



**Leukocyte Adhesion Defect (LAD) Registry Data Collection Form**

Patient Initials: \_\_\_\_/\_\_\_\_/\_\_\_\_

**Patient Identification:**

Patient Name (first, middle, last) \_\_\_\_\_

Patient's USIDNET Registry Number assigned after online enrollment \_\_\_\_\_

Date of Birth \_\_\_\_/\_\_\_\_/\_\_\_\_(mm/dd/yyyy) or Year of Birth \_\_\_\_\_

Gender: male [ ], female [ ]

**Home Address:**

Address: \_\_\_\_\_

State: \_\_\_\_\_

Zip Code: \_\_\_\_\_

Phone: \_\_\_\_\_

Email: \_\_\_\_\_

State or Province of birth: \_\_\_\_\_

Country of birth: \_\_\_\_\_

Date of this Record Completion (mm/dd/yyyy): \_\_\_\_/\_\_\_\_/\_\_\_\_

Date of Visit (mm/dd/yyyy): \_\_\_\_/\_\_\_\_/\_\_\_\_

Is this the initial registration of this patient[ ] or follow-up?[ ]

**Submitting Physician Information:**

Name: \_\_\_\_\_

Address: \_\_\_\_\_

State: \_\_\_\_\_

Zip Code: \_\_\_\_\_

Phone: \_\_\_\_\_

Email: \_\_\_\_\_

Fax: \_\_\_\_\_

The hallmarks of leukocyte adhesion deficiency (LAD) are defects in the leukocyte adhesion process, marked leukocytosis and recurrent infections. These molecular and clinical manifestations result from an impaired step in the inflammatory process, namely, the emigration of leukocytes from the blood vessels to sites of infection, which requires adhesion of leukocytes to the endothelium. In the last 20 years, three distinctive defects in the leukocyte adhesion cascade, involving several precise ordered steps such as rolling, integrin activation and firm adhesion of the leukocytes have been described. While LAD I and II are clearly autosomal recessive disorders, the mode of inheritance of LAD III is still not clear. LAD I is due to structural defects in the integrin molecule, preventing a firm adhesion to occur. In LAD II, the primary genetic defect is in a specific Golgi GDP-fucose transporter that leads to absence of the selectin ligand on the leukocyte and a defective rolling. LAD III or LADI/variant, which was last described, is due to defects in the integrin activation process and also includes a severe bleeding tendency due to a platelet adhesion defect.. All three syndromes are very rare, LAD I being more frequent than LAD II and III, with LAD I being described in more than 300 patients worldwide and LAD II and III in less than 10 children each. The most important focus should be to control infections. Treatment includes antibiotics and in many cases bone marrow transplantation.

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### Diagnostic Criteria LAD-1

Definitive [ ]

A male or female patient with decreased intensity of expression of CD18 on neutrophils (less than 5% of normal) and **at least one** of the following:

Mutation in the  $\beta 2$  integrin gene [ ]

Absence of  $\beta 2$  integrin mRNA in leukocytes [ ]

Probable [ ]

A male or female patient with defective expression of CD18 on leukocytes (less than 5% of normal) and **all** of the following:

Recurrent or persistent bacterial or fungal infections [ ]

Leukocytosis (WBC greater than 25,000/mm<sup>3</sup>) [ ]

Delayed separation of the umbilical cord and/or defective wound healing [ ]

Possible [ ]

Infant with marked leukocytosis (WBC greater than 25,000/mm<sup>3</sup>) and **one** of the following:

Recurrent bacterial infections [ ]

Severe deep seated infection [ ]

Absence of pus at sites of infection [ ]

### Spectrum of disease

Marked leukocytosis and recurrent bacterial infections are the hallmarks of LAD. Staphylococcus, gram negative enteric bacteria and fungal infections are particularly troublesome. Periodontitis is a very common persistent finding. In the severe form, no expression of CD18 is detected on neutrophils and early death occurs without BMT. In the moderate form, a small amount of CD18 is expressed and patients can survive to adulthood. Some patients may have normal CD18 expression with a defective CD18 ( $\beta 2$  integrin) activity.

Exclusion criteria

Normal CD18 and CD15s expression on neutrophils

Normal neutrophil counts

Normal neutrophil adhesion

Rare leukocyte adhesion deficiency type II (**LAD II**) is due to an inborn error in fucose metabolism caused by mutations in the guanosine diphosphate-fucose transporter gene. There is a failure to express the ligand for E and P selectin, sialyl Lewis-X (**CD15s**), which is expressed on leukocytes. The patients are unable to fucosylate other glycoproteins, including the H blood group polysaccharide, so they are Bombay phenotype, ie, negative for the O and H blood group antigens and capable of making anti-H antibody. IgM and IgG are present in normal amounts. Patients have an increased incidence of bacterial infections, persistent leukocytosis, poor pus formation and a number of neurological, developmental and physical abnormalities, typical dysmorphic features, the Bombay (hh) blood phenotype and severe growth and psychomotor retardation. Infections of the skin, lungs, and gums resemble those seen in the moderate type of LAD-1, but the frequency and severity of infections tend to decrease with age.

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**Tests Performed** (check all that apply)

Indicate those tests / data used to establish the diagnosis by checking the indicated box [ ]

**Flow Cytometry (FACS)**

	Absent	present	If present, mean channel fluorescence (MCF)		Increase w activation?	Not Tested
			Patient MCF	Normal MCF	% expression	
CD18	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
CD11a	[ ]	[ ]	[ ]	[ ]		[ ]
CD11b	[ ]	[ ]	[ ]	[ ]		[ ]
CD11c	[ ]	[ ]	[ ]	[ ]		[ ]
CD15a	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
CD15s	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
Other (specify)						

**Adherence**

- Nylon wool [ ]
- Glass/plastic [ ]
- Cell to cell [ ]

**Blood counts** WBC elevated [ ] PMN elevated [ ]

Latest WBC and PMN (date \_\_\_/\_\_\_/\_\_\_) WBC \_\_\_\_\_ PMN \_\_\_\_\_ %  
 Maximum WBC & PMN (date \_\_\_/\_\_\_/\_\_\_) WBC \_\_\_\_\_ PMN \_\_\_\_\_ %

Bombay {hh} blood phenotype [ ]                      yes [ ] no [ ]  
 Anti-H antibody    yes [ ] no [ ]

**Genetic Information**

Sporadic [ ] (no family history) or [ ] \_\_\_\_\_ pattern of inheritance

**Pedigree Analysis**

Family history unknown [ ]

Please list additional relationships. If more space is needed, please use the Memo section at the end of this form.

Relation	LAD – alive	LAD – deceased	Tested Normal	Carrier	Not Tested	Unknown	Undiagnosed with suggestive symptoms
Mother							
Father							

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**Information on Other Affected Kindred Members listed above (e.g., sibling, cousin, other):**

Relation	Initials	Gender	Year of Birth	Listed in Registry? Yes/No/Unknown

**Gene Mutation**

LAD 1 [ ], LAD 2 [ ], LAD 3 [ ]  
 (Number nucleotides for CD18 using Kishimoto, *Cell* 48:681-689,1987)

Nucleotides affected (e.g., 361C>T) \_\_\_\_\_  
 Predicted Amino Acid Change (e.g., W140R) \_\_\_\_\_  
 Insertion / Deletion / Frameshift / Splice Site (please explain) \_\_\_\_\_  
 Mutation tested but not found [ ] which gene(s) tested \_\_\_\_\_  
 Publications (please give citation - if published) \_\_\_\_\_  
 Protein expressed? Yes\_\_\_\_\_, No\_\_\_\_\_, Not tested\_\_\_\_\_ Western [ ] FACS [ ]

**Clinical Features of Special Note**

	Not Seen	Observed	Prominent in this Patient	Unknown
Infectious Episode				
Skin wound				
Gingivitis				
Pneumonia				
Central line infection				
GI infection				
GU infection				
Sepsis				
Recurrent infections without pus formation				
Omphalitis				
Delayed separation of umbilical cord				
Dysmorphic features				
Psychomotor/growth retardation				
Bombay blood group				
Severe bleeding tendency				
Other (explain)				
None of the above				
<b>Comments:</b>				

**Other treatments used** List all complications at the end of this section \*.

**Cytokine Therapy**

	Yes	No	Unknown	Age	Date (dd/mm/yyyy)	Response
Gamma-interferon						
G-CSF						
GM-CSF						
IL-2						
Other (list):						

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Did this treatment lead to significant complications? Yes [ ], no [ ], unknown [ ]

*Complications:

	Yes	No	Unknown	Age begun	Date begun (mm/dd/yyyy)	Duration	Still needed?	
							Yes	No
Chronic oxygen								
Parenteral nutrition								

	Yes	No	Age or Date	Cells:	Vector	Outcome
Gene Therapy						
Publication?						

Other Treatments?	Yes	No	Age begun	Date begun (mm/dd/yyyy)	Duration	Still needed?	
						Yes	No

Did any of these treatments lead to significant complications? Yes [ ], no [ ], unknown [ ], explain:

*Complications:

Was steroid / immunosuppressive therapy needed for management? Yes [ ], No [ ], unknown [ ]

What kind? \_\_\_\_\_ dose \_\_\_\_\_ duration \_\_\_\_\_

What reason? Check appropriate boxes or add under 'other':

ITP	<input type="checkbox"/>	IBD or other gastrointestinal disease	<input type="checkbox"/>
Hemolytic Anemia	<input type="checkbox"/>	Lymphoma	<input type="checkbox"/>
Lung Disease	<input type="checkbox"/>	Vasculitis	<input type="checkbox"/>
Other (specify): _____			

Did this treatment lead to significant complications? Yes [ ], no [ ], unknown [ ]

*Complications:

**Additional comments:**

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