# Leukocyte Adhesion Deficiency

## Clinical Background

Leukocyte adhesion disorders (LAD) are a primary immune deficiency affecting phagocytic blood cells.

### Epidemiology

- Incidence – <1/1,000,000
- Age – usually identified in infancy or early childhood

### Inheritance

- Heterogeneous mutations in the CD18 leukocyte integrin gene
- At least 3 defects known (LAD-I, LAD-II, LAD-III)
  - LAD I – integrin expression defect
  - LAD II – selectin defect
  - LAD III – defect in integrin activation
- Autosomal recessive inheritance

### Pathophysiology

- Blood neutrophils are the first line of defense against bacterial and fungal infection
- Initial neutrophil adherence is weak but becomes strong with the aid of beta integrin interactions
- LAD involve defects in integrin expression leading to defective adhesion of neutrophils, leading to increased susceptibility to bacterial and fungal infections

### Clinical Presentation

- LAD I – characterized by delayed separation of the umbilical cord, recurrent soft tissue infections, chronic periodontitis, marked leukocytosis and lack of neutrophils in tissue infections
- LAD II – same features as LAD I, but also growth and mental retardation abnormalities but with no delay in separation of umbilical cord
- LAD III – same features as LAD I and severe bleeding tendency

### Treatment

- Early intervention for periodontal disease
- Preventive antibiotics for infection
- Allogeneic bone marrow transplant for severe disease

## Diagnosis

- Indications for testing – child with recurrent infections and in whom more common immunodeficiencies have been ruled out; tissue infections with absence of inflammatory cells
- Laboratory testing
  - CBC reveals leukocytosis with neutrophilia (even in the absence of infection but exaggerated during infection)
  - Flow cytometric analysis
    - CD11b and CD18 expression on leukocytes
      - No expression – 75% die in infancy
      - 1-10% – 33% survive to age 40 years
      - >10% – mild deficiency which may not be recognized until late teen years

Differential Diagnosis

- Neutropenic disorders
- Agranulocytosis
- IRAK-4 deficiency
- Job syndrome
- Chronic granulomatous disease
- Myeloperoxidase deficiency

## Lab Tests

**Indications for Laboratory Testing**

Tests generally appear in the order most useful for common clinical situations. For test-specific information, refer to the test number in the ARUP Laboratory Test Directory on the ARUP Web site at www.aruplab.com.

| Test Name and Number | Recommended Use | Limitations | Follow Up |
|---|---|---|---|
| CBC with Platelet Count & Automated Differential<br>0040003<br><br>Method:<br>Automated Cell Count with Flow Cell Differential | Recommended testing to reveal leukocytosis with neutrophilia | | |
| Neutrophil Receptor Profile<br>0095921<br><br>Method:<br>Flow Cytometry | Diagnose LAD | | |

**General References**

Bunting M, Harris ES, McIntyre TM, Prescott SM, Zimmerman GA. Leukocyte adhesion deficiency syndromes: adhesion and tethering defects involving beta 2 integrins and selectin ligands.Curr Opin Hematol. 2002; 9 (1) 30-35.

Cox DP, Weathers DR. Leukocyte adhesion deficiency type 1: an important consideration in the clinical differential diagnosis of prepubertal periodontitis. A case report and review of the literature.Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008; 105 (1) 86-90.

Etzioni A. Leukocyte adhesion deficiencies: molecular basis, clinical findings, and therapeutic options.Adv Exp Med Biol. 2007; 601 51-60.

Immune Deficiency Foundation. [Accessed: 17 Apr 2009]

Lakshman R, Finn A. Neutrophil disorders and their management.J Clin Pathol. 2001; 54 (1) 7-19.

Shyur SD, Hill HR. Recent advances in the genetics of primary immunodeficiency syndromes.J Pediatr. 1996; 129 (1) 8-24.

Webber EC, Church J, Rand TH, Shah AJ. Leukocyte adhesion deficiency in a female patient without delayed umbilical cord separation.J Paediatr Child Health. 2007; 43 (5) 406-408.

**Reviewed by**

Hill, Harry R., MD. Group Medical Director, Laboratory of Immunology, ARUP Laboratories, and Executive Director of the ARUP Institute for Clinical and Experimental Pathology; Professor and Division Head, Pathology (Clinical), University of Utah

Wittwer, Carl T., MD, PhD. Medical Director, General Flow Cytometry Laboratory and Advanced Technology Group at ARUP Laboratories; Professor of Pathology, and Adjunct Professor of Biomedical Engineering, University of Utah

**Diagnostic Algorithm(s)**

PDF algorithm(s) available at www.arupconsult.com.

Immunodeficiency Evaluation for Chronic Infections in Adults and Older Children Testing Algorithm

Immunodeficiency Evaluation for Chronic Infections in Infants and Children Testing Algorithm

**Related Content**

Bruton Agammaglobulinemia - X-Linked Agammaglobulinemia

Chronic Granulomatous Disease - CGD

Complement Deficiency

Immunodeficiency, Innate System

Immunoglobulin Disorders

Neutrophil Disorders

Severe Combined Immunodeficiencies - SCID

T-Cell Deficiency Disorders, Inherited

Comprehensive Review: May 2009
Last Update: May 2009