Variations in the incidence and the spatial distribution of patients with primary acute pancreatitis in Nottingham 1969-76

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SUMMARY During the eight year period 1969-76, 214 patients with primary acute pancreatitis were admitted to Nottingham hospitals from the Nottingham defined population area (the City of Nottingham and the four adjacent urban districts, which had a population of 469 720 in 1971). There was considerable variation in both the incidence and distribution of the disease within the study area and the crude average incidence rates ranged between 31.8 and 388.7 per million. Six of the eight wards with rates in excess of 200 per million were contiguous with similar wards; together these formed a U-shaped area extending from the city centre to the eastern boundary of the study area. These findings could not be accounted for by the age structure of the population or its social class structure. Although the Nottingham defined population area is relatively small (147 km² or 57 sq. miles), it is subdivided into distinct and fixed domestic water supply areas. The distribution of patients among the six water supply areas showed that the Burton Joyce supply area, which is a particularly 'hard' water, contained significantly more patients than could have occurred by chance ($P < 0.002$). This investigation of some social and geographical factors suggests that the chemical composition of the domestic water supply may affect the distribution of this disease within this particular urban area. This concentration of patients in the Burton Joyce water supply area suggests that some, as yet unidentified, property of the water supply may be an aetiological factor.

Careful local inquiry should produce details of all patients admitted to hospital in their first attack of acute pancreatitis. A previous study has shown that there was a four-fold variation in the incidence of primary acute pancreatitis within the Nottingham defined population area (Miller *et al.*, 1974), during the six year period, 1969 to 1974 (Bourke, 1975). The peak incidence of 83.0 per million population occurred in 1974, while the lowest incidence was 21.2 per million in 1970. This study has now been extended to cover the eight year period to 1976 and spatial variation analysis has been undertaken to see if population and/or environmental factors could be identified among the patients in their first attack of acute pancreatitis.

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Method

PATIENTS AND DIAGNOSTIC CRITERIA

All case reports of all patients in whom pancreatitis was diagnosed were sought by searching the Nottingham hospitals inpatient diagnostic indexes for the period 1969-76. This was supplemented by a personal diagnostic index and post-mortem reports.

These case reports were reviewed, and the diagnosis of acute pancreatitis was accepted only with a compatible clinical history, physical examination, and a greater than four-fold increase in serum amylase level. Laparotomy and/or necropsy evidence was also accepted.

Only patients in their first attack of acute pancreatitis were included, while those with recurrent, chronic, traumatic, or postoperative pancreatitis were excluded. The presence of associated factors such as gallstones was recorded.

CALCULATION OF INCIDENCE

The former City of Nottingham and the four former Urban Districts of Arnold, Beeston and Stapleford, Carlton, and West Bridgford had a population of 469 720 in 1971. This area lies within an approximate radius of five miles around the centre of Nottingham. This population has remained constant during the study and the census figures for 1971 have been used in calculating incidence data for individual years.

INVESTIGATION OF GEOGRAPHICAL DISTRIBUTION

Primary acute pancreatitis is an uncommon disease found chiefly among the middle-aged and elderly, and the investigation of the geographical distribution of the disease within the Nottingham defined population area was consequently structured to take account of these two important characteristics. In 1971, the population 'at risk'—that is, 45 years and over—amounted to only 170 493 persons, or 36.3% of the total population. The home address of these patients was identified and coded for the 37 electoral wards within the Nottingham defined population area. Crude average annual incidence rates were calculated and mapped for each ward (Fig. 1). Age and sex differentials were not considered, given the small number of patients and the relatively large number of wards.

Fig. 1 Average annual incidence rates per million for wards: 1969-76.

A Poisson probability test (Choynowski, 1959; White, 1972) was applied to these data in order to determine whether the overall distribution of patients could be considered random. The 0.05 level was selected as the cut-off point for values which were significantly higher, or lower, than average. The probabilities derived from this analysis were then plotted for each ward to produce a probability map (Fig. 2). The probability of relationships between age, social class, and the domestic drinking water supply was investigated.

Fig. 2 Distribution of probability values for primary acute pancreatitis.

Although the Nottingham defined population area is relatively small (147 km² or 57 sq. miles), it is subdivided into distinct and fixed domestic water supply areas. These are served by six different major sources (Fig. 3). Table 1 shows that the chemical composition of the water supplies from these sources varies considerably between areas. Very little mixing of supplies occurs, and only those supplies for central Nottingham (Bellevue Reservoir) are affected during temporary shortages. The chemical composition of these water supplies has also been stable for many years. The sole exception is provided by the water taken from the River Derwent. In 1970, the hardness of the domestic water supplied from this source to the population of the western part of the study area

(Fig. 3) was increased considerably. In 1971, the population living in the Derwent supply area was 31 493 persons.

Fig. 3 Average annual incidence rates per million for water supply areas: 1969-76.

The remarkable combination of factors outlined above provided an opportunity to test whether the incidence of primary acute pancreatitis within the study area varied significantly among the population living in the six distinct water supply areas. The published census data for electoral wards could not be used in this particular analysis because the ward boundaries cut across those of the six water supply areas (compare Figs 1 and 3). However, the un-

published 1971 census tabulations provided by the Registrar General gave population data for the much smaller areas (enumeration districts) assigned to the local census enumeration officers. Accordingly, the 914 enumeration districts within the Nottingham defined population area were assigned to the appropriate water supply areas and their populations aggregated. The population 'at risk'—that is, aged 45 and over—in these areas ranged between 20 005 (Burton Joyce) and 35 520 (Bellevue).

Results

Two-hundred-and-fourteen patients from within the Nottingham defined population area were accepted on review as having primary acute pancreatitis during the period 1969 to 1976, and their associated aetiological factors are shown in Table 2. These factors are similar to those reported previously (Bourke, 1975). Table 3 shows the pattern of incidence of primary acute pancreatitis by age and sex. The youngest patient in the series was 18 years old, and there was a predominance of females. The incidence rates rose sharply with age, particularly from 45 years onwards. In four of the five age groups, the rate for females was higher than that for males:

Table 2 Associated aetiological factors in primary acute pancreatitis in Nottingham defined population area (n = 214)

Factor	No.	%
Gallstones	99	46.3
Previous cholecystectomy	5	2.3
Gallstones/carcinoma of pancreas	1	—
Gallstones/alcohol	1	—
Alcohol	17	7.9
Alcohol/hypothermia	1	—
Hypothermia	1	—
Hyperparathyroidism	1	—
Chronic renal failure	2	0.9
Cushing's syndrome	1	—
Idiopathic	59	27.5
Unclassified	26	12.1

Table 1 Chemical composition of water supply from major sources in Nottingham defined population area (1975)

	Burton Joyce	Bellevue	Derwent (before 1970)	Redhill	Oxton	Ramsdale
Ph	7.7	8.2	8.4	7.9	8.1	7.9
Free CO ₂	7	—	—	5	2	4
Total hardness as:						
CaCO ₃	300	164	197	196	151	173
Carb.	184	115	115	110	140	65
Calcium	142	80	138	102	45	101
Magnesium	158	84	59	94	106	72
Total dissolved solids	377	240	470	276	160	321
Chloride as Cl	16	26	91	38	11	90
Nitrate as N	0.6	9.3	2.4	8.3	0.7	3.0
Ammonia as N	—	—	0.02	—	—	—
Sulphate as SO ₄	120	59	140	47	11.2	44
Silica as SiO ₂	7	7	4	7	7	7

Table 3 Average annual incidence of primary acute pancreatitis (rates per million persons) by age and sex; Nottingham defined population area, 1969-76

Age groups (years)	Males		Females		Total	
	Patients	Rate	Patients	Rate	Patients	Rate
15-29	6	14.5	11	30.9	17	22.1
30-44	10	31.3	8	19.8	18	24.9
45-59	26	74.0	27	78.0	53	76.0
60-74	37	161.9	51	181.2	88	172.5
75+	9	182.7	29	290.8	38	255.0
Total	88	64.6	126	84.8	214	75.1

the exception being in the 30-44 year age group. The geographical analysis was, therefore, restricted to the 179 patients aged 45 years and over, and this accounted for 83.6% of the entire cohort. The crude average annual incidence rate among this segment of the population was 138.6 per million and was calculated and mapped for each ward (Fig. 1).

Figure 1 shows that there were considerable variations in both the incidence and distribution of the disease within the study area. The crude average annual incidence rates ranged between 31.8 and 388.7 per million. Six of the eight wards with rates in excess of 200 per million were contiguous with similar wards; together these formed a U-shaped area extending from the city centre to the eastern boundary of the Nottingham defined population area.

The Poisson probability test analysis showed that the numbers of patients found in five wards were greater than could be expected by chance. In only one ward was the number significantly lower than might have been expected by chance.

Figure 2 shows that the five wards with significantly large numbers of cases formed a single region extending from the city centre to the eastern fringes of the Nottingham defined population area. The highest incidence rates may be found in electoral wards with populations which were predominantly middle-aged and elderly. This possibility was tested by using information on electoral wards and age abstracted from the 1971 census. The Pearson product moment correlation coefficient was calculated between mean age and incidence rate for the 37 electoral wards. The correlation coefficient was only -0.180 ($P > 0.1$).

The relationship between social class and incidence rate was also tested. Information by ward on social class was obtained from the 1971 census. Three variables were calculated for each ward—namely, high social class (% persons in socioeconomic groups I and II), low social class (% persons in socioeconomic groups IV and V), and mean social class. The correlation coefficients between these

three variables and incidence rate were $+0.179$ ($P > 0.1$), $+0.306$ ($P > 0.1$), and $+0.135$ ($P > 0.1$) respectively.

Table 4 shows the pattern of incidence among the populations of the six domestic water supply areas by sex. In every case, the rates for females exceeded those for males. There was considerable variation in the incidence of the disease between water supply areas. The highest rates for both sexes were found among persons living in the Burton Joyce water supply area. The distribution of crude total incidence rates is shown in Fig. 3. Water supplied to homes in this area has significantly high concentrations of calcium carbonate and carbonate (Table 1). The configuration of the high-rate Burton Joyce water supply area is remarkably similar to the high-rate region formed by electoral wards shown in Figs 1 and 2.

Table 4 Average annual incidence rates of primary acute pancreatitis by sex, Nottingham defined population area, 1969-76

Water supply areas	Rates per million		
	Males	Females	Total
Derwent	68.2	160.0	115.1
Redhill	83.5	169.8	131.1
Oxton	111.6	106.8	108.8
Ramsdale	115.9	166.8	134.2
Bellevue	144.1	144.4	144.3
Burton Joyce	166.1	296.2	237.4
Total	125.4	154.5	138.6

The Poisson probability test was applied to the data for males, females, and total patients in order to determine whether the distribution of patients among the six water supply areas could be considered random. The results of these analyses showed that the numbers of females and total cases in the Burton Joyce supply area were significantly greater than could have occurred by chance ($P < 0.002$). In every other case, the probabilities did not exceed 0.05.

The six water supply areas also provided a convenient spatial framework to explore variations in the incidence of different kinds of primary acute pancreatitis. However, the rather small number of cases available inevitably limited the scope of this part of the investigation. Analysis was, therefore, limited to two major groups—namely, gallstone patients (90 persons) and all other patients (89 persons). The incidence rates of these two groups are presented in Table 5. Substantial variations were evident, but the highest rates for both groups were found in the Burton Joyce water supply area. The Poisson probability test revealed that for the two groups, the numbers of cases occurring in the Burton

Table 5 Average annual incidence rates of primary acute pancreatitis by major diagnostic classes, Nottingham defined population area, 1969-76

Water supply areas	Rates per million	
	Gallstones	Other types
Derwent	51.6	63.5
Redhill	84.3	46.8
Oxton	57.0	51.8
Ramsdale	63.1	71.1
Bellevue	59.8	84.5
Burton Joyce	125.0	112.4

Joyce area were much greater than could have been expected by chance (gallstones, $P = 0.013$; other types, $P = 0.038$). In the other water supply areas, the probabilities did not exceed 0.05.

Discussion

Marked variations in the geographical distribution of different forms of pancreatitis have been observed at an international level (White, 1966; Sarles, 1965, 1972, 1973). However, diagnostic reliability and uniformity and case identification and enumeration are two important problems inherent in comparative international studies. By using a much smaller spatial unit (the Nottingham defined population area) and one reviewer (J.B.B.), it was hoped to eliminate these problems.

On review, the diagnosis of acute pancreatitis was accepted only with a compatible clinical history, physical examination, and a greater than four-fold increase in serum amylase level. Laparotomy and/or necropsy diagnosis was also accepted. Only patients in their first attack of acute pancreatitis were included, while those with recurrent, chronic, traumatic, or postoperative pancreatitis were excluded. These restrictions were applied, as mortality is greatest in the initial attack of pancreatitis (Trapnell, 1972) and this is important in clinical practice in the United Kingdom. Also, this definition of primary acute pancreatitis aids the calculation of accurate incidence as opposed to prevalence data, and helps to identify patients who correctly contribute to the disease incidence.

Considerable geographical variations in the incidence of the disease were identified among the 37 wards in this large urban area. In six wards, the incidence was significantly different from the average for the study area. The five wards with significantly high rates formed a single region, which was strikingly linear in form.

The identification of large local variations in the geographical distribution of primary acute pancreatitis and of a single high rate region within the

Nottingham defined population area provides an opportunity to test various hypotheses concerning the aetiology of pancreatitis. However, this work can only be exploratory. At present, we have relatively little demographic information concerning acute pancreatitis. The main types of pancreatitis in the Nottingham defined population area series are shown in Table 2.

In the Nottingham series, as in other British series (Imrie, 1974; Imrie *et al.*, 1975; Trapnell and Duncan, 1975), gallstones are the commonest associated aetiological factor.

The information presented in Table 3 shows that the disease becomes progressively more common with increasing age. However, there was no significant association of primary acute pancreatitis with increasing age in the population at ward level. The spatial pattern of incidence of primary acute pancreatitis in the study area is thus not simply a reflection of the spatial pattern of age distribution.

One possibly significant aetiological factor which has been explored at the international level is nutrition (Sarles, 1965, 1972, 1973). Unfortunately, we have no information concerning the dietary patterns either of our patients or of the general population of the Nottingham defined population area. It would also be interesting to study any variation in alcohol consumption within the defined population area; such data are not available. However, social class has been invoked in a similar study for diverticular disease as a useful surrogate variable (Eastwood *et al.*, 1977). It was inferred that differences in social class were reflected in parallel variations in income, life style, spending habits, and hence dietary patterns. However, no relationship was found between social class and incidence rate for primary acute pancreatitis in this study.

Detailed information is available for only one important dietary element of the population of the Nottingham defined population area—namely, the domestic drinking water supply. The effects of regional variations in the chemical composition of domestic water supply upon the incidence of cardiovascular and other disease are well known (Howe, 1970, 1972; Howe *et al.*, 1977; Platts *et al.*, 1977).

This study has identified statistically significant variations in the distribution of primary acute pancreatitis within the Nottingham defined population area. The brief investigation of social and geographical factors suggests that the composition of the domestic water supply may affect the distribution of the disease in this particular urban area. Specifically, the very significant concentration of patients in the Burton Joyce area suggests that some (as yet unidentified) property of the water supply may be an important aetiological factor.

'Hard' water, such as the water in the Burton Joyce area, is associated with cardiovascular disease (Howe, 1970, 1972; Howe *et al.*, 1977) and this study has shown an association between acute pancreatitis and water. It may be that this present study simply reflects the high incidence of cardiovascular disease, which may be related to the water supply and is reflected in the high incidence of pancreatitis, for vascular disease has been thought to predispose to pancreatitis (Nakashima and Howard, 1977). This can remain only a possible explanation, as data are not available about the incidence of cardiovascular disease in the patients studied. There is clearly a need for more detailed epidemiological studies of primary acute pancreatitis.

One potentially fruitful line of investigation involves tracing the residential histories of patients before their first attack. Many of the elderly patients in the study area were admitted to Nottingham hospitals from suburban addresses between 1969 and 1976. However, we know that many of them have been rehoused fairly recently. Since Spring 1968, 45 500 people have been moved and rehoused from two comprehensive redevelopment areas—that is, St Ann's and The Meadows—near the city centre. Figure 3 shows that these two large clearance areas are located almost completely within the Burton Joyce water supply area. The authors are currently engaged in tracing the residential histories of the 1969-76 cohort. It should then be possible to calculate incidence rates for previous census years—that is, 1951, 1961, and 1966—and to determine how many of the cases lived in each of the six water supply areas. The duration of residence in these areas may provide a useful measure of length of exposure to potential risk factors.

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