Comment

The survey clearly disclosed widespread public ignorance of the elementary facts relating to testicular cancer. Hence, not surprisingly, most of the respondents had never heard of a self examination procedure and only five men (1·3%) examined themselves regularly. The biased nature of the study group in favour of better education highlights the findings. We should reasonably expect a better appreciation of health matters in these men than in the general population.

The positive aspects of the results indicate the way for future action. The affirmed interest by nine out of 10 men for more information assures any prospective health campaign of a receptive target group. The excellent cure prospects in testicular cancer will allow an education programme to be conducted in a very open manner; this does not apply to tumours of other sites. On the basis of these and more extended results a national publicity campaign is now under way by the Irish Testicular Tumour Registry.[3]

We thank the Irish Civil Service Building Society, the Educational Building Society, and the Electricity Supply Board for their help in this study. The Irish Testicular Tumour Registry is funded by the Irish Cancer Society.

1 Scher H, Bosl G, Geller N, Cirrincione C, Whitmore W, Golby R. Impact of symptomatic interval on prognosis of patients with stage III testicular cancer. *Urology* 1983;**21**:559-61.
2 Cummings KM, Lampone D, Mettlin C, Edson Pontes J. What young men know about testicular cancer. *Prev Med* 1983;**12**:326-30.
3 Thornhill JA. *Testicular cancer and self-examination: what you should know*. Dublin: Irish Cancer Society, 1986.

(Accepted 10 June 1986)

Irish Testicular Tumour Registry, Dublin 4, Ireland
JOHN A THORNHILL, FRCSI, research fellow
RONAN M CONROY, BA, medical statistician
DANIEL G KELLY, MCH, FRCSI, consultant urologist
ANTHONY WALSH, FRCSI, consultant urologist
JAMES J FENNELLY, MD, FRCPI, consultant oncologist and professor
JOHN M FITZPATRICK, MCH, FRCSI, consultant urologist and professor of surgery

Correspondence to: Mr Thornhill.

Smoking and colonic mucus in ulcerative colitis

Patients with ulcerative colitis tend to be non-smokers,[1] and it has been suggested that smoking may protect against the disease.[2] Colonic mucus in ulcerative colitis has been shown to be qualitatively and quantitatively abnormal,[3] and cigarette smoking is known to produce hypersecretion and modification of respiratory mucus by systemic as well as local effects.[4] We have therefore investigated colonic mucus production in vitro in patients with ulcerative colitis and assessed the possible influence of smoking.

Patients, methods, and results

Patients attending for routine colonoscopy answered a detailed questionnaire which included details of smoking habits and other relevant social and clinical data. Patients were then divided into a group with ulcerative colitis and a "control" group (comprising 63 subjects with diverticular disease or irritable bowel syndrome, 18 with colonic carcinoma, and 40 with colonic polyps). Clinical diagnosis was confirmed by independent histological examination of fixed biopsy material.

The control group contained 70 non-smokers and 51 current smokers (42%), while the ulcerative colitis group contained 71 non-smokers and 11 current smokers (13%), emphasising the infrequency of smoking among patients with ulcerative colitis.

Biopsy specimens were obtained from the descending colon (adjacent to the site used for histological diagnosis) and, using established tissue culture techniques, incubated in Roswell Park Memorial Institute culture medium 1840 containing 10 mg fetal calf serum per ml, 100 μg gentamicin per ml, and 1·25 μCi (46·2 kBq) D-[l-^{3}H]-glucosamine hydrochloride (specific activity 2·2 Ci (81·4 GBq)/mmol) at 37°C in a mixture of 5% carbon dioxide and 95% air for 24 hours. Glucosamine is incorporated into the carbohydrate chains of the newly synthesised mucus glycoproteins. After tissue culture the specimens were homogenised and an aliquot of the homogenate assayed for total protein concentration by a modified Lowry method. The mucus glycoproteins were extracted by precipitation with trichloroacetic acid and phosphotungstic acid.[5] The resultant protein and glycoprotein pellet was solubilised and synthesised mucus quantified by liquid scintillation counting of the newly incorporated tritiated glucosamine. After extensive dialysis to remove unincorporated label the culture medium was precipitated and counted in the same way. The results from the biopsy and medium fractions were combined to give total mucus glycoprotein production.

Compared with the controls incorporation of tritiated glucosamine was significantly less ($p<0·05$) in patients with ulcerative colitis (table). In the non-smoking patients the total mucus production was significantly less ($p<0·05$) than in non-smoking controls, but there was no difference between the ulcerative colitis patients who smoked and smoking controls. Smoking had no apparent effect on control patients.

Total glycoprotein production (dpm/mg) biopsy protein x 10^{-4}). Values are means (standard errors in parentheses)

	All patients	Non-smokers	Smokers
Controls	152·6 (11·1) [n=121]	151·7 (27·3) [n=70]	146·4 (16·3) [n=51]
Ulcerative colitis	117·6 (10·1)* [n=82]	112·1 (10·2)† [n=71]	153·4 (35·6) [n=11]

*Significantly less than controls (Mann-Whitney U test: $p<0·05$).
†Significantly less than non-smoking controls (Mann-Whitney U test: $p<0·05$).

Comment

Mucus is an essential component of the intestinal mucosal defences. The colonic mucus of patients with ulcerative colitis is structurally altered and may be defective, possibly by not possessing the functional integrity for complete epithelial protection. Incorporation of glucosamine into newly synthesised glycoprotein is a well established procedure for assessing mucus biosynthesis in vitro.[5] In our study patients with ulcerative colitis showed reduced glucosamine incorporation into colonic mucus compared with controls, and ulcerative colitis patients who did not smoke showed reduced mucus production compared with non-smoking controls. Ulcerative colitis patients who smoked, however, had mucus production similar to that of all control patients.

The increased mucus production seen in colitic patients who smoke may be important in increasing the quantity and improving the quality of the mucosal barrier and may be a factor in explaining how cigarette smoking, or the use of nicotine, might protect against ulcerative colitis, as has been suggested.[2]

We acknowledge helpful discussion with Professors A Allen and J Clamp and Dr F Roe, and financial support from the Tobacco Advisory Council.

1 Heatley RV, Thomas P, Prokipchuk EJ, Gauldie J, Sieniewicz DJ, Bienenstock J. Pulmonary function abnormalities in patients with inflammatory bowel disease. *Q J Med* 1982;**203**:241-50.
2 De Castella H. Non-smoking: a feature of ulcerative colitis. *Br Med J* 1982;**284**:1706.
3 Podolsky DK, Isselbacher KJ. Glycoprotein composition of colonic mucosa. *Gastroenterology* 1984;**87**:991-8.
4 Kollerstrom N, Lord PW, Whimster WF. A difference in the composition of bronchial mucus between smokers and non-smokers. *Thorax* 1977;**32**:155-9.
5 MacDermott RP, Donaldson RM, Trier JS. Glycoprotein synthesis and secretion by mucosal biopsies of rabbit colon and human rectum. *J Clin Invest* 1974;**54**:545-54.

(Accepted 9 June 1986)

Department of Medicine, St James's University Hospital, Leeds LS9 7TF
G F COPE, BSC, MIBIOL, research assistant
R V HEATLEY, MD, MRCP, senior lecturer in medicine and consultant physician
J KELLEHER, PHD, senior lecturer in biochemistry in relation to medicine

Correspondence to: Mr Cope.

Treatment of functional abdominal pain by transcutaneous electrical nerve stimulation

Functional abdominal pain may be defined as pain for which no structural, biochemical, or infective cause can be determined. Transcutaneous electrical nerve stimulation has been used for years to alleviate chronic pain,[1] but to our knowledge this is the first report of its use for the relief of functional abdominal pain.

Patients, methods, and results

Twenty nine patients with intractable abdominal pain diagnosed as functional in a gastroenterological clinic by an appropriate history[2] with normal findings on physical examination, sigmoidoscopy, and investigations (full blood count, sedimentation rate, serum urea and electrolyte concentrations, liver function values, and barium enema as a minimum) were treated with transcutaneous

electrical nerve stimulation for at least one month. None had been helped by diet or drug treatment.

A physiotherapist explained the nature of transcutaneous nerve stimulation and assessed the intensity of pain using a visual analogue scale.[3] Transcutaneous nerve stimulation was given using a Neen system 7737 stimulator (Neen Pain Management Systems, Swanton Morley, Dereham, Norfolk), which delivered an electrical stimulus of 9 V, frequency 30-100 Hz, pulse width 200 μs. The stimulating electrodes were initially placed over the site of the pain, but if this produced no effect other positions were tried, either paraspinally over the dorsal root of the affected dermatome or on the appropriate acupuncture sites. After an instruction period of one hour the patients were lent a machine to assess its benefit over one month. During this time they were seen at two and four weeks, when further assessments of pain severity were made. Changes in pain intensity were calculated as the percentage alteration in the visual analogue score from the original reading[3] and the patients divided into three groups: no response (<33% reduction), moderate response (33-66% reduction), and good response (>66% reduction).[2] Eight patients with no response stopped treatment within the first four weeks; the remainder were followed up for at least six months (maximum 11 months).

The initial mean values on the visual analogue scale were the same in the three groups whatever the response (8·7, 8·7, and 9·2 respectively). Twenty one patients reported benefit from the treatment at one month, and 15 of these continued the treatment for at least six months (table). At six months 10 reported a good response and five a moderate response. The effective sites of electrode placement in those who initially responded (n=21) were over the site of pain in 17, paraspinally in five, and at the acupuncture points in two; three patients responded at more than one site. In those who continued treatment the mean pain score on the visual analogue scale at six months was 4·1 in those with a moderate response and 1·4 in those with a good response. The six people who discontinued treatment between one and six months did so either because of a loss of effect (four cases) or because they were unable to afford a machine (two cases).

Numbers of patients with functional abdminal pain responding to transcutaneous nerve stimulation at one, three, and six months

	Follow up (months)		
	1	3	6
Good response	15	13	10
Moderate response	6	6	5
Stopped treatment	8	10	14
Total	29	29	29

Comment

Severe functional abdominal pain is often difficult to treat. The results of this open trial show that transcutaneous electrical nerve stimulation may provide relief from this condition over at least six months. The treatment is acceptable to the patients (15 bought their own machines) and is harmless.

We accept that the pain reduction seen in these patients may have been placebo response but we doubt that this is the whole explanation. A placebo response to any treatment in functional abdominal pain may initially be as high as 70%, but this response is rarely maintained for more than two months.[4] Unfortunately, it is difficult to undertake a blinded trial of transcutaneous electrical nerve stimulation because of the associated tingling. Attempts have been made in the laboratory to compare transcutaneous nerve stimulation with a supposed subthreshold electrical stimulation reinforced by a visual wave seen on an oscillograph,[5] but this technique did not seem appropriate for our study. Whatever the mechanism we conclude that transcutaneous nerve stimulation may help some patients with functional abdominal pain unresponsive to drugs.

GK is the W E G Knott research fellow of the British Digestive Foundation.

1 Loeser JD, Black RG, Christmas A. Relief of pain by transcutaneous stimulation. *J Neurosurg* 1975;42:308-14.
2 Manning AP, Thompson WG, Heaton KW, Morris AF. Towards a positive diagnosis of the irritable bowel. *Br Med J* 1978;ii:653-4.
3 Huskisson EC. Measurement of pain. *Lancet* 1974;ii:1127-31.
4 Holdsworth CD. Drug treatment of irritable bowel syndrome. In: Read NW, ed. *Irritable bowel syndrome*. London: Grune and Stratton, 1985:223-32.
5 Thorsteinsson G, Stonnington HH, Stillwell GK, Elveback LR. The placebo effect of transcutaneous electrical stimulation. *Pain* 1978;5:31-41.

(Accepted 12 June 1986)

St Mark's Hospital, London EC1V 2PS
KAREN SYLVESTER, MCSP, physiotherapist
G P N KENDALL, MRCP, clinical assistant, department of medical research
J E LENNARD-JONES, MD, professor of medical research

Correspondence to: Dr Kendall.

Cigarette smoking and prolactin in women

Recent reports have shown that cigarette smoking may be associated with low prolactin concentrations in premenopausal women.[1] Although this has been confirmed experimentally in rats,[1,2] there has been no investigation in postmenopausal or younger women in the general population. We present an analysis of cigarette smoking and prolactin concentrations in a large group of healthy premenopausal and postmenopausal women.

Methods and results

All data were from the third phase of the Guernsey study, a prospective investigation of hormones and risk of breast cancer. Over 5000 women aged 30 or over and living on Guernsey volunteered to provide blood and urine specimens and complete a health questionnaire. Although a history of cigarette smoking was not routinely gathered, the first 732 subjects were questioned about their smoking habits for another study.

Blood samples were drawn between 1300 and 1930 hours, and serum was frozen at −20°C. Prolactin was measured using the method of Kwa and Wang (normal concentration ≤1·2 nmol/l (30 μg/l)).[3] Women who had menstruated in the six months previously were considered premenopausal; all others were considered postmenopausal. Women who had had a hysterectomy (with or without oophorectomy) formed a separate group for analysis. Women taking drugs that alter the concentration of prolactin (phenothiazines, reserpine, methyldopa, tricyclic antidepressants, metaclopramide, oral contraceptives, and oestrogens) were excluded from analysis, as were those for whom drug information was incomplete.

Because of the skewed distribution of prolactin measurements geometric means were used to summarise the data, and analysis of covariance was performed on log transformed values to assess the impact of various factors.

After exclusions for missing data and drugs 508 subjects remained for analysis. The table summarises geometric mean prolactin concentrations by smoking and menopausal state. In both smoking and non-smoking groups premenopausal women had higher prolactin concentrations than postmenopausal women.

Subject details and geometric mean prolactin concentrations

	Smokers*	Non-smokers*
Mean (SD) age (years)	47·6 (8·8)	48·7 (9·2)
Mean (SD) weight (kg)	64·0 (10·9)	64·5 (10·0)
Mean (SD) parity	2·4 (1·6)	2·2 (1·3)
Mean (SD) hour of blood draw	1649 (113 min)	1646 (109 min)
Geometric mean prolactin (nmol/l):		
Premenopausal women (No)	0·38 (60)	0·44 (213)
Naturally menopausal women (No)	0·29 (33)	0·32 (119)
Surgically menopausal women (No)	0·24 (11)	0·34 (70)

*Excluding women taking prolactin altering drugs.
Conversion: SI to traditional units—Prolactin: 1 nmol/l=0·04 μg/l.

Conversely, within both the premenopausal and postmenopausal groups women who smoked had lower prolactin concentrations than non-smokers. Analysis of covariance showed that after control for age and weight, menopausal state and smoking were highly significant (p<0·01). There was no support for variation in the smoking effect by menopausal state, as the interaction between these two variables was not significant.

Comment

The differences we found were unlikely to have been due to intake of drugs because of the strict inclusion criteria used. Age and weight were considered as covariates and could not explain these effects. Meals may alter prolactin concentrations, but there was no indication that the subjects who smoked differed from non-smokers in the time their blood was taken.

Our results agree with previous findings that smoking or parenteral nicotine is associated with low prolactin concentrations.[1,2] Some studies using human subjects found smoking to be associated with increased prolactin concentrations but these assessed acute changes after smoking.[4] All studies, like ours, that compared long term smokers with long term non-smokers have found lower concentrations among smokers. A similar distinction between short term and longer term effects has been found in rats.[5]

As dopamine inhibits prolactin secretion our results suggest that smoking has a clinically important dopaminergic influence in the central nervous system. The negative association between Parkinson's disease and smoking is consistent with this view.[1] Indeed, experiments with rodents have confirmed that cigarette smoke increases dopamine turnover in the central nervous system.[2] Because dopamine may inhibit secretion of luteinising