Plasma $\text{PGF}_{2\alpha}$ concentrations in female genital tract malignancy

Patient No	Age (years)	Diagnosis	Plasma $\text{PGF}_{2\alpha}$ concentration (ng/l)
1	65	Carcinoma ovary stage III	88
2	41	Carcinoma ovary stage III	97
3	52	Carcinoma ovary stage III	70
4	58	Carcinoma ovary stage III	65
5	59	Carcinoma ovary stage III	45
6	16	Carcinoma ovary stage IV	61
7	76	Carcinoma ovary stage IV	92
8	62	Carcinoma ovary stage IV	59
9	65	Carcinoma endometrium stage I	34
10	64	Carcinoma endometrium stage I	39
11	57	Carcinoma cervix stage I	25
12	60	Carcinoma cervix stage IV	94
13	69	Mixed Mullerian tumour stage IV	94

Blood $\text{PGF}_{2\alpha}$ levels were measured by radioimmunoassay² in 13 untreated patients with gynaecological cancer presenting to this centre. The results are shown in the table and indicate a uniform elevation above the range (9–24 ng/l) established in our laboratory for normal adult women. A positive correlation with the stage of the disease is also apparent.

In common with other forms of malignant disease tumours of the female genital tract are associated with raised blood levels of $\text{PGF}_{2\alpha}$. The mechanism of this association is unclear but most likely reflects abnormal PG production by neoplastic cells. One practical implication of this finding is the possibility that hypercalcaemia and osteolysis occurring in advanced malignancy³ may be caused by the osteolytic effect of $\text{PGF}_{2\alpha}$ and not be due to bone secondaries.

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² Dray, F, Charbonnel, B, and MacLough, J, *European Journal of Clinical Investigation*, 1975, **5**, 311.

³ Powles, T J, *Proceedings of the Royal Society of Medicine*, 1977, **70**, 199.

Schizophrenia and neurosis

SIR,—Your leading article (8 July, p 76) on the predominance of neurotic complaints in a group of chronic schizophrenics treated in the community quotes, from Cheadle *et al*¹, surprise that this should be the case. It furthermore reiterates their assertion that neurotic symptoms are the major stumbling block to rehabilitation within the community.

Might I suggest that the work of Cheadle *et al* merely confirms something which has been known for the greater part of this century—that premorbid adaptation has a considerable bearing on recovery from schizophrenic breakdown? A 100-year review² of the literature on premorbid personality and schizophrenia illustrated well that in many

studies chronicity has a relationship to poor premorbid personality, and presumably the latter is a major determinant in so-called neurotic symptoms in the group studied.

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¹ Cheadle, A J, Freeman, H L, and Korner, J R, *British Journal of Psychiatry*, 1978, **132**, 221.

² Fritsch, W, *Fortschritte der Neurologie, Psychiatrie und ihrer Grenzgebiete*, 1976, **44**, 323.

Colonoscopy in the diagnosis of pseudomembranous colitis

SIR,—Dr A Kappas and his colleagues (18 March, p 675) are of the opinion that pseudomembranous colitis (PMC) is far more common than the sporadic published reports would suggest, a view which, as stated in your leading article in the same issue (p 669) has also been expressed by others.¹ Dr Kappas and his co-workers believe also that the only means of avoiding a high mortality rate is to establish the diagnosis promptly and give early supportive treatment. They conclude that careful, repeated sigmoidoscopy should be performed in all clinically suspected cases and in any patient with an unexplained complication after a colorectal operation.

But, as Bartlett and Gorbach in their excellent review of PMC pointed out,² one must also remember that the anatomical location of pseudomembranes includes virtually all portions of the intestinal tract. When the colon is attacked the more severe lesions occur in the proximal portion—the caecum and ascending colon. In patients with antibiotic-related disease the major impact of the disease is in the colon. This is evident also in some clinical studies. For example, Dr Kappas and his colleagues performed sigmoidoscopy on 20 patients with PMC but found membranes in only 13, while the appearances were normal in two. Price and Davies³ found typical plaques on sigmoidoscopy in only 14 out of 21 cases. Bearing in mind how serious a disease PMC can be, it does not seem to me that investigation by repeated sigmoidoscopy with biopsy and faecal toxin tests is sufficient to make an early diagnosis of PMC in all cases. Colonoscopy in skilled hands is safe,⁴ and I believe that the risk of perforation is not very great in the early stages of PMC with less severe mucosal changes. My own experience of colonoscopy for the diagnosis of PMC has been good, as the following case history shows.

A 27-year-old electrician was admitted with severe abdominal pain and bloody diarrhoea after three days' amoxicillin treatment (total dose 3.375 g). He had previously had abdominal pain and diarrhoea after penicillin treatment five years previously but had since been well except for symptoms of allergic rhinitis.

In the emergency room his temperature was 37.5°C, leucocyte count $21.9 \times 10^9/\text{l}$ ($29\,000/\text{mm}^3$), serum total protein 55 g/l. Sigmoidoscopy showed a totally normal rectal mucosa, but the contents of the sigmoid colon were brightly bloodstained. Next day I carried out a bedside colonoscopy with biopsy without x-ray or special bowel preparation. The rectum was normal, but at a height of 30 cm there was a heavily bleeding mucosa with gray plaques. The examination was stopped when it was seen that the whole descending colon was diseased except for some small areas with visible blood vessels. Although it was impossible to make a definite diagnosis because of the similarity of the colonoscopic picture to that of ulcerative

colitis and our case, a tentative diagnosis of PMC was made. The patient was treated with intravenous fluids and orally metronidazole 500 mg twice daily. The abdominal pain and bloody diarrhoea disappeared in five days and the patient made a full recovery.

The biopsy specimens taken at colonoscopy from diseased areas at the level of the sigmoid and ascending colon were later found to show the typical diagnostic features of PMC. After 10 days a control colonoscopy was performed, with normal findings. Faecal and biopsy specimen cultures taken during the first days in hospital showed only a growth of *Klebsiella pneumoniae* and *Pseudomonas maltophilia* with an otherwise normal flora. Unfortunately, no special investigations for the detection of *Clostridium difficile* or *C. sordelli* were carried out.

I suggest that careful colonoscopy is indicated for the early diagnosis of potentially fatal PMC if the key investigation, sigmoidoscopy, gives negative results.

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¹ Tedesco, F J, Barton, R W, and Alpers, D H, *Annals of Internal Medicine*, 1974, **81**, 429.

² Bartlett, J G, and Gorbach, S L, *Advances in Internal Medicine*, 1977, **22**, 455.

³ Price, A B, and Davies, D R, *Journal of Clinical Pathology*, 1977, **30**, 1.

⁴ Britton, D C, *et al*, *British Medical Journal*, 1977, **1**, 149.

Sulphinpyrazone and prevention of death after myocardial infarction

SIR,—Your leading article (15 April, p 42) which discussed the report of the sulphinpyrazone trial¹ rightly calls for caution in accepting the favourable results without further information. One reason mentioned is the disparity between groups in the incidence and characteristics of arrhythmias. Another perhaps more obvious reason for doubting the results is the fortuitously high incidence of death in the placebo group (9.5%). For patients surviving the first month following myocardial infarction, especially when those with cardiomegaly were excluded, a death rate of 5% per annum or less might have been expected, more in line with the figure of 4.9% for the treated group in the trial. The data for the placebo group in the long-term practolol post-infarction trial² indicate the importance of heart size in prognosis (see table).

Death rate related to cardiac width (data from placebo group in Multicentre International Study¹)

Cardiac width (cm)	Deaths	No of patients	Death rate (%)
≤13	7	309	2.3
14–15	24	658	3.6
16–17	30	316	9.5
≥20	4	33	12.1

Armitage test for linear trend relating increasing death rate with increasing cardiac width significant at 1% level ($P < 0.001$).

A positive role for the platelet in the development of ischaemic heart disease seems very probable and the mode of action of sulphinpyrazone is therefore attractive. However, the long-term use of the drug following infarction should be postponed until a further large trial has confirmed benefit against placebo group figures which are more in accord with general experience. Perhaps