All lacked plasma cells and cells exhibiting *cytoplasmic* fluorescence with fluorescine-labeled antibodies to IgM, IgG, and IgA in biopsies of ileum and stimulated lymph node. In contrast to the patient with XLA, patients with SA had prominent germinal centers in stimulated nodes; one had the syndrome of nodular lymphoid hyperplasia (NLH). Using criteria established for identification of bursa-derived lymphocytes in chickens, B-lymphocytes were identified by electron microscopy in the lymph node of one patient with SA; only T-lymphocytes were found in the patient with XLA. *Membrane-bound* immunoglobulins (IgM, IgG, and IgA) were detected by immunofluorescent studies of living peripheral blood lymphocytes of both patients with SA, but were not found on cells from the patient with XLA. The results indicate that in these patients with SA, lymphocytes of the plasma cell line are able to synthesize surface immunoglobulins and to respond to antigenic stimulation by germinal center formation but fail to differentiate to the stage of antibody secretion; lack of antibody-mediated "feedback" inhibition of antigen-induced proliferation may account for the NLH often observed in SA. Our observations also provide preliminary evidence that B and T lymphocytes can be distinguished at an ultrastructural level in man.

Phytohemagglutinin (PHA) skin test: A measure of intact cell-mediated immunity. RICHARD J. BONFORTE, R. MICHAEL BLAESE, MARCEL TOPILSKY, LOUIS E. SILTZBACH, and PHILIP R. GLADE. *Mt. Sinai Sch. Med., City Univ. N. Y., N. Y.*

PHA is a non-specific stimulant of normal lymphocytes resulting in vitro in their blast-like transformation with increased RNA and DNA synthesis, mitosis, and the release of putative mediators of cell-mediated immunity. Histologically the skin reaction to intradermal PHA shows perivascular infiltration of mononuclear cells, the hallmark of delayed-type hypersensitivity. Since prior exposure is not required—only the capacity to respond—PHA appears to be the ideal agent to assess cell-mediated immunity in vivo. In a continuing series of more than 30 individuals 2 μg of PHA intradermally produces erythema and induration in 24–48 hrs., despite the presence or absence of cutaneous reactivity to other skin-test antigens (PPD-S, histoplasmin, mumps, SK-SD, candida, and trichophyton). In a selected group of patients in vivo skin reaction to PHA correlates with in vitro response of the individual's peripheral blood lymphocytes to PHA. PHA in vivo thus appears to be an effective measure of intact cell-mediated immunity and is especially useful in infants and children who have had limited prior exposure to those antigens normally used as skin-test reagents.

Pernicious anemia, concordant twins, and immune dysfunction. ERWIN W. GELFAND, A. IZZET BERKEL, HERMAN A. GODWIN, ROSS E. ROCKLIN, JOHN R. DAVID, and FRED S. ROSEN. *Children's Hosp. Med. Ctr., Boston City Hosp., and Robert B. Brigham Hosp., Boston, Mass.*

The pathogenesis of pernicious anemia (PA) may be mediated by auto-immune mechanisms. However, the presence or absence of antibodies to intrinsic factor has not been clearly correlated with the clinical course of the disease. Three members of one family, a mother and identical twin daughters, were found to have classical PA and achlorhydria. Schillings tests revealed less than 1% excretion of the $Co^{57}B_{12}$ isotope. Repeat tests with orally administered intrinsic factor increased the isotope excretion to 10% or more. The twins, unlike their mother, had low levels of serum γG, absent γA, and normal γM globulins, and impaired antibody responses. The serum of the mother and only one of the twins contained antibodies to intrinsic factor and gastric parietal cells. Lymphocytes from the mother and the twins, cultured in the presence of intrinsic factor, underwent transformation with increased uptake of H^3-thymidine into DNA (stimulation indices—9.8, 2.5, 1.4). Production of migration inhibition factor in similar cultures in these three patients resulted in 17, 37, and 9% inhibition of macrophage migration. These studies suggest that cell-mediated immunity, rather than humoral immunity, may play a critical role in the development of PA.

Lymphopenia, dysgammaglobulinemia and decreased cellular immunity: A genetic lymphocyte defect. ARMOND S. GOLDMAN, C. WAYNE SMITH, and ELTON DUPREE. *Univ. of Tex. Med. Branch and Shriner's Burns Inst., Galveston, Tex.*

A previously unrecognized genetic immunologic disorder is reported. The patient a 13-year-old female, presented with recurrent viral and bacterial infections, eczema and acute allergic reactions. Humoral and cellular immunity were reduced, the serum IgG and IgM were low; IgD was normal; IgA and IgE were increased. She was lymphopenic, but her thymus appeared normal microscopically. In comparison to normal lymphocytes, her blood lymphocytes in culture did not suppress the life-span of PMNs. In those leukocyte cultures, the PMNs inhibited blastogenesis due to phytohemagglutinin, concanavalin A, pokeweed mitogen and antigens. However, in PMN-depleted cultures the relative frequency of blastogenesis became normal but lymphocyte survival and quantitative blastogenesis due to antigens and mitogens were reduced.

The parents' lymphocytes were unable to limit PMN survival *in vitro* and the relative frequency of transformation of their lymphocytes was reduced. However, the functions of their lymphocytes in PMN-depleted cultures seemed normal. These findings suggest that the principal defect in this disease is in the lymphocytes and that the propositus is homozygous for the defective gene, whereas, the asymptomatic carriers are heterozygous. Although this disorder resembles the Wiskott-Aldrich syndrome, the genetic aspect of the disease, the lack of thrombocytopenia, the low IgG and other features indicate that this is a previously undescribed primary immunologic disorder.

Macrophage function in severe combined immunodeficiency. RICHARD A. GATTI and ROBERT A. GOOD. *Univ. of Minn., Minneapolis, Minn.*

In patients with severe combined immunodeficiency (i.e., lymphopenic agammaglobulinemia), both humoral and cell-mediated forms of immunity are lacking as a result of absence of immunoblasts or lymphoid precursor cells capable of differentiating into plasma cells and small lymphocytes. The small lymphocytes of these infants do not respond to stimulation in vitro with phytohemagglutinin, allogeneic cells or antigens. This situation can be corrected by transplanting bone marrow from an HL-A compatible healthy donor. This finding establishes that the differentiative sites are intact. Macrophage function has not been evaluated in these patients. Nor is there clear evidence to indicate whether macrophages derive from the same defective precursor stem cells as lymphocytes. In these experiments, a glass-adherent cell population was obtained from two patients with severe combined immunodeficiency. After three days incubation, these adherent cells (i.e., macrophages) were added to highly purified lymphocytes from two PPD-sensitive donors. Such highly purified lymphocytes do not respond to antigens in the absence of at