Synovasure®

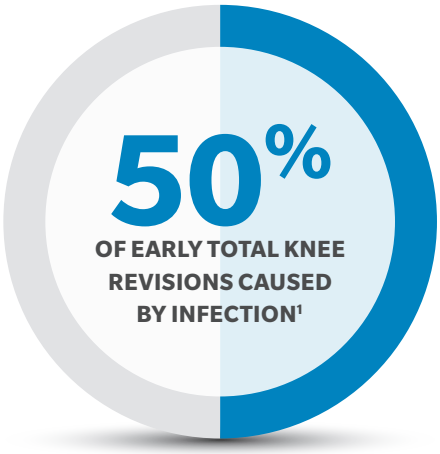
Comprehensive Infection Panel

Laboratory Testing for Joint Infection

ZIMMER BIOMET

IMPACT OF PERIPROSTHETIC JOINT INFECTION

Periprosthetic Joint Infection (PJI) is one of the most common complications following total joint arthroplasty. Over 50% of early (<2 years) total knee arthroplasty revisions are caused by infection.[1] Additionally, the management costs of a septic revision are nearly double that of an aseptic revision.[2] Therefore, a comprehensive diagnosis of PJI is crucial.



MANAGEMENT COSTS NEARLY
2X HIGHER
FOR SEPTIC VS ASEPTIC REVISION[2]

Diagnosing PJI is Challenging

There is currently no single test to diagnose PJI, which can make diagnosing an infection difficult. However, there are a few industry-developed criteria used to support PJI diagnosis including:

- Musculoskeletal Infection Society (MSIS)
- International Consensus Meeting (ICM)
- European Bone & Joint Infection Society (EBJIS)

2018 ICM PJI DIAGNOSIS CRITERIA[3]:

Major Criteria includes:	Decision
Two positive periprosthetic cultures with phenotypically identical organisms	Infected
A sinus tract communicating with the joint	

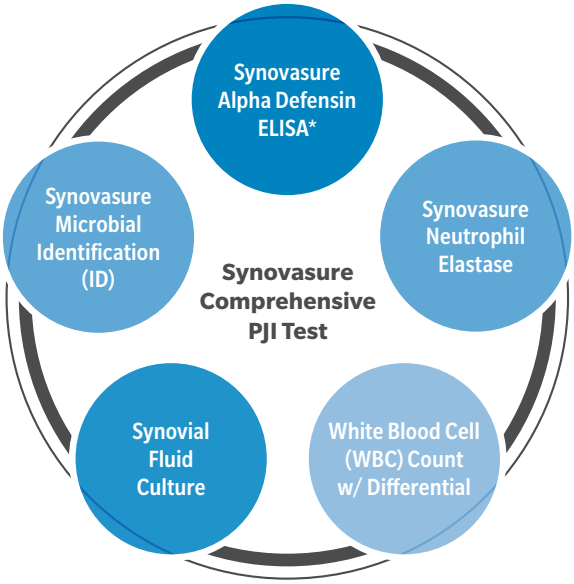
Test	Threshold		Score	Decision
	Acute*	Chronic		
Serum CRP (mg/L) **OR** D-Dimer (µg/L)	100 Unknown	10 860	2	Combined preoperative and postoperative score: ≥ 6 = Infected 4-5 = Inconclusive** ≤ 3 = Not Infected
Elevated Serum ESR (mm/hr)	No role	30	1	
Elevated Synovial WBC (cells/µL) **OR** Leukocyte Esterase **OR** Positive Alpha Defensin (signal/cutoff)	10,000 ++ 1.0	3,000 ++ 1.0	3	
Elevated Synovial PMN (%)	90	70	2	
Single Positive Culture			2	
Positive Histology			3	
Positive Intraoperative Purulence***			3	

*Proceed with caution in: Adverse local tissue reaction, crystal deposition disease and slow growing organisms. *Further studies needed to validate a specific threshold. **Consider further molecular diagnostics such as next-generation sequencing. ***Has no role in patients with suspected adverse local tissue reaction*

SYNOVASURE
COMPREHENSIVE PJI TEST PANEL

A SINGLE SOURCE FOR JOINT INFECTION DIAGNOSIS

The Synovasure Comprehensive PJI Test Panel combines common standard of care (SoC) tests with proprietary tests only offered by Zimmer Biomet, through its subsidiary CD Laboratories.



*Includes alpha defensin and C-reactive protein (CRP)

Proprietary Testing Included
Synovasure Alpha Defensin ELISA, Synovasure Microbial Identification, Synovasure Neutrophil Elastase testing are included as part of the panel.

Integrity Assessments on All Specimens
Approximately 8% of specimens are affected by specimen integrity, impacting the accuracy of tests.[4] As part of the panel, every specimen is tested for Absorbance at 280nm (A280) and Red Blood Cell Count to ensure the specimen is not diluted by added fluid or blood.

Fulfills Industry-Developed Criteria
Panel includes tests that fulfill MSIS, ICM and EBJIS criterias.

Easy-to-Read Results Report in 24 Hours
Providers receive an easy-to-read report typically within 24-hours of receipt at CD Laboratories, except culture. Cultures are held for 7 days (14 for shoulder specimens).

ABOUT CD LABORATORIES

CD Laboratories, located in Baltimore, MD, is a CLIA-certified clinical laboratory specialized in synovial fluid testing for joint pain and inflammation, including infection. Since 2013, we have processed over 180,000 synovial fluid specimens from across the United States and leverage this expertise to provide accurate and timely results to aid physicians and patients in their treatment journey.

SYNOVASURE ALPHA DEFENSIN ELISA TEST

Alpha defensin is an antimicrobial peptide released by neutrophils in response to pathogens and has been well published as a biomarker to aid in PJI diagnosis.[5-14] The Synovasure Alpha Defensin ELISA Test is a laboratory-based test that detects elevated levels of the alpha defensin biomarker in synovial fluid. The results for alpha defensin levels are combined with synovial fluid CRP and lactate for PJI and Native Septic Arthritis (NSA), respectively. The Synovasure Alpha Defensin ELISA Test can be ordered individually or as part of the Synovasure Comprehensive PJI Test Panel

First and Only Test Specifically Designed and Validated to Aid in the Diagnosis of PJI

Highly Sensitive and Specific Based on 2013 MSIS Criteria for PJI[5-11]

- 95% Sensitivity
- 97% Specificity

Performance Unaffected by:

- Prior antibiotic administration[6,12]
- Comorbidities related to inflammation[6,13]
- Type and/or virulence of organism[6,14]

Study	N	Sensitivity	Specificity
Rothman Institute[6]	149	97% (36/37)	96% (107/112)
Mayo Clinic[7]	61	100% (19/19)	95% (40/42)
Cleveland Clinic[8]	78	100% (24/24)	98% (53/54)
Endo Klinik[9]	156	97% (28/29)	97% (123/127)
Cleveland Florida[10]	70	97% (34/35)	97% (34/35)
Charite – Universitatsmedizin Berlin[5]	71	85% (11/13)*	98% (57/58)
Multi-center Study[11]**	369	93% (113/122)	98% (241/247)
Combined	**954**	**95% (265/279)**	**97% (655/675)**

**Includes patients with a draining sinus*

***Mayo Clinic, Cleveland Clinic – Florida, Sinai Hospital of Baltimore*

If results are needed in less than 24 hours, the **Synovasure Alpha Defensin Lateral Flow Test** offers comparable performance with results in 10 minutes.[11]

SYNOVASURE MICROBIAL IDENTIFICATION (MID)

The Synovasure Microbial ID Test is a test that utilizes a novel bead-based test for identifying infecting organisms and a bead-based test for early detection (typically within 24 hours) of microbial antigen in synovial fluid by binding genera-specific antibodies to a corresponding antigen. The Synovasure ID Identification Test can be ordered individually or as part of the Synovasure Comprehensive PJI Test Panel.

Validated Test Panel for Common Species

Designed to identify the organisms in synovial fluid responsible for more than 70% of PJIs[15,16] including:

- *Staphylococcus* species
- *Enterococcus* species
- *Candida* species
- *Cutibacterium acnes* (formerly *P. acnes*)

Performance Backed by Data

Highly sensitive and specific compared to synovial fluid culture techniques

Organism genus	Sensitivity[15]	Specificity[15]
Staphylococcus species	94%	99%
Enterococcus species	97%	99%
Candida species	90%	99%

Note: *Due to difficult nature of culturing C. acnes, sensitivity and specificity data is unavailable*

Performance in Culture-negative Specimens

Identifies more than 54% of culture-negative PJI specimens[17]

SYNOVASURE NEUTROPHIL ELASTASE

The Synovasure Neutrophil Elastase ELISA Test measures the elastase enzyme released by neutrophils in synovial fluid.

Designed Specifically for Synovial Fluid

- Proxy for neutrophil count in synovial fluid
- Not prone to high invalid rate due to blood contamination compared to LE test strip[16]

Performance Backed by Data[17]

- Compared to against LE test strip, demonstrated a 95.5% sensitivity and 88.5% specificity
- Compared against PMN count demonstrated a 100% sensitivity and 91.8% specificity

STANDARD OF CARE TESTING

In addition to the proprietary tests offered only through Zimmer Biomet, the Synovasure Comprehensive PJI Test Panel also includes standard of care (SoC) tests:

Synovial Fluid Culture

Aerobic and anaerobic culture is performed on synovial specimens to determine identity and susceptibility of organisms. Cultures are held for seven (7) days on all samples and 14 days for shoulder specimens.

White Blood Cell Count w/ Differential

An automated, high-performance cell count that provides overall number of white blood cells, as well as the percentage breakdown of white blood cell type in synovial fluid. There is evidence that an automated WBC count can be affected by the presence of a total joint arthroplasty, leading to higher rates of false-positive results[18], therefore elevated white blood cells (>3000 cells/mm^3) are confirmed by a manual count as part of the PJI comprehensive panel testing.

Crystal Analysis

Specimens are tested with polarized microscopy to detect monosodium urate (MSU) and calcium pyrophosphate dihydrate (CPPD) crystals to aid in identifying the presence of gout and pseudogout/CPPD disease.

SYNOVASURE COMPREHENSIVE NSA TEST PANEL

Similar to PJI, infection can affect native joints in the form of septic arthritis. In these cases, CD Laboratories and Zimmer Biomet offer a comprehensive test panel similar to PJI but fine-tuned for the nuances associated with a native joint by testing for lactate (vs CRP) as part of the Alpha Defensin ELISA and the inclusion of crystal analysis.

A STREAMLINED PROCESS

Submitting synovial specimens to CD Laboratories uses a simple, streamlined process following aspiration to result reporting.

ASPIRATE JOINT

TRANSFER FLUID TO PROVIDED TUBES

PACKAGE TUBES AND REQUISITION IN SHIPPER

OVERNIGHT SHIPMENT TO CD LABORATORIES

TESTS PERFORMED AND RESULTS SENT TO PROVIDER

Uniting Innovative Solutions

TRUSTED PARTNER IN REVISION

From diagnostics to patient-specific re-implantation, we unite customizable services and solutions to address each unique episode of care. We are your trusted partner in delivering optimal clinical and economic outcomes in revision arthroplasties.

Learn more on our Revision Solutions on www.zimmerbiomet.com/revision

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