treatment of asthma. Indeed, it became clear in the course of discussion that the company itself had anticipated many of the objections to the compound aerosol and it tacitly acknowledged that the proposed development was related to the imminent expiry of the patent applying to Ventolin.

I have no means of knowing whether the company's medical division attempted to persuade those responsible for developing Ventide that its introduction would be as undesirable as it was unnecessary: if any attempt was made, it did not prevail. Consequently, some special pleading has been made to justify Ventide's introduction. It has been claimed that it will "improve compliance, especially with the Becotide component" on the ground that some patients who have been prescribed beclomethasone diproprionate alone "stop taking it or use it only intermittently because it does not have an instant effect."[3]

There are better ways to solve this problem than by misleading patients into believing that beclomethasone diproprionate, the more important of Ventide's two constituents, confers immediate benefit. While I do not wish to imply that Allen and Hanburys regarded this as a commercially attractive aspect in the marketing of Ventide, I cannot believe that the company did not foresee the likely consequences of confusion among patients, particularly with the precedent of Intal Compound. At the time of the introduction of Intal Compound, however, there appeared to be valid reasons for combining cromoglycate with isoprenaline to facilitate inhalation. No such justification can be offered for combining beclomethasone diproprionate with salbutamol. In the first place, a more rapidly acting beta agonist would have been a more logical choice than salbutamol and, secondly, it was shown in a recent trial that the inhalation of salbutamol either 10 minutes before or after beclomethasone diproprionate made no difference to the overall control of asthma.[4]

The data sheet describing Ventide states that the compound aerosol has been "specially provided for those patients who require regular doses of both drugs." Yet the principal objection to it (which applies to all compound preparations) is that it permits no flexibility of dosage of its individual constituents. Hence, 600-800 μg of salbutamol per day must be taken in order to attain the conventional daily dose of 300-400 μg of beclomethasone diproprionate. The conventional dose of beclomethasone diproprionate, however, often proves inadequate to control asthma during exacerbations, and in some patients a higher dose is permanently required.

In few other diseases is it as important as in asthma to instruct patients about the action and purpose of whatever treatment they have been advised to take. If all doctors invariably give a clear explanation about the purpose of beclomethasone diproprionate and emphasised that it does not give rise to any immediately perceived relief, non-compliance, which Ventide has been claimed to prevent, would become much less frequent.

It is ironic that at the very time it has marketed Ventide Allen and Hanburys is about to embark on educational programmes for general practitioners in the management of asthma. The findings from some of my own research studies (which it gives me pleasure to acknowledge have received generous support from Allen and Hanburys) suggest that improved management of asthma in general practice will come about only when treatment is prescribed on a rational basis. This depends on a full assessment of the patient and of the prevailing circumstances, then making inferences about the mechanisms responsible for airflow limitation. This procedure will suggest the form of treatment that is most appropriate.

I would hope that the educational programmes planned by Allen and Hanburys will endorse this principle of rational treatment. If so, their sales force will have an unenviably difficult task in promoting Ventide and it will be interesting to see whether their representatives perform it with the same probity and responsibility as they showed over the promotion of Becotide.

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****Allen and Hanburys reply below.—ED, *BMJ*.

SIR,—The many factors that affect the decision to market a new product—albeit in this case a combination of two well established compounds—are extremely complex. They include pharmaceutical, pharmacological, medical, and commercial principles, and advice on all these aspects is taken from a large number of experts, both from within the company and externally. We are grateful to Dr Gregg for his help and counsel but should emphasise that his view was one of a wide variety of clinical opinions that were expressed.

The commercial considerations were of minor importance. Contrary to Dr Gregg's assertion, the patent on Ventolin has still a number of years to run. Allen and Hanburys is concerned with and has a major interest in the sound management of patients with asthma. We therefore agree with all that Dr Gregg says regarding the importance of a rational approach to treatment.

Ventide is formulated to provide the most commonly used maintenance doses of Ventolin and Becotide in one inhaler and is primarily for use by those patients who have previously been stabilised with Ventolin and Becotide in this dose ratio. Our promotion of the product, an example of which is appearing in the *BMJ*, reinforces this message and is not aimed at misleading either doctors or patients.

The convenience of one inhaler for maintenance treatment should improve compliance and ensure that patients actually take their beclomethasone dipropionate. It is well recognised that when patients have to use both Ventolin and Becotide inhalers regularly there is a tendency to default on one. It is usually Becotide that is missed out, sometimes with serious consequences. By combining both drugs in one inhaler we hope that this problem will be avoided.

Beclomethasone dipropionate is an important therapeutic agent for those patients with chronic forms of asthma, and we believe that Ventide will make a positive contribution to patient management.

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Vaginal discharge

SIR,—Professor Michael W Adler's ABC of vaginal discharge (19 November, p 1529) puts *Gardnerella vaginalis* sixth in a list of pathological causes and goes on to describe the clinical and diagnostic features of this infection. Our experience with this organism differs in several aspects. Firstly, we find that *G vaginalis* rarely occurs on its own in non-candidal, non-trichomonal vaginal infection, large numbers of anaerobic bacteria being an almost invariable accompaniment.[1 2] It was for this reason (among others) that a more descriptive and microbiologically accurate name, anaerobic vaginosis has been proposed.[2 3] Secondly, we feel that the long held view of *Candida* as the most common cause of vaginal infection may need to be revised. In 1982 we saw 2860 women with anaerobic vaginosis, 2337 women with candidiasis, and 1074 women with trichomoniasis. Anaerobic vaginosis may be underdiagnosed elsewhere. On the exceptionally rare occasions that *G vaginalis* is found alone, the vaginal pH may not be raised but the amine test is always negative.[2]

The suggestion that, when only limited culture facilities are available, investigation for chlamydial infection should be restricted to contacts of men with non-specific urethritis or gonorrhoea is topsy turvy. It is widespread practice to treat the former with antichlamydial antibiotics anyway and the latter are known to have a high incidence of positive isolations.[4] Surely the group to be investigated are those with no history of contact, for whom the lack of a diagnosis may give rise to complications both social and clinical?[5]

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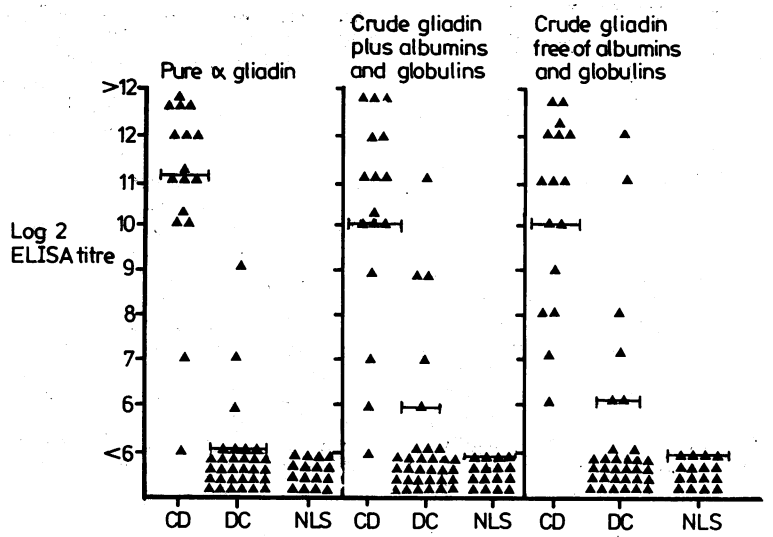
Gliadin antibody levels in screening tests for coeliac disease

SIR,—Dr Cliona O'Farrelly and others claim that an enzyme linked immunosorbent assay test using purified α gliadin rather than crude gliadin (containing α, β, γ and ω gliadins) improves discrimination between untreated patients with coeliac disease and control subjects.

We performed essentially similar studies some time ago, and our results point to a different conclusion. In our enzyme linked immunosorbent assay test, we coated the wells overnight at 4°C with wheat protein at a concentration of 20 μg/ml in 60% ethanol/water, but otherwise the methods were similar.[1] We compared three different wheat protein preparations, each derived from the wheat variety known as Flander's. α Gliadin (preparation 1) was prepared as described by Patey and Evans[2]; crude gliadin contaminated with wheat albumins and globulins was prepared by direct extraction of flour with 70% ethanol (preparation 2); and crude gliadin free of albumins and globulins (preparation 3) was prepared by salt precipitation (1·5% sodium chloride) of preparation 2. The preparations were carefully characterised by polyacrylamide gel electrophoresis in aluminium lactate buffer pH 3·1.[3]

We first tested serum from 16 adults (mean age 47·5 years) with coeliac disease proved on biopsy, 32 adults (mean age 43 years) with miscellaneous

gastrointestinal complaints (including Crohn's disease, ulcerative colitis, aphthous ulceration, duodenal ulcer, liver disease), and 16 healthy laboratory staff (mean age 34·5). Each serum sample was screened by enzyme linked immunosorbent assay against the three wheat protein preparations mentioned above, and the antibody titre determined with an antihuman Ig reagent capable of detecting all classes of immunoglobulin. The figure summarises these preliminary results.



Antibody titres of serum samples from patients with coeliac disease (CD), disease controls (DC), and normal laboratory staff (NLS). ELISA=Enzyme linked immunosorbent assay.

Good discrimination was found between untreated patients with coeliac disease and control subjects irrespective of whether α gliadin or crude gliadin preparations were used. The number of "false negative" results—that is, untreated patients found to be gliadin antibody negative—was lowest when crude gliadin contaminated with wheat albumins and globulins was used as antigen. This was achieved at the cost of increased "false positive" results—that is, control subjects positive for gliadin antibodies—on the basis of these results we decided to use preparation 3 as antigen in an enzyme linked immunosorbent assay,[1] and in a new immunofluorescence test that uses rat tissue sections treated with gliadin as substrate to detect gliadin antibody in patients' sera.[4] Both tests were used in a larger survey of the incidence of serum antigliadin antibodies in adults with gastrointestinal complaints. The table summarises the results, which were the same whichever test was used.

The incidence of false negative results we obtained (15%) is similar to that found by Dr O'Farrelly and others (11%) in spite of our use of crude gliadin as antigen. Although our incidence of false positive results (8%) is slightly higher than theirs (7%), ours was a much larger study. The possibility that the use of α gliadin as antigen in screening tests reduces the incidence of false positives thus remains to be proved.

It is not clear why our findings differ from those of Dr O'Farrelly and others. They cite the results of Kieffer *et al* in support of their view that patients with coeliac disease tend to develop higher antibody titres to α gliadin than to the other gliadins.[5] The titres of α gliadin antibody and crude gliadin antibody found in sera by Kieffer *et al*, however, differed only by one tube dilution. Indeed, these authors concluded that crude gliadin extracts are "a satisfactory antigen for screening for coeliac antibody." It should also be noted that although Kieffer *et al* found α gliadin antibody titres in patients with coeliac disease to be higher than β, γ, and ω gliadin antibody titres, the relative differences were the same in both untreated patients with coeliac disease and normal individuals, the difference between these two groups being one of magnitude and not of preference.

In conclusion, we see no advantage in using purified α gliadin (which is difficult to prepare) as opposed to crude gliadin in screening tests for gluten sensitivity. Our previous work and that of others does, however, show that the presence of IgA antigliadin antibody is more closely associated with gluten induced mucosal atrophy than IgG antigliadin antibody.[6-9] Thus, in the context of screening for gluten sensitivity the antibody class seems to be more important than the range of antibody specificities.

Incidence of antigliadin antibodies in adults with gastrointestinal complaints

	No of patients	No gliadin antibody positive* %
Coeliac disease:		
Untreated	60	51 (85)
Gluten-free diet for 3-6 months	86	16 (13)
Total	146	67 (46)
Disease controls:		
Crohn's disease	47	9 (19)
Ulcerative colitis	46	3 (7)
Liver disease	22	1 (6)
Aphthous ulcers	29	4† (14)
Duodenal ulcer	30	0 (0)
Miscellaneous	40	0 (0)
Total	214	17 (8)

*A negative result was recorded when the antibody titre lay within the normal range.
†Two of these also had coeliac disease.

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SIR,—In agreement with Dr Cliona O'Farrelly and others (25 June, p 2007) we have found that measurement of gliadin antibodies is useful in screening for adult coeliac disease.

We have recently determined IgG gliadin antibodies by a solid phase radioimmunoassay in serum samples from 14 untreated adults with coeliac disease, 13 patients with chronic inflammatory bowel disease (nine with ulcerative colitis and four with Crohn's disease), and 54 normal controls.[1]

Eleven of the 14 untreated patients (mean (SD) of log values: 2·3 (0·7)) had significantly increased levels (more than twice the mean of the control group); only one of the 54 controls (0·9 (0·5) and none of the patients with inflammatory bowel disease (1·1 (0·3)) had high gliadin antibody levels. Thus, our results confirm the good sensitivity (79%) as well as the high specificity (98%) of the test in adults, even though levels found in adult patients are about 10 times lower than those observed in affected infants (unpublished observations).

In contrast to the findings of Dr O'Farrelly and others, our assay showed a good discriminatory value also when crude gliadin was used as antigen; indeed, tested serum samples showed a similar pattern of reactivity to crude gliadin and to A gliadin (kindly provided by Dr Kasarda), a highly purified fraction of α gliadin.[2]

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**The authors reply below.—ED, *BMJ*.

SIR,—The findings of Dr Unsworth and colleagues and of Dr Truncone and colleagues confirm our recently published results that patients with coeliac disease show a significant humoral response to wheat protein antigens. In our study, the use of α gliadin was required to allow good differentiation between patients with coeliac disease and controls. Dr Unsworth and Dr Truncone report that crude (unfractionated) gliadin was an equally effective