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Viewpoint

Should obesity be the main game? Or do we need an environmental makeover to combat the inflammatory and chronic disease epidemics?

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Summary

There is a link between obesity and chronic disease. However, the causal relationship is complicated. Some forms of obesity are associated with low-level systemic inflammation, which is linked to disease. But lifestyle behaviours that may not necessarily cause obesity (poor diet, inadequate sleep, smoking, etc.) can independently cause inflammation and consequent disease. It is proposed here that it is the environment driving modern lifestyles, which is the true cause of much chronic disease, rather than obesity *per se*, and that obesity may be a marker of environmental derangement, rather than the primary cause of the problem. Attempts to clinically manage obesity alone on a large scale are therefore unlikely to be successful at the population level without significant lifestyle or environmental change. Environmental factors influencing obesity and health have now also been implicated in ecological perturbations such as climate change, through the shift to positive energy balance in humans caused by the exponential use of fossil fuels in such areas as transport, and consequent rises in carbon emissions into the atmosphere. It is proposed therefore that a more policy-based approach to dealing with obesity, which attacks the common causes of both biological and ecological 'dis-ease', could have positive effects on both chronic disease and environmental problems. A plea is thus made for a greater health input into discussions on environmental regulation for chronic disease control, as well as climate change.

Keywords: environment, inflammation, obesity.

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Introduction

Obesity is collateral damage in the battle for modernity. It is the burden many of us bear as a result of our inability, or unwillingness, to adjust to the energy surpluses emanating from economic advancement. A causal association between obesity and a wide range of diseases has been well documented (1). However, recent findings suggest a more complicated aetiological role than just a simple weight–disease association (2). Dependent largely on the site of fat storage, obesity can be relatively benign, with little negative impact on physical health (3) (although admittedly with an often significant psychological effect), or metabolic, with significant links to metabolic and other disorders (4). On the other hand, a clear link has been established between certain lifestyle factors (aspects of nutrition, inactivity, inadequate sleep, stress, depression, excessive alcohol intake, smoking), which sometimes, but not always, lead to obesity, and a type of low-grade systemic inflammation (5), which is associated with a range of chronic diseases (5,6).

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It is proposed here that obvious (in contrast to visceral) obesity may be simply a marker of an aberrant human lifestyle, which is mediated by aspects of the modern technological environment to which humans have had little time to adapt physiologically, a feature seen most prominently in indigenous populations thrust into modernity (7). As a result, a low-level immune reaction, resulting in a cascade of potentially pathological events, occurs not just in association with metabolic forms of obesity but to these lifestyle behaviours, with or without obesity. If correct, this implies the need for an altered approach to the management of chronic disease, with a greater emphasis on changes to influence lifestyle and the environment, than on personal changes, such as diets and exercise routines, which can be overwhelmed by the modern 'obesogenic' (8) environment. Because of the synergies in factors causing obesity and environmental damage (9,10), such as the decrease in human energy use and increase in carbon emissions from fossil fuel use in transport and the processing of energy-dense foods, policies to do this may have the dual effect of moderating obesity and environmental problems such as climate change (10).

The following viewpoint, in which these propositions are canvassed, is thus in three parts: First, the importance of adipose tissue and tissue stores is considered in relation to its risk for disease. The conclusions from this are that the obesity–disease relationship is complex and obesity *per se* may not provide a satisfactory causal explanation for many of the chronic diseases for which it has often been blamed. Second, inflammatory processes, which are now regarded as a potent indicator of disease risk, are linked with individual lifestyle behaviours that often, but not always, cause weight gain. This implies that the modern environment driving lifestyle behaviours is the distal cause not only of obesity but also of much modern chronic disease, and that this needs to be acknowledged and dealt with in any comprehensive disease management programme. Finally, ways of mitigating the adverse biological, as well as ecological, effects of the modern environment, which do not discount the significant gains made from economic development, are considered. This includes a discussion of various proposed environmental processes such as carbon trading, for the management of obesity as well as climate change, thus extending a previous review of the underlying common link between biological and ecological concerns (10). Because of the novelty of this approach and the broad ranging nature of its implications, we have chosen to concentrate more on breadth rather than depth of the topic, without intending it to be a comprehensive review of component issues.

Human body fat stores

A certain amount of body fat in mammals is essential for survival (11). It serves as an energy reserve, a storage mechanism for vital nutrients and a form of insulation. Recent findings have shown that it also acts as an endocrine organ (12), as well as having a close link to the immune system (5). Lack of fat, as in the lipodystrophic state, is linked with insulin resistance and associated health conditions (13). Excessive fat stores, on the other hand, have also been regarded as a health hazard (14). This was thought to apply to all forms of obesity, but since Vague's (15) findings on the metabolic differences between abdominal and gluteal fat in the 1940s, the focus has been more on the location of fat stores.

Recently, it has been shown that excessive visceral adipose tissue (VAT) is even more predictive of the metabolic disorders originally associated with subcutaneous adipose tissue (SAT) (14,16,17), and that there may even be an inverse association with metabolic problems and gluteal fat stores (18). Variability in VAT has been proposed as the underlying cause for the significant proportion of obese individuals (estimated to be around 20%), without health risks, and the similar proportion of lean individuals with such risks (19).

While there is a positive correlation between SAT and VAT, excessive VAT can exist with minimal SAT stores (20) or be largely absent in the presence of excessive SAT (21). VAT in the absence of SAT can predispose to insulin resistance and an unfavourable inflammatory profile (20). However, this is not always the case (13), suggesting that while VAT may be important, the portal drainage hypothesis based around this (22) may not fully explain the fat–disease link. To add to this, it appears that an intermediatory layer of abdominal fat, called deep superficial adipose tissue (dSAT), may exist in larger individuals, with a pathogenic effect midway between superficial subcutaneous adipose tissue (sSAT) and VAT (23). As an energy source, VAT seems to be preferentially mobilized after initial weight loss, but the effect is attenuated with greater loss (24), supporting the idea of a dynamic metabolic effect of VAT.

The effects of the thiazodiazenoles, a class of nuclear transcription factor facilitators that increase adipocyte progeneration, have added another layer of complexity to the issue (11). These medications increase insulin sensitivity while increasing, rather than decreasing SAT, and not changing VAT levels, suggesting that the VAT/SAT ratio could be the important factor in risk. Current evidence also suggests that while fat expansion can occur through hyperplasia or hypertrophy, the ultimate limitations come in adipose cell size, or hypertrophy (13). Hormonal messages from adipocytes expanded to capacity may lead to spillover into visceral, then hepatic and intramyocellular fat stores, which are known to have a strong association with insulin resistance. Using a mouse model, Akagiri *et al.* (25) have shown a >500% increase in epididymal adipocyte size in mice fed a high-fat diet before significant spillover into

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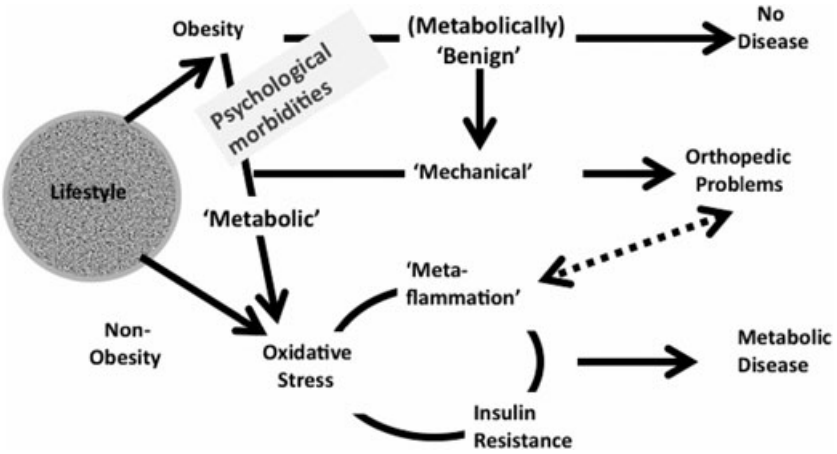

Figure 1 A proposed model of the effects of lifestyle on metabolic outcome with and without accompanying obesity.

hepatic stores. Insulin resistance then appears in association with fatty liver and inflammatory markers. Genetic manipulation studies suggest that this is because fat expansion to a certain level prevents spillover, which would otherwise cause metabolic problems (26), possibly through a rise in inflammatory cytokines kept in check to that point by anti-inflammatory chemokines (27).

It is thus apparent that the relationship between body fat and metabolic disease is more complex than earlier findings implied. While obesity clearly is important, not all fatness indicates disease risk, and not all leanness indicates lack of risk. The discovery of a form of low-grade systemic inflammation (since labelled 'metaflammation', (5) 'para-flammation' (28) or 'smouldering inflammation' (29)) associated with obesity in the early 1990s (30), as well as a more detailed understanding of oxidative stress (31), and insulin resistance (32) in chronic disease, is now helping to clarify the situation.

Adiposity, inflammation and disease

As discussed earlier, fat stores can be physiologically benign, or metabolic, depending on their level of pathological activity. The benign form is usually based in peripheral stores, but may also exist in subcutaneous stores with a capacity for greater than expected expansion (at least to a point), without metabolic consequences. The metabolic form, which is more pathological, is more likely to be linked to VAT and associated pathological markers.

Excessive VAT, or an increased VAT/SAT ratio is strongly associated with macrophage infiltration and is an inflammatory state (33), which has possible links with oxidative stress. Oxidative stress (34) and inflammation (35), in turn, have been linked to insulin resistance, and ultimately, to cardio-metabolic disorders (36). Obesity is thought to be an instigator of this process (30). However, recent research has shown that modern lifestyle factors that are not always mediated through obesity (i.e. over-nutrition, poor nutrition, inactivity, inadequate sleep, smoking, excessive alcohol, stress, depression) are also associated with inflammation, suggesting a more extensive cause than obesity *per se* in metabolic disease. This is illustrated in the model proposed in Fig. 1.

As shown in Fig. 1, there are a number of lifestyle stimuli that may or may not lead to obesity. Even where they do, this may be physiologically benign, as shown across the top of the figure, or metabolic as shown below. This is not to deny of course that psychological morbidities, such as depression, anxiety, eating disorders or inability to cope, may exist even in the presence of what we have here labelled benign obesity. With no further gain in weight, the benign form poses risks mainly from mechanical overload (which may, however, lead to orthopaedic problems such as arthritis), physical disability, disordered eating and psychological comorbidity. The metabolic form, on the other hand, as well as certain lifestyle factors (discussed below) that may not necessarily cause obesity, is associated with a cascade of oxidative, metabolic and inflammatory events, shown in the circle at the base of Fig. 1, which can ultimately lead to disease. An increase in our understanding of the processes in this reaction now makes it possible to follow this trail more closely.

Metaflammation and inflammatory markers

Classical inflammation usually represents a local acute immune reaction associated with infection or injury. Standard symptoms are rubor, tumour, calor and dolour (redness, swelling, pain and fever), and physiological indicators are a multi-fold increase in biochemical inflammatory markers. Metaflammation is distinguished from this by its systemic and chronic nature, but only a 2–4 fold elevation of inflammatory markers (5). Typically, the metaflammatory 'antigens' are also less apparent as 'foreign agents' or microbial organisms, do not result in obvious antibody production, and hence may be better

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referred to as 'inducers' (28).The link between metaflammation and a range of chronic diseases such as type 2 diabetes (37), heart disease (36,38), certain cancers (29,39), erectile dysfunction (40) and even Alzheimer's (41) is demonstrated in humans by the expression of these inflammatory markers.

In general, markers classified as pro- or anti-inflammatory are expressed through a range of immune mediators such as cytokines, chemokines, adipokines, myokines and transcription factors (42). Certain markers such as C-reactive protein have gained more attention than others, such as TNF alpha, Il-6 and transcription factors such as NFkB, which are now receiving more attention as interest in the inflammatory process widens. Many of these have now been used to identify metaflammatory, and hence potentially unhealthy inducers. Increased adiposity was one of the first of these identified (30). However, as suggested earlier, and discussed in more detail further in the article, obesity itself may be a marker for other lifestyle factors which may or may not necessarily cause obesity.

Inflammatory processes are also linked with oxidative stress and insulin resistance in cell tissue, although the links have not yet been fully elucidated. A possible scenario is that oxidative stress from metabolic overload or an immune reaction resulting from a range of endogenous or exogenous inducers, incites an immune alarm through the production of pro-inflammatory molecules. This, in turn, causes disruption of insulin receptor signalling leading to the build-up of insulin resistance and, ultimately, to the development of metabolic and other disorders (30). An important issue in this process is the cause(s), or inducers of the initial stress, and the relationship of these to body fat stores.

Inflammatory stimulants ('Inducers')

There are a number of lifestyle-related inducers that have been associated with oxidative stress and/or inflammatory processes in the body, as well as with insulin resistance and potential cardio-metabolic disease. Within these categories, there are also inducers associated with pro- and anti-inflammatory, or neutral processes. The discussion to follow identifies these, considers the link with obesity, and attempts to explain the underlying causal factors[1]. With many, if not most factors considered, there appears to be a 'hormetic' effect (where hormesis refers to the reverse effects of too little or too much of a substance/activity, compared with a mid-range level) (43).

[1]A more extensive list of references on lifestyle and environmental inflammatory inducers is available at http://www.lifestylemedicine.net.au/staging/health-information/lifestyle-medicine-evidence-base/inflammation-database/index.htm

Nutrition

Postprandial responses to certain nutritive stimuli can trigger a biochemical cascade causing inflammation, endothelial dysfunction and sympathetic hyperactivity (44), resulting in postprandial dysmetabolism (45). It has been proposed that postprandial indices of inflammation, which can be measured directly through inflammatory cytokines (5), or indirectly through postprandial hyperglycaemia or hyper-triglyceridaemia (45), when occurring chronically, can be indicative of increased cardio-metabolic risk (45). This information can thus be used to assess the effects of various nutritive processes on potential health outcomes. [More detail on nutritive processes in inflammation is also provided in published reviews on the topic (45,46).]

Nutritive overload

While obesity is known to be associated with inflammatory processes (30,47), as well as oxidative stress (48) and insulin resistance (49), it is not clear whether it is obesity *per se*, or the nutritive excesses and/or inactivity (i.e. positive energy balance) leading to obesity, which cause this effect. Inflammatory cytokines, even those originating in adipocytes, may be regulated by the nutritional state (50), and subcutaneous obesity is not necessary for the increased inflammatory responses which characterize a systemic immune reaction (20,51). Several recent studies have shown changes in inflammatory markers owing to dietary intake in the absence of significant weight gain (52–54). From a mechanistic perspective, oxidative stress is a consequence of flooding of the Krebs cycle, thus outstripping the capacity of oxidative phosphorylation and creating free radicals (55,56). Recent findings suggest that resulting endoplasmic reticular stress can lead to an unfolded protein response and cascade of resultant events (57). It is also notable that an increase in inflammatory mediators or indices can predict the future development of obesity and diabetes (58), as well as *vice versa*, and that negative metabolic outcomes can result from acute nutritive excesses (59). In mice, genetically limiting fat expansion results in early type 2 diabetes from nutritive overload, whereas fat expansion in normal mice actually delays this process (26). These findings are also indirectly supported by the fact that caloric restriction is one of the most robust, non-genetic means known to increase longevity and cardio-metabolic health (60–62), possibly through biogenetic factors (63,64), but that fasting (65), in a typical hormetic fashion, can cause an increase in inflammatory responses, suggesting a limited range of nutritive intake (probably related to energy expenditure), outside of which pathological processes, often marked by obesity (or anorexia) may develop. More direct effects have been associated with specific nutrients, as discussed below.

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Type and amount of carbohydrate

The amount and type of carbohydrate consumed is a major determinant of postprandial excursions in glucose and triglycerides associated with inflammation and oxidative stress (66–68). Minimally processed low glycaemic index (GI) foods such as vegetables, fruits, nuts, seeds and grains, or meals with a low glycaemic load (GL), do not result in adverse postprandial inflammatory effects (68–70). High GI foods, or meals with a high GL on the other hand, do cause an increase in postprandial inflammatory markers (66,67,71). However, supporting the nutritive overload results discussed earlier, large amounts of otherwise benign low GI foods have a similar effect on postprandial glucose excursion (and presumably inflammation) to small amounts of high GI foods(72), suggesting that too much of an otherwise anti-inflammatory or neutral food may cause this to become inflammatory. Inflammatory factors have even been associated with glycaemic status in middle-aged population samples (73).

Other nutrients

It is not the intention here to extensively review all nutrients identified in an inflammatory reaction. This is the subject of a wider review to follow, and can be sourced in other available reviews (53,74). A summary of nutrients for which pro-inflammatory reactions have been reported however includes the following: ***Dietary fats***: Saturated and trans-fats are among the most commonly reported nutrients inducing an inflammatory reaction, both chronically (75–78) and acutely(79,80), particularly when compared with unsaturated fats. Fast food (77) and modern takeaway meals (81–83), which are generally high in saturated and trans-fats, have similar acute pro-inflammatory effects, suggesting that while fat is a common cause of obesity, nutrient sensing can occur to a fat overload without obvious obesity. A similar pattern occurs with a low N3/N6 fatty acid ratio in the diet (84). Finally, an inflammatory response has been reported in one study (72), but not another (85), to a fatty beef meal, and low-grade endotoxemia in another (80). Lean meat, which is more characteristic of game animals, does not appear to have this effect (86). ***Alcohol***: The response to alcohol is biphasic (87), with pro-inflammatory effects from excessive consumption (87,88), but a large body of research (89) showing anti-inflammatory benefits from a moderate intake (see below). ***Fructose*** and soft drinks: Fructose has been found to induce inflammatory reactions (90,91), as well as stimulate fatty acid synthesis in adults (92). An acute pro-inflammatory response has also been found with both fructose (93) and sucrose-sweetened soft drinks (94). ***'Unhealthy' diets***: Overall healthy diet scores have been shown to be negatively related to inflammatory markers (95), independently of body weight (52).

On the other hand, significantly lower postprandial glucose and fat excursions and/or anti-inflammatory responses as indicated by anti-inflammatory biomarkers, have been associated with a range of foods such as high fruit and vegetable intake (96), low GI (72), and high-fibre foods (97), tea (98,99), mono-unsaturated fats (96,100), a high N3/N6 dietary ratio (84), moderate alcohol intake (87,101,102), with particular benefits of red wine (103,104), capsaicin in spicy foods (105), as well as other herbs and spices (106), olive oil (107) and the Mediterranean diet (108,109). It has been suggested that such dietary processes can have these effects without significant changes in body weight (52).

A close examination of these pro- and anti-inflammatory nutritive inducers suggests a link with 'evolutionary adaptation'. As expressed previously in anthropological literature (110–112), aspects of the modern diet are at complete variance to traditional human evolutionary dietary intakes. Developments in our understanding of inflammatory processes are now helping to verify the potentially damaging health effects of this, supporting the anthropological view by showing a low-grade immune reaction to those foods that are a product of the modern environment and which are consumed on a regular basis. A similar process may also be associated with beverages (113), although space limits a detailed review of this here.

Inactivity

As with particular foods, humans have evolved in an environment requiring 3–4 times the level of physical activity carried out today (110–112,114). Hence, it is not surprising that there is a physiological cost for the modern sedentary environment. This comes in the form of obesity with its accompanying health problems. However, several lines of evidence suggest that inactivity, without weight gain, can increase dysmetabolic processes (115), while increased activity without weight loss can lead to improvements in inflammatory and metabolic processes (116). Modelling the modern sedentary state of humans with rats in a wheel lock situation, Booth *et al.* (117) found a rapid increase in insulin resistance, which replicates findings in humans (118), followed by increases in VAT which they attribute to the need to rapidly adjust to energy scarcity in a traditional hunter-gatherer environment. While the reasons for this seem apparent (i.e. conservation of glucose supplies during energy scarcity), the mechanisms and sequence are a little less clear. Brunsgaard (119), Brunsgaard and Pedersen (120), and Pedersen (121) have reviewed the evidence on inflammatory processes and exercise, which suggests a rapid but complicated stress and inflammatory response to inactivity, which could be responsible for the changes in insulin signalling. Reductions in a range of inflammatory cytokines have also been shown to occur with chronic

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exercise training (38), although interestingly, extreme exercise can have the opposite, pro-inflammatory effect (122). Thus, it is apparent that exercise too, has a hormetic effect. Inactivity significantly below the level to which humans have evolved, and excessive exercise, such as in modern endurance events above that level, can feed forward to dysmetabolism and potential chronic disease. More importantly, inactivity can do this in the absence of obvious weight gain.

Inadequate sleep

Yet another lifestyle pattern that has changed significantly in humans in recent times is sleep. This appears to have decreased significantly since the invention of the light bulb (123). From a suggested level of around 10 h per night in the 18th century, recent evidence suggests that >30% of humans in industrialized economies get <7 h of sleep a night (124), a level at which big increases in pro-inflammatory markers are noticed (125). This is apparent not just with sleep deprivation, but with decreased sleep quality, such as through insomnia (126), and other sleep disorders (127). Proposed reasons are the 'stress-like' effect of sleep deprivation (128) and hormonal changes (129). And while inadequate sleep has been found in cross-sectional studies to be associated with obesity (130), and to increased appetitive hormones associated with obesity (131), some inflammatory markers associated with inadequate sleep are independent of body mass index (BMI) (132). The fact that these occur after one night's sleep deprivation (133) and that sleep disturbances can follow administration of pro-inflammatory cytokines (134) suggests that obesity is not a necessary condition for sleep-related dsymetabolism (for a more detailed review of sleep and inflammation see reference 125).

Stress, anxiety and depression

The stress reaction is a normal response in humans. However, it is reasonable to suggest that chronic exposure to a stressor, without traditional cultural support, and reduced options for a biological adaptive reaction (flight or fight), is more characteristic of modern industrialised societies. Although interacting, the link between stress, anxiety and depression is complicated (135). However, all three appear to be rising in advanced societies, and a link has been shown through immune activation as indicated by the presence of inflammatory cytokines (136). A possible function of this is to prepare the immune system for healing following an anticipated physical challenge (137), as shown in the different immune sensitivity reactions in defeated mice compared with victorious mice in social challenge situations (138). But while stress may instigate visceral forms of obesity (139), it appears that obesity is not a necessary precursor to inflammatory states associated with stress, anxiety or depression. In addition, in an obese population depression is an independent risk factor for raised inflammatory markers (140). This is also obvious from the acute inflammatory reaction noted to imposed psychological stress in the laboratory situation (141), and to depression induced by administration of inflammatory cytokines (142). Obesity, perhaps understandably, can cause depression (140), and other psychological pathologies which have not been canvassed here, but a causal link in the other direction could be through dietary changes induced by the stress response (143), or changes in population activity levels leading to central neural degeneration (144). Physical activity, which has an anti-inflammatory effect (see above), may be effective in reducing depression, possibly through central neurogenesis (144). 'Burnout', and exhaustion, both outcome effects of chronic stress, have clear links with pro-inflammatory processes (145,146).

Smoking

Cigarette smoking was introduced to the 'old world' around the middle of the second millennium. As a developed habit, prevalence rapidly increased with commercialization following WWII, making it one of the most recent and recognizable lifestyle habits of the industrialized environment. Since the initial warning of its dangers, garnered from epidemiological evidence of Sir Richard Doll in the early 1950s, smoking has been shown to have a range of respiratory, cardiovascular and carcinogenic outcomes. More recently, it has been shown to be associated with oxidative stress (147) and metainflammatory processes (148,149), which decrease on quitting (150), although still remain higher in ex-smokers than non-smokers (151). Smokers in general have a lower BMI, although greater proportion of VAT than non-smokers (152,153), but obesity-related disease remains high even in lean smokers (154), suggesting that body weight is not an issue in smoking-related disease.

Summary

Figure 2 shows environmental inducers with evidence of a causal link with metaflammation and consequent chronic disease. Some of these have dependent links with obesity, as well as independent effects, but some also affect metaflammation without any connection to obesity. A summary of metaflammatory inducers with evidence of pro- or anti-inflammatory (or neutral in the case where there are similar pro-inflammatory inducers) effects is shown in Table 1. This clearly differentiates between behaviours associated with environments with which humans have evolved over a long time, and those modernized by industrialization. And while obesity is often a result of such lifestyles (155), it

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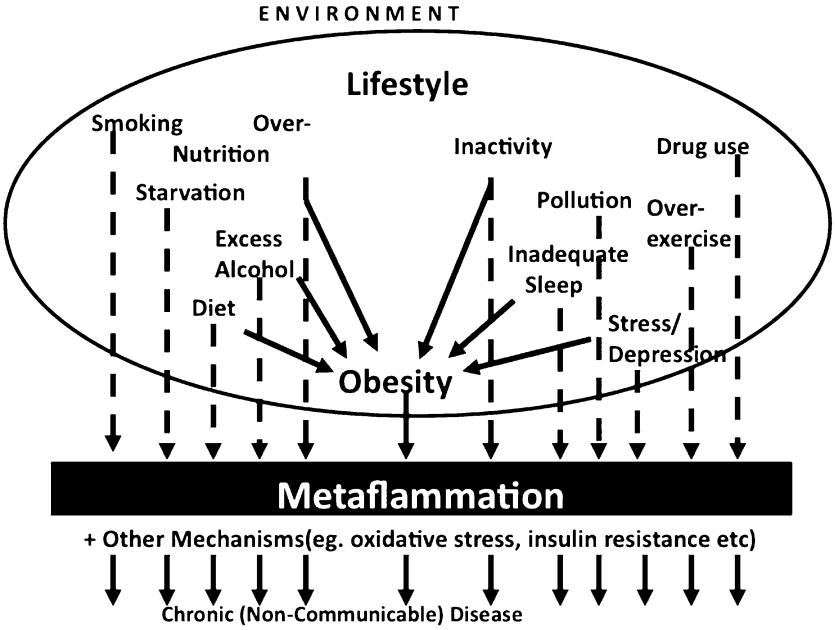

Figure 2 Environmental and lifestyle 'inducers' of metaflammation, showing both independent and dependant effects through obesity (expanded from reference 168).

Table 1 Lifestyle-related metaflammatory 'inducers' with biochemical evidence for a pro-, or anti-inflammatory (or neutral in the case where there are similar pro-inflammatory inducers) response in humans

Pro-inflammatory	Anti-inflammatory
Obesity	Weight loss
Nutrition	Nutrition
Excessive energy intake	Fruits/vegetables
Starvation	Nuts
Saturated fatty acids;	High MUFA foods
'Trans' fats	Fish/fish oils
High glycaemic load diet	Tea/green tea
High GI foods	Garlic
Fructose	Herbs and spices
Refined carbohydrate	Capsaicin
Low N3/N6 ratio	Lean game meats
Excess salt	Vinegar
Excessive alcohol	Low GI foods
High fat/western style diet	High fibre diet
'Fast food'	Olive oil
Inactivity	Grapes/raisons
Excessive exercise	Dark chocolate
Smoking	High N3 : N6 ratio
Sleep deprivation	Red wine/moderate alcohol intake
Stress/anxiety/depression	Mediterranean diet
Low humidity	Calorie restriction
Air pollution	Physical activity
'Sick building syndrome'	Smoking cessation
	Intensive lifestyle change

Inducers shown on the left-hand side (below 'obesity') can cause rises in pro-inflammatory markers, often without obesity, whereas those on the right-hand side (under 'weight loss') can cause an opposite reaction, often without weight loss (see text and http://www.lifestylemedicine.net.au/staging/health-information/lifestyle-medicine-evidence-base/inflammation-database/index.htm).

seems it is not a necessary prerequisite for the disease outcomes associated with aspects of this modern lifestyle [other potential environmental influences with possible inflammatory effects not discussed here include air pollution, low humidity 'sick building' syndrome, and the effects of industrial chemicals (for more detail see footnote 1)]. The implications from this are that the stresses of the modern environment are similar enough to the stresses of an infection that the body reacts to the environment as it would to an invading microbial organism. Hence, while reducing obesity remains a priority in public health, treating obesity alone, or even the proximal risk factors associated with this (hypertension, dyslipidaemia, hyperglycaemia), appears unlikely to significantly impact the global chronic disease epidemic.

It is thus not surprising that single initiatives aimed specifically at weight control, such as dieting, have been found to be less than fully effective over the long term (156), although weight loss has been shown to be a contributing factor in the prevention of diabetes progression in several prospective lifestyle-based programmes (157–159). Inflammatory markers have been reduced with lifestyle change in some of these studies (157), with an increasing degree of effectiveness clearly related to the number of lifestyle changes adopted (159), supporting the hypothesis that it is more than just obesity associated with the disease. It is unreasonable however, to expect success from a large-scale roll-out of these locally based programmes in the absence of significant environmental change. Similarities with other prevention programmes such as smoking reduction, drink-driving, bicycle safety, etc., testify to the fact that regulatory change usually has a more widespread and quicker

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impact on population behaviour than educational initiatives. This suggests that a more lateral and multidisciplinary approach than just health education or pharmaco-medical interventions is required.

Changing environments

It has been proposed previously that obesity and its related disorders are an expected phenotypic reaction to an abnormal environment (8), and that the modern environment is 'abnormal' when seen in an evolutionary context (10). The proposition put forward here is that lifestyle behaviours facilitated by an 'obesogenic' environment, rather than obesity *per se*, are responsible for much modern chronic disease previously attributed solely to obesity. And while the original proposal is still valid, it might be expanded to suggest that (much) chronic disease is a normal reaction to an abnormal environment, sometimes, but not always, in the presence of obesity. This results from lifestyles facilitated by an environment that humans have adopted with relish psychologically, but have not adapted to successfully physiologically. It is the modern 'effort-free' industrial lifestyle, driven by our exponential use of non-renewable energy sources, and increased consumption of processed, energy-dense foods, which has also led to aspects of environmental deterioration resulting in, among other things, climate change. The shift to positive energy balance in humans caused by the exponential use of fossil fuels in such areas as transport, and consequent rises in carbon emissions into the atmosphere have thus had an impact on both obesity and climate change. Hence, the convergence in the 21st century of biological disease sharing causes with ecological 'dis-ease'(9), with 'inflammation', both biological and ecological, being an underlying metaphorical cause (10). The question is how to deal with such a situation.

Managing obesity is clearly still an issue, as processes to do this will also modify lifestyle factors causing other problems (e.g. increasing physical activity can improve sleep, decrease depression, etc.). Environmental initiatives, which identify the population as the unit of intervention, are likely to have most impact on this (160). Reductions in chronic disease, associated particularly with the more 'pervasive' causes of lifestyle-related disease and/or weight gain (e.g. poor nutrition and inactivity), occur rapidly to environmental manipulation, as shown following the Cuban economic crisis of 1990–2000 (161), resource depletion in the Pacific Island of Nauru, and return to a subsistence environment in Indigenous Australian men (162). A preferable option, however, would be a more controlled intervention that is socially equitable, relatively painless and easy to instigate, in order to secure public support. The expanded use of a technique proposed for managing climate change, i.e. carbon trading, may help do this (10,163).

Carbon trading and chronic disease

Clearly, an economic system promoting indefinite exponential growth cannot be sustained and must inevitably be modified in the long term. However, in the short term, intermediate measures aimed at improving both personal and environmental health need to be considered. Carbon trading, both corporate, as currently being discussed in several countries, and personal, as proposed in the UK by the Global Commons Institute (164) and elaborated on by others (165,166), offers the potential to act on obesity and climate change simultaneously. It should do this by reducing carbon emissions causing greenhouse gases and climate change, while increasing personal energy expenditure and reducing high-energy-dense food consumption to reduce obesity and chronic disease. This is provided that consideration is given to health, and not just climate concerns, in the establishment of details relating to carbon trading regulations.

In the case of corporate carbon trading, the price of locally produced, non-processed, low-energy-dense foods might be expected to be reduced, relative to carbon emitting processed, and usually high-energy-dense foods. Corporate trading however accounts for only around 50–60% of human carbon emissions, the remainder coming from individuals and households. Hence, the value of a system is more likely to impact on the energy expenditure side of the human energy equation, but has been less recognized to date. The details and potential of this in relation to health have been discussed elsewhere (10,163).

The potential benefits of a personal carbon trading scheme reside not so much in its expected direct effects, but in the potential modification of the existing chronic disease environment through encouraging changing attitudes to energy use (10). A desired long-term outcome is a shift in consumer aspirations from conspicuous consumption, to conspicuous non-consumption, where the lust for non-renewable (and often unhealthy) consumables is reduced, and the importance of health is elevated, almost coincidentally. As suggested (and largely misunderstood) by former UK chief scientist Sir David King, when asked by a young woman what she could do personally to prevent climate change: 'Stop admiring young men who drive Ferraris.'

While carbon trading is not likely to impact all of the lifestyle factors facilitated by the modern environment considered here (e.g. sleep, stress and smoking would be unlikely to be directly effected), it may be part of a preventive portfolio of actions which includes awareness raising, education and regulation. In order to do this, more detailed input and modelling is required from specialist health scientists as well as climate change experts. It is in the early stages of development, such as now, that this needs to occur in order to capitalize on the opportunities that exist in an inevitably modified world environment. A major positive to

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this is that even if such an action does not impact on obesity (and this still needs to be proven), it will have benefits for the broader environment. Any disruptions to the current 'business as usual schedule' should also be outweighed by the entrepreneurial advantages of such a modified, but more sustainable approach.

Conclusion

Increasing evidence suggests that while obesity is a health risk, it may not necessarily be the direct cause, but may instead be a marker of many modern chronic diseases. The distal cause appears to lie in a maladaptive environment facilitating lifestyle behaviours and stimuli to which humans have not had time to adjust, leading us to 'treat our own cells like invading microbes' (167). Modifying the environment, while not losing the undoubted benefits of modern economic development, thus becomes a key health priority. As there is a common environmental cause between several forms of chronic disease, as indicated by obesity, and climate change, major interdisciplinary initiatives like carbon trading, which have the potential to reduce both biological and ecological disorder, should be considered as part of future health planning. For this to happen, it is vital that health specialists are both aware of the significance of, and provide input to, the planning and initiation of developing carbon trading systems and other environmental initiatives often not seen to be directly linked to obesity. It is vital, therefore, that health professionals provide greater input into discussions on environmental regulation for chronic disease control, as well as for climate change.

Conflict of Interest Statement

No conflict of interest was declared.

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