DISARMED ANTI-MALIGNIN ANTIBODY IN HUMAN CANCER

SIR,—The purification of an anti-cancer-cell antibody from human cancer sera has revealed much of the antibody to be structurally impaired—in fact, disarmed.

Malignin, a highly acidic polypeptide of approximately 10 000 molecular weight and unusual amino-acid composition, was produced from human malignant glial cells grown in tissue culture after a closely related polypeptide, astrocytin, had been obtained from human gliomas in vivo.[1] The quantitative demonstration of increased human anti-malignin antibody, first observed in brain-tumour patients,[2] has lately been extended to non-brain cancers. In a seven-hospital blind study on 290 sera[3] the antibody levels in both brain and non-brain cancer groups were significantly ($P<0.00001$ higher than those in medical or surgical patients without cancer and in healthy controls. These results suggested there might be cancer-cell antigen products in non-brain cancer cells which are closely related to malignin. These antigens have now been produced from the first two other human cancer cell types examined after growth in tissue culture—namely, recognin M from MCF-7 mammary cancer cells and recognin L from P,G lymphoma cells. They are both structurally and immunologically closely related to malignin.[3,4] Anti-malignin antibody, at approximately 1 ng protein, stains one cancer cell in Coons double-layer immunofluorescence[1,2,5] and has been used successfully in Papanicolaou smears of brain and a variety of types of non-brain cancer cells including lung, breast, and ovary. Thus studies on both antigens and antibodies, point clearly to there being a new family of immunochemically closely related cancer-cell antigens, reflecting the process of malignancy rather than the cell type, which we have called "recognins" because they are derived from glycoprotein fractions thought to be involved in cell recognition.[6]

The survival-rate of cancer patients with low serum anti-malignin antibody has now been compared retrospectively with that of patients with increased antibody. Of seven patients with low antibody (less than 135 μg/ml) five (71%) died within 8 months of diagnosis, whereas of sixty patients with increased antibody (greater than 135 μg/ml), seventeen (28%) were dead in the same period. In serial determinations a drop in anti-malignin antibody seemed to signal impending death. Thus the antibody seems to be beneficial—indeed, the intact antibody has been shown to be cytotoxic to malignant glial cells in vitro at approximately the same concentration as that which stains cancer cells in immunofluorescence.[6] A further property of the antibody is its ability to localise in vivo. ^{99m}Technetium-labelled anti-malignin antibody has been found to localise in vivo in rats preferentially in brain gliomas at a ratio of 10:1 over normal brain tissue.[6]

Using a variety of cancer sera, we have now further purified human anti-malignin antibody in milligram quantities by immunoadsorption to malignin antigen immobilised on bromoacetylcellulose (Brain Research, Inc.), followed by column chromatography on 'Cellex D' (Bio-Rad) and 'Sepharose CL6B' (Pharmacia). We have studied the resultant subfractions of the antibody by polyacrylamide gel electrophoresis, by immunofluorescent staining of biopsy material and Papanicolaou smear cancer cells, and by Ouchterlony double diffusion against anti-human immune globulin specific for gamma-globulin chains and specific for anti-human Fab and for anti-human Fc fragments (Miles) (detailed report in preparation). We found that a third or more of the antibody from human cancer sera is recovered in an incomplete form so that Fab fragments were free of Fc fragments. Other antibody Fab fragments separated from their Fc attachment lose several of their powers, including that of cytotoxicity.[7] This fragmented state would thus represent disarming of anti-malignin antibody in terms of its ability to destroy cancer cells.

The disarming of antibody may be one of the cancer cell's successful defences against host attack. It will have to be taken into account in the therapeutic attempts with purified anti-malignin antibody now underway.

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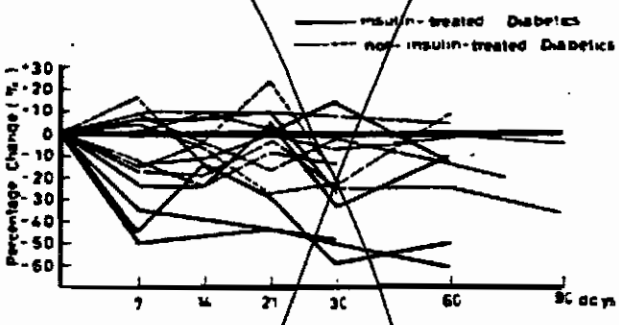
TREATMENT OF DIABETES WITH GLUCOMANNAN (KONJAC MANNAN)

SIR,—Dietary fibres have been used successfully to treat diabetes,[8-12] with a reduction of the doses of insulin or hypoglycæmic drugs. The mechanism of action of these fibres is thought to relate to the ability of fibre to increase the viscosity[13] of gastrointestinal contents, slow gastric emptying, and act as a barrier to diffusion by increasing the width of the unstirred layer. Among dietary fibres, guar gum[12] (galactomannan) has been found the most effective in reducing blood-sugar or glycosuria in diabetics.



Individual percentage changes in fasting blood-glucose concentrations of thirteen diabetics after they had taken glucomannan.

We have been studying konjac mannan (glucomannan) which is one of the unabsorbable polysaccharides and prepared from tubers of the *Amorphophallus* plant.[14] Konjac mannan is composed of glucose and mannose (molar ratio, 1:1·6), while guar gum is of galactose and mannose (molar ratio, 1:2). Konjac mannan is a normal Japanese foodstuff taken in gelled form.

When thirteen diabetic patients (adult type) had their metabolic ward diets supplemented with 3·6 or 7·2 g konjac mannan daily for 90 days, their mean serum-cholesterol at 20 days fell by 11·2% and their mean fasting glucose fell by 29% ($P<0.025$, for 30 days, see figure), and insulin or hypoglycæmic agents were reduced in dose or, in some patients, withdrawn.

Five healthy men underwent a 50 g glucose-tolerance test (G.T.T.) with and without 2·6 g konjac mannan. The additional

1. Bogoch, S. *Nat. Cancer Inst. Monogr.* 1977, 46, 133
2. Bogoch, S., Bogoch, E. S., Fager, C. A., Goldensohn, E., Harris, J. H., Hickok, D. F., Lowden, J. A., Lux, W. E., Ransohoff, J., Walker, M. D. *Neurology.* 1979, 29, 584.
3. Bogoch, S., Bogoch, E. S. *Am. Soc. Neurochem.* 1979, 10, 78 (abstr.)
4. Bogoch, S., Bogoch, E. S. *Neurochem. Res.* (in the press).
5. Harris, J. H., Gohara, A., Bogoch, S. *J. Neuropath. exp. Neurol.* 1978, 37, 623.
6. Bogoch, S. in *Current Trends in Sphingolipidoses and Allied Disorders* (edited by B. W. Volk and L. Schneck), p. 555. New York, 1976.
7. Winkelhake, J. L. *Immunochemistry.* 1978, 15, 965.
8. Jenkins, D. J. A., Wolever, T. M. S., Haworth, R., Lands, A. R., Hockaday, T. D. R. *Lancet*, 1976, ii, 172
9. Jenkins, D. J. A., Wolever, T. M. S., Haworth, R., Lands, A. R., Hockaday, T. D. R. *ibid* 1976, ii, 1086
10. Jenkins, D. J. A., Hockaday, T. D. R., Haworth, R., Apling, E. C., Wolever, T. M. S., Leeds, A. R., Bacon, S., Dilawari, J. *ibid.* 1977, ii, 779.
11. Kiehm, T. G., Anderson, J. W., Ward, K. *Am. J. clin. Nutr.* 1976, 29, 895
12. Jenkins, D. J. A., Wolever, T. M. S., Lands, A. R., Gassull, M. A., Hazzman, P., Dilawari, J., Goff, D. V., Metz, G. L., Alberti, K. M. G. M. M. *Br. med. J.* 1978, i, 1392
13. Wolever, T. M. S., Taylor, R., Goff, D. V. *Lancet*, 1978, ii, 1351
14. Kiriyama, S., Eanbi, A., Yuru, K. *J. Nutr.* 1974, 104, 69