

4. **Diet, nutrition and chronic diseases in context**

4.1 **Introduction**

The diets people eat, in all their cultural variety, define to a large extent people's health, growth and development. Risk behaviours, such as tobacco use and physical inactivity, modify the result for better or worse. All this takes place in a social, cultural, political and economic environment that can aggravate the health of populations unless active measures are taken to make the environment a health-promoting one.

Although this report has taken a disease approach for convenience, the Expert Consultation was mindful in all its discussions that diet, nutrition and physical activity do not take place in a vacuum. Since the publication of the earlier report in 1990 (*1*), there have been great advances in basic research, considerable expansion of knowledge, and much community and international experience in the prevention and control of chronic diseases. At the same time, the human genome has been mapped and must now enter any discussion of chronic disease.

Concurrently there has been a return to the concept of the basic life course, i.e. of the continuity of human lives from fetus to old age. The influences in the womb work differently from later influences, but clearly have a strong effect on the subsequent manifestation of chronic disease. The known risk factors are now recognized as being amenable to alleviation throughout life, even into old age. The continuity of the life course is seen in the way that both undernutrition and overnutrition (as well as a host of other factors) play a role in the development of chronic disease. The effects of man-made and natural environments (and the interaction between the two) on the development of chronic diseases are increasingly recognized. Such factors are also being recognized as happening further and further “upstream” in the chain of events predisposing humans to chronic disease. All these broadening perceptions not only give a clearer picture of what is happening in the current epidemic of chronic diseases, but also present many opportunities to address them. The identities of those affected are now better recognized: those most disadvantaged in more affluent countries, and – in numerical terms far greater – the populations of the developing and transitional worlds.

There is a continuity in the influences contributing to chronic disease development, and thus also to the opportunities for prevention. These influences include the life course; the microscopic environment of the gene to macroscopic urban and rural environments; the impact of social and political events in one sphere affecting the health and diet of populations far distant; and the way in which already stretched agriculture and oceanic systems will affect the choices available and

the recommendations that can be made. For chronic diseases, risks occur at all ages; conversely, all ages are part of the continuum of opportunities for their prevention and control. Both undernutrition and overnutrition are negative influences in terms of disease development, and possibly a combination is even worse; consequently the developing world needs additional targeting. Those with least power need different preventive approaches from the more affluent. Work has to start with the individual risk factors, but, critically, attempts at prevention and health promotion must also take account of the wider social, political and economic environment. Economics, industry, consumer groups and advertising all must be included in the prevention equation.

4.2 **Diet, nutrition and the prevention of chronic diseases through the life course**

The rapidly increasing burden of chronic diseases is a key determinant of global public health. Already 79% of deaths attributable to chronic diseases are occurring in developing countries, predominantly in middle-aged men (2). There is increasing evidence that chronic disease risks begin in fetal life and continue into old age (3–9). Adult chronic disease, therefore, reflects cumulative differential lifetime exposures to damaging physical and social environments.

For these reasons a life-course approach that captures both the cumulative risk and the many opportunities to intervene that this affords, was adopted by the Expert Consultation. While accepting the imperceptible progression from one life stage to the next, five stages were identified for convenience. These are: fetal development and the maternal environment; infancy; childhood and adolescence; adulthood; and ageing and older people.

4.2.1 ***Fetal development and the maternal environment***

The four relevant factors in fetal life are: (i) intrauterine growth retardation (IUGR); (ii) premature delivery of a normal growth for gestational age fetus; (iii) overnutrition in utero; and (iv) intergenerational factors. There is considerable evidence, mostly from developed countries, that IUGR is associated with an increased risk of coronary heart disease, stroke, diabetes and raised blood pressure (9–20). It may rather be the pattern of growth, i.e. restricted fetal growth followed by very rapid postnatal catch-up growth, that is important in the underlying disease pathways. On the other hand, large size at birth (macrosomia) is also associated with an increased risk of diabetes and cardiovascular disease (16, 21). Among the adult population in India, an association was found between impaired glucose tolerance and high ponderal index (i.e. fatness) at birth (22). In Pima Indians, a U-shaped relationship to birth

weight was found, whereas no such relationship was found amongst Mexican Americans (21, 23). Higher birth weight has also been related to an increased risk of breast and other cancers (24).

In sum, the evidence suggests that optimal birth weight and length distribution should be considered, not only in terms of immediate morbidity and mortality but also in regard to long-term outcomes such as susceptibility to diet-related chronic disease later in life.

4.2.2 *Infancy*

Retarded growth in infancy can be reflected in a failure to gain weight and a failure to gain height. Both retarded growth and excessive weight or height gain (“crossing the centiles”) can be factors in later incidence of chronic disease. An association between low growth in early infancy (low weight at 1 year) and an increased risk of coronary heart disease (CHD) has been described, irrespective of size at birth (3, 25). Blood pressure has been found to be highest in those with retarded fetal growth and greater weight gain in infancy (26). Short stature, a reflection of socioeconomic deprivation in childhood (27), is also associated with an increased risk of CHD and stroke, and to some extent, diabetes (10, 15, 28–34). The risk of stroke, and also of cancer mortality at several sites, including breast, uterus and colon, is increased if shorter children display an accelerated growth in height (35, 36).

Breastfeeding

There is increasing evidence that among term and pre-term infants, breastfeeding is associated with significantly lower blood pressure levels in childhood (37, 38). Consumption of formula instead of breast milk in infancy has also been shown to increase diastolic and mean arterial blood pressure in later life (37). Nevertheless, studies with older cohorts (22) and the Dutch study of famine (39) have not identified such associations. There is increasingly strong evidence suggesting that a lower risk of developing obesity (40–43) may be directly related to length of exclusive breastfeeding although it may not become evident until later in childhood (44). Some of the discrepancy may be explained by socioeconomic and maternal education factors confounding the findings.

Data from most, but not all, observational studies of term infants have generally suggested adverse effects of formula consumption on the other risk factors for cardiovascular disease (as well as blood pressure), but little information to support this finding is available from controlled clinical trials (45). Nevertheless, the weight of current evidence indicates adverse effects of formula milk on cardiovascular disease risk factors; this is consistent with the observations of increased mortality among older adults who were fed formula as infants (45–47). The risk for several

chronic diseases of childhood and adolescence (e.g. type 1 diabetes, coeliac disease, some childhood cancers, inflammatory bowel disease) have also been associated with infant feeding on breast-milk substitutes and short-term breastfeeding (48).

There has been great interest in the possible effect of high-cholesterol feeding in early life. Reiser et al. (49) proposed the hypothesis that high-cholesterol feeding in early life may serve to regulate cholesterol and lipoprotein metabolism in later life. Animal data in support of this hypothesis are limited, but the idea of a possible metabolic imprinting served to trigger several retrospective and prospective studies in which cholesterol and lipoprotein metabolism in infants fed human milk were compared with those fed formula. Studies in suckling rats have suggested that the presence of cholesterol in the early diet may serve to define a metabolic pattern for lipoproteins and plasma cholesterol that could be of benefit later in life. The study by Mott, Lewis & McGill (50) on differential diets in infant baboons, however, provided evidence to the contrary in terms of benefit. Nevertheless, the observation of modified responses of adult cholesterol production rates, bile cholesterol saturation indices, and bile acid turnover, depending on whether the baboons were fed breast milk or formula, served to attract further interest. It was noted that increased atherosclerotic lesions associated with increased levels of plasma total cholesterol were related to increased dietary cholesterol in early life. No long-term human morbidity and mortality data supporting this notion have been reported.

Short-term human studies have been in part confounded by diversity in solid food weaning regimens, as well as by the varied composition of fatty acid components of the early diet. The latter are now known to have an impact on circulating lipoprotein cholesterol species (51). Mean plasma total cholesterol by age 4 months in infants fed breast milk reached 180 mg/dl or greater, while cholesterol values in infants fed formula tended to remain under 150 mg/dl. In a study by Carlson, DeVoe & Barness (52), infants receiving predominantly a linoleic acid-enriched oil blend exhibited a mean cholesterol concentration of approximately 110 mg/dl. A separate group of infants in that study who received predominantly oleic acid had a mean cholesterol concentration of 133 mg/dl. Moreover, infants who were fed breast milk and oleic acid-enriched formula had higher high-density lipoprotein (HDL) cholesterol and apoproteins A-I and A-II than the predominantly linoleic acid-enriched oil diet group. The ratio of low-density lipoprotein (LDL) cholesterol plus very low-density lipoprotein (VLDL) cholesterol to HDL cholesterol was lowest for infants receiving the formula in which oleic acid was predominant. Using a similar oleic acid predominant formula, Darmady, Fosbrooke & Lloyd (53) reported

a mean value of 149 mg/dl at age 4 months, compared with 196 mg/dl in a parallel breast-fed group. Most of those infants then received an uncontrolled mixed diet and cow's milk, with no evident differences in plasma cholesterol levels by 12 months, independent of the type of early feeding they had received. A more recent controlled study (54) suggests that the specific fatty acid intake plays a predominant role in determining total and LDL cholesterol. The significance of high dietary cholesterol associated with exclusive human milk feeding during the first 4 months of life has no demonstrated adverse effect. Measurements of serum lipoprotein concentrations and LDL receptor activity in infants suggests that it is the fatty acid content rather than the cholesterol in the diet which regulates cholesterol homeostasis. The regulation of endogenous cholesterol synthesis in infants appears to be regulated in a similar manner to that of adults (55, 56).

4.2.3 ***Childhood and adolescence***

An association between low growth in childhood and an increased risk of CHD has been described, irrespective of size at birth (3, 25). Although based only on developed country research at this point, this finding gives credence to the importance that is currently attached to the role of immediate postnatal factors in shaping disease risk. Growth rates in infants in Bangladesh, most of whom had chronic intrauterine under-nourishment and were breastfed, were similar to growth rates of breastfed infants in industrialized countries, but catch-up growth was limited and weight at 12 months was largely a function of weight at birth (57).

In a study of 11–12 year-old Jamaican children (26), blood pressure levels were found to be highest in those with retarded fetal growth and greater weight gain between the ages of 7 and 11 years. Similar results were found in India (58). Low birth weight Indian babies have been described as having a characteristic poor muscle but high fat preservation, so-called “thin-fat” babies. This phenotype persists throughout the postnatal period and is associated with an increased central adiposity in childhood that is linked to the highest risk of raised blood pressure and disease (59–61). In most studies, the association between low birth weight and high blood pressure has been found to be particularly strong if adjusted to current body size – body mass index (BMI) – suggesting the importance of weight gain after birth (62).

Relative weight in adulthood and weight gain have been found to be associated with increased risk of cancer of the breast, colon, rectum, prostate and other sites (36). Whether there is an independent effect of childhood weight is difficult to determine, as childhood overweight is usually continued into adulthood. Relative weight in adolescence was

significantly associated with colon cancer in one retrospective cohort study (63). Frankel, Gunnell & Peters (64), in the follow-up to an earlier survey by Boyd Orr in the late 1930s, found that for both sexes, after accounting for the confounding effects of social class, there was a significant positive relationship between childhood energy intake and adult cancer mortality. The recent review by the International Agency for Research on Cancer (IARC) in Lyon, France, concluded that there was clear evidence of a relationship between onset of obesity (both early and later) and cancer risk (65).

Short stature (including measures of childhood leg length), a reflection of socioeconomic deprivation in childhood, is associated with an increased risk of CHD and stroke, and to some extent diabetes (10, 15, 28–34). Given that short stature, and specifically short leglength, are particularly sensitive indicators of early socioeconomic deprivation, their association with later disease very likely reflects an association between early undernutrition and infectious disease load (27, 66).

Height serves partly as an indicator of socioeconomic and nutritional status in childhood. As has been seen, poor fetal development and poor growth during childhood have been associated with increased cardiovascular disease risk in adulthood, as have indicators of unfavourable social circumstances in childhood. Conversely, a high calorie intake in childhood may be related to an increased risk of cancer in later life (64). Height is inversely associated with mortality among men and women from all causes, including coronary heart disease, stroke and respiratory disease (67).

Height has also been used as a proxy for usual childhood energy intake, which is particularly related to body mass and the child's level of activity. However, it is clearly an imperfect proxy because when protein intake is adequate (energy appears to be important in this regard only in the first 3 months of life), genetics will define adult height (36). Protein, particularly animal protein, has been shown to have a selective effect in promoting height growth. It has been suggested that childhood obesity is related to excess protein intake and, of course, overweight or obese children tend to be in the upper percentiles for height. Height has been shown to be related to cancer mortality at several sites, including breast, uterus and colon (36). The risk of stroke is increased by accelerated growth in height during childhood (35). As accelerated growth has been linked to development of hypertension in adult life, this may be the mechanism (plus an association with low socioeconomic status).

There is a higher prevalence of raised blood pressure not only in adults of low socioeconomic status (68–74), but also in children from low socioeconomic backgrounds, although the latter is not always associated

with higher blood pressure later in life (10). Blood pressure has been found to track from childhood to predict hypertension in adulthood, but with stronger tracking seen in older ages of childhood and in adolescence (75).

Higher blood pressure in childhood (in combination with other risk factors) causes target organ and anatomical changes that are associated with cardiovascular risk, including reduction in artery elasticity, increased ventricular size and mass, haemodynamic increase in cardiac output and peripheral resistance (10, 76, 77). High blood pressure in children is strongly associated with obesity, in particular central obesity, and clusters and tracks with an adverse serum lipid profile (especially LDL cholesterol) and glucose intolerance (76, 78, 79). There may be some ethnic differences, although these often seem to be explained by differences in body mass index. A retrospective mortality follow-up of a survey of family diet and health in the United Kingdom (1937–1939) identified significant associations between childhood energy intake and mortality from cancer (64).

The presence and tracking of high blood pressure in children and adolescents occurs against a background of unhealthy lifestyles, including excessive intakes of total and saturated fats, cholesterol and salt, inadequate intakes of potassium, and reduced physical activity, often accompanied by high levels of television viewing (10). In adolescents, habitual alcohol and tobacco use contributes to raised blood pressure (76, 80).

There are three critical aspects of adolescence that have an impact on chronic diseases: (i) the development of risk factors during this period; (ii) the tracking of risk factors throughout life; and, in terms of prevention, (iii) the development of healthy or unhealthy habits that tend to stay throughout life, for example physical inactivity because of television viewing. In older children and adolescents, habitual alcohol and tobacco use contribute to raised blood pressure and the development of other risk factors in early life, most of which track into adulthood.

The clustering of risk factor variables occurs as early as childhood and adolescence, and is associated with atherosclerosis in young adulthood and thus risk of later cardiovascular disease (81, 82). This clustering has been described as the metabolic – or “syndrome X” – clustering of physiological disturbances associated with insulin resistance, including hyperinsulinaemia, impaired glucose tolerance, hypertension, elevated plasma triglyceride and low HDL cholesterol (83, 84). Raised serum cholesterol both in middle age and in early life are known to be associated with an increased risk of disease later on. The Johns Hopkins Precursor Study showed that serum cholesterol levels in adolescents and young white males were strongly related to subsequent risk of cardiovascular disease mortality and morbidity (85).

Although the risk of obesity does not apparently increase in adults who were overweight at 1 and 3 years old, the risk rises steadily thereafter, regardless of parental weight (86). Tracking has also been reported in China, where overweight children were 2.8 times as likely to become overweight adolescents; conversely, underweight children were 3.6 times as likely to remain underweight as adolescents (87). The study found that parental obesity and underweight, and the child's initial body mass index, dietary fat intake and family income helped predict tracking and changes. However, in a prospective cohort study conducted in the United Kingdom, little tracking from childhood overweight to adulthood obesity was found when using a measure of fatness (percentage body fat for age) that was independent of build (88). The authors also found that only children obese at 13 years of age had an increased risk of obesity as adults, and that there was no excess adult health risk from childhood or adolescent overweight. Interestingly, they found that in the thinnest children, the more obese they became as adults, the greater was their subsequent risk of developing chronic diseases.

The real concern about these early manifestations of chronic disease, besides the fact that they are occurring earlier and earlier, is that once they have developed they tend to track in that individual throughout life. On the more positive side, there is evidence that they can be corrected. Overweight and obesity are, however, notoriously difficult to correct after becoming established, and there is an established risk of overweight during childhood persisting into adolescence and adulthood (89). Recent analyses (90, 91) have shown that the later the weight gain in childhood and adolescence, the greater the persistence. More than 60% of overweight children have at least one additional risk factor for cardiovascular disease, such as raised blood pressure, hyperlipidaemia or hyperinsulinaemia, and more than 20% have two or more risk factors (89).

Habits leading to noncommunicable disease development during adolescence

It seems increasingly likely that there are widespread effects of early diet on later body composition, physiology and cognition (45). Such observations “provide strong support for the recent shift away from defining nutritional needs for prevention of acute deficiency symptoms towards long-term prevention of morbidity and mortality” (45).

Increased birth weight increases the risk of obesity later, but children with low birth weight tend to remain small into adulthood (89, 92). In industrialized countries there have been only modest increases in birth weight so the increased levels of obesity described earlier must reflect environmental changes (89).

The “obesogenic” environment appears to be largely directed at the adolescent market, making healthy choices that much more difficult. At the same time, exercise patterns have changed and considerable parts of the day are spent sitting at school, in a factory, or in front of a television or computer. Raised blood pressure, impaired glucose tolerance and dyslipidaemia are associated in children and adolescents with unhealthy lifestyles, such as diets containing excessive intakes of fats (especially saturated), cholesterol and salt, an inadequate intake of fibre and potassium, a lack of exercise, and increased television viewing (10). Physical inactivity and smoking have been found independently to predict CHD and stroke in later life.

It is increasingly recognized that unhealthy lifestyles do not just appear in adulthood but drive the early development of obesity, dyslipidaemia, high blood pressure, impaired glucose tolerance and associated disease risk. In many countries, perhaps most typified by the United States, changes in family eating patterns, including the increased consumption of fast foods, pre-prepared meals and carbonated drinks, have taken place over the past 30 years (89). At the same time, the amount of physical activity has been greatly reduced both at home and in school, as well as by increasing use of mechanized transport.

4.2.4 **Adulthood**

The three critical questions relating to adulthood were identified as: (i) to what extent do risk factors continue to be important in the development of chronic diseases; (ii) to what extent will modifying such risk factors make a difference to the emergence of disease; and (iii) what is the role of risk factor reduction and modification in secondary prevention and the treatment of those with disease? Reviewing the evidence within the framework of a life-course approach highlights the importance of the adult phase of life, it being both the period during which most chronic diseases are expressed, as well as a critical time for the preventive reduction of risk factors and for increasing effective treatment (93).

The most firmly established associations between cardiovascular disease or diabetes and factors in the lifespan are the ones between those diseases and the major known “adult” risk factors, such as tobacco use, obesity, physical inactivity, cholesterol, high blood pressure and alcohol consumption (94). The factors that have been confirmed to lead to an increased risk of CHD, stroke and diabetes are: high blood pressure for CHD or stroke (95, 96); high cholesterol (diet) for CHD (97, 98), and tobacco use for CHD (99). Other associations are robust and consistent, although they have not necessarily been shown to be reversible (10): obesity and physical inactivity for CHD, diabetes and

stroke (100–102); and heavy or binge drinking for CHD and stroke (99, 103). Most of the studies are from developed countries, but supporting evidence from developing countries is beginning to emerge, for example, from India (104).

In developed countries, low socioeconomic status is associated with higher risk of cardiovascular disease and diabetes (105). As in the affluent industrialized countries, there appears to be an initial preponderance of cardiovascular disease among the higher socioeconomic groups, for example, as has been found in China (98). It is presumed that the disease will progressively shift to the more disadvantaged sectors of society (10). There is some evidence that this is already happening, especially among women in low-income groups, for example in Brazil (106) and South Africa (107), as well as in countries in economic transition such as Morocco (108).

Other risk factors are continually being recognized or proposed. These include the role of high levels of homocysteine, the related factor of low folate, and the role of iron (109). From a social sciences perspective, Losier (110) has suggested that socioeconomic level is less important than a certain stability in the physical and social environment. In other words, an individual's sense of understanding of his or her environment, coupled with control over the course and setting of his or her own life appears to be the most important determinant of health. Marmot (111), among others, has demonstrated the impact of the wider environment and societal and individual stress on the development of chronic disease.

4.2.5 ***Ageing and older people***

There are three critical aspects relating to chronic diseases in the later part of the life-cycle: (i) most chronic diseases will be manifested in this later stage of life; (ii) there is an absolute benefit for ageing individuals and populations in changing risk factors and adopting health-promoting behaviours such as exercise and healthy diets; and (iii) the need to maximize health by avoiding or delaying preventable disability. Along with the societal and disease transitions, there has been a major demographic shift. Although older people are currently defined as those aged 60 years and above (112), this definition of older people has a very different meaning from the middle of the last century, when 60 years of age and above often exceeded the average life expectancy, especially in industrialized countries. It is worth remembering, however, that the majority of elderly people will, in fact, be living in the developing world.

Most chronic diseases are present at this period of life – the result of interactions between multiple disease processes as well as more general

losses in physiological functions (113, 114). Cardiovascular disease peaks at this period, as does type 2 diabetes and some cancers. The main burden of chronic diseases is observed at this stage of life and, therefore, needs to be addressed.

Changing behaviours in older people

In the 1970s, it was thought that risks were not significantly increased after certain late ages and that there would be no benefit in changing habits, such as dietary habits, after 80 years old (115) as there was no epidemiological evidence that changing habits would affect mortality or even health conditions among older people. There was also a feeling that people “earned” some unhealthy behaviours simply because of reaching “old age”. Then there was a more active intervention phase, when older people were encouraged to change their diets in ways that were probably overly rigorous for the expected benefit. More recently, older people have been encouraged to eat a healthy diet – as large and as varied as possible while maintaining their weight – and particularly to continue exercise (113, 116). Liu et al. (117) have reported an observed risk of atherosclerotic disease among older women that was approximately 30% less in women who ate 5–10 servings of fruits and vegetables per day than in those who ate 2–5 servings per day. It seems that, as elderly patients have a higher cardiovascular risk, they are more likely to gain from risk factor modification (118).

Although this age group has received relatively little attention as regards primary prevention, the acceleration in decline caused by external factors is generally believed to be reversible at any age (119). Interventions aimed at supporting the individual and promoting healthier environments will often lead to increased independence in older age.

4.3 **Interactions between early and later factors throughout the life course**

Low birth weight, followed by subsequent adult obesity, has been shown to impart a particularly high risk of CHD (120, 121), as well as diabetes (18). Risk of impaired glucose tolerance has been found to be highest in those who had low birth weight, but who subsequently became obese as adults (18). A number of recent studies (12, 13, 25, 59–61, 120) have demonstrated that there is an increased risk of adult disease when IUGR is followed by rapid catch-up growth in weight and height. Conversely, there is also fairly consistent evidence of higher risk of CHD, stroke, and probably adult onset diabetes with shorter stature (122, 123). Further research is needed to define optimal growth in infancy in terms of prevention of chronic disease. A WHO multicentre growth reference study (124) currently under way may serve to generate much needed information on this matter.

4.3.1 **Clustering of risk factors**

Impaired glucose tolerance and an adverse lipid profile are seen as early as childhood and adolescence, where they typically appear clustered together with higher blood pressure and relate strongly to obesity, in particular central obesity (76, 78, 125, 126). Raised blood pressure, impaired glucose tolerance and dyslipidaemia also tend to be clustered in children and adolescents with unhealthy lifestyles and diets, such as those with excessive intakes of saturated fats, cholesterol and salt, and inadequate intake of fibre. Lack of exercise and increased television viewing add to the risk (10). In older children and adolescents, habitual alcohol and tobacco use also contribute to raised blood pressure and to the development of other risk factors in early adulthood. Many of the same factors continue to act throughout the life course. Such clustering represents an opportunity to address more than one risk at a time. The clustering of health-related behaviours is also a well described phenomenon (127).

4.3.2 **Intergenerational effects**

Young girls who grow poorly become stunted women and are more likely to give birth to low-birth-weight babies who are then likely to continue the cycle by being stunted in adulthood, and so on (128). Maternal birth size is a significant predictor of a child's birth size after controlling for gestational age, sex of the child, socioeconomic status, and maternal age, height and pre-pregnant weight (129). There are clear indications of intergenerational factors in obesity, such as parental obesity, maternal gestational diabetes and maternal birth weight. Low maternal birth weight is associated with higher blood pressure levels in the offspring, independent of the relation between the offspring's own birth weight and blood pressure (7). Unhealthy lifestyles can also have a direct effect on the health of the next generation, for example, smoking during pregnancy (9, 130).

4.4 **Gene–nutrient interactions and genetic susceptibility**

There is good evidence that nutrients and physical activity influence gene expression and have shaped the genome over several million years of human evolution. Genes define opportunities for health and susceptibility to disease, while environmental factors determine which susceptible individuals will develop illness. In view of changing socio-economic conditions in developing countries, such added stress may result in exposure of underlying genetic predisposition to chronic diseases. Gene–nutrient interactions also involve the environment. The dynamics of the relationships are becoming better understood but there is still a long way to go in this area, and also in other aspects, such as

disease prevention and control. Studies continue on the role of nutrients in gene expression; for example, researchers are currently trying to understand why omega-3 fatty acids suppress or decrease the mRNA of interleukin, which is elevated in atherosclerosis, arthritis and other autoimmune diseases, whereas the omega-6 fatty acids do not (131). Studies on genetic variability to dietary response indicate that specific genotypes raise cholesterol levels more than others. The need for targeted diets for individuals and subgroups to prevent chronic diseases was acknowledged as being part of an overall approach to prevention at the population level. However, the practical implications of this issue for public health policy have only begun to be addressed. For example, a recent study of the relationship between folate and cardiovascular disease revealed that a common single gene mutation that reduces the activity of an enzyme involved in folate metabolism (MTHFR) is associated with a moderate (20%) increase in serum homocysteine and higher risk of both ischaemic heart disease and deep vein thrombosis (132).

Although humans have evolved being able to feed on a variety of foods and to adapt to them, certain genetic adaptations and limitations have occurred in relation to diet. Understanding the evolutionary aspects of diet and its composition might suggest a diet that would be consistent with the diet to which our genes were programmed to respond. However, the early diet was presumably one which gave evolutionary advantage to reproduction in the early part of life, and so may be less indicative of guidance for healthy eating, in terms of lifelong health and prevention of chronic disease after reproduction has been achieved. Because there are genetic variations among individuals, changes in dietary patterns have a differential impact on a genetically heterogeneous population, although populations with a similar evolutionary background have more similar genotypes. While targeted dietary advice for susceptible populations, subgroups or individuals is desirable, it is not feasible at present for the important chronic diseases considered in this report. Most are polygenic in nature and rapidly escalating rates suggest the importance of environmental change rather than change in genetic susceptibility.

4.5 **Intervening throughout life**

There is a vast volume of scientific evidence highlighting the importance of applying a life-course approach to the prevention and control of chronic disease. The picture is, however, still not complete, and the evidence sometimes contradictory. From the available evidence, it is possible to state the following:

- Unhealthy diets, physical inactivity and smoking are confirmed risk behaviours for chronic diseases.

- The biological risk factors of hypertension, obesity and lipidaemia are firmly established as risk factors for coronary heart disease, stroke and diabetes.
- Nutrients and physical activity influence gene expression and may define susceptibility.
- The major biological and behavioural risk factors emerge and act in early life, and continue to have a negative impact throughout the life course.
- The major biological risk factors can continue to affect the health of the next generation.
- An adequate and appropriate postnatal nutritional environment is important.
- Globally, trends in the prevalence of many risk factors are upwards, especially those for obesity, physical inactivity and, in the developing world particularly, smoking.
- Selected interventions are effective but must extend beyond individual risk factors and continue throughout the life course.
- Some preventive interventions early in the life course offer lifelong benefits.
- Improving diets and increasing levels of physical activity in adults and older people will reduce chronic disease risks for death and disability.
- Secondary prevention through diet and physical activity is a complementary strategy in retarding the progression of existing chronic diseases and decreasing mortality and the disease burden from such diseases.

From the above, it is clear that risk factors must be addressed throughout the life course. As well as preventing chronic diseases, there are clearly many other reasons to improve the quality of life of people throughout their lifespan. The intention of primary prevention interventions is to move the profile of the whole population in a healthier direction. Small changes in risk factors in the majority who are at moderate risk can have an enormous impact in terms of population-attributable risk of death and disability. By preventing disease in large populations, small reductions in blood pressure, blood cholesterol and so on can dramatically reduce health costs. For example, it has been demonstrated that improved lifestyles can reduce the risk of progression to diabetes by a striking 58% over 4 years (133, 134). Other population studies have shown that up to 80% of cases of coronary heart disease, and up to 90% of cases of type 2 diabetes, could potentially be avoided through changing lifestyle factors, and about one-third of cancers could be

avoided by eating healthily, maintaining normal weight and exercising throughout life (135–137).

For interventions to have a lasting effect on the risk factor prevalence and the health of societies, it is also essential to change or modify the environment in which these diseases develop. Changes in dietary patterns, the influence of advertising and the globalization of diets, and widespread reduction in physical activity have generally had negative impacts in terms of risk factors, and presumably also in terms of subsequent disease (138, 139). Reversing current trends will require a multifaceted public health policy approach.

While it is important to avoid inappropriately applying nutritional guidelines to populations that may differ genetically from those for whom the dietary and risk data were originally determined, to date the information regarding genes or gene combinations is insufficient to define specific dietary recommendations based on a population distribution of specific genetic polymorphisms. Guidelines should try to ensure that the overall benefit of recommendations to the majority of the population substantially outweighs any potential adverse effects on selected subgroups of the population. For example, population-wide efforts to prevent weight gain may trigger a fear of fatness and, therefore, undernutrition in adolescent girls.

The population nutrient goals recommended by the Joint WHO/FAO Expert Consultation at the present meeting are based on current scientific knowledge and evidence, and are intended to be further adapted and tailored to local or national diets and populations, where diet has evolved to be appropriate for the culture and local environment.

The goals are intended to reverse or reduce the impact of unfavourable dietary changes that have occurred over the past century in the industrialized world and more recently in many developing countries. Present nutrient intake goals also need to take into account the effects of long-term environmental changes, i.e. those that have occurred over time-scales of hundreds of years. For example, the metabolic response to periodic famine and chronic food shortage may no longer represent a selective advantage but instead may increase susceptibility to chronic diseases. An abundant stable food supply is a recent phenomenon; it was not a factor until the advent of the industrial revolution (or the equivalent process in more recently industrialized countries).

A combination of physical activity, food variety and extensive social interaction is the most likely lifestyle profile to optimize health, as reflected in increased longevity and healthy ageing. Some available evidence suggests that, within the time frame of a week, at least 20 and

probably as many as 30 biologically distinct types of foods, with the emphasis on plant foods, are required for healthy diets.

The recommendations given in this report consider the wider environment, of which the food supply is a major part (see Chapter 3). The implications of the recommendations would be to increase the consumption of fruits and vegetables, to increase the consumption of fish, and to alter the types of fats and oils, as well as the amount of sugars and starch consumed, especially in developed countries. The current move towards increasing animal protein in diets in countries in economic transition is unlikely to be reversed in those countries where there are increased consumer resources, but is unlikely to be conducive to adult health, at least in terms of preventing chronic diseases.

Finally, what success can be expected by developing and updating the scientific basis for national guidelines? The percentage of British adults complying with national dietary guidelines is discouraging; for example, only 2–4% of the population are currently consuming the recommended level of saturated fat, and 5–25% are achieving the recommended levels of fibre. The figures would not be dissimilar in many other developed countries, where the majority of people are not aware of what exactly the dietary guidelines suggest. In using the updated and evidence-based recommendations in this report, national governments should aim to produce dietary guidelines that are simple, realistic and food-based. There is an increasing need, recognized at all levels, for the wider implications to be specifically addressed; these include the implications for agriculture and fisheries, the role of international trade in a globalized world, the impact on countries dependent on primary produce, the effect of macroeconomic policies, and the need for sustainability. The greatest burden of disease will be in the developing world and, in the transitional and industrialized world, amongst the most disadvantaged socioeconomically.

In conclusion, it may be necessary to have three mutually reinforcing strategies that will have different magnitudes of impact over differing time frames. First, with the greatest and most immediate impact, there is the need to address risk factors in adulthood and, increasingly, among older people. Risk-factor behaviours can be modified in these groups and benefits seen within 3–5 years. With all populations ageing, the sheer numbers and potential cost savings are enormous and realizable. Secondly, societal changes towards health-promoting environments need to be greatly expanded as an integral part of any intervention. Ways to reduce the intake of sugars-sweetened drinks (particularly by children) and of high-energy density foods that are micronutrient poor, as well as efforts to curb cigarette smoking and to increase physical activity will have an impact

throughout society. Such changes need the active participation of communities, politicians, health systems, town planners and municipalities, as well as the food and leisure industries. Thirdly, the health environment, in which those who are most at risk grow up, needs to change. This is a more targeted and potentially costly approach, but one that has the potential for cost-effective returns even though they are longer term.

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