Testing for and identifying lupus-like anticoagulant

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Department of Medical and Surgical Procedures Assessment
THE TEAM

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The final report was validated by the HAS Committee for the Assessment of Diagnostic and Therapeutic procedures in September 2006.

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**SUMMARY**

1. Introduction

Lupus-like anticoagulant is an acquired abnormality affecting about 2% of the general population. It is associated with a risk of thrombosis that can give rise to obstetric, neurological, renal or pulmonary events.

The procedure called by CNAMTS¹ “Additional investigation and identification of a lupus-like inhibitor (or antiphospholipid or antiprothrombinase)” is also called "Investigation for lupus-like anticoagulant". It is a biological procedure mainly used during workup for venous or arterial thrombosis, or after repeated spontaneous abortion, and is one of the procedures used to diagnose antiphospholipid syndrome (APS).

In France, the procedure is not reimbursed. It is included in the 4 foreign health insurance schedules consulted (United States, Australian, Belgian, Canadian).

At the request of the Social Security Directorate and as part of the revision of the "Haemostasis" section of the NABM², the Haute Autorité de Santé assessed the expected benefit of this procedure in order to give an opinion on its inclusion in the NABM.

2. Assessment method

The HAS method for assessing expected or actual benefit of procedures is based on a review of the literature and expert opinion (members of the NABM committee in this instance). The main medical databases (Medline, Cochrane Library, Cochrane Library, National Guideline Clearinghouse and HTA Database) were searched over the period January 1999 to July 2005.

A total of 245 articles were retrieved of which 30 were analysed and 10 finally selected: 3 national multicentre studies of the validity of the procedure, 4 guidelines, 1 systematic review and 2 randomised controlled trials.

3. Results of the literature review

Indications

The indications established in the 4 guidelines based on expert opinion were:

- deep vein thrombosis or pulmonary embolism with no apparent cause;
- recurrent deep vein thrombosis or pulmonary embolism (even if there are other risk factors for thrombosis);
- young subject (under 50 years) who has had a stroke or peripheral arterial thrombosis;
- older subject (over 50 years) who has had a stroke or peripheral arterial thrombosis in the absence of risk factors;
- recurrent arterial thrombosis despite preventive anticoagulant therapy;
- disseminated lupus erythematosus, to assess the risk of thrombosis;
- multiple spontaneous abortions;
- early or severe pre-eclampsia or severe placental insufficiency;
- unexplained intrauterine death;
- unexplained severe intrauterine growth retardation.

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¹ CNAMTS: National Health Insurance Fund for salaried workers
² NABM: French Health Insurance Schedule of reimbursed biological procedures
Diagnostic performance
The sensitivity of the test for (and identification of) lupus-like anticoagulant was 82%–99%, the specificity was 80%–99%, depending on the type and composition of plasma used in the 3 studies selected.

Safety
The procedure does not raise any issues of safety as it only requires a venous blood sample.

Test conditions
The procedure should be performed in accordance with the French code of practice for tests (GBEA).
It consists of a series of successive tests:
(i) detection of prolonged coagulation time in phospholipid-dependent coagulation tests (at least two tests);
(ii) identification of the presence of a coagulation inhibitor using sensitive tests;
(iii) confirmation that the inhibitor is phospholipid-dependent;
(iv) exclusion of another coagulation disorder.
The plasma samples used (patient and control) should be platelet-poor in order to improve the sensitivity of the tests. The laboratory should state the reagents used and give an interpretation of the results.

Contribution to the treatment strategy
If lupus-like anticoagulant is identified, treatment can be adjusted to prevent the onset or recurrence of thrombosis (start anticoagulant therapy, adjust the dose and duration of anticoagulant therapy, etc.), whilst taking into account the risk of bleeding associated with anticoagulant therapy.

These treatment adjustments were established in 4 guidelines based on expert opinion, observational studies or randomised trials with methodological limitations. Subsequently, 2 randomised trials showed that intensive anticoagulant therapy was not superior to moderate therapy in preventing onset of recurrence. No randomised trials were found that compared incidence of recurrent thrombosis with and without preventive therapy.

There are no published data on the impact of the procedure on the healthcare system and public health programmes.

4. Position of the NABM Committee
According to the Committee, the test is used to identify a risk factor for thrombosis. If an abnormally prolonged activated partial thromboplastin time (APTT) is not related to anticoagulant therapy, a corrected APTT test for circulating anticoagulant may be performed at the initiative of the laboratory director.

This test should be performed using at least two antiphospholipid-dependent tests based on different principles. The report should state the methods and reagents used, and give an interpretation of the results.

The NABM Committee voted in favour of including this procedure in the NABM.
### 5. Conclusion

**Diagnostic benefit**  
Antiphospholipid syndrome (APS) is a serious disease. Testing for lupus-like anticoagulants is one of the diagnostic factors for APS. It satisfies an unfulfilled diagnostic need.

The sensitivity and specificity of the lupus-like anticoagulant test is over 80%, and may be as high as 99% depending on the type and composition of plasma. It does not pose any safety problems.

**Treatment benefit**  
The main indications for this procedure and its contribution to the treatment strategy were established in 4 guidelines based on expert opinion.

If lupus-like anticoagulant is identified, treatment can be adjusted, with a positive impact on patient morbidity and mortality (according to 4 guidelines based on expert opinion, observational studies or randomised trials with methodological limitations).

There are no published data on the impact of this procedure on the healthcare system and public health programmes.

**The expected benefit is judged to be sufficient**  
because the test:  
- satisfies an unfulfilled diagnostic need;  
- is a diagnostic factor for APS;  
- has good diagnostic power.

**The improvement in expected benefit is judged to be moderate (level III)**  
because the test:  
- allows treatment to be adjusted (no randomised trials with an untreated group);  
- should be followed by other diagnostic procedures (determination of antiphospholipid auto-antibodies).