Case–control studies of risk factors for primary biliary cirrhosis in two United Kingdom populations

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Case—control studies of risk factors for primary biliary cirrhosis in two United Kingdom populations

M I Prince,1 S J Ducker,2 O FW James2

ABSTRACT

Objective The aetiology of primary biliary cirrhosis (PBC) is largely unknown. Previous studies have indicated that both environmental and genetic risk factors may be important.

Design We undertook a large case—control study to study possible risk factors in more detail. All patients were sent postal questionnaires on risk factors.

Patients We identified two sets of PBC cases from a geographically defined epidemiology study (epidemiological cases) and from a survey of the national patient support group (Foundation cases). Controls were selected from the electoral roll in strata matched to epidemiological cases by quartiles of age and sex.

Results Analysable questionnaires were received from 318 epidemiological cases, 2258 Foundation cases and 2438 controls. Statistically significant associations were seen with smoking (OR = 1.63 (95% CI, 1.27 to 2.09)), epidemiological cases versus controls (1.57 (1.39 to 1.78)), Foundation cases versus controls, hair dye use (1.37 (0.98 to 1.80)), 1.25 (1.07 to 1.46)), and with previous histories of psoriasis (1.90 (1.21 to 1.91), 2.33 (1.03 to 1.73)), urinary infections (2.06 (1.56 to 1.73)), and shingles (2.38 (1.82 to 3.11), 1.23 (1.08 to 1.43)) and previous autoimmune diseases. Alcohol consumption was negatively associated with PBC (0.57 (0.39 to 0.83), 0.73 (0.61 to 0.79)). We did not identify any associations with obstetric risk factors except a previous history of obstetric cholestasis (2.13 (1.25 to 3.59), 2.20 (1.61 to 3.03)).

Conclusion We have confirmed that among environmental risk factors, smoking and the use of some cosmetics as well as urinary infections appear important. Among possible genetic risk factors a family history of PBC is a strong association and that a previous history of obstetric cholestasis as another putative ‘genetic’ risk.

INTRODUCTION

Primary biliary cirrhosis (PBC) is a chronic autoimmune cholestatic liver disease characterised by destruction of medium and small calibre intrahepatic bile ducts and by the presence of anti-mitochondrial antibodies (AMAs) in around 95% of sufferers.1 The aetiology of PBC is uncertain but is likely to include both genetic and environmental components. Whilst the genetic basis of PBC has been studied extensively, for example in twin concordance,2 family history3–5 and human leucocyte antigen (HLA) genotyping studies,7 8 Environmental risk factors are less clear. Several groups have suggested roles for a variety of infectious agents (as reviewed in detail by Haydon and Neuberger),9 including, most recently, retroviruses.10 However, further studies have usually failed to confirm these associations.

Two early studies used traditional epidemiological case—control methods to identify environmental risk factors for PBC.11 12 One of these, an earlier study from our own unit, suggested possible positive associations with smoking and psoriasis, with eczema having a protective effect.12 However, this study was limited by a relatively small sample size and large number of risk factors investigated. A second study carried out by Parikh-Patel et al in association with patient support groups suggested smoking, shingles and tonsillectomy as risk factors.11 However, this study should be interpreted with caution since cases were recruited from membership of internet fora and controls were recruited by patients themselves, leading to the potential for significant selection biases. Against this background we undertook a larger case—control study that we report here.

A third, large, well performed case—control study from several American centres has been reported since we undertook this study.13 We will compare the results of the present United Kingdom based study with the recent American study to see what ‘consensus’ can be reached.

METHODS

Case selection

Two cohorts of patients with PBC were used in this study. The primary cohort (‘epidemiological cases’) consisted of cases of PBC who were identified from part of a new comprehensive case-finding epidemiological study of the frequency and distribution of PBC in northeast England. Cases were recruited from five adjacent areas (representing old district health authority regions) in northeast England (Newcastle, North Tyneside, Gateshead & South Tyneside, Durham and Sunderland). Cases were identified through a survey of consultant gastroenterologists and hepatologists in the region, follow-up of patients with positive AMAs on serum testing and review of hospital discharge data. The criteria for a diagnosis of PBC were at least two of persistently cholestatic liver function tests over a period of greater than 3 months, positive mitochondrial antibody at a titre of 1 in 40 or greater twice or more, and compatible liver histology. The date of diagnosis was taken as the first date when two of these criteria were met. All cases were incident between 1997 and 2005. Patients questioned in the previous case—control study from our group were excluded. Permission from the consultant looking after each patient was obtained prior to patients being approached for inclusion in this study.

A second case series (‘Foundation cases’) was selected from the membership of the United Kingdom PBC Foundation (the national support
group for patients with PBC). To avoid cases appearing in both study groups, PBC Foundation members resident in the study area were excluded as they were included in the ‘epidemiological cases’. As it was not possible to verify case status from hospital records for these patients all Foundation members were asked a series of ‘screening questions’ and were excluded from the analysis if they did not meet at least one of the following criteria: Having attended a hospital specialist for a diagnosis they were told was PBC, being prescribed treatment for PBC by a secondary care consultant (either ursodeoxycholic acid or cholestryamine), having had a liver transplant, or knowing that they were AMA positive.

Control selection

Controls were selected randomly from electoral roll datasets. To comply with relevant data protection legislation the selection process excluded people who had specifically requested not to receive direct marketing mail-shots via the United Kingdom mail preference service. Controls were selected by age—sex stratification to be of similar demographic distribution to the epidemiological case series. Ninety per cent of controls were female. Female controls were selected in four quartiles of age to match the age distribution quartiles of the epidemiological cases. As the number of male cases was much smaller it was not possible to use quartiles of age in the analysis and therefore male controls were selected to be within the age range of male epidemiological cases.

Questionnaire

Epidemiological cases and controls were sent identical postal questionnaires. PBC Foundation cases received postal questionnaires. Epidemiological cases and controls were sent identical postal questionnaires. Wherever possible questions regarding risk factors (eg, smoking and drinking alcohol) were taken from a questionnaire previously validated in local epidemiological studies. All non-respondents were sent up to two reminders by post. The questionnaires used in this study are available as an online appendix.

Data analysis

All data were entered onto Microsoft access databases using an established data preparation service. Analysis was performed using SPSS (version 10, SPSS Corps) and epi info (CCDC, USA). All analysis was performed using stratified significance tests with subjects stratified by their age—sex quartile. Univariate analysis used Mantel–Haentzel statistics. Multivariate analysis was carried out using logistic regression adjusted for both stratification and patient age. All datasets complied with UK data protection legislation.

RESULTS

The epidemiological survey identified 381 patients with PBC. No cases were excluded because the clinician in charge of their care considered contact clinically inappropriate. Three hundred and fifty-three (92%) were female and their median age was 68 years. The age quartiles (strata for control selection) for female patients were selected with 900 in each female age stratum and 318 (95%) were female and their median age was 68 years. Three thousand, two hundred and seventeen patients from the PBC Foundation (0.7%) and 33 (1.4%) controls. These patients were excluded from the analysis as it was not possible to place them in an age—sex stratum.

The age and sex distribution of excluded Foundation members did not differ significantly from those included (median age in both groups 60 years and both were 95% female).

The matching of epidemiological patients and controls was highly successful with equal proportions of respondents in each group. (χ² p=0.97). In comparison, the PBC Foundation members were over-represented in the younger strata and were more likely to be female (χ² p<0.001).

Table 1 gives the stratified odds ratios (ORs) for the environmental risk factors for PBC examined. Compared to controls both groups of patients with PBC were more likely to have ever smoked, although a dose—response relationship was not identified. This association was observed across all age strata when analysed separately and also both sexes (data for individual strata not shown). The mean age when respondents started smoking was similar in all three groups and also within each stratum at around 18 years and was earlier than the date of diagnosis in 100% of cases in both groups.

Patients with PBC from both sets of cases were less likely to have ever drunk alcohol regularly than controls, although this difference was not statistically significant for patients from the PBC Foundation when men were included (stratified ORs for women only for epidemiological cases, OR=0.58 (0.59 to 0.85); Foundation cases, OR=0.82 (0.65 to 1.05)).

Patterns of hair dye usage differed markedly between the sexes with less than 1% of male respondents in all groups using hair dye compared to greater than 50% of women in all strata.

Table 1 (ORs) in univariate stratified analysis for environmental risk factors for primary biliary cirrhosis (PBC)

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>OR compared to epidemiological cases (95% CI)</th>
<th>OR compared to PBC Foundation cases (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever smoked</td>
<td>1.63 (1.27 to 2.09)</td>
<td>1.57 (1.39 to 1.78)</td>
</tr>
<tr>
<td>Regularly &gt; 20 cigarettes per day</td>
<td>1.46 (1.11 to 1.93)</td>
<td>1.43 (1.24 to 1.65)</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drunk alcohol regularly ever</td>
<td>0.57 (0.39 to 0.83)</td>
<td>0.73 (0.61 to 0.79)</td>
</tr>
<tr>
<td>Use of hair products</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hair dye †</td>
<td>1.29 (1.00 to 1.80)</td>
<td>1.25 (1.07 to 1.46)</td>
</tr>
<tr>
<td>Hair perms †</td>
<td>1.13 (0.78 to 1.65)</td>
<td>0.95 (0.80 to 1.13)</td>
</tr>
<tr>
<td>Co-existent conditions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psoriasis</td>
<td>1.90 (1.21 to 2.91)</td>
<td>1.33 (1.03 to 1.73)</td>
</tr>
<tr>
<td>Eczema</td>
<td>0.96 (0.63 to 1.46)</td>
<td>1.41 (1.04 to 1.55)</td>
</tr>
<tr>
<td>Urinary tract infections</td>
<td>2.06 (1.56 to 2.73)</td>
<td>1.80 (1.54 to 2.11)</td>
</tr>
<tr>
<td>Shingles</td>
<td>2.38 (1.82 to 3.11)</td>
<td>1.23 (1.04 to 1.43)</td>
</tr>
<tr>
<td>Appendectomy</td>
<td>1.27 (0.91 to 1.76)</td>
<td>1.62 (1.38 to 1.72)</td>
</tr>
<tr>
<td>Tonsillitis</td>
<td>1.09 (0.82 to 1.45)</td>
<td>1.69 (1.48 to 1.93)</td>
</tr>
<tr>
<td>Connective tissue disease*</td>
<td>2.02 (0.93 to 4.26)</td>
<td>2.02 (1.33 to 3.08)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>1.52 (1.12 to 2.10)</td>
<td>1.21 (1.01 to 1.45)</td>
</tr>
<tr>
<td>Thyroid disease</td>
<td>2.35 (1.79 to 3.14)</td>
<td>1.62 (1.37 to 1.91)</td>
</tr>
<tr>
<td>Breast fed as child</td>
<td>1.01 (0.72 to 1.41)</td>
<td>1.15 (0.98 to 1.36)</td>
</tr>
</tbody>
</table>

*Unstratified analysis.
† Analysis restricted to women due to low numbers of men reporting risk factor.
CI, confidence interval.
hair dye usage amongst women only was investigated the association was significant in both arms (stratified OR for female epidemiological cases 1.29 (1.00–1.00), Foundation cases (1.25 (1.07–1.46)). The date that patients first dyed their hair preceded the date of diagnosis in 86% of local cases and 87% of Foundation cases. In stratified analysis the age of first dyeing hair was similar in cases and controls. Use of hair perms was not significantly associated with case status. We did not ask patients about the frequency with which dye or perms were used.

Psoriasis, urinary tract infections and shingles were associated with PBC in both groups. Associations with appendectomy and tonsillectomy were only seen with Foundation cases. As expected, rheumatoid arthritis, thyroid disease and coeliac disease were more common in patients with PBC. The low numbers of patients with coeliac disease (10 (3.1%) epidemiological cases, 68 (5.1%) Foundation cases and 38 (1.4%) controls) meant this analysis could only be performed in an unstratified manner.

Table 2 shows the relationship between PBC and obstetric and gynaecological risk factors in female respondents. There was no apparent association between PBC and ever having been pregnant, or the sex of offspring. The mean number of all offspring was similar in all groups (epidemiological cases, 2.96; Foundation cases, 3.07; controls, 3.04) as were the numbers of male (1.66, 1.50, 1.45) and female (1.52, 1.26, 1.29) offspring (all p>0.05). There was a weak association between a previous hysterectomy and PBC for Foundation but not epidemiological cases. However, this association arose almost exclusively from a high number of patients reporting surgery in the youngest stratum of Foundation patients (OR in this stratum, 1.80 (1.32–2.51)). Analysis of the other strata did not show such an association individually or when combined (OR when excluding the first stratum=1.16 (0.95–1.33)). No association was observed with either miscarriage or stillbirths. Patients from both groups were more likely to recall suffering from itching during their pregnancy. Patients with PBC were more likely to have a family history of PBC than were controls (OR for epidemiological cases, 2.26 (1.05 to 5.21); Foundation cases, 4.43 (2.83 to 7.01)).

Table 3 shows the results of multivariate analysis, accounting for patient age, sex and stratification. Consistently significant associations were seen for both case populations and smoking, hair dye, urinary tract infections and thyroid disease. Associations with appendectomy, tonsillectomy, coeliac disease and pruritus in pregnancy and were seen only for the Foundation cases.

**CONCLUSIONS**

We have carried a large case–control study to investigate risk factors for PBC. At the time this study was undertaken the epidemiological evidence for risk factors for PBC was limited, coming mainly from two earlier pilot studies that were flawed, as discussed above, by small sample size and potential selection biases.11 12

The present study improves on the methods used in the earlier local case–control study from our unit in that it includes a larger number of patients and examines fewer risk factors (chosen on the basis of previous epidemiological and laboratory studies) reducing the risk both of type 2 and type 1 errors, respectively. In addition, we have examined not only a larger unselected group of local patients but also a much larger group of patients from a national source. All of the univariate associations seen in the epidemiological survey were reproduced in the Foundation cases, adding to the likely validity of these results. However, some further risk factors (eg, appendectomy and tonsillectomy) were only seen when Foundation cases and controls were compared. These inconsistent findings are probably less reliable. They may reflect the different geographical location of cases and controls, or socio-economic confounding (members of PBC support groups tend to be more educated).14 Despite our stratification this may have also reflected a difference of age distribution occurring within the strata.

The large American multicentre study by Gershwin et al has been reported since the start of our study.15 This study used different methods from our own (eg, telephone interviews) and was extremely well performed. It studied a very large cohort of well characterised patients (n=1052) and controls (n=1041) recruited from several secondary care centres. Apart from slight differences in the socio-economic status (patients with PBC earned significantly more than controls), cases and controls were well matched. The survey used a validated telephone survey tool to ask about multiple risk factors. Risk factors identified on multivariate analysis in this study included family history of PBC, lupus or Sjögren’s syndrome, smoking, and the use of nail polish. Patients with PBC were also more likely to currently or previously have used hormone replacement therapy and were younger at their first pregnancy.

The current study confirms the associations we previously identified with smoking, drinking alcohol (negative association) and psoriasis (in univariate analysis only). We did not detail use of nail polish or age at first pregnancy. In addition, we identified use of hair dyes as a risk factor for PBC. Gershwin et al also identified that patients with PBC used hair dye slightly more frequently than controls although this was only of borderline statistical significance in univariate analysis (p=0.04) and was not significant in multivariate analysis. It is not possible to identify exactly which component of hair dyes might be responsible for this association as they are complex products

**Table 2 Analysis of associations between primary biliary cirrhosis (PBC) and obstetric and gynaecological risk factors in female patients and controls**

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>OR compared to epidemiological cases (95% CI)</th>
<th>OR compared to PBC Foundation cases (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous pregnancy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever pregnant</td>
<td>0.80 (0.54 to 1.18)</td>
<td>0.84 (0.68 to 1.03)</td>
</tr>
<tr>
<td>Any male children</td>
<td>1.34 (0.75 to 2.43)</td>
<td>0.77 (0.59 to 1.01)</td>
</tr>
<tr>
<td>Any female children</td>
<td>0.93 (0.59 to 1.35)</td>
<td>1.01 (0.78 to 1.38)</td>
</tr>
<tr>
<td>Previous history of miscarriage</td>
<td>0.81 (0.53 to 1.23)</td>
<td>0.81 (0.64 to 1.03)</td>
</tr>
<tr>
<td>Previous history of still births</td>
<td>0.97 (0.70 to 1.37)</td>
<td>1.12 (0.94 to 1.33)</td>
</tr>
<tr>
<td>Previous hysterectomy</td>
<td>1.02 (0.75 to 1.39)</td>
<td>1.27 (1.08 to 1.47)</td>
</tr>
<tr>
<td>Presence of itch during pregnancy</td>
<td>2.13 (1.25 to 3.59)</td>
<td>2.20 (1.61 to 3.03)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Adjusted OR compared to epidemiological cases (95% CI)</th>
<th>Adjusted OR compared to PBC Foundation cases (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>1.6 (1.2 to 2.3)</td>
<td>1.5 (1.3 to 1.7)</td>
</tr>
<tr>
<td>Any alcohol</td>
<td>0.6 (0.4 to 1.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Hair dye</td>
<td>1.8 (1.2 to 2.7)</td>
<td>1.3 (1.0 to 1.5)</td>
</tr>
<tr>
<td>Appendectomy</td>
<td>NS</td>
<td>1.4 (1.2 to 1.7)</td>
</tr>
<tr>
<td>Tonsillectomy</td>
<td>NS</td>
<td>1.6 (1.4 to 1.9)</td>
</tr>
<tr>
<td>Thyroid disease</td>
<td>2.0 (1.4 to 2.9)</td>
<td>1.6 (1.3 to 1.9)</td>
</tr>
<tr>
<td>Coeliac disease</td>
<td>NS</td>
<td>2.3 (1.3 to 3.8)</td>
</tr>
<tr>
<td>Urinary tract infections</td>
<td>2.4 (1.7 to 3.4)</td>
<td>1.7 (1.5 to 2.1)</td>
</tr>
<tr>
<td>Shingles</td>
<td>2.5 (1.7 to 3.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Obstetric pruritus</td>
<td>NS</td>
<td>2.1 (1.6 to 2.7)</td>
</tr>
</tbody>
</table>

PBC, primary biliary cirrhosis
containing a variety of chemicals. However, intriguingly, other work by Gershwin’s groups has found that several chemicals (most notably octynoic acid) commonly found in cosmetics, including hair dye and nail polish, may react with endogenous pyruvate dehydrogenase increasing its immunogenicity, and may lead to reduced immunotolerance in animal models. This has been proposed as a potential route for breakdown of immunotolerance. The lack of an association with hair perming, a previously unstudied risk factor, in the current study suggests that this is a specific association with particular xenobiotics and adds further weight to these theories concerning cosmetic usage. Ala et al undertook a geographical case-control study and identified proximity to ‘superfund’ waste disposal sites as a further risk factor for PBC, postulating that as yet unidentified environmental xenobiotics may explain this link.

The association between PBC and smoking has been consistently observed across all four epidemiological studies of PBC. At present there is no clear explanation of this association. One recent study reported that smoking is associated with more advanced hepatic fibrosis in PBC. The authors did not have a clear explanation for this association but postulated that it might result from alterations in the balance of T lymphocyte sub-types or increased levels of the pro-fibrotic cytokine interleukin 13. Screening studies have shown that it is likely that the majority of cases of PBC are sub-clinical. It is possible therefore that the observed association with smoking is due to smoking being a risk factor for more advanced disease that is more likely to be diagnosed rather than development of PBC per se.

The negative association between PBC and recent alcohol intake has previously been reported by Gershwin et al. Recall bias, confounding or reduction in alcohol intake after a patient has been told he/she has a ‘liver condition’ may also explain the finding in our study. Patients with PBC often report feeling a stigma that ‘liver disease must be due to drinking’. Our results, taken together those of Gershwin, suggest that it is very unlikely indeed that alcohol consumption has any causal relationship with PBC, a finding that is important to many patients. However, we can find no plausible biological explanation to support a true negative link, and think this too is unlikely.

We did not identify any association between being breast fed as a child and PBC. This potential risk factor had not previously been reported from case-control studies. This has been suggested as a route of exposure to a mouse mammary tumour virus, like retrovirus, described by Mason et al, although not by other authors. The association seen with urinary tract infections has been reported in several previous studies. Although associations with Escherichia coli have been reported by a number of authors, it is not possible on the basis of our study to separate a possible causative role for urinary pathogens from increased urinary tract infections reflecting general ill health secondary to PBC itself.

In keeping with all previous studies we found that PBC was more common in patients with a family history of the disease. This is likely to reflect shared genetic vulnerability factors (eg HLA haplotypes). This result is in keeping with several other studies that have shown a higher than expected frequency of PBC in family members of index cases (and the sibling relative risk of 10.5). The apparent association with obstetric pruritus has not been identified previously. The nature of our study meant it was not possible to verify whether any of the respondents describing this had documented objective markers of obstetric cholestasis and thus it is not possible to exclude this association resulting from recall bias. However, further work is needed to identify whether there may be any shared, possibly genetic, risk factors for obstetric cholestasis and PBC or possibly that pregnancy unMASKS symptomst of otherwise sub-clinical PBC. We did not confirm any other obstetric risk factors for PBC development. Unlike Parikh-Patel we did not find an association with gravidity. Parikh-Patel did not report the sex of patients’ offspring. Our finding of a lack of an association with male offspring adds further evidence against theories of fetal chimerism.

In summary, we have conducted a large case-control study of risk factors for PBC. We confirmed previous results from studies using other survey methods implicating genetic and environmental risk factors for PBC, including smoking, hair dye use and family history of autoimmune disease. This indicates that these associations are extremely likely to be true associations rather than due to type 1 error or artefact. We have also identified obstetric cholestasis as a risk factor. This has not previously been examined in the previous studies and thus requires further study. Some of the risk factors identified (notably hair dye) have plausible mechanisms for inducing disease. Overall, the present study, taken with that by Gershwin et al, lends strong support to the concept of PBC as an autoimmune disorder in which both genetic and multiple environmental factors are very likely to play roles in pathogenesis and clinical expression.

**Acknowledgements** The authors are grateful to the members of the PBC Foundation for their help and cooperation throughout this study.

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**Competing interests** None.

**Ethics approval** The study received ethics approval from all relevant local ethics committees. The study was approved by Northern and Yorkshire MREC [approval reference 1/3/34] and by the following LREC’s: Newcastle and North Tyneside, Gateshead and South Tyneside, County Durham, Northumberland and Sunderland.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**REFERENCES**


Koizumi H, Prolene mesh is seen eroding the sigmoid colon (evidence of diverticulitis or malignancy. At laparotomy the (Permacol) (rhabdies was repaired with porcine collagen prosthesis The abdominal wall defect previously subject to three herniorrhaphies was repaired with porcine collagen prosthesis.


From the question on page 480

The endoscopic views demonstrate intraluminal prosthetic mesh (figure 1, in the question) also seen on axial and sagittal CT (figures 2 and 3, in the question). Histological examination confirmed localised infarction and perforation of the sigmoid colon adherent to the mesh within a field of diverticulosis, but no evidence of diverticulitis or malignancy. At laparotomy the prolene mesh is seen eroding the sigmoid colon (figure 1, below). The abdominal wall defect previously subject to three herniorrhaphies was repaired with porcine collagen prosthesis (Permacol) (figure 2 below).

Prosthetic mesh was first introduced in the 1940s. Initially, only steel mesh was available, but Usher claimed mechanical advantage. Prosthetic mesh was introduced in the 1940s. Initially, only steel mesh was available, but Usher claimed mechanical advantage. But in 1981 Kaufman first reported enterocutaneous fistula formation as a late complication of intraperitoneal placement. Synthetic meshes can produce micro-erosions in adjacent tissues precipitating migration and fistula formation. The asymptomatic detection of this complication through the Bowel Cancer Screening Programme (BCSP) facilitated elective colonic resection with primary anastomosis. Today, problematic hernia are usually repaired with an extraperitoneal approach. If only an extraperitoneal repair is possible; repair utilising collagens such as Permacol, or synthetic composite meshes which employ a conventional prolene layer and a non-adhesive polytetrafluoroethylene layer.

Gut 2010;59:512. doi:10.1136/gut.2009.177170a

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