Indications for operation in suspected appendicitis and incidence of perforation

Roland Andersson, Anders Hugander, Anders Thulin, Per Olof Nyström, Gunnar Olaison

Abstract

***Objective*—To clarify poorly understood epidemiological features of appendicitis.**

***Design*—Retrospective study of consecutive cases from a defined population and analysis of data from published studies.**

***Setting*—County of Jönköping, Sweden. 3029 patients who underwent operation in 1984-9 and 4717 patients from the county town who underwent operation in 1970-89, all for suspected appendicitis, plus 48 426 cases from six reported studies.**

***Main outcome measures*—Incidences specific for age and sex and temporal trends of perforating and non-perforating appendicitis and removal of a normal appendix. Associations between diagnostic accuracy, rate of perforation, and incidences of removal of a normal appendix and of perforating and non-perforating appendicitis.**

***Results*—The incidence of appendicitis was 116/100 000 inhabitants. Appendicitis was more common in male patients. The incidence of perforating appendicitis was independent of age, stable over time, and uninfluenced by the rate of laparotomy, whereas the incidence of non-perforating appendicitis was age dependent, decreasing over time, and related to the diagnostic accuracy and rate of removal of a normal appendix.**

***Conclusions*—Perforating and non-perforating appendicitis seem to be separate entities, and appendicitis that resolves spontaneously is common. This may have important implications for managing suspected appendicitis.**

Introduction

The many poorly understood epidemiological features of acute appendicitis include a widely varying incidence even within the same country,[1-4] trends towards a falling incidence,[5-7] and rising rate of perforation.[8,9]

We surveyed the epidemiology of appendicitis in terms of the patients' age and sex and the changes associated with time in a Swedish county. We also analysed how varying rates of exploratory laparotomy in suspected appendicitis influenced the incidence of perforating and non-perforating appendicitis.

Department of Surgery, Ryhov Hospital, S-551 85 Jönköping, Sweden
Roland Andersson, *registrar*
Anders Hugander, *senior consultant*
Anders Thulin, *head of department*

Department of Surgery, University Hospital, Linköping, Sweden
Per Olof Nyström, *associate professor*
Gunnar Olaison, *associate professor*

Correspondence to:
Dr Andersson.

BMJ 1994;308:107-10

Subjects and methods

AGE AND SEX SPECIFIC INCIDENCES

From the computerised hospital register for Jönköping county (population 302 475 in 1987) we identified 3029 consecutive patients who underwent appendicectomy for suspected appendicitis in 1984-9. Patients who had incidental appendicectomies were excluded. The quality of the database is high, and errors in registration are avoided by continuous checks of extracts from the database with the original discharge letter.

A total of 1470 males and 1559 females had undergone an appendicectomy. Their median age was 21 years. Histological examination of excised tissue had been performed in 2509 (83%). An inconsistency between the discharge diagnosis and the results of the microscopic examination was found in 219 (9%) of the 2509 examined specimens. There were 179/1840 (10%) false positive diagnoses and 40/669 (6%) false negative diagnoses. The net error because of these false diagnoses was an overestimation of appendicitis in 139/2509 cases (6%).

In the 250 cases in which no histological examination of excised tissue took place the patients were slightly younger (mean (SD) age 25·1 (17·3) *v* 27·4 (17·9) years; $P < 0.007$) and were more often male (52·7% *v* 47·6%; $P < 0.05$). There was, however, no difference in diagnostic accuracy (78% *v* 73%; $P = 0.15$) and rate of perforation (16% in both groups) before the correction.

The final diagnosis corrected in accordance with the histological findings was appendicitis in 2100 cases, giving a diagnostic accuracy (ratio of inflamed appendixes to all appendicectomies) of 69%. The appendix was perforated in 330 cases (perforation rate 16%).

An abdominal pathological condition other than acute appendicitis was the cause of symptoms in 382 (13%) cases, of which 105 (4%) required an operation. The most common cause was lymphadenitis mesenterica (193 (6%) cases). A gynaecological disorder was found in 64 (4%) female patients. Further details of the patients have been published elsewhere.[10]

The incidence of perforating and non-perforating appendicitis and of removal of a normal appendix were calculated in relation to the patients' age and sex. Because of the age related rise in the proportion of people who underwent appendicectomy the population at risk of acquiring appendicitis was adjusted by subtracting the estimated number of people who had previously undergone the operation according to the cumulative age specific incidence of appendicectomy, assuming a constant rate of appendicectomy over time.

TEMPORAL TRENDS

To study temporal trends we analysed the results of 4717 appendicectomies performed in the town of Jönköping (population 108 235 in 1987) in 1970-89. We chose this town because in other parts of the county the hospital register for the period was incomplete. The incidence of perforating and non-perforating appendicitis and of removal of a normal appendix, standardised for age and sex to the demographic state in 1987, were calculated for each of the four component periods of five years. No correction of discharge diagnosis was made as results from histological examinations were not available before 1984.

ASSOCIATION BETWEEN LAPAROTOMY RATE AND APPENDICITIS RATE

The influence of the rate of laparotomy on incidences of perforating and non-perforating appendicitis was analysed by reviewing previously published studies from defined populations. Diagnostic accuracy and rates of negative results from laparotomy were used as indicators of the attitude to surgical exploration in suspected appendicitis as the numbers and the proportion of operations that yielded negative results are directly related to readiness to explore.

A search of *Index Medicus* back to 1970 found six relevant studies.[7,11-16] With our data these studies

included 53 143 patients from 15 defined geographical areas who had undergone laparotomy. As some series represented more than one time period from the same area there were in total 23 sets of data from different times and places.

STATISTICAL METHODS

The χ^2 test was used for analysis of categorical data and the t test for normally distributed continuous variables. Relative risks were calculated with Taylor series 95% confidence intervals. Correlation analysis was performed with Pearson coefficient and P values of $<0{\cdot}05$ were considered significant. Calculations were done with EPI INFO[17] and STATGRAPHICS.

Results

RELATION OF INCIDENCE OF APPENDICITIS TO AGE AND SEX

From 1984 to 1989 the incidence of appendicectomy per 100 000 people in Jönköping county was 167 and that of appendicitis 116. Appendicectomy was equally common in both sexes, whereas the incidence of appendicitis had a male to female ratio of 129:102 (relative risk 1·27; 95% confidence interval 1·16 to 1·38; $P<0{\cdot}0001$). The incidence of perforating appendicitis was 18/100 000, with a male to female ratio of 23:14 (1·71; 1·37 to 2·14; $P<0{\cdot}0001$). The corresponding figure for non-perforating appendicitis was 97 per 100 000, with a male to female ratio of 106:89 (1·20; 1·09 to 1·32; $P<0{\cdot}0002$).

The incidence of appendicitis was strongly age dependent, peaking at 10-14 years. This variation, however, was mainly among cases of non-perforating appendicitis, and the incidence of perforating disease was almost stable at all ages (fig 1).

The rate of removal of a normal appendix was 51 per 100 000, with a male to female ratio of 34:69 (0·50; 0·43 to 0·57; $P<0{\cdot}00001$), reflecting the lower diagnostic accuracy in female patients (60% *v* 79%).

TEMPORAL TRENDS, 1970-89

The incidence of appendicectomy in the town of Jönköping fell by 29% (from 256 to 182 per 100 000, $P<0{\cdot}0001$) between 1970-4 and 1985-9 (table I). The corresponding figure for appendicitis was 24% (from 173 to 132 per 100 000; $P<0{\cdot}0001$). A trend towards more conservative management was indicated by a 40% drop in the number of operations to remove a normal appendix (from 84 to 50 per 100 000 population; $P<0{\cdot}0001$) and a rise in diagnostic accuracy from 67% to 73% ($P<0{\cdot}01$). Concomitantly the incidence of non-perforating appendicitis fell by 27% from 152 to 111 per 100 000 ($P<0{\cdot}00001$), while that of perforating appendicitis remained stable at around 21 per 100 000. As a result the perforation rate rose from 12% to 16% ($P<0{\cdot}05$).

INFLUENCE OF MANAGEMENT POLICY

Among the 23 sets of data from defined places and times there were wide variations in the incidence of appendicectomy and appendicitis. The variation, however, was mainly in the incidence of non-perforating appendicitis and removal of a normal appendix, whereas the incidence of perforating appendicitis was less variable. For non-perforating appendicitis the highest rate (235 per 100 000) was reported from the Republic of Ireland[11] and the lowest (11 per 100 000) from Melanesia,[12] but the rate of perforating appendicitis in the Republic of Ireland was only double that in Melanesia (20 *v* 9 per 100 000 population).

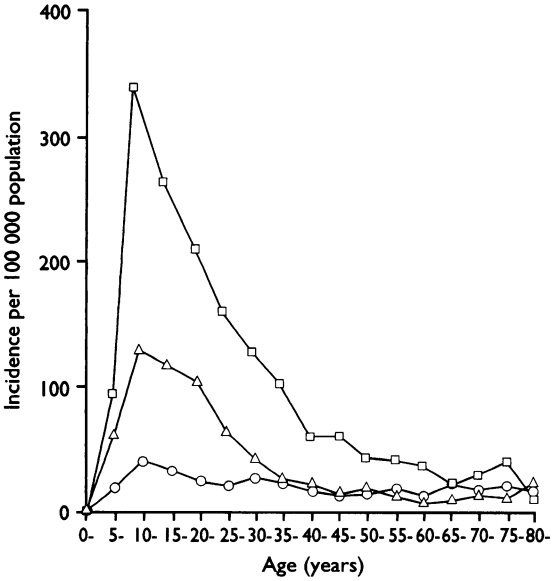

FIG 1—*Adjusted age specific incidence of perforating (○—○) and non-perforating (□—□) appendicitis and of removal of normal appendix (△—△) in Jönköping county, 1984-9*

The influence of the readiness to explore in suspected appendicitis, expressed as diagnostic accuracy and incidence of removal of a normal appendix was studied by correlation analysis (table II). The extreme results from Melanesia and the Republic of Ireland were excluded from this analysis.

The incidence of perforating appendicitis was unrelated to diagnostic accuracy and rates of removal of a normal appendix. The figures for non-perforating appendicitis, however, correlated strongly with those for removal of a normal appendix ($r=0{\cdot}85$; $P<0{\cdot}0001$; fig 2) and were inversely related to diagnostic accuracy ($r=-0{\cdot}59$; $P=0{\cdot}005$; fig 3).

The perforation rate was unrelated to diagnostic accuracy and to the incidence of perforating appendicitis but was inversely related to the rate of non-perforating appendicitis ($r=-0{\cdot}62$; $P=0{\cdot}003$) and removal of a normal appendix ($r=-0{\cdot}52$; $P=0{\cdot}02$).

TABLE I—*Incidences of perforating and non-perforating appendicitis and of removal of normal appendix per 100 000 population, standardised for age and sex, and diagnostic accuracy and perforation rate in four consecutive periods of five years (Jönköping town)*

Year	Appendicectomy	Non-perforating appendicitis	Perforating appendicitis	Removal of normal appendix	Diagnostic accuracy (%)	Perforation rate (%)
1970-4	256	152	21	84	67	12
1975-9	216	130	18	69	68	12
1980-4	203	123	22	58	71	15
1985-9	182	111	21	50	73	16

TABLE II—*Correlation matrix of 23 data sets from previous and present studies. Numbers are correlation coefficients (95% confidence interval) and P values*

	Incidence of:			
Correlate	Perforating appendicitis	Removal of normal appendix	Non-perforating appendicitis	Perforation rate
Incidence of removal of normal appendix	0·34 (−0·11 to 0·67) P=0·13			
Incidence of non-perforating appendicitis	0·45 (0·02 to 0·74) P=0·04	0·85 (0·66 to 0·94) P<0·0001		
Perforation rate	0·40 (−0·03 to 0·71) P=0·07	−0·52 (−0·78 to 0·11) P=0·02	−0·62 (−0·83 to 0·25) P=0·003	
Diagnostic accuracy	−0·17 (−0·56 to 0·28) P=0·46	−0·91 (−0·96 to 0·79) P<0·00001	−0·59 (−0·8 to 0·21) P=0·005	0·39 (−0·05 to 0·7) P=0·08

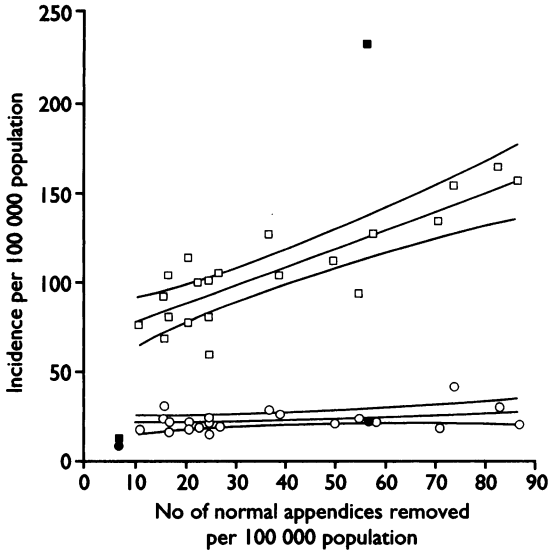

FIG 2—*Incidence of perforating (○—○) and non-perforating (□—□) appendicitis in relation to removal of normal appendix in 23 sets of data obtained from previous and present studies. Regression lines exclude two outliers (● and ■)*

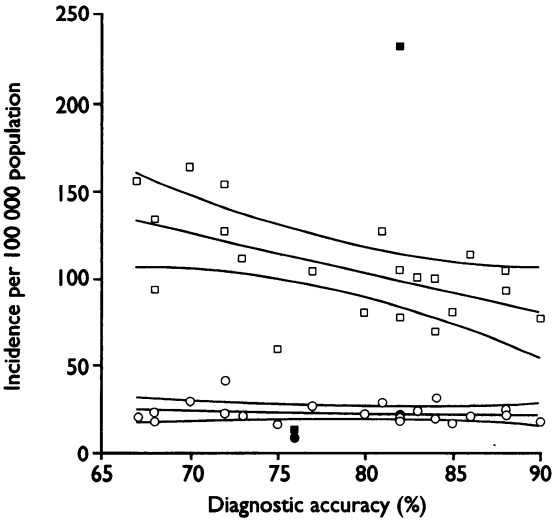

FIG 3—*Incidence of perforating (○—○) and non-perforating (□—□) appendicitis in relation to diagnostic accuracy in 23 sets of data obtained from previous and present studies. Regression lines exclude two outliers (● and ■)*

Discussion

In this study the incidence of perforating appendicitis was independent of time, place, patients' age, and rates of exploratory laparotomy in suspected appendicitis. The contrast with the widely varying incidence of non-perforating appendicitis supports Luckman's proposition that perforating and non-perforating appendicitis are separate entities,[16] as do earlier observations of higher rate of obstruction and faecaliths in gangrenous and perforating appendices than in phlegmonous appendixes.[18]

The natural course of non-perforating appendicitis is not known. Many surgeons regard acute appendicitis as a progressive inflammation,[19] but spontaneous resolution may occur[20-22] and microscopy of excised appendixes may show signs of healed inflammation.[23] Recurrent appendicitis has also been reported.[24]

CHANGES IN MANAGEMENT

A high rate of exploratory laparotomy in suspected appendicitis increases the number of confirmed cases,[25] presumably by adding cases of self limiting inflammation which otherwise would have escaped detection. Inflammation without symptoms, which is seen in up to 35% of incidentally removed appendixes,[26] may also be erroneously diagnosed at laparotomy as appendicitis. The observed incidence of non-perforating appendicitis will therefore be influenced by a willingness to perform exploratory laparotomy in cases of suspected appendicitis.

This hypothesis is confirmed by our findings of a strong association between the incidence of non-perforating appendicitis and rate of laparotomy with a stable incidence of perforating appendicitis and indicates that appendicitis commonly resolves. The declining registered incidence of appendicitis in the town of Jönköping and the observed geographical variations may therfore be explained by differences in the management of patients with suspected appendicitis. The increase in diagnostic accuracy in the town of Jönköping was not the result of any new diagnostic methods.

The diagnosis of appendicitis is usually overestimated clinically at operation (in 6% according to our study). Histological confirmation, which is usually mandatory, was lacking in 17% of the cohort from Jönköping county for 1984-9. These patients did not represent any selected subgroup as the characteristics were almost identical to the remaining cases. The error induced by this group is therefore only marginal (less than 1%).

Changes in the clinical diagnosis of appendicitis at operation could be an alternative explanation to the decreasing incidence of appendicitis as clinical diagnosis of appendicitis without histological confirmation was used in the temporal trend analysis. This trend has, however, continued after 1984 and after histological confirmation and is consistent with the unanimous reports of a decreasing incidence of appendicitis from other countries.[5-7]

Removal of a normal appendix was more common in women. A lower diagnostic accuracy in women is a common finding in most studies. Gynaecological diseases may mimic appendicitis because of the proximity to the female pelvic organs, but this is probably not the only explanation.[10]

GOALS OF TREATMENT

The ultimate goal in treating suspected appendicitis is to minimise the number of unnecessary laparotomies without increasing the incidence of perforated appendixes. Diagnostic accuracy may be increased by a conservative attitude to explore in uncertain cases.[27] This strategy is criticised, however, for giving an increased perforation rate. Our study shows that a seemingly increased perforation rate can be explained

Clinical implications

- The incidence of appendicitis is declining and shows large geographical variations
- A liberal attitude to exploration with an accompanying high rate of negative results (up to 50% in women) has been accepted in the hope of preventing perforation
- In this study perforating and non-perforating appendicitis seemed to be different entities, and spontaneously resolving appendicitis was common
- The readiness to explore influences the detection of resolving appendicitis and may explain variations in incidence of appendicitis and perforation rate
- Perforation rate is useless as a measure of quality of management in suspected appendicitis

by misclassification of spontaneously resolving cases. Reported rises in perforation rates with duration of symptoms may also be explained by selection bias due to spontaneous resolution of milder inflammation.[15] The perforation rate is therefore worthless as a measure of quality in the management of appendicitis.

That appendicitis commonly resolves implies that future diagnostic and therapeutic policies should aim at early detection and operation in patients with perforating appendicitis or progressive inflammation and at active observation and investigation of alternative diagnoses in other patients. Studies on clinical signs and laboratory findings in relation to the degree of inflammation or perforation have shown promising results.[28,29] The role of explorative laparoscopy in this context is as yet unclear but may increase the yield of alternative diagnoses in prolonged abdominal pain.[30]

We thank Mrs R McVeigh Källqvist for linguistic revision. The study was supported by a grant from the committee for research and development, Jönköping County Council.

1 Barker DJP, Liggins A. Acute appendicitis in nine British towns. *BMJ* 1981;283:1083-5.
2 Attwood SE, Cafferkey MT, West AB. High appendectomy rates in Ireland: why? *J Epidemiol Community Health* 1987;41:72-3.
3 Lichtner S, Pflanz M. Appendectomy in the Federal Republic of Germany. *Med Care* 1971;9:311-30.
4 West RR, Carey MJ. Variation in rates of hospital admission for appendicitis in Wales. *BMJ* 1978;i:1662-4.
5 Rutkow IM, Zuidema GD. Surgical rates in the United States: 1966 to 1978. *Surgery* 1981;89:151-62.
6 Arnbjörnsson E, Asp NG, Westin SI. Decreasing incidence of acute appendicitis with special reference to the consumption of dietary fiber. *Acta Chir Scand* 1982;148:461-4.
7 Noer T. Decreasing incidence of acute appendicitis. *Acta Chir Scand* 1975;141:431-2.
8 Peltakallio P, Tykkä H. Evolution of the age distribution and mortality of acute appendicitis. *Arch Surg* 1981;116:153-6.
9 Ricci MA, Cuasay RS, Beck WC. Appendicitis: the perforation rate when reviewed by decades in a general hospital. *Am Surg* 1988;54:273-5.
10 Andersson RE, Hugander A, Thulin AJG. Diagnostic accuracy and perforation rate in appendicitis: association with age and sex of the patient and with appendicectomy rate. *European Journal of Surgery* 1992;158:37-41.
11 Waldron R, Johnston JG. Appendicitis: 357 consecutive cases. *Ir Med J* 1983;76:446-8.
12 Foster HMcA, Webb SJ. Appendicitis and appendectomy in a Melanesian population. *Br J Surg* 1989;76:368-9.
13 Addiss DG, Shaffer N, Fowler BS, Tauxe RV. The epidemiology of appendicitis and appendectomy in the United States. *Am J Epidemiol* 1990;132:910-25.
14 Pieper R, Kager L. The incidence of acute appendicitis and appendectomy. *Acta Chir Scand* 1982;148:45-9.
15 Pieper R, Kager L, Näsman P. Acute appendicitis: a clinical study of 1018 cases of emergency appendectomy. *Acta Chir Scand* 1982;148:51-62.
16 Luckman R. Incidence and case fatality rates for acute appendicitis in California. *Am J Epidemiol* 1989;129:905-18.
17 Dean AD, Dean JA, Burton AH, Dicker RC. *EPI INFO, version 5: a word processing, database, and statistics program for epidemiology on microcomputers.* Stone Mountain, GA: USD Incorporated, 1990.
18 Arnbjörnsson E, Bengmark S. Obstruction of the appendix lumen in relation to pathogenesis of acute appendicitis. *Acta Chir Scand* 1983;149:789-91.
19 Condon RE. Appendicitis. In: Sabiston DC, ed. *Textbook of surgery.* 13th ed. Philadelphia: W B Saunders, 1986:967-82.
20 Puylaert JB, Rutgers PH. Lalisang RI, de Vries BC, van der Werf SD, Dörr JP. A prospective study of ultrasonography in the diagnosis of appendicitis. *N Engl J Med* 1987;317:666-9.
21 Amland PF, Skaane P, Ronningen H, Nordshus T, Solheim K. Ultrasonography and parameters of inflammation in acute appendicitis. *Acta Chir Scand* 1989;155:185-9.
22 Heller MB, Skolnick LM. Ultrasound documention of spontaneously resolving appendicitis. *Am J Emerg Med* 1993;11:51-3.
23 Williams GT. The vermiform appendix. In: Morson BC, ed. *Systemic pathology.* Vol 3. *Alimentary tract.* 3rd ed. Edinburgh: Churchill Livingstone, 1987:292-312.
24 Butsch DW, Jothi R, Butsch WL, Butsch JL. Recurrent appendicitis. Fact not fallacy. *Postgrad Med* 1973;54:132-7.
25 Howie JGR. Too few appendectomies? *Lancet* 1964;i:1240-2.
26 Pieper R, Kager L, Näsman P. Clinical significance of mucosal inflammation of the vermiform appendix. *Ann Surg* 1983;197:368-74.
27 Thomson HJ, Jones PF. Active observation in acute abdominal pain. *Am J Surg* 1986;152:522-5.
28 Graham DF. Computer-aided prediction of gangrenous and perforating appendicitis. *BMJ* 1977;ii:1375-7.
29 Van Dieijen-Visser MP, Go PMNYH, Brombacher PJ. The value of laboratory tests in patients suspected of acute appendicitis. *European Journal of Clinical Chemistry and Clinical Biochemistry* 1991;29:749-52.
30 Olsen JB, Myrén CJ, Haahr PE. Randomized study of the value of laparoscopy before appendectomy. *Br J Surg* 1993;80:922-3.

(Accepted 19 October 1993)

Renal disease and use of topical non-steroidal anti-inflammatory drugs

C A O'Callaghan, P A Andrews, C S Ogg

Renal Unit, Guy's Hospital, London SE1 9RT
C A O'Callaghan, *renal registrar*
P A Andrews, *Wingate lecturer*
C S Ogg, *consultant renal physician*

Correspondence to:
Dr O'Callaghan.

BMJ 1994;308:110-1

Renal impairment is a recognised complication of oral, rectal, and intramuscular non-steroidal anti-inflammatory drugs. We report cases of renal disease associated with a topical preparation.

Case report

CASE 1

A 74 year old woman presented with a six week history of breathlessness and oedema. Investigations showed proteinuria (+++ by dipstick), a serum albumin concentration of 17 g/l, and a creatinine concentration of 169 μmol/l. Her urine contained no leucocytes but grew *Escherichia coli* in culture and she was prescribed trimethoprim, frusemide, and prophylactic heparin. Her renal function deteriorated, and three days later she was transferred to our care. She was not volume depleted but remained grossly nephrotic with proteinuria of 18 g/day. There was no eosinophilia or eosinophiluria, and results of renal phlebography and ultrasonography were normal. Renal biopsy showed a florid interstitial nephritis with normal glomeruli.

The combination of nephrotic syndrome and interstitial nephritis was highly suggestive of use of non-steroidal anti-inflammatory drugs, but this was denied by the patient, her relatives, and her general practitioner. All drugs were therefore changed or stopped, and she was given high doses of steroids. Her renal function worsened, however, and she started haemodialysis. Shortly afterwards she became confused, possibly because of her uraemia, steroid treatment, or dialysis. A tube of piroxicam gel was then discovered in her locker, which she had been applying regularly to her shoulder and back for musculoskeletal pains. Over six weeks she had used three 60 g tubes of 0·5% piroxicam and had been applying it in the ward bathroom at least twice daily until her confusion. After its removal her renal function rapidly recovered so that 10 days later she stopped dialysis and three weeks later her oedema was reduced with proteinuria only +, serum albumin concentration 32 g/l, and creatinine concentration 110 μmol/l. The figure shows the changes in creatinine concentration over time.

CASE 2

A 57 year old woman had been using a topical cream of 3% benzydamine hydrochloride for four months and had used a total of 400 g of cream. She was referred for investigation of plasma concentrations of creatinine and urea of 137 μmol and 13·2 mmol/l respectively. When the drug was stopped these concentrations fell to 96 μmol/l and 6·5 mmol respectively, results consistent with the drug causing a substantial reduction in glomerular filtration rates. No other cause was found.

Comment

About 5-18% of outpatients taking non-steroidal anti-inflammatory drugs have renal impairment.[1] Case-control studies suggest that use of these drugs doubles the risk of renal disease; in men aged over 65