CHROMOSOMAL ANOMALIES—"PRENATAL DETECTION"

By

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SUMMARY

Methods of prenatal detection of chromosomal anomalies have been discussed. Recent advanced method of chorionic villi culture is included. Different situations of chromosomal abnormalities evaluated.

Prenatal detection of chromosomal anomalies is now a well established procedure. Several reviews have appeared on prenatal detection of genetic anomalies in general and chromosomal anomalies in particular.

The amniotic fluid

It is preferable to sample the fluid after the 16th week, Therkelson (1972) reports hundred per cent successful cultures for this period. The relative abundance of cells in fluid surrounding female foetuses is a reliable diagnostic criteria for sex (Hudson, 1975). During amniocentesis contamination of the fluid with maternal cells derived from skin, fascia, connective tissue and blood are known to occur but their incidence is very low.

Culture

Many minor variations are used, however basically they all consist of setting up the cells in a culture system. Natural media is the amniotic fluid itself or an artificial media fortified with foetal calf serum is used (Abbo and Zell weger, 1970). The latter procedure is most popular method.

From: Kasturba Medical College, Mangalore. Accepted for publication on 3-3-87.

In all cases a gas phase of 5% CO_2 in air is recommended. Culture time varies from sample to sample, generally speaking between one to three weeks. Ferguson (1971) in his series noted a variation between 7-31 days.

Three main types of cells proliferate (1) Epitheloid like (2) Thin elongated fibroblasts like (3) Short, squat, fusiform like, in that order of frequency (Schmid, 1972). Following a 4-6 hour colchicine treatment; cells if on coverslips are directly placed in hypotonic solution, cells in flasks or bottles are trypsinized. Fixation is the routine 3:1 alcohol acetic mixture. The sophisticated banding techniques are used.

Preparation of chromosomes from chorionic villi sample

Collect sample in Han's F-10 media (heparinized) wash off blood cells and debris by fresh media. Transfer villi to silliconised petri dish. Add 5 ml chang medium with colcemid (0.1 mcg/ml),

Chop tissue finely and incubate for 2 hours at 37°C. Transfer to siliconised centrifuge tube and centrifuge at 500 rpm for 8 minutes and discard supernatant. Add 4 ml 1% trisodium citrate, leave for 4 minutes on bench, then centrifuge at 500 rpm for 6 minutes, discard supernatant. Add 3:1 methanol: aceticacid fix, centrifuge at 500 rpm for 5 minutes. Discard supernatant and leave sample to air-dry for several minutes. Transfer material to clean dry slides.

The cells derived by modified direct method are treated for trypsin banding.

Indications

The most important is in familial translocation. With one of the parents most usually the mother known to be a translocation carrier, the risks of an abnormal child vary with the exact type of translocation. Most of the times it may not be possible to be certain of the phenotype in a balanced carrier. Usually investigators predict a normal foetus if the translocation is exactly like that of the parent.

The second indication is following the birth of a child with a chromosomal error, the rationale being that a second trisomy is more frequent in these cases than in the general population.

A third indication is in all pregnancies where the mother is over 40 years, for the well known reason that non-disjunctional errors are many times more frequent in this group. A fourth indication is in sex linked conditions to detect the sex of the foetus. This can be resolved by the much simpler sexchromatin determination.

A fifth indication is inadvertant intrauterine insult like accidental exposure to radiation or the ingestion of a clastogen. Assessing the amount or nature of damage in these cases however poses problems.

Evaluation

A straight forward trisomy rarely poses a problem. Structural anomalies can be detected by banding procedures; once detected, if they are of the balanced variety, it may be impossible to be certain of the phenotype. The family history and comparison with similar karyotypes in the family may be of some help. When a structural heterozygosity is seen for the first time in the foetus, the siuation may be difficult.

Aneuploidy and polyploidy is another difficult situation. Aneuploidy of sexchromosoms or autosomes may be very difficult to resolve. Polyploidy is a case in point for the uncertainities.

Chromosomal aberrations in the form of fragments etc., are again difficult to assess. As pointed out by Schmid (1972) it is very necessary that each lab establishes its own criteria. Frequency of aberrations may suddenly increase with unknown clastogens introduced into the culture medida via serum etc.; monitoring these should be a must if any conclusions are to be drawn.

References

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