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Field E J & Caspary E A. Lymphocyte sensitisation: an in-vitro test for cancer? *Lancet* 2:1337-41, 1970. [Medical Res. Council Demyelinating Diseases Unit, Newcastle General Hosp., Newcastle upon Tyne, England]

Blood lymphocytes of patients with a malignant neoplasm were sensitized to basic proteins derived from both the central and peripheral nervous system. If certain clearly defined limitations are observed, this lymphocyte sensitization could be employed as a diagnostic or screening procedure. [The *SCI*® indicates that this paper has been cited in over 280 publications since 1970.]

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The Medical Research Council (MRC) Demyelinating Unit, of which I was then honorary director, was employed in "follow my leader" research (Sir Peter Medawar), studying varying lymphocyte sensitization in multiple sclerosis (MS), a disease then "known" to be of immunological nature. David and colleagues' macrophage migration inhibition (MMI) method[1] depended upon lymphokine production.[2] It appeared to me that altered charge might accompany migration inhibition and be measured accurately by electrophoresis. Blood lymphocyte sensitization to purified protein derivative and thyroid extract was measured with peritoneal macrophages[3] from a closed colony of healthy guinea pigs as indicator cells. Infection (cf. Lewkonia and colleagues[4]) mars all results. Incubation of lymphocytes, antigen, and macrophages in medium 199, at room temperature, led to marked slowing of the indicator cells only when lymphokine had been produced. To eliminate possible mixed lymphocyte reaction between the 20-percent lymphocytes in peritoneal exudate and added human cells, we irradiated with 100-200 rads from a cobalt bomb. This fertile error, a dosage grossly inadequate for its purpose, nevertheless "tickled up" macrophages, making them more avid for lymphokine. This "tickling up" became integral to the method. Control experiments eliminated the effect of antigen or lymphocytes alone.

Casting around for a problem to which our method (meanwhile proven in Hashimoto's disease and MS) might be applied, we chanced upon carcinomatous neuropathy. Naturally, we found sensitization to both encephalitogenic factor[5] (EF) and sciatic nerve basic protein (SNBP). As controls, we used malignancies without nervous system involvement and, to our utter astonishment, found that they gave precisely identical levels. And so the method—very sensitive—was born. Quickly cancer basic protein (CaBP) was prepared, and lymphocytes from *all* malignant tumors were found to give positive results compared with controls and nonmalignant tumors. Malignancy of any sort produced a common surface epitope that, by a "quirk of nature," shared antigenic determinant(s) with EF and CaBP. Throughout biology and medicine, the macrophage electrophoretic mobility (MEM) test offers an accurate means of assessment of lymphocyte sensitization to any (clean) antigen. Research clearly is "inspired fumbling."

John Humphrey and A.J. Forrester vetted the method "blind" for the MRC and reported it valid.

In 1972-1973, however, "political warfare" with the then-secretary of the MRC as to the effort expected from senior staff halted work, and I resigned from the MRC to learn how it can be damaging to be right at the wrong time (Laqueur). Inevitably, an MRC trial became enmeshed in snags we had learned to avoid, but condemnation by such a prestigious body (in the true sense of the word—*Oxford English Dictionary*) made access to quality English journals impossible overnight. However, in Eastern Europe, confirmations appeared from Dresden (Müller),[6] Berlin (Pasternak),[7] and Rostock (symposium, September 1984).[8,9] A detailed and novel plan for cancer research laid before the MRC was shelved, and an "unpersoning" procedure initiated, which has smeared over into later studies of the genetics of MS, though confirmations have come frequently.[4,5]

The many safeguards needed for success have been set out in two recent works.[10,11] One author in Rostock, however, found the method "too much bother!" The original work was carried out in the MRC unit in collaboration with E.A. Caspary, whose health, I am sorry to say, has deteriorated badly recently.

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