PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Geochemistry and Cardiovascular Diseases [and Discussion]

R. Masironi, J. R. Todd, P. Elwood and D. B. R. Poole

Phil. Trans. R. Soc. Lond. B 1979 **288**, 193-203
doi: 10.1098/rstb.1979.0101

Phil. Trans. R. Soc. Lond. B **288**, 193–203 (1979) [193]
Printed in Great Britain

Geochemistry and cardiovascular diseases

By R. Masironi

Cardiovascular Diseases Unit, World Health Organization,
1211 *Geneva* 27, *Switzerland*

Deficiencies or excesses in the content or availability of trace elements in rocks and soils, or in water flowing through them, is hypothesized as a possible cause of certain chronic diseases, including cardiovascular diseases. Geographic distribution of cardiovascular diseases is often associated with geochemical differences. This trend is particularly evident in the United States and in Europe, with higher rates for cardiovascular mortalities being present in areas underlain by soils that are poor in most essential trace elements. Confirmation of this trend is found in connection with the degree of mineralization of local water supplies. Areas that are served by soft waters usually show higher rates of cardiovascular mortality and other forms of cardiovascular pathology, compared with the areas that are served by hard waters. Such a negative association between water hardness and cardiovascular pathology is evident in many countries, both industrialized and developing.

Cardiovascular diseases are the leading cause of death in the industrialized countries, and tend increasingly to strike at relatively young age groups. They have reached epidemic proportions and are therefore a major public health problem. Their occurrence is also increasing in the developing parts of the world, where they were practically unknown until relatively recent times.

Although the multi-causal nature of these diseases is well established and clinical (hypertension, hyperlipidaemia) as well as behavioural (overnutrition, smoking, sedentarism, stressful living) factors play a predominant role in their aetiology and pathogenesis, attempts were made to correlate the geographic distribution of cardiovascular diseases with the characteristics of the geological and geochemical environments. Some years ago, a W.H.O. meeting of experts emphasized the importance of this type of investigation (World Health Organization 1971).

In studying the relations between environments and cardiovascular, as well as other, diseases, two approaches are possible: (*a*) field studies and analyses of local rock and soil samples associated with local epidemiological surveys, and (*b*) the use of geological, geochemical, and soil maps for comparison with epidemiological maps, when available. The first approach is more precise but, often, it may not be feasible on a large scale. The second approach is easier and may indicate contrasting situations, but it calls for greater caution in the interpretation of any apparent association.

To my knowledge, one of the earliest investigations that associated geographical distribution of cardiovascular diseases with the type of soil was that by Tromp (1958) in the Netherlands, where mortality rates from arteriosclerotic heart disease were found to be highest in those areas which were underlain by sea-clay soils and peat soils, and lowest on sandy soils of glacial origin. Later on, several investigations have revealed that higher cardiovascular pathology is almost consistently associated with environments – be these rocks, soils or water – that are generally deficient in trace elements.

For instance, the eastern part of the United States, where cardiovascular diseases are more prevalent, is underlain by sands and silts and is characterized by soils that are generally deficient in many trace elements, among which are the biologically essential ones. Waters are also demineralized relative to the western part. In contrast, most of the Great Plains region to the west is underlain by limestone and shale. Many of the elements in limestone are readily available through solution, and shales are notably richer in trace elements than other sedimentary rocks. This situation is outlined in table 1. The eastern and western United States are separated by the 97th meridian, which corresponds to the boundary dividing the dry soils of the western United States from the wet and moist soils of the eastern United States (Shacklette *et al.* 1971).

TABLE 1. DEATH RATES FROM CARDIOVASCULAR DISEASES RELATED TO ELEMENT CONCENTRATIONS IN SOIL AND WATER HARDNESS IN THE U.S.A.

	metal content of soil†/(μg/g)		
	west U.S.A.‡	east U.S.A.‡	
Al	54000	33000	
Fe	20000	15000	
Ca	18000	3200	
K	17000	7400	
Na	10200	2600	
Mg	7800	2300	
Ba	560	300	
Mn	389	285	
Sr	210	51	
V	66	46	
Zn	51	36	
Cu	21	14	
water hardness/(μg/g)	154 ± 71	81 ± 56	$p < 0.001$
cardiovascular death rates§	366 ± 32	429 ± 39	$p < 0.001$
non-cardiovascular death rates	432 ± 70	424 ± 44	n.s.

† From Schacklette *et al.* (1971).
‡ East–west boundary is the 97th meridian.
§ From Schroeder (1960). Death rates per 100000 white persons of both sexes and all ages.

Shacklette *et al.* (1972) studied the occurrence of heart disease in Georgia, U.S.A., in relation to the geochemical environments and the trace eleme t content of the soil. Counties located in the southeastern coastal plains of this State showed death rates from cardiovascular diseases that were twice as high as those of counties from the northwestern, mountainous, Appalachian region. The coastal plains lie on marine sediments that have been extensively weathered and leached so that the overlying soils are depleted of most trace elements. The low death rate counties lie instead on igneous and metamorphic rocks which are rich in minerals and continuously supply trace elements to the soils (figure 1).

A clustering of high death rate counties in the southeastern coastal plains, and of low death rate counties in the northwestern Appalachian highlands was similarly found by Voors (1971) in neighbouring North Carolina.

Shamberger (1976) demonstrated lower human heart disease mortality in states where the soil is rich in Se, especially the six states (Colorado, Kansas, Nebraska, North Dakota, South

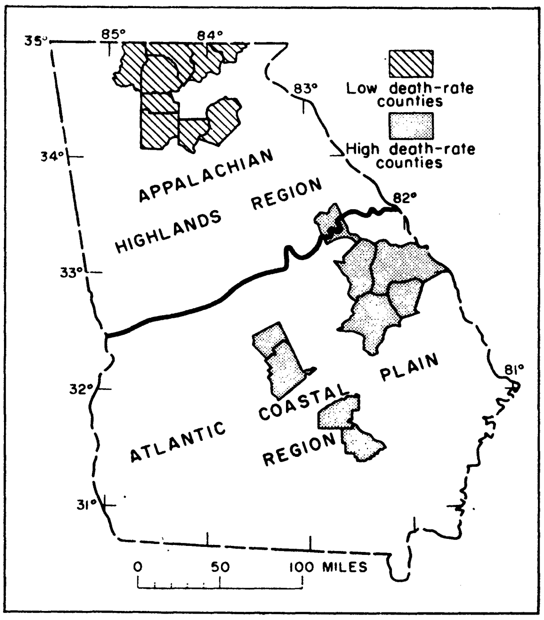

FIGURE 1. Physiographic regions of Georgia, and groups of counties having high and low rates of death due to cardiovascular diseases (from Shacklette *et al.* 1972).

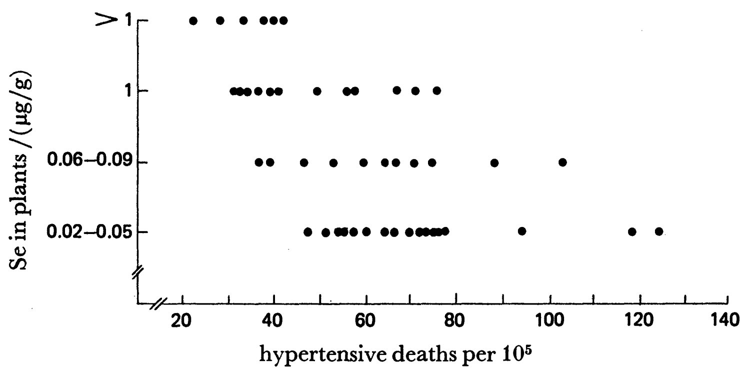

FIGURE 2. Cardiovascular diseases and environmental Se in the U.S.A. (from Shamberger 1976).

Dakota and Wyoming) that are very high in Se. In 17 cities located in high-Se areas, hypertensive heart disease and arteriosclerotic heart disease were significantly lower than in 17 matched low-Se cities (figure 2).

The Se story described above seems to apply also on a larger geographic scale in Europe. For instance, Scotland and the Scandinavian countries, with their very high cardiovascular death rate, are 'low-Se' countries whose soils are strongly leached glacial deposits. Countries in central Europe, where cardiovascular death rates are lower, have adequate Se supply from their soils (Gissel-Nielsen 1976).

Eastern Finland is unfortunately notorious for its very high cardiovascular death rates which are perhaps the highest in the world. They are higher there than in western Finland. This difference between adjacent regions of the same country is considered to be related to the lower average content of exchangeable Ca and Mg in the soils of the eastern part, compared with the western soils (Karppanen & Neuvonen 1973).

Soils and rocks in the high mortality countries of northern Europe are poor sources of many essential trace elements. Those countries are generally underlain by rocks of great geological age, especially Precambrian, which are sometimes characterized by a low availability of trace elements and by soft waters. Another feature of the major areas of the world with underlying Precambrian rocks is that, in general, they are covered by podzol or podzolic soils, the upper layers of which have been leached. On the other hand, countries of the Mediterranean region with underlying geological formations of the Mesozoic and Cainozoic eras have characteristically

TABLE 2. DEATH RATES FROM ISCHAEMIC HEART DISEASE (ALL AGES, BOTH SEXES, PER 100000, 1967) IN EUROPE RELATED TO SURFACE ROCKS AND UNDERLYING STRATA

Precambrian (> 600 Ma old)		early Palaeozoic (600–300 Ma old)		late Palaeozoic (300–180 Ma old)		Mesozoic (< 180 Ma old)	
Sweden	320	Norway	263	Ireland	294	Italy	200
Finland	274	Northern Ireland	302	Austria	256	Yugoslavia	129
Denmark	318	England	308	Hungary	259	Bulgaria	144
Scotland	345			France	83	Greece	100
				Germany (F.R.)	226	Switzerland	220
				Netherlands	186		
				Belgium	180		
				Czechoslovakia	197		
				Poland	92		
				Spain	68		
				Portugal	119		
				Rumania	144		
mean	314†		291		175		159†
s.d.	±29		±24		±75		±50

† Difference significant at $p \leqslant 0.001$.

low death rates from cardiovascular diseases. Unlike the podzols which, in the northern latitudes, originate largely from relatively insoluble granites and gneisses, the red and brown Mediterranean soils are formed mainly from the more soluble calcareous rocks. Plants and water may thus extract larger amounts of minerals from these soils (Masironi *et al.* 1972) (table 2).

A similar pattern of lower cardiovascular mortality associated with younger geological environments appears to be present also within the United Kingdom. Lower death rates from cardiovascular and cerebrovascular diseases occur in the southeastern areas, which are underlain by comparatively recent strata of the Cretaceous and Tertiary periods. Significantly higher death rates are instead found in the northwestern, geologically much older areas (Takahashi 1967; Stocks 1970; Masironi *et al.* 1972 (figure 3).

Takahashi (1967) examined the geographic distribution of cardiovascular and cerebrovascular diseases in 18 European countries and in Japan and found associations with the type of geological substrate in many of them, usually in the direction of higher mortality associated with older terrains.

A much larger body of evidence that relates cardiovascular diseases to factors of the geochemical environment comes from numerous investigations on the inverse association between death rates from cardiovascular diseases and hardness of water, which was found in the United States of America (Schroeder 1960), in the United Kingdom (Crawford 1972), in Canada (Neri *et al.* 1972), and in other countries as well. The voluminous literature in this field was reviewed recently by Neri & Johansen (1978). All of the large national and international epidemiological studies consistently showed a higher cardiovascular pathology in areas served by relatively soft water than in areas served by relatively hard water. The negative association shown in figure 4, which exemplifies the associations reported in several other similar studies,

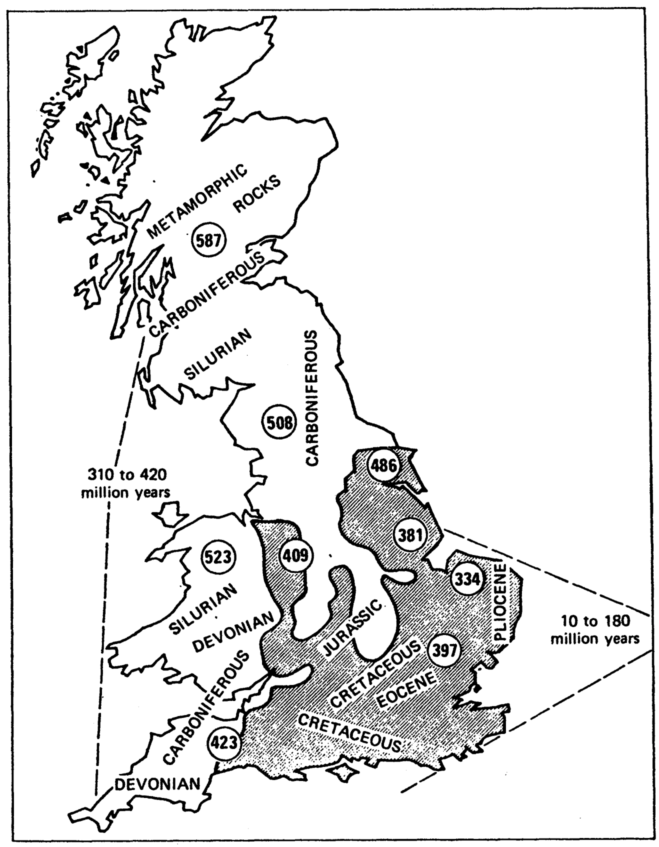

FIGURE 3. Coronary heart disease mortality in relation to hardness of water and to geology in the U.K. Unshaded areas, very soft to slightly hard water (less than 50–150 μg/l); shaded areas, moderately hard to very hard water (150–300 μg/l or more); numbers in circles are coronary heart disease death rates per 10^5m ales 45–60 years old.

results from a recent survey coordinated by W.H.O., of myocardial infarction in 15 large European towns (World Health Organization 1976). Final results of this investigation are published elsewhere (Masironi *et al.* 1978).

Some of the smaller studies, which only involved a few towns, however, gave contrasting results (Bierenbaum *et al.* 1973; Meyers & Williams 1977).

Whereas the studies mentioned above dealt with treated municipal water supplies, the influence of broader geochemical environmental factors, as expressed by data on raw river waters, was investigated by Kobayashi (1957) on cerebrovascular apoplexy in Japan, by Masironi (1970) on hypertensive heart disease in the U.S.A., and by Masironi *et al.* (1976) on blood pressure in New Guinea villagers.

Kobayashi (1957), who with his investigation unknowingly initiated what is now called the 'water story' in cardiovascular diseases, found a parallel between the geographic distribution of apoplexy and the acidity of river water in Japan. Masironi (1970) examined the cardiovascular

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

mortality rates in populations living along four rivers in the U.S.A., the Ohio, Missouri, Colorado and Columbia rivers, whose waters contrast in hardness (figure 5*a*). Mortality rates from hypertensive heart disease and, less markedly, from arteriosclerotic heart disease, were significantly lower in the populations living along the hard-water Colorado river than in the

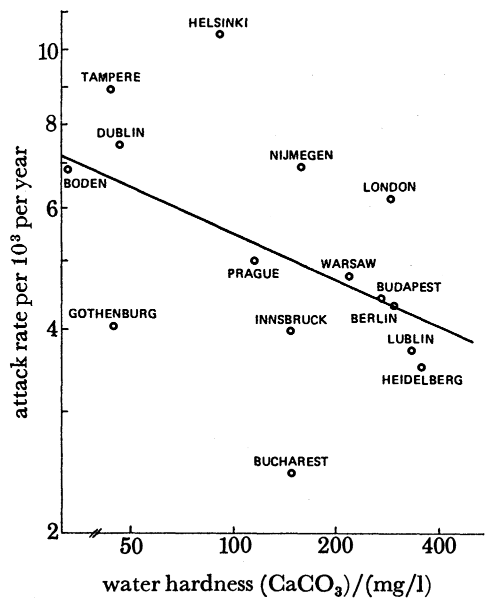

FIGURE 4. Heart attack rate standardized by age and sex (age 45–64); for the regression line the parameters are $r = -0.477$ and $\rho = -0.536$.

populations living along the soft-water Columbia and Ohio rivers. The non-cardiovascular mortality rates did not differ in the four areas (figure 5*b*).

The choice of primitive communities living in a relatively isolated area with very little exposure to industrialization is likely to ensure a closer relationship between the population and the geochemical environment. One such community was found in New Guinea, and blood pressure was measured in villagers living along the banks of the Wogupmeri river. These villagers subsist on a non-cash economy and drink the river water as such. The Wogupmeri river originates in limestone mountains and flows into the Sepik river. The Ca content of the water decreases downstream, as the river flows away from the mountains. Contrary to this trend, the mean of the blood pressure measurements taken in inhabitants of the eleven villages increases (figure 6) (Masironi *et al.* 1976).

Of course, the chemical composition of natural waters is influenced by the type of soils and rocks through which the water flows. Water hardness as used in all the studies outlined above is only an indicator of something in the water that may be beneficial to the cardiovascular function and is missing in soft water. Cr, I, F, Li and Mg are thought by some investigators to be the beneficial factor(s) in hard water. It may also well be that soft treated waters contain something harmful that has been leached out of water pipes, for instance Cd, which is thought to exert a hypertensive effect.

Major elements or trace elements may thus be involved, but no consensus has yet been reached.

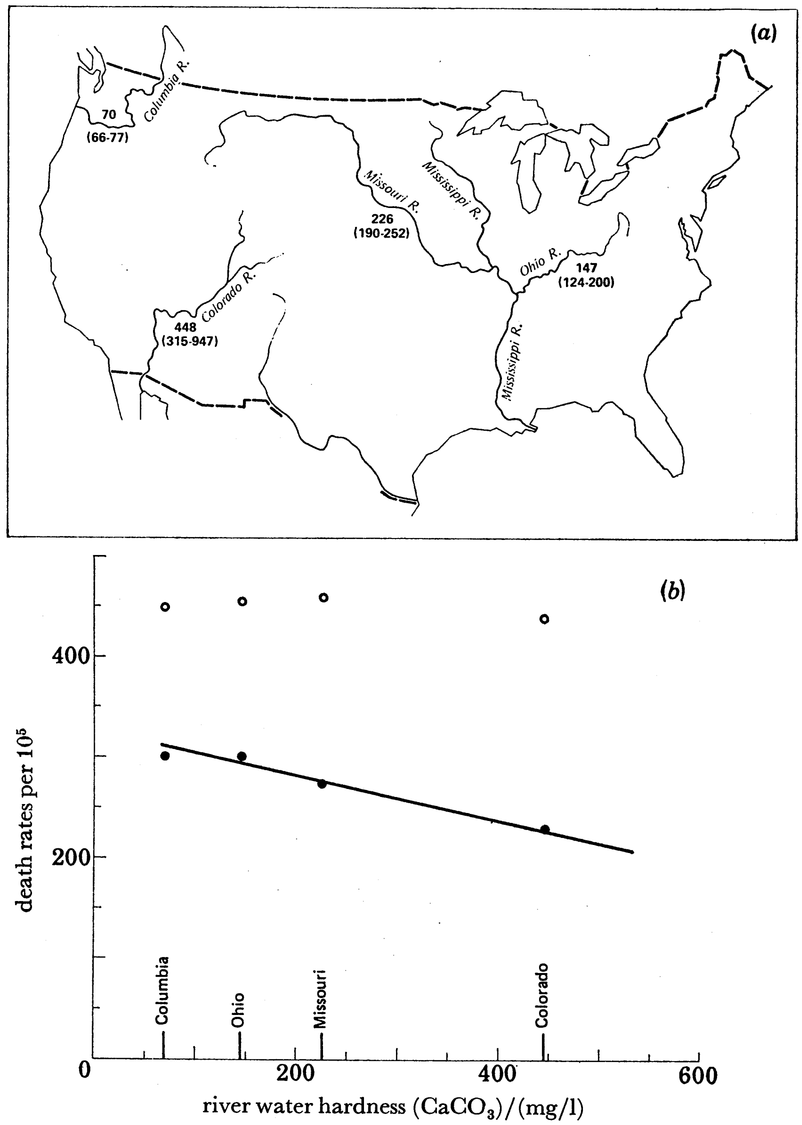

FIGURE 5. Cardiovascular mortality rates along U.S. rivers differing in water hardness. (*a*) Water hardness ($CaCO_3$) of the four rivers under study (mean and range in milligrams per litre; from Masironi 1970). (*b*) Coronary heart disease (●) and non-cardiovascular diseases (○) in relation to hardness of river water; all ages, both sexes.

In conclusion, cardiovascular diseases have been shown to be geographically distributed, both intranationally and internationally, in a fashion generally similar to the distribution of certain geochemical characteristics. The analysis of data obtained by numerous investigators, who followed different geographical and epidemiological approaches and used different geochemical indicators – rock age, soil type, water hardness – consistently point to a higher cardiovascular pathology in areas where the geochemical environments are, broadly speaking, poor in mineral content or availability. Such situations are found, for instance, in regions of extensively weathered rock, or in areas where the water is soft and the soils are low in essential trace elements. The nature of these associations is unknown, and whether or not they reflect a cause–effect

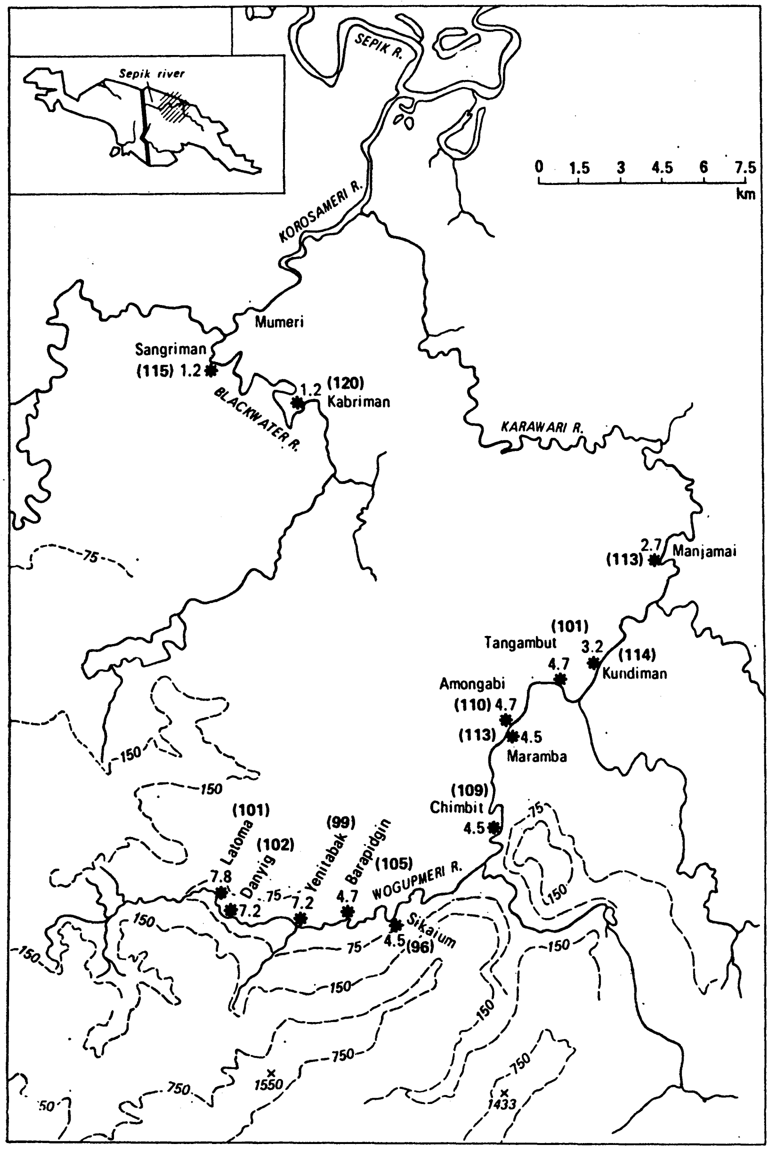

FIGURE 6. Villages surveyed in Sepik river basin and Ca content (milligrams per litre) of local river water. Numbers in parentheses are systolic blood pressure (both sexes) in millimetres of Hg (1 mmHg ≈ 133.3 Pa).

relation has yet to be ascertained. It can, however, be hypothesized that geochemical environments that do not supply optimal amounts of the biologically essential minerals – through water and the food chain – to the populations living locally may, in the long run, cause the unsuspected, slow development of a chronic cardiovascular or circulatory impairment. This would later on become manifested as increased mortality from heart diseases in comparison with populations living in other, more beneficial, geochemical environments. Of course these tentative observations appear to be an overwhelmingly simple generalization and may merely indicate just a working hypothesis. Cardiovascular diseases have a complex multifactoral pathogenesis in which clinical and behavioural factors play predominant roles; the geochemical environment, however, may also be relevant in this connection.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

References (Masironi)

Bierenbaum, M. L., Fleischman, A. I., Dunn, J. P., Hayton, T., Pattison, D. C. & Watson, P. B. 1973 Serum parameters in hard and soft water communities *Am. J. publ. Hlth* **63**, 169–173.

Crawford, M. D. 1972 Hardness of drinking water and cardiovascular diseases. *Proc. Nutr. Soc.* **31**, 347–353.

Elliott, G. B. & Alexander, E. A. 1961 Sodium from drinking water as an unsuspected cause of cardiac decomposition. *Circulation* **23**, 562–566.

Gissel-Nielsen, G. 1976 Selenium in soils and plants. In *Proceedings of a Symposium on Selenium and Tellurium in the Environment*, Notre Dame, Indiana, pp. 10–25. Pittsburgh: Industrial Health Foundation.

Karppanen, H. & Neuvonen, P. J. 1973 Ischaemic heart disease and soil magnesium in Finland. *Lancet* i, 1390.

Kobayashi, J. 1957 Geographical relationship between chemical nature of river water and death rate from apoplexy. *Ber. Ohara Inst. landw. Biol.* **11**, 12–21.

Masironi, R. 1970 Cardiovascular mortality in relation to radioactivity and hardness of local water supplies in the U.S.A. *Bull. Wld Hlth Org.* **43**, 687–697.

Masironi, R., Miesch, A. T., Crawford, M. D. & Hamilton, E. I. 1972 Geochemical environments, trace elements, and cardiovascular diseases. *Bull. Wld Hlth Org.* **47**, 139–150.

Masironi, R., Koirtyohann, S. R., Pierce, J. O. & Schamschula, R. G. 1976 Calcium content of river water, trace element concentrations in toenails, and blood pressure in village populations in New Guinea. *Sci. tot. Envir.* **6**, 41–53.

Masironi, R., Pisa, Z. & Clayton, D. 1978 Myocardial infarction and water hardness within the WHO network of myocardial infarction community registers. *Bull. Wld Hlth Org.* **57**, 291–299.

Meyers, D. H. & Williams, G. 1977 Mortality from all causes and from ischaemic heart disease in the Australian capital cities. *Med. J. Aust.* **2**, 504–505.

Neri, L. C. & Johansen, H. 1978 Water hardness and cardiovascular mortality. *Ann. N.Y. Acad. Med.* (In the press.)

Neri, L. C., Mandel, J. S. & Hewitt, D. 1972 Relation between mortality and water hardness in Canada. *Lancet* i, 931–934.

Shacklette, H. T., Hamilton, J. C., Boerngen, J. G. & Bowles, J. W. 1971 Elemental composition of surficial materials in the conterminous United States. *U.S. geol. Surv. prof. Pap.* no. 574-D. Washington, D.C.: U.S. Govt Printing Office.

Shacklette, H. T., Sauer, H. I. & Miesch, A. T. 1972 Distribution of trace elements in the environment and the occurrence of heart disease in Georgia. *Bull geol. Soc. Am.* **83**, 1077.

Shamberger, R. J. 1976 Selenium in health and disease. In *Proceedings of a Symposium on Selenium and Tellurium in the Environment*, Notre Dame, Indiana, pp. 253–267. Pittsburgh: Industrial Health Foundation.

Schroeder, H. A. 1960 Relation between mortality from cardiovascular diseases and treated water supplies. *J. Am. med. Ass.* **172**, 1902–1908.

Stocks. P. 1970 Incidence of congenital malformations in the regions of England and Wales. *Br. J. prev. soc. Med.* **24**, 67–77.

Takahashi, E. 1967 Geographic distribution of mortality rate from cerebrovascular disease in European countries. *Tohoku J. exp. Med.* **92**, 345–378.

Tromp, S. W. 1958 *The geographical distribution of arteriosclerotic heart disease in the Netherlands (1936–1945)*, vol. 3. Leiden: Bioclimatological Research Centre.

Voors, A. W. 1971 Atherosclerotic heart disease and drinking water trace metals in North Carolina. In *Trace substances in environmental health*, vol. 5 (ed. D. D. Hemphill), pp. 523–534. Columbia: University of Missouri.

World Health Organization 1971 Trace elements and cardiovascular diseases. *W.H.O. Chronicle*, **26** (2), 51–59.

World Health Organization 1976 Myocardial infarction community registers. *Public health in Europe*, no. 5. Copenhagen: W.H.O. Regional Office for Europe.

Discussion

J. R. Todd (*Department of Agriculture for N. Ireland, and Queen's University, Belfast, U.K.*). The evidence relating hardness of water and cardiovascular disease has all been in relation to incidence in man. Animals, and particularly grazing livestock, must also be subject to the effects of drinking water composition in the areas where they are reared. Is there any evidence of cardiovascular lesions in animals and, if so, can the incidence be related to the composition of water supplies?

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

R. Masironi. Atherosclerosis and ischaemic heart disease are, unfortunately, human diseases only. Animal models are rather unsatisfactory. This is why studies on water hardness and cardiovascular pathology in animals are very scarce. I know of only three such studies and they tend to confirm the trends found in human studies.

P. Elwood (*M.R.C. Unit*, 4 *Richmond Road*, *Cardiff*, *U.K.*). I wonder if Dr Masironi has been just a little selective in the evidence he has presented in support of the hard water cardiovascular disease association.

(1) There have been a number of studies in which the association has not been found, notably the 'two town' studies.

(2) When it has been looked for, a negative association has been detected for conditions other than ischaemic heart disease, e.g. bronchitis and congenital malformation.

(3) A great natural experiment to which no allusion has been made is in the West Midlands conurbation. Birmingham has a very soft water, and an ischaemic heart disease mortality identical with a number of very hard water areas immediately adjacent.

(4) Dr Masironi referred to one study in which small differences in blood pressure and very small differences in cholesterol levels were detected in men living in hard and soft water areas, and of course, areas of very different mortalities. Yet two studies along identical lines failed to find any such differences.

R. Masironi. (1) We cannot always expect to find absolutely consistent results in such studies where a geochemical factor like water hardness and a multifactorial disease group like cardiovascular diseases are compared. All of these parameters are poorly definable, and sometimes these change with the season, with the fashion of reporting, and with other confounding circumstances.

Nevertheless, the large geographical studies which covered wide national or international areas in the U.S.A., Canada, U.K. and continental Europe, and were based on mortality data from several million people, all showed a consistent negative association between water hardness and cardiovascular mortality. The 'two town' studies and all the other small-scale studies, some of which merely compared sections of the same towns, and the statistics which were based on, for example, less than ten deaths, gave inconsistent results. In these small-scale studies, seasonal variations in water hardness and in cardiovascular mortality, the use of domestic water softeners, the mobility of the populations living in one section of the town and working and eating in another, play, of course, an overwhelmingly confounding role.

(2) Several other diseases have been found to be associated with water hardness in one study or another. However, these diseases were never the same in the different, large-scale, studies. Cardiovascular diseases, instead, always showed a negative association.

(3) The same answer as in point number 1 may apply here. We must consider associations based on data from a large number of population groups. If we compare just a few such population groups it is very likely that one group may show, for example, higher death rates in spite of harder water, than another group nearby.

(4) The association of water hardness to such cardiovascular parameters as blood pressure and blood cholesterol, if any, is not really well established. It is still a working hypothesis based on limited observations.

D. B. R. Poole (*The Agricultural Institute*, *Dunsinea Research Centre*, *Castleknock*, *Co. Dublin*, *Ireland*). Referring to figure 2 in Dr Masironi's paper, can Dr Masironi explain the basis that Ireland

and indeed Britain too are classed as high-Se areas. Our work on soil Se and on blood glutathione peroxidase levels in cattle and sheep strongly suggest that most of Ireland may have a low or marginal Se status. On a more general level, in relation to the mapping of human mortality figures, in the light of our knowledge (in animals) of the more profound effects for example of Cu deficiency on the young growing animal, or of Zn deficiency on the foetus, might it not be more valuable to map mortality, say for cardiovascular disease on the birth place of the deceased rather than on the place of death?

R. Masironi. The map of Se adequacy in Europe is taken from published data and I cannot therefore comment on the discrepancy between the published finding of Se adequacy in Ireland and your finding of possible inadequacy. Certainly this is a field of marked research interest. As to the suggestion of mapping mortality based on the place of birth rather than on the place of death, I think it would be a very interesting exercise. It could yield a new insight into geographic distribution of diseases, but I am unaware of any such approach having been attempted so far.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES