GASTROINTESTINAL INVOLVEMENT IN CHRONIC GRANULOMATOUS DISEASE


Purpose of the Study. To evaluate the clinical presentation, prevalence, and consequences of gastrointestinal (GI) involvement in patients with chronic granulomatous disease (CGD).

Study Population. A registry of 140 patients with CGD (67% X-linked) maintained at the National Institutes of Health.

Methods. This was a retrospective review of records from 1988–2002. GI involvement was defined as abdominal pain, diarrhea, constipation, obstruction or fistulas, and involvement of the esophagus, stomach, or bowel confirmed by endoscopy and/or histology. Other causes of GI involvement were excluded from analysis.

Results. Forty-six (33%) patients had documented GI involvement; 44 (96%) were male. Mean age of CGD diagnosis was 2 years (range: birth to 27 years), and median age of GI involvement was 5 years (range: 10 months to 30 years). Thirty-two (70%) patients experienced GI symptoms in the first decade of life, 9 (20%) in the second decade, and 5 (10%) in the third decade. In 8 (17%) patients, GI manifestations preceded the diagnosis of CGD. A high proportion (89%) of those with GI manifestations had X-linked inheritance. All patients experienced severe infections except for 2 kindred, who only experienced GI involvement. Mortality was equal in GI-affected and unaffected groups and was a result of severe infection. Although all patients experienced abdominal pain, it was the primary presenting complaint in 33% of patients. Other symptoms included diarrhea (39%), nausea and vomiting (24%), and constipation (2%). Obstruction occurred in 35% of patients involving gastric, esophageal, duodenal, and other locations. Despite interferon γ prophylaxis in 89% of GI patients, there seemed to be no protection; 81% of unaffected patients had received similar prophylaxis. After endoscopic confirmation of GI granuloma, successful treatment was initiated by using prednisone (1 mg/kg per day with taper to ~0.25 mg/kg every other day), but 71% experienced relapse. Two patients became hypertensive, and 1 developed cataracts. After bone marrow transplantation, 3 patients experienced remission of GI involvement.

Conclusions. GI involvement in CGD is common and recurring, especially in those with X-linked inheritance. Interferon γ prophylaxis does not reduce involvement or affect mortality.

Reviewers’ Comments. Although CGD is a rare disorder, the pediatrician must be aware of the classic presentation involving infection of the skin, deep tissues, and bone and complications such as GI granuloma formation. This is especially true in those with X-linked disease. Abdominal pain or abdominal symptoms voiced by a child with CGD must be evaluated thoroughly and, when not infection-related, treated with corticosteroids (in some cases, long-term). Bone marrow transplantation can be effective in inducing remission of the disease including the GI manifestations.

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HEALTH-RELATED QUALITY OF LIFE OF CHILDREN WITH PRIMARY IMMUNODEFICIENCY DISEASE: A COMPARISON STUDY


Purpose of the Study. To compare parental perceptions of health-related quality of life (HRQOL) in children with primary immunodeficiency (PI) with children with juvenile idiopathic arthritis (JIA) and healthy children.

Study Population. Thirty-six children in each of 3 groups (108 total): those with PI, those with JIA, and those who were healthy. Patients were matched for age, ethnicity, and parental marital status. The age ranged from 4 to 18 years, and 94% were white. All patients with PI received regular infusions of intravenous immunoglobulin. Of the patients with JIA, 77% had either oligoarthritis or polyarthritis. The JIA group had a significantly higher proportion of females.

Methods. Parents were interviewed and completed the Child Health Questionnaire-Parental Form 50. Treating physicians completed forms documenting any complications of the underlying disease.

Results. In comparison to healthy children, those with PI had significantly lower scores on physical functioning, school and social activities, limitations on parental time and family activities, and parental emotional distress. They were equivalent to the healthy group with respect to overall psychosocial health, daily pain and discomfort, social limitations, self-esteem, mental health, general behavior, and family cohesion. In comparison to the JIA group, children with PI were similar. However, they scored lower than the JIA group with respect to perception of general health and limitations on parental time and family activities. The children with JIA had more bodily pain and discomfort than the children with PI.

Conclusions. Children with PI have significant impairment in several measures of HRQOL in comparison to healthy children. These limitations are similar to, and in some cases more severe than, those occurring in another group of chronically ill children, those with JIA.

Reviewers’ Comments. This study begins to fill the gap in our understanding of the impact of PI on the quality of life of children and families. Despite some limitations in size and scope, it is clear that HRQOL in children and families with PI is impaired (even when the disease is treated with intravenous immunoglobulin) to a degree that is on a par with other serious chronic disorders that are generally better recognized. Overall, PI is underdiagnosed, to what extent is unknown. This study suggests that not only is there room for improvement in HRQOL aspects of disease management or patient care in those who already have a diagnosis of PI but also implies that there are gains in HRQOL to be made with improved diagnosis of PI.

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CHILDREN AND ADULTS WITH PRIMARY ANTIBODY DEFICIENCIES GAIN QUALITY OF LIFE BY SUBCUTANEOUS IgG SELF-INFUSIONS AT HOME


Purpose of the Study. To determine the impact of a change from in-hospital infusion of intravenous immunoglobulin (IVIG) to in-home infusion of subcutaneous immunoglobulin (SCIG) on health-related quality of life (HRQOL) and treatment satisfaction.

Study Population. Fifty-eight patients between the ages of 2 and 75 years (17 patients <14 years old [“children” for the purposes of this study]; 41 patients ≥14 years old [“adults”]) with primary antibody deficiency. Thirty-seven patients were receiving IVIG, and 10 were receiving SCIG.
(a control group to compare for effects specifically related to the switch from IVIG to SCIG); priority therapy for 1 patient was not stated.

**Methods.** Patients received weekly SCIG infusions at home over a period of 10 months (43 infusions). Questionnaires were administered at baseline and at 6 and 10 months. For assessment of HRQOL in children, parents completed the Child Health Questionnaire-Parental Form 50; adults used the Short Form 36. For assessment of treatment satisfaction, the authors adapted a Life Quality Index instrument previously developed in a study of antibody-deficient patients receiving IVIG.

**Results.** On the Child Health Questionnaire-Parental Form 50, the children demonstrated significant improvement in 6 of 14 concepts analyzed: “role/social-emotional, behavioral,” “general health perceptions,” “parental impact-emotional,” “parental impact-time,” “family activities,” and “global health.” On the Short Form 36, adults had improvements in vitality, mental health, and social functioning. These differences were found only in those adults who switched from IVIG to SCIG, not in those who were already receiving SCIG, suggesting that the improvement resulted from the change in therapy. Both children and adults had significant improvements in Life Quality Index. Again, in the adults, no change was seen in the group that was already receiving SCIG at enrollment. At study end, all children/parents, the 10 adults on SCIG at enrollment, and 73% of the adults who switched preferred to continue SCIG at home. Two expressed a preference for SCIG regardless of setting, 1 expressed a preference for home regardless of method, 1 expressed no preference for anything, and only 1 expressed a preference for IVIG in the hospital.

**Conclusions.** Home therapy with SCIG in children and adults with antibody deficiency is generally self-perceived as superior to in-hospital therapy with IVIG with respect to several validated measures of HRQOL.

**Reviewer’s Comments.** IVIG has been a major mode of therapy for immunodeficiency for 30 years. Many primary care providers have 1 or a few patients who receive this therapy. Less widely recognized, SCIG has also been used with safety and efficacy equivalent to IVIG and has been the major mode of immunoglobulin delivery in some countries (although this is an off-label use in the United States). For a variety of reasons, SCIG is gaining in popularity and may replace IVIG for many patients with immunodeficiency diseases.

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**HUMAN IMMUNODEFICIENCY VIRUS**

**PERFORMANCE CHARACTERISTICS OF HIV-1 CULTURE AND HIV-1 DNA AND RNA AMPLIFICATION ASSAYS FOR EARLY DIAGNOSIS OF PERINATAL HIV-1 INFECTION**


**Purpose of the Study.** The diagnosis of HIV infection in a newborn exposed to HIV in utero is a challenge. In the early years of the epidemic, HIV clinicians monitored the decline of HIV antibody levels for up to 2 years after birth to confirm that a child was not HIV-infected. HIV infection in infants is now typically made by the detection of viral DNA sequences in peripheral blood mononuclear cells by means of a DNA polymerase chain reaction (PCR). Plasma HIV-RNA measurements with PCR may also be valuable but has the theoretic limitation of false-negative reactions resulting from early treatment of the mother and infant. The purpose of this study was to evaluate the performance of HIV DNA PCR, HIV RNA PCR, and HIV culture to identify infected infants exposed to the virus in utero.

**Study Population.** Infants participating in the Pediatric AIDS Clinical Trials Group protocol 185.

**Methods.** Specimens from the infants (24 infected and 100 uninfected) obtained prospectively were studied with standard nucleic acid–amplification assays and peripheral blood mononuclear cell microcultures. The sensitivities, specificities, and positive and negative predictive values were calculated for each of the 3 assay systems.

**Results.** At birth the sensitivity of culture, DNA PCR, and RNA PCR were 21%, 11%, and 27%, respectively. By 6 weeks, the sensitivity had improved to 90%, 83%, and 95%. The specificity was 99% to 100% for all assays at all times.

**Conclusions.** The authors concluded that the diagnostic performance of the RNA PCR assay matched or exceeded that of culture and DNA PCR. Because RNA assays require less blood volume and often can be performed more quickly at reference laboratories, it is suggested that RNA assays may be used for early diagnosis of HIV infection in infants.

**Reviewer’s Comments.** This study demonstrates that RNA PCR assays are effective for the diagnosis of HIV infection. However, it must be noted that cryopreserved specimens were used for these PCR assays and may have impacted the sensitivity of the DNA PCR. Additionally, we have had 3 false-positive RNA PCR assays in 2 newborns and 1 adolescent exposed to HIV. A negative RNA PCR at or after 6 weeks of age strongly indicates that an infant is not infected.

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**GROWTH HORMONE IN T-LYMPHOCYTE THYMIC AND POSTTHYMIC DEVELOPMENT: A STUDY IN HIV-INFECTED CHILDREN**


**Purpose of the Study.** Growth hormone (GH) plays a role in thymic function, and decreased hormone secretion has been reported in HIV-infected children. Highly active antiretroviral therapy suppresses HIV replication and results in increases in CD4+ T cells in HIV-infected patients. The aim of this study was to determine if the level of immune reconstitution associated with antiretroviral therapy is influenced by the status of the GH insulin-like growth factor 1 axis.

**Study Population.** HIV-infected children (n = 26) were studied. Half of them had GH deficiency as defined by a reduced peak GH response to GH-releasing hormone and arginine-stimulation test. These patients were matched to 13 patients of similar age, pubertal status, and clinical findings but with normal GH-response tests.

**Methods.** Thymic volume was measured with magnetic resonance imaging. Peripheral blood lymphocyte subsets were evaluated with standard monoclonal antibody techniques. Serum interleukin 7 levels were measured with an enzyme-linked immunosorbent assay.

**Results.** The 2 patient populations did not differ in age, weight, height, body mass index, pubertal status, clinical or immunologic stage of disease, or number and percentage of CD4+ T cells before beginning antiretroviral therapy. After antiretroviral therapy, children with GH deficiency had reduced CD4+ T-cell numbers and percentages, reduced interleukin 7 concentrations, and reduced thymic
Children and Adults With Primary Antibody Deficiencies Gain Quality of Life by Subcutaneous IgG Self-Infusions at Home

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