placebo might influence ulcer healing and, by inference, ulcer relapse. In addition, patients could not be allowed access to any antacids as there is now accumulating evidence that even very low doses of antacid may increase ulcer healing rates.[1,2] Clearly, such a study would not be considered ethically justifiable, despite the fact that patients taking "placebo" have a low rate of ulcer related complications.[3]

Although the natural relapse rate of duodenal ulcer remains unknown, some workers have speculated that treatment with H_2 antagonists might actually increase the relapse rate above normal.[4] Several possible explanations, including increased parietal cell mass secondary to hypergastrinaemia, have been proposed but not conclusively shown. It is therefore of great interest that treatment with ranitidine increases the acid output in response to sham feeding.[5] There is now preliminary evidence that acid output in response to the specific H_2 agonist inpromidine is also increased after treatment with a maintenance dose of ranitidine.[6] This observation suggests that the H_2 receptor may be rendered more sensitive to stimulation after treatment with a competitive antagonist—a well recognised phenomenon in other fields. If maximal stimulated acid output is temporarily increased after treatment with an H_2 antagonist then patients might be more likely to sustain an ulcer relapse. This situation would not arise if the patient were treated with a drug which did not affect acid secretion, such as tripotassium di-citrato bismuthate.[7]

Lower relapse rates after treatment with a mucosal protective drug than with an H_2 antagonist may well be genuine but should be confirmed in a single large multicentre trial. There may be theoretical reasons to explain the higher rates with H_2 antagonists when compared with non-acid suppressing drugs, but we still do not really know the natural relapse rate.

COLIN HOWDEN

University Department of Materia Medica,
Stobhill General Hospital,
Glasgow G21 3UW

G D KERR

Royal Shrewsbury Hospital,
Shrewsbury SY3 8XF

1 Kumar N, Vij JC, Karol A, Anand BS. Controlled therapeutic trial to determine the optimum dose of antacids in duodenal ulcer. *Gut* 1984;**25**:1199-202.
2 Weberg R, Berstad A, Large O, Schultz T, Aubert E. Duodenal ulcer healing with four antacid tablets daily. *Scand J Gastroenterol* 1985;**20**:1041-5.
3 Schiller LR, Fordtran JS. Ulcer complication during short-term therapy of duodenal ulcer with active agents and placebo. *Gastroenterology* 1986;**90**:478-81.
4 McLean AJ, Harrison PM, Ioannides-Demos LL, Byrne AJ, McCarthy P, Dudley FJ. Microbes, peptic ulcer and relapse rates with different drugs. *Lancet* 1984;ii:525-6.
5 Frislid K, Aadland E, Berstad A. Augmented postprandial gastric acid secretion due to exposure to ranitidine in healthy subjects. *Scand J Gastroenterol* 1986;**21**:119-22.
6 Jones DB, Howden CW, Burget DW, Silletti C, Hunt RH. Alteration of H_2 receptor sensitivity during maintenance ranitidine treatment. *Gut* 1986;**27**:A1255.
7 Baron JH, Barr J, Batten J, Sidebotham R, Spencer J. Acid, pepsin and mucus secretion in patients with gastric and duodenal ulcer before and after treatment with colloidal bismuth subcitrate (De-Nol). *Gut* 1986;**27**:486-90.

Effect of aspirin on pruritus

SIR,—We wonder why the *BMJ* should publish articles like that by Dr B Martina Daly and Professor Sam Shuster (11 October, p 907). Their unqualified conclusions are not justified from an open study that stood little chance of detecting a clinically important effect with only 13 patients. The data presented in the table are of limited value, as the standard errors quoted are not those of differences. This means that no confidence intervals can be calculated to examine what potential benefit there may be (a policy that we thought your journal had taken on[1]).

Rather than ending the report with a sentence stating that their study gives no support to the view that prostaglandins play a part in the itch of inflammatory dermatoses, they should have ended by saying that their study gives no evidence either way.

JOHN THORNE
SIMON J DAY

Department of Clinical Epidemiology,
London Hospital Medical College,
London E1 1BB

1 Gardner JR, Altman DG. Confidence intervals rather than P values: estimation rather than hypothesis testing. *Br Med J* 1986;**292**:746-50.

AUTHORS' REPLY,—Our wonder is how the editor found our paper under the heap of statistician led studies, the dementing effect of which is spreading into clinical research like the acquired immune deficiency syndrome.

The idea that you cannot detect any clinically important effect in an open study of 13 patients is at best a statistical scotoma and at worst an economy of truth. If you sharpen your question and refine your measuring technique you can detect the effect of drugs in as few as 6-10 patients, as we have shown for sebum and antiandrogens, wealing and antihistamines, sweating and anticholinergics, lesion thickness and anthralin, and many other activities. But very many more patients would have been required had we left definition of response in the statistically acceptable but scientifically soft reaches of clinically assessed acne, urticaria, sweating, and psoriasis. The ability to detect change is a function of method, which is why we prefer to design and use objective methods of measurement. Using one such method to measure the subjective sensation of itch by nocturnal scratch movement we found no effect of aspirin on itch, and analysis of the data as difference does not negate that negative finding.

Of course, a double blind regimen would have improved the study (as would randomisation, placebo control, and group homogeneity of disease and severity), but the need for that design would have had more force had we actually found an antipruritic effect and therefore needed a placebo and bias control. Or do Messrs Thorne and Day think that our patients, perversely, and in concert, as well as in their sleep, were deliberately scratching more than they should have been so as to conceal from mankind a beneficial antipruritic effect of aspirin, which, in any case, none of us would have known was there until the study was complete? Statistical rigour and good design are essential to clinical trials, but much of their unreliability and tedium could be avoided if less time were spent on their execution and more on the definition of useful questions and development of objective methods for measuring biological answers.

Statistics is a small part of methodology; it says more about what you cannot do than what you can do and is rarely creative. It cannot therefore be allowed to dictate the needs of clinical science; we have too many studies with a reliable statistical provenance and a negligible biological future. The impending season of good will should help as the hard line statistical Cassandras are replaced by user friendly software packages on the Christmas tree.

MARTINA DALY
SAM SHUSTER

University Department of Dermatology,
Newcastle upon Tyne NE1 4LP

Clinical and bronchoscopic diagnosis of suspected pneumonia related to AIDS

SIR,—A clear division is emerging in the recommended optimal management of suspected pulmonary complications in patients infected with human immunodeficiency virus. The recent report from the Middlesex Hospital (27 September, p 797) attempts to provide support for a non-invasive "best guess" approach, in which a presumptive pathogen is treated and investigation reserved for those who fail to respond. We have adopted a different policy of investigating all patients before treatment with fibreoptic bronchoscopy, bronchoalveolar lavage, and transbronchial biopsy.[1] To date over 100 examinations have been performed with few complications.

There are three main advantages in this approach. Firstly, the pathogen causing the infection is known, and appropriate treatment can be instigated with confidence. A wide variety of pathogens, which may be multiple, are recognised,[1,2] and, although helpful, chest radiology is certainly not diagnostic. A therapeutic response to "high dose" co-trimoxazole does not preclude the possibility of an infection with bacteria sensitive to co-trimoxazole. Secondly, identification of *Pneumocystis carinii*, or another opportunist organism, establishes the diagnosis of the acquired immmune deficiency syndrome (AIDS). This allows appropriate discussion of the disease and prognosis with the patient in a way not possible if the diagnosis has only the precision of "co-trimoxazole responsive pneumonia." This aspect is also likely to be of ever greater importance as the disease spreads into the lower risk heterosexual community. Thirdly, confirmation of the diagnosis of AIDS, on the basis of identifying a recognised opportunist infection, allows rational decisions to be made on the appropriateness of assisted ventilation in a patient deteriorating despite high dose co-trimoxazole. This is impossible if other differential diagnoses such as tuberculosis, cytomegalovirus, cryptococcus, pneumococcus, and legionnaires' disease have not been excluded.

Our policy in managing pulmonary complications in patients suspected of having AIDS has been very similar to that followed in the United States centres, which have greater experience. A clinical algorithm outlining the recommended diagnostic procedures has been presented,[2] which we believe presents a more appropriate approach than that indicated by the Middlesex team. We think that British physicians should take the opportunity to assess the full range of current thinking in this increasingly important subject before adopting the technically easier, but in our view less satisfactory, "best guess" approach.

R J SHAW
A J PINCHING
E E KEAL

Department of Immunology,
St Mary's Hospital Medical School,
London W2 1PG

1 Warren JB, Shaw RJ, Weber JN, Holt DA, Keal EE, Pinching AJ. Role of fibre-optic bronchoscopy in management of pneumonia in acquired immune deficiency syndrome. *Br Med J* 1985;**291**:1012-3.
2 Hopewell PC, Luce JM. Pulmonary manifestations of the acquired immunodeficiency syndrome. In: Pinching AJ, ed. *Clinics in immunology and allergy: AIDS and HIV infection*. Philadelphia: W B Saunders Co, 1986.

SIR,—The approach of Dr A L Posniak and others (27 September, p 797) should be welcomed as an attempt to simplify the diagnosis of the patient with AIDS associated pneumonia, but it does raise