THE ROLE OF PEYER'S PATCHES IN THE MODULATION OF IMMUNE RESPONSES

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SUMMARY

This thesis is concerned with the characterization and modulation of immune responses to V.cholerae presented by different routes, in mice.

A key question examined is whether the preponderance of IgA found after oral immunization is due to the modulation of the response by cells in the Peyer's patches (PP). An alternative hypothesis examined is whether the antigen is processed in some way by the PP so that it specifically stimulates IgA forming cells.

The Jerne plaque forming cell assay was used for the estimations of antibody responses in spleen and gut lamina propria.

The following are the salient observations:

(1) Although the individual IgM or IgA spleenic response in systemically primed and boosted mice is dose dependent, the combination of a very low IgA/IgM ratio and absence of gut response seem to be a function of the route and schedule of the immunization.

(2) Repeated oral immunization followed by systemic boosting leads to a high response in the spleen with a high IgA/IgM ratio. No gut response is detected.

(3) Good responses in the gut are only obtained by repeated high-dose oral priming followed by an oral boosting. The IgA/IgM ratios are highest by this regimen in both spleen and gut lamina propria.

(4) By the nature of IgA/IgM ratios of antibody responses in the spleen it is possible to differentiate between a systemic and a local (intestinal) immune stimulus.

(5) The IgM spleenic antibody responses in mice to V.cholerae following adoptive transfer of PPL from antigen-fed syngeneic donors are profoundly suppressed as compared with the responses obtained in control mice receiving antigen only or antigen plus unprimed PPL from normal conventional donors. The IgA responses in the same experiments are variable, being enhanced, suppressed or remaining unchanged.

(6) When the mixed population of PPL from antigen-fed donors are partitioned into purified T and B cell subsets and are injected separately into the recipients along with the antigen, either T or B cell subset is shown to bring forth concurrent suppression of IgM and enhancement of IgA response in the spleen as compared with results of the control mice described above.

The finding of concurrent IgM suppression and IgA enhancement by gut-presentation of antigen is discussed in the light of earlier evidence. The implication of these phenomena in the immunologic homeostasis of the host is considered.