research is showing powerful and complex mechanisms for adjustment of appetite and energy expenditure, involving especially the gut and the hypothalamus. Because of this, loss of weight is less than the expected 1.0 kg for eating a deficit of 7,000 calories [121].

Some genetic control is obvious from Mendelian human studies, though the main individual genes at play await discovery. When people take in less energy than they need, their metabolic rate goes down faster than their body weight – which helped our species survive food shortages.

There are two concepts of obesity. One is social (and varies with the society); the other is medical, the BMI at which risk of disease starts to increase. Hippocrates observed that very fat people are apt to die younger than slender people. In the first half of the 20th century life insurance actuaries found that above a weight-for-height corresponding to a BMI of 25kg/m² mortality started to increase. The WHO classified BMIs between 25 and 30 as "overweight" with "obesity" above 30 kg/m². However in the last years of the 20th century (in USA and Canada) BMIs 25 to 30 were not associated with increased mortality, though there was more diabetic morbidity.

There was an unexpected surge in overweight and obesity starting around 1980 in developed countries and beyond. Faced with this, doctors and dietitians find it very difficult to treat obesity. Physicians are accustomed to treat most complaints with medication, but obesity stands out as having no effective safe pharmacotherapy. Dietitians are accustomed to treat patients with diet plans – how much to eat of which foods at

each meal, but it has become clear that most obese people cannot manage to follow their diet prescription. "Doctor has put me on a diet", but the diet is on paper, not in their stomach. With obesity it's not the health professional that does the treatment, it's the fat person themselves – and some people can achieve substantial weight reduction without professional help. They have great difficulty, unfortunately in visualising the calorie value of foods and drinks as easily as they can see their dollar value. We are all very confused by Calories, kilocalories, kilojoules and megajoules and whether these are per 100 g (even kg) or per usual serving.

When type 2 diabetes is part of the diagnosis, weight reduction is more than cosmetic and preventive, it is a major part of the medical management because weight loss alleviates and can cure diabetes. Diabetologists in the second half of the 20th century focused on different types of insulin and drugs and neglected dieting. They had forgotten that Joslin showed back in 1921 that "diabetes is largely a penalty of obesity".

Many strategies have been tried to help with weight reduction: very low calorie diets (VLCDs); many celebrity named diets; commercial diet instructors; behaviour modification; low fat, or the opposite – low carbohydrate "Atkins" diets. The Cambridge diet looks the best of VLCDs; Weight Watchers have performed best in trials of commercial diets. Behaviour modification was shown, round 1970, to help more than usual advice and some of its methods are now commonly used. In Atkins (type) diets the extra protein provides satiation and some thermogenic effect. Several large trials have found rather more weight loss with low carbohydrate than with other low calorie diets in first months, but not later. It is very hard for anyone to eat the same weight-reducing diet month after month, even with trained support. So what was eaten in the trials published in high impact journals was not actually the planned

food prescription. The only doctors who can directly TREAT obesity are bariatric surgeons. With advances in surgery, gastric banding and gastric bypass are now serious options for very obese people with diabetes.

The food and drink industries have been the background of the obesity epidemic and so has agriculture's efficiency in making foods much cheaper. Fogel⁽⁴⁾ has shown these achievements over the last one & a half centuries made major contributions to longer life expectancy and economic growth [172]. The recent overshoot of society's energy balance now requires policies and work by sections of society beyond the health profession. General practitioners should, however, measure and record weights regularly and advise overweight patients how to minimise further weight gain.

Obesity, like tetanus and poliomyelitis, is much easier to prevent than cure. Lack of exercise at work, in transportation and in recreation is part of the explanation for the obesity epidemic. Health professionals cannot correct it on their own. Town planners, architects, developers and schools should all work to make it easier for people to get recreational exercise and to move more by walking and cycling. Caterers at all levels should be seriously aware of the calorie contents of the foods and drinks they are offering.

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⁽⁴⁾ Nobel prize for Economics

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