Autoantibodies: The mystery revealed

Connective Tissue Diseases

Insaf FENNICHE & **Ons ELHMADI**

Faculty of medicine of Tunis — *Faculty of pharmacy of Monastir*

Rheumatoid factors (RFs) s are immunoglobulins (IgM (fig.1), IgG, IgA, IgE, IgD) reacting with epitopes in the Fc fragment of the IgG heavy chain.

- **1940, Waaler** demonstrated the agglutinating power of IgM antibodies to sheep red blood cells sensitized with rabbit anti-sheep red blood cells serum.
- **1948, Rose** described antibodies in Rheumatoid Arthritis (RA) patients.
- **1952, named RF** due to association with rheumatoid arthritis.

- **Physiological polyreactive RFs: Low-affinity, seen in up to 4% of young, healthy and elderly.**
- **Pathological monoreactive RFs:**

❖ **Polyclonal, high affinity in infectious and rheumatic diseases**
❖ **Monoclonal, high affinity in Waldenstrom macroglobulinemia or chronic lymphocytic leukemia, often linked to cryoglobulinemia.**

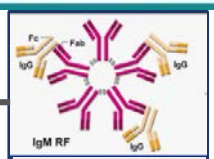

Fig.1: IgM RF

Rheumatoid factors

Main disease: RA

- RFs are included in 2010 ACR/EULAR RA criteria.
- **IgM** in RA diagnosis: valuable but **non-specific**; present in various **inflammatory** and **infectious** diseases.
- **Low sensitivity**: 50% in early forms, 75% in advanced stages.
- **IgA** determination offers **highest specificity**, serves as the **earliest marker**, and **correlates** better **with disease activity**. Usefulness remains unproven.

High RF (>3N): Strongly linked to
- **Rapid**, **severe**, **erosive** RA
- **Extra-articular involvement** (nodules, pulmonary issues, vasculitis)
- **Poor prognosis**

RFs are mainly detected in :

Rheumatoid arthritis (RA)	70-90%
Primary Sjögren's syndrome	75-95%
Systemic lupus erythematosus	15–35%
Systemic sclerosis	20–30%
Periarteritis nodosa	5–20%
Lymphoproliferative syndrome	10-20%
Primary biliary cholangitis	45-70%

Liver cirrhosis		25%
Subacute endocarditis		40%
Viral hepatitis		40%
Syphilis		40%
EBV and CMV		20%
Normal subjects	**< 30 years**	**1%**
	30-65 years	**5%**
	>65 years	**15%**

Detection techniques	**Nephelometry/Turbidimetry**	**ELISA**		**Waaler Rose**	**Latex**
Advantages	• Quantitative • Standardized • Automatisable • reproducible • Sensitive • Specific • Rapid • Detects all isotypes of the RF without distinction between them	• Quantitative • Possible standardisation • More sensitive and specific(/nephelometry) • Reproducible • Determines the different isotypes of the RF		• Specific • Not expensive	• Not expensive
Limits	• Costly instrumentation	• False positives • Time consuming • Requires technical expertise		• Lack of sensitivity • Lack of reproducibility • Semiquantitative • Detects only IgM RF • **Not recommended anymore (HAS 2007)**	
Antigen used	Human IgG	Human IgG	Animal IgG	Animal IgG	Human IgG
Sensitivity	60 to 83%	52 to 85%	42 to 75%	43 to 80 %	39 to 75%
Specificity	80 to 90%	46 to 90 %	42 to 95 %	87 to 90%	75 to 85 %

References

Rev Tun Biol Clin 2024 31(2)