Regulatory Mechanisms in Reagin Synthesis

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Several factors have been shown to regulate the production of reaginic antibodies. The formation of reagins in rabbits may be suppressed by IgG antibodies [Strannegard and Belin, 1970], whereas IgM antibodies may stimulate reagin production [Strannegard and Belin, 1971]. Although the induction of a reagin response is very sensitive to the suppressive effect of IgG antibody, we have not been able to significantly influence an already induced response with passively transferred antibody. Thus it is not known to what extent antibody-induced suppression of reagin synthesis operates in vivo.

The effect of varying dosages of antigen on the reagin response may bear some relationship to antibody-induced suppression. We have found that very high or very low doses of haemocyanin incorporated in Freund's adjuvant failed to give rise to reagin response although antibodies of other classes were produced. The dose-response curve had a peak at 0.5–5 mg and also a low peak at 50 ng of antigen. Thus, dependent on what reference point on the curve that was chosen, an increase of antigen dose could lead to either an increased or a decreased reagin formation. Although footpad immunization with adjuvant-incorporated antigen was superior to other modes of immunization in inducing reagin response, such responses were also demonstrated after intravenous, intranasal and oral administration of antigen. Intravenous injection of 1 µg haemocyanin resulted in a reagin response, initially in the absence of demonstrable IgG or IgM antibodies. One explanation for this finding could be that re-agin-forming cell precursors have a very high affinity for antigen.

Several components of birch pollen have been found to induce reagin formation when injected with adjuvant, whereas only heat-stable components do so when the pollen is introduced intranasally [Belin and Strannegard, 1971]. This finding would indicate that allergenicity of a substance is not solely dependent on its capacity to induce reagin formation. The studies with birch pollen suggested that part of the explanation as to

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why the pollen grains are allergenic may be that they have an adjuvant effect on antibody production. Thus in experiments using BSA as antigen, birch pollen was found to significantly increase the responsiveness to the antigen, as regards both production of reagins and haemagglutinating antibodies. In other experiments polymerization of BGG did not increase the reaginic response to this substance significantly. It is therefore not probable that the capacity of birch pollen to induce an allergic state is dependent upon its particulate nature.

Recent experiments have suggested that thymocytes may negatively regulate reagin formation [Okumura and Tada, 1971]. Similar experiments performed in rabbits suggested that thymocytes may either stimulate or suppress reagin formation, probably in a non-specific manner. In inbred mice the reagin response was enhanced when F1 hybrid animals were injected with parental spleen cells from unimmunized animals. Thus, in some as yet unclarified manner, thymus-derived lymphocytes seem to have a regulatory effect on reagin synthesis.

In conclusion, several factors have been found to regulate reagin synthesis. The nature and dose of allergen, the route of administration and formation of other classes of antibodies seem to be very important for the regulation. A regulatory role can probably also be attributed to thymus-derived lymphocytes. In addition to the factors discussed in this paper, reagin synthesis appears to be dependent on genetic factors, the age of the individual, hormonal influences and probably also other factors. Since some of the factors appear to have different effects on IgE and IgG synthesis it should be possible to find means of manipulating antibody responses towards less production of IgE-antibodies. With such manipulations it should then be possible to treat atopic disease more efficiently than what is presently done.

References

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