Critical Review Form

Diagnostic Test

Synovial fluid lactic acid in septic arthritis, *NZ Med J*; 1981; 93:115-117

Objectives: **"…to determine the usefulness of elevated synovial fluid lactic acid concentrations in the diagnosis of septic arthritis using an enzyme method currently available in many New Zealand hospitals." (p. 115)**

Methods: **Non-randomized, prospective, blind, case-control study of "every clinically suspected case of septic arthritis attending Middlemore Hospital" (p. 115) over an unspecified period. The control cohort of non-septic arthritis was a non-random sample of Rheumatology Department patients.**

In addition to assessing synovial lactate levels in septic arthritis and non-septic arthritis patients, the investigators assessed other factors that could also demonstrate an elevated synovial lactate, including: partially treated septic arthritis, gonococcal arthritis, the volume of synovial fluid, collection container preservation fluid (fluoride vs. citrate), and the delay before putting the specimen on ice.

Synovial fluid lactate levels were assessed using the Calbiochem-Behring Rapid Lactate Kit, which oxidizes lactate to pyruvate using a LDH catalyst and a molar equivalent of nicotimamide. The change in absorbance at 340 mm is proportional to the concentration of lactate. Presumably, the specimen was analyzed with photospectrometry, but the authors do not provide these details.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did clinicians face diagnostic uncertainty?**	No, there is no clear statement that either the clinician or the outcome assessor was blinded to the synovial lactate level.
B.	**Was there a blind comparison with an independent gold standard applied similarly to the treatment group and to the control group?** **(Confirmation Bias)**	Uncertain. The authors do not clearly state that all control patients had a synovial culture. However, "the definitive study was non-randomised, prospective and blind, in that the technician determining the lactic acid concentration was unaware of the clinical details of the patient." (p. 115)

C.	**Did the results of the test being evaluated influence the decision to perform the gold standard?** **(Ascertainment Bias)**	Uncertain. Did all control patients have a synovial culture? If not did the synovial lactate level impact clinicians' decisions to obtain a synovial culture?
II.	**What are the results?**	
A.	**What likelihood ratios were associated with the range of possible test results?**	• No patient demographics or details about the infecting organisms or joint affected are provided. • The concentration of lactic acid varied up to 55% when collected in citrate vs. fluoride, but when specimens from 14 patients were placed in fluoride the lactate level for individual patients did not significantly vary by time until placed on ice for up to 3-hours. Therefore, **when using a fluoride preservative, putting the synovial fluid on ice may not be crucial for up to 3-hours.** • The non-specific inflammatory arthritides had mean lactic acid 4.27 mmol/L (range 0.8-10.2 mmol/L vs. nongonococcal SA mean 21.2 mmol/L (range 11.0-35.2). • There was significant negative correlation between synovial lactate and synovial glucose (R=-0.74, p<0.001). • Although not reported by the investigators, dichotomous diagnostic accuracy for synovial lactate can be computed at various thresholds from Figure 2 (see the 2x2 tables constructed on the left): **Threshold of ≥ 10 mM** Sensitivity 100% (95% CI 73%-100%) Specificity 96% (95% CI 91%-96%) LR+ 22 (95% CI 8-22) LR- 0 (95% CI 0-0.29) **Threshold of ≥ 5 mM** Sensitivity 100% (95% CI 73%-100%) Specificity 63% (95% CI 58%-63%) LR+ 2.7 (95% CI 1.7-2.7) LR- 0 (95% CI 0-0.51)

Synovial Lactate	SA+	SA-
≥ 10 mmoL/L	11	3
<10	0	63

Synovial Lactate	SA+	SA-
≥ 5 mmoL/L	11	23
<5	0	40

		• More importantly, one can use Figure 2 to compute interval LR's. Synovial lactate range (mmoL/L) / Interval LR 0-5 / 0 5-10 / 0 10-20 / 17.2 >20 / ∞
III.	**How can I apply the results to patient care?**	
A.	**Will the reproducibility of the test result and its interpretation be satisfactory in my clinical setting?**	Uncertain since synovial lactate levels were not tested in the ED setting using currently available L-lactate assays or point-of-care tests, but since history/physical exam are inaccurate and a superior screening test does not exist, both D- and L-lactate are most definitely worth exploring within the context of acute monoarticular arthritis with clinical concern for septic arthritis.
B.	**Are the results applicable to the patients in my practice?**	Uncertain since not conducted in an ED setting. In general, one would expect patients with monoarticular arthritis presenting to Rheumatology clinic to be less acutely ill and probably of higher socioeconomic status. Furthermore, the investigators provide no patient demographics by which to compare our patients with theirs. Theoretically, test accuracy may vary from one setting to another (see also Leeflang 2009).
C.	**Will the results change my management strategy?**	Not in isolation, but when reviewing the entire body of literature available in 2013, both L-lactate and D-lactate levels in synovial fluid are worth exploring further. Future studies should assess diagnostic accuracy in a consecutive sample of ED patients with monoarticular arthritis and sufficient suspicion of non-GC SA to obtain arthrocentesis. These studies should follow STARD criteria and report interval LR's. If these "level 2" diagnostic accuracy studies confirm synovial lactate as a useful adjust to sWBC, the logical progression in research would be to assess the impact of awareness of synovial lactate on clinician decision-making.

D.	**Will patients be better off as a result of the test?**	Yes, if the studies hypothesized above confirm the diagnostic accuracy and reliability of synovial lactate to distinguish non-GC septic arthritis from other forms of acute monoarticular arthritis in ED patients using a readily available assay or point of care test. If confirmed, synovial lactate could reduce unnecessary admissions and orthopedic surgery consults, as well as antibiotic misuse/resistance/adverse consequences.

Limitations

1) **No clear statement to delineate whether L-lactate (vs. D-lactate) is being measured (STARD criteria).**

2) **Pragmatic? Lactate not measured real-time so clinical relevance difficult to judge.**

3) **Case-control design likely to bias estimates of both sensitivity and specificity upwards.**

4) **No clear blinding of clinicians or outcome assessors (co-intervention bias, incorporation bias).**

5) **No attempt to report diagnostic accuracy (STARD criteria).**

6) **No patient demographics provided (STARD criteria).**

7) **Limited external validity (single-center, Rheumatology clinic). Explicit description of the study setting and population evaluated is one of the STARD criteria and essential to delineate since test accuracy may vary from one setting to another (see also Leeflang 2009).**

Bottom Line

Based on this case-control, single-center, Rheumatology clinic study, synovial lactate assays (probably L-lactate based on the investigator's discussion) using the Calbiochem-Behring Rapid Lactate Kit accurately discriminates non-GC septic arthritis from other etiologies of acute monoarticular joint pain/swelling. At a threshold of 10 mmoL/L (which is nearly two-fold the 5.5 mmoL/L threshold proposed by Brook 1978) the LR^+ is 22 and the LR^- is 0. Using the Brook 5 mmoL/L threshold, the current study demonstrates LR^+ 2.7 and LR^- 0 (compared with 5.9 and 0.04 for Brook, respectively) for lactate. The interval LR for 0-10 mmol/L is zero versus 17.2 for 10-20 mmoL/L and ∞ for synovial lactate >20 mmoL/L. Future studies should assess diagnostic accuracy in a consecutive sample of ED patients with monoarticular arthritis in whom there is sufficient suspicion of non-GC septic arthritis to perform an arthrocentesis. It will be essential for these future studies to follow the STARD criteria and to report interval LR's. If these "level 2" diagnostic accuracy studies confirm synovial lactate as a useful adjust to sWBC, the logical progression in research would be to assess the impact of awareness of synovial lactate on clinician decision-making.