MEDICAL PRACTICE

Occasional Survey

Chronic Pancreatitis in England: A Changing Picture?

OLIVER JAMES, J. E. AGNEW, IAN A. D. BOUCHIER

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Summary

A total of 107 patients with chronic pancreatitis from the London area seen between 1968 and 1973 have been reviewed; they comprised 30 with calcific pancreatitis and 77 with chronic or chronic relapsing pancreatitis without calcification. The commonest clinical features were pain, diabetes, malabsorption, and peptic ulcer. Alcohol was a probable aetiology in nearly half the cases, a different finding from those of previous surveys and possibly associated with the increased consumption of alcohol in England in the last 20 years.

Introduction

The study of chronic pancreatic inflammatory disease has been beset with problems of classification and nomenclature and comparison of patients from different centres and countries has been difficult. Here we define pancreatitis as an inflammatory condition characterized by permanent pancreatic damage which persists even if the primary cause or factors are eliminated: the patients we studied thus fall into clinical groups 3 and 4 of the Marseilles classification.[1]

The introduction of well-recognized tests of pancreatic secretory function—the secretin, secretin/pancreozymin, and Lundh tests—and the increasing reliability of ^{75}Se-selenomethionine scanning of the pancreas in larger centres and improvements in radiology, particularly hypotonic duodenography, have led to better assessment of pancreatic function and pathology in the past 10 years. Comparison between groups of patients with chronic pancreatitis is therefore easier and may be more fruitful than in the past. The suggestion that the pattern of chronic pancreatic inflammatory disease may be changing in England and in other countries, together with the impression that chronic pancreatitis is becoming more frequent, have led to this retrospective study of 107 patients with chronic pancreatitis seen at the Royal Free Hospital in the six-year period 1968-73.

We made no distinction between chronic relapsing pancreatitis (Marseilles category 3), in which the evolution is characterized by intermittent attacks of pain, often of growing severity, and chronic pancreatitis, in which symptoms are more persistent (Marseilles category 4). We believe that there is a spectrum of chronic inflammatory disease in this country and that a division of this type is unhelpful. Some patients with relapsing symptoms, often with raised serum amylase values during attacks, were excluded because they did not have residual pancreatic damage—as shown by pancreatic function tests and laparotomy—and were excluded from the series by definition (Marseilles category 2).

Patients and Methods

The Royal Free Hospital provides a pancreatic scanning service for many hospitals in the Greater London area, particularly in North London. Our series was drawn from 1,230 patients referred for pancreatic scans. At the time of scanning a full clinical history of each patient was obtained from the medical records, with details of investigations carried out, and a Lundh test was performed on many patients. Follow-up information was obtained on those patients about whom there was insufficient information on which to base a confident diagnosis of chronic pancreatitis at the time of scan.

Pancreatic disease is comparatively uncommon and therefore many patients can be gathered only at centres known for their interest in this field. These centres often show a medical or

Royal Free Hospital, London WC1X 8LF

O. JAMES, M.B., M.R.C.P., Registrar, Department of Medicine (Present appointment: First Assistant, Department of Medicine, University of Newcastle upon Tyne)

J. E. AGNEW, B.A., M.SC., Senior Physicist

I. A. D. BOUCHIER, M.D., F.R.C.P., Reader in Medicine (Present appointment: Professor of Medicine, University of Dundee)

surgical bias or are known to be particularly interested in one aspect of pancreatic disease. Hence possibly considerable selection of patients occurs before referral to these large centres. In this series, however, because patients were referred for pancreatic scanning from over 10 hospitals throughout London and because referral was made for investigation of all possible pancreatic conditions our group represented a fairly unselected cross-section of patients with chronic pancreatitis.

As patients came from different hospitals a constant data base was not obtained on all patients. Our criteria for diagnosing chronic pancreatitis are shown in table I. Abnormal results of pancreatic biopsy at laparotomy were sufficient criteria for diagnosis of chronic pancreatitis but if patients had a strongly suggestive history and abnormal responses to two or more primary diagnostic investigations the diagnosis was also established.

Primary pancreatic investigations were regarded as those in which pancreatic function or disease was assessed directly at the time of investigation. Secondary investigations were regarded as those where a measurement was made in which an abnormality while not necessarily implying pancreatic disease was often associated with it; these were not used in establishing the diagnosis of chronic pancreatitis.

TABLE I—*Results of Investigations performed to establish Diagnosis of Chronic Pancreatitis in 107 Patients. (Mean Age at Onset of Symptoms 46·9 years; M.:F. 71:36)*

Investigations	No. of Patients Investigated	Patients with Abnormalities	
		No.	%
Primary:			
Pancreatic scan	107	101	94·4
Lundh test	46	41	89·1
Radiology (pancreatic, calcification, barium studies, arteriography)	84	68	81·0
Laparotomy	60	60	100
Secondary:			
Glucose tolerance test	81	49	60·5
Faecal fat estimation	65	37	56·9
Increased serum amylase in early history		35	

TABLE II—*Investigations in 30 Patients with Calcific Pancreatitis. (Mean Age at Onset of Symptoms 46·1 years)*

	Patients with Alcoholic Calcific Pancreatitis (n=19; M.:F. 14:5)*		Patients with Non-alcoholic Calcific Pancreatitis (n=11; M.:F. 4:7)†		Total	
	No. Investigated	No. with Abnormalities	No. Investigated	No. with Abnormalities	No. Investigated	No. with Abnormalities
Pancreatic scan	19	17	11	11	30	28
Lundh test	10	8	8	7	18	15
Glucose tolerance test	17	9	8	6	25	15
Faecal fat estimations	14	5	8	7	22	12

*Mean age at onset of symptoms 46·5 years.
†Mean age at onset of symptoms 45·8 years.

TABLE III—*Associated Findings in 30 Patients with Calcific Pancreatitis. (Mean Age at Onset of Symptoms 46·1 years)*

	No. of Patients with Alcoholic Calcific Pancreatitis (n=19; M.:F. 14:5)*	No. of Patients with Non-alcoholic Calcific Pancreatitis (n=11; M.:F. 4:7)†	Total
Pain	17	10	27
Biliary disease	0	2	2
Duodenal ulcer	1	3	4
Pancreatic cyst	2	2	4
α-Cell adenoma	1	0	1
Crohn's disease of duodenum	0	1	1

*Mean age at onset of symptoms 46·5 years.
†Mean age at onset of symptoms 45·8 years.

Results

Of the 107 patients who had chronic pancreatitis, 30 showed radiological evidence of pancreatic calcification. The clinical features and results of investigations are shown in tables I-V.

TABLE V—*Associated Findings in 77 Patients with Non-calcific Chronic Pancreatitis. (Mean Age at Onset of Symptoms 47·3 years)*

	No. of Patients with Alcoholic Non-calcific Pancreatitis (n=26; M.:F. 25:1)*	No. of Patients with Gall Stone Non-calcific Pancreatitis (n=17; M.:F. 8:9)†	No. of Patients with Non-gall Stone Non-alcoholic Pancreatitis (n=35; M.:F. 21:14)‡	Total
Pain	25	17	30	72
Biliary disease	1	17		17§
Duodenal ulcer	3		9	12
Gastric ulcer			2	2
Duodenal polyp	1			1
Carcinoma of pancreas			1	1
Islet cell tumour			1	1
Cystic fibrosis			1	1

*Mean age at onset of symptoms 46·0 years.
†Mean age at onset of symptoms 50·5 years.
‡Mean age at onset of symptoms 46·5 years.
§One patient had both gall stones and heavy alcoholic consumption.

Pain.—Pain was the outstanding clinical feature in 99 patients. There was no difference in the clinical presentation between alcoholic and non-alcoholic patients. Out of three patients with painless calcific pancreatitis two presented with malabsorption and steatorrhoea and one was asymptomatic who was investigated after visualization of pancreatic calcification on a plain *x*-ray film of the abdomen for an unrelated complaint. Among the 77 patients who did not have pancreatic calcification were five who did not complain of abdominal pain and who all presented with gross malabsorption and diabetes.

Diabetes.—A total of 49 patients had greatly impaired response to glucose tolerance tests or frank diabetes. There was no significant difference between the proportion found in calcific (50%) and non-calcific disease (44%).

Malabsorption.—Faecal fat levels of over 6 g/day were found in 37 out of 65 patients tested. There was no difference between

TABLE IV—*Investigations in 77 Patients with Non-calcific Chronic Pancreatitis. (Mean Age at Onset of Symptoms 47·3 years)*

	Patients with Alcoholic Non-calcific Pancreatitis (n=26*; M.:F. 25:1)†		Patients with Gall Stone Non-calcific Pancreatitis (n=17*; M.:F. 8:9)‡		Patients with Non-gall Stone Non-alcoholic Non-calcific Pancreatitis (n=35; M.:F. 21:14)§		Total	
	No. Investigated	No. with Abnormalities	No. Investigated	No. with Abnormalities	No. Investigated	No. with Abnormalities	No. Investigated	No. with Abnormalities
Pancreatic scan	25	24	17	16	35	33	77	73
Lundh test	7	7	5	4	16	15	28	26
Glucose tolerance test	18	13	12	6	26	15	56	34
Faecal fat estimation	10	5	9	4	24	16	43	25

*One of these patients had both gall stones and heavy alcoholic consumption.
†Mean age at onset of symptoms 46·0 years
‡Mean age at onset of symptoms 50·5 years
§Mean age at onset of symptoms 46·5 years.

the proportion found in patients with calcific or non-calcific disease.

Peptic Ulcer.—Duodenal ulcer was found in 16 patients and gastric ulcer in two; thus 17% of the patients had associated peptic ulcer disease. The number of duodenal ulcer patients (12) and the proportion (16%) found in the non-calcific group was scarcely higher than that found in the calcific group, where there were only four.

Other Findings.—One carcinoma of the pancreas was seen in a patient with a history of symptoms going back over 10 years and a long history of malabsorption. One patient had an islet cell tumour of the pancreas and associated longstanding chronic pancreatic inflammation, one had fibrocystic disease, one had Crohn's disease of the duodenum, four had pancreatic cysts, one had pancreatic adenoma, and one had a duodenal polyp. Our information on follow-up and family history of all patients was incomplete but we found no patients with parathyroid adenoma, hyperlipaemia, or a family history of chronic pancreatitis.

Alcohol.—A history of heavy alcohol ingestion is notoriously difficult to obtain from patients who are naturally reluctant to disclose the full extent of their consumption. A definite history of heavy alcohol consumption was obtained in 31 patients. Heavy consumption was regarded as daily consumption of over one bottle of wine, half a bottle of whisky or other spirits, or eight pints (4·5 l.) of beer. Most heavy drinkers chose spirits or wine rather than beer and many mixed the type of beverage consumed. In addition, a history of what was regarded as moderate to heavy social drinking was obtained in a further 14 patients. This was defined as daily consumption of half a bottle of wine, quarter-bottle of spirits, or four pints (2·3 l.) of beer, and consumption was often increased at weekends. In view of the underestimation of alcohol consumption among such social drinkers, they were included in the total number of patients in whom alcohol was thought to be an important aetiological factor. Thus a history of appreciable alcohol consumption was found in 45 patients. We recognized that this might still have been an underestimate of the true state of affairs. There was a significant difference between the proportion of patients with marked alcohol consumption among those who had calcific pancreatitis (63%) and among those with non-calcific pancreatitis (34%; $P<0.01$ by 2×2 χ^2 test). Nevertheless, 26 patients with non-calcific disease had a significant alcohol consumption.

Biliary Tract Disease.—Out of 19 patients with biliary tract disease only two had pancreatic calcification. Of the 17 patients with biliary tract disease and no pancreatic calcification 15 had stones in the biliary tree, only two having stones in the gall bladder alone. Only one patient out of the 17 with non-calcific pancreatitis also had a heavy consumption of alcohol.

Discussion

AETIOLOGICAL FACTORS

Alcohol.—The proportion of patients with high alcohol intake was greater in patients with pancreatic calcification than in those without. Some features, however, support the suggestion that, whether calcific or not, alcoholic chronic pancreatitis is one entity. There were more men than women in both groups, similar proportions of diabetic subjects and patients with frank steatorrhoea in both groups, and a lack of other associated possible aetiological factors among all the alcoholic patients except one, who also had biliary disease. Possibly, as Sarles[2] has suggested, pancreatic calcification will eventually occur in the natural history of the disease in most cases.

Gall Stones.—Gall stone pancreatitis rarely caused pancreatic calcification, only two patients out of 19 having pancreatic calcification. The fact that only two patients had stones solely in the gall bladder emphasizes that stones in the biliary tree are far more likely to cause pancreatic inflammation, presumably by direct or indirect pancreatic duct obstruction. The degree of pancreatic malfunction as judged by steatorrhoea and diabetes was less noticeable in this group than in patients with alcoholic or other aetiological factors.

Idiopathic.—In 44 patients neither alcohol nor biliary tract disease could be implicated as a cause of the disease. Of these patients 14 had peptic ulcer (12 duodenal ulcer) and it is hard to believe that there was no relation between duodenal ulcer and chronic pancreatitis. Whether this was a causal relation or whether the two conditions were manifestations of a common aetiological agent was not clear. Eight patients (three calcific) experienced no pain and of the seven who presented with malabsorption all had diabetes. This group had also been identified by Howat,[3] Fitzgerald,[4] and Goulston and Gallaher[5] since Bartholomew and Comfort[6] first described it and may well represent a separate disease entity. The subject of painless pancreatitis has been recently reviewed by Fitzgerald.[4]

AGE INCIDENCE

There was no appreciable difference in the mean age at onset of symptoms in the three main aetiological groups (alcoholic, biliary tract, idiopathic). Though Sarles[1] has suggested that alcoholic pancreatitis is seen in a younger age group than other forms of the disease we found no evidence to support this.

SEX INCIDENCE

As expected there were many more men than women among the alcoholic patients but there was no appreciable difference between the sexes in the other groups. Among patients with gall stones women only slightly outnumbered men.

PANCREATIC FUNCTION TESTS

Our findings do not assess the reliability of the contribution of the ^{75}Se-selenomethionine scan or of the Lundh test in the diagnosis of chronic pancreatitis, as these tests were used in selecting the patients. Nevertheless, 35 patients who received both scan and Lundh test meal had sufficient evidence of chronic pancreatitis without reference to either test. There were 18 patients with calcific pancreatitis in whom, therefore, the diagnosis of chronic pancreatic disease was not in doubt and a further 17 patients who had laparotomy proof of chronic pancreatitis. The results of both investigations were abnormal in 85% of cases—in 86% of cases of calcific disease and in 83% of cases without calcification. These figures may be compared with those of Leger *et al.*,[7] who found an abnormal pancreatic scan in 49 out of 52 patients with calcific pancreatitis and 16 out of 28 patients with chronic non-calcific pancreatitis proved at laparotomy.

We recognize that they may be a sizeable proportion—perhaps 30% of falsely abnormal scans.[8] Nevertheless, the combination of abnormal responses to both pancreatic scan and pancreatic stimulation test, in this case the Lundh test, and the presence of a suggestive history seems to be of value in the diagnosis of chronic pancreatitis.[9]

COMPARISON

The symptoms and effects of chronic pancreatitis vary little from country to country but the factors implicated in its causation differ. They fall broadly into three groups, depending on the proportion of patients in each series in whom alcohol has been implicated as the aetiological factor, which is responsible for over 60%, 30-60%, and less than 30%, in groups 1, 2, and 3 respectively (table VI).

TABLE VI—*Comparison of Findings in Studies of Chronic Pancreatitis*

Studies	No. of Patients	% with Calcification	% Alcoholic	% with Biliary Disease	Other Findings	% with Diabetic Curve	% with Steathorrea
Group 1—Over 60% of Cases with Alcoholic Aetiology							
France:							
Gullo and Sarles[22]	150*	100	82	2		60·5	34
Sarles *et al.*[30]	115	87	82	4·5	4 Carcinoma of pancreas	41	36
Levrat *et al.*[23]	113	46	⩾60	10·5		66	18
S. Africa:							
Marks *et al.*[10]	100*	100	93	5		50	31
Marks *et al.*	621†	16	60	16	18% Painless	20	10
U.S.A.:							
Owens and Howard[18]	32*	100	100	0	6 Peptic ulcers	34	37·5
Berman *et al.*[24]	123	4	⩾60	22			
Switzerland:							
Haemmerli *et al.*[25]	15	20	87	13	4 Painless patients		
Liem[26]	39	54	100	3		28	31
Group 2—30-60% of Cases with Alcoholic Aetiology							
U.S.A.:							
Kelley *et al.*[12]	31*	100	48	39		39	
Warren[19]	160	40	37		17% Peptic ulcer	33	
Gambill *et al.*[13]	56	39	29	48		54	43
Paulino-Netto *et al.*[27]	124	19	38	39	6 Carcinoma of pancreas		
Group 3—Less than 30% of Cases with Alcoholic Aetiology							
U.S.A.:							
O'Sullivan *et al.*[28]	35	49	8·5			26	5·7
Czechoslovakia:							
Herfort[15]	151	0	4·6	55			
Spain:							
Artigas[14]	72	5·5	4	93			
England:							
Howat[17]	44	20	4·5	32	5 Duodenal ulcers	46	33
Howat[3]	54	33	20	15		7·5	24
Ireland:							
Fitzgerald *et al.*[16]	53	11	7·5	41·5			

*Series of patients with calcific chronic pancreatitis.
†Both acute and chronic pancreatitis.

Very few epidemiological studies have been made on the prevalence of chronic pancreatitis in different communities but the strong impression is that chronic pancreatitis, whether calcific, relapsing chronic, or chronic, is more common in those countries or communities in which there is a high per capita consumption of alcohol. While the typical clinical presentation may vary somewhat according to whether heavy alcohol consumption occurs usually in bouts, as in South Africa,[10] or steadily, as in France,[11] the end result seems to be the same. Possibly also the underlying pathological process is the same.[11] The type of alcohol drunk is apparently not important, as our series also showed.

In the group 2 series the proportion of patients in whom biliary tract disease has been implicated as a cause has been surprisingly constant, varying from about 39%[12] to 48% only.[13] In the group 3 series biliary tract disease was said to be very common in Spain,[14] 67 out of 72 patients with chronic pancreatitis having biliary tract disease, and in Czechoslovakia,[15] being implicated in 83 out of 151 patients. Fitzgerald *et al.*[16] also found that it was the most common aetiological factor, being present in 22 out of 53 patients seen with chronic pancreatitis—though only 33 of these had been investigated for biliary tract disease.

The series which compares most closely to ours, however, are those of Howat.[3 17] In 1963 he reported biliary tract disease in 14 out of 44 patients with chronic pancreatitis and alcoholism in only two. In 1968 the corresponding figures were eight out of 54 and 11 out of 54. Duodenal ulcer was associated with their illness in five patients and seven patients had painless pancreatitis with weight loss and steatorrhoea as prominent symptoms.

Probably our patients should be assigned to group 2 since a significant history of alcohol ingestion was found in 45 of the 107 patients. Like Howat, but unlike other centres with low alcohol groups, we found biliary tract disease present in less than 20% of our patients. This form of disease rarely led to pancreatic calcification, possibly because patients came to surgical treatment earlier in the course of the disease. In common with findings in other studies from the British Isles[3 16] and elsewhere,[18 19] relatively many (17%) of our patients had peptic ulcers.

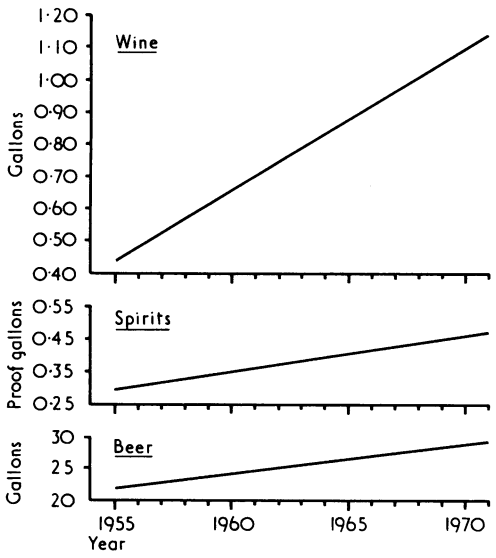
Our patients may be ascribed to several categories according to the possible aetiology or associated aetiological factors of their disease: (*a*) alcohol, 45 patients; (*b*) biliary tract disease, 19 patients; (*c*) painless pancreatitis with malabsorption (cause unknown), eight patients; (*d*) miscellaneous, including fibrocystic disease in one patient, islet cell tumour in one, Crohn's disease of the duodenum in one, pancreatic adenoma in one, duodenal polyp in one, carcinoma of the pancreas in one, and pancreatic cysts in four.

In addition, duodenal ulcer was found in 12 patients with no other feature which might have been associated in the aetiology of the pancreatitis in these patients. Thus there were 88 patients in whom an associated aetiological factor was found (or 76 excluding the patients with duodenal ulcer). No cause was therefore found in 18% of the patients (or 29% including those with duodenal ulcer). This compares with 52% in Howat's[3] series and 51% in the series of Fitzgerald *et al.*[16]

INCREASING TREND OF ALCOHOLISM

Compared with the three previously published accounts from Britain the increase in the proportion of alcoholic patients seen in our series supports the suggestion put forward by Sarles[20] and Howat[3] that there is a changing pattern of chronic pancreatic inflammatory disease.

The consumption of alcohol has risen steadily over the past decade in England, particularly that of wine and spirits (see chart). The number of people suffering from alcoholism is also increasing: figures from the Department of Health show that admissions to mental hospitals in England and Wales of patients with a diagnosis of alcoholism or alcoholic psychosis rose from 799 in 1954 to 5,423 in 1964 and 10,167 in 1972. While these figures represent a less reliable numerical index than those shown in the chart they nevertheless reflect the large rise in the number of heavy alcohol drinkers in England in the past 20 years. Though the number of deaths attributed to chronic pancreatitis in the Registrar General's annual reports has not increased over the past 10 years we consider that chronic pancreatitis is becoming more common.[21] Two factors may explain why there has not been a rise in recorded mortality from chronic



Annual per capita consumption of alcoholic beverages in England and Wales, 1955-71. (Erroll Report[29].)

pancreatitis: firstly, it is often not the cause of death even in patients who have suffered from its effects for many years; secondly, it is a long lasting illness and if there is to be any increase in mortality from chronic pancreatitis in England it may occur over the next decade rather than the past one.

If this impression that the incidence of chronic pancreatitis is increasing is correct then increasing alcohol consumption, particularly consumption of wine and spirits, seems to be playing an important part in causing this increase. Certainly, increased alcoholism is changing the aetiological pattern of chronic pancreatitis in England.

Conclusion

The aetiology of chronic pancreatitis seen in England seems to have changed. Alcohol was implicated as a probably aetiology in nearly half of the 107 patients seen with chronic pancreatitis during 1968-73. This may be related to a definite increase in per capita alcohol consumption in England over the past 15 years. In earlier series from Great Britain heavy alcohol consumption was seen in less than 10% of the patients with chronic pancreatitis. Biliary tract disease was found in less than 20% of our patients. Our study confirms the existence of a small but well-defined group of patients with chronic painless pancreatic disease whose aetiology is obscure and in whom malabsorption and diabetes are the principal complaints. We also found a definite association between chronic pancreatitis and duodenal ulcer as 16 patients had both conditions.

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