

PROPOSAL: TEST WITHDRAWAL

SUMMARY

See also chart “Legionella Urinary Antigen Test”

Test description: Legionellae, detection of antibodies against

Sample type(s): serum

Procedure: immunofluorescence test (ELISA or microagglutination)

Can be ordered by: primary care physician and specialists

Pricing: 7.70 € = B250 x 0.030811

Estimated number of tests/year: 15.474 in 2008

Estimated total budget/year: 15.474 x 250 x 0.030811= 119.192 €

Estimated cost savings/year: 119.192 €

Expected impact of (new) concurrent test ordering: 110.920 € (see Legionella urinary antigen) > final impact: - 8.273 €

Nederlandstalige omschrijving voorstel

Schrap 551036 en 551040 Legionellae, opsporen van antilichamen tegen

Franstalige omschrijving voorstel

Biffez 551036 et 551040 Legionellae, recherche des anticorps

CLINICAL/DIAGNOSTIC SCENARIO

The diagnosis of Legionella pneumophila infection remains very difficult:

- *Culture has a low sensitivity (<50% when golden standard is serology), is slow (turnaround-time 3-7 days) and often not possible (<50% of patients produce adequate sputum).*
- *Direct fluorescent antigen staining on LRT secretions has a sensitivity of 25-70%, but is technically demanding.*
- *Serology is not useful for acute diagnosis, as more than 3 weeks up to 10 weeks are needed for a seroconversion or 4-fold increase in titers, and this with a sensitivity of 60-80%. Single titer results can be misleading.*
- *Single serum titers (acute or convalescent) cannot confirm Legionnaires' disease. Elevated titers have been found in 1 to 16% of healthy adults, thereby hampering the use in acute phase. On the other hand, the positive predictive value of a convalescent-phase titer is unacceptably low.*
- *Molecular techniques are promising, but more evaluation and standardisation are needed before introducing in routine clinical diagnosis.*

APPRAISAL

1) Analytical performance characteristics (analytical validation report)

1.1 *Preanalytical considerations (patient variables, sample stability)*

- *Biological variation detection from 3 to 10 weeks after onset of disease*
- *Interferences none*
- *Patient variables impaired production of antibodies in immunosuppressed patients*
- *Sample stability good*
- *Sample type serum*
- *Sample volume < 1 ml (more if concentration technique is used)*
- *Prevalence 90 cases reported by sentinel-laboratories in 2006; estimation about 500 cases*
- *Target population severe pneumonia*

1.2 *Analytical considerations (reproducibility, accuracy, correlation, linearity, reference range)*

- *(Im)Precision:*
- *Accuracy (bias):*
- *Correlation with current method/ standard Sensitivity sensitivity 60 to 80% when seroconversion is detected and specificity of 98% in Legionella type 1 infection; sensitivity only 50% in other serogroups*
- *Reproducibility (within run, between run) very good*
- *Reference range*
- *Analytical range/Linearity*
- *Turn around time (TAT)*

1.3 *Quality issues*

- /

2) Diagnostic performance

2.1 Sensitivity, specificity

- /

2.2 Likelihood ratio's (LR)

2.3 NND (number needed to diagnose)

2.4 Other

- ROC-curves (other methods)
- Are other results needed tot interpret this lab test? *no*

3) Clinical impact

3.1 Diagnostic

- /

3.2 Treatment

- /

3.3 Health outcome

- /

3.4 Other

- /

4) Organizational impact

4.1 Impact in the hospital

- /

4.2 Impact outside the hospital

- /

5) Cost impact: in and outside the laboratory

5.1 (Activity-Based) Cost/test (reagents, personnel, overhead (housing, QC, ...))

- /

5.2 Reimbursement

- /

5.3 Profit elsewhere in the hospital? *no*

6) Decision making

6.1 *Impact on the clinical decision making process and patient management very low (results too late)*

RELEVANT EVIDENCE/REFERENCES

1) Guidelines and Recommendations (most recent topics on top)

Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, Dowell SF, File TM Jr, Musher DM, Niederman MS, Torres A, Whitney CG; *Infectious Diseases Society of America; American Thoracic Society. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults Clin Infect Dis. 2007 Mar 1;44 Suppl 2:S27-72.*

Woodhead M, Blasi F, Ewig S, Huchon G, Ieven M, Ortqvist A, Schaberg T, Torres A, van der Heijden G, Verheij TJ; **European Respiratory Society; European Society of Clinical Microbiology and Infectious Diseases.** Guidelines for the management of adult lower respiratory tract infections. *Eur Respir J. 2005 Dec;26(6):1138-80.*

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Canadian Infectious Diseases Society and Canadian Thoracic Society. Mandell LA, Marrie TJ, Grossman RF, et al. Canadian guidelines for the initial management of community-acquired pneumonia: an evidence-based update by the Canadian Infectious Diseases Society and Canadian Thoracic Society. *Clin Infect Dis 2000; 31: 383-421.*

2) Systematic Reviews and Meta-analyses

3) Reviews

Diederens BMW Op zoek naar nieuwe diagnostische mogelijkheden voor patiënten met de veteranenziekte. *Tijdschrift voor Infectieziekten 2008, 3:36-39.*

Richtlijn LCI dec 2007 met wijziging juni 2008. <http://www.rivm.nl/cib/infectieziekten-A-Z/infectieziekten/legionellose/index.jsp> 2003; 9: 175-80

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Pimentel L, McPherson SJ. Community-acquired pneumonia in the emergency department: a practical approach to diagnosis and management. *Emerg Med Clin N Am 2003; 21: 395-420*

Murdoch DR. Nucleic acid amplification test for diagnosis of pneumonia. *Clin Infect Dis 2003; 36: 1162-1170.*

File TM. Community-acquired pneumonia. *Lancet 2003; 362: 1991-2001.*

Andrews J, Nadjm B, Gant V and Shetty N. Community-acquired pneumonia. *Curr Opin Pulm Med 2003; 9: 175-180.*

Carroll KC. Laboratory diagnosis of lower respiratory tract infections: controversy and conundrums. *J Clin Microbiol 2002; 40: 3115-3120.*

Saubolle MA and McKellar PP. Laboratory diagnosis of community-acquired lower respiratory tract infection. *Infect Dis Clin North Am 2001; 15: 1025-1045.*

Skerrett SJ. Diagnostic testing for community-acquired pneumonia. *Clin Chest Med 1999; 20: 531-548.*

Plouffe JF, McNally C, File TM. Value of noninvasive studies in community-acquired pneumonia. *Infect Dis Clin North Am 1998; 12: 689-699*

Stout JE, Yu VL. Legionellosis. *N Engl J Med* 1997;337:682-7

4) Original Articles

Helbig JH, Uldum, SA, Bernander, S, et al. Clinical utility of urinary antigen detection for diagnosis of community-acquired, travel-associated, and nosocomial legionnaires' disease. *J Clin Microbiol* 2003; 41:838.

Trends in legionnaires disease, 1980-1998: declining mortality and new patterns of diagnosis. Benin AL; Benson RF; Besser RE *Clin Infect Dis* 2002 Nov 1;35(9):1039-46. Epub 2002 Oct 14.

Deforges L, Legrand P, Tankovic J, Brun-Buisson C, Lang P, Soussy CJ. Case of false-positive results of the urinary antigen test for *Legionella pneumophila*. *Clin Infect Dis*. 1999 Oct;29(4):953-4.

A recurrent outbreak of nosocomial legionnaires' disease detected by urinary antigen testing: evidence for long-term colonization of a hospital plumbing system Lepine LA; Jernigan DB; Butler JC; Pruckler JM; Benson RF; Kim G; Hadler JL; Cartter ML; Fields BS *Infect Control Hosp Epidemiol* 1998 Dec;19(12):905-10

Dirven K, Ieven M, Peeters MF, van der Zee A, De Schrijver K, Goossens H. Comparison of three *Legionella* urinary antigen assays during an outbreak of legionellosis in Belgium. *J Med Microbiol*. 2005 Dec;54(Pt 12):1213-6.

Struelens MJ, Costers M. Hospital antibiotic management in Belgium – results of the ABS maturity survey of the ABS International group. *Wien Klin. Wochenschr* 2008; 10:284-288.

Plouffe TF, File TM jr, Breiman RF, et al. Reevaluation of the definition of legionnaires' disease: use of the urinary antigen assay. *Clin Infect Dis* 1995; May 20(5): 1286-91

5) Reference Works, Handbooks and Databases

Isenberg H. *Clinical Microbiology Procedures Handbook*, 2nd edition, ASM: see section 3.11.4 RIVM
Murray P. *Manual of Clinical Microbiology*, ASM, 2007

Mandell. *Principles and Practice of Infectious Diseases*. 6th Edition
(<http://www.ppidonline.com>)

Uptodate (online). Diagnostic approach to the patient with community-acquired pneumonia

6) Posters, "grey literature", presentations

Evaluation of the Uni-Gold™ *Legionella* Urinary Antigen Test, a new immunochromatographic test in comparison with the Binax NOW test Abstract number: P1381 ESCMID 2008 Freydiere A.M., Lagrange N., Vandenesch F., Etienne J., Jarraud S.

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