Evaluation of rheumatoid factor by a new latex enhanced immuno-turbidimetric assay

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Rheumatoid factor (RF) is an autoantibody with specificity for the Fc portion of polyclonal immunoglobulin G (IgG). It can occur in all the different types of classes of immunoglobulins (Igs) including IgG, IgA, IgE, IgM. However, the most important class is the IgM and which is routinely measured in the clinical immunology laboratory.[1] Rheumatoid factor has been classically associated with rheumatoid arthritis (RA) and many clinicians still regard the presence of RF as an indication of the disease.[2] However, RF is found in many other conditions than RA as well as in many elderly people (**Table 1**) and therefore, on its own, has very little diagnostic significance.[3]

Rheumatoid arthritis is a chronic inflammatory condition affecting predominantly the small joints of the hands, feet, wrists and knees at least initially. The course of the disease can range from a self-limiting illness to a severe erosive disease that progress rapidly with destruction of the joints. The latter form is also associated with extra-articular manifestations comprising of serositis, anemia, sicca syndrome and vasculitis.[4]

The role of RF in the pathogenesis of RA is still controversial; however, its role in the diagnosis and the prognosis of RA is well established.[5] Although by its own, RF has very little diagnostic significance, under appropriate clinical setting, it can be used to aid the diagnosis of RA. Indeed, it has been included amongst the diagnostic criteria for RA by the American association for rheumatologists.[6] However, the most important role of RF is in the prognosis of patients with RA. Patients who show persistently high concentrations of RF tend to follow an aggressive form of the disease, with severe destruction of the joints and extra-articular manifestations.[7] Such patients are generally treated more aggressively from the onset of the disease with disease modifying anti rheumatic drugs. The prevalence of RA in the general population is estimated to vary between 1 and 5%[8] and therefore the RF test tend to be one of the most commonly requested tests in the clinical immunology laboratory.

Testing for RF has been performed by the classic latex agglutination technique and positive samples are then quantified by the classical Rose Waaler assay. However, the latter assay is semi-quantitative, time consuming and involves a number of non-specific reactions that tend to contribute to the imprecision of the results. As the concentration of RF is used in the prognosis and treatment of RA and as the RF test is amongst the most commonly requested test in the laboratory, the method used to quantify RF should therefore

Table 1 - Conditions associated with positive RF antibody.

Conditions	Prevalence %
CTD	
Rheumatoid Arthritis	50-90
Systemic Lupus Erythematosus	15-35
Sjogren's syndrome	90
Polymyositis	5-10
Systemic sclerosis	20-35
Juvenile Rheumatoid Arthritis	7-10
Mixed Cryoglobulinaemia	90
Other diseases	
Interstitial lung disease	-
Liver Cirrhosis	-
Sarcoidosis	-
Malignancies	-
Infections	
Hepatitis C infection	-
Acute viral infections	-
Endocarditis	-
Tuberculosis	-
Elderly people	1-5

(-) results not available, RF - rheumatoid factor, CTD - connective tissue disease

Table 2 - RF results obtained by the Rose Waaler and a latex enhanced immuno-turbidimetric assay.

Rose Waaler assay (titres)	Turbidimetric assay (IU/ml) Mean±SD	Ranges
Negative	10±2	8-13
16	29±23	11-79
32	45±36	10-107
64	44±24	12-76
128	59±27	34-100
256	119±113	25-220
512	237±183	41-637
1024	273±121	24-401
2048	550±183	389-794

Positive values > 20IU/ml, RF- rheumatoid factor, SD - standard deviation

produce precise results and have a quick turn around time. In the present study we have evaluated a new latex enhanced immuno-turbidimetric assay and compared the results with that produced by the Rose Waaler assay. The study was conducted at the Department of Immunology, Birmingham Heartlands Hospital, between 2002 and 2003. Approximately 100 samples, previously found to contain different concentrations of the RF by a combination of a simple Latex agglutination and the Rose Waaler assays, were re-evaluated by a Latex enhanced immuno-turbidimetric assay using automated analyser. Preliminary experiments showed that, unlike the Rose Waaler assay, the new turbidimetric assay produced both precise and highly reproducible results. **Table 2** shows results obtained by both the Rose Waaler and the new latex enhanced immuno-turbidimetric assays. The results between the 2 assays correlated poorly. Thus many samples tested positive for RF, low and moderate titres, by the Rose Waaler assay, turned out to be negative by the new turbidimetric assay. Moreover, some samples tested strongly positive for RF (high titres) by the Rose Waaler assay, again turned out to have weak positive results by the turbidimetric assay. Regarding the costing of the new assay, the cost of testing for RF by the turbidimetric assay is more than twice as expensive as the Rose Waaler assay. However, the time taken to run a batch of samples is reduced considerably by using the new assay (the time taken to run 100 samples is reduced from 6 hours, using the Rose Waaler assay, to just 20 min by the new turbidmetric assay).

This brief study has indicated that the results produced by the classical Rose Waaler assay do not reflect the true picture of the levels of RF in many patient samples. As the concentrations of RF are used in the prognosis and treatment of patients with RA,[7] continual use of the Rose Waaler assay can no longer be justified and therefore clinical immunology laboratories still using this out dated method should consider moving to newer methods. We have shown that, unlike the Rose Waaler assay, the fully automated latex enhanced immuno-turbidimetric assay produces both quantitative and highly precise and reproducible results. Moreover, the cost of using this new assay would be nearly comparable to that of the Rose Waaler assay, when the cost of both reagents and personnel time are taken into consideration. Laboratory with limited resources can screen samples for RF by a simple Latex agglutination assay and positive samples can then be quantified by the latex enhanced immuno-turbidimetric assay, or alternatively by enzyme-linked immunosorbent assay.

In conclusion, the present study has clearly demonstrated that continual use of the Rose Waaler assay can no longer be justified and laboratories still using this out-dated assay should consider moving to new assays.

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