


Ursula Turpeinen1
Caj Haglund2
Peter Roberts1
Ulf Håkan Stenman1

1 Dept Obst. and Gynecol., Lab., 2 Fourth Dept. Surgery
Helsinki Univ. Central Hosp.
Haartmaninkatu 2, 00290 Helsinki,
Finland

Healthy individuals Seropositive for Rheumatoid Factor

To the Editor:

Several authors have described frequencies of seropositive results for rheumatoid factor (RF) in healthy individuals without rheumatoid arthritis (1, 2). In a recent paper in this journal, Ailus et al. (3) show this prevalence in a subgroup of pregnant women.

However, there is no consensus on the extent of this clinical false-positivity (true positivity being given by subjects with rheumatoid arthritis diagnosed according to criteria of The American College of Rheumatology). These rates are probably mainly dependent on the methodology used, as Ailus et al. show.

We would like to mention two ideas. Many commercial kits for RF measurement have the drawback of requiring heat inactivation of sera at 56°C for 30 min to denature the complement component C1q, which causes a positive interference in some RF assays. Nevertheless, heat inactivation produces erroneous results by leading to the aggregation of endoge-

nous IgG, which inhibits the binding of RF to the aggregated IgG added with the reagents. C1q interference can easily be avoided by including a chemical inhibitor of C1q (polyvinyl sulphonate, sodium salt) in the reaction medium (4).

Second, using two methods that do not require sample pretreatment (5), we recently confirmed that some RF-positive sera become negative after heat treatment, as determined with a nephelometric or a turbidimetric RF test.

These results indicate that methods requiring heat inactivation of sera may present a high rate of false-negative results, especially for RF concentrations in the range of 20–45 kIU/L, and should not be used for RF quantification.

Establishing RF reference values is very difficult because of the poor analytical sensitivity of the various available methods and the extremely low RF values in healthy individuals. In many RF assays, the upper “normal” limit is not in accordance with recent foundations of the International Federation of Clinical Chemistry or simply is not stated (6–8). We found that 96% of sera from a group of blood donors gave values <10 kIU/L (9) when assayed with a very sensitive method (detection limit, 10 IU/L). Therefore, when the clinical decision limit is arbitrarily set to coincide with the upper reference limit, the frequency of seropositive RF in a healthy population should be 5% if the test is sensitive enough.

We suggest that studies about frequencies of seropositive RF in healthy individuals should be carried out with methodologies having good analytical sensitivity and not requiring heat treatment of sera.

References


5. Borque L, Ruiz R, Ruiz A. Effect of serum heat treatment on rheumatoid factor meas-


Reliability of Immunoassays of Cyclosporin A in Blood

To the Editor:

The need to monitor blood concentrations of cyclosporin A (CaA) in patients with organ transplantation or autoimmune disorders has stimulated the introduction of commercial immunoassays with high throughput and ease of operation. The performance of these methods has usually been evaluated by comparison with existing immunoassays and with HPLC, where the main statistical parameters used have been the equation for the regression line and the correlation coefficient (r) (1, 2). This information is certainly relevant for comparison of the overall analytical performance of the method, but overlooks the importance of using the scatter around the regression line for a further evaluation of clinical acceptability of the new method, e.g., within a certain therapeutic range.

We provide an illustrative example of this situation, based on a comparison of two immunoassays of CaA with an HPLC method that compared well with an in-house mass spectrometry method (manuscript in preparation).

EDTA-anticoagulated blood was collected from pediatric patients with organ transplantation (heart, heart-lung, renal, and bone marrow), autoimmune diseases, or nephrotic syndrome, all of whom were receiving CsA therapy. Whole-blood samples