A COHORT STUDY OF NEURODEVELOPMENTAL OUTCOME IN CHILDREN WITH DIGEORGE SYNDROME FOLLOWING CARDIAC SURGERY

Maharasingam M, Ostman-Smith I, Pike MG. Arch Dis Child. 2003;88:61–64

Purpose of the Study. To examine whether cognitive impairment among patients with DiGeorge syndrome (DGS) is secondary to cardiac pathologic conditions and their treatment or is a feature of the DGS phenotype.

Study Population. Ten patients with 22q11 deletions who had undergone cardiac repair in infancy, along with 2 control subjects for each patient, matched with respect to gender and age and having the same or similar cardiac defects and normal 22q11, were studied. Children ranged from <1 year to ~8 years of age at the time of developmental testing.

Methods. Patient records were reviewed retrospectively for features of DGS (hypocalcemia and immunodeficiency), operative data such as duration of bypass and postoperative ventilation, and episodes of hypotension or hypoxia and acidosis. Determinations of developmental quotients (DQs) were performed (in an unblinded manner, because DGS is associated with characteristic facial features) by a single investigator, using the Ruth Griffiths Abilities of Infants and Young Children tool. Patient and control groups were compared with multiple analyses of variance.

Results. There were no significant differences between patients and control subjects with respect to age at presentation or surgery or with respect to operative characteristics and complications. Associations with DQs of 22q11 deletions with hypocalcemia and immunodeficiency were highly significant (p = .004-.009); the associations were not independent, because all are linked features of DGS. The DQs for DGS patients (mean: 71; 95% confidence interval: 113; 95% confidence interval: 108–118; P = .0001). Perioperative acidosis was strongly associated with lower DQs among children with DGS (P < .005) but not among control subjects.

Conclusions. Abnormal neurodevelopmental outcomes in DGS are not solely the result of cardiac lesions and their surgical repair. Also, DGS may predispose patients to worse neurodevelopmental outcomes after cardiac surgery because of factors intrinsic to the disease, 1 of which appears to be hypocalcemia.

Reviewer’s Comments. DGS occurs at a rate of ~1 case per 3000 live births. Previous studies showed developmental delays or cognitive impairment in a subset. This study shows that little is attributable to cardiac complications themselves. However, it suggests that DGS may predispose patients to greater susceptibility to poor neurodevelopmental outcomes after surgery because of associated conditions, such as hypocalcemia.

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SAFETY OF LIVE VIRAL VACCINES IN PATIENTS WITH CHROMOSOME 22Q11.2 DELETION SYNDROME (DIGEORGE SYNDROME/VELOCARDIOFACIAL SYNDROME)

Perez EE, Bokszczanin A, McDonald-McGinn D, Zackai EH, Sullivan KE. Pediatrics. 2003;112:e325–e327

Purpose of the Study. To investigate the incidence of side effects after live viral vaccine administration in a population with chromosome 22q11.2 deletion syndrome.

Study Population. A total of 174 patients with chromosome 22q11.2 deletions were evaluated at Children’s Hospital of Philadelphia between 1994 and 2002. Of these, 59 patients completed a questionnaire regarding live viral vaccination; these constituted the study population.

Methods. Patient records were reviewed retrospectively. Data acquisition was designed to record the clinical consequences of vaccination or of withholding the vaccines.

Results. Thirty-two patients received varicella vaccine. Of those, 12 (23%) reported mild adverse reactions, consisting of fever, rash, and malaise. None of the unvaccinated patients developed wild-type measles, mumps, or rubella infection. For neither varicella vaccine nor measles-mumps-rubella vaccine were T cell counts correlated with the occurrence of adverse effects.

Conclusions. Adverse reactions to common, live, attenuated, viral vaccines among patients with 22q11.2 deletions were similar in frequency and severity to those in the general population. Varicella vaccine appeared to be very protective in this population.

Reviewer’s Comments. As the authors noted, this study was limited by size, by its retrospective nature, by comparison with the general population, and by relying on parental recollection of adverse events. Also, T cell counts at the time of immunization were not available for many patients, because the diagnosis was not yet established. However, this analysis provides a very reasonable basis for the general safety and efficacy of these vaccines among patients with 22q11.2 deletions and lays the groundwork for a more definitive prospective study.

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TARGET CELLS OF EPSTEIN-BARR VIRUS-POSITIVE POSTTRANSPLANT LYMPHOPROLIFERATIVE DISEASE: SIMILARITIES TO EPSTEIN-BARR VIRUS-POSITIVE HODGKIN’S LYMPHOMA


Purpose of the Study. To determine the types of B cells from which posttransplant lymphoproliferative disease (PTLD) arises.

Study Population. Tissue samples and DNA extracted from fresh tumors were obtained from 13 patients with PTLD.

Methods. Tumor suspensions were stained with monoclonal antibodies to surface B-cell (CD20 and CD38) and T-cell (CD3) markers and cell surface and cytoplasmic immunoglobulin heavy and light chains. The presence of Epstein-Barr virus (EBV) was detected with in situ hybridization assays for EBV-encoded RNA. Immunoglobulin heavy chain sequences corresponding to framework regions and complementarity-determining (antigen-binding) regions were determined with polymerase chain reaction assays. The sequences were analyzed for suggestions of antigen-selected genotypes (normal memory B cells).
Results. Twelve tumors were of B cell origin and expressed surface or cytoplasmic immunoglobulin. One tumor was a B cell–T cell composite. All 13 malignant B cell populations were positive for EBV-encoded RNA. Of the 11 biclonal and monoclonal tumors, 4 appeared to arise from memory B cells, 5 seemed to be derived from somatically mutated non-memory B cells, and 2 had inactivated immunoglobulin heavy chain sequences, because of a stop codon and a large deletion causing an out-of-frame mutation.

Conclusions. PTLD can arise from atypical, post-germinal center, B cells that have failed selection into memory cells, like the monoclonal tumors of Hodgkin’s lymphoma, as well as from the antigen-selected memory cells that are usually colonized by EBV in immunocompetent individuals.

Reviewers’ Comments. Although the ages of the patients with PTLD were not reported in this study, young children receiving posttransplant immunosuppressive therapy are at increased risk for this disease, because they are more likely to be EBV-susceptible at the time of transplantation. The suggestion of a common initiation step in the pathogenesis of PTLD and Hodgkin’s lymphoma may lead to future diagnostic and therapeutic breakthroughs.

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HUMAN IMMUNODEFICIENCY VIRUS

FAILURE OF 1 WEEK ON/1 WEEK OFF ANTIRETROVIRAL THERAPIES IN A RANDOMIZED TRIAL


Purpose of the Study. Although highly active antiretroviral therapy (HAART) has dramatically improved the duration and quality of life of human immunodeficiency virus (HIV)-infected individuals, an increasing number of serious complications are being identified among patients who are treated with these agents for long periods of time. Strategies that reduce the total drug exposure among infected patients while maintaining the stability of HIV and T cell levels would be welcomed. Scheduled or structured treatment interruptions are being evaluated in an effort to decrease the costs and side effects of HAART.

Methods. In this study, 600 patients receiving successful HAART were randomized to either continuous therapy, CD4+ T cell count-guided therapy, or 1 week on/1 week off therapy.

Results. This report described the preliminary analysis of data for the 1 week on/1 week off arm. Of 36 evaluable patients, 19 had 2 successive HIV RNA plasma concentrations of ≥500 copies/mL after 1 week off therapy; those cases were classified as virologic failures. Most of the patients who experienced failure were receiving didanosine, stavudine, saquinavir, and ritonavir. Among those patients, there was no evidence of mutations suggesting drug resistance. Plasma saquinavir levels were within the expected range.

Conclusions. The 1 week on/1 week off schedule tested in this study showed an unacceptably high failure rate and was therefore terminated early.

Reviewer’s Comments. Early anecdotal reports suggested that HIV-specific immune responses were boosted after discontinuation of therapy. Clinical trials based on this concept were developed for both acute and chronic HIV infections. The most promising results were from studies involving subjects who were treated for acute HIV infections; specific T cell responses to HIV were enhanced after interruptions in therapy. Similar findings have not been demonstrated for patients with chronic HIV infections. The results of this study are certainly disappointing. However, the definition of virologic failure in this study was a rebound to ≥500 copies/mL, which may be acceptable. The major concern with this approach would be the development of resistance to the antiretroviral therapy if repeated rebounds were allowed to continue in the off weeks. Studies of scheduled or structured treatment interruptions will continue. Perhaps a 2 weeks on/1 week off or 3 weeks on/1 week off schedule would limit the viral rebounds and still reduce the cumulative drug exposure for patients.

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USING POINT-OF-CARE TESTING TO MAKE RAPID HUMAN IMMUNODEFICIENCY VIRUS-1 TESTS IN LABOR REALLY RAPID


Purpose of the Study. The US Food and Drug Administration recently approved the OraQuick rapid human immunodeficiency virus-1 (HIV-1) antibody test (OraSure Technologies, Bethlehem, PA). The test is designed for point-of-care testing for HIV. The test is performed with a small amount of blood, and results are available within 20 to 30 minutes. Remarkably, this test is as sensitive and specific as the standard enzyme-linked immunosorbent assay for HIV-specific antibodies. The purpose of this study was to evaluate the differences in turnaround times between hospitals where obstetric staff members performed the rapid test at the point of care and a hospital where testing was performed in the hospital laboratory.

Results. During a 7-month period, 5771 women were evaluated in the labor and delivery areas of the target hospitals, and 514 met the criteria for rapid HIV testing. Of those, a total of 225 women were tested at 3 hospitals that used point-of-care testing and 155 were tested at a hospital that used the laboratory for the same test. Standard enzyme-linked immunosorbent assays confirmed 100% of the rapid test results. Three women were identified as being HIV infected; in those instances, antiretroviral therapy was administered during labor and delivery and/or administered to the neonate. The median turnaround time at the 3 hospitals that used point-of-care testing was 45 minutes (range: 30 minutes to 2.5 hours); the hospital that used the laboratory had a median time of 3.5 hours (range: 94 minutes to >16 hours; P < .0001).

Conclusions. The OraQuick rapid HIV-1 antibody test is a highly accurate measure of HIV risk, for use in a number of clinical settings. With the OraQuick test, hospitals can rapidly identify HIV-infected individuals. This study demonstrates that true point-of-care testing dramatically reduces the time needed for test result availability and allows clinical interventions in a timely manner.

Reviewer’s Comments. Same-day access to HIV test results could greatly reduce the number of adults who are tested but never return to the test site for their HIV test results. The availability of the OraQuick test also has the potential to reduce the already low incidence of perinatal HIV transmission. It currently takes days to obtain HIV antibody test results for individuals presenting to a hospi-
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Elinor Simons and Robert A. Wood

*Pediatrics* 2004;114;550

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