Medical genetics: advances in brief

Failure of amniotic-fluid-cell growth; is it related to fetal aneuploidy?

Persutte WH, Lenke RR. *Lancet* 1995;345:96-7.

When amniotic fluid cells do not grow
Gosden CM. *Lancet* 1995;345:78.

Failure of amniotic fluid cell cultures is well recognised to occur in a small percentage of samples and has been suggested to be a random event. Persutte and Lenke retrospectively reviewed the outcome of 7872 amniocenteses. The samples were taken for a range of indications: 55% for advanced maternal age, 11% for low maternal serum alpha-fetoprotein, 10% for family history, 10% for fetal abnormality detected on ultrasound examination. A small number of samples were excluded where there were technical sampling problems (14) or fetal death (10) before the amniocentesis. Thirty two (0.5%) of the remaining samples failed to grow. Ten of these 32 pregnancies were not subject to repeat sampling, six of this group ended in the birth of normal babies, but of the remaining four, two ended in third trimester stillbirths, one pregnancy was terminated for bladder outflow obstruction, and one was from an acardiac twin pregnancy. Twenty two women had repeat procedures; 18 of the 22 had normal karyotypes and delivered normal babies, two fetuses had trisomy 21, one had trisomy 13, and one had Pallister-Killian syndrome. A result was obtained on 7816 samples after the first procedure; 161 were excluded because of fetal death, and of the remainder 82 (1%) had aneuploid results. This compares to 13% in the group in which the initial culture failed. In her commentary Gosden discusses the possible reasons for this finding. Pregnancies with structural abnormalities of the gastrointestinal or urogenital tract, oligo- or polyhydramnios may be at risk of culture failure because of low cell counts, and these pregnancies have a higher chance of being associated with aneuploidy. She emphasises the importance of validating the findings in other laboratories and reviewing the most appropriate management in culture failure. An anomaly scan with cordocentesis rather than a simple repeat amniocentesis may be a more appropriate intervention. Finally, the potential harm that may be done by inducing anxiety in those women with normal pregnancies is discussed.

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Prenatal genetic counselling for haemoglobinopathy carriers: a comparison of primary providers of prenatal care and professional genetic counselors

Rowley PT, Loader S, Sutera CJ, Kozyra A. *Am J Hum Genet* 1995;56:769-76.

All geneticists are aware of the increasing demands on their time from patients as many common disorders are found to have a genetic component (for example, several cancers), and more and more genes implicated in single gene disorders are mapped and cloned. Clearly the limited number of health personnel trained in genetics will be insufficient to meet the demand, and so the question arises as to who else could assist in the provision of a comprehensive genetics service. Methods which would enable primary care providers to offer the more straightforward genetic services are evolving and being tested, and in this paper, focusing on haemoglobinopathies, a comparison is made between the outcome of counselling provided by primary care personnel and professional genetic counsellors. (The former were instructed by geneticists on counselling technique, and provided with videotapes, patient information leaflets, and visual teaching aids for use with patients.) The authors have previously reported that in a community wide prenatal screening programme for haemoglobinopathies, 36% of women found to have a haemoglobinopathy did not go to a tertiary centre for counselling, and thus may not have benefited from testing. The authors wished to determine if the provision of counselling by the prenatal care provider (obstetrician or family doctor) would increase the efficiency of the programme. It did not. The proportion of patients found to have a haemoglobinopathy who received counselling was similar in primary and tertiary care for both sickle cell and β thalassaemia. Knowledge after counselling was the same in both groups as well. The only significant difference arose in the proportion of patients whose partner had been tested: 25% for primary providers compared with 49% for tertiary providers with sickle trait; and 47% versus 78% for the same groups with β thalassaemia trait. Overall it seems that haemoglobinopathy screening and genetic counselling can be provided by the prenatal care provider, but an important challenge which remains to be resolved is an improvement in effective partner testing.

FRANCES FLINTER

Uniparental disomy 7 in Silver-Russell syndrome and primordial growth retardation

Kotzot D, Schmitt S, Bernasconi F, et al. *Hum Molec Genet* 1995;4:583-7.

Uniparental disomy (UPD) in which both chromosomes of a given pair are inherited from a single parent is a generally rare phenomenon. Its frequency is, however, increased among patients with isochromosomes, Prader-Willi or Angelman syndromes, Beckwith-Wiedemann syndrome, transient neonatal diabetes, and trisomic conceptions which survive as a result of reduction from trisomy to disomy. There is always a risk that UPD will unmask recessive alleles and the first cases of UPD for chromosome 7 were identified in children with cystic fibrosis and short stature. These authors have, therefore, prospectively searched for UPD (7) in 35 patients ascertained with pre- and postnatal growth retardation; 25 of them had additional dysmorphic features consistent with a clinical diagnosis of Silver-Russell syndrome (SRS). Among the syndromic group 3/25 had maternal UPD (7) and among the 10 with growth retardation a further case was found. Minor dysmorphic features in this growth retarded patient as well as some of the previously reported UPD (7) cases suggest consistent short stature with variable expression of SRS features. The association of SRS with both maternal heterodisomy as well as isodisomy argues against the unmasking of a recessive allele and for the existence of a maternally imprinted gene or region associated with pre- and postnatal growth. Chromosome 7 has two large areas of homology to regions of the mouse genome which show imprinting effects and SRS has previously been mapped to 17q25. The next challenge is, therefore, to establish to what extent microdeletions or mutations within these areas are responsible for the phenotype of SRS patients without UPD. In the meantime, these findings mean that it is appropriate to apply molecular genetic testing for UPD (7) to another group of patients who have traditionally been examined by cytogenetics only.

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