CLINICAL RESEARCH

British Regional Heart Study: cardiovascular risk factors in middle-aged men in 24 towns

A G SHAPER, S J POCOCK, MARY WALKER, N M COHEN, C J WALE, A G THOMSON

Abstract

The British Regional Heart Study seeks to define risk factors for cardiovascular disease, to examine their interrelationships, and to explain the geographic variations in cardiovascular disease in Britain. A clinical survey of men aged 40-59 in 24 British towns was carried out and preliminary data from the survey analysed. On a town basis cardiovascular mortality was associated with mean systolic blood pressure and the prevalence of heavy cigarette smoking and heavy alcohol consumption. No such association was seen for body mass index or mean serum total cholesterol or high-density-lipoprotein cholesterol concentration. Cigarette smoking and alcohol intake and, to a less degree, systolic blood pressure were related to the social class (percentage of manual workers) of a town, and these factors may determine to some extent the increased risk of cardiovascular disease in manual workers.

Blood pressure in individual subjects was affected predominantly by age, body mass index, and alcohol intake. Body mass index appeared to affect blood pressure to a greater extent than alcohol intake and did so with a consistent and positive linear trend. Nevertheless, the differences between towns in mean blood pressure readings appeared to be more closely associated with variations in the prevalence of heavy drinking than with variations in body mass index. Alcohol intake and body mass index explained only a part of the striking differences between towns in mean blood pressure readings, and some important "town" factors remained unexplained.

Department of Clinical Epidemiology and General Practice, Royal Free Hospital School of Medicine, London NW3 2QG

A G SHAPER, FRCP, FRCPATH, professor of clinical epidemiology
S J POCOCK, MSC, PHD, senior lecturer in medical statistics
MARY WALKER, SRN, SCM, research administrator
N M COHEN, MD, MRCP, senior research fellow
C J WALE, statistical technician
A G THOMSON, BA, programmer

Introduction

There is a twofold range in mortality from ischaemic heart disease and stroke in the towns of Britain, the highest mortality being in the west of Scotland and the lowest in south-east England. The British Regional Heart Study was undertaken to explain these substantial variations in cardiovascular mortality by assessing the role of environmental, socioeconomic, and personal risk factors. The study falls into three main phases.

Phase 1 related cardiovascular mortality over five years (1969-73) in 253 towns in England, Wales, and Scotland to a wide range of environmental and socioeconomic data.[1] A multifactorial approach in analysing this information showed that the geographic variation in cardiovascular mortality was related to water hardness, rainfall, temperature, and socioeconomic factors. Water hardness was negatively associated with cardiovascular mortality, even after allowing for climatic and socioeconomic effects, and this apparent effect was present for both stroke and ischaemic heart disease but not for non-cardiovascular disease.

Phase 2 was a clinical survey of middle-aged men in 25 towns selected from the broad data base of phase 1 to represent the wide distribution of cardiovascular mortality and water hardness. The principal objectives of this phase were (*a*) to examine the variation between towns in the distribution of established and possible risk factors for cardiovascular disease and to relate these variations to the known cardiovascular mortality rates; (*b*) to examine the relations between risk factors and variables of water quality, and to assess whether water quality affects cardiovascular mortality via any of the risk factors; and (*c*) to examine the interrelationships between the personal risk factors.

Phase 3 is a prospective study of cardiovascular morbidity and mortality in the same group of middle-aged men to determine which of the many personal risk factors are most strongly related to cardiovascular events and to assess their behaviour under differing environmental conditions.

The fieldwork for phase 2 was begun in January 1978 and completed in June 1980, by which time 8241 men had been examined. This paper is concerned with the prevalence of individual cardiovascular risk factors in 7727 middle-aged men in 24 towns in England, Wales, and Scotland; with their interrelationships; and with their relation to cardiovascular mortality in these towns. The analysis excludes the pilot town and a repeat visit to one town (514 men in all).

Materials and methods

SELECTION OF TOWNS

In selecting the towns for phase 2 we were primarily concerned with regional variations in cardiovascular disease and with variations in water quality, particularly hardness. We intended that the towns should represent all major geographic regions (including Scotland) and at the same time reflect the variations in mortality from cardiovascular disease and water hardness. Seven criteria were established.[1]

(1) All standard regions should be represented.

(2) Towns should be discrete entities, separated from major conurbations, and with populations of 50 000-100 000 at the 1971 Census. In England one larger town was included (Ipswich, 122 700). To obtain a reasonable number of suitable towns in Scotland, some towns below 50 000 were considered there.

(3) The choice of towns within regions should adequately reflect the variations in mortality from cardiovascular disease and water hardness.

(4) Whenever possible towns should be chosen which are representative of the region in socioeconomic terms.[2]

(5) Towns with large, recent housing developments, with noticeable population movement, or with an unusual population structure should be avoided.

(6) The study should include some of the towns that were apparently "outliers" when mortality from cardiovascular disease and water hardness were plotted against each other—for example, Hartlepool, Exeter, and Harrogate.[1]

(7) When similar towns meet the above criteria random selection should be made.

Table I lists the 25 towns selected and gives the standardised mortality ratios for cardiovascular disease in men aged 35-64, total water hardness, population, number of men examined, and the percentage response rate. "Cardiovascular disease" includes all forms of cardiovascular disease except rheumatic heart disease (*International Classification of Diseases*, 8th revision, codes B27-30).

TABLE I—*Towns included in regional heart study*

Town	Standardised mortality ratios for all cardiovascular disease in men aged 35-64	Water hardness (mmol/l)	Population size (1971 census)	No of men examined	Response rate (%)
Ayr	140	0·27	47 890	301	70
Bedford	80	3·27	72 880	303	73
Burnley	114	0·37	76 130	286	80
Carlisle	121	0·90	71 820	389	85
Darlington	109	0·98	85 900	382	82
Dewsbury	142	0·33	51 130	326	79
Dunfermline	118	0·41	49 890	350	80
Exeter	90	0·72	93 800	332	84
Falkirk	98	0·38	37 600	308	75
Gloucester	84	2·08	89 980	309	73
Grimsby	96	2·60	95 610	318	71
Guildford	78	2·50	58 090	335	82
Harrogate	82	0·73	63 470	280	77
Hartlepool	101	5·28	97 110	334	70
Ipswich	92	3·84	122 700	362	85
Lowestoft	85	3·19	52 120	324	83
Maidstone	99	3·01	71 250	319	72
Mansfield	95	2·30	57 820	321	80
Merthyr Tydfil	135	0·39	55 100	282	76
Newcastle-under-Lyme	115	2·08	77 320	293	77
Peterborough (pilot town)	92	3·72	70 100	279	80
Scunthorpe	109	2·88	70 900	313	76
Shrewsbury	95	1·13	56 630	310	83
Southport	114	3·00	84 870	322	80
Wigan	134	0·55	81 140	337	77

Conversion: SI to traditional units—Water hardness: 1 mmol/l = calcium carbonate equivalent 100 mg/l.

SELECTION OF PRACTICE

To find a representative group of men in each town in whom it would be likely that there would be a good initial response and good subsequent follow-up, we decided to select subjects from one group practice in each town. This also facilitated organisation and administration. Criteria for selecting a practice included its size (practice population over 7500 and two or more principals) and its representativeness of socioeconomic composition and characteristics of the town population. A full list of all practices was obtained from the appropriate family practitioner committee and discussed with the area medical officer or district community physician, or both. A short list of possible practices was drawn up and all were sent information about the regional heart study and asked to indicate their interest and willingness to discuss participation. Each interested practice was then visited and a further assessment made of its representativeness through discussions with doctors and ancillary staff. After this a decision was made and one group practice invited to participate. If no age and sex register existed one was prepared by the study.

SELECTION OF SUBJECTS

To have enough men in each town to study differences in the prevalence rates of the personal risk factors we calculated that about 300 men per town should be studied. This number provided about 7500 men, which were enough for the prospective study (phase 3). From the age and sex register we selected at random some 450 men aged 40-59 years, stratified into equal five-year age groups. This list of names was sent to the general practice and the doctors asked to exclude those whom they considered would be unable to participate because of severe mental or physical disability. We emphasised that no attempt should be made to exclude subjects with cardiovascular problems, and close scrutiny of the returned annotated lists reduced the exclusions to about six to 10 per practice. The remaining subjects were invited to take part in the study in a letter signed by all the practice doctors. Invitations which were returned undelivered were removed from the denominator in assessing response rates. Non-responders were sent a second invitation. Those who accepted an appointment but did not turn up were posted a reminder card asking them to attend at any time convenient to themselves while the survey team were in the practice.

MEASUREMENTS

All measurements were made by a team of three nurses. Training for standardisation of procedures, including administering the questionnaire, was carried out before the study and repeated at intervals throughout. A *feasibility* study was carried out in one town in order to test all methods and procedures, and the results for that town are not included in the study. A *pilot* study was then carried out in a further town to test the finalised methods and procedures, and the results for that town are not presented here.

A questionnaire was administered by a nurse and details of personal and family history including duration of residence, previous residence, and past and present occupations obtained. Questions on chest pain, leg pain, respiratory symptoms, medical history, and drug usage were included and data obtained on smoking, diet, alcohol intake, and physical activity at work and in leisure time. (Copies of questionnaire available on request.)

Height and weight—Height was measured without shoes using a Harpenden Stadiometer with digital meter which recorded to the nearest millimetre. Weight in trousers and socks was measured to the nearest 0·1 kg on an MPS110 field survey scale (beam balance).

Blood pressure—The London School of Hygiene sphygmomanometer was used to measure the blood pressure twice in succession with the subject seated and the arm supported on a cushion. Diastolic blood pressure was recorded at disappearance of sounds (phase V). Room temperature was recorded for each session

Lung function was determined with a Vitalograph (model J49-B2) with a digital meter indicating forced vital capacity and forced expiratory volume in one second.

Electrocardiograms were recorded on computer tape using the three-lead orthogonal system[3] and viewed on an oscilloscope for any major abnormalities. The completed tapes for each town were sent to a collaborating centre for analysis by computer. On a few occasions when technical problems occurred with this apparatus 12-lead electrocardiograms were recorded on a Hewlett-Packard (1515-B) machine and sent to the centre for analysis.

Blood samples were taken, using evacuated tubes, for biochemical analysis, haematological study, and blood grouping (ABO and rhesus). Serum was analysed for concentrations of sodium, potassium, urea, creatinine, urate, calcium, phosphate, albumin, globulin, bilirubin, glucose, total cholesterol, and high-density-lipoprotein cholesterol and activities of alkaline phosphatase, aspartate transaminase, and gammaglutamyltranspeptidase. Lead concentrations were measured, and cadmium concentrations are also to be determined. High-speed liquid chromatography is being carried out for serum fatty-acid analysis in certain subgroups. The time at which samples were obtained was recorded.

Consistency of recording—The flow pattern of the above investigations took the men through three successive stations, (*a*) the questionnaire; (*b*) measurements of height, weight, blood pressure, and respiratory function; and (*c*) electrocardiography and blood sampling. The data obtained at each station could be attributed to a specific nurse for purposes of checking quality control.

Personality and attitudes—While the men were waiting to start the above series of investigations they completed a simple 14-item questionnaire on personality and attitudes.[4]

Water supplies—A team from the Water Research Centre (Medmenham, Bucks) joined the survey team for two days during the study in each town, administered a questionnaire on water-usage patterns to about 15% of the sample (about 40 men in each town), and arranged for collection of tap-water supplies from their homes. The samples were analysed for a wide range of bulk and trace elements.

Urine samples—In the last five towns casual urine samples from all men were collected into normal hydrochloric acid (1/20 dilution). The men being studied by the Water Research Centre provided an overnight 12-hour sample, which was collected into 50 ml normal hydrochloric acid. Samples were analysed for creatinine, sodium, potassium, calcium, and magnesium concentrations.

There were 25 towns in the study, including the pilot town, and a repeat visit was made to one town (because of a low response rate at an unrepresentative practice on the first visit), making 26 town visits in all. Four different nurses took part in the study and participated in 26, 26, 19, and eight visits, respectively. A briefing was carried out before each visit and a debriefing meeting was held after each visit to review any problems in methods or procedures. Each town visit lasted two weeks, and during this period the survey co-ordinator (MW) visited the team to strengthen relationships with the practice staff, and a study director (AGS or NMC) held meetings with the doctors and practice staff to provide information and encourage full participation in phase 3. During these visits to the team and practice, periods were spent with each nurse as part of the quality-control system.

RESPONSE RATES

The number of men examined in each town is expressed as a percentage of those invited to participate and who were presumed to have received the invitations. The response rate (table 1) averaged 78% (range 70-85%), 18 of the 24 towns having a response rate of 75% or more.

Presentation of results

The field work on the 25 towns was completed in June 1980, but it will be some time before all the data are ready for analysis and comment. The results presented here relate to a limited number of variables in 24 towns (excluding the pilot town), and the data are presented in two main ways.

Cardiovascular mortality—This "town-based" analysis relates the standardised mortality ratio (SMR) for cardiovascular disease (1969-73) for a town to the mean values of several variables derived from men studied in that town—for example, blood pressure, body mass index, smoking, drinking, and social class. In this approach we were looking for associations which could then be explored further by other methods to see if they might be causal.

Blood pressure—This "individual-based" analysis treats the 7727 men in the 24 towns as one large group of middle-aged British men and explores the relations between blood pressure and several other variables measured in these men.

Cardiovascular mortality

This form of presentation allows examination of the extent to which established or possible cardiovascular risk factors varied between towns differing in cardiovascular mortality. Figure 1 uses the SMRs for cardiovascular disease (ICD codes B27-30) for men aged 35-64 years for the period 1969-73. The SMRs for all cardiovascular disease (excluding rheumatic heart disease) are used in this presentation because they correlated strongly and positively with the SMRs for both ischaemic heart disease ($r=0{\cdot}99$) and cerebrovascular disease ($r=0{\cdot}87$). The term ischaemic heart disease includes hypertensive disease and "other forms of heart disease" (ICD codes B27-29) and conforms with recommendations that we have made for international and regional studies.[5]

These SMRs are plotted against the mean values of systolic and diastolic blood pressure, serum total cholesterol and serum high-density-lipoprotein cholesterol concentrations, and body mass index and also against the percentage of "heavy" smokers, percentage of "heavy" drinkers, and percentage of manual workers among the men surveyed in each town.

BLOOD PRESSURE

There was a pronounced between-town variation in both mean systolic and mean diastolic blood pressure. Mean systolic blood pressure ranged from 136 mm Hg in Guildford and Shrewsbury to 153 mm Hg in Dunfermline, while mean diastolic pressures ranged from 77 mm Hg in Lowestoft to 88 mg Hg in Dunfermline. There was a positive association between mean systolic pressure and the SMR for cardiovascular disease ($r=0{\cdot}55$, $p<0{\cdot}01$). The association with mean diastolic blood pressure was less pronounced and not statistically significant ($r=0{\cdot}30$). Towns with a low mean systolic (<140 mm Hg) or diastolic (<80 mm Hg) blood pressure had an SMR below 100, except Scunthorpe with a mean diastolic pressure of 78 mm Hg and an SMR of 109. Towns with a higher mean systolic or diastolic pressure showed a substantial variation in SMR.

SMOKING

The percentage of heavy smokers (men smoking 20 or more cigarettes daily) ranged from 12% in Guildford to 40% in Grimsby, and there was a positive association between the percentage of heavy smokers and a town's SMR for cardiovascular disease ($r=0{\cdot}50$, $p<0{\cdot}05$).

ALCOHOL

Each man interviewed answered three questions on alcohol consumption (frequency, type, and quantity) based on the General Household Survey (1972-3) questionnaire.[6] A "heavy" drinker is one who has *more* than six drinks either daily or on each day at the weekend, a drink being either a half-pint of beer, a glass of wine, or a single tot of spirits. On this basis, the proportions of heavy drinkers ranged from 7% in Guildford to 45% in Merthyr Tydfil. There was a strong positive association with the SMR for cardiovascular disease and the percentage of heavy drinkers ($r=0{\cdot}67$, $p<0{\cdot}001$). Those towns with a less than 25% prevalence of heavy drinkers were predominantly below average for mortality from cardiovascular disease (10 out of 14 had SMRs below 100), while those with a higher prevalence of heavy drinkers were predominantly above average for mortality from the disease (seven out of 10 had SMRs over 110). Nevertheless, a positive association was found between the percentage of heavy smokers and percentage of heavy drinkers in these towns ($r=0{\cdot}71$, $p<0{\cdot}001$), so that it was impossible on a town basis to separate the possible effects on cardiovascular mortality of these two factors.

SERUM TOTAL CHOLESTEROL AND HIGH-DENSITY LIPOPROTEIN

The mean concentrations of serum total cholesterol showed only a small range between towns (5·99-6·59 mmol/l; 231-254 mg/100 ml), and no association was seen with cardiovascular disease mortality. Similarly, the range of mean concentrations of high-density-lipoprotein cholesterol was small (1·07-1·22 mmol/l; 41-47 mg/100 ml) and no association was seen with cardiovascular disease mortality. There was certainly no suggestion on a town basis that higher mean concentrations of high-density-lipoprotein cholesterol were associated with lower cardiovascular disease mortality.

BODY MASS INDEX

The body mass index (weight/height^2) was used as a measure of adiposity for the men in each town. Guildford, the town with the lowest SMR, had an exceptionally low body mass index, but there was no overall association between the mean body mass index and town SMR.

SOCIOECONOMIC AND GEOGRAPHIC PATTERNS

In this analysis the socioeconomic state (social class) of a town is expressed as the percentage of manual workers in the sample of men drawn from the participating general practice. Social class was based on the occupation which each man had held for the longest period, rather than on his current occupation. The proportion of manual workers ranged from 24% in Guildford to 84% in Grimsby (fig 1), and there was a positive association between the social class of the town and the SMRs for cardiovascular disease ($r=0.40$, $p=0.05$). It was not a strong association and, while towns with less than 50% manual workers ("non-manual" towns) mainly had SMRs below 100, those with more than 50% manual workers ("manual" towns) showed a very wide range of SMRs. The four towns with the highest SMRs (Dewsbury, Ayr, Wigan, Merthyr Tydfil) were all "manual" towns.

It is widely recognised that smoking and alcohol consumption are influenced by socioeconomic and geographic factors. In this study the proportion of manual workers in the 24 towns correlated positively with both heavy smoking ($r=0.84$) and heavy drinking ($r=0.72$). There was also a significant correlation between the proportion of manual workers and the mean systolic blood pressure ($r=0.55$, $p<0.01$) but not with mean diastolic blood pressure ($r=0.33$). Thus three factors which correlate with cardiovascular mortality in the analysis of town-based data (cigarette smoking, alcohol intake, and systolic blood pressure) were all associated to a greater or less degree with social class.

The "non-manual" towns (fig 1) were on the whole those with relatively low alcohol consumption, low prevalence of smoking, and lower mean blood pressures. They tended to be in the southern half of England, and there were more towns with a hard water supply (>1·7 mmol/l; >170 mg/l) than with a soft water supply. In the manual towns, those with SMRs over 100 differed from those with SMRs below 100 by having in general a higher mean systolic blood pressure, much higher prevalences of heavy smoking and heavy drinking, and predominantly a soft water supply. Mean body mass indices and serum total cholesterol and high-density-lipoprotein cholesterol concentrations did not differ between the manual towns with high SMRs and those with low SMRs for cardiovascular disease.

Blood pressure

The following results relate to the 7727 men aged 40-59 years from the 24 towns in the study. This analysis concerns *blood pressure* in particular, because blood pressure is a well-established risk factor in cardiovascular disease of all kinds and because of the striking differences in mean blood pressures between the towns. Simple univariate associations are examined initially and then multiple regression techniques used to establish the relevance to blood pressure of various factors when all are considered simultaneously. Table II shows the mean systolic and diastolic blood pressures for subjects classified according to age, body mass index, cigarette smoking, alcohol consumption, social class, and marital state.

AGE

In most communities blood pressure increases with age, and in our data there was a clear increase in systolic pressure with each five-year increase in age. Diastolic pressure showed only a small increase with age.

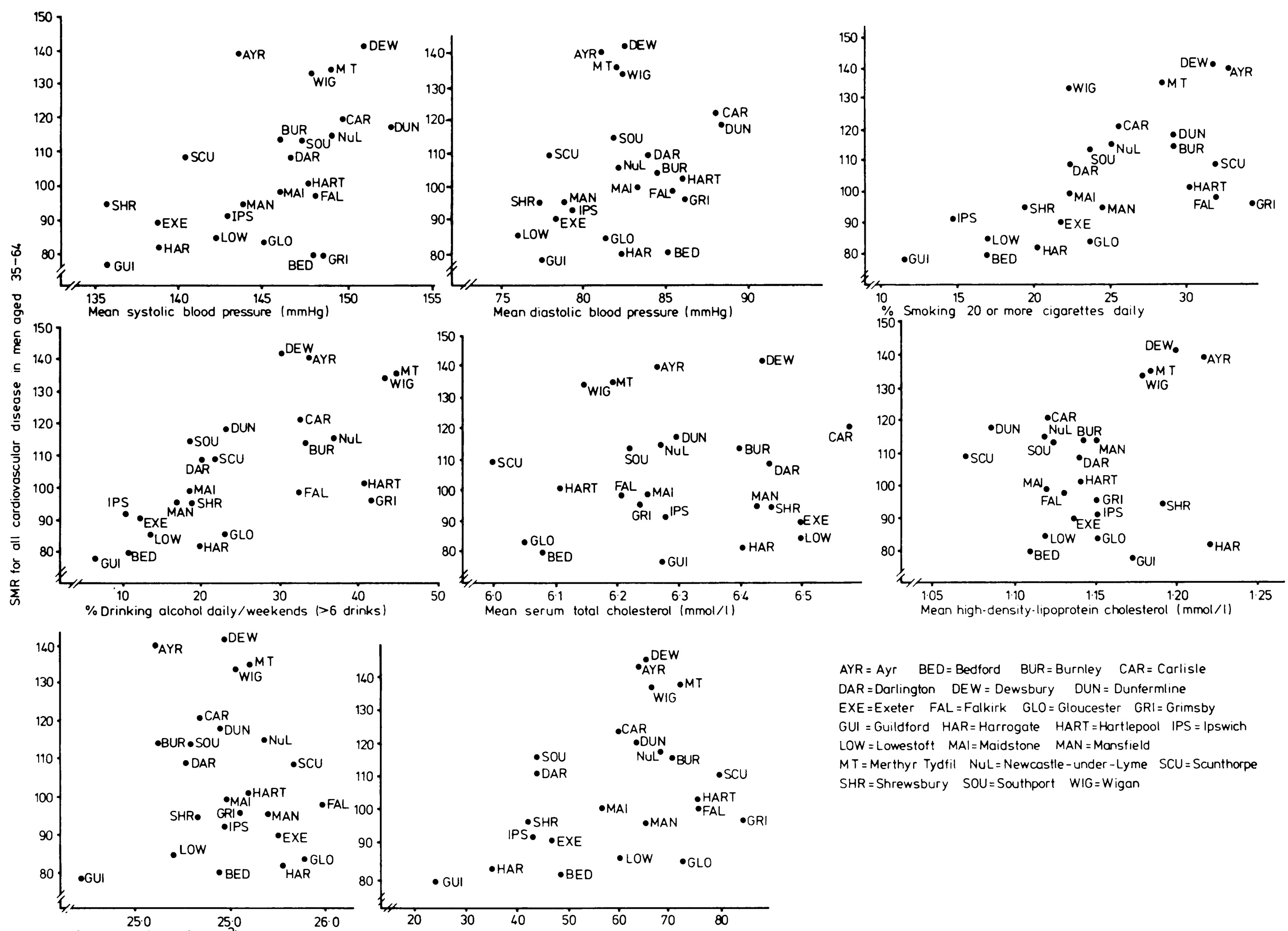

FIG 1—Standardised mortality ratios (SMRs) for all cardiovascular diseases in men aged 35-64 years in 24 British towns (1969-73) plotted against means of several variables measured in middle-aged men in same towns during regional heart study.

Conversion: SI to traditional units—Cholesterol and high-density-lipoprotein cholesterol: 1 mmol/l ± 38·6 mg/100 ml.

TABLE II—*Personal factors associated with blood-pressure in middle-aged men in regional heart study*

Factor	No of men	Mean blood pressure (mm Hg) Systolic	Diastolic
Age in years:			
40-44	1836	139·7	80·7
45-49	1896	143·1	82·4
50-54	1974	146·8	83·1
55-59	2021	150·9	82·7
Body mass index (wt/ht²) in kg/m²:			
<22·5	1256	137·4	75·4
22·5-24·4	1763	141·5	79·1
24·5-26·4	2044	145·7	82·4
26·5-28·4	1420	148·6	85·4
≥28·5	1241	153·9	90·0
Cigarette smoking:			
None	2501	143·8	82·6
Ex-smokers	2030	147·7	83·6
1-19/day	1185	144·6	81·3
20/day	835	145·1	81·1
21-40/day	1068	145·3	81·3
>40/day	92	141·1	78·2
Alcohol consumption:			
None	466	144·4	81·6
Monthly or special occasions only	1842	143·8	81·1
1-2 drinks/day At weekends	724	143·6	81·1
1-2 drinks/day Daily	584	142·5	81·0
3-6 drinks/day At weekends	1234	145·2	82·1
3-6 drinks/day Daily	947	144·6	82·1
>6 drinks/day At weekends	1094	147·2	83·9
>6 drinks/day Daily	830	150·5	83·3
Social class distribution:			
I	607	141·2	80·9
II	1733	142·9	81·2
III non-manual	719	146·2	83·2
III manual	3323	147·1	82·8
IV	783	145·5	82·9
V	316	146·9	82·8
Armed services	231	140·4	80·7
Marital state:			
Single	374	148·6	85·0
Married	6982	145·1	82·1
Widowed	98	145·3	81·5
Other	273	143·8	82·1

BODY MASS INDEX (WEIGHT/HEIGHT²)

There was a definite positive trend with body mass index for both systolic and diastolic blood pressures. To illustrate the clinical significance of the units for body mass index (kg/m²), consider a 6 ft (183 cm) man weighing 11½ stone (73 kg). He has a body mass index of 21·7 and falls into the lowest category (table II). Each stone (6·35 kg) increase in weight moves him successively into a higher category of body mass index, with estimated mean increases in systolic and diastolic blood pressures of about 4 mm Hg and 3·5 mm Hg per stone, respectively. At each body mass index there was considerable individual variation in blood pressure, but the correlation coefficient between blood pressure and body mass index, though highly significant, was only moderate in size (systolic pressure, $r=0·26$; diastolic pressure, $r=0·36$; $p<0·001$ in each case).

CIGARETTE SMOKING

Cigarette smoking had no apparent effect on blood pressure. There was a suggestion of a slight reduction in systolic pressure in those smoking over 40 a day, but this was a very small group. Ex-smokers (including ex-cigarette smokers who were currently pipe or cigar smokers) had a higher mean systolic blood pressure than non-smokers or current smokers.

ALCOHOL

The highest systolic and diastolic blood pressures were found in men having more than six drinks either daily or on each day at weekends, with higher pressures in those doing so daily than in those doing so only at the weekends. This level of drinking was reported by 25% of all men in the study. Compared with abstainers and occasional drinkers these increases in mean systolic and diastolic pressures for heavy drinkers were highly significant ($p<0·01$ in each case). The mean systolic blood pressure in men having one or two drinks daily was slightly lower than in abstainers and occasional drinkers, but this difference was not statistically significant.

SOCIAL CLASS

Men in social classes I and II had significantly lower mean systolic and diastolic blood pressures than manual workers (classes III manual, IV, and V). The association of social class with blood pressure appeared to be relatively weak compared with the effects of age or body mass index.

MARITAL STATE

The very small group of single men showed significantly higher mean systolic and diastolic blood pressures.

BODY MASS INDEX, ALCOHOL, AND BLOOD PRESSURE

The findings for body mass index presented in table II were also tabulated separately for each social class, age group, and cigarette smoking and alcohol consumption category, and in each case the same strong relation between body mass index and blood pressure was present.

The association of alcohol intake with blood pressure shown in table II was also examined separately for each social class, age group, body mass index group, and cigarette-smoking group. The higher blood pressures in heavy drinkers (over six drinks daily or on each day at weekends) appeared consistently for each age group, for each cigarette-smoking category, and for each social class.

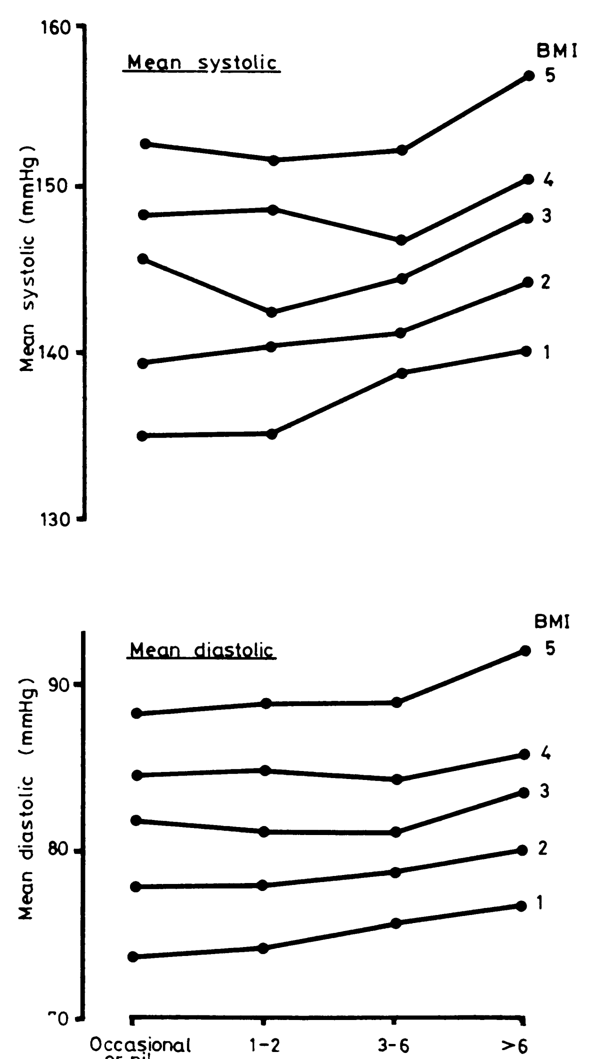

FIG 2—Systolic and diastolic blood pressure and alcohol intake in men aged 40-59 years at various body mass indices (BMI: 1, <22·5 kg/m²; 2, 22·5-24·4 kg/m²; 3, 24·5-26·4 kg/m²; 4, 26·5-28·4 kg/m²; 5, ≥28·5 kg/m²).

Body mass index and alcohol intake seemed largely to operate independently of one another as regards their effect on blood pressure (fig 2). The effects of body mass index were particularly clear cut for diastolic blood pressure, with a consistent mean difference of around 15 mm Hg between the heaviest and lightest groups at each alcohol intake. The heavy drinkers showed consistently higher mean systolic and diastolic pressures compared with abstainers and occasional drinkers for each category of body mass index. Moderate drinking—that is, three to six drinks daily or on each day at weekends—was not associated with any consistent increase in blood pressure, once body mass index was taken into account. In the lightest groups of men (body mass index <22.5), however, there was a statistically significant increase in both mean systolic and mean diastolic blood pressure in the moderate drinkers compared with abstainers and occasional drinkers or with light drinkers ($p<0.01$ in each case). There was no evidence that light drinkers (one or two drinks/day, daily or at weekends) had lower blood pressures than non-drinkers.

MULTIPLE REGRESSION ANALYSIS OF VARIABLES AFFECTING BLOOD PRESSURE

Multiple regression techniques were used to establish to what extent systolic and diastolic blood pressure *in individuals* was associated with age, observer, body mass index, alcohol intake, smoking behaviour, social class, marital state, and town when all of these factors were considered simultaneously.

Highly significant associations continued to be present between blood pressure (systolic and diastolic) and age, body mass index, observer, alcohol intake, marital state, and town. Body mass index emerged as the factor most significantly associated with individual blood pressure. Even within the limited age range of this study (40-59 years) a significant age trend persisted after multiple regression analysis, more pronounced for systolic than diastolic blood pressure. The effect of heavy drinking, particularly on a daily basis, continued to show a significant effect on blood pressure after adjustment for all other factors. The raised systolic blood pressure in ex-smokers was considerably reduced after allowing for other factors but remained significant ($p=0.02$), while the low systolic pressure in very heavy smokers was not significant after adjustment for other factors. The mean diastolic blood pressure was significantly lower in cigarette smokers than in current non-smokers (-1.4 mm Hg after adjustment), and this effect was most noticeable for those smoking more than 40 cigarettes a day (-4.6 mm Hg after adjustment).

The difference in systolic blood pressure between social classes I and II (combined) and manual workers (III manual, IV, and V) remained significant though somewhat reduced, since half of the difference in table II had been accounted for by other factors such as body mass index and alcohol. The social class difference in diastolic blood pressure was not significant. Single men, after all other factors had been considered, continued to have a significantly higher systolic blood pressure ($+3.2$ mm Hg) and diastolic blood pressure ($+2.5$ mm Hg) than married men.

When all these factors had been taken into account major differences in mean systolic blood pressure remained between the towns, with little alteration in their rank order or in the range of mean systolic pressure. The implication of this observation was that while these factors significantly affected individual systolic blood pressures they still did not explain the major differences *between* towns in mean systolic pressures. The effect of observer differences cannot contribute to solving this problem, as each observer dealt randomly with roughly similar numbers of men in each town.

BODY MASS INDEX, ALCOHOL, AND BLOOD PRESSURE (TOWN-BASED DATA)

The relation between body mass index, alcohol intake, and blood pressure may also be examined using town-based information. The variables measured on the men in each town may be correlated, using the mean values—for example, blood pressure and body mass index—or the percentage prevalence—for example, alcohol and smoking. As shown in fig 1, the mean body mass indices did not vary much between towns and did not correlate with the SMRs for cardiovascular disease. The percentage of heavy drinkers varied widely between towns and correlated positively with the SMR for cardiovascular disease (fig 1). On an intertown basis, there was no relation between mean body mass index and blood pressure but there was a positive association between heavy drinking and blood pressure (systolic, $r=0.53$, $p<0.01$; diastolic, $r=0.46$, $p<0.05$).

BLOOD PRESSURE AND WATER HARDNESS (TOWN BASED DATA)

There was no overall relation between water hardness and mean systolic or diastolic blood pressure (systolic, $r=0.10$; diastolic, $r=0.16$); however, the five towns with the highest mean diastolic pressures (Dunfermline, Carlisle, Falkirk, Burnley, Darlington) were all towns with soft water (<1.1 mmol/l; <110 mg/l).

Discussion

The regional variations in cardiovascular mortality in Britain have been recognised for many years and examined in various ways.[7-10] Recently, we related cardiovascular mortality for 1969-73 in 253 towns in England, Wales, and Scotland to environmental and socioeconomic variables and estimated the contribution made to the variation in mortality from cardiovascular disease by water hardness, rainfall, temperature, and socioeconomic factors.[1] Differences in the distribution of individual risk factors could also contribute to the striking regional variations in mortality, and almost certainly many of these are included under the heading of "socioeconomic" factors. We know little, however, about geographic variations in the distribution of the established risk factors such as smoking, hypertension, and hyperlipidaemia. Information is available on diet, tobacco, and alcohol intake for the standard regions covering England, Wales, and Scotland[11 12] and therefore attempts to explain the geographic variations in mortality from cardiovascular disease in terms of diet or smoking have been based on these large standard regions.[13-15] Data of this kind are not available for individual towns. Each standard region is a complex mixture of smaller areas which differ considerably in mortality from various disorders and will certainly differ considerably in smoking, drinking, and dietary patterns. Although these region-based studies may provide leads to more detailed investigation, conclusions based on them must of necessity be tentative.

No single study of cardiovascular disease or its risk factors can provide comprehensive information applicable to the whole British population. We chose to study middle-aged men recruited through representative towns. For organisational reasons it was necessary to concentrate on urban areas but we wished to avoid large towns and conurbations because of their greater complexity and heterogeneity in respect of many variables. The size of our towns made it practicable to select one general practice per town, and recruitment through general practice provided an unselected sample of the general male population and allowed prospective morbidity studies in these men. The use of general practices, no matter how carefully chosen, carries the risk that the men in any one such practice may not be truly representative of the town. We checked this issue subsequently by comparing the social class distribution of the men examined in each town and the social class composition of men in that town at the 1971 Census. The 1971 Census data relate to all heads of households (all ages), while the regional heart study concerns men aged 40-59 years. The correlation coefficient of 0·76 for these two sets of data in respect of the percentage of manual workers is therefore reassuring. The scale of our investigations over 25 towns ensured that any possible inappropriate choice of practice in one town could not seriously bias our findings.

We have shown that several environmental factors—water hardness, rainfall, temperature, and certain social factors—substantially explain the geographic variations in cardiovascular mortality in Britain. Broad terms like "social factors" obviously cover a wide range of behavioural variables and phenomena associated with living standards and conditions. Even climatic factors may have an effect on "life style" in terms of physical activity in leisure time, smoking and drinking habits, and dietary preferences. The clinical study (phase 2) described in this paper set out to explore the ways in which social factors might be reflected in behaviour—for example, smoking and drinking—and in physiological measurements—for example, body mass index, blood pressure, and blood lipids.

CARDIOVASCULAR MORTALITY

We have related the information obtained on the sample of men examined in each town (blood pressure, smoking, and so on) to the most recently available measure of cardiovascular mortality for that town (1969-73). The associations seen in these 24 towns suggest that blood pressure, cigarette smoking, and alcohol intake contribute to geographic variations in cardiovascular mortality while serum total cholesterol and high-density-lipoprotein cholesterol and body mass index do not appear to do so. This town-based approach is part of the search for variables which may differ sufficiently in their distribution between towns to account to some degree for the differences observed in SMRs between towns. Caution is required in interpreting these town-based comparisons, for the absence of an association does not imply that the variable being examined is not important in cardiovascular disease, but merely that it does not obviously contribute to intertown variation in cardiovascular mortality. The presence of an association may merely reflect interrelationships between the variables and may not have direct (causal) significance. This approach must therefore be regarded as useful but preliminary.

BLOOD PRESSURE

The mean blood pressures in these middle-aged men varied widely between the 24 towns and we therefore examined the variables associated with blood pressure in all the men regarded as one group. We hesitate to call these variables "determinants" of blood pressure except in a statistical sense and the word "effect" is also used in terms of statistical association rather than with causal inference.

The strong associations between blood pressure and age, body mass index, and alcohol intake seen on univariate analysis (table II) were confirmed on cross-tabulation and on analysis by multiple regression techniques. Body mass index appeared to affect individual blood pressure to a greater extent than alcohol and did so with a consistent and linear positive trend over the whole range of body mass indices. Alcohol and body mass index operated independently of one another as regards their effect on blood pressure. Heavy drinking, as defined in this study, had a pronounced and consistent effect on blood pressure, though even moderate drinking appeared to be associated with increased blood pressure in the lowest body mass index group. In the heavier men, the effects of moderate drinking may have been confounded by the body mass index reached and its strong independent effect on blood pressure. In an atmosphere which regards light drinking as beneficial to health in general and to the cardiovascular system in particular[16 17] we emphasise that our data do not disclose any beneficial effect on blood pressure of light drinking. The effects of cigarette smoking on blood pressure did not appear to be important, and the lower diastolic blood pressure in very heavy smokers was not explained by the variables included in the analysis. Social class continued to have a small unexplained independent effect on systolic blood pressure; this could have been due to the failure of our questionnaire to elicit "very heavy" drinking.

Multiple regression analysis indicated that only 21% of the between-town variance in systolic blood pressure was explained statistically by the effects of body mass index and heavy drinking. We presume that most of this explained variation was due to heavy drinking, as examination of the relationship between the town-based mean levels of blood pressure, body mass index, and heavy drinking showed a significant association between heavy drinking and mean blood pressure but not between mean body mass index and mean blood pressure. Because of the high prevalence of heavy drinking in Britain, this may be an important contributor to community levels of hypertension. Heavy drinking may also have effects on the heart and circulation which could affect cardiovascular mortality through mechanisms other than blood pressure. Indeed, heavy drinking could be an important and rather neglected factor in cardiovascular disease. We anticipate that the prospective part of the regional heart study (phase 3) will contribute to determining the validity of this suggestion.

BODY MASS INDEX, ALCOHOL, AND BLOOD PRESSURE

The relevance of body mass as a determinant of individual blood pressure has been established,[18] and the positive association of alcohol intake with blood pressure has been reported in the United States.[19 20] In those studies, as in ours, the effect of alcohol on blood pressure was largely confined to heavy drinkers, but since a substantial proportion of men in the British study are thus categorised, its impact on hypertension in Britain may be considerable. Geographic variations in smoking and drinking have been shown in the standard British regions, and because smoking is an established risk factor for cardiovascular disease the geographic association between smoking and cardiovascular mortality is accepted as causal.[15] The close but complex relation between smoking and drinking habits in the individual, however, clearly indicates that the impact of one factor on health cannot be studied without taking the other into account. Studies which apparently show that alcohol may be associated with reduced rates of ischaemic heart disease cannot be regarded as sound if they do not take smoking habits into account. Conversely, if alcohol does have effects on blood pressure in particular and on cardiovascular disease in general, then failure to allow for alcohol intake may exaggerate the effects apparently associated with smoking.

SOCIAL CLASS AND RISK FACTORS

There is considerable interest in the relation between social class and cardiovascular mortality, and recent data show that working-class men and women have a higher mortality from ischaemic heart disease (ICD codes B27-29) than the non-manual classes.[21] Working-class men had slightly lower mortality rates from ischaemic heart disease than non-manual workers (social classes I and II) in 1931 and 1951. By 1961 the mortality rates in the non-manual male workers had levelled off while they continued to rise in manual workers. By 1971 the rates in manual workers exceeded those in non-manual workers.[22] A prospective study of London male civil servants showed that men in the lowest grades of employment had more than three times the mortality from ischaemic heart disease (B27-29) of men in the highest grades.[23] The men in the lowest grades smoked more, exercised less, were shorter and more overweight, and had higher blood pressures and lower glucose tolerance levels than men in the highest grades. These differences, however, were thought to explain only a part of the higher mortality from ischaemic heart disease. In the British Regional Heart Study there was an association on a town basis between social class and cardiovascular mortality, but it was not strong and appeared to be related to a considerable extent to town differences in smoking, drinking, blood pressure, and the hardness of drinking water.

Conclusion

This report presents the aims and objectives of the British Regional Heart Study, details the methods used in the clinical survey, and provides some of the initial findings in the 24 towns; many variables remain to be analysed. It will be some time before adequate material is available for relating the incidence of cardiovascular events to established or suspected risk factors (phase 3). We hope that this study will help to explain the striking geographic variations in cardiovascular mortality in Britain and thereby provide means of postponing or preventing the onset of cardiovascular disease.

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Requests for reprints should be addressed to Professor A G Shaper.

References

1 Pocock SJ, Shaper AG, Cook DG, *et al.* British Regional Heart Study: geographic variations in cardiovascular mortality, and the role of water quality. *Br Med J* 1980;**280**:1243-9.

2 Webber R, Craig J. Socioeconomic classification of local authority areas. *OPCS studies on medical and population subjects.* No 35. London: HMSO, 1978.

3 MacFarlane PW, Lawrie TDV. *An introduction to automated electrocardiogram interpretation.* London: Butterworths, 1974.

4 Bortner RW. A short rating scale as a potential measure of pattern of behaviour. *J Chronic Dis* 1969;**22**:87-91.

5 Clayton DG, Taylor D, Shaper AG. Trends in heart disease in England and Wales 1950-1973. *Health Trends* 1977:**9**:1-6.

6 Office of Population Censuses and Surveys. *General household survey* 1972-3. London: HMSO, 1974-5.

7 Morris JN, Crawford MD, Heady JA. Hardness of local water supplies and mortality from cardiovascular disease. *Lancet* 1961;i:860-2.

8 Crawford MD, Gardner MJ, Morris JN. Mortality and hardness of local water supplies. *Lancet* 1968;i:827-31.

9 Howe GM. *National atlas of disease mortality in the United Kingdom.* 2nd ed. London: Nelson, 1979.

10 Fulton M, Adams W, Lutz W, Oliver MF. Regional variations in mortality from ischaemic heart and cerebrovascular disease in Britain. *Br Heart J* 1978;**40**:563-8.

11 Ministry of Agriculture, Fisheries and Fooa. Household food consumption and expenditure 1969-1973. *Annual reports of the National Food Survey Committee.* London: HMSO, 1971-5.

12 Department of Employment. *Family expenditure survey 1969-73.* London: HMSO, 1970-4.

13 Knox EG. Ischaemic-heart-disease mortality and dietary intake of calcium. *Lancet* 1974;i:1465-7.

14 Armstrong BK, Mann JI, Adelstein AM, Eskin F. Commodity consumption and ischaemic heart disease mortality with special reference to dietary practice. *J Chronic Dis* 1975;**28**:455-69.

15 Chilvers C, Adelstein AM. Interpreting patterns of mortality from circulatory disease in the regions of England and Wales: results from the decennial supplement on area mortality, 1969-73. *Health Trends* 1981; **13**:28-31.

16 Anonymous. Need pleasure be harmful? *Lancet* 1980;i:350.

17 Turner TB, Bennett VL, Hervandez H. The beneficial role of moderate alcohol use. *Johns Hopkins Med J* 1981;**148**:53-63.

18 Taylor HL. Body composition and elevated blood pressure: a comment. In: Stamler J, Stamler R, Pullman TN, eds. *The epidemiology of hypertension.* New York: Grune and Stratton, 1967:101-9.

19 Klatsky AL, Friedman GD, Siegelaub AB, Gerart MJ. Alcohol consumption and blood pressure. Kaiser-Permanente Multiphase Health Examination Data. *N Engl J Med* 1977;**296**:1194-9.

20 Harburg E, Ozgoren F, Hawthorne VM, Schork MA. Community norms of alcohol usage and blood pressure: Tecumseh, Michigan. *Am J Public Health* 1980;**70**:813-20.

21 Office of Population Censuses and Surveys. *Occupational mortality, the Registrar General's decennial supplement for England and Wales 1970-72.* London: HMSO, 1978. (Series DS No 1.)

22 Marmot MG, Adelstein AM, Robinson N, Rose GA. Changing social class distribution of heart disease. *Br Med J* 1978;ii:1109-12.

23 Rose G, Marmot MG. Social class and coronary heart disease. *Br Heart J* 1981;**45**:13-9.

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OF THE PARAPHRENITIS.

THE *paraphrenitis*, or inflammation of the diaphragm, is ſo nearly connected with the pleuriſy, and reſembles it ſo much in the manner of treatment, that it is ſcarce neceſſary to conſider it as a ſeparate diſeaſe.

IT is attended with a very acute fever, and an extreme pain of the part affected, which is generally augmented by coughing, ſneezing, drawing in the breath, taking food, going to ſtool, making water, &c. Hence the patient breathes quick, and draws in his bowels to prevent the motion of the diaphragm; is reſtleſs, anxious, has a dry cough, a hiccup, and often a delirium. A convulſive laugh, or rather a kind of involuntary grin, is no uncommon ſymptom of this diſeaſe.

EVERY method muſt be taken to prevent a ſuppuration, as it is impoſſible to ſave the patient's life when this happens. The regimen and medicine are in all reſpects the ſame as in the pleuriſy. We ſhall only add, that in this diſeaſe emollient clyſters are peculiarly uſeful, as they relax the bowels, and by that means make a derivation from the part affected.

OF THE PLEURISY.

THE true pleuriſy is an inflammation of that membrane called the *pleura*, which lines the inſide of the breaſt. It is diſtinguiſhed into the moiſt and dry. In the former, the patient ſpits freely; in the latter, little or none at all. There is likewiſe a ſpecies of this diſeaſe, which is called the *ſpurious* or *baſtard pleuriſy*, in which the pain is more external, and chiefly affects the muſcles between the ribs. The pleuriſy prevails among labouring people, eſpecially ſuch as work without doors, and are of a ſanguine conſtitution. It is moſt frequent in the ſpring ſeaſon.

CAUSES.—The pleuriſy may be occaſioned by whatever obſtructs the perſpiration; as cold northerly winds; drinking cold liquors when the body is hot; ſleeping without doors, on the damp ground; wet clothes; plunging the body into cold water, or expoſing it to the cold air, when covered with ſweat, &c. It may likewiſe be occaſioned by drinking ſtrong liquors; by the ſtoppage of uſual evacuations; as old ulcers, iſſues, ſweating of the feet or hands, &c. the ſudden ſtriking in of any eruption, as the itch, the meaſles, or the ſmall-pox. Thoſe who have been accuſtomed to bleed at a certain ſeaſon of the year, are apt, if they neglect it, to be ſeized with a pleuriſy. Keeping the body too warm by means of fire, clothes, &c. renders it more liable to this diſeaſe. A pleuriſy may likewiſe be occaſioned by violent exerciſe, as running, wreſtling, leaping, or by ſupporting great weight, blows on the breaſt, &c. A bad conformation of the body ſometimes renders perſons more liable to this diſeaſe, as a narrow cheſt, a ſtraitneſs of the arteries of the pleura, &c.

SYMPTOMS.—This, like moſt other fevers, generally begins with chillneſs and ſhivering, which are followed by heat, thirſt, and reſtleſſneſs. To theſe ſucceeds a violent pricking pain in one of the ſides among the ribs. Sometimes the pain extends towards the backbone, ſometimes towards the forepart of the breaſt, and at other times towards the ſhoulder-blades. The pain is generally moſt violent when the patient draws in his breath.

THE pulſe in this diſeaſe is commonly quick and hard, the urine high-coloured; and if blood be let, it is covered with a tough cruſt, or buffy coat. The patient's ſpittle is at firſt thin, but afterwards it becomes groſſer, and is often ſtreaked with blood.

REGIMEN.—Nature generally endeavours to carry off this diſeaſe by a critical diſcharge of blood from ſome part of the body, by expectoration, ſweat, looſe ſtools, thick urine, or the like. We ought therefore to ſecond her intentions by leſſening the force of the circulation, relaxing the veſſels, diluting the humours, and promoting expectoration.

(Buchan's *Domestic Medicine*, 1786.)