# Evaluation of a 'DIY' test for the detection of colorectal cancer

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## Summary
A new type of faecal occult blood test, EZ-Detect™, has been evaluated in 404 patients presenting with symptoms suggestive of colorectal disease. The test avoids handling of stools and gives a result which patients can read themselves - factors which may increase patient compliance. In comparison with the Haemoccult™ test, EZ-Detect has the same sensitivity for blood in laboratory conditions. In clinical use 98% of patients expressed a preference for EZ-Detect but it detected significantly fewer patients with cancer than did Haemoccult ($P = < 0.05$). In its present form, this type of test would be unsuitable for population screening for colorectal cancer even if improved compliance is achieved.

## Introduction
Population screening for colorectal cancer by faecal occult blood testing is presently subject to clinical trials[1]. One of the major problems of such screening programs is poor compliance - often below 50%[1,2]. This not only reduces the effectiveness of screening but increases the cost of each tumour detected. The method of specimen collection may have an important influence on compliance[2,3]. New occult blood tests are available which require no handling of the stool by the patient and, therefore, can improve compliance[4].

One such test is EZ-Detect (NMS Pharmaceuticals Inc, USA). The test reagents are all present on a paper sheet which is placed in the lavatory and which changes colour to give a positive result. A further advantage of this method of testing is that there is no cost to the health service for processing the test and no results service to administer.

However, little is known of the clinical performance of such tests. Therefore, we have compared EZ-Detect (EZD) with the most popular faecal occult blood test, Haemoccult (HO) (Röhm Pharma, FRG), to determine their ability to detect neoplasia in patients with symptoms of colorectal disease.

## Methods
The EZD test consists of five paper sheets impregnated with test reagents in the shape of a cross (Figure 1). A single sheet is placed in the lavatory pan after passing a stool. If blood is present in the stool it will diffuse into the water in the pan and activate the test. The cross turns blue to indicate a positive result. When no blood is present there is no colour change. The test is repeated on three consecutive days. A positive and negative control technique is used with the two remaining sheets. For the positive control test, a sachet of powdered chemical is provided which is poured into the lavatory water and triggers the test paper to demonstrate a positive result. For the negative control, a test paper is simply placed in the lavatory to exclude a reaction with substances in the water supply.

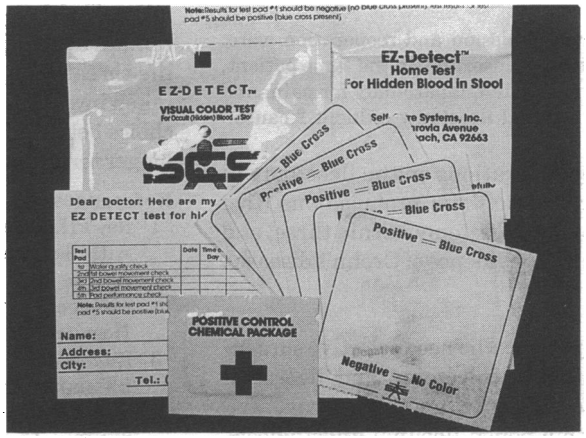


*Figure 1. The EZ-Detect test*

Haemoccult was used in the usual manner by smearing a stool sample collected with a spatula onto the test card. Patients collected two separate samples of faeces on each of three consecutive bowel movements. Haemoccult slides were processed without rehydration.

### *Experimental*
The sensitivity of both EZD and HO was compared in vitro; firstly with aqueous solutions of blood of different concentration and secondly with model stools (120 g crushed biscuit mixed with 20 ml water) containing differing volumes of blood evenly distributed.

### *Clinical*
Studies were performed on 460 consecutive patients with symptoms of large bowel disease presenting to surgical outpatient clinics. Each patient was sent EZD and HO by post with instructions and asked to use both tests concurrently on the same three bowel movements. Every patient was investigated by double-contrast barium enema or colonoscopy except those patients in whom a tumour was discovered on clinical examination of the rectum.

## Results
### *Experimental*
The lowest concentration of haemoglobin in aqueous solution at which EZD and HO gave a positive result was the same - a dilution of 1/5000. With the model

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stool, both tests gave a positive result when the stool contained 2 ml of blood and this result was repeated when several different batches of the two tests were studied.

*Clinical*

The 460 patients in the study were aged 17-89 years (median 65 years). An EZD test was completed by 404 (compliance 88%) and 275 completed a Haemoccult test in addition (compliance to two faecal occult blood tests 60%). Forty-eight patients (12%) recorded the EZD positive control test result as negative. All patients were investigated (253 patients by barium enema and 147 by colonoscopy) except four patients with palpable rectal tumours.

A positive EZD result was recorded by 49 patients (12.1%) and a positive Haemoccult result by 42 (15.3%) of the 275 patients who completed this test also. The results of investigation are shown in Table 1.

A total of 22 patients had colorectal cancer, EZD was positive in 8 of these (sensitivity 36.4%, specificity 89.3%, positive predictive value 16.3%) and Haemoccult was positive in 12 of 15 cases (sensitivity 80%, specificity 88.5%, positive predictive value 28.6%) (Table 2). The difference is statistically significant (Chi-squared test with Yates correction, $P = < 0.05$).

For the detection of all neoplasia (adenomatous polyps as well as cancer) EZD achieved a sensitivity and positive predictive value of 25.9% and 28.6% respectively whereas the results for Haemoccult were 46.2% and 42.9%. The difference in sensitivity fails to reach statistical significance.

Among the 15 patients with cancer who did both tests, EZD was positive in one case when HO was negative but EZD was negative in nine patients who had a positive HO result (Table 2). When asked which they would choose if they had to test their stool again, patients who had completed both tests preferred EZD in 98% of cases.

*Table 1. Result of investigation of large bowel in 404 patients*

| | *EZ (n=404)* | | *HO (n=275)* | |
|---|---|---|---|---|
| *Diagnosis* | *Positive* | *Negative* | *Positive* | *Negative* |
| Cancer | 8 | 14 | 12 | 3 |
| Adenoma (>5 mm) | 6 | 26 | 6 | 18 |
| Colitis | 2 | 12 | 3 | 8 |
| Diverticulosis | 10 | 80 | 5 | 43 |
| No abnormality | 23 | 223 | 16 | 161 |
| Total | 49 | 355 | 42 | 233 |
| Overall positive rate | 12.1% | | 15.3% | |
| False positive rate | 10.0% | | 10.2% | |

*Table 2. Comparison of EZD and HO result in patients with colorectal cancer* (na=not available, test not done)

| *Site* | *Stage* | *EZD* | *HO* |
|---|---|---|---|
| 1 Recto-sig | C | − | + |
| 2 Recto-sig | A | − | + |
| 3 Rectum | A | − | + |
| 4 Sigmoid | C | − | + |
| 5 Sigmoid | C | − | + |
| 6 Recto-sig | C | − | + |
| 7 Sigmoid | C | − | + |
| 8 Sigmoid | C | − | + |
| 9 Ascending | B | − | + |
| 10 Sigmoid | B | + | + |
| 11 Rectum | A | + | + |
| 12 Recto-sig | B | + | + |
| 13 Sigmoid | 2° | + | − |
| 14 Rectum | A | − | − |
| 15 Sigmoid | B | − | − |
| 16 Hep flex | B | + | na |
| 17 Caecum | C | + | na |
| 18 Recto-sig | C | + | na |
| 19 Rectum | B | + | na |
| 20 Sigmoid | B | − | na |
| 21 Descending | B | − | na |
| 22 Recto-sig | B | − | na |

## Discussion

This study investigates the ability of EZD to detect colonic cancer in symptomatic patients. Patients due to have investigation of the colon have been studied in order that false negative occult blood results might be identified. Compliance among symptomatic patients is greater than in asymptomatic populations[1,5] and this fact, combined with the design of our study, prevents any conclusion being drawn about increased compliance in a screened population using EZD; although the stated preference for EZD of the majority of patients (98%) who completed both tests supports the hypothesis.

The laboratory studies confirm that EZD is sensitive to blood and to approximately the same degree as Haemoccult. An aqueous solution of blood can be a poor method of predicting clinical sensitivity[6], while the model stool is a more valid comparison. However, the rate of diffusion of blood out of a stool into water in a lavatory pan will vary according to the surface area of stool (a constant in our studies) and other physical characteristics. Therefore, the in vitro measurement of sensitivity may be unreliable. It was of note that, in laboratory testing, blood diffusing out of the stool tended to sink to the bottom of the pan while the EZD test paper floats on the surface. Therefore, blood which was obviously present in the stool occasionally failed to trigger the test. If a suitable method, possibly chemical, of fragmenting the stool could be achieved, blood within the stool might be released in a quantity sufficient to activate the EZD test before sinking from the surface. With Haemoccult there is direct application of stool to the test paper avoiding this problem.

In clinical use EZD is significantly worse than Haemoccult at detecting cancer. Our results with Haemoccult are similar to those previously reported with symptomatic patients[5]. In an asymptomatic population the sensitivity for cancer is likely to be lower[7], presumably because asymptomatic tumours are less advanced. Therefore, the results suggest that EZD would be unsuitable for population screening - as many as two-thirds of cancers could give a false negative result. If the test were performed by a patient with symptoms, false reassurance due to a negative result may result in delay in seeking medical attention.

We found EZD to have a false positive rate virtually identical to Haemoccult; therefore, there does not appear to be the opportunity simply to increase the sensitivity of the chemicals in the EZD test paper to blood. While this might lead to detection of more cancers it would decrease specificity - for population

screening specificity is of equal importance to sensitivity.

Also of concern is the fact that 12% of patients read the EZD positive control test as negative. This could be due to failure on the part of the patients to carry out the procedure properly; indeed four patients recorded the positive control results as negative but reported the test result as positive. However, some patients may have been unable to detect the colour change of the test. This is a problem of interpretation which will be common to any test which patients have to read for themselves and the manufacturer includes a warning that the test should not be used by persons who are colour-blind.

EZ-Detect is an example of a new type of faecal occult blood test. While its novel method of use may be advantageous in comparison with existing products, its ability to detect cancer is not as good as that of Haemoccult.

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