

Critical Review Form

Meta-analysis

Does this Adult Patient Have Septic Arthritis?
JAMA 2007; 297: 1497-1488

Objective: “To determine the diagnostic value of the history, physical examination, and routine laboratory testing for identifying patients with septic arthritis”. (p.1479)

Methods: English-language search of PUBMED and EMBASE using Medical Subject Headings (MeSH): arthritis, infectious, physical examinations, medical history taking, diagnostic tests, and sensitivity and specificity, combined with other terms. Identified articles’ reference lists were also reviewed. One author screened the abstracts of the search results and identified relevant articles which three authors then independently reviewed and abstracted.

Studies were included if they described patients presenting with an acutely painful or swollen joint and contained original diagnostic data on accuracy and precision. An adequate Gold standard was any combination of positive Gram stain, blood cultures, macroscopic pus aspirated from the joint, or anti-microbial response. Literature quality was assessed for potential selection bias (Study Quality from Box 2, p.1480) and design quality limiting ascertainment bias (Level of Evidence from Box 2). The primary outcome measures were the LR’s for all signs/symptoms which were summarized using a random-effects model.

Abnormal results were defined as follows:

Fever > 37.5°C
WBC > 10
ESR > 30 mm/h
C-reactive protein > 100 ng/L

| Guide | Question | Comments |
|--------------|---|--|
| I | <i>Are the results valid?</i> | |
| 1. | Did the review explicitly address a sensible question? | Yes. What is the diagnostic value of history, physical exam, and routinely available lab testing for septic arthritis? |
| 2. | Was the search for relevant studies details and exhaustive? | Yes. The authors describe a reasonable search for peer-reviewed literature, but they could have explored non-English reports, grey literature (conference proceedings, industrial reports) and text book references. |
| 3. | Were the primary studies of high methodological quality? | “The quality scores were relatively low, with only three studies attaining a level 1 score.” (p.1481) |
| 4. | Were the assessments of the included studies reproducible? | Uncertain. “Differences in assessment were discussed and resolved by consensus”, (p.1480) but the authors don’t report how frequently that occurred. |
| II. | <i>What are the results?</i> | |

| 1. | What are the overall results of the study? | <ul style="list-style-type: none"> 14 studies of 6,242 patients met inclusion criteria, but one study (4,889 patients) accounted for 78% of this total. The overall prevalence of septic arthritis was 10.5% (653/6242), but <u>only two studies prospectively assessed prevalence with their rates reported at 8% and 27%</u>. The 27% rate was the only study recruiting patients exclusively for the ED. Three studies assessing synovial fluid lactic acid were excluded. Only six studies assessed the sensitivity of symptoms and <u>none assessed specificity</u> (Table 3, p.1484). <table border="0" style="margin-left: 20px;"> <thead> <tr> <th></th> <th style="text-align: right;"><u>Sensitivity (95% CI)</u></th> </tr> </thead> <tbody> <tr> <td>Joint pain</td> <td style="text-align: right;">85% (78-90%)</td> </tr> <tr> <td>Hx of joint edema</td> <td style="text-align: right;">78% (71-85%)</td> </tr> <tr> <td>Fever</td> <td style="text-align: right;">57% (52-62%)</td> </tr> <tr> <td>Sweats</td> <td style="text-align: right;">27% (20-34%)</td> </tr> <tr> <td>Rigors</td> <td style="text-align: right;">19% (15-24%)</td> </tr> </tbody> </table> Only one study prospectively assessed fever and found that the presence of fever actually <i>decreases</i> the likelihood of septic arthritis (LR+ 0.67, LR- 1.7). Two studies assessed septic arthritis risk factors: <table border="0" style="margin-left: 20px;"> <thead> <tr> <th><u>Risk Factor</u></th> <th><u>Sen</u></th> <th><u>Spec</u></th> <th><u>LR⁺ (95% CI)</u></th> <th><u>LR⁻ (95%CI)</u></th> </tr> </thead> <tbody> <tr> <td>Age > 80</td> <td>19%</td> <td>95%</td> <td>3.5 (1.8-7.0)</td> <td>0.86 (0.73-1.0)</td> </tr> <tr> <td>DM</td> <td>12%</td> <td>96%</td> <td>2.7 (1.0-6.9)</td> <td>0.93 (0.83-1.0)</td> </tr> <tr> <td>Rheumatoid</td> <td>68%</td> <td>73%</td> <td>2.5 (2.0-3.1)</td> <td>0.45 (0.32-0.72)</td> </tr> <tr> <td>Recent joint surgery</td> <td>24%</td> <td>96%</td> <td>6.9 (3.8-12.0)</td> <td>0.78 (0.64-0.94)</td> </tr> <tr> <td>Hip or knee prosthesis</td> <td>35%</td> <td>89%</td> <td>3.1 (2.0-4.9)</td> <td>0.73 (0.57-0.93)</td> </tr> <tr> <td>Skin infection</td> <td>32%</td> <td>88%</td> <td>2.8 (1.7-4.5)</td> <td>0.76 (0.60-0.96)</td> </tr> <tr> <td>Hip or knee prosthesis and skin infection</td> <td>24%</td> <td>98%</td> <td>15.0 (8.1-28.0)</td> <td>0.77 (0.64-0.93)</td> </tr> <tr> <td>HIV +</td> <td>79%</td> <td>50%</td> <td>1.7 (1.0-2.8)</td> <td>0.47 (0.25-0.90)</td> </tr> </tbody> </table> Percentage synovial PMN >90% LR+ 3.4, LR- 0.34. Lab values (except synovial WBC) are of limited value. <table border="0" style="margin-left: 20px;"> <thead> <tr> <th><u>Test</u></th> <th><u>Sen</u></th> <th><u>Spec</u></th> <th><u>LR+ (95% CI)</u></th> <th><u>LR- (95% CI)</u></th> </tr> </thead> <tbody> <tr> <td>WBC >10</td> <td>90</td> <td>36</td> <td>1.4 (1.1-1.8)</td> <td>0.28 (0.07-1.10)</td> </tr> <tr> <td>ESR > 30</td> <td>95</td> <td>29</td> <td>1.3 (1.1-1.8)</td> <td>0.17 (0.20-1.30)</td> </tr> <tr> <td>CRP > 100</td> <td>77</td> <td>53</td> <td>1.6 (1.1-2.5)</td> <td>0.44 (0.24-0.82)</td> </tr> <tr> <td>jWBC > 100</td> <td>29</td> <td>99</td> <td>28.0 (12.0-66.0)</td> <td>0.71 (0.64-0.79)</td> </tr> <tr> <td>jWBC > 50</td> <td>62</td> <td>92</td> <td>7.7 (5.7-11.0)</td> <td>0.42 (0.34-0.51)</td> </tr> </tbody> </table> | | <u>Sensitivity (95% CI)</u> | Joint pain | 85% (78-90%) | Hx of joint edema | 78% (71-85%) | Fever | 57% (52-62%) | Sweats | 27% (20-34%) | Rigors | 19% (15-24%) | <u>Risk Factor</u> | <u>Sen</u> | <u>Spec</u> | <u>LR⁺ (95% CI)</u> | <u>LR⁻ (95%CI)</u> | Age > 80 | 19% | 95% | 3.5 (1.8-7.0) | 0.86 (0.73-1.0) | DM | 12% | 96% | 2.7 (1.0-6.9) | 0.93 (0.83-1.0) | Rheumatoid | 68% | 73% | 2.5 (2.0-3.1) | 0.45 (0.32-0.72) | Recent joint surgery | 24% | 96% | 6.9 (3.8-12.0) | 0.78 (0.64-0.94) | Hip or knee prosthesis | 35% | 89% | 3.1 (2.0-4.9) | 0.73 (0.57-0.93) | Skin infection | 32% | 88% | 2.8 (1.7-4.5) | 0.76 (0.60-0.96) | Hip or knee prosthesis and skin infection | 24% | 98% | 15.0 (8.1-28.0) | 0.77 (0.64-0.93) | HIV + | 79% | 50% | 1.7 (1.0-2.8) | 0.47 (0.25-0.90) | <u>Test</u> | <u>Sen</u> | <u>Spec</u> | <u>LR+ (95% CI)</u> | <u>LR- (95% CI)</u> | WBC >10 | 90 | 36 | 1.4 (1.1-1.8) | 0.28 (0.07-1.10) | ESR > 30 | 95 | 29 | 1.3 (1.1-1.8) | 0.17 (0.20-1.30) | CRP > 100 | 77 | 53 | 1.6 (1.1-2.5) | 0.44 (0.24-0.82) | jWBC > 100 | 29 | 99 | 28.0 (12.0-66.0) | 0.71 (0.64-0.79) | jWBC > 50 | 62 | 92 | 7.7 (5.7-11.0) | 0.42 (0.34-0.51) |
|---|--|---|--------------------------------|-------------------------------|------------|--------------|-------------------|--------------|-------|--------------|--------|--------------|--------|--------------|--------------------|------------|-------------|--------------------------------|-------------------------------|----------|-----|-----|---------------|-----------------|----|-----|-----|---------------|-----------------|------------|-----|-----|---------------|------------------|----------------------|-----|-----|-----------------------|------------------|------------------------|-----|-----|---------------|------------------|----------------|-----|-----|---------------|------------------|---|-----|-----|------------------------|------------------|-------|-----|-----|---------------|------------------|-------------|------------|-------------|---------------------|---------------------|---------|----|----|---------------|------------------|----------|----|----|---------------|-------------------------|-----------|----|----|---------------|------------------|------------|----|----|-------------------------|------------------|-----------|----|----|-----------------------|------------------|
| | <u>Sensitivity (95% CI)</u> | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Joint pain | 85% (78-90%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hx of joint edema | 78% (71-85%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Fever | 57% (52-62%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Sweats | 27% (20-34%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Rigors | 19% (15-24%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <u>Risk Factor</u> | <u>Sen</u> | <u>Spec</u> | <u>LR⁺ (95% CI)</u> | <u>LR⁻ (95%CI)</u> | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Age > 80 | 19% | 95% | 3.5 (1.8-7.0) | 0.86 (0.73-1.0) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| <u>Test</u> | <u>Sen</u> | <u>Spec</u> | <u>LR+ (95% CI)</u> | <u>LR- (95% CI)</u> | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| 2. | How precise are the results? | Sufficiently narrow CI's (see above) |
| 3. | Were the results similar from study to study? | For the most useful lab test, synovial WBC, the results were impressively similar (Table 4, p.1485). |
| III. | <i>Will the results help me in caring for my patients?</i> | |
| 1. | How can I best interpret the results to apply them to the care of my patients? | <p><u>“The history and physical examination are not able to substantially change the pre-test probability of septic arthritis in patients with acutely painful swollen joints”.</u> (p 1486).</p> <p>The pre-test probability of septic arthritis of such patients who present to the ED is about 18% (midway between out patient 8% value and Taiwan ED value of 27%) and this probability can be modified upward by several demographic risk factors. Peripheral WBC, ESR, and CRP have high sensitivity but their poor specificity makes them useless for the EM diagnosis of septic arthritis. In the ED, any patient with suspected septic arthritis absolutely requires arthrocentesis with synovial WBC and differential (above and beyond Gram stain, culture, protein, glucose, or LDH).</p> |
| 2. | Were all patient important outcomes considered? | No specific patient outcomes were considered. |
| 3. | Are the benefits worth the costs and potential risks? | Yes, if joint destruction related morbidity (and rare septic mortality) can be avoided by early identification of septic arthritis and appropriate treatment. |

Limitations:

- 1. Incomplete search strategy.**
- 2. No assessment of patient-important outcomes.**
- 3. Exclusion of synovial lactate (now readily available) from analysis.**
- 4. Lack of high-quality studies.**
- 5. Imperfect Gold standard utilized. Perhaps operative diagnosis would be defacto Gold standard given culture sensitivity 82% and Gram stain 39-50%.**
- 6. Inability to assess synovial WBC diagnostic tests characteristics among high risk subjects.**

Bottom Line:

History and physical exam, CBC, ESR, and CRP are useless for the diagnosis of septic arthritis since they do not substantially change the pre-test in patients with acutely painful, swollen joint. On the other hand, synovial WBC and PMN percentage can change pre-test probability sufficiently to cross the treatment threshold and modify management. A 10-year old ED based study of 75 patients suggests that synovial fluid TNF_{α} may be a useful marker meriting further evaluation (LR+ 3.3, LR- 0.07).

