Patients with common variable hypogammaglobulinemia (CVH) often have circulating suppressor cells that profoundly inhibit normal immunoglobulin (Ig) production in vitro. We have examined the nature of signals operating in the interaction between CVH-associated suppressor cells and their targets, and explored the possibility that lectin-like receptor molecules and their specific sugars might contribute to the specificity of these interactions. When D-mannose was added to suppressed cocultures of normal PWM-activated mononuclear cells and patient T cells a significant enhancement of Ig production was observed. N-acetyl-D-glucosamine had a similar enhancing effect when added to suppressed cocultures of normal mononuclear cells and patient non-T cells. Since D-mannose and N-acetyl-D-glucosamine did not enhance Ig production by normal cells when cultured alone, these sugars were interfering with the process of suppression. In contrast, a number of other saccharides had no effect on suppression. These results suggest that selected saccharides may represent critical components in the cellular receptors involved in suppressor cell interactions.

Introduction

Little is known about the molecular nature of signals operating in the interaction between suppressor cells and
their targets. In other systems it has been shown that specific cell surface carbohydrates may serve as recognition and interaction structures (Shen et al., 1968; Reisner et al., 1977; Ofek et al., 1977; Muramatsu et al., 1979; Sharon, 1983). We have recently reported that D-mannose and some of its derivatives can significantly reverse inhibition of immunoglobulin production mediated by suppressor T cells activated during the course of acute EBV-induced infectious mononucleosis (Tosato et al., 1983). This finding indicated that D-mannose and selected mannose derivatives were interfering with the process of suppression, and suggested that certain carbohydrates may represent critical components involved in physiologic suppressor cell interactions.

In the present study we have tested the hypothesis that specific carbohydrate molecules might be involved in other suppressor cell interactions, and looked at the in vitro effects of a panel of sugars on suppression mediated by T cells as well as non-T cells from a selected group of patients with common variable hypogammaglobulinemia (CVH).

Patients and Methods

Mononuclear cells were obtained from peripheral blood of normal individuals and 11 patients with CVH. These patients were known to have circulating suppressor cells (Waldmann et al., 1974). Selected clinical and laboratory data relating to these patients are shown in Table I. Of interest, patient no. 2 developed hypogammaglobulinemia 1 year earlier, following an illness clinically and serologically defined as acute Epstein-Barr virus (EBV)-induced infectious mononucleosis (Henle et al., 1974). B cell-enriched and T cell-enriched cell subsets were obtained by incubating the mononuclear cells with AET-sensitized sheep red blood cells and separating the rosette forming cells on Ficoll-Hypaque gradients, as described (Tosato et al., 1983). Normal and patient mononuclear cells (1x10^6) were cultured alone in the presence of pokeweed mitogen (PWM) or EBV. In addition, normal mononuclear cells (0.5x10^6) were cultured in the presence of PWM either alone or mixed in culture with patient T (0.5x10^6) or non-T cells (0.25x10^6). At the end of a 6-8 day culture period the number of immunoglobulin (Ig) secreting cells was determined.