

Sunlight, cholesterol and coronary heart disease

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Summary

We investigated the relationship between geography and incidence of coronary heart disease, looking at deficiency of sunlight and thus of vitamin D as a factor that might influence susceptibility and thus disease incidence. Sunlight deficiency could increase blood cholesterol by allowing squalene metabolism to progress to cholesterol synthesis rather than to vitamin D synthesis as would occur with greater amounts of sunlight exposure, and the increased concentration of blood cholesterol during the winter

months, confirmed in this study, may well be due to reduced sunlight exposure. We show evidence that outdoor activity (gardening) is associated with a lower concentration of blood cholesterol in the summer but not in the winter. We suggest that the geographical variation of coronary heart disease is not specific, but is seen in other diseases and sunlight influences susceptibility to a number of chronic diseases, of which coronary heart disease is one.

Introduction

The geography of coronary heart disease is characterized by two factors which are not readily explained. Firstly, deaths are more common with increasing distance of residence from the equator,^{1,2} and are especially common on the Atlantic fringes of north-west Europe—the British Isles (the north-western parts in particular^{3,4}) and northern Scandinavia. In the last of these, the high death rate cannot be explained by known risk factors.⁵ The mortality risk of an individual also changes with migration to that of the new place of residence.⁴ Secondly, in studies from the US, the death rate from coronary heart disease decreased with increasing altitude of residence.^{6–8}

These observations suggest that differential rates of sunlight exposure might be the common factor which determines susceptibility to coronary heart disease, the high levels of sunlight exposure at low latitudes and high altitudes being protective and the relative deficiency at high latitudes being responsible for a high incidence.

A high level of blood cholesterol is a strong indicator of risk of coronary heart disease in a population.^{9,10} At an individual level, in those with

coronary heart disease a high blood cholesterol is associated with a greatly increased risk of death,¹¹ and lowering the cholesterol level by drugs has been shown to be effective in reducing the incidence of death and other cardiovascular events.¹² However the risk to individuals *without* coronary heart disease is very small,¹¹ and in such 'normal' people lowering blood cholesterol by drugs is of much less benefit¹³ (some people who are considered 'normal' because they have no history or symptoms of coronary heart disease will however have the disease in a subclinical form, but as yet there are no simple markers for it). Dietary manipulation aimed at reducing blood cholesterol has not shown any benefit.^{14,15}

The structural similarities of cholesterol and vitamin D and their common precursor led us to wonder whether a high level of blood cholesterol within a population might be a manifestation of sunlight deficiency.

We studied this by looking at: (i) the relationship between population mean cholesterol and latitude of residence; (ii) the relationship between hours of sunshine per annum and age-adjusted death rates for coronary heart disease in the health districts and

regions of the UK; (iii) the mean blood cholesterol in our laboratory throughout the year, relating it to hours of sunshine; (iv) the influence of garden ownership on blood cholesterol and vitamin D.

Methods

Using data from Keys epidemiological work 'Seven Countries',¹⁶ we were able to determine the population mean blood cholesterol for a number of towns, shown in Table 1. We determined the latitude of these towns to regress cholesterol on latitude.

We obtained from the Meteorological Office the recorded hours of sunshine at 136 centres in the UK. To these we added age-adjusted death rates for coronary heart disease, data supplied by The Coronary Prevention Group/British Heart Foundation Statistics Database (1991). We regressed death rates for coronary heart disease on hours of sunshine and repeated this for the means of each of the regions into which the NHS is divided.

The biochemistry laboratory of the Blackburn Royal Infirmary performs about 1500 blood cholesterol estimations per month, receiving requests from the hospital wards, outpatient departments and from general practice. There is no designated lipid clinic. We have recorded these prospectively for 2 years from September 1991, calculating means for each day, each week and each month. We obtained from the Meteorological Office the hours of sunshine for each day as recorded at Myerscough, Lancashire, the nearest recording centre to Blackburn.

To separate hours of sunshine from latitude, we looked at the data for Blackpool, Preston, Blackburn and Burnley, four towns in Lancashire lying on the same latitude but progressively distant from the west coast of north-west England (the altitude change of populated areas above sea level is only 200 m). We

regressed the age-adjusted death rate for coronary heart disease on hours of sunshine per annum.

We obtained from the secretariat of the European Union details of agricultural productions of the constituent nations (1987), and from the World Health Annual Report (1985) the standardized mortality rates for myocardial infarction.

We obtained from the National Household Survey (1992) details of national dietary patterns and in particular seasonal variations of consumption.

During the summer of 1992, we took random samples of blood which were received by the laboratory for cholesterol estimation, and we also estimated vitamin D (25-hydroxycholecalciferol). We then identified whether the addresses on the request forms were houses with or without a garden, and we compared the cholesterol and vitamin D levels of these two groups. We repeated this study during the winter of 1992–93.

To separate *in vitro* from *in vivo* effects of the photometabolism of cholesterol, we took a number of blood specimens during the month of January, carefully avoiding casual exposure to light. We separated the serum and measured cholesterol levels before and after exposure to ultraviolet light for 24 h.

Cholesterol was measured by an enzymic colorimetric method (CHOD-PAP, Bio-Stat Diagnostics) on a RA-XT analyser (Bayer Diagnostics). The analytical detail is that cholesterol is determined after enzymic hydrolysis and oxidation (cholesterol oxidase). The indicator quioneimine is formed from hydrogen peroxide and 4-aminoantipyrine in the presence of 4-chlorophenol and peroxidase. Between batch precision was determined at two levels using an unassayed quality control material, included within each analytical run. The mean between-batch CVs were 2.4% and 3.08% for mean cholesterol levels of 6.08 and 3.44 mmol/l, respectively.

Vitamin D levels were measured using a radioimmunoassay (RIA) kit obtained from INSTAR. Blood specimens were taken, the plasma separated and frozen, being stored for batch analysis. The assay detects 25-hydroxy-vitamin D (25-OH-D) and consists of a two-step procedure. The first step is a rapid extraction of 25-OH-D and other hydroxylated metabolites from plasma or serum with acetonitrile. Following extraction, the treated samples are then assayed using an equilibrium RIA procedure. The RIA method is based on an antibody with specificity to 25-OH-D. The sample, antibody and tracer are incubated for 90 min at 20–25 °C. Phase separation is accomplished after a 20-min incubation at 20–25 °C with a second antibody-precipitating procedure.

Results

The population mean blood cholesterol levels of the towns of Keys' study show a clear regression on

Table 1 Mean blood cholesterol and latitude

| Country (town) | Latitude (°N) | Mean cholesterol (mmol/l) |
|------------------------|---------------|---------------------------|
| Japan (Kyushu) | 33 | 4.14 |
| Crete | 35 | 5.10 |
| Corfu | 40 | 5.10 |
| Italy (Monte Giorgio) | 42 | 5.18 |
| Croatia (Makarska) | 43 | 4.79 |
| Serbia (Velika Krsna) | 45 | 5.34 |
| Slovenia (Dalj) | 46 | 5.00 |
| Netherlands (Zutphen) | 52 | 6.01 |
| West Finland (Turku) | 60 | 6.50 |
| East Finland (Joensuu) | 63 | 6.86 |

Data from Keys (1980).¹⁶

latitude, blood cholesterol increasing with distance from the equator ($r=0.936$; $df=8$; $p<0.001$) (Figure 1).

The regressions of age-adjusted death rates for coronary heart disease on hours of sunshine per annum for regions and districts can be seen in Figures 2 and 3. There is a clear increase in death rates with decreasing hours of sunshine (for the regions $r=-0.85$, $df=15$, $p<0.001$; for the districts $r=-0.59$, $df=134$, $p<0.001$).

The relationship between hours of sunshine per annum and death rate due to coronary heart disease can be seen in the four Lancashire towns, in Figure 4. There is a negative regression as death rates increase with distance from the coast and reduction of hours of sunshine per annum ($r=-0.97$, $df=2$, $p<0.001$).

There was a clear seasonal variation of the population mean blood cholesterol, shown in Figures 5 and 6 with the means and 99% confidence intervals for each of the two years in the study. The mean cholesterol for each month was below the annual

mean during the summer months, and above the annual mean during the winter months, in keeping with the hypothesis presented. There is an inverse relationship with hours of sunshine per month (Figure 7).

The mean blood cholesterol of the first year of the study was lower than that of the second (6.228 and 6.353 mmol/l), the hours of sunshine being higher and lower, respectively (1105.7 and 844 h).

Table 2 shows the consumption of a variety of foods in the UK, comparing the first and second quarters of the year. It can be seen that there is no obvious difference which might explain the changes that are displayed in Figures 5 and 6.

Exposure of plasma to ultraviolet light for 24 h had no effect on the cholesterol concentration, mean 6.02 mmol/l before and 6.05 mmol/l after (paired t-test, not significant).

The blood cholesterol and vitamin D levels of people with and without gardens can be seen in Table 3. In the summer, vitamin D levels were higher in those with gardens (mean 27.08 and 24.19 ng/ml;

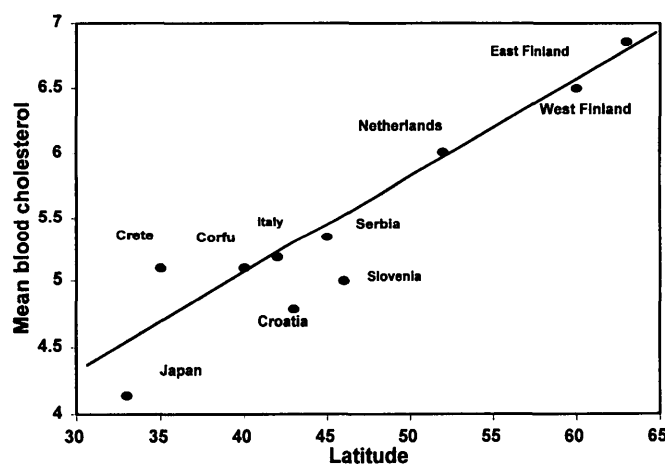


Figure 1. Blood cholesterol (population mean, mmol/l) and latitude. $y=1.8+0.078x$; $r=0.936$; $p<0.001$. Data from Keys.¹⁶

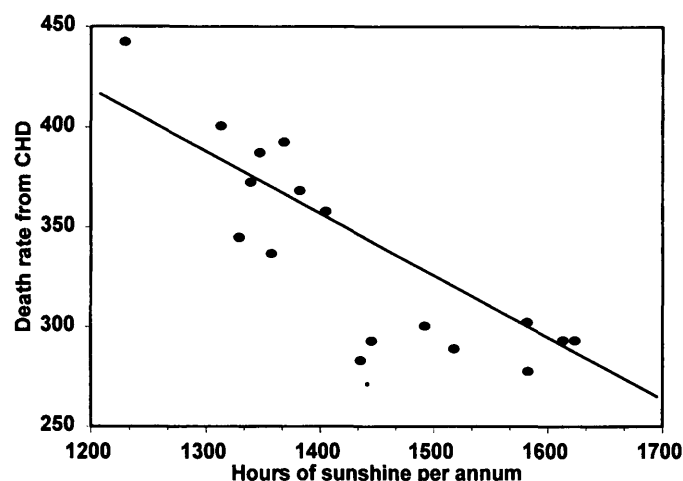


Figure 2. Sunshine per year and coronary heart disease death rate per 100 000 males, within the regions of the NHS. $y=862-0.37x$; $r=-0.85$; $p<0.001$.

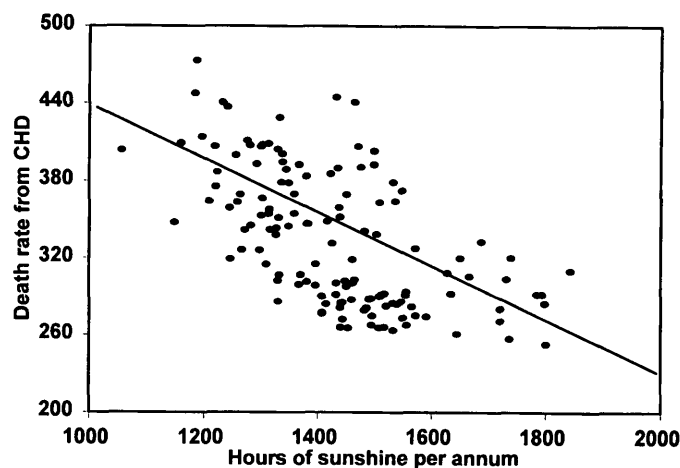


Figure 3. Sunshine per year and coronary heart disease death rate per 100 000 males, within the 200 districts of the NHS. $y = 628 - 0.2x$; $r = -0.59$; $p < 0.001$.

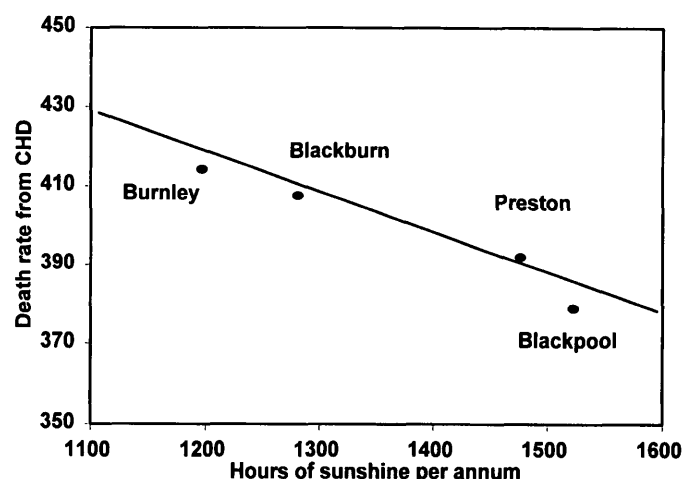


Figure 4. Sunshine per year and coronary heart disease death rate per 100 000 males in four towns in Lancashire at 54 °N. $y = 536 - 0.1x$; $r = 0.974$; $p < 0.001$.

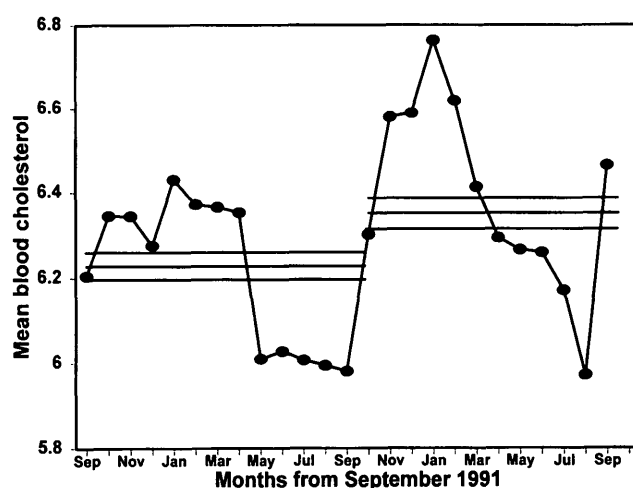


Figure 5. Population mean cholesterol (mmol/l) in Blackburn, Lancashire (54 °N) each month from September 1991 to September 1993 (means of first and second twelve-month periods also shown, together with 99% confidence intervals).

$t = 2.147$, $p < 0.025$) and cholesterol levels were correspondingly lower (5.84 and 6.34 mmol/l; $t = 2.629$, $p < 0.01$). In the winter, vitamin D levels

remained higher in those with gardens (24.25 and 18.62 ng/ml; $t = 2.348$, $p < 0.025$) but the cholesterol levels became equal (6.68 and 6.59 mmol/l).

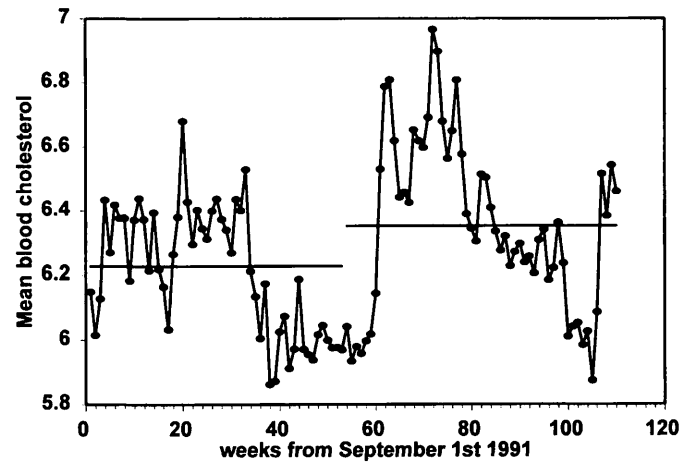


Figure 6. Population mean cholesterol (mmol/l) in Blackburn, Lancashire (54°N) each week from September 1991 to September 1993 (means of first and second twelve-month periods also shown).

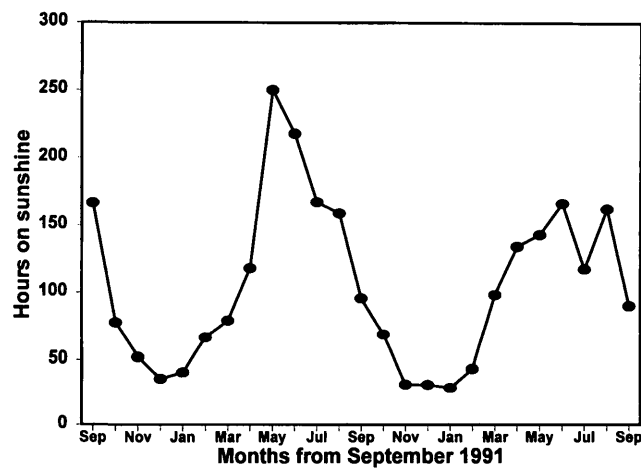


Figure 7. Hours of sunshine per month Myerscough, Lancashire (54°N) from September 1991 to September 1993.

Table 2 UK household consumption of foods, ounces per person per week

| Food item | Jan/Mar | Apr/Jun | Change | % |
|---------------------|---------|---------|--------|-------|
| Milk and cream | 3.87 | 3.73 | 0.20 | −5.17 |
| Cheese | 3.93 | 4.28 | 0.35 | 8.91 |
| Meat | 11.54 | 11.57 | 0.10 | 0.87 |
| Meat products | 21.43 | 23.49 | 2.06 | 9.61 |
| Fish | 4.64 | 4.96 | 0.40 | 8.62 |
| Eggs | 2.22 | 2.42 | 0.20 | 9.01 |
| Fats | 8.95 | 8.95 | 0 | 0 |
| Sugar and preserves | 7.28 | 7.95 | 0.67 | 9.20 |
| Vegetables | 82.13 | 76.77 | −5.30 | −6.45 |
| Fruit | 31.21 | 34.14 | 2.93 | 9.39 |
| Bread | 25.70 | 26.85 | 1.15 | 4.47 |
| Cereals | 51.06 | 52.05 | 0.99 | 1.94 |
| Beverages | 2.71 | 2.53 | −0.18 | −6.64 |

Data from National Household Survey 1991.

The agricultural productions of the countries of the European Community are shown in Table 4, together with the standardized mortality rates for

myocardial infarction. The populations of countries in which the olive and the vine grow to agricultural maturity enjoy low mortality rates for coronary heart

Table 3 Garden ownership, vitamin D and cholesterol

| | Summer | | Winter | |
|-----------------|--------|-----------|--------|-----------|
| | Garden | No garden | Garden | No garden |
| Sample size (n) | 81 | 61 | 35 | 37 |
| Vitamin D | | | | |
| Mean (ng/ml) | 27.08 | 24.19 | 24.25 | 18.62 |
| SD | 8.17 | 7.76 | 11.57 | 8.44 |
| Cholesterol | | | | |
| Mean (mmol/l) | 5.84 | 6.34 | 6.68 | 6.59 |
| SD | 1.04 | 1.18 | 1.37 | 1.24 |

Table 4 European agricultural production (kHa in production) and deaths per 100 000 males from myocardial infarction

| | Olive | Vine | Wheat | Barley | Grass | Deaths from MI |
|-------------|-------|------|-------|--------|-------|----------------|
| UK | 0 | 1 | 1944 | 1831 | 11069 | 251 |
| Ireland | 0 | 0 | 57 | 276 | 4654 | 242 |
| Denmark | 0 | 0 | 398 | 943 | 210 | N/A |
| Netherlands | 0 | 0 | 111 | 50 | 1090 | 174 |
| Belgium | 0 | 0 | 194 | 123 | 626 | N/A |
| Germany | 0 | 101 | 1671 | 1850 | 4481 | 159 |
| Luxembourg | 0 | 1 | 8 | 17 | 70 | 104 |
| France | 18 | 1033 | 4909 | 1975 | 11894 | 84 |
| Greece | 655 | 170 | 886 | 241 | 5255 | 110 |
| Italy | 1175 | 1082 | 3087 | 445 | 4952 | 98 |
| Spain | 2099 | 1514 | 2221 | 4401 | 6685 | 75 |
| Portugal | 317 | 299 | 324 | 84 | 972 | 76 |

Agricultural data from Eurostat 1987, MI data from WHO 1985.

disease, whereas those of countries in which only grass and barley reach agricultural maturity have high rates.

Table 5 shows the agricultural patterns of the regions of the United Kingdom together with age-adjusted death rates for coronary heart disease. Once again, grass and barley production is associated with high death rates, and in regions in which wheat is produced the death rate is lower.

Discussion

It is well known that death rates from coronary heart disease are much lower in the Mediterranean countries of southern Europe than in the Atlantic fringes of north west Europe, and it is usually assumed that this is due to different dietary patterns reflecting local agriculture. Hence we in north-west England are advised to drink red wine and to add garlic and olive oil to our diets and at the same time to stop eating 'fish and chips'. But whereas migration has an effect on mortality risk,⁴ the individual adopting the risk of the place to which he has migrated, people who migrate tend to take their dietary patterns

with them. Furthermore, the dietary manipulation that has been part of prevention trials of coronary heart disease has been very disappointing, and overviews of the many dietary primary prevention trials have shown that there is no overall benefit.^{14,15} These observations suggest that agricultural production and local diet might not be the explanation of susceptibility to coronary heart disease in a given country, and we suggest that local agriculture is a reflection of local climate, sun exposure in particular, and that this is directly cardioprotective.

The relationship between population average cholesterol and latitude is clearly shown in Figure 3 with a highly significant regression, cholesterol rising with increasing distance from the equator. It is those countries on the Atlantic fringe of north-west Europe that have the highest cholesterol levels, and similarly they have the highest coronary heart disease death rates. Although once again conventional wisdom is that this is a reflection of agriculture and diet, we propose that it is a manifestation of differential rates of sunlight energy at ground level, influenced by the angle of incidence of the sun at noon and the amount of cloud cover.

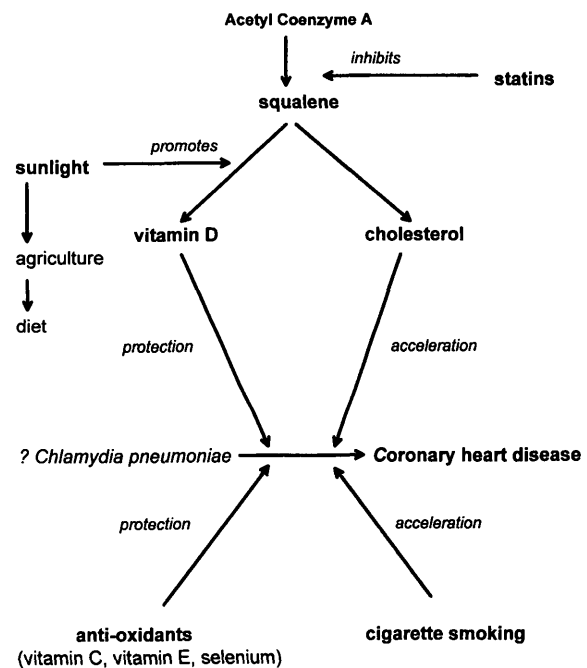
Table 5 UK agricultural production (kHa in production) and age-adjusted death rates from coronary heart disease

| | Olive | Vine | Wheat | Barley | Grass | Deaths from CHD |
|---------------|-------|------|-------|--------|-------|-----------------|
| South East | 0 | 1 | 492 | 262 | 446 | 293 |
| South West | 0 | 0 | 194 | 219 | 979 | 302 |
| East Anglia | 0 | 0 | 343 | 204 | 105 | 289 |
| East Midlands | 0 | 0 | 389 | 188 | 324 | 337 |
| West Midlands | 0 | 0 | 143 | 137 | 428 | 345 |
| Yorkshire | 0 | 0 | 231 | 196 | 431 | 373 |
| North | 0 | 0 | 61 | 93 | 736 | 387 |
| North West | 0 | 0 | 19 | 45 | 300 | 393 |
| Wales | 0 | 0 | 11 | 51 | 1395 | 358 |
| Scotland | 0 | 0 | 104 | 387 | 4691 | 401 |
| N. Ireland | 0 | 0 | 5 | 45 | 766 | 443 |

Agricultural data from Eurostat 1987, CHD data from Coronary Prevention Group.

We propose that the seasonal variation of blood cholesterol is due to the direct effect of sunlight acting on the skin. This is supported by the observation that the mean blood cholesterol of the population of Blackburn varies throughout the year and appears to depend on hours of sunshine. The data from the National Household Survey clearly fail to show a dietary explanation for the fall in blood cholesterol that occurs between the first and second quarters of the year.

The identification of the precise pathway of the proposed involvement of cholesterol in human photometabolism is beyond the scope of this study, but it is worth noting that both vitamin D and cholesterol are derived from squalene.¹⁷ Although photometabolic involvement of cholesterol may occur in other ways, it is possible that whereas in the presence of sunlight squalene in exposed skin is converted into 7-dehydrocholesterol and vitamin D (and photometabolites of vitamin D), in the absence of effective sunlight its metabolic pathway is diverted into the formation of cholesterol (Figure 8). The high cholesterol levels seen in populations residing at high latitudes is thus seen to be a result of sunlight deficiency and as such a powerful risk indicator but not necessarily a cause of coronary heart disease. This does not exclude the probability that a high blood cholesterol might further damage diseased endothelial cells and coronary arteries by accretion, and indeed high blood cholesterol presents a much greater risk to people with coronary heart disease than to those without.¹¹ In other words we envisage cholesterol in the blood as *accelerating* coronary heart disease but not *causing* it. In the '4S' secondary prevention trial, 78 coronary deaths were prevented in 2221 subjects given simvastatin,¹² whereas in the west of Scotland primary prevention trial, only 14 coronary deaths were prevented in 3302 subjects given pravastatin.¹³ This trial demonstrated preven-

**Figure 8.** Proposed model linking sunlight, cholesterol and vitamin D with coronary heart disease.

tion of the clinical manifestations of coronary heart disease, not prevention of the disease itself. It is interesting to note that statins lower blood cholesterol by limiting the rate of metabolic progression from acetyl co-enzyme A to squalene to thus to cholesterol, whereas we envisage sunlight diverting further metabolism of squalene from cholesterol to vitamin D.

The seasonal variation of blood cholesterol has been described previously: 'Seasonal variations in circulating lipid levels have long been suspected by biologists interested in the regulation of lipid metabolism, yet proof of their existence has been elusive. Several small longitudinal studies during the past 60 years have broadly suggested that cholesterol levels

are higher in fall and winter than in spring and summer'.¹⁸ Sunshine was considered only briefly in that review, and no mention was made of a possible relationship with vitamin D metabolism. Seasonal variations of diet and body weight were studied but found to be insignificant. An unsigned editorial in the *Lancet* in 1984 mentioned 'the well-recognised seasonal variation which occurs in plasma cholesterol' without giving any references.¹⁹

We were not able to study controlled exposure of individuals to sunlight, but we used the natural experiment of sun exposure resulting from garden ownership. We used blood vitamin D levels as an index of sun exposure, and the higher levels in those with gardens is in keeping with this. The lower blood cholesterol levels in those with gardens supports the hypothesis that sun exposure reduces cholesterol by a direct effect.

The geographical variation of mortality rates for coronary heart disease within the UK is both puzzling and worrying. Susceptibility is highest in Scotland and Northern Ireland, but generally higher in the north than in the south. It is politically convenient to blame dietary misbehaviour of individuals for this variation, thus putting responsibility for the misfortune of the sufferers on themselves, an attitude of 'victim blaming' that has been clearly criticized.²⁰ The Three Towns study demonstrated the north-south variation but failed to find a dietary or other explanation²¹ and the study of the cold parts of Sweden failed to find the cause of the particularly high death rate from coronary heart disease.⁵ If dietary change is without effect, then diet can hardly be held responsible.

A recent publication from the WHO MONICA project compared death rates in Belfast and Toulouse. During the period of study, the death rate for all causes per 100 000 men aged 55–64 was 2112 in Belfast compared to 1197 in Toulouse, and the comparable numbers for coronary heart disease were 761 and 175.²² There was no obvious explanation for this, and the diets were remarkably similar considering major differences in climate and agriculture, but there was a suggestion of higher vitamin C intake in Toulouse. The important thing however is the difference in deaths from all causes: it is important to look not just at coronary heart disease and its possible causes but at an overall susceptibility factor to disease, related to geography.

We propose that the high mortality rate for coronary heart disease in the British Isles (north-west England, Northern Ireland and Scotland in particular) and the Atlantic fringe of north-west Europe in general is due to the high latitude and the prevailing climate, with low inclination of the sun and a great deal of cloud cover, which together result in low exposure of the population to sunshine.

There are two major features which control the weather of Europe. The first is geothermal energy in the western central Atlantic which produces the hot water of the Gulf Stream and the North Atlantic current, which keeps the sea surrounding the British Isles at a temperature higher than would be expected for its latitude. It continues northwards round the coast of Norway in the Norwegian Drift passing round the North Cape to northern Finland and keeping the sea around Murmansk free of ice. The second energy source controlling the weather of Europe is the Tibetan plateau. It is only 50 million years ago, with the collision of the Indian tectonic plate into that of Asia, that the area which is now Tibet was elevated to its present position of 5 km above sea level. The air is very thin and sunlight penetration at ground level is very high. The Tibetan plateau thus absorbs enormous amounts of energy from the sun, creating a large volume of hot dry air which rises off the Tibetan plateau to great heights and falls to the west as a result of the rotation of the earth. This hot dry air descends over western Asia and most of Europe, including the Mediterranean basin, as warm dry air at high pressure.²³ Although this weather from Tibet creates a very pleasant climate in most of Europe, only occasionally does it extend to the north-western parts of the United Kingdom, as during the summer months of 1995. North-western parts of the British Isles are much more influenced by the Gulf Stream which warms up the air immediately above the ocean. When it reaches the British Isles this air comes into contact with the cold air from the Arctic. The warm air above the water is very moist, and the contact point of the cold air above it produces cloud, resulting in the land mass of north-west Britain having a large amount of cloud cover and reduced hours of sunshine per annum.

Although north-west England has one of the highest death rates for coronary heart disease in the world, there are local significant variations. For example, the inner-city areas of Blackburn and Accrington have an SMR (Standardized Mortality Ratio) for coronary heart disease of 144 and 148, whereas the Ribble Valley, just five miles to the north has an SMR of 90.²⁴ The climate is the same, but the inner-city areas are characterized by terraced housing without gardens, a population mainly social classes 4 and 5 and a large number of Asian immigrants. The Ribble Valley has a middle-class population, villages, and larger houses most of which have a garden. Deaths from coronary heart disease are more common in social classes 4 and 5 than in social classes 1 and 2.^{25,26} This has never been convincingly explained. In the UK it is usually blamed on cigarette smoking, which has a strong social class 4 and 5 bias. However, this is not the

case in Sweden, where about 48% of all social classes smoke, but where there is still a strong gradient of deaths from coronary heart disease, low in professional classes and high in manual workers.²⁷

We further propose that the high incidence of death from coronary heart disease in social classes 4 and 5 in the north west of the British Isles is the result of sunlight deprivation, itself a result of poor housing, lack of recreational opportunity and inadequate money to allow holidays in sunnier places. Adults from social classes 4 and 5 have a higher likelihood of a sedentary lifestyle and are less likely to take regular outdoor physical activity than those in social classes 1 and 2.²⁸

The risk of death from coronary heart disease is particularly high in Indo-Asian immigrants into the UK,^{29–31} and as this risk is common to all Indo-Asian ethnic groups it is thought to be independent of dietary factors.³¹ Indo-Asian immigrants also have a high incidence of privational rickets and osteomalacia and of tuberculosis, which are considered to be the result of inadequate sunlight exposure.^{32–34} This is a common factor to all Indo-Asian groups who have adapted their lifestyles to semi-tropical areas, lifestyles not at all appropriate to living on the fringes of the Arctic. We suggest that the Indo-Asian immigrants into the UK are at a particularly high risk of death from coronary heart disease because of their behaviour; in particular a mainly indoor life, almost total skin cover with clothes and no incentive to sunbathe or take holidays in the sun. The high susceptibility may thus be seen as difficulty in adapting to a new environment.

The incidence of death from coronary heart disease appears to have fallen in recent years.^{35,36} Although the reason for this is not known for certain it could be the result of clean air legislation of the 1950s, increased leisure time of the population and the availability of cheap holidays in the sun of Florida and the Mediterranean coast.

There has been a recent suggestion that the latitude and social class variations of the incidence of coronary heart disease might be climatic, broadly agreeing with our view, but that the intervening mechanism might be related to cold.³⁷ Temperature at sea level is mainly the result of sunlight energy reaching ground level, and in respect of latitude it is perhaps difficult to separate the two. However, temperature falls with increasing altitude whereas susceptibility to coronary also diminishes.^{6–8} The altitude effect cannot be attributed to ethnicity, as it was present in a study of white males only.⁷ Similarly, hardness of water was not a satisfactory explanation.⁸ We feel therefore that sunlight is more likely to be the climatic factor determining coronary risk. This view is also supported by the association between particulate air pollution and cardiorespiratory mortality in

six US cities.³⁸ This form of pollution would diminish the penetration of sunlight energy to ground level and might be important in the emergence of coronary heart disease in the newly industrialized cities of developing countries.

The week-by-week analysis of the seasonal variation of blood cholesterol presented in Figure 6 allows us to look in more detail at the timing of the change. Our observations show that in Blackburn the population mean cholesterol dropped during April at the same time of the year that a study in Edmonton, Alberta (54°N, the same latitude as Blackburn, England), demonstrated that vitamin D synthesis in human skin commences.³⁹ This suggests that changes in blood cholesterol might be a manifestation of the same photometabolic process.

If the link between sunshine and coronary heart disease is indeed via a photometabolic process in which cholesterol is involved, then it is important to speculate on the next link in the chain of events. It is probable that the first stage in the pathological lesion in the coronary arteries is the impairment of function of the vascular endothelium, which is metabolically active producing antithrombins, thrombolytics and nitric oxide all of which maintain vascular integrity.^{40–42} Perhaps this metabolic activity requires the hormonal action of a photometabolite, which may or may not be vitamin D, but perhaps it is the elusive 'maternal factor' which seems to be a determinant of coronary heart disease risk later in life.⁴³

Niels Ryberg Finsen was awarded the Nobel Prize for Medicine in 1903 for his work in identifying the therapeutic powers of sunlight and in particular for using sunlight to heal tuberculosis of the skin (he identified ultraviolet light as being the active wavelength). More recently sunlight deficiency has been thought to precipitate clinical tuberculosis in Indo-Asian immigrants into this country. That vegetarian Hindus are more at risk than Muslims suggests that the latter obtain some vitamin D from meat and fish,⁴⁴ and it is suggested that vitamin D deficiency suppresses immunity. There is a distinct possibility that coronary heart disease has a microbial cause⁴⁵ and at present the low-grade respiratory pathogen *Chlamydia pneumoniae* (initially called *Chlamydia TWAR*⁴⁶) is the chief contender.^{47–49} We suggest that sunlight deficiency increases the opportunism of such an organism in the same way as with tuberculosis. Indo-Asian immigrants tend to develop clinical tuberculosis about 5 years after arrival in the UK, during which interval their vitamin D stores become depleted. This allows activation of an organism previously lying dormant. They might only come into contact with *Chlamydia pneumoniae* (or whichever organism might cause coronary heart disease) after arrival in this country but have no natural

immunity to it as well as diminished immunocompetence resulting from sunlight deficiency.

It is interesting to consider Crohn's disease in this respect. A 'north-south divide' has been identified, the incidence being much lower in Greece than in north-west Europe.⁵⁰ It is a transmissible disease, almost certainly microbial and the chief contender is *Mycobacterium paratuberculosis*.⁵¹ The geographical feature of sunlight could once again be protective by enhancing immunity, thus reducing the incidence in the Mediterranean countries (in contrast ulcerative colitis, the cause of which is unknown, does not exhibit this north-south divide).

Medicine, like science in general, works through a series of paradigms which, in the absence of 'proof', create a conventional understanding of the way illnesses come about. The paradigm for coronary heart disease in recent years has been along the lines that it is mainly self-induced through cigarette smoking and dietary misbehaviour, together with some family tendency or ill-defined genetic problem. The paradigm has been that coronary heart disease is 'multifactorial' and in some people effectively caused by one factor and in other people, by something else. We wish to challenge the traditional paradigm, and we propose a model as outlined in Figure 8. We propose that coronary heart disease is a specific disease with a specific cause which is probably a microbe and perhaps *Chlamydia pneumoniae*. We suggest that the rate of progress of the disease process can be modified by accelerating and inhibiting factors. We suggest that high blood cholesterol and cigarette smoking are accelerating factors of coronary heart disease but are not initiating factors. We propose that Vitamin D, or possibly one of its photometabolites, is an inhibiting factor, slowing down the rate of progress of disease. Other inhibiting factors are anti-oxidants such as Vitamin C¹⁹ and selenium,⁵² and it is clear that free oxygen radicals can increase the rate of progression of the disease.⁵³

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