Beyond Obesity and Lifestyle: A Review of 21st Century Chronic Disease Determinants

Garry Egger1 and John Dixon2

1 School of Health and Human Sciences, Southern Cross University, P.O. Box 313, Balgowlah, Lismore, NSW 2093, Australia
2 Clinical Obesity Research, Baker IDI Heart and Diabetes Institute, Melbourne, VIC, Australia

Correspondence should be addressed to Garry Egger; eggergj@ozemail.com.au

Received 4 February 2014; Accepted 10 March 2014; Published 7 April 2014

Academic Editor: Tanya Chikritzhs

Copyright © 2014 G. Egger and J. Dixon. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

The obesity epidemic and associated chronic diseases are often attributed to modern lifestyles. The term “lifestyle” however, ignores broader social, economic, and environmental determinants while inadvertently “blaming the victim.” Seen more eclectically, lifestyle encompasses distal, medial, and proximal determinants. Hence any analysis of causality should include all these levels. The term “anthropogens,” or “…man-made environments, their by-products and/or lifestyles encouraged by these, some of which may be detrimental to human health” provides a monocausal focus for chronic diseases similar to that which the germ theory afforded infectious diseases. Anthropogens have in common an ability to induce a form of chronic, low-level systemic inflammation (“metaflammation”). A review of anthropogens, based on inducers with a metaflammatory association, is conducted here, together with the evidence for each in connection with a number of chronic diseases. This suggests a broader view of lifestyle and a focus on determinants, rather than obesity and lifestyle per se as the specific causes of modern chronic disease. Under such an analysis, obesity is seen more as “a canary in a mineshaft” signaling problems in the broader environment, suggesting that population obesity management should be focused more upstream if chronic diseases are to be better managed.

1. Introduction

Modern western lifestyles are often blamed for the current obesity and associated chronic disease pandemics [1]. This seems plausible as such problems, at a population level, only really began 3-4 decades ago [2]. They are also not usually caused by any microbial agent and have occurred too quickly for genome changes to be a factor [2] (although this does not preclude environmental influences on gene expression). The increased aging of the population is a consideration, but increased risk factors across all age groups limit aging as a sole explanation [3]. Other behaviors [4] and environmental factors [5] have been implicated, but a single causal underpinning is illusive, thus making “lifestyle” an attractive proposition.

However, lifestyle (“a mode of life chosen by a person or group”-Macquarie Dictionary) infers volitional behavior on the part of an individual. This has a pejorative meaning for some social scientists as it is thought to ignore the deeper social, economic, and environmental determinants of both lifestyle and disease, while focusing on individual responsibility, that is, “victim blaming” [6]. A more holistic view would involve not only looking at the “cause” of a disease, but also, as Rose has pointed out in [7], looking at the “cause of the cause,” and even the “cause of the cause of the cause.” This is particularly relevant for an understanding of the chronic, noncommunicable diseases (NCDs) often linked to obesity, in contrast to infectious/communicable diseases that have prevailed historically [8].

Infectious diseases benefited from a monocausal focus [9] provided by the “germ theory,” which culminated in improvements in public health, hygiene, immunization, and the development of antibiotics in the early 20th century [10]. Chronic diseases began to replace the decline in infections in the west in the late 20th century, taking health experts somewhat by surprise. Epidemiologists noted a phase in the development of a country called the “epidemiological transition” [11] when chronic diseases take over from infections as the main disease burden. This occurred in the 1970s and 1980s for many developed economies in North America, Europe,
and the Asian-Pacific region and is currently occurring in others, such as Brazil, Russia, India, and China. The double-edged sword of progress, which facilitated control over infectious diseases, instigated an unhealthy trend in chronic diseases. The worldwide rise in obesity has been an accompaniment to this.

2. Causality in Disease

While infectious disease can usually be ascribed to microbial causes, causality in NCDs is more problematic. In most cases the agent of causality is ill-defined, but there are layers of influence. As shown in Figure 1, most immediate to the cases the agent of causality is ill-defined, but there are layers of determinants that influence the disease risk. The determinants shown in Figure 1 and chronic diseases. Such a hierarchy of determinants and risk factors/markers is given in Table 1.

Figure 1: A hierarchy of determinants and risk factors/markers in chronic disease aetiology.

and the Asian-Pacific region and is currently occurring in others, such as Brazil, Russia, India, and China. The double-edged sword of progress, which facilitated control over infectious diseases, instigated an unhealthy trend in chronic diseases. The worldwide rise in obesity has been an accompaniment to this.

2. Causality in Disease

While infectious disease can usually be ascribed to microbial causes, causality in NCDs is more problematic. In most cases, the agent of causality is ill-defined, but there are layers of influence. As shown in Figure 1, most immediate to the cases, the agent of causality is ill-defined, but there are layers of determinants that influence the disease risk. The determinants shown in Figure 1 and chronic diseases. Such a hierarchy of determinants and risk factors/markers is given in Table 1.

Figure 1: A hierarchy of determinants and risk factors/markers in chronic disease aetiology.

A summary of anthropogens associated with these diseases, discussed in the text, is given in Table 2 using the acronym NASTIE ODOURS.

Table 1: Chronic disease categories with lifestyle/environmental determinants.

| Chronic disease category                  | Lifestyle/environmental determinant |
|------------------------------------------|-------------------------------------|
| Cardio- and cerebrovascular diseases     |                                     |
| Cancers with lifestyle component        |                                     |
| Endocrine/metabolic disorders            |                                     |
| Gastrointestinal diseases                |                                     |
| Kidney disease                           |                                     |
| Mental/CNS health                        |                                     |
| Musculoskeletal disorders                |                                     |
| Respiratory diseases                     |                                     |
| Reproductive disorders                   |                                     |
| Dermatological disorders                 |                                     |

Obviously, not all anthropogens are unhealthy for all people. The identification of those that have negative health effects however is important for developing a focus on chronic disease aetiology. We consider that a review of anthropogens could focus the attention of health workers and hence provide such a review below. We provide evidence of metaflammatory reactions from either inadequate or excessive exposure to these and evidence for their association with a number of chronic diseases. A list of disease categories is shown in Table 1.

An individual’s susceptibility to a range of anthropogens clearly varies with genetic predisposition to chronic diseases carried through the genome including obesity, diabetes, many cancers, and cardiovascular disease. However, during the second half of the 20th century, a revolution in our understanding of environmental influences and lifelong gene expression has emphasized the importance of early environmental influences on the later development of chronic disease. It is now clear that epigenetics, the heritable changes in gene activity not driven by change in the DNA sequence, has a major influence on the susceptibility to chronic disease for both individuals and their offspring. Chronic disease driven by a mismatch between the environment one is programmed for and the environment one is born into is highlighted by the extreme susceptibility of indigenous and developing communities to anthropogens and related chronic diseases.

Obviously, not all anthropogens are unhealthy for all people. The identification of those that have negative health effects however is important for developing a focus on chronic disease aetiology. We consider that a review of anthropogens could focus the attention of health workers and hence provide such a review below. We provide evidence of metaflammatory reactions from either inadequate or excessive exposure to these and evidence for their association with a number of chronic diseases. A list of disease categories is shown in Table 1.

A summary of anthropogens associated with these disease categories, discussed in the text, is given in Table 2 using the acronym NASTIE ODOURS.
| Determinants                                      | Decreases risk                                                                 | Increases risk                                                                 | Moderators                                                                 |
|--------------------------------------------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------|----------------------------------------------------------------------------|
| Nutrition                                        | Fruit/vegetables                                                               | High total energy                                                              | Binge eating/drinking                                                     |
|                                                  | Dietary fibre                                                                  | High energy density                                                            | Social/holiday eating                                                     |
| 1, 2, 3, 4, 5, 6                                 | Whole grains                                                                   | Excess processed foods                                                         | “Restrained” eating                                                       |
|                                                  | Food variety                                                                    | High GI foods                                                                  | Feasting                                                                  |
|                                                  | Seafood                                                                        | Sat./trans fats                                                                | Culture                                                                   |
|                                                  | Healthy eating patterns                                                        | Sugars                                                                        | Habits                                                                    |
|                                                  |                                                                               | Salt                                                                           |                                                                            |
|                                                  |                                                                               | Excessive alcohol                                                               |                                                                            |
|                                                  |                                                                               | Sugared soft drinks                                                            |                                                                            |
|                                                  |                                                                               | Processed/red meat                                                            |                                                                            |
| (In)Activity                                     | Aerobic exercise                                                                | Overload                                                                      | Peer/social/pressure                                                      |
| 1, 2, 3, 6, 7, 8, 9                              | Resistance exercise                                                             | “Learned helplessness”                                                         | Uncontrollable thoughts                                                   |
|                                                  | Stretching                                                                     | Early trauma                                                                   | Worry                                                                     |
|                                                  | Stability                                                                       | Boredom                                                                       | Fear of the unknown                                                      |
|                                                  | Leisure activity                                                                | Caffeine/drug use                                                              | Obesity                                                                   |
|                                                  | Incidental activity                                                            |                                                                               |                                                                            |
| Stress, anxiety, and depression                   | Exercise/fitness                                                                | Overload                                                                       |                                                                            |
| 1, 3, 4, 9                                       | Healthy nutrition                                                               | “Learned helplessness”                                                         |                                                                            |
|                                                  | Perceived control                                                              | Early trauma                                                                   |                                                                            |
|                                                  | Self-efficacy                                                                   | Boredom                                                                       |                                                                            |
|                                                  | Coping skills                                                                   | Caffeine/drug use                                                              |                                                                            |
|                                                  | Meaning                                                                         |                                                                               |                                                                            |
| Technology-induced-pathology                      |                                                                               | Motor vehicle use                                                              | Peer/social pressure                                                      |
| 7, 10                                            |                                                                               | Machinery                                                                     | Legislation/regulation                                                    |
|                                                  |                                                                               | TV/small screens                                                               | Habits                                                                    |
|                                                  |                                                                               | Repetitive actions                                                             |                                                                            |
|                                                  |                                                                               | Noise pollution                                                                |                                                                            |
|                                                  |                                                                               | Processed foods                                                                |                                                                            |
|                                                  |                                                                               | Weapons of war                                                                |                                                                            |
| Inadequate sleep                                  |                                                                               | Stress                                                                         | Activity before sleep                                                     |
| 1, 3, 6, 10                                       | REM sleep                                                                       | Entertainment                                                                  |                                                                            |
|                                                  | Bed-time                                                                        | Sleep disorders                                                                | Stress                                                                    |
|                                                  | Hypersomnia                                                                     | Overheating                                                                    | Anxiety/depression                                                        |
|                                                  | Nutrition                                                                       | Interactive media                                                             | Obesity habits                                                            |
|                                                  | Exercise/fitness                                                                | Alcohol/drugs                                                                  |                                                                            |
| Environment                                       |                                                                               | Passive influences                                                             | Social proof                                                              |
| 2, 3, 6, 9, 10                                    | Political/economic structure                                                    | Second-hand smoke                                                             | “Tipping point”                                                           |
|                                                  | Recreational space                                                              | Particle pollution                                                             | Social/peer pressure                                                      |
|                                                  | “Green” exposure                                                                | Endocrine disrupting Chemicals (EDCs)                                         | Cultural influences                                                       |
|                                                  | Infrastructure for walking and cycling                                          | Home chemicals                                                                | Habit                                                                     |
|                                                  | Plant-based nutrition                                                           | Drug-immunity (e.g., antibiotics)                                             |                                                                            |
| Occupation                                        |                                                                               | Stress                                                                         |                                                                            |
| 1, 2, 8, 10                                       | Social justice                                                                  | Shift-work                                                                     | Peer pressure                                                             |
|                                                  | Work equality                                                                   | Hazard exposure                                                                |                                                                            |
|                                                  | Security of employment                                                          | Conflict                                                                       |                                                                            |
| Drugs, smoking, and alcohol                      |                                                                               | Work stress                                                                    | Stress, anxiety, and depression                                          |
| 1–10                                             | Appropriate medication                                                         | Peer pressure                                                                   |                                                                            |
|                                                  |                                                                               | Recreational drugs                                                             |                                                                            |
|                                                  |                                                                               | Cigarette smoking                                                              |                                                                            |
|                                                  |                                                                               | Alcohol use                                                                    |                                                                            |
|                                                  |                                                                               | Iatrogenesis                                                                   |                                                                            |
Table 2: Continued.

| Determinants          | Decreases risk    | Increases risk                           | Moderators                |
|-----------------------|-------------------|------------------------------------------|---------------------------|
| Over- and underexposure 1, 2, 3 | Sunlight light stimulation | Sunlight (excess) Sunlight (inadequate) Low humidity/ asbestos Radiation | Peer/social pressure Cultural influences Habit |
| Relationships 1, 3, 6 | Companionship Peer support Maternal support in childhood “Love” | Interpersonal conflict Loneliness Lack of support | Peer pressure Early experience |
| Social factors 1–10 | Trust Income security Market regulation SE status Education | Inequality Poverty Deregulated markets | Stress Bullying Cognitive processes Peer/social pressure |

3. Identifying “Anthropogens”

In discussions of modern chronic disease etiology, smoking, poor nutrition, excess weight, and alcohol use stand out as the dominant preventable determinants [20]. However recent research has expanded this considerably to take account of social, cultural, occupational, environmental, and other factors (“anthropogens”) in the hierarchical structure (Figure 1). A list of these is described below. The discussion is not meant to be an extensive review of each topic area but rather to cover the main components of each identified here as being associated with chronic disease and with a common metaflammatory base. Each is also considered in its own right an independent determinant in the absence of obesity or weight gain.

Nutrition. The importance of nutrition for the prevention and management of chronic disease is well known [21]. Inadequate or overnutrition has been proposed to account for up to two-thirds of risk for certain chronic problems like type 2 diabetes and cardiovascular disease [22] and a significant proportion of other chronic ailments [23]. Health problems have been related to both specific nutrients [24] and overall meal patterns [25], with inflammatory biomarkers generally accompanying those foods/eating patterns associated with disease risk in the presence and the absence of obesity [17, 26].

Excessive energy intake, particularly of high energy-dense, but low nutrient-dense products, is a major problem of industrialised societies. Still, excessive intake of even healthy foods can increase postprandial (and potentially chronic) metaflammation [27], suggesting negative long-term outcomes. At the other extreme, chronic energy restriction is now well documented as being associated with increased longevity and improved health [28].

In relation to nutrition quality, studies have reported increased risk and elevated metaflammation from excessive amounts of sugars, salt, alcohol, and (saturated and trans) fats, as well as inadequate levels of fibre, fruit, vegetables, grains, and certain nutrients [17, 26]. Levels of processing have been proposed as a general indication of risk [29], and there appears to be a clear postprandial “metaflammatory” trail from processed versus whole foods, suggesting an evolutionary role in nutritional health [18, 30, 31]. Although individual and genetic factors influence outcomes [32], the worst-case scenario for obesity and chronic disease based on current evidence would be an excessive amount of a modern, western diet made up of highly processed foods [25]. While there may be controversy over an ideal diet (mediterranean, anti-inflammatory, paleo, etc.), Michael Pollan’s [33] dictum to “Eat food. Mostly plants. Not too much”, provides a simple, concise, and accurate long-term nutritional goal.

(In)Activity. Inactivity, as well as sedentary activities like sitting, in contrast to insufficient physical activity, is an independent risk factor for disease [34]. It is one of the major unhealthy anthropogens of our times with links to over 35 different diseases [35].

Movement, physical activity, and exercise can be conceived of as gradations along a scale and all have a role, to different degrees, in primary prevention of a range of diseases and, in some cases, treatment and reversal of risks and/or disease entities (namely, type 2 diabetes). This is mainly through the modems of aerobic capacity and/or muscle strength and integrity. Flexibility and balance provide musculoskeletal integrity that can enhance quality of life.

While controversies exist about type, intensity, frequency, and duration of physical activity, there is no dispute about the health value of an optimal physical activity requirement for humans. A generic prescription based on “volume” (intensity $\times$ frequency $\times$ duration) incorporating both aerobic and resistance training is appropriate in the absence of a more detailed individual-genetic understanding [36]. In the absence of this, recommendations that “…any activity is better than none, and more is better than a little”, and for individuals to “think of movement as an opportunity, not an inconvenience” [37] are appropriate. The relationship between activity and health has been referred to as a U-shaped function, with excessive exercise having diminishing health benefits as reflected in increased metaflammation, similar to that of inactivity [38, 39].
Poor nutrition and inactivity are the best-known inducers of weight gain. Several studies however now show that either poor nutrition or inactivity can independently modify obesity, as well as other chronic disease risks like obesity [60] and smoking [61]. Control of technology misuse is traditionally through legislative restrictions (i.e., use of cell phones while driving) but personal controls on behavior are also likely to be necessary.

Stress, Anxiety, and Depression. The nature of stress has changed in recent times from an acute warning signal to a chronic strain on physiological adaptation. Typically, the body's reaction to a stressor has been "flight" or "fight," but these options are less viable in the modern environment, leading to chronic effects such as elevated adrenocortical hormone concentrations, activation of the sympathetic nervous system [42], ailments like heart disease [43], and accompanying vascular, metabolic, and inflammatory processes [43, 44]. Of itself, stress is not a health issue, and a certain amount within the coping capacity of the individual [45] is vital for a healthy life. It is the "strain," resulting from excessive stress, outside the limitations of the stressor to cope, and resulting in anxiety and depression that can lead to allostatic and chronic disease.

Anxiety is a form of "feared helplessness" defined as "...a thin stream of fear trickling through the mind. If encouraged, it cuts a channel into which all other thoughts are drained" [46]. Anxiety occurs while an individual is striving to adapt and the association of this with ill-health is diffuse. However it is when striving ceases that depression or "learned helplessness" [47] can result, with more defined channels into a range of chronic diseases. High levels of depression have been shown to be related to a range of chronic diseases from type 2 diabetes [48] to Alzheimer's [49]. A consistent finding is a link between stress, anxiety, and depression and increased inflammatory markers, which can be associated with [50] or independent of body weight [51].

Technology-Pathology. The association of chronic disease with certain modern forms of technology is often overlooked or disregarded. This can range from death or chronic pain initiated from motor vehicle or machine injuries to auditory problems from amplified music [52]. At the extremes, it can range from mortality and morbidity from firearms and high tech weapons used in warfare to apparently obscure problems like dermatoses [53], other skin disorders [54], impaired vision [55], and repetitive strain injury from excessive computer and small screen use [56].

Other recent problems within this category are acute and chronic problems that occur while focusing on use of social media (e.g., texting and tweeting) whilst carrying out other activities, such as driving [57]. Because of its immediacy, social media bullying and intimidation can also lead to psychological morbidities and even suicide amongst youth, although this is not as yet well documented in the medical literature. Other problems such as "facebook depression" [58] are only beginning to emerge. Social contagion [59] effects on disease are amplified through the use of social media as shown in the association between social networks and chronic disease risks like obesity [60] and smoking [61]. Control of technology misuse is traditionally through legislative restrictions (i.e., use of cell phones while

Environment. Aspects of the environment have always been a consideration in public health. However the rise of chronic diseases has led to a more structured approach to this. Swinburn et al. [74], for example, consider four types (physical, economic, policy, and sociocultural) and two sizes (micro and macro) of "obesogenic" [75] environments, which serve to draw attention away from purely biological explanations of obesity and by extension chronic disease.

Small particle pollution from exhaust and industrial fumes [76] as well as a wide range of chemicals in the air, water, soil, and households [77] makes up the natural physical environment. A large group of such pollutants, labeled endocrine disrupting chemicals (EDCs) [78], has been attributed to significant physiological and even behavioural changes such as increased hunger, which can lead to obesity [79]. Exposure data (e.g., to bisphenol A) suggests
a link between this and obesity in children [80], leading to
the suggestion of some chemicals being "obesogens" [81].
Increases in carbon in the atmosphere are an example of a
dramatic macroenvironmental change with potential health
(as well as climate change) impacts [82]. Many environmental
factors have also been shown to lead to increased metaflam-
mation as an intermediary process with links to chronic
disease [78, 83].

Sociocultural influences are reflected, for example, in
attitudes to feasting in some cultures which may have been
suitable in historical times but are contraindicated with the
imposition of a western culture and diets. Political environ-
ments make the “rules” that allow, for example, smoking or
drinking in the family or unrestricted sales of unhealthy foods
and products (e.g., cigarettes) in society. Overarching all of
this is the macroeconomic system, including the modern
economic growth model which demands consumption that
is not necessarily conducive to health [84, 85].

Recent findings relating to the gut microbiome suggest
that the inner environment ("in"-vironment in contrast to
“en”-vironment) should also be considered within this cate-
gory [86]. Changes in the gut microbiome not only appear to
result from unhealthy activities but also influence outcomes,
such as obesity through better energy harvesting through a
“leaky gut” [87, 88].

Some protection against unhealthy environments may
be provided by positive lifestyle changes [77, 89]. It should
be obvious however that significant macroenvironmental
reforms through legislative change, some of which may
crossover with those required to moderate climate change
[90] and other environmental degradation, are necessary.

**Occupation.** Meaningful work is an important component
of good health. Generally however it is the direct effects on
health and safety—exposure to machinery, chemicals, injury,
and so forth—or the adverse health effects of work hours and
shift work [91] and their effects on inflammation [92] that
are considered. Recent concern has turned more to social
factors. Job insecurity and job strain, for example, have been
shown to increase the risk of heart disease (although the effect
may be modest and largely explainable by socioeconomic
factors [93]). Poor job satisfaction is linked to “burn out,” low
self-esteem, depression, and anxiety [94] and excessive work
hours to a risk of ill-health and damage to social relationships
[95]. In work with the British Civil Service, Marmot and
colleagues have reported on the health effects of perceived
social justice [96], “burn out” [97], and social standing [98,
99] relating to occupational status. Changes in the nature and
security of work in the modern world mean that both the
physical and psychological components of occupations need
to be considered part of a lifestyle/environmental perspective
on health. Hence some forms of occupation can be seen as
modern-day, chronic disease promoting anthropogens.

**Drugs, Cigarettes, and (Excessive) Alcohol.** Drugs, both licit
and illicit, are responsible for a significant and increasing
degree of morbidity and mortality in modern societies.
The stand-out amongst licit products is cigarette smoking
and its links with cancers, heart disease, and respiratory
problems [100]. Legal medications form another category of
drug related mortality and morbidity. Shapiro et al.
[101] categorise problematic drug use into hazardous use,
substance abuse, or substance dependence. Unfortunately
some of the most effective medications for disorders such as
schizophrenia, depression, and certain forms of epilepsy
increase hunger, weight gain, and cardio-metabolic risk [102].
Illicit drug use (and the accompanying health effects) appears
to increase with increased urbanization, economic prosperity,
and inequality.

Its more ambiguous outcomes make alcohol a more
diverse problem. Some health and social benefits of moderate
consumption [103] are difficult to weigh up against the severe
health and social disruption of excessive consumption, binge
drinking, social and economic costs [104], and other chronic
disease outcomes [100]. Overuse of alcohol is also known to
have deleterious effects on several forms of disease including
cancers, although this literature is not expanded on here.
While excessive alcohol intake is inflammatory, moderate
intake has an anti-inflammatory effect [105].

**Over- and Underexposure.** While many lifestyle-related beha-
vours have a linear association with health (e.g., smoking and
sleep), others have a “U” or “tick-shaped” relationship (e.g.,
physical activity, alcohol, and sleep). Exposure to ultraviolet
radiation (UVR) from sunlight is a case in point. UVR is
classified as a carcinogen and a major determinant for several
forms of skin disorders. The incidence of melanoma, the most
deadly form of skin cancers, has doubled in recent years
[106, 107], although this is less common than other forms
of skin cancers and photoaging [108]. Intermittent extreme
exposures and sunburn, as well as chronic overexposure can
have differing degrees of risk [109]. Overexposure to heat
and dryness (low humidity) is also thought to have adverse
effects on the skin [110]. Passive smoking is yet another form
of overexposure with increased risks of chronic diseases like
type 2 diabetes [111].

At the other extremes, underexposure to sunlight can
lead to deficiencies in vitamin D, thus increasing risks of
heart disease [112], type 2 diabetes [113], and depression
[114], as well as more well-known problems such as rickets
[115]. Underexposure to daylight can also have unhealthy
consequences in seasonal affective disorders (SAD) suffered
at extreme latitudes [116].

**Relationships.** The quality of personal and social relationships
is clearly linked to chronic disease outcomes [117] including
heart disease [118], stroke [119], some cancers [120], and all-
disease mortality [121].

The pathways for this are, as yet, unclear and psycholog-
ical mediators have not been proven [122], but inflammatory
processes have been associated with poor social relations
[123] such as spousal ambivalence [124] and isolation [125]
and can even stem back to maternal separation in childhood
[126]. People who have supportive close relationships have
lower levels of systemic inflammation compared to people
who have unsatisfactory relationships [127]. Negative and
competitive social interactions can even increase proinflam-
matory cytokine activity on a daily level [128]. In reverse,
a Finnish study has shown that social support can alleviate the inflammation associated with childhood adversities [129]. Improving awareness of the importance of social support and assisting in finding such support should be integral to chronic disease management.

**Social Disadvantage.** Social disadvantage is associated with diseases like type 2 diabetes [130] and cardiovascular disease [131]. Disadvantage exists not only through socioeconomic status [98] and income inequalities [132] but also through economic stress and security, with metaflammation as a possible link [133].

According to the Commission on Social Determinants of Health [134], inequities in power, money, and resources are responsible for much of the inequalities in health within and between countries. While the effects of socioeconomic status on health (and inflammation) are relatively clear [135, 136], the effects of income disparities on health have been more controversial. Wilkinson and Pickett [132] in a descriptive analysis of ratios of rich to poor within and between OECD countries show a linear worsening of a number of health and social problems (obesity, infant mortality, teenage pregnancies, etc.) in countries with greater income gradients.

Much has been made of the mechanisms underlying social disadvantage, socioeconomic status, and inequality. Stringhini et al. [137] show that modifiable health behaviours and obesity could explain around 50% of the incidence in type 2 diabetes. Increases in inflammatory processes are also common with social disadvantage in different forms [138, 139] (see Figure 2).

### 4. Discussion

We have categorized a number of determinants of modern chronic diseases within a hierarchy using the acronym NASTIE ODOURS (Table 2). In doing so, we have extended the concept of lifestyle to include broader aspects of the social, political, and economic environments. Because of their man-made nature (in contrast to the microbial nature of infectious disease determinants), these have been collectively called anthropogens [19]. In addition, we have shown that most of the anthropogens discussed here have a common physiological link through chronic, systemic inflammatory (metaflammation) processes.

An obvious omission from our classification is obesity. There are two reasons for this. In the first place, obesity should be seen as a risk factor, rather than a primary determinant of disease, which is downstream, sometimes, but not always resulting from some of the determinants considered here, like overnutrition, inactivity, stress, social pressure, and so forth. A second reason is the variability of causal links between obesity and disease as exemplified in the “obesity paradox” [140] and metaflammatory associations with disease preceding or in the absence and presence of obesity [15, 17, 18]. Hence obesity is probably more a “canary in a mineshaft,” warning of problems in the broader environment than a universal cause of disease [141, 142].

There are a number of implications stemming from this discussion. Firstly, arguments about the best “diets” for weight loss and chronic disease become less relevant when looking at this big picture pattern of disease [84]. Secondly, the presence of independent upstream determinants means that weight loss should not be the sole focus of chronic disease management. Losses can be expected from changing aspects of the NASTIE ODOURS formula, but weight loss should not be seen as the sole driver of the process. Third, it would be wrong to assume that chronic disease determinants should be managed singly. The interactive nature of these determinants suggests more of a “systems” model approach to
managing chronic disease problems than is often considered. Inadequate sleep and resultant fatigue, for example, can lead to a reduction in physical activity and a change in dietary patterns, uptake of technology-based entertainment, increased obesity, and resultant depression, which can continue and/or widen the cycle. The use of a “diet” for treating obesity, when underlying inflammatory processes may be related to all these more obscure determinants, is unlikely to provide optimal health. Finally a concentration on lifestyle through simply proximal and even medial determinants as defined here is unlikely to significantly influence the problem while more dominant upstream determinants remain. Effective management of modern chronic disease thus needs to be broadened to encompass a greater sphere of influence than is often publically perceived or politically popular.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

References

[1] M. L. Power and J. Schulkin, *The Evolution of Obesity*, Johns Hopkins University Press, Baltimore, Md, USA, 2009.

[2] M. M. Finucane, G. A. Stevens, M. J. Cowan et al., “National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants,” *The Lancet*, vol. 377, no. 9765, pp. 557–567, 2011.

[3] D. E. King, E. Matheson, S. Chirina, A. Shankar, and J. Broman-Fulks, “The status of baby boomers’ health in the United States: the healthiest generation?” *Journal of the American Medical Association*, vol. 173, no. 5, pp. 385–386, 2013.

[4] J. L. Ochsman, “Chronic disease: are we missing something?” *Journal of Alternative and Complementary Medicine*, vol. 17, no. 4, pp. 283–285, 2011.

[5] S. J. Genuis, “What’s out there making us sick?” *Journal of Environmental and Public Health*, vol. 2012, Article ID 605137, 10 pages, 2012.

[6] M. T. Have, A. van der Heide, J. P. Mackenbach, and I. D. de Beaufort, “An ethical framework for the prevention of overweight and obesity: a tool for thinking through a programme’s ethical aspects,” *European Journal of Public Health*, vol. 23, no. 2, pp. 299–305, 2013.

[7] G. Rose, *The Strategy of Preventive Medicine*, Oxford University Press, Oxford, UK, 1992.

[8] B. Harris, “Public health, nutrition, and the decline of mortality: the McKeown thesis revisited,” *Social History of Medicine*, vol. 17, no. 3, pp. 379–407, 2004.

[9] H. Anderson, “History and philosophy of modern epidemiology,” 2011, http://philsci-archive.pitt.edu/id/eprint/4159.

[10] T. McKeown, *The Origins of Human Disease*, Basil Blackwell, New York, NY, USA, 1998.

[11] J. W. Sanders, G. S. Fuhrer, M. D. Johnson, and M. S. Riddle, “The epidemiological transition: the current status of infectious diseases in the developed world versus the developing world,” *Science Progress*, vol. 91, no. 1, pp. 1–38, 2008.

[12] G. S. Hotamisligil, “Inflammation and metabolic disorders,” *Nature*, vol. 444, no. 7121, pp. 860–867, 2006.

[13] G. S. Hotamisligil, N. S. Shargill, and B. M. Spiegelman, “Adipose expression of tumor necrosis factor-α: direct role in obesity-linked insulin resistance,” *Science*, vol. 259, no. 5091, pp. 87–91, 1993.

[14] R. Medzhitov, “Origin and physiological roles of inflammation,” *Nature*, vol. 454, no. 7203, pp. 428–435, 2008.

[15] P. Libby, “Inflammatory mechanisms: the molecular basis of inflammation and disease,” *Nutrition Reviews*, vol. 65, no. 12, pp. S40–S46, 2007.

[16] M. F. Gregor and G. S. Hotamisligil, “Inflammatory mechanisms in obesity,” *Annual Review of Immunology*, vol. 29, pp. 415–445, 2011.

[17] G. Egger and J. Dixon, “Inflammatory effects of nutritional stimuli: further support for the need for a big picture approach to tackling obesity and chronic disease,” *Obesity Reviews*, vol. 11, no. 2, pp. 137–149, 2010.

[18] G. Egger and J. Dixon, “Non-nutrient causes of low-grade, systemic inflammation: support for a ‘canary in the mineshaft’ view of obesity in chronic disease,” *Obesity Reviews*, vol. 12, no. 5, pp. 339–345, 2011.

[19] G. Egger, “In search of a ‘germ theory’ equivalent for chronic disease,” *Preventing Chronic Disease*, vol. 9, no. 11, pp. 1–7, 2012.

[20] M. Ezzati and E. Riboli, “Behavioral and dietary risk factors for non-communicable diseases,” *The New England Journal of Medicine*, vol. 369, pp. 954–964, 2013.

[21] World Health Organization, *Diet, Nutrition, and the Prevention of Chronic Diseases*, vol. 916, WHO, Geneva, Switzerland, 2003.

[22] L. Nicholas, D. Roberts, and D. Pond, “The role of the general practitioner and the dietitian in patient nutrition management,” *Asia Pacific Journal of Clinical Nutrition*, vol. 12, no. 1, pp. 3–8, 2003.

[23] Australian Institute of Health and Welfare, “Chronic diseases,” 2013, http://www.aihw.gov.au/chronic-diseases/.

[24] L. Galland, “Diet and inflammation,” *Nutrition in Clinical Practice*, vol. 25, pp. 634–664, 2010.

[25] J. Barbareiko, M. Koch, M. B. Schulze, and U. Nothlings, “Dietary pattern analysis and biomarkers of low-grade inflammation: a systematic literature review,” *Nutrition Reviews*, vol. 71, no. 8, pp. 511–527, 2013.

[26] P. C. Calder, N. Ahluwalia, F. Brouns et al., “Dietary factors and low-grade inflammation in relation to overweight and obesity,” *British Journal of Nutrition*, vol. 106, supplement 3, pp. S75–S78, 2011.

[27] J. H. O’Keefe, N. M. Gheewala, and J. O. O’Keefe, “Dietary strategies for improving post-prandial glucose, lipids, inflammation, and cardiovascular health,” *Journal of the American College of Cardiology*, vol. 51, no. 3, pp. 249–255, 2008.

[28] C. W. Bales and W. E. Kraus, “Calorie restriction: implications for human cardiometabolic health,” *Journal of Cardiopulmonary Rehabilitation and Prevention*, vol. 33, no. 4, pp. 201–208, 2013.

[29] C. A. Monteiro, “Nutrition and health. The issue is not food, nor nutrients, so much as processing,” *Public Health Nutrition*, vol. 12, no. 5, pp. 729–731, 2009.

[30] L. Cordain, *The Paleo Answer*, John Wiley and Sons, New Jersey, NJ, USA, 2012.

[31] T. C. Campbell and T. M. Campbell, *The China Study*, Bebella Books, Dallas, Tex, USA, 2006.

[32] D. M. Minich and J. S. Bland, “Personalized lifestyle medicine: relevance for nutrition and lifestyle recommendations,” *The Scientific World Journal*, vol. 2013, Article ID 129841, 14 pages, 2013.
[33] M. Pollan, In Defense of Food: An Eater’s Manifesto, Penguin Books, New York, NY, USA, 2008.

[34] D. Dunstan, H. Howard, G. N. Healy, and N. Owen, “Too much sitting—a health hazard,” Diabetes Research and Clinical Practice, vol. 97, no. 3, pp. 368–376, 2012.

[35] F. W. Booth, M. V. Chakravartly, S. E. Gordon, and E. E. Spangelo, “Waging war on physical inactivity: using modern molecular ammunition against an ancient enemy,” Journal of Applied Physiology, vol. 93, no. 1, pp. 3–30, 2002.

[36] P. L. Greenhaff and M. Hargreaves, “‘Systemsbiology’ in human exercise physiology: is it something different from integrative physiology?” Journal of Physiology, vol. 589, no. 5, pp. 1031–1036, 2011.

[37] National Health and Medical Research Council, National Physical Activity Guidelines, Department of Health and Ageing, Australian Government Publishing Services, ACT, Canberra, Australia, 1999.

[38] R. A. Pinho, L. A. Silva, C. A. Pinheiro et al., “Oxidative stress and inflammatory parameters after an ironman race,” Clinical Journal of Sport Medicine, vol. 20, no. 4, pp. 306–311, 2010.

[39] B. K. Pedersen, “The anti-inflammatory effect of exercise: its role in diabetes and cardiovascular disease control,” Essays in Biochemistry, vol. 42, pp. 105–117, 2006.

[40] M. C. de la Camara, J. Santabarbara et al., “Depression and incident Alzheimer disease: the impact of disease severity,” The American Journal of Geriatric Psychiatry, 2013.

[41] M. Hamer and E. Stamatakis, “Inflammation as an intermediate pathway in the association between psychosocial stress and obesity,” Physiology and Behavior, vol. 94, no. 4, pp. 536–539, 2008.

[42] E. A. Lambert and G. W. Lambert, “Stress and its role in systemic inflammation: is it something different from integrative physiology?” European Journal of Epidemiology, vol. 23, no. 2, pp. 95–103, 2008.

[43] T. Almadi, I. Cathers, and C. M. Chow, “Associations among anxiety, depression, and obesity,” Diabetes Research and Clinical Practice, vol. 101, no. 2, pp. 131–140, 2013.

[44] P. Gracia-García, C. de-la-Cámara, J. Santabárbara et al., “Depression and incident Alzheimer disease: the impact of disease severity,” The American Journal of Geriatric Psychiatry, 2013.

[45] M. Hamer, G. J. Molloy, C. de Oliveira, and P. Demakakos, “Persistent depressive symptomatology and inflammation: to what extent do health behaviours and weight control mediate this relationship?” Brain, Behavior, and Immunity, vol. 23, no. 4, pp. 413–418, 2009.

[46] E. Henderson, M. A. Testa, and C. Hartnick, “Prevalence of noise-induced hearing-threshold shifts and hearing loss among US youths,” Pediatrics, vol. 127, no. 1, pp. e39–e46, 2011.

[47] M. E. Seligman, Helplessness: On Depression, Development and Death, Freeman, San Francisco, Calif, USA, 1975.

[48] J. B. Dixon, J. L. Browne, G. W. Lambert et al., “Severely obese people with diabetes experience impaired emotional well-being associated with socioeconomic disadvantage: results from diabetes MILES—Australia,” Diabetes Research and Clinical Practice, vol. 101, no. 2, pp. 131–140, 2013.

[49] G. Alvarez and N. T. Ayas, “The impact of sleep duration and inflammation: findings on C-reactive protein and interleukin 6 in the Whitehall II study,” The American Journal of Epidemiology, vol. 178, no. 6, pp. 595–961, 2013.

[50] G. E. Alvarez and N. T. Ayas, “The impact of sleep duration on health: a review of the literature,” Progress in Cardiovascular Nursing, vol. 19, no. 2, pp. 56–59, 2004.

[51] H. R. Colten and B. M. Altevogt, Eds., Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem, National Academies Press, Washington, DC, USA, 2006.

[52] M. A. Carskadon and W. C. Dement, “Normal human sleep: an overview,” in Principles and Practice of Sleep Medicine, M. H. Kryger, T. H. Roth, and W. C. Dement, Eds., Elsevier, St. Louis, Mo, USA, 5th edition, 2010.

[53] US National Sleep Foundation, “International bedroom poll,” 2013, http://now.msn.com/trenddetails?q=international+bedroom+poll.
[69] M. P. Hoevenaar-Blom, A. M. Spijkerkerman, D. Kromhout, and W. M. Verschuren, “Sufficient sleep duration contributes to lower cardiovascular disease risk in addition to four traditional lifestyle factors: the MORGEN study,” European Journal of Preventive Cardiology, 2013.

[70] S. M. Greer, A. N. Goldstein, and M. P. Walker, “The impact of sleep deprivation on the human brain,” Nature Communications, vol. 2259, 2013.

[71] S. J. Motivala, “Sleep and inflammation: psychoneuroimmunology in the context of cardiovascular disease,” Annals of Behavioral Medicine, vol. 42, no. 2, pp. 141–152, 2011.

[72] N. Nishinoue, T. Takano, A. Kaku et al., “Effects of sleep hygiene education and behavioral therapy on sleep quality of white-collar workers: a randomized controlled trial,” Industrial Health, vol. 50, no. 2, pp. 123–131, 2012.

[73] G. S. Brunborg, R. A. Mentzoni, H. Molde et al., “The relationship between media use in the bedroom, sleep habits and symptoms of insomnia,” Journal of Sleep Research, vol. 20, no. 4, pp. 569–575, 2011.

[74] B. Swinburn, G. Egger, and F. Raza, “Dissecting obesogenic environments: the development and application of a framework for identifying and prioritizing environmental interventions for obesity,” Preventive Medicine, vol. 29, no. 6, pp. 563–570, 1999.

[75] G. Egger and B. Swinburn, “An “ecological” approach to the obesity pandemic,” British Medical Journal, vol. 315, no. 7106, pp. 477–480, 1997.

[76] R. J. Laumbach and H. M. Kipen, “Acute effects of motor vehicle traffic-related air pollution exposures on measures of oxidative stress in human airways,” Annals of the New York Academy of Sciences, vol. 1203, pp. 107–112, 2010.

[77] M. E. Sears and S. J. Genuis, “Environmental determinants of chronic disease and medical approaches: recognition, avoidance, supportive therapy, and detoxification,” Journal of Environmental and Public Health, vol. 2012, Article ID 356798, 15 pages, 2012.

[78] R. R. Dietert, “Misregulated inflammation as an outcome of early-life exposure to endocrine-disrupting chemicals,” Reviews on Environmental Health, vol. 27, no. 2-3, pp. 117–131, 2012.

[79] R. Kelishai, P. Poursafa, and F. Jamshidi, “Role of environmental and public health in early-life exposure to endocrine-disrupting chemicals,” International Journal of Environmental Research and Public Health, vol. 12, no. 4, pp. 381–387, 2015.

[80] F. Bäckhed, “99th dahlem conference on infection, inflammation and chronic inflammatory disorders: the normal gut microbiota in health and disease,” Clinical and Experimental Immunology, vol. 160, no. 1, pp. 80–84, 2010.

[81] M. Hasnain, W. V. Vieweg, and B. Hollett, “Weight gain and glucose dysregulation with second-generation antipsychotics and antidepressants: a review for primary care physicians,” Postgraduate Medicine, vol. 124, no. 4, pp. 154–167, 2012.
D. Huang, Z. Hunter, and L. H. Francescutti, “Alcohol, health, and injuries,” The American Journal of Lifestyle Medicine, vol. 7, no. 4, pp. 232–240, 2013.

J. H. O’Keefe, K. A. Bybee, and C. J. Lavie, “Alcohol and cardiovascular health. The razor-sharp double-edged sword,” Journal of the American College of Cardiology, vol. 50, no. 11, pp. 1009–1014, 2007.

W. Garibyan and D. E. Fisher, “How sunlight causes melanoma,” Current Oncology Reports, vol. 12, no. 5, pp. 319–326, 2010.

M. Pinquart and P. R. Duberstein, “Associations of social networks, inflammation, and health,” Psychoneuroendocrinology, vol. 35, no. 1, pp. 33–38, 2010.

J. K. Kiecolt-Glaser, J.-P. Gouin, and L. Hantsoo, “Close relationships, inflammation, and health,” Neuroscience and Biobehavioral Reviews, vol. 35, no. 1, pp. 487–4504, 2013.

B. N. Uchino, J. A. Bosch, T. W. Smith et al., “Relationships and cardiovascular risk: perceived spousal ambivalence in specific relationship contexts and its links to inflammation,” Health Psychology, 2013.
[138] E. M. Friedman and P. Herd, “Income, education, and inflammation: differential associations in a national probability sample (The MIDUS Study),” Psychosomatic Medicine, vol. 72, no. 3, pp. 290–300, 2010.

[139] M. G. Marmot, M. J. Shipley, H. Hemingway, J. Head, and E. J. Brunner, “Biological and behavioural explanations of social inequalities in coronary heart disease: the Whitehall II study,” Diabetologia, vol. 51, no. 11, pp. 1980–1988, 2008.

[140] K. M. Flegal and K. Kalantar-Zadeh, “Perspective: mortality and survival,” Obesity, 2013.

[141] G. J. Egger and J. B. Dixon, “Obesity and global warming: are they similar “canaries” in the same “mineshaft”?” Medical Journal of Australia, vol. 193, no. 11-12, pp. 635–637, 2010.

[142] S. L. Pagoto and B. M. Appelhans, “A call to the end of the diet debate,” The Journal of the American Medical Association, vol. 310, pp. 687–688, 2013.