Procalcitonin test in the diagnosis of bacteremia: a meta-analysis
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CRD summary
This review concluded that the procalcitonin test has moderate ability to diagnose bacterial bloodstream infections in patients seen in emergency departments, and further research is needed before its widespread clinical use. Although the review had some limitations, the authors’ conclusions are in line with the evidence presented and seem likely to be reliable.

Authors' objectives
To evaluate the diagnostic performance of the procalcitonin test for bacteraemia in the emergency department (ED) setting.

Searching
MEDLINE was searched from 1970 to September 2006 for studies reported in the English language; the search terms were reported. Abstracts from annual meetings of three emergency medicine societies (1995 to 2005), and the reference lists of included articles and a previous systematic review, were also searched.

Study selection
Study designs of evaluations included in the review
Clinical studies assessing diagnostic performance were eligible for inclusion. Case series and studies with ambiguous inclusion criteria were excluded from the review. It appears that the included studies were diagnostic cohort studies.

Specific interventions included in the review
Studies of testing for serum procalcitonin were eligible for the review. The cut-off level used in the included studies ranged from 0.4 to 2.0 ng/mL, a value of 0.4 or 0.5 ng/mL being most common.

Participants included in the review
Eligible participants were out-patients with suspected infection studied either in the ED or on admission to hospital. Studies of adult, paediatric and mixed populations were eligible. The prevalence of infection in the included studies ranged from 4.2 to 53.7%, and patients were either self-referred or physician referred.

Outcomes assessed in the review
Studies had to report sufficient data to enable calculation of the sensitivity, specificity and diagnostic odds ratio (OR).

How were decisions on the relevance of primary studies made?
Two reviewers independently selected studies for the review. Any disagreements were referred to a third reviewer and consensus was reached among all three reviewers.

Assessment of study quality
Two independent reviewers assessed validity on the basis of the reference standard used, the risk of differential reference standard bias and the risk of spectrum bias. Any disagreements were resolved by consensus. For risk of spectrum bias, studies were graded A (consecutive or random sampling from an out-patient population with signs and symptoms from infection), B (selected subgroups of out-patients with selected infection) or C (case series or studies with ambiguous inclusion criteria). Studies graded C were excluded from the review.

Data extraction
One reviewer extracted the data using a standardised collection form, which a second reviewer then checked. Authors of included studies were contacted for additional information if necessary. Data on the numbers of true and false positives and negatives were used to derive the sensitivity and specificity, with associated 95% confidence intervals (CIs), of the procalcitonin test in each study. Diagnostic ORs were also derived, although the results were not reported.
Methods of synthesis
How were the studies combined?
The studies were combined by summary receiver operating characteristic (SROC) curve analysis. Diagnostic ORs and sensitivity and specificity values were pooled using a random-effects model if the studies were considered sufficiently homogeneous.

How were differences between studies investigated?
Heterogeneity of the diagnostic ORs was assessed using the I-squared statistic. A regression equation derived from the SROC curve analysis was used to assess the presence of any threshold effect. A sensitivity analysis was performed in which studies rated B for patient spectrum were excluded. Subgroup analyses were performed of studies in adult and paediatric populations and of studies using the most common cut-off values for procalcitonin (0.4 or 0.5 ng/mL).

Results of the review
Seventeen studies with 2,008 participants were included.

Eight of the included studies were rated A for patient spectrum and nine were rated B. There was no evidence of a threshold effect but heterogeneity was significant for the diagnostic OR (I-squared 64%). The SROC curve had an area under the curve (AUC; a measure of the probability of classifying diseased and non-diseased patients correctly) of 0.84 (95% CI: 0.75, 0.9). Sensitivity analysis involving only studies rated A for patient spectrum resulted in similar test performance (AUC 0.86, 95% CI: 0.78, 0.9) without substantial heterogeneity (I-squared 31%), as did the subgroup analysis for paediatric studies (AUC 0.85, 95% CI: 0.63, 0.95). Subgroup analysis of studies with a cut-off of 0.4 or 0.5 ng/mL revealed moderate heterogeneity (I-squared 46%); pooled estimates for sensitivity and specificity were 76% (95% CI: 66, 84) and 70% (95% CI: 60, 79), respectively.

Authors' conclusions
The procalcitonin test has moderate ability to diagnose bacteraemia in ED patients.

CRD commentary
The review objectives and inclusion criteria for the participants, intervention and reference standard were clear. Inclusion criteria for the study design were not stated, but it appears that the included studies had a relatively strong (diagnostic cohort) design. The authors searched one electronic database plus supplementary sources, and the search was limited to English language material, so it is possible that relevant studies could have been missed. The risk of publication bias was not assessed. Validity was assessed using a limited number of criteria that addressed risk of spectrum bias and differential reference standard bias; study quality was used in selecting studies for the review and in the analysis. Relevant details of the included studies were presented. The methods of analysis, including the investigation of heterogeneity, seem appropriate. Although the review had some limitations, the authors’ conclusions are in line with the evidence presented and seem likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that further research is needed before the procalcitonin test can be recommended for widespread clinical use.

Research: The authors stated that future studies should examine the performance of the test in combination with other laboratory, diagnostic or clinical characteristics.

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Bibliographic details
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.