

## This Week's Citation Classic

**Bendixen G & Søborg M.** A leucocyte migration technique for in vitro detection of cellular (delayed type) hypersensitivity in man. *Dan. Med. Bull.* **16**:1-6, 1969.  
[Medical Depts. P and A, Rigshospitalet, Univ. Copenhagen, Denmark]

A capillary tube migration technique for investigation of specific antigen-induced migration inhibition of human peripheral blood cells is described. The method, which is a modification of similar preexisting techniques used in animal experiments, can detect lymphocyte-mediated immunity (delayed hypersensitivity) associated with, e.g., immunity of infection and autoimmunity. [The *SCI*<sup>®</sup> indicates that this paper has been cited over 270 times since 1969.1

Gunnar Bendixen  
Medical Department TA  
and  
Laboratory of Medical Immunology  
Rigshospitalet  
University of Copenhagen  
DK 2200 Copenhagen N  
Denmark

October 20, 1981

"This paper describes the technique of antigen-induced peripheral blood leucocyte migration inhibition in man as it was performed when it was developed and fully established as scientific routine in our laboratory. The first publication on the subject appeared in 1967.<sup>1</sup>

"At the beginning of the 1960s, immunobiologists hypothesized that cell-mediated immune reactions as known from infectious disease and contact hypersensitivity were probably of pathogenetic importance also in tissue lesions in autoimmune conditions, transplantation syndromes, and tumour diseases. Their assumptions were supported partly by logical deduction and partly by extrapolation from animal experimental evidence. So far, however, an appropriate method for such studies in clinical research has not been developed.

"The idea to develop this *in vitro* technique for detection of cell-mediated immunity in man was inspired by the studies by John David and his group<sup>2</sup> on tuberculin-induced, lymphocyte dependent migration inhibition of guinea pig peritoneal

macrophages. Peripheral blood lymphocytes might be assumed representative of the cell-mediated immunity of any organism at any time, and antigen-lymphocyte interaction might cause inhibition of monocytes and/or granulocytes from peripheral blood in a way similar to the migration inhibition of guinea pig peritoneal macrophages. The capillary tube migration technique originally described by George and Vaughan<sup>3</sup> was therefore modified for use with peripheral human blood cells. At this time, my good friend Mogens Søborg obtained a position as research fellow and joined me in the laboratory.

"Results with tuberculin hypersensitivity were disappointing in these first experiments, but the *Brucella* model showed very clear results indeed. There was no doubt that this type of antimicrobial, cell-mediated immunity was associated with an antigen-specific reactivity of peripheral blood cells, demonstrable as antigen-induced migration inhibition *in vitro*. And the reactivity was closely related to the delayed type intracutaneous reaction to the same antigen. These results initially attracted only limited interest, since it was generally assumed that the system could only work with guinea pig macrophages. Søborg continued to explore the mechanism of the reaction, using *Brucella* hypersensitivity as a model, whereas, in my own studies, the technique was used to detect pathogenetic mechanisms in clinical immune disorders.

"The present paper was published at a time when significant results had shown that organ specific, cell-mediated immunity could be demonstrated with this technique in ulcerative colitis and glomerulonephritis. Later on, several other expectations were fulfilled: organ specific, cell-mediated immunity was demonstrated in other autoimmune conditions, and the method could detect cell-mediated immunity to tumours, transplants, and infection. Furthermore, this initially very crude technique could be refined and thereby contribute considerably to developments in the field of human lymphokine (lymphocyte hormone) research.<sup>4,5</sup> If the paper has been often cited, the reason may be both its clinical applicability within a field which at the time greatly needed an assay of this type and also its early initiation of improved techniques in basic lymphocyte research."

1. **Søborg M & Bendixen G.** Human lymphocyte migration as a parameter of hypersensitivity. *Acta Med. Scand.* **181**:247-56, 1967.
2. **David J R, Al-Askari S, Lawrence H S & Thomas L.** Delayed hypersensitivity in vitro. I. The specificity of inhibition of cell migration by antigens. *J. Immunology* **93**:264-73, 1964.
3. **George M & Vaughan J H.** In vitro cell migration as a model for delayed hypersensitivity. *Proc. Soc. Exp. Biol. Med.* **111**:514-21, 1962.
4. **Bendixen G, Bendtzen K, Clausen J E, Kjaer M & Søborg M.** Human leucocyte migration inhibition. *Scand. J. Immunol.* **5**(Suppl. 5): 175-84, 1976.
5. **Rocklin R E, Bendtzen K A Greineder D.** Mediators of immunity: lymphokines and monokines. *Advan. Immunol.* **29**:56-136, 1980.