Synovasure® Diagnostics

Annotated Lab Report

ZIMMER BIOMET
Your progress. Our promise.®

CD Laboratories' Exclusive Comprehensive Infection Panels

CD Laboratories provides healthcare professionals with a simple and comprehensive diagnostic report typically within one business day. Six diagnostic tests are available and can be ordered based on patient need and surgeon preference.

Diagnostic Test Options:

1. Synovasure Alpha Defensin
   - Periprosthetic Joint Infection (PJI)
   - Native Septic Arthritis (NSA)
2. WBC Count with Differential
3. Synovasure Neutrophil Elastase
4. Crystal ID
5. Synovasure Microbial ID Panel
6. Synovial Fluid Culture with Antibiotic Susceptibility

The following diagnostic report is an annotated example to provide further explanation of results that can be expected from each test.

CD Laboratories
Citrano Diagnostic Labs
810 Gleneagles Court, Suite 100
Baltimore, Maryland 21286
Office: (888) 981-8378 | Fax: (443) 279-2935

Reported as Positive, Negative, or Indeterminate. Result is 97% sensitive and 96% specific for PJI vs MSIS.[1] Usually reported within 1 business day.

Patient: TEST, PATIENT
Provider: PROVIDER, UNSPECIFIED
Home Phone: (888) 555-6666
Birth:
Age: 62 Years
Gender: Male
Acct#:
Collection Date: 3/8/2017
Received in Lab: 3/9/2017 1:05 PM
Organization: CD LABORATORIES

CRP < 3 mg/L combined with positive alpha defensin triggers potential metallosis warning in prosthetic joint samples. Approximately 10% of PJIs are CRP negative.[2]

Test Name	Result	U	
			/2017 1:07 PM
1 SYNOVASURE ALPHA DEFENSIN PJI	POSITIVE		
SPECIMEN SITE	LEFT KNEE		
ALPHA DEFENSIN-SF	POSITIVE		
CRP-SF	>60	mg/L	
HEMOGLOBIN-SF	NORMAL		

Hemoglobin is measured as a proxy for cell lysis to adjust results from blood contamination. The Indeterminate range is expanded to adjust for potential white cells present from blood contamination.

For technical assistance regarding the Synovasure® Alpha

Synovasure® Alpha Defensin is a laboratory developed tes
for the detection of infection in synovial fluid in patie
inflammation in a joint. Synovasure® Alpha Defensin LDT u
measure markers, including alpha-defensin, in the synovial fluid of joints that are infected.
The alpha-defensin cutoff is adjusted for cell lysis using hemoglobin concentration.
Synovasure® Alpha Defensin LDT results are intended to be used in conjunction with other
n a patient's diagnosis of infection.

Native Septic Arthritis (NSA) Reported Test uses a dual analyte algorithm that combines alpha defensin and lactate. Reported as Positive, Negative, or Indeterminate. Result is 96% Sensitive and 90% Specific.[3]

o determine whether there is an infection present
identify a specific type of infection or to
nfection. It is intended to provide the physician
t for the presence of biomarkers that are in
on.

Test Name	Result	Units	Flag	Ref. Range
				Run by: ~LD on 11/8/2017 1:09 PM
SYNOVASURE ALPHA DEFENSIN NSA	POSITIVE		ABNORMAL	
SPECIMEN SITE	LEFT KNEE			
ALPHA DEFENSIN-SF	POSITIVE			
HEMOGLOBIN-SF	NORMAL			
LACTATE - SF	80.0	mg/L		

For technical assistance regarding the Synovasure® Alpha Defensin assay call 1-888-981-8378.

Synovasure® Alpha Defensin NSA is a laboratory developed test (LDT) intended as an adjunct for the detection of infection in synovial fluid in patients experiencing pain and or inflammation in a joint. Synovasure® Alpha Defensin NSA LDT utilizes a panel of tests that measure markers, including alpha-defensin and lactate, in the synovial fluid of joints that are infected. The alpha-defensin cutoff is adjusted for cell lysis using hemoglobin concentration. Synovasure® Alpha Defensin LDT results are intended to be used in conjunction with other clinical and diagnostic findings to aid in a patient's diagnosis of infection.

An analysis has shown that almost 14% of automated synovial cell counts can be falsely elevated.[4] Therefore, all automated counts >3000 c/ul are verified by manual count.

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Organization: CD LABORATORIES

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Test Name	Result	Units	Flag	Ref. Range
CELL COUNT/DIFF, SYNOVIAL				*Run by: MAC on 3/9/2017 1:11 PM*
RED BLOOD CELL COUNT. FLUID	241000	/uL		
TOTAL NUCLEATED CELL COUNT	206000	/uL	HIGH	<150
NEUTROPHILS	87.9	%	HIGH	<25.0
MONONUCLEAR CELLS	12.1	%		<75.0

***Result was verified by manual cell count.

MSIS guidance of cell count differs from standard reference ranges.

There have been a number of reported cutoff[illegible] Arthritis (NSA) in the literature. The literature bel[illegible] for the interpretation of your result.

Periprosthetic Joint Infection

The Musculoskeletal Infection Society (MSIS) currently recommends that any:
White cell count over 3000 cells/uL meets a minor criterion for PJI
Percent PMN over 80% meets a minor criterion for PJI

Native Septic Arthritis (NSA)

Guidance on cell count for native joints.

There is no fixed cutoff for NSA. A number of cutoffs (1700 - 100,000 cells/uL) have been reported with varying sensitivities and specificities. The commonly referenced cutoff of 50,000 white cell count/uL provides only 50% sensitivity for septic arthritis. Elevated white cell counts and %PMNs need to be interpreted along with all other clinical information available.

1) ***http://www.msis-na.org/international-consensus***
2) ***Carpenter CR, Schuur JD, Everett WW, Pines JM. Acad Emerg Med. 2011Aug;18(8):781-96.***

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SYNOVASURE® NEUTROPHIL ELASTASE	POSITIVE	ABNORMAL

The Synovasure® Neutrophil Elastase (NE) LDT was designed to be a replacement for the Leukocyte Esterase (LE) test strip which can serve as one of the criteria in the MSIS infection algorithm. The Neutorphil Elastase LDT has been shown to out perform the LE test strip in internal studies. The NE LDT is not prone to the high rate of invalid results due to blood contamination that have been reported with the LE test strip. A positive NE result should be interpreted as meeting the MSIS criteria of a positive LE test strip.

Proprietary immunoassay to measure Neutrophil Elastase (NE), the enzyme detected by the Leukocyte Esterase (LE) test strip

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Test Name	Result	Units	Flag	Ref. Range

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CRYSTAL ID, SYNOVIAL FLUID
POSITIVE FOR INTRACELLULAR AND EXTRACELLULAR

Assesses for presence of CPPD (Calcium pyrophosphate dehydrate) and /or MSU (Monosodium urate) crystals. The presence of crystals does not rule out infection.[5]

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EXPANDED SYNOVASURE® MICROBIAL ID PANEL	
STAPHYLOCOCCUS PANEL	POSITIVE
CANDIDA PANEL	NEGATIVE
P. ACNES	NEGATIVE
ENTEROCOCCUS PANEL	NEGATIVE

Exclusive diagnostic technology enables identification of common infecting organisms through direct detection of microbial antigens. Results usually reported within 1 business day. May identify microbial organisms that do not culture.[6]

The Synovasure® Microbial ID Test is a qualitative in vitro diagnostic test intended for the early detection of microbial antigen in synovial fluid of patients experiencing joint pain and/or inflammation. The Synovasure® Microbial ID Test measures antigen from bacterial and fungal species in the synovial fluid from organisms which commonly cause joint infections. The Synovasure® Microbial ID Test results are intended to be used as an additional test to microbial culture and can provide detection of an organism in some samples where there is microbial organism present, but was not able to be cultured.

Notes: Protein A found on cell surface of S. aureus can result in low-level cross-reactivity in Candida and E. faecalis assays

CULTURE, FLUID

Run by: SG on 3/9/2017 1:16 PM

Site:
Left Knee

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Organism 1: Staphylococcus aureus
Growth: In Aerobic and Anaerobic Bottle

Sensitivities	Organism 1	
Ciprofloxacin	<=0.5	S
Clindamycin	0.25	S
Daptomycin	0.25	S
Doxycycline	<=0.5	S
Erythromycin	<=0.25	S
Gentamicin	<=0.5	S
Levofloxacin	0.25	S
Linezolid	2	S
Moxifloxacin	0.25	S
Nitrofurantoin	<=16	S
Oxacillin MIC	<=0.25	S
Rifampicin	<=0.5	S
Tetracycline	<=1	S
Tigecycline	<=0.12	S
Trimethoprim/Sulfamethox	<=10	S
Vancomycin	1	S

S = Susceptible R = Resistant I = Intermediate

Blood culture bottle is reported to be the most sensitive method for synovial fluid culture.[7] We utilize a BACT/ALERT® system and always run both aerobic and anaerobic bottles.

Upon positive culture and identification of the organism, susceptibility profile is performed.

Easy to Use

- Simple sample submission process, including pre-paid shipping
- No out of pocket costs, covered by most insurance companies
- Experienced customer support team ready to assist

Surgeon injects synovial fluid into tubes provided with kit

Complete the test requisition form, and package sample using provided instructions and materials

Call FedEx at 1-800-GOFEDEX for Pre-Paid Package Pick-Up

Testing is performed at CD Laboratories, Inc. Results are sent to surgeons via secure fax or email within one business day of sample receipt.

For additional information please phone: CD Laboratories Customer Service **888-981-8378,** email: **customerservice@cdlaboratories.com** or contact your Zimmer Biomet Representative

ZIMMER BIOMET
Your progress. Our promise.®

1535.1-US-en-REV0718

References

1. Instructions for use. Synovasure PJI ELISA Test. CD Diagnostics. Claymont, DE.
2. Wang C, *et al.* Synovial Fluid C-reactive Protein as a Diagnostic Marker for Periprosthetic Joint Infection:A Systematic Review and Meta-analysis. Chinese Medical Journal. 129:1987-93, 2016
3. Instructions for use. Synovasure L-Lactate LDT. CD Diagnostics. Claymont, DE.
4. Deirmengian C, et al. Automated Synovial Fluid Cell Counts are Often Aberrantly Elevated. Poster presented at: AAOS 2017 Annual Meeting; March 14, 2017; San Diego, CA.
5. Deirmengian C, et al. Crystal Positive Synovial Fluid: Do Not Dismiss the Likelihood of Infection. Abstract presented at: MSIS 2017 Annual Meeting; August 4-5, 2017; Boston, MA.
6. CD Diagnostics, June 30th, 2017. What assays are available to provide additional information on culture negative infections? Technical Bulletin Ed 1, Vol. 2.
7. Bourbeau P., *et al.* Use of the BacT/Alert blood culture system for culture of sterile body fluids other than blood. *Journal of Clinical Microbiology* 36(11):3273-7, 1998. PubMed PMID: 9774578; PubMed. Central PMCID: PMC105314.