Dr Stenkvist replies as follows:

In relation to Dr Paul Sillocks comments on observer variation I wish to make the following comment:

The breast cancer classification systems we analysed not only have a poor reproducibility but they also lack clinical value in that they do not take into account rate of recurrence. However, parameters whose measurement is easily reproducible, such as "tumour markers" (CEA etc), DNA distribution among tumour cell nuclei, measures of tumour size, etc, although clearly correlated with prognosis when you compare groups of patients, are of little or no value for prognosis in the individual patient unless they are combined in a reliable way into a malignancy index that can be obtained by step-wise logistic regression analysis. We have recently addressed this problem, and we think it is time that pathologists and clinicians start to look for optimal combinations of parameters to create "malignancy indices" for tumour diseases in order to have practicable methods in daily clinical work.

Breast cancer patients deserve the greatest possible assurance in estimates of the severity of their disease and in the selection of their treatment, just as the clinician should receive the most complete information possible about his patient's condition. Our study indicates that it will be possible to give the clinician such complete information (superior to so-called clinical staging), provided that the significant variables are recorded in a meticulous way and combined into a risk curve. Patients with low malignancy grade as demonstrated in our study could then be confidently reassured that they will not suffer from recurrent disease, and resources for adjuvant therapy and follow-up can be saved for those patients who really need them (i.e patients with a high malignancy grade).

Our study further emphasises that there is no evidence that THE factor, a single entity of absolute prognosis, exists or is likely to exist.

We regret our mistake in proof-reading the standard error of kappa of Dr Jacob Cohen's formula. The computation, however, was performed using the correct formula.

**References**


2 Cohen J. Weighted kappa: nominal scale agreement with provision for scaled disagreement or partial credit. Psychol Bull 1968;70:213-20.

Professor Horne and Dr McHardy reply as follows:

Although we did not screen the ANA-negative sera against human tissues we agree with Watson and Kerr that a small number of sera will react with such tissues. However, we must point out that we never claimed that the radioimmunoassay kit supplied by RC Amersham did not give false positive results. They most certainly do. It was for this reason that we only studied sera where a value of 40 U/ml or greater had been obtained. The main point of our argument in this paper is simply that if clinicians rely solely on the conventional immunofluorescence screening procedure for antibodies to nuclear constituents these are likely to be missed if they hold the traditional view that ANA are present in over 98% of SLE cases.

Finally, we accept that an immunofluorescence screening test based on *Crithidial luciliae* is of diagnostic value and we are currently comparing it with the RIA kits.

**IgA pyroglobulinaemia in lymphoma**

Pyroglobulins are abnormal immunoglobulins, usually IgG or IgM, which when heated to 56°C form a gel irreversible by changes of temperature, pH or dilution. They were first recognised in 1953, and since then have been reported in a variety of conditions, mainly multiple myeloma, Waldenström's macroglobulinaemia, and lymphoma. We would like to report a patient with an unusual pyroglobulin. The patient had abnormal bleeding associated with defective ristocetin-induced platelet aggregation. This appeared to be related to the presence of the abnormal globulin. When the patient's serum was fractionated to obtain the abnormal pyroglobulin and when this fraction was added to normal plasma it produced a similar defect in platelet aggregation.

**Case report**

The patient was a 72-year-old woman. Six weeks prior to admission, she complained of arthralgia, involving both ankles, wrists, and knees. She was admitted after the development of a purpuric rash.

On examination, she had a marked purpuric rash over both legs. There was no lymphadenopathy and no hepatomegaly but her spleen was palpable 4-5 cm below.