Rapid Prenatal Exome Sequencing (R21) Inclusion Criteria

NHS East Genomics

Checklist: ✓ Trio testing advised ✓ MDT with Genetics ✓ Record of discussion and request forms ✓ R21 information leaflet

Multiple anomalies

Inclusion	Exclusion
✓ **≥ 2 major structural anomalies.**	✗ Minor markers for aneuploidy, e.g. • Choroid plexus cysts • Echogenic foci • Mild renal pelvis dilation • Small nasal bone • Long bones on 3rd centile.

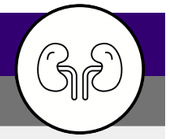
Brain anomalies

Inclusion	Exclusion
✓ **Major Central Nervous System (CNS) anomalies.**	✗ Neural tube defects (NTDs).
✓ **Anomalies of the corpus callosum** (partial or complete agenesis) either in isolation or with other anomalies.	
✓ **Ventriculomegaly -** Posterior horn persistently >11mm on ≥ 2 scans + another anomaly.	✗ It is not a CNS anomaly in isolation AND must be with another anomaly.

Skeletal / growth

Inclusion	Exclusion
✓ **Multiple contractures.**	✗ Bilateral talipes.
✓ **Isolated short long bones** all <3rd percentile with AC+HC >3rd percentile.	✗ EDD confirmed with early USS. No evidence of placental insufficiency, normal fetal & maternal dopplers, PAPP-A >0.41 (if taken), no previous FGR, no previous stillbirth, no maternal history of SLE etc.
✓ **Small for Gestational Age (SGA)** AC+ HC <3rd centile.	

Renal anomalies



Inclusion	Exclusion
✓ **Large echogenic kidneys** with a normal bladder.	

Additional indications

Inclusion	Exclusion
✓ **Nuchal translucency (NT)** • Measured between 11-14 weeks • >6.5mm + anomaly (can be a minor finding) • Normal array CGH.	✗ NT >3.5 but <6.5mm can only be considered in the presence of other structural anomalies in ≥ 2 body systems.
✓ **Isolated non-immune fetal hydrops** Defined as fluid/oedema in at least 2 physical compartments, e.g.: • Skin • Pleural • Pericardium • Ascities	✗ Detected at or after anomaly scan (18-20 weeks) with normal array CGH.
When the same couple has another and similar fetal anomaly in their current pregnancy that may be monogenic, despite it not meeting the inclusion criteria.	✗ Neural tube defects.

Pregnancies occurring in couples related by blood that do not strictly fulfil testing criteria but where there is a likelihood of a monogenic cause.

Please discuss further with Genetics MDT if the R21 inclusion criteria is not met, but there is a concern of a monogenic cause.

National Genomic Test Directory (V.5 April 2023) - for current testing criteria please refer directly to the National Genomic Test Directory

Rapid Prenatal Exome Sequencing (R21) Exclusion criteria

NHS East Genomics

- Termination of pregnancy has already been decided.
- Fetal demise has occurred.
- Fetal demise is imminent.

R27 or R412 (if not enough DNA is available for testing)
Clinical Indication - Congenital malformation and dysmorphism syndromes.
Sequencing should be offered if QF-PCR and Microarray are normal.

For cases where the sonographic findings indicate a specific monogenic disorder:

- Targeted testing should be applied where appropriate.

Confirmed aneuploidy or pathogenic copy number variant consistent with anomalies detected by microarray.

Fetuses with confirmed thanatophoric dysplasia, achondroplasia or Apert syndrome on other relevant rapid tests (R23,R24,R25,R306 or R309).

Cases where familial causative variant(s) are known:

- Targeted testing should be performed.

Useful links

GeNotes Fetal and Women's Health

bit.ly/GeNotes_FetoMaternal

Record of discussion form (Prenatal)

bit.ly/recordofdiscussion_rPES

NHS National Genomic Test Directory

bit.ly/national_test_directory

R21 Request form

bit.ly/R21_requestform

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