Fecal screening tests in the approach to acute infectious diarrhea: a scientific overview

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Authors' objectives
To evaluate the value of faecal leukocyte, faecal occult blood, faecal lactoferrin, and a combination of faecal leukocytes with clinical data in the workup of patients with inflammatory diarrhoea.

Searching
MEDLINE was searched from 1970 to September 1994 (the search terms were given). Additional relevant articles were identified by consulting experts in the field, and by examining review articles and references in retrieved articles.

Study selection
Study designs of evaluations included in the review
All study designs reporting original data were eligible for inclusion. Technical articles which contained no clinical information were excluded. Studies where diagnostic tests were performed without medical supervision were also excluded.

Specific interventions included in the review
Articles including information on clinical data and/or faecal screening tests (faecal leukocytes, faecal occult blood, faecal lactoferrin), assessed individually or in combination, were eligible for inclusion.

Reference standard test against which the new test was compared
The included studies were required to use stool culture in all patients as the reference standard. Diarrhoea was considered inflammatory if the stool culture was positive for Salmonella, Shigella, Campylobacter, enteroinvasive E. coli, enteropathogenic E. coli, or cytotoxigenic C. difficile.

Participants included in the review
Only articles relating to acute infectious diarrhoea in humans were eligible for inclusion.

Outcomes assessed in the review
The included articles were required to report sensitivity, specificity, and positive and negative predictive values, or to provide sufficient data for the construction of a 2x2 contingency table.

How were decisions on the relevance of primary studies made?
All studies were reviewed independently by two reviewers who were not co-authors of the studies, using defined inclusion criteria. A final decision was reached by consensus.

Assessment of study quality
The overall scientific quality of each study was rated on a 16-point scale (described in detail in the report), in which 16 represented a study with minimal flaws and 1 a study with extensive flaws. All studies were reviewed independently by two reviewers who were not co-authors of the studies, using defined validity criteria. A final validity score was reached by consensus.

Data extraction
The data were extracted independently by the two reviewers and any differences were resolved by consensus.

Methods of synthesis
How were the studies combined?
The sensitivity, specificity, and positive and negative predictive values were calculated from each study using the method of Sackett et al. (see Other Publications of Related Interest no.1). The studies were pooled, grouped by test or combination of tests, using sROC curves generated by the method of Littenberg and Moses (see Other Publications of Related Interest no.2). The area under the sROC curve was used as the summary measure to rank test performance.

How were differences between studies investigated?
Differences between the studies were investigated through discussion of the validity assessment. The threshold effect was evaluated using weighted linear regression (see Other Publications of Related Interest no.2).

**Results of the review**
Twenty-five studies were included, of which 24 were used to produce summary receiver operating characteristic (sROC) curves (19,036 patients). There were 4 studies (138 patients) of faecal lactoferrin, 3 studies (517 patients) of clinical data and faecal leukocytes, 5 studies (834 patients) of occult blood, and 20 studies (18,490 patients) of faecal leukocytes.

The accuracy of the index tests, as assessed by the area under the sROC curve where the intercept is the intercept of the logit transformation of the sROC curve, was as follows (hierarchical order, least accurate first):

- faecal leukocytes (intercept 1.097; sensitivity, SE 0.100),
- occult blood (intercept 1.504; SE 0.171),
- clinical data and faecal leukocytes (intercept 1.568; SE 0.356),
- faecal lactoferrin (intercept 3.645; SE 0.457).

**Authors’ conclusions**
Faecal lactoferrin appears to be the most accurate index test. A limited number of studies (faecal lactoferrin and leukocytes with clinical data) and methodological flaws identified in the assessed studies must be solved in future primary studies, to improve the usefulness of the meta-analytical approach used by the authors.

**CRD commentary**
This was a methodologically-sound review that has been well documented. The results indicate that faecal lactoferrin is the most accurate index test. This statement is based on only a small number of studies with relatively few participants that examine faecal lactoferrin, and it would only take a few larger trials with an opposing outcome to overturn this result. It is interesting to note that those diagnostic tests with the largest number of studies and participants are judged to be the least effective by the meta-analysis. This may imply that the differences in test accuracy, as inferred by the meta-analysis, could be a real indication of relative accuracy or an artifact resulting from differential study power.

**Implications of the review for practice and research**
Research: Further larger trials are needed to test the robustness of this review's conclusions.

**Bibliographic details**

**PubMedID**
8783344

**Other publications of related interest**
1. Sackett DL, Haynes RB, Guyatt GH, Tugwell P. Clinical epidemiology. A basic science for clinical medicine. 2nd

**Indexing Status**
Subject indexing assigned by NLM

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Blood; Communicable Diseases /diagnosis /etiology; Diarrhea /diagnosis /etiology; False Negative Reactions; False Positive Reactions; Feces /chemistry /cytology; Humans; Inflammation /diagnosis; Lactoferrin /analysis; Leukocytes

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**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.