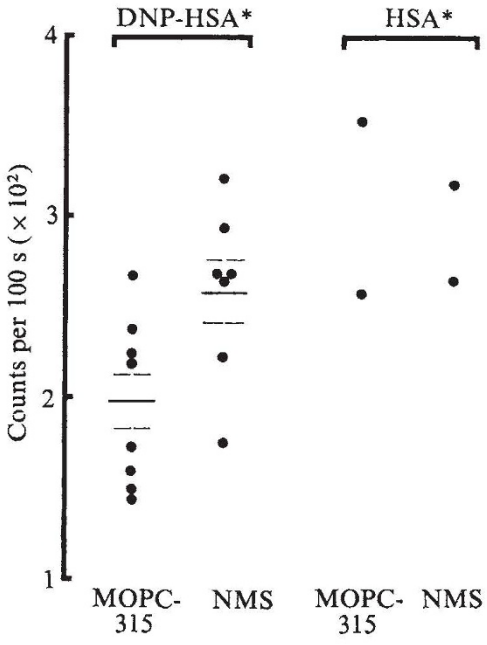


**Fig. 2** Serum radioactivity in rats 20 min after intratracheal injections of either $^{125}$I-labelled DNP-HSA (DNP–HSA*) or $^{125}$I-labelled HSA (HSA*). They had received either mouse serum containing MOPC-315 IgA myeloma protein or normal mouse serum (NMS) into the trachea 15 min before. Mean ± s.e.m. are shown.

In a second experiment, rats were bled only at 20 min. The radioactivity in the serum was rather higher in both groups than in the initial experiments but it was significantly less ($t = 2.54$; $P < 0.025$) in the group receiving MOPC 315 serum than in that receiving NMS (Fig. 2). There was no such obvious difference in the serum radioactivity in four rats receiving $^{125}$I-HSA instead of DNP-$^{125}$I-HSA, after either MOPC-315 or normal mouse serum.

These experiments show that an IgA myeloma protein, injected into the rat respiratory tract, can specifically prevent entry into the blood of antigen for which it has binding affinity. This strengthens the view that IgA may be responsible for this process in both the respiratory tract, in which this is the first evidence of specific immune exclusion, as well, presumably, as in the gut where such a phenomenon has already been demonstrated[2] without the mechanism being established. The evidence that this mechanism is defective in IgA deficient individuals, namely their antibodies to food proteins[4] and allergy[5,6,11], supports the view that IgA is important for this function, but immunodeficiency is often complex and other mechanisms might have been defective in such patients. Limited experiments with IgG rabbit anti-HSA antibody suggest that IgG may also be effective in our system. Walker and his colleagues[12] detected IgG1 anti-BSA antibody in extracts of intestinal mucosa and in intestinal secretions of rats immunised with BSA, so the IgG class may also be important, but the predominance of IgA in the secretions suggests that this is the main mechanism.

The use of the IgA myeloma protein avoids all the usual problems of establishing immunoglobulin class specificity of the observed biological effect, since the animals were not immunised. The negative controls using the DNP-$^{125}$I-HSA with normal mouse serum and using $^{125}$I-HSA with both MOPC 315 serum and NMS establish that it was an effect of IgA and exclude the possibility of nonspecific binding to HSA, a property of many IgA myeloma proteins[13].

The observed antigen exclusion in our experiments was an effect of IgA which probably lacked secretory component. It is likely that normal secretory IgA antibody, with its reported resistance to proteolysis[14], would be much more efficient. It is also possible, however, that the effect was due to polymerised IgA associated with secretory component derived from secretions of the recipient rats. In either case we have shown that IgA can produce this effect, even though the artificial system used may be suboptimal.

It is attractive to suggest that in the gut the complexes of IgA antibody with antigen are retained in the lumen till the antigen is digested. In the respiratory tract they may be swept up by cilliary action, swallowed and similarly digested, although most of the antigen remained in the lungs in our acute experiments. If the adherence of IgA to mucous membranes[15] is important in this system, it is possible that macrophages would be attracted by the chemotactic effect of complement, activated through the alternative pathway[16].

If the function of immune exclusion were defective in an individual capable of eliciting IgE, IgG or cell mediated responses to the antigen, local allergic lung or gut damage or generalised soluble complex disease could occur. Even a transient defect such as in presymptomatic atopic infants[6] could lead to persistent disease, since, once a population of sensitised cells is established, very little subsequent antigen entry would be required to maintain the process. Defects of the system we have described may, therefore, be the basis of many common diseases.

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## Erratum

In the article "Role of macrophages in *in vitro* induction of T-helper cells" by P. Erb and M. Feldmann (*Nature*, **254**, 352; 1975), page 353, column 2, line 3, for presence read absence.

In the article "Centrometric asymmetry and induction of translocations and sister chromatid exchanges in mouse chromosomes" by M. S. Lin and R. L. Davidson (*Nature*, **254**, 354; 1975) Figs 1 and 3 were transposed. The captions are correct as they stand.

In the article "Synthesis of ribosomal RNA during sporulation in *Bacillus subtilis*" by D. Testa and R. Rudner (*Nature*, **254**, 632; 1975) Fig. 1 was rotated through 90°. The time scale should have been on the abscissa.

In the article "Crystallisation of troponin-C" by D. Mercola, B. Bullard and J. Priest (*Nature*, **254**, 634; 1975) the results in the first sentence of paragraph 4 are not attributable to ref. 12.