

# Obesity — the inevitable penalty of civilisation?

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The modern inhabitants of 17th century cottages are reminded of the way in which the human form has changed every time they hit their head on a beam or stoop to pass through a doorway. The secular changes in the height of the Japanese over the past 50 years are an accelerated version of the same phenomenon. These are changes that we accept as being permanent and natural. We talk of 'reaching our genetic potential' in response to better nutrition, and view the changes as beneficial, since height is positively associated with health and social status. Are we now on the verge of another anthropometric transition — this time in weight? The evidence suggests that we are, but that this time the trend will be far from beneficial.

Data stretching back to the turn of the century show that the average body mass index ( $BMI = \text{weight (kg)} / \text{height} \times \text{height (m)}^2$ ) has increased steadily in the UK (where the best data are available) and other affluent countries. Such changes are graphically illustrated by the fact that Boeing's aeroplane designers have had to increase the assumed weight of each passenger by over 20 pounds since their first airliners took to the skies. Designers of clothes, and beds and chairs and cars, are all acknowledging that this increase in girth is not a temporary deviation in the statistics; it is here to stay and shows every sign of accelerating rapidly.

If left unchecked the future effects on society could be profound. In this book, Gill quotes Rose's statistical demonstration that when the mean weight of a population rises there comes a point when there is a sudden and disproportionate rise in the number of people who are seriously obese. The US passed this critical point some years ago and now has subgroups of the population (black, Hispanic and mid-American women) in whom the prevalence of clinical obesity exceeds 50%. Overseas visitors to the US will have no difficulty in reconciling these statistics with their own personal impressions, and will be struck by the massive, debilitating obesity that afflicts so many. The chapter by Seidell and Flegal shows that other affluent nations are close on the heels of the US, and that developing nations have no room for complacency especially among the urban rich.

In these days of political correctness, the gloomy tone of these predictions may appear hostile to the many self-help and self-protective organisations such as NAAFA (the North American Association for Fatness Acceptance) whose view is that the risks of obesity, and the

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benefits of weight loss are grossly overstated by a tyrannous medical profession bent on making their life a misery. This is a serious view, worthy of every sympathy, and it imposes on us a responsibility to critically examine the evidence of risk upon which we base our medico-centric attitudes.

## Is obesity really harmful?

Jung's chapter provides an overview of the health risks of being obese, and the chapters by Kopelman & Albon and Pettigrew & Hamilton-Fairley examine two specific examples with illustrations of the likely mechanistic pathways.

Jung provides a condensed list of the morbidities associated with obesity. Even this shortened list runs to 45 diseases for which there is unequivocal statistical proof of increased risk. Among these are some of the biggest killers in modern societies including coronary heart disease, stroke, diabetes, and certain cancers.

Diabetes is one of the most thoroughly researched of the obesity-related syndromes and reveals some salutary messages. The incidence of new cases of NIDDM in previously healthy individuals has been carefully measured over an 8 year follow-up in over 50,000 middle-aged US male health professionals<sup>1</sup> and over a 14 year follow-up in over 110,000 US female nurses<sup>2</sup>. Body weight and weight change emerge as the most important predictors of the likelihood of developing diabetes with odds ratios rising to over 40-fold in men and over 90-fold in women who are seriously obese. Perhaps more worrying for health economists is the finding that the risk of NIDDM is significantly raised, by up to 8-fold, in people who are only mildly overweight.

Several arguments have been marshalled by those who wish to downplay the risks of obesity. The first is that some obese people are perfectly healthy; an argument which is extended to imply that it is something other than obesity which is causing illhealth. Of course some obese people are healthy, just as some 80-year-olds can run a marathon, a fact which does not disprove that ageing is associated with a general decline in physiological function. A corollary of this argument is the claim that obesity is not an *independent* risk factor for heart disease because it is displaced from regression analyses by other risk factors such as hypertension, hyperlipidaemia and hyperinsulinaemia. The fallacy inherent in this argument is the failure to accept that obesity is often the direct and pivotal cause of the hypertension, hyperlipidaemia and hyperinsulinaemia. A second argument has been that the curve for mortality is J-shaped with an increased risk among thin people as well as

among fat people. As reported by Jung, this apparent excess risk among thin people has now been clearly shown to be due to an over-representation of smokers and people with pre-existing disease among the thin groups<sup>3</sup>. The third popular argument has been that the nadir of the mortality risk curve moves to the right (i.e. favouring fatter people) with increasing age, thus suggesting that it is natural and healthy to gain weight as we age. This claim has never been properly substantiated and is now largely discredited.

None of these arguments undermine the conclusion that serious obesity is seriously damaging to a person's health, and that mild obesity has a range of progressive effects on physiological function which ultimately cause a deterioration in health. Economic analyses as summarised by Hughes and McGuire suggest that the direct and indirect health costs attributable to obesity are around 5% of the total health budgets of affluent countries, equivalent to an astonishing \$69 billion in the US.

These physical health effects are compounded by psychological and social burdens. Kolanowski's chapter on surgical interventions touches on the issue of quality of life for obese people, and records the benefits that many feel when they achieve substantial weight loss. The size of the benefit gives an indirect measure of the quality-of-life penalties borne by the seriously obese. Obese patients are reported to score worse than multiple amputees and tetraplegics on quality-of-life questionnaires. They have suffered a lifetime of bullying, social castigation and prejudice which result in prejudice and impaired opportunities in education, employment and marriage. Surveys in the US, during the 1970s, showed that obesity rated worse than a criminal conviction for rape as an undesirable feature in a potential marriage partner. Fortunately, these attitudes are now very different as a result of the effective lobbying by organisations such as NAAFA, and as a result of the fact that most people in the US now have at least one family member with obesity. The stigma is lessening, but the anguish remains acute for many sufferers.

Such a catalogue of side effects surely argues strongly in favour of a concerted, seriously-resourced national or international effort to combat the problem. But should we concentrate on prevention or cure? Can we effectively treat obese patients? And is it safe to do so? These issues are raised in the final chapters of this book. Let us first examine the question of safety.

## **Is weight loss beneficial?**

Jung's chapter tabulates the benefits of a 10 kg weight loss, and shows substantial advantage in terms of co-morbidities and mortality. His

interpretation is probably a balanced representation of current knowledge, but would not be universally accepted especially with respect to mortality. It has to be admitted that there are disquieting data available in the literature which still require explanation. For instance, the Harvard Alumni Study shows that weight stability is the optimal strategy for minimising coronary heart disease (CHD) and all-cause mortality, and that weight loss was associated with a *raised* mortality (even after allowing a considerable wash-out period to allow for deaths in people with pre-existing disease)<sup>4</sup>. Similar findings emerged from the NHANES follow-up studies<sup>5</sup>, and there are repeated epidemiological surveys illustrating that weight-cycling (or yo-yo dieting) is associated with raised CHD mortality<sup>6</sup>.

The defence that is usually mounted against these challenging findings is that they do not reflect the result of *intentional* weight loss achieved using modern dietary and pharmacological therapies. Some support for this claim is provided by recent analyses which do reveal reductions in mortality in people who intentionally and successfully lose weight<sup>7</sup>.

In a similar vein of caution, we must also be careful not to assume that the obesity-related hypertension and insulin resistance carry the same mortality risks as hypertension and insulin resistance of other origin. It is known, for instance, that, although obesity is a major risk factor for hypertension, the incidence of stroke per case of hypertension is lower in the obese than in lean essential hypertensives<sup>8</sup>. We need new research to explore whether the physiological dysfunctions generated by obesity carry as much risk as the same dysfunction in a non-obese person. If this is not the case, it would support the view of those who believe that the risks have been exaggerated.

## Can obesity be successfully treated?

Anyone working in this field will be familiar with Stunkard's famous adage that 'most obese people won't enter treatment, most who do won't lose weight, and most who lose weight regain it'. This nihilistic view is supported by statistics showing that the long-term cure rate for obesity is worse than for most forms of cancer.

Part of the explanation for such a poor treatment record lies with the fact that the statistics are derived from specialist tertiary referral centres which only receive the most severe cases; those who have failed all other attempts. In fact, broader community-based audits show that many people are very successful at long-term weight loss and management, but such people never appear in treatment statistics because they never seek formal treatment.

However, even allowing for this factor, the current treatment paradigms for obesity (with the possible exception of surgery) would not be described as successful by any truly impartial observer. The lifestyle and behavioural management strategies described by Cowburn, Hillsdon and Hankey are still in the infancy of their development as we start to learn some of the deeply-complex psychological factors underlying some obesities. The emerging pharmacotherapies described in Finer's chapter are likewise the first generations of drugs which will ultimately be much more effective. It is in this context that the new developments in neurobiology outlined in the chapter by Wilding, Widdowson and Williams may provide the vital insights into how we can ultimately design pharmacotherapies capable of disrupting the feeding drive which we are now learning has multiple fail-safe back-up systems.

But, even when such drugs are developed, we will be faced with some testing ethical and economic decisions. What will be the potential for abuse of such drugs by a population which is increasingly obsessed by their body image, and in which eating disorders are a major concern? Will we be able to afford to maintain a substantial proportion of the population on lifelong therapy? Is this the best way to allocate resources or should we focus on prevention?

## **Prevention or treatment — where should we prioritise?**

Notwithstanding the compassionate need to help people who are already obese, there would be few analysts who would argue with the view that prevention of obesity is the only viable long-term strategy if we are seriously to tackle the problem. In this context, we need to understand the causes of the current epidemic before we can institute effective remedial measures. The chapter by Jebb analyses the likely aetiological factors.

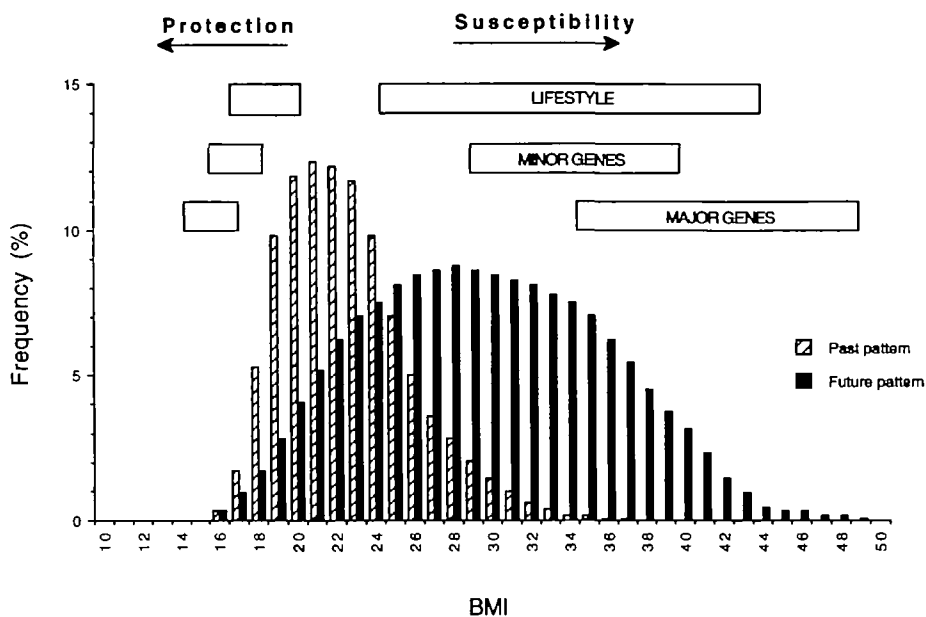
On the one hand the search for causes seems impossible since energy balance only needs to be displaced by a tiny fraction for the cumulative effects to result in obesity. The fattest man in the world died recently in his mid-forties weighing 465 kg (73 stone). Even this enormous accumulation of fat required an excess equivalent to only a small bar of chocolate each day. The smaller changes characteristic of most obesities are, therefore, beyond the limits of detection of most metabolic measurements. This problem is reinforced by the now well known fact that it is virtually impossible to obtain an accurate record of habitual food intake in obese people because of the layers of psychoses and

subconscious self-deception which have built up as a protection against social stigma.

However, the quest is not hopeless and certain useful observations can be made with some certainty. The first is that there are many different types of obesity ranging from the purely genetic (e.g. Prader-Willi syndrome) through the purely environmental (e.g. pastry cooks and sweet-shop owners) to the purely behavioural (e.g. Sumo wrestlers). Within this spectrum there are certain categories, such as sufferers of binge eating disorder, which are becoming clinically recognised as discrete aetiologies. There is an urgent need to progress our understanding of the different phenotypes of obesity so that each can be targeted with appropriate therapeutic measures. The current approach, which often applies the same therapeutic methods to all patients, must be inefficient and may actually be harmful since some components, such as restrictive dieting, might actually reinforce some of the causal factors such as bingeing.

The second useful observation that can be made with certainty is that most modern obesities must be caused by environmental and lifestyle factors in modern life, since the epidemic is emerging within a relatively constant gene pool. This does not mean that genetic effects are unimportant; there is ample evidence to prove that some individuals, and some tribal groups, are more genetically susceptible than others, and the concept of the 'thrifty genotype' probably remains valid 30 years after it was initially proposed. But the balance of genetic versus environmental influences is changing. Figure 1 gives a schematic representation of what is happening. In the past, average BMI was around 21–22 kg/m<sup>2</sup> and there was only a shallow right hand tail to the distribution pattern. Under such conditions it was highly likely that any seriously obese person would have a definite genetic susceptibility perhaps resulting from a single major gene defect, or more likely arising from a cluster of minor genetic variants. The situation has already moved to one in which the genuine genetic susceptibilities are being obscured by the sheer volume of lifestyle obesities. As more and more people become obese the concept of genetic susceptibility loses value, and attention will be turned to those who seem to be genetically resistant to weight gain.

Jebb's chapter identifies high-fat diets and physical inactivity as the prime aetiological candidates. High-fat diets have a high energy density and result in so called 'passive overconsumption' where people accidentally overconsume energy without necessarily eating a large bulk of food. Physiological studies show that human metabolism is very poorly adapted to recognise excess fat consumption and to re-establish fat balance. This effect interacts with physical inactivity such that the combination of inactivity and high-fat foods is especially adipogenic.



**Fig. 1** A schematic illustration of the changing role of genetic and lifestyle influences on obesity.

Analysis of secular and cross-sectional epidemiological data from a variety of sources suggests that the physical inactivity characteristic of modern sedentary lifestyles is possibly the dominant factor in inducing obesity. This is key to the preventative strategies outlined by Gill and to the behavioural therapeutics outlined by Cowburn, Hillsdon and Hankey. The data in this area suggest that inactivity is not just the reciprocal of activity. It is often a specific trait, such as obsessive TV viewing, and one which is actively promoted by marketing of TV and video programmes, home computers, video games, and energy-sparing domestic devices. The increasing use of motorised transport, lifts and escalators, mobile telephones, central heating and so on, all conspire to save energy. Unfortunately, our physiological homeostatic mechanisms fail to detect this and to adequately down-regulate food intake with the result that the excess has to be stored as fat unless we use cognitive controls (restrained eating and/or exercising to maintain healthy weight) to take over from the fallible innate mechanisms.

## Is there hope for the future?

It is easy to become demoralised by the enormity of the task involved in trying to reverse the current trends in obesity, but there is hope. At the extremes of obesity the present spate of 'gene-a-month' discoveries will

soon have identified most of the major and minor genes involved in pathological weight gain. This will aid our understanding of the principles involved, help to develop improved pharmacotherapy, and perhaps even lead to gene therapies in the longer term. Advances in our understanding of the psychological aspects of obesity are also leading to greatly improved behavioural change models for treatment. The importance of an increased research effort into the fundamental causes of obesity cannot be overstated.

But at a more general societal level the omens are less encouraging. Whatever advice we offer in terms of environmental modifications always appears to be swimming against the rip tide of 'progress' which is backed by the enormous resources of global TV giants, motorcar manufacturers, multinational fast-food chains, and such like. Surely we will never stop this particular juggernaut. So the glimmer of hope lies in the fact that many individuals do in fact manage to maintain a lifetime's healthy weight in spite of living within such an obesogenic environment. Knowledge and motivation seem to be key elements of success, and the best riposte to those who claim that behavioural changes are ineffective comes from the observation that obesity shows a strong inverse correlation with level of education in most affluent countries.

We have elsewhere argued that increasing peoples' activity levels and reducing their fat intake are likely to be the critical components in successful weight management<sup>9</sup>. This advice is absolutely in line with recommendations emanating from other disease areas such as CHD, diabetes and cancer. There is a powerful synergism developing, and we now need to persuade the general public of the immense benefits to health and well-being that would accrue if they would adopt more healthy lifestyles. Education appears to be the only really viable option in tackling the current epidemic of obesity, but that education needs to be based on a solid foundation of knowledge about the causes and consequences of obesity of the type contained in the following chapters.

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