
MEMORANDUM

To: All Laboratory Users
From: Molecular Diagnosis Centre, Department of Laboratory Medicine
Date: 09 September 2025
Re: **Discontinuation of Methylene tetrahydrofolate reductase (MTHFR) c.665C>T variant testing**

Dear Users of Laboratory Medicine,

Please be informed that the Molecular Diagnosis Centre, Department of Laboratory Medicine, will discontinue the following test, effective **01 October 2025**:

- Methylene tetrahydrofolate reductase (MTHFR) c.665C>T variant [LAB3040432]

This follows recommendations from ACOG, RCOG, ESHRE, ACMG, and RCPA*, which state that MTHFR testing has no proven clinical utility and should not be ordered as part of routine evaluation for thrombophilia or recurrent pregnancy loss (PRL) / adverse pregnancy outcomes.

1. Recurrent Pregnancy Loss (RPL) Work-up

Current international guidelines (ACOG, RCOG, ESHRE) advise against routine testing for inherited thrombophilia testing, including Factor V Leiden and Prothrombin G20210A, in women with RPL. These variants are not consistently associated with miscarriage, and testing does not alter management or improve outcomes.

Recommended tests in RPL may include:

- Antiphospholipid antibody panel (anticardiolipin, lupus anticoagulant, anti-β₂ glycoprotein I)
- Parental karyotyping
- Uterine cavity assessment
- Endocrine and systemic disease screening for thyroid dysfunction, diabetes mellitus

2. Inherited Thrombophilia Evaluation

Inherited thrombophilia testing should be reserved for patients with a personal history of venous thromboembolism (VTE), or a strong family history of thrombosis at a young age. In such cases, the following may be appropriate:

- Factor V Leiden mutation
- Prothrombin G20210A mutation
- Antithrombin III activity
- Protein C activity
- Protein S activity

These tests should not be ordered as part of routine RPL work-up in the absence of thrombotic history.

References:

1. ACOG Practice Bulletin No. 197: Inherited Thrombophilias in Pregnancy (2018)
2. RCOG Green-top Guideline No. 17: Recurrent Miscarriage (2011, updated)
3. ESHRE Guideline: Recurrent Pregnancy Loss (2017, reaffirmed 2022)
4. ACMG Practice Guideline: Lack of evidence for MTHFR polymorphism testing (2013)

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American College of Obstetricians and Gynecologists (ACOG)
Royal College of Obstetricians & Gynaecologists (RCOG)
European Society of Human Reproduction and Embryology (ESHRE)
American College of Medical Genetics and Genomics (ACMG)
Royal College of Pathologists of Australasia.(RCPA)

We appreciate your understanding and cooperation during this transition.

Should you have any questions or require further information, please contact the laboratory staff at 6772 4384.

Thank you.

Yours sincerely

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