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Singer J M & Plotz C M. The latex fixation test. I. Application to the serologic diagnosis of rheumatoid arthritis. *American Journal of Medicine* **21**:888-92, 1956.

The authors describe a latex fixation test for the serologic diagnosis of rheumatoid arthritis which improves on standard tests depending on erythrocyte agglutination by using biologically inert polyvinyl toluene and polysterene latex particles of uniform size. [The *SCI*® indicates that this paper was cited 566 times in the period 1961-1976.]

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"Science is a puzzle-solving activity based upon one or more scientific achievements, while the perception of scientific novelties emerge as unpredictable events.

"Cecil, Nicholls and Stainsby (1931)[1] described the agglutination by rheumatoid arthritis sera of streptococci isolated from patients with RA. Later Waaler (1940)[1] and subsequently Rose and Ragan[2] showed that sheep cells coated with antibody against sheep blood would also agglutinate in the presence of RA sera. Thus two puzzles based on a similar agglutination system were presented.

"In 1946 Wallis[1] was able to demonstrate that a small percentage of patients with RA could agglutinate collodion particles, a substitute for sheep cells, previously suggested by Goodner (1941).[1] Although collodion particles were thought to react nonspecifically in sera of RA, Charles Plotz, in 1953, began a new study at Mount Sinai Hospital (New York) designed to utilize carrier particles. In 1954 Heller, Jaobson, Kolodny, and Kammerer[1] identified the antigen as being human IgG. When I started working as a fellow in 1955, I continued to work on this project, but for six months results were very discouraging. Prior to discontinuance of this work. Dr. Orenstein, from the electron microscopy section of Mount Sinai, was asked to look at collodion particles and determine their size if possible.

"In 1954 the first latex particles of uniform size were developed by Backus and Vanderhoff.[2] This followed the observations of Williams (1947)2 that latex paints using particles of various sizes could be utilized in electron microscopy for secondary measurements of virus particles. Dr. Orenstein imbedded these particles in a micrograph grill. A print of the electron micrograph showed two or three perfect spherical, well dispersed latex particles, surrounded by a mass of particles which were clumped and unequal in size (our collodion particles). It was at this moment that the use of latex particles was visualized and their novel significance for many other applications fully perceived.

"Combining Heller's findings and our new latex, the latex fixation test was born. Clinical investigation of this test began, and in 1955 the second paper, 'Results in RA' by Plotz and Singer, appeared. Soon the last part of the puzzle was solved, the nature of the agglutinating factor of sheep cells or latex particles coated with HGG. Epstein, Johnson and Ragan (1956)[1] demonstrated that HGG reacts with sera of RA in a true immunological (precipitin) reaction. Franklin, Holman, Muller-Eberhard and Kunkel (1957)1 found that the antibody in RA sera is a 19S and 22S component called rheumatoid factor (RF). This opened the vista for further development of the latex test and, in immunology, the concept of auto-antibodies in RA sera and further development of the latex test.

"The principle involved, the use of latex particles which can be coated with antigens or antibodies, found applications in a great variety of serological tests as well as many other applications (in medicoserological tests, in the study of phagocytosis *in vivo* and *in vitro,* as immunological markers, in electron microscope scanning, adjuvancy, etc.). A new industry has been created producing and using these particles for scientific purposes including the development of kits for use in doctors' offices and laboratories.

"With all the vast number of developments over the past 22 years it is of interest that the original latex fixation test utilizing the same 0.8 latex particles has remained unchallenged and the standard by which other tests are judged."

REFERENCES

1. **Singer J M.** Latex fixation test in rheumatic diseases —a review. *American Journal of Medicine* **31**:766-79, 1961.
2. **Vanderhoff J W.** The use of monodisperse latex particles in medical research. American Chemical Society, Division of Organic Coatings and Plastic Chemistry. *Preprints* **24**:223-32, 1964.