# MEDICAL PRACTICE

## *Clinical Topics*

# Clinical findings, early endoscopy, and multivariate analysis in patients bleeding from the upper gastrointestinal tract

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*British Medical Journal*, 1977, **2**, 237-240


### Summary

**A simple system has been developed to identify patients with upper gastrointestinal tract haemorrhage who run a high risk of continued bleeding or rebleeding. The system is based on six items of patient data available at or soon after arrival in hospital. It was evaluated in a prospective study of 66 patients with upper gastrointestinal tract haemorrhage. Over half of the patients classified by the system into a high-risk category either continued bleeding or rebled after apparent cessation (as against one out of 33 patients in the low-risk category). The high-risk group also had a higher mortality (21%) than those in the low-risk group (nil). The addition or subtraction of early endoscopic findings made little difference to the accuracy of prognosis.**


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### Introduction

Patients admitted to hospital with acute upper gastrointestinal tract haemorrhage present many problems in practical management. Perhaps one of the most difficult is to assess whether the bleeding will settle on conservative management, continue, or recur after a few days' apparent cessation. Several workers have attempted to investigate this problem, and recently there has been a lively discussion over the merits of early and "aggressive" investigation of these patients.[1-7]

Unfortunately, authors of previous studies have often omitted to define the terms used in describing upper gastrointestinal tract haemorrhage. Moreover, most have either studied non-consecutive series or restricted their analysis to one aspect of the patient's presentation and analysed this in terms of the final outcome of the patient.

We therefore thought that it would be interesting to study a consecutive prospective series of patients with upper gastrointestinal tract haemorrhage (having first defined the terminology to be used). In addition, as well as looking at single attributes, we would study combinations to see whether an accurate individual short-term prognosis could be derived from a patient's initial clinical state. Our attempts to do this in 66 patients form the basis of this paper.

### Patients and methods

All patients presented with acute upper gastrointestinal tract haemorrhage (to be defined) and were admitted as emergencies to the Airedale District General Hospital from January 1975 to March 1976. This hospital serves a population of about 165 000 in a mixed urban and rural environment and is the only district general hospital in this

geographical area of Yorkshire. Each physician within the hospital contributed all his cases to the trial, and the resulting prospective series is therefore representative and unselected. A breakdown of the patients by diagnosis is shown in table I.

TABLE I—*Diagnosis and outcome in 66 patients*

| Diagnosis | Settled | Rebled | Total |
|---|---|---|---|
| Gastric ulcer | 9 | 4 | 13 |
| Duodenal ulcer | 10 | 3 | 13 |
| Hiatus hernia with and without oesophagitis | 7 | 1 | 8 |
| Pyloric ulcer | 4 | 2 | 6 |
| Neoplastic lesion | 3 | 2 | 5 |
| Gastric erosions | 4 | | 4 |
| Mallory-Weiss syndrome | 2 | 1 | 3 |
| Oesophageal varices | | 1 | 1 |
| Multiple diagnoses | 1 | 2 | 3 |
| Other | 2 | 1 | 3 |
| No lesion found* | 6 | 1 | 7 |
| Total | 48 | 18 | 66 |

*One patient with Crohn's disease later shown to be bleeding from ileal lesions and not from upper gastrointestinal tract. One other patient with positive hepatitis B antigen died in hepatic coma before full investigation could be performed.

As soon as each patient was admitted to hospital a detailed analysis was carried out of his clinical state using a form specially designed for the purpose (see appendix). Endoscopy was performed (almost always within 24 hours of admission and in every instance within 72 hours). Two patients did not undergo endoscopy because they were positive for hepatitis B antigen; in one a barium meal examination was substituted, and in the other hepatic coma precluded all investigation. Each patient was followed up for 10 days, the short-term outcome was noted, and the patient was then placed in one of two categories—either "bleeding settled" or "continued bleeding or rebled."

The survey was divided into two parts. For the first six months a series of 40 cases was collected. Analysis of these, coupled with a search through published reports, enabled us to identify several useful factors for multivariate analysis. In the second phase of the trial proper (nine months, 66 patients) the hypotheses generated in the first phase were tested on a further prospective consecutive series of patients.

### DEFINITIONS

Before the trial began it was necessary to define terminology. We therefore reviewed previous workers' definitions. As mentioned already, many studies had none, but we adopted the following definitions.

#### *Upper gastrointestinal tract haemorrhage*

To be admitted into the study an adult patient had to have either (*a*) clinical evidence of gastrointestinal bleeding on admission or (*b*) a history of having experienced upper gastrointestinal bleeding within 10 days before admission. (In practice all but one of the patients suffered from bleeding within 24 hours of the patient's admission to hospital, and most were actively bleeding on admission.)

*Haematemesis* was defined as vomiting blood or blood clots. Coffee-ground vomit was accepted as evidence of haematemesis only if witnessed by nursing or medical staff.

*Melaena* was defined as the passage of dark tarry stools or fresh blood, and was again accepted as having occurred only if witnessed by nursing or medical staff.

#### *Continued bleeding or rebleeding*

Continued bleeding was defined as having occurred if (*a*) bleeding had continued for more than 48 hours, or (*b*) the haematemesis or malaena was of sufficiently massive nature to warrant urgent surgery. Evidence of continued bleeding consisted of a high pulse rate and low blood pressure without other obvious cause, continued haematemesis, passage of fresh melaena, and a falling haemoglobin concentration (more than would be accounted for by haemodilution).

The patient was defined as having rebled if the signs of bleeding, already outlined, recurred in the first 10 days after admission. To be classified as having rebled the patient must first of all have given evidence that bleeding had ceased after the first episode. This evidence consisted of a stabilised blood pressure and pulse rate together with a stable haemoglobin concentration, and the passage of either normal stools or stale melaena. This state must have lasted for at least 24 hours before rebleeding for a patient to be put into this category. In practice, the categories of continued bleeding and rebleeding were amalgamated for this analysis.

## Findings

### FIRST STUDIES

Initially 40 patients were studied, and for each patient we recorded the attributes set out in the appendix. It quickly became apparent that several of these attributes were of no value for prognosis. None the less, from the first group of 40 patients a short list of the six most potentially valuable attributes were produced (table II). In subsequent months these attributes were then studied to test their individual and combined prognostic influence in a prospective series of 66 patients.

TABLE II—*List of short-term attributes found useful in terms of prognosis*

| Attributes | Sign of "poor prognostic significance" |
|---|---|
| Patient's age | Age ⩾60 |
| Past medical history | Positive past medical history of cardiac, respiratory, hepatic, or renal disease (deemed clinically significant by admitting doctor) |
| Alcohol intake | Teetotal |
| Endoscopy | Endoscopic diagnosis of ulcer or cancer |
| Drug history | On *no* drugs (over last month) |
| Cardiovascular system | Congestive heart failure on admission |

### SUBSEQUENT STUDIES

At first the effect of each of the six helpful factors *on its own* was examined with results that are shown in table III. For example, of the patients aged 60 or more at the time of their admission, 14 rebled or continued to bleed, and 24 settled. By contrast, of the patients aged under 60 at the time of admission, only four out of 28 failed to settle. Age, therefore, has a strong influence on prognosis, but nevertheless, age alone does not offer a prognosis that can be used in the individual patient. Similar considerations apply to the patients with a past medical history (as defined in table II): a total of 15 of these 36 patients rebled. By contrast, only three of the 30 patients without a past medical history rebled or failed to settle. The same considerations hold for most of the other prognostic factors in table IV.

All six factors in combination were then studied, and a system was developed that amounted to a simple discriminant analysis—that is, if the patients had three or more "poor prognostic factors" it was

TABLE III—*Analysis of six single prognostic factors (results expressed as numbers of patients)*

| | Correct prediction | | Incorrect prediction | |
|---|---|---|---|---|
| | True positive | True negative | False positive | False negative |
| Age ⩾60 | 14 | 24 | 24 | 4 |
| Positive past medical history | 15 | 27 | 21 | 3 |
| No history of alcohol (teetotal) | 9 | 37 | 11 | 9 |
| Ulcer or cancer on endoscopy | 14 | 26 | 22 | 4 |
| *Not* on drugs | 6 | 32 | 16 | 12 |
| Heart failure on admission | 3 | 47 | 1 | 15 |

TABLE IV—*Patient outcome in terms of continued bleeding and mortality*

| No of poor prognostic factors | No of patients | No continued bleeding | Percentage continued bleeding | No (%) died |
|---|---|---|---|---|
| 2 or less | 33 | 1 | 3 | — |
| 3 or more | 33 | 17 | 52 | 7 (21) |

predicted that they would rebleed; if two or less that they would settle. In the event, of the 33 patients with three or more poor prognostic factors, 17 (52%) either rebled or failed to settle. By contrast, of the 33 patients with two or less poor prognostic factors, only one (3%) failed to settle promptly on conservative management (table IV).

The effects of this in terms of the patient's survival are also listed in table IV. Of 33 patients in the high-risk category seven (21%) died; while of the 33 patients with two or less poor prognostic factors, none died. We conclude from this that the factors outlined in table II, taken together, have a quite profound influence on patient mortality. Indeed, of the 15 patients with four or more poor prognostic factors, 10 rebled and four died.

*Role of endoscopy*

Five of the six factors listed in table II are simple clinical variables, readily elicited as soon as the patient arrives in hospital. The sixth, endoscopy, is more complex. Not only does an urgent endoscopy cause the patient some discomfort, but in many hospitals facilities for urgent endoscopy may not be available. We therefore decided to repeat the analysis shown in table IV, but this time restricting consideration solely to the five simple clinical variables and ignoring endoscopy.

Of the 26 patients with one (or none) of the poor prognostic factors, one rebled (3·8%) and none died. Of those with two poor prognostic factors, seven out of 23 rebled (30·4%), and one died (4·3%). Of those with three or more poor prognostic factors, 10 out of 17 rebled (58·8%) and six died (35·3%). Therefore the inclusion or exclusion of endoscopy findings makes little difference to the accuracy of prognosis.

*Comparison with clinicians*

It is reasonable to argue that clinicians might be able to make this prognostic discrimination by themselves. To test this hypothesis we copied out 10 case histories and gave these to a group of eight clinicians (four consultants and four junior staff) who were unaware of the scoring system. The system correctly identified nine out of 10 cases whereas the clinicians' range was from four to seven (three identified seven cases, one identified six, two identified five, and two identified four). We concluded from this additional data that clinicians as a group do not appear able to discriminate between patients who rebleed or settle.

## Discussion

It has been known for many years that certain clinical factors influence the outcome of acute upper gastrointestinal tract haemorrhage. As long ago as 1937, Allen[1] showed that the mortality depended to some extent on the patient's age and this finding was confirmed by Avery Jones.[2] More recently a high mortality has been shown in patients with chest, cardiovascular, and liver disease.[8–10]

What has been in doubt is whether combinations of these clinical features could be used to give a prognosis that would be accurate enough to be of value in managing the individual patient. Here our evidence is perhaps encouraging: the high-risk patients have been shown in a prospective consecutive series to have a better than even chance of failing to settle. By contrast, only one patient out of the 33 in the low-risk group failed to settle promptly on conservative management. As regards mortality, this was 21% in the high-risk group of patients, and nil in the low-risk group.

A more precise scoring system might well have given better separation, but we would defend our decision to use a crude discriminant system on two grounds. Firstly, the number of patients in the present series was relatively small. Secondly, and perhaps more important, the purpose of the present study was *not* to produce an "optimum" scoring system but to determine whether combinations of features gave a prognosis superior to that given by single features. This has been confirmed, even using a crude system of analysis.

The Airedale District General Hospital takes all such cases from an urban and rural population of about 165 000 people. Since each physician in the hospital participated in this trial, the series is at least locally representative. On a wider scale, however, geographical differences in presentation may necessitate revising part or all of the scoring system; and eight or 10 other hospital units are currently engaged in a multicentre trial.

Such a trial, with its greater number of patients, may well enable us to overcome a further difficulty. It is undoubtedly a weakness of the present scoring system that it refers merely to "drugs" that have been recently ingested or to "chest diseases." It would be of more value if we could identify specific drugs and specific diseases and apply a prognostic feature to each. To do so requires large numbers of patients and was quite clearly impossible in the present circumstances.

Some results came as a considerable surprise to many of us—for example, most clinicians think that recent ingestion of alcohol has an adverse prognostic influence; whereas actually its influence is in the reverse direction. This is perhaps because—like most clinicians—on hearing about alcohol ingestion we immediately associated this with cirrhosis and oesophageal varices. Such cases may be frequent in specialised units. In the spectrum of disease presenting routinely to a district general hospital, however, most patients who ingest alcohol just before vomiting blood prove to have a minor gastric erosion that rapidly heals. The results of the study therefore are useful in that they point to a different pattern of disease presenting routinely to specialised units and to a district general hospital.

As regards endoscopy, we have shown that, for patients with less than two prognostic factors, emergency endoscopy contributes little in terms of knowledge concerning immediate prognosis. It may be argued that endoscopy is valuable in other senses ("it tells the surgeon where to look") but in patients with less than two factors the chance of coming to surgery or needing urgent endoscopy is so small that it would seem more logical to perform endoscopy in these patients as a more leisurely procedure, allowing the patients to get over their initial episode of haematemesis before subjecting them to additional stress.

The practical relevance of the present study is therefore two-fold. Firstly, patients with two or more poor prognostic factors are shown to have such a poor outlook that early surgery should be considered in every one of the patients in this group. The situation is perhaps analogous to that in severe ulcerative colitis, when some 10 years ago high-risk groups of patients were clearly identified.[11] Of course, it remains to be seen whether, as in the case of ulcerative colitis, early surgery will lower the mortality rate. $H^2$-receptor blockers appear to have evoked a mixed response—being of value in patients with erosive gastritis,[12] but not in more serious conditions[13]—which rather underlines the need to discriminate prognostically at an early stage. Secondly, we have identified a group of patients in whom early endoscopy is not helpful in prognostic terms (table IV). In centres where emergency endoscopy facilities are limited, concentration of endoscopic facilities on patients with two or more clinical poor prognostic factors would enable most benefit to be gained from scarce resources.

We thank our consultant colleagues at the Airedale General Hospital for their support and access to patients under their care, and those of our clinical colleagues who completed the proforma. Jane C Horrocks and G L Walmsley were aided by a grant from the Medical Research Council, which we also acknowledge with gratitude.

## Appendix

CRITERIA NOTED ON ADMISSION AND FOLLOW-UP INVESTIGATIONS

*Criteria noted on admission*—Sex; age; presentation of upper gastrointestinal bleed; symptoms before upper gastrointestinal bleed; drug history; past medical history; smoking habit; alcohol intake; family history; social history; general appearance; and finding on examination in cardiovascular system, respiratory system, abdomen, and central nervous system.

*Follow-up investigations*—Haemoglobin, blood urea, and serum

calcium concentrations; units of blood transfused; blood group; evidence of further rebleed/continued bleeding (see text); findings on endoscopy or barium meal examination; final diagnosis; and final outcome.

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(*Accepted 22 April 1977*)

# *Letter from . . . Chicago*

# Shopping-bag syndrome

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*British Medical Journal*, 1977, **2**, 240-241

Recently at a party a shapely blonde took me aside to ask if she could make an appointment at my clinic at the county hospital. She then explained, somewhat to my disappointment, that the prospective patient was not herself but her aging mother and that she needed not my superior diagnostic skills but relief from the monthly drug bill. Reaching into her handbag, she produced a list showing that her mother was taking 13 different drugs:—thrice weekly methyldopa, allopurinol, spironolactone, paracetamol, tripelennamine, quinidine, thiamine, and adiphenine; twice daily multivitamin tablets; and once daily diphenhydramine, hydroflumethiazide, oestrogens, and thyroid extract. Yet she was a sturdy 72-year-old lady who could have outpaced many a sedentary middle-aged doctor—including the aetiological agent of her shopping-bag syndrome.

The syndrome is never seen in hospital patients—who receive an average of eight medications per hospital admission but do not have to carry them. Ambulatory patients, however, often leave the clinics and doctors' offices loaded with bags full of bottles of medicine; and the natural history of these bags has been only incompletely described. Hospital consultants can help but little, since they rarely see the patients in their normal surroundings. But family practice residents, who make house-calls as part of their training, afford interesting insights—as exemplified by the rare "case" of hypertension, arthritis, easy bruising, and light-chain proteinuria. The case turned out to be a poor old lady, living alone in a tiny room without a kitchen, bathroom, or medicine cupboard. On a shelf in her room, the resident reported, 10 brown paper bags were lined up in a row, each representing one visit to the clinic, each full of bottles of medicine labelled with instructions that clearly were not followed. The bags, it appears, were not necessarily in chronological order, having a tendency to fall off the shelf. Moreover, the bag currently in use contained two methyldopa bottles, each labelled "take one tablet four times daily," apparently because the pharmacy had run out of larger containers. So she was taking a full dose from each bottle, since "They would not have given them to me had they not wanted me to take them." A study of shopping bags and brown bags could turn up some nasty surprises—this at a time when the medical profession is constantly being besieged by complaints about rising costs.

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## Cost of drugs

Within the span of a decade the national expenditure on drugs has doubled. In 1973 doctors wrote 2·8 billion* prescriptions or drug orders, representing an average of 10 prescriptions per person and an annual cost of $11 billion. Tranquillisers, antibiotics, and non-narcotic analgesics topped the list, followed by contraceptive steroids, expectorants, antispasmodics, and diuretics. Some 30m restless Americans take sleeping pills. One in 10 takes benzodiazepines, for at least a week a year; and the consumption of these drugs has more than doubled in a decade. Some 97% of general practitioners or internists prescribe diazepam. In 1974 doctors wrote 60m prescriptions for 3 billion tablets of diazepam and 20m prescriptions for one billion tablets of chlordiazepoxide—to tranquillise, to relieve anxiety, perhaps to satisfy the prevailing belief that happiness is a constitutional right. Furthermore, writing prescriptions helps terminate the interview, makes up for lack of time, mollifies the chronic complainer—and provides an adequate supply for diversion to those who occasionally or continuously need to feel "high." This drug orgy can, however, be curbed with remarkable ease—as shown by the experience at this hospital, where in any one day medical residents would issue prescriptions for psychoactive or analgesic drugs to 125 of 200 visiting outpatients. Yet after a directive from the chief of medicine, the use of propoxyphene and pentazocine was stopped; and prescriptions for tranquillisers, limited to 10 tablets at a time unless countersigned by a staff physician, fell to 12 a day—with an incidental yearly saving of $150 000, and no appreciable outcry from deprived patients or restricted house officers.

*US billion = $10^9$.