PAPERS AND ORIGINALS

Prevalence of gall stones at necropsy in nine British towns: a collaborative study*

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Summary and conclusions

A prospective study of the prevalence of gall stones at necropsy in nine towns in England and Wales showed considerable geographical variations. The age- and sex-standardised prevalence ranged from 20.6% in Ipswich to 9.2% in Wakefield. The distribution of gall stones differed from that of all-cause mortality and was negatively correlated with that of mortality from ischaemic heart disease.

Socioeconomic influences related to affluence do not appear to be major determinants of the distribution of gall stones.

Introduction

Mortality is higher in the north and west of Great Britain than in the south and east. The variation is large—twofold among county boroughs, for example¹—and the reasons for it unknown. Socioeconomic influences account for only part of the variation, and latitude is one of several factors that have an independent relation with mortality. To what extent the higher mortality in the north and west is associated with higher morbidity from common diseases is not known. We describe here the results of a

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prospective study of the prevalence of gall stones at necropsy in nine county boroughs in England and Wales. We analysed variations in the prevalence of gall stones between the nine towns in relation to socioeconomic conditions and latitude.

Methods

Selection of towns—We used a range of intercorrelated socioeconomic indices—for example, population density, income, and car ownership—to produce a single social-factor score for each of the 83 county boroughs in England and Wales.¹ On the basis of the score we divided the towns into three equal groups having better, intermediate, and worse social and economic conditions. Figure 1 shows the distribution

FIG 1—Distribution of 83 county boroughs in England and Wales according to social and economic conditions (see text).

of the towns, the horizontal lines dividing them into three equal groups according to latitude. As would be expected there was an aggregation of towns with better social and economic conditions in the south, and of towns with worse conditions in the north. Table I shows the mean standardised mortality ratio for towns in each socioeconomic group and latitude during 1969-73.² Mortality increased with both increasing latitude and worsening socioeconomic conditions.

TABLE I—Mean standardised mortality ratios in nine groups of county boroughs during 1969-73.

Latitude	Social and economic conditions		
	Better	Intermediate	Worse
North	105	114	113
Central	99	108	117
South	95	106	108

Data on gall stones—For the study of gall-stone prevalence we chose one town from each of the nine groups (table II)—in the north York, Wakefield, and Preston; in the central latitude band Chester, Derby, and Stoke; and in the south Ipswich, Plymouth, and Newport. The pathologists in each town all agreed to collaborate in the prospective study. From 1 January 1977 they recorded the presence or absence of gall stones at each necropsy carried out on a person aged 18 or over who was resident within the town at the time of death. Our findings are based on a total of 5571 necropsies carried out from January 1977 to May 1978. These included necropsies carried out for the coroner as well as routine hospital necropsies. In 115 cases the gall bladder had been removed surgically: these were excluded from the analysis, which therefore related to 5456 necropsies.

TABLE II—Nine towns selected for study of prevalence of gall stones at necropsy according to latitude and socioeconomic conditions

Latitude	Social and economic conditions		
	Better	Intermediate	Worse
North	York	Wakefield	Preston
Central	Chester	Derby	Stoke
South	Ipswich	Plymouth	Newport

Results

Figure 2 shows the percentage prevalence of gall stones by age and sex when the results were combined for all the towns. The prevalence among women increased from 6% among those aged under 45 to 25% among those aged 75 and over. Among men the prevalence at each age was lower and rose from 4 to 17%.

Table III shows the prevalence of gall stones in each town expressed as age- and sex-standardised rates. The towns are listed in descending

FIG 2—Percentage prevalence of gall stones at necropsy by age and sex.

order of the rates. The highest prevalence (20.6) was in Ipswich, the southern town with the best social and economic conditions; the lowest (9.2) was in Wakefield. The number of necropsies performed in each town varied considerably, this variation being mainly determined by the size of the population. Fewest necropsies were carried out in Chester and Wakefield, and the prevalences derived from them are correspondingly less reliable.

TABLE III—Prevalence of gall stones at necropsy in nine towns

Town	Necropsies		Age-sex standardised rate (%)
	No carried out	No at which gall stones found	
Ipswich	594	131	20.6
Preston	463	90	19.2
Plymouth	973	181	18.8
Chester	242	38	16.1
York	582	90	15.1
Stoke	1001	151	15.0
Derby	992	141	14.1
Newport	335	44	13.9
Wakefield	274	26	9.2
All towns	5456	892	16.3

Table IV shows the prevalence of gall stones among women. The highest rates were in the three southern towns Ipswich, Plymouth, and Newport and in Preston. The rate of 29.0% in Ipswich was around double the rates in Wakefield and York, where the prevalence was lowest. The combined figures for each latitude fell from 25.4 in the south to 17.9 (central) and 18.3 (north). Combined figures for the three social and economic groupings showed little variation. Among men (table V) Wakefield, Newport, and Derby, towns with intermediate and worse social and economic conditions, had the lowest rates (6.1, 7.1, and 10.2 respectively), compared with rates of around 14 and 15 in the other towns. There was no evidence of any variation with latitude.

TABLE IV—Prevalence of gall stones at necropsy among women expressed as age-standardised rates (%)

Latitude	Social and economic conditions			All towns
	Better	Intermediate	Worse	
North	16.0 (York)	13.4 (Wakefield)	25.4 (Preston)	18.3
Central	17.0 (Chester)	19.4 (Derby)	17.1 (Stoke)	17.9
South	29.0 (Ipswich)	24.3 (Plymouth)	23.0 (Newport)	25.4
All towns	20.7	19.0	21.8	

TABLE V—Prevalence of gall stones at necropsy among men expressed as age-standardised rates (%)

Latitude	Social and economic conditions			All towns
	Better	Intermediate	Worse	
North	14.4 (York)	6.1 (Wakefield)	14.5 (Preston)	11.7
Central	15.3 (Chester)	10.2 (Derby)	13.5 (Stoke)	13.0
South	14.4 (Ipswich)	14.7 (Plymouth)	7.1 (Newport)	12.1
All towns	14.7	10.3	11.7	

The pathologists were asked to record the number of stones (solitary, from two to 10, or more than 10). The findings are shown in table VI, in which the towns are listed in the same descending order of age- and sex-standardised prevalence as in table III. In a small proportion of records the pathologists had noted the occurrence of multiple stones without saying whether there were more or less than 10. The results show that the variation in prevalence between the towns derived from multiple stones, there being little variation in the prevalence of solitary stones. Almost all the gall stones were pure or

compound cholesterol or multifaceted. Only 2.3% were pigment stones.

The numbers of necropsies performed in each town during 1977 were expressed as a percentage of all deaths in the town during the year. The results were as follows, with the towns again listed in descending order of age- and sex-standardised prevalence: Ipswich 36%, Preston 28%, Plymouth 27%, York 33%, Chester 25%, Stoke 31%, Derby 40%, Newport 19%, and Wakefield 24%. These results give no evidence of an association between prevalence and the percentage of cases in which necropsy was performed.

TABLE VI—Prevalence (%) of gall stones at necropsy by number of stones

Town	Solitary stone	Multiple stones			
		2-10	11 or more	No not recorded	All multiple
Ipswich	4.0	9.9	6.7	1.3	18.0
Preston	5.2	5.6	7.6	1.1	14.3
Plymouth	4.9	7.6	4.9	1.1	13.7
Chester	3.7	6.2	5.4	0.4	12.0
York	3.8	5.5	6.2	0	11.7
Stoke	3.8	5.7	2.8	2.8	11.3
Derby	4.3	6.4	3.3	0.2	9.9
Newport	4.8	5.4	3.0	0	8.4
Wakefield	3.6	3.6	1.8	0.4	5.8
All towns	4.3	6.5	4.5	1.0	12.1

Table VII shows the prevalence of gall stones (all necropsies from all towns combined) according to the three major causes of death (comprising 79% of all deaths). Prevalences were similar for the different causes of death, and there is therefore no indication that the geographical variations in gall-stone prevalence depend on variations in mortality from a disease with which gall stones are associated.

TABLE VII—Prevalence of gall stones at necropsy by major causes of death

Cause of death	No of deaths	Age-sex standardised rate (%)
Cardiovascular	2884	16.8
Respiratory	942	15.4
Gastrointestinal	507	17.1

Discussion

This prospective survey shows considerable variation in the prevalence of gall stones at necropsy in nine towns within England and Wales. Prevalence at necropsy was used as an indicator of prevalence in the population because a large proportion of people with gall stones suffer no symptoms from them, and indices related to medical care are therefore poor measures of prevalence. Because deaths that lead to necropsy are a selected group of all deaths the necropsy prevalence of gall stones must be a biased index of prevalence in the population. We do not think, however, that this invalidates its use for comparative studies between towns.

The increasing prevalence of gall stones with age and the higher prevalence among women (fig 2) are well known. Hormonal influences, both endogenous and exogenous (for example, oral contraceptives and postmenopausal oestrogen treatment), may be important influences in the occurrence of gall stones among women.³

The variations in gall-stone prevalence indicated by our findings do not follow those in all-cause mortality (tables I, II, III). Ipswich, for example, which has the lowest standardised mortality ratio of the nine towns, and indeed has one of the lowest such ratios of any county borough in England and Wales, had the highest prevalence of gall stones. Although available data suggest that several other diseases—for example, renal stones⁴ and breast cancer⁵—have patterns of incidence quite different from that of all-cause mortality, the difficulties of obtaining morbidity data make us ignorant of whether these form a minority

or majority of diseases. The importance of this issue when discussing health-resource allocation, currently determined by regional mortality, is obvious. The aetiological implications are of great interest.

Table VIII compares the prevalence of gall stones at necropsy with standardised mortality ratios for ischaemic heart disease, a leading cause of death among both men and women. The distributions of the two disorders are negatively correlated (correlation coefficient -0.68 ; $P < 0.05$), yet both have been classified as "diseases of civilisation" and similar causes—for example, low dietary-fibre intake⁶—have been postulated for both.

TABLE VIII—Prevalence of gall stones, expressed as age-sex standardised rates (%), and mortality from ischaemic heart disease (standardised mortality ratios 1969-73)

Town	Gall-stone prevalence	Mortality from ischaemic heart disease
Ipswich	20.6	88
Preston	19.2	114
Plymouth	18.8	107
Chester	16.1	88
York	15.1	103
Stoke	15.0	110
Derby	14.1	114
Newport	13.9	112
Wakefield	9.2	130

Cholesterol gall stones are almost confined to the affluent countries of the world,⁷ yet our findings suggest that socio-economic influences are not a major determinant of gall-stone distribution within England and Wales. Among women (table IV) two of the three towns with worse socioeconomic conditions, Newport and Preston, had high prevalences, and there was no overall trend with socioeconomic conditions. Among men (table V) there was some evidence of an association with socioeconomic influences, since Newport, Wakefield, and Derby—towns with intermediate or worse socioeconomic conditions—had the lowest rates.

An association exists between gall stones and obesity.³ Retailers of clothes in Britain recognise that the distribution of adult body sizes varies from one part of the country to another. For example, one leading retailer distributes women's blouses (for which it controls over a quarter of the total British market) to its stores in two standard packs. Pack A has a small-size and pack B a large-size emphasis. This retailer has branches in each of the towns included in this survey. The store in Plymouth, a town with high gall-stone prevalence among women (24.3%), requires only B packs, while Ipswich, another town with high prevalence (29.0%), requires two B packs to one A. The remaining towns receive two A packs to one B, except Newport, which receives only A packs. The pattern of distribution of brassières (for which the retailer controls more than a third of the market) is similar.

The data from Plymouth and Ipswich suggest an association between geographical variations in gall-stone prevalence among women and obesity. The findings in Newport (prevalence 23.0%), however, indicate that this association does not dominate gall-stone distribution. No comparable data exist for men, since this retailer does not have so large a share of the national market for any single item of men's clothing. We think that distribution of clothes' sizes is a potentially useful method for exploring geographical variations in body size in relation to other diseases—for example, late-onset diabetes—but the method requires validation by data from other sources.

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References

- ¹ Gardner, M J, *Journal of the Royal Statistical Society*, series A, 1973, **136**, 421.
- ² Registrar General, *Area Mortality 1969-73: Decennial Supplement, DS3*. London, HMSO. In press.
- ³ Bennion, L J, and Grundy, S M, *New England Journal of Medicine*, 1978, **299**, 1221.
- ⁴ Barker, D J P, and Donnan, S P B, *British Medical Journal*, 1978, **1**, 67.
- ⁵ Office of Population Censuses and Surveys, *Registrar General's Statistical Review of England and Wales 1968-1970: Supplement on Cancer*. London, HMSO, 1975.
- ⁶ Burkitt, D P, *British Medical Journal*, 1973, **1**, 274.
- ⁷ Brett, M, and Barker, D J P, *International Journal of Epidemiology*, 1976, **5**, 335.

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Immunoreactive calcitonin in leukaemia

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Summary and conclusions

A radioimmunoassay was used to measure concentrations of immunoreactive human calcitonin (HCT) in plasma and leucocytes from patients with various leukaemic and myeloproliferative disorders. Plasma immunoreactive HCT concentrations were increased in 32 out of 33 patients with chronic granulocytic leukaemia (CGL) and in all eight patients with acute myeloid leukaemia (AML) at presentation or in relapse. Out of 11 patients with other myeloproliferative disorders, eight had increased plasma immunoreactive HCT concentrations. Buffy-coat-cell extracts and culture media from peripheral leucocytes of patients with CGL also contained increased immunoreactive HCT concentrations. In contrast, plasma from patients with chronic lymphocytic leukaemia, acute lymphoblastic leukaemia, and AML in remission had low or undetectable immunoreactive HCT concentrations.

Increased plasma and cellular concentrations of immunoreactive HCT may be a consequence of abnormal proliferation of myeloid cells and might prove to be valuable in predicting relapse in patients with myeloid leukaemias.

Introduction

Increased hormone concentrations may be associated with various non-endocrine tumours,¹ and immunoreactive human calcitonin (HCT) has been found in several different non-thyroid tumours.² In some cases immunoreactive HCT may be shown to be of ectopic origin by in-vitro techniques.^{3,4}

We have measured calcitonin concentrations in the plasma and cells of patients with different types of leukaemia and myeloproliferative disorders. The finding of increased concentrations in several of these conditions may help in assessing such patients, and changes in immunoreactive HCT concentrations during the course of the disease could lead to changes in therapeutic strategy.

Subjects and methods

The subjects studied were divided into seven groups: (1) 33 patients with chronic granulocytic leukaemia (CGL), 27 in chronic phase and six in blast-cell transformation before undergoing intensive treatment; (2) six patients with acute myeloid leukaemia (AML) at presentation and two in relapse before reinduction treatment; (3) five patients with AML in remission; (4) 10 patients with chronic lymphocytic leukaemia (CLL); (5) two patients with acute lymphoblastic leukaemia (ALL); (6) 11 patients with chronic myeloproliferative disorders (eight with myeloid leukaemia, one with polycythaemia rubra vera, and two with essential thrombocythaemia); and (7) 113 normal volunteers.

Plasma calcitonin assay—Peripheral blood samples from all the patients and normal controls were collected into cold heparinised tubes, centrifuged, and separated immediately. Plasma samples were frozen and stored at -20°C until assayed. Calcitonin concentrations were measured by an overnight radioimmunoassay similar to that described.⁵ The antiserum used is directed against the central and C-terminal parts of the calcitonin molecule. Normal calcitonin concentrations ($<0.08\text{ }\mu\text{g/l}$) are undetectable with this assay.

Cell extraction procedure—In ten cases CGL cryopreserved buffy-coat cells were used as these were readily available in adequate quantities.⁶ Fresh cells were obtained from two patients with CGL and two controls. The frozen cells were thawed in a water bath at 37°C and washed in TC-199 and saline to remove residual plasma. Fresh cells were washed in saline. The cells were weighed and extracted as described.⁶ After centrifuging at $10\,000\text{ g}$ the supernatants were decanted and applied to ODS-porasil columns twice.⁷ The columns were then eluted with 80% methanol and 1% trifluoroacetic acid, the eluate being vacuum-dried and reconstituted in phosphate buffer before calcitonin assay.

Leucocyte cultures—Heparinised peripheral blood samples from patients with CGL and controls were collected and allowed to stand at room temperature for one to two hours. The leucocyte-rich plasma was collected and the leucocytes washed three times and resuspended in McCoy's 5A modified medium supplemented with 20% horse serum. A total of 12×10^6 leucocytes in 6 ml McCoy's 5A modified medium was placed in a 90 mm sterile plastic Petri dish and incubated in a 5% CO_2 incubator in air. After seven days' incubation the culture medium was collected, centrifuged to remove all cells, and the supernatant tested for calcitonin.

Results

With one exception all patients with CGL whether in chronic phase or in blast-cell transformation had increased plasma immunoreactive HCT concentrations (mean $0.78 \pm \text{SE of mean } 0.35\text{ }\mu\text{g/l}$) (figure). Patients in blast-cell transformation tended to have higher concentrations (mean $3.14 \pm 2.21\text{ }\mu\text{g/l}$) than those in chronic phase ($0.36 \pm 0.04\text{ }\mu\text{g/l}$). There was no correlation between immunoreactive HCT concentrations and the patients' leucocyte counts, though all counts were high (range 86×10^9 – $572 \times 10^9/\text{l}$).

The patients with AML studied at diagnosis and in relapse had increased plasma immunoreactive HCT concentrations (mean $0.97 \pm 0.45\text{ }\mu\text{g/l}$). In contrast, four of the five patients with AML

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