Defects in cellular immune responsiveness have been repeatedly described in patients after serious injury or major burns. The exact relationship between impairment of cellular immunity and septic complications in such injured patients is unknown. Nevertheless, there are several reports which indicate that clinical anergy in patients with major burns, for example, is significantly correlated with mortality, particularly with death from sepsis. A number of years ago, we reported anergy in patients after major burn injury was associated both with failure of circulating lymphocytes from such patients to respond normally to the T cell mitogens phytohemagglutinin (PHA) and Concanavalin A (Con A), and with the presence in the patients' serum of circulating substances suppressive of activation of normal human T lymphocytes.

In order to investigate the apparently abnormal T lymphocyte function in injured patients and burn patients, we investigated circulating T lymphocyte subsets with monoclonal antibodies in patients with burns of greater than 30% body surface area and those with lesser degrees of burn injury. We showed that patients after major burn injury had a significant early alteration in the ratio of circulating helper-inducer to cytotoxic-suppressor T cell phenotypes. This reduction tended to return towards normal several weeks after burn injury, and it was again altered in association with the appearance of systemic sepsis. We also found similar changes in patients suffering from major traumatic injury. More recent studies have indicated that patients with severe burns have an early and persistent reduction in the percentage of circulating T cells (Figure 1), and that the reversal of the ratio of T helper-inducer to cytotoxic-suppressor subsets is caused chiefly by an absolute diminution in the number of circulating T helper cells. This diminution was not found consistently in trauma patients. As a correlative to these studies, we also found that patients after serious thermal injury often had circulating lymphocytes of immature phenotypes not normally seen in the circulating blood, including lymphocytes expressing the OKT6 and OKT9 antigens.

We and others have examined the question of whether or not increased circulating suppressor cell activity could account for the impairment of T lymphocyte activation seen in patients following major injury. In patients with major burns, we found that circulating peripheral blood mononuclear cells (PBMC) were on some occasions capable of inhibiting proliferation of lymphocytes from normal human volunteers in response to T cell mitogens or alloantigens in vitro. However, because of

Fig. 1. OKT3 positive cells (total circulating T cells) following burns. 17 patients with burns, 30% total body surface area or greater (▲) are compared to 8 with burns less than 30% total body surface area (▲) and shown as the mean±1SEM. The control range is shown. (⁎p < 0.05 patients versus controls, †p < 0.05 burns greater than 30% versus burns less than 30%). (Reprinted from Annals of Surgery)

potentially factitious results inherent in assays which involve the simultaneous culture of multiple allogeneic cell populations, these results and similar results reported from other laboratories clearly must be interpreted with caution. Experiments to demonstrate suppressor cell activity in autologous culture systems by subtracting and re-adding appropriate cell types have proved difficult and so far have not produced sufficiently consistent results to permit firm conclusions.

One assay used in many laboratories for the detection of suppressor cell activity in an autologous system, namely the inhibition of polyclonal immunoglobulin (Ig) production by T lymphocytes in response to pokeweed mitogen (PWM) has not yielded positive results in seriously injured patients (Figure 2). In fact, patients with major burns, for example, often have background polyclonal Ig production by circulating B cells that is in excess of PWM stimulated Ig production by similar cells from normal control individuals. Thus, circulating suppressor T cells in burn patients, if present, are clearly not effective in inhibiting PWM stimulated B cell Ig production, a finding consistent with the observation that there is not an increased percentage of cells bearing the cytotoxic-suppressor phenotype in the PBMC of these patients.

Because of the persistent impairment of T lymphocyte activation seen in seriously injured and burn patients, we have more recently studied the ability of PBMC from such individuals to produce the cytokines necessary for the initiation of the immune response. Adherent cells from the PBMC population of seriously injured patients and patients with major burns were studied for their ability to produce interleukin 1 (IL 1) in response to endotoxin and the PBMC of the same individuals were studied for their ability to produce interleukin 2 (IL 2) in response to PHA stimulation in vitro. We have found that IL 1 production by the