North Thames
Genomic Medicine Service

Bitesize basics - The importance of knowing ethnicity in Cystic Fibrosis carrier testing

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Go to our **WEBSITE** for up-to-date genetic testing information.

This is one segment of an eight-part bitesize basics learning series for Primary Care, focusing on ordering Cystic fibrosis (CF) carrier testing:

1. How genetic testing is changing in Primary Care
2. What is CF carrier testing?
3. Should I order a CF carrier test?
4. Is ethnicity important in CF carrier testing?
5. Consenting for CF carrier testing
6. How to order a CF carrier test?
7. What do I do with a CF carrier test result?
8. Genetics quiz – CF carrier testing

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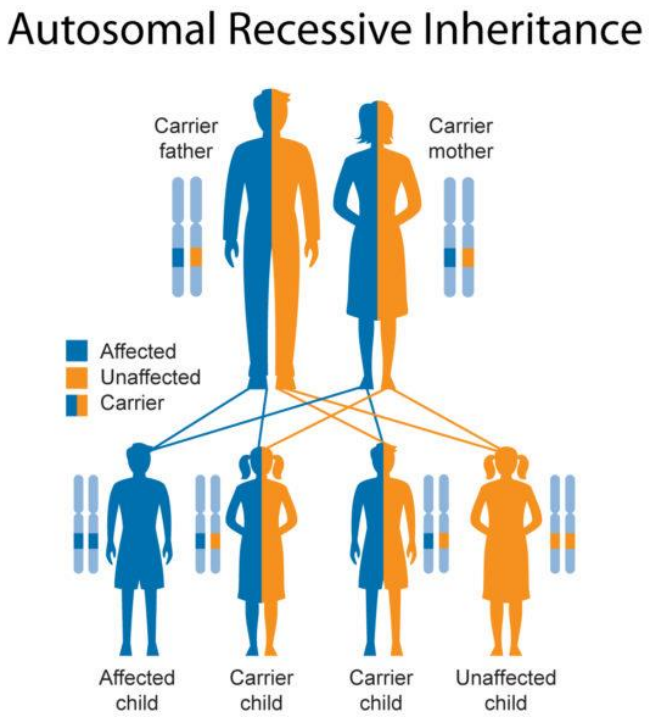
Autosomal recessive inheritance

Cystic fibrosis is inherited through a family in an "autosomal recessive" pattern.

If an individual has a genetic variant in one of their two copies of the *CFTR* gene, then the second copy compensates, and they are known as an unaffected carrier.

If an individual has no working copies of the *CFTR* gene, they would be affected with cystic fibrosis.



Ethnicity and recessive genetic conditions

The chance that an individual is a carrier of a recessive condition depends upon their family history and their ethnicity.

Some genetic conditions are more common in specific ethnic groups. The table below shows the chance that an individual is a CF carrier based on their ethnicity.

Carrier frequency of *CFTR* mutations	Ethnicity	Incidence of CF	Carrier frequency
	Northern European	1 in 2000-3000	1 in 22 –27
	African	1 in 28500	1 in 85
	Ashkenazi Jewish	1 in 3300	1 in 29
	Bahraini	1 in 5000	1 in 36
	Mexican	1 in 8500	1 in 46

Ethnicity can determine eligibility for CF carrier testing

Currently (publication date 27 May 2024), ethnicity is included in the criteria for CF carrier testing. These criteria are given in the NHS National Genomic Test Directory.

R185 Cystic fibrosis carrier testing

Testing Criteria

1. Prospective egg or sperm donor
2. Family history of CF in close relative (up to 4th degree, i.e. in 1st cousin's child or closer relative), or in a similar close relative of partner
3. Partner of a known CF carrier
4. Close consanguineous couple (1st cousins), AND from an ethnic group with a high carrier frequency
5. Both parents of a fetus with echogenic bowel (where both parents are available)
6. Both parents of a fetus with dilated bowel (where both parents are available)

Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Ethnicity can impact CF carrier test reporting

Knowing a patient's ethnicity is important for reporting CF carrier test results. This is particularly true for results where no *CFTR* variant is found.

CF carrier testing only looks for the 50 most common variants that cause CF in the Northern European population. If a variant is not found, this test reduces the chance that they are a carrier but does not rule it out entirely.

The remaining chance that your patient is a carrier of a variant that would not be detected by this test is called their "residual risk."

Remember…

To include ethnicity information on a CF carrier test referral form.

This way the genetics laboratory can assess your patient's residual risk in an individualised and accurate way.

National Test Directory

Up-to-date eligibility criteria and who can order genetic tests in England are given in the NHS National Genomic Test Directory.

NHS England » National genomic test directory
https://www.england.nhs.uk/publication/national-genomic-test-directories/

Contacts and information

To contact the North Thames Genomic Medicine Service, email: nt-gmsa@gosh.nhs.uk

To contact the North Thames Genomic Medicine laboratory hub, email: gos-tr.norththamesgenomics@nhs.net

Visit our website: https://norththamesgenomics.nhs.uk

For a more comprehensive understanding of the information provided in this bitesize resource, please download our *CF Carrier Testing Toolkit:*

https://norththamesgenomics.nhs.uk/wp-content/uploads/2024/05/20240905-NTGMS-Toolkit-Cystic-Fibrosis-CF-Carrier-Testing-in-Primary-Care.ppt

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Helpful references

Autosomal recessive inheritance diagram can be found at: https://nfed.org/learn/genetics-inheritance/

Northern European population CF incidence and carrier frequency:
https://www.genomicseducation.hee.nhs.uk/documents/cystic-fibrosis/

African population carrier frequency: Goldman, A., Labrum, R., Claustres, M., Desgeorges, M., Guittard, C., Wallace, A. and Ramsay, M. (2001) The molecular basis of cystic fibrosis in South Africa. Clin Genet 59, 37-41.

Ashkenazi Jewish population carrier frequency: Kerem E, Kalman YM, Yahav Y, Shoshani T, Abeliovich D, Szeinberg A, Rivlin J, Blau H, Tal A, Ben-Tur L, et al. Highly variable incidence of cystic fibrosis and different mutation distribution among different Jewish ethnic groups in Israel. Hum Genet. 1995 Aug;96(2):193-7. doi: 10.1007/BF00207378. PMID: 7635469.

Bahraini population carrier frequency: Al-Mahroos F. Cystic fibrosis in Bahrain incidence, phenotype, and outcome. J. Trop. Pediatr. 1998; **44**: 35–39.

Mexican population carrier frequency: Orozco, L., Velazquez, R., Zielenski, J., Tsui, L.C., Chavez, M., Lezana, J.L., Saldana, Y., Hernandez, E. and Carnevale, A. (2000) Spectrum of CFTR mutations in Mexican cystic fibrosis patients: identification of five novel mutations (W1098C, 846delT, P750L, 4160insGGGG and 297-1G-->A). Hum Genet 106, 360-365.