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Immunodiagnosis of Cancer

SIR,—The letter from Professor E. J. Field and others on immunodiagnosis of cancer (9 September, p. 641), the publicity resulting from it, and the fact that we have now provided the first independent confirmation¹ of the macrophage electrophoretic mobility (M.E.M.) test as a technique for the early detection of cancer encourage us to bring to your attention the latest facts concerning this important development. In our preliminary series we examined blood specimens from 72 patients with cancer and 31 hospital staff using techniques similar to those of Field and Caspary.² With encephalitogenic factor (E.F.), a basic protein from human brain) as antigen, patients gave macrophage percentage slowing in the range 13-29% while all healthy staff were below 3.4% (with the exception of three sarcoidosis subjects who gave fully-positive results). The complete absence to date of any overlap in our results from the two groups is perhaps the most surprising feature of the M.E.M. test and the one which may keep it from joining the long line of past cancer tests now in limbo.

The test as described by Field and Caspary is technically difficult on anything but a small laboratory scale, and the next phase of development must be aimed at removing enough of the difficulties to allow the test to be tried in a wide range of pre-clinical feasibility studies. On this aspect we can already report considerable progress. Early studies showed that 100 rad of gamma

rays to the guinea-pig macrophages used as the indicator cells in the test could suppress most of the mixed lymphocyte interaction between the human lymphocytes and the guinea-pig lymphocytes removed along with the macrophages in the peritoneal exudate, but increasing the dose to 2,500 rad raised the percentage slowing from 14.8 to 22.3 in a typical case. To avoid such high doses we investigated a split incubation technique in which human lymphocytes are first incubated with the antigen to release the soluble macrophage slowing factor, which is then separated from the cells by centrifugation and added as a cell-free supernatant to the macrophage suspension for a second period of incubation. In this way the two lymphocyte populations are kept apart and a mixed interaction should not occur.

We found that when the second incubation is carried out at 37°C for 90 min irradiation of the macrophages can be omitted while still retaining a percentage slowing slightly greater than originally claimed by Field and Caspary. To our surprise we then found that irradiation of the macrophages to a modest 200 rad before this second 37°C-incubation caused the results from a group of patients with cancer to jump from the range 15.6%-21.0% to the new range 22.6%-40.0% without any corresponding effect on the low values from "normals," thereby making the gap between "malignant" and "normal" even wider. We have now adopted this MOD-MEM test

as a basis for all further development, and a full report of our findings is in press.³

It is not immediately clear why the 200-rad irradiation should have this effect, but the implication for the future of the MOD-MEM test is encouraging. The wider gap between malignant and normal reduces some of the technical difficulty at present impeding the test, since the larger difference is more easily seen against a background of apparatus instability or by an inexperienced operator, and it may allow some relaxation in sample-handling for greater clinical convenience. Even with further simplification the test will have limited value as a screening procedure for patients who do not display specific localizing signs or symptoms since there is at present no simple way to locate early malignant disease, except for a few sites such as cancer of the cervix. In view of this, we are now applying the MOD-MEM test to situations where it can be used in conjunction with existing clinical and ancillary investigations.—We are, etc.,

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¹ Pritchard, J. A. V., Moore, J. L., Sutherland, W. H., and Joslin, C. A. F., *Lancet*, 1972, 2, 627.

² Field, E. J., and Caspary, E. A., *Lancet*, 1970, 2, 1337.

³ Pritchard, J. A. V., Moore, J. L., Sutherland, W. H., and Joslin, C. A. F., *British Journal of Cancer*, submitted.