what was found in this study. I found it discouraging that two thirds of the people who should have been receiving γ globulin were not.

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**Recognition, Clinical Diagnosis and Management of Patients With Primary Antibody Deficiencies: A Systematic Review**


**PURPOSE OF THE STUDY.** To create an evidence-based literature review of clinical diagnosis and management of primary antibody deficiency.

**METHODS.** Computer literature searches were conducted for randomized clinical trials in medical literature databases including the US National Library of Medicine (Medline), the Excerpta Medica database (EMBASE), the Cochrane Library, the Database of Abstracts of Reviews of Effects (DARE) of the Centre for Reviews and Dissemination (University of York), and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) up to June 2006. Reports were rated on the basis of relevance and quality or type of evidence. Disease entities included were X-linked agammaglobulinemia, common variable immunodeficiency, hyper–immunoglobulin M (IgM) syndromes, IgG subclass deficiency with and without IgA deficiency, and specific antibody deficiency. Reports that involved only a limited number of patients were not included.

**RESULTS.** Individuals who present with recurrent respiratory infections of all types, especially with excessive frequency and severity, should be screened for antibody deficiency. In children, common associations included growth delay and failure to thrive, recurrent fevers without a source, and poor school attendance or performance. Chronic diarrhea was found in 40% to 60% of the patients at all ages. The median delay in diagnosis was 1 year but ranged to >10 years. Delayed diagnosis led to increased risk of bronchiectasis, pulmonary hypertension, and cor pulmonale. Randomized trials of the efficacy of γ-globulin replacement versus placebo do not currently exist. Many observational studies have confirmed the benefit of IgG therapy for reducing infectious morbidity. Higher IgG doses are associated with reduced incidence and severity of infections.

**CONCLUSIONS.** Delayed diagnosis was common as a result of lack of recognition of presenting symptoms and signs. Delay was less frequent when patients were referred to specialists. Delayed diagnosis led to delayed therapy (IgG) and a higher rate of infections and morbidity. Several areas for additional research were identified, including studies of efficacy and dose of IgG and adjunct therapies (antibiotics), microbiologic study of pathogens, identification of prognostic markers, and effective monitoring of disease (eg, lung function, other organs, cancer). Collaboration and pooling of data among centers nationally and internationally would likely lead to better data.

**REVIEWER COMMENTS.** This study again points out the human cost of delayed or undiagnosed immunodeficiency and the difficulties in accumulating high-quality data on therapy and outcomes. Several initiatives are taking shape in the United States and abroad to collaborate to answer many of the remaining questions points out in this study.

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**HUMAN IMMUNODEFICIENCY VIRUS**

**Functional Patterns of HIV-1-Specific CD4 T-Cell Responses in Children Are Influenced by the Extent of Virus Suppression and Exposure**


**PURPOSE OF THE STUDY.** HIV-specific CD4+ T cells seem to play a critical role in antiretroviral immunity and particularly in maintaining cytotoxic T-cell responses. The objective of this study was to evaluate the function of HIV-specific T cells in antiviral treated, HIV-infected children.

**STUDY POPULATION.** The researchers evaluated 23 HIV-infected children who were treated with antiretroviral therapy for a mean of 7 years.

**METHODS.** Flow-cytometric analysis was used to measure the ability of HIV-specific T cells to secrete interleukin 2 (IL-2) and interferon γ (IFN-γ) after stimulation of patient cells with p55 gag protein.

**RESULTS.** Three patterns of intracellular cytokine generation were identified: in 10 subjects, antigen-specific cytokine production was characterized by IL-2 production, 8 subjects’ CD4+ T cells expressed IL-2 and IFN-γ, and 5 subjects’ T cells expressed IFN-γ alone. These 3 groups were then analyzed for factors that might explain the different patterns. The patterns correlated with viral load at the time of functional analysis and over the previous 2 years. The group with dominant IFN-γ responses had high viremia levels, a pattern similar to that observed in patients with uncontrolled viral replication. Patients with combined IL-2 and IFN-γ production had relatively lower viral loads but had experienced viral “blips” over the 2 years before analysis. This pattern was similar to...
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