Neural Tube Defects (NTDs) and genetic testing
Information for CLINICIANS

The vast majority of patients with an isolated neural tube defect do **NOT** need to be seen by Clinical Genetics.

It is believed that neural tube defects are the result of a complex interaction between polygenic and environmental factors. There are no genetic tests recommended for isolated neural tube defects.

However, if there are additional features to suggest an underlying syndromic diagnosis, or a strong family history of neural tube defects, these patients may benefit from a referral to Clinical Genetics.

WHO TO REFER

- ✓ Patients with additional structural anomalies (e.g. cleft palate, cystic kidneys, polydactyly, skeletal anomalies, congenital heart defects).
- ✓ Patients with a strong family history of neural tube defects (e.g. ≥1 first-degree relatives, ≥2 second-degree relatives on the same side of the family).

HOW TO REFER / CONTACT CLINICAL GENETICS FOR ADVICE

- **You may find useful information, including how to refer and a copy of the genetics test request form on our website:** https://belfasttrust.hscni.net/service/laboratory-services/clinical-genetics/
- **Clinical queries:** genetic.medicine@belfasttrust.hscni.net / 028 9504 8022 / via Belfast Trust Switchboard. There is an on-call consultant available 9am-5pm Mon-Friday.
- **Lab queries:** GeneticsLabs@belfasttrust.hscni.net / 028 9504 7353

Please consider sending an EDTA sample for microarray alongside a referral.

RISK OF RECURRENCE AND ADVICE

Couples, who have one or more pregnancies affected by a neural tube defect, have an increased risk of this happening again (see Table 1).

The risk of recurrence can be significantly reduced by supplementation with high dose folic acid (5mg) in future pregnancies. This advice also applies to women where the female herself, or her partner, has a personal or family history of neural tube defects.

Table 1: Risk (%) of neural tube defect (NTD) in a fetus, depending on family history.

Population	Risk of neural tube defect (to the fetus)
General population	~0.2%
One sibling with NTD	~3%
Two siblings with NTD	~6%
Parent with NTD	~1%
Half sibling with NTD	~1%
First cousin (e.g. mother's sister's child)	~1%

Adapted from Rose, N., & Mennuti, M. (2009). Fetal neural tube defects: diagnosis, management, and treatment. Glob. libr. women's med.

Please note, if the neural tube defect has occurred as part of a genetic syndrome, the recurrence risk may be higher.

MTHFR GENE TESTING

Testing of the *MTHFR* gene is **not** currently recommended in the case of isolated neural tube defects.

Some private companies offer direct-to-consumer testing of *MTHFR*. There are some variants or 'polymorphisms' in *MTHFR*, which are commonly found in the general population. It is estimated that ~10% of individuals in the UK & Ireland are homozygous for the C667T variant ("TT homozygous"). A1298C is another commonly observed *MTHFR* polymorphism. At present, there are no specific recommendations for women who are homozygous carriers for these common variants, and we would reassure these individuals that, based on the scientific evidence currently available, we would not expect them to be at a significantly increased risk of having a child with a neural tube defect, and no specific supplements are recommended.

Other useful resources:

https://www.shinecharity.org.uk/support-for-professionals/specialist-support-for-professionals
https://www.nice.org.uk/guidance/PH11/chapter/4-Recommendations#folic-acid-2
https://www.gov.uk/government/publications/anencephaly-description-in-brief/anencephaly-information-for-parents
https://www.gov.uk/government/publications/spina-bifida-information-for-parents