Test Definition: CIB

Cutaneous Direct Immunofluorescence Assay, Varies

Overview

Useful For

Confirming a diagnosis of bullous pemphigoid, cicatricial pemphigoid, pemphigoid gestationis and other variants of pemphigoid, all types of pemphigus, including paraneoplastic pemphigus (paraneoplastic multiorgan syndrome), dermatitis herpetiformis, linear IgA bullous dermatosis, chronic bullous disease of childhood, epidermolysis bullosa acquisita, porphyria cutanea tarda, bullous eruption of lupus erythematosus, and atypical or mixed forms of bullous disease, systemic lupus erythematosus, cutaneous lupus erythematosus, or other variants, vasculitis, lichen planus, and other inflammatory diseases

This test is **not useful** for diagnosis of malignancies involving the skin.

Testing Algorithm

For information see:
Autoimmune Blistering Disease Diagnostic Algorithm
Pathology Consultation Ordering Algorithm

Special Instructions

- Pathology Consultation Ordering Algorithm
- Autoimmune Blistering Disease Diagnostic Algorithm

Method Name

Direct Immunofluorescence Assay (IFA)

NY State Available

Yes

Specimen

Specimen Type

Varies

Necessary Information

All requisition and supporting information must be submitted in English.

Each of the following items is required:
1. All requisitions must be labeled with:
-Patient name, date of birth, and medical record number
-Name and phone number of the referring pathologist or ordering healthcare professional
-Anatomic site and collection date

2. A suspected diagnosis and reason for testing

See Specimen Required - Recommended Biopsy Site Selection Based on Disease State for how to label biopsy site specimens.

Specimen Required

Each biopsy requires **separate** specimen vials. If 2 or more biopsies are received in 1 specimen vial, expect testing delay. Note: Multiple biopsies can be ordered together. Tests performed on each site will be billed accordingly.

Transport Medium Method

Specimen Type: Tissue

Supplies: Michel's Transport Media for Immunofluorescent Testing on Tissue (T321)

Sources: Skin or 1 of the following mucosae: oral (oropharyngeal), nasal, genital, esophageal, conjunctival, laryngeal, or epiglottis

Container/Tube: Screw-capped container or vial containing transport medium (Michel's, also called Zeus media)

Specimen Volume: 2- to 8-mm punch specimen, intact or bisected; excisional biopsy specimen intact or bisected

Collection Instructions:

1. Collect biopsy of skin or mucosa avoiding old lesions (including facial), ulcers, erosions, or bullae. Refer to Recommended Biopsy Site Selection Based on Disease State below.
2. Immediately place specimen into a labeled vial of transport medium and seal tightly.

Acceptable

Snap-Frozen Method

Specimen Type: Tissue

Sources: Skin or 1 of the following mucosae: oral (oropharyngeal), nasal, genital, esophageal, conjunctival, laryngeal, or epiglottis

Container/Tube: Plastic vial

Specimen Volume: 2- to 8-mm punch specimen, intact or bisected; excisional biopsy specimen, intact or bisected

Collection Instructions:

1. Collect biopsy of skin or mucosa avoiding old lesions (including facial), ulcers, erosions, or bullae. Refer to Recommended Biopsy Site Selection Based on Disease State below.
2. Immediately place specimen into liquid nitrogen and allow to freeze thoroughly (do not allow specimen to desiccate). If liquid nitrogen is not available, specimen may be frozen by placing it on a small square of aluminum foil on a block of dry ice. Liquid nitrogen is preferred.
3. Immediately wrap specimen carefully in aluminum foil. At no time should the specimen be allowed to thaw.
4. Place the wrapped specimen into the prelabeled plastic vial and seal tightly. Ship frozen.

Recommended Biopsy Site Selection Based on Disease State

1. Pemphigus and pemphigoid groups (including linear IgA bullous dermatosis and chronic bullous disease of childhood)**:** Biopsy erythematous perilesional skin or mucosa. Avoid erosions, ulcers, and bullae while obtaining tissue adjacent to active lesions. Label as perilesional skin.

2. Dermatitis herpetiformis: Biopsy normal-appearing skin, 0.5-1 cm away from lesion. Label as perilesional skin.

3. Lupus erythematosus: Involved areas of skin such as erythematous or active borders are preferred biopsy sites to confirm the diagnosis of lupus erythematosus, either discoid or systemic. Label as involved skin. Avoid ulcers, old lesions, and facial lesions, if possible. Uninvolved, nonexposed skin is the preferred site to detect a lupus band as may be found

in systemic lupus erythematosus. Should unexposed skin be desired, buttock or medial thigh is suggested. Label as uninvolved, nonexposed skin.

4. Mixed connective tissue disease: Biopsy as for lupus erythematosus except when sclerodermoid features are present. For sclerodermoid features, biopsy inflamed area. Label as involved or uninvolved, exposed or nonexposed skin.

5. Vasculitis and urticaria: The erythematous or active border of a new lesion is preferred. Avoid old lesions and ulcers. Label as involved skin. If appropriate, skin lesion is not present, diagnosis may sometimes be made from uninvolved skin.

6. Porphyria: Biopsy involved skin. Avoid old lesions and ulcers. Label as involved skin.

7. Lichen planus and lichenoid reactions: Biopsy involved skin. Avoid old lesions and ulcers. Label as involved skin.

Specimen Minimum Volume

See Specimen Required

Reject Due To

Biopsy tissue from lung, kidney, muscle, salivary gland, veins, synovial tissue, bronchial tissue, or bronchial lavage	Reject
Formalin-fixed biopsy tissue	Reject
Biopsy tissue frozen in alcohol	Reject
Biopsy tissue in Trumps media	Reject
Biopsy tissue in glutaraldehyde	Reject
Biopsy tissue in Hank's media	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)	30 days	
	Refrigerated	30 days	
	Frozen	120 days	

Clinical & Interpretive

Clinical Information

Skin or mucosal tissue from patients with autoimmune bullous diseases, connective tissue disease, vasculitis, lichen planus, and other inflammatory conditions often contains bound immunoglobulin, complement, or fibrinogen.

Biopsy specimens are examined for the presence of bound IgG, IgM, IgA, third component of complement (C3), fibrinogen, and IgG4.

Reference Values

An interpretive report will be provided.

Interpretation

A board-certified Dermatopathologist will review and interpret the test results in correlation with other clinical findings as provided.

Cautions

This test is an adjunctive test to be interpreted in the context of clinical information, histologic studies, and serologic studies as clinically indicated.

Clinical Reference

1. Jain S, Basavaraj V, Vimala MG. Utility of direct immunofluorescence studies in subclassification of autoimmune sub-epidermal bullous diseases: A 2-year study in a tertiary care hospital. Turk Patoloji Derg. 2016;32(2):91-98. doi:10.5146/tjpath.2015.01345
2. Diercks GF, Pas HH, Jonkman MF. Immunofluorescence of autoimmune bullous siseases. Surg Pathol Clin. 2017;10(2):505-512. doi:10.1016/j.path.2017.01.011
3. Kershenovich R, Hodak E, Mimouni D. Diagnosis and classification of pemphigus and bullous pemphigoid. Autoimmun Rev. 2014;13(4-5):477-481. doi:10.1016/j.autrev.2014.01.011
4. Buschman KE, Seraly M, Thong HY, Deng JS, Draviam RP, Abernethy JL. A predominant IgG4 subclass may be responsible for false-negative direct immunofluorescence in bullous pemphigoid. J Cutan Pathol. 2002;29(5):282-286. doi:10.1034/j.1600-0560.2002.290504.x
5. Lamb PM, Patton T, Deng JS. The predominance of IgG4 in prodromal bullous pemphigoid. Int J Dermatol. 2008;47(2):150-153. doi:10.1111/j.1365-4632.2008.03361.x
6. Lehman JS, Ferringer TC, Fung MA, Cassarino DS, Shalin SC. Diagnostic utility of direct immunofluorescence test panels for cutaneous vasculitis: A scoping review. J Cutan Pathol. 2024;51(12):987-999. doi:10.1111/cup.14722
7. Lehman JS, Johnson EF, Camilleri MJ, et al. Impact of adding an IgG4 conjugate to routine direct immunofluorescence testing for subepithelial and intraepithelial autoimmune blistering disorders. J Cutan Pathol. 2022;49(4):358-362. doi:10.1111/cup.14176
8. Lehman JS, Fernandez AP, Leiferman KM, et al. Assessment of cutaneous and mucosal direct immunofluorescence testing practices in the US. JAMA Dermatol. 2025;161(7):747-754. doi:10.1001/jamadermatol.2025.0339

Performance

Method Description

Frozen sections of biopsy specimens are brought to ambient temperature, air dried, washed with phosphate-buffered saline (PBS), and then layered with fluorescein isothiocyanate (FITC)-conjugated rabbit antihuman IgG, IgA, IgM, C3, fibrinogen, and IgG4. These slides are incubated in a moist chamber at ambient temperature. The sections are then washed with PBS, mounted in buffered glycerine, and viewed under a fluorescence microscope.(Mysorekar VV, Sumathy TK, Shyam Prasad AL. Role of direct immunofluorescence in dermatological disorders. Indian Dermatol Online J. 2015;6[3]:172-180. doi:10.4103/2229-5178.156386)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

2 to 5 days

Specimen Retention Time

Stained slides:14 days; Remaining biopsy tissue: 30 days

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed using an analyte specific reagent. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

Per biopsy:
88346
88350 x 5

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value

CIB	Cutaneous Direct IFA, Biopsy	In Process

Result ID	Test Result Name	Result LOINC® Value
71145	Interpretation	66121-5
71146	Participated in the Interpretation	No LOINC Needed
71147	Report electronically signed by	19139-5
71610	Addendum	35265-8
71855	Case Number	80398-1