Diagnosing Anaemia

Bandolier is always on the lookout for good papers which help in making a diagnosis. A number of papers on the diagnosis of anaemia have come our way this month. Interestingly, they include the issues of clinical evaluation, and of laboratory diagnosis.

Conjunctival pallor

Dr Findlay could always diagnose anaemia by just looking at a patient's nails, or pulling down an eyelid and seeing conjunctival pallor. But how good is conjunctival pallor, or its absence, in predicting anaemia? A study from Toronto tells us [1].

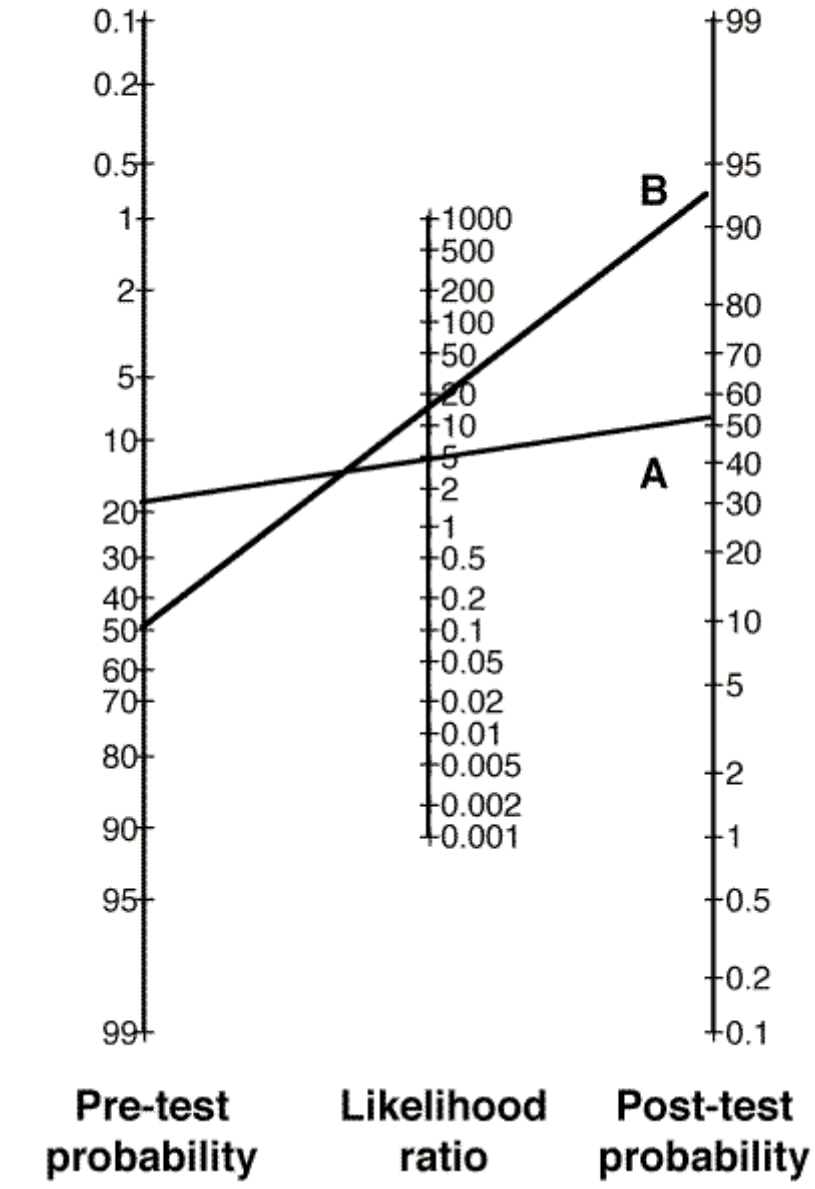
A total of 302 inpatients were examined who were over 18 years of age, able to consent and willing to participate and who had a haemoglobin measurement taken within three days of assessment of conjunctival pallor (but no transfusion in between). Three observers examined them for conjunctival pallor - after an initial 25 patients were seen to agree definitions. Pallor was described thus:

- Pale conjunctiva were those with very little or no evidence of red colour on the anterior rim, which matched the fleshy colour of the posterior aspect of the palpebral conjunctiva.
- Conjunctivae that were normal had full or nearly full redness of the anterior rim.
- Borderline conjunctivae were those with neither clearly red nor clearly pale anterior rims, or those in which one conjunctiva was pale and the other was normal.

Results

Of the 302 patients, 55 (18%) had Hb levels of 90g/L or below. Of the 55 with Hb <=90 g/L, 8 had conjunctival pallor, and 22 had borderline pallor. So on this basis, the results were modest, with a likelihood ratio for the presence of conjunctival pallor of 4.5 (95% confidence interval 1.8 to 11), and a likelihood ratio for the absence of pallor of 0.6 (0.4 to 0.8).

However, a post-hoc analysis using different haemoglobin cut offs found that the presence of conjunctival pallor was highly predictive of a Hb value of below 110 g/L (Figure).

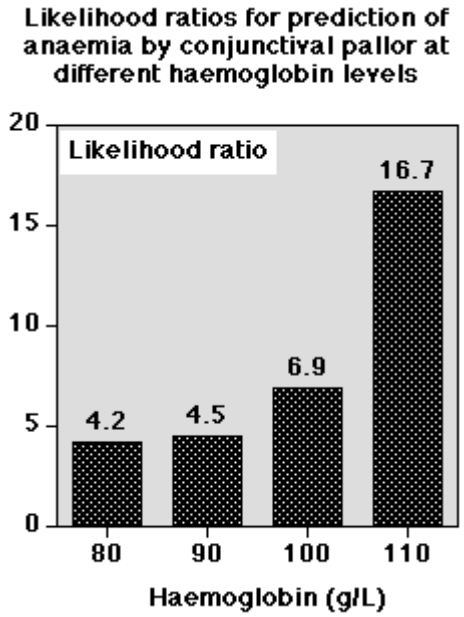


But neither borderline pallor nor absence of pallor were particularly helpful at any level of Hb - with likelihood ratios close to 1.

Useful information?

Yes it is. Given that 18% of patients in this Toronto hospital (including those with cancer and HIV) had Hb values of 90 g/L or below, and 47% had values of 110 g/L or below, the presence of conjunctival pallor should at least prompt a test for haemoglobin (and probably for serum ferritin, as will become apparent in a moment). The likelihood ratios and prevalences are combined in the likelihood ratio nomogram. Using an 18% prevalence for Hb <=90 g/L, a LR of 4.5 gives a post-test probability of about 50% (line A). Using a 47%

prevalence for Hb <=110 g/L, a LR of 16 gives a post-test probability above 90% (line B).



It also tells us that in patients where there is evidence from other signs, symptoms or history, the presence of full conjunctival redness does not exclude significant anaemia.

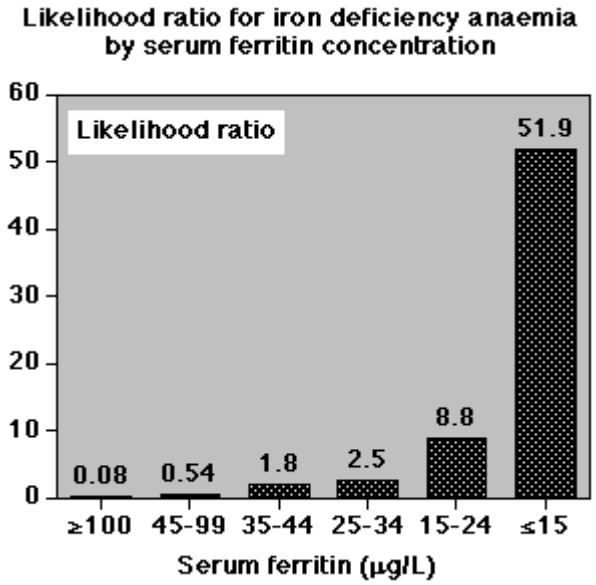
And this ought to prompt some research elsewhere. This is just the sort of informative research that could be done in general practice in the UK, with large numbers of patients to tighten confidence intervals and provide results for particular patient groups. Is anyone doing it?

Serum ferritin predicts iron-deficiency anaemia

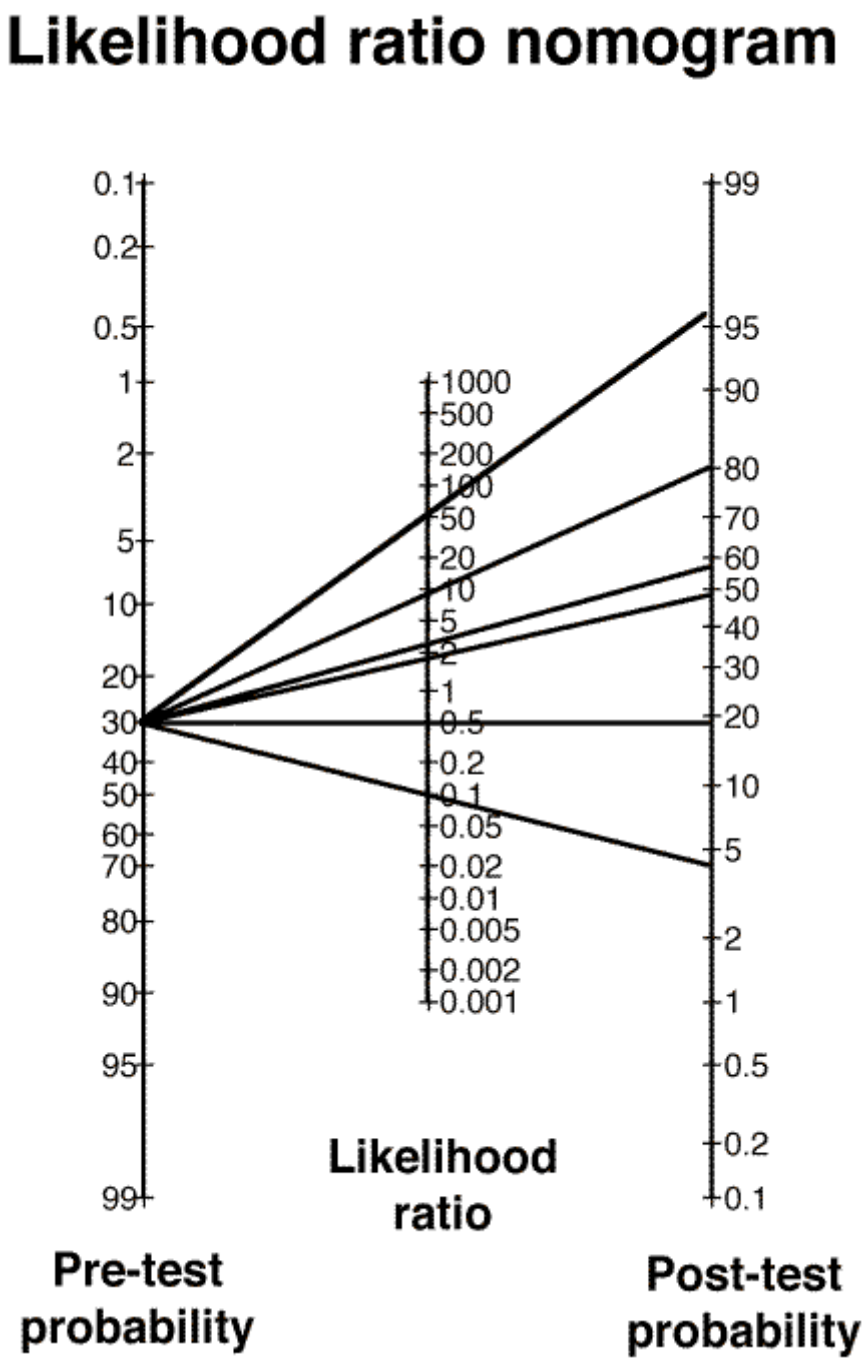
There was a great systematic review of tests to diagnose iron deficiency anaemia from McMaster published a few years ago [2]. The authors sought reports in which the target population was over 18 years with low levels of haemoglobin (<130 g/L for men and <110 g/L for women), with histological appearance of bone marrow aspirates as the gold standard criterion for diagnosis.
The review showed clearly that a number of tests were not up to the job - notably mean cell volume, transferrin saturation, red cell protoporphyrin, red cell volume distribution and red cell ferritin. Serum ferritin was streets ahead in terms of diagnostic accuracy.

Serum ferritin results

There was information on 2669 patients for serum ferritin, of whom 809 (30%) were iron deficient. Likelihood ratios were calculated for patients with inflammatory diseases, and with non-inflammatory disease, but in the Figure below the combined results are given for likelihood ratios calculated at different serum ferritin levels.



How these might be used for a patient is shown in the likelihood ratio nomogram. Using a 30% figure for a pre-test probability (obtained here from prevalence, but it might just as easily come from clinical experience or history), post-test probabilities from serum ferritin of >=100 µg/L down to <=15 µg/L are 4, 20, 50, 60, 80 and >95% respectively. Other ways of using these data are explored in the book by David Sackett and others on how to practice and teach evidence-based medicine [3].



Comment

There is some instructive material beginning to be produced on more rational and insightful ways of using diagnostic tests. We still lack a number of really good examples where clinical experience, clinical history, and diagnostic tests can be combined to provide a rational diagnostic process. The key has to be an incremental approach in which simple and immediate tests are used first to increase the probability of the diagnosis. More complicated and costly tests can then be used to conclude the process. For aficionados of diagnostic testing, there is another interesting paper to read [4].

References:

1. TS Sheth, NK Choudhry, M Bowes, AS Detsky. The relation of conjunctival pallor to the presence of anaemia. Journal of General Internal Medicine 1997 12: 102-6.
2. GH Guyatt, AD Oxman, M Ali et al. Laboratory diagnosis of iron-deficiency anaemia: an overview. Journal of General Internal Medicine 1992 7: 145-53.
3. DL Sackett, WS Richardson, W Rosenberg, RB Haynes. Evidence-based medicine: How to practice and teach EBM. 1997 Churchill Livingstone, ISBN 0-443-05686-2.
4. C Patterson, GH Guyatt, J Singer, M Ali, I Turpie. Iron deficiency anemia in the elderly: the diagnostic process. Canadian Medical Association Journal 1991 144: 435-40.