

Rapid Prenatal Exome Sequencing (R21) Inclusion Criteria

Checklist:



Trio testing advised



MDT with Genetics



Record of discussion and request forms



R21 information leaflet

Multiple anomalies



Inclusion

- ✓ **≥ 2 major structural anomalies.**

Exclusion

- ✗ 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

- ✓ **Major Central Nervous System (CNS) anomalies.**
- ✓ **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.

Exclusion

- ✗ Neural tube defects (NTDs).
- ✗ It is not a CNS anomaly in isolation AND must be with another anomaly.

Skeletal / growth



Inclusion

- ✓ **Multiple contractures.**
- ✓ **Isolated short long bones** all <3rd percentile with AC+HC >3rd percentile.
- ✓ **Small for Gestational Age (SGA)** AC+ HC <3rd centile.

Exclusion

- ✗ Bilateral talipes.
- ✗ 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.

Renal anomalies



Inclusion

- ✓ **Large echogenic kidneys** with a normal bladder.

Exclusion

Additional indications

Inclusion

- ✓ **Nuchal translucency (NT)**
 - Measured between 11-14 weeks
 - >6.5mm + anomaly (can be a minor finding)
 - Normal array CGH.

Exclusion

- ✗ 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.

Rapid Prenatal Exome Sequencing (R21) Exclusion criteria

- 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**

<https://tinyurl.com/ed62u9sb>



**NHS National Genomic
Test Directory**

<https://tinyurl.com/mwh367cd>



**Record of discussion
form (Prenatal)**

<https://tinyurl.com/hhet9pc7>



R21 Request form

<https://tinyurl.com/mr2ueubj>

