

## Screening brief

### Antenatal screening for neural tube defects

#### Background

- Neural tube defects result from a failure of closure of the neural tube early in pregnancy. They include mainly anencephaly and spina bifida; encephalocele is rare
- Anencephaly is fatal, but most infants with other neural tube defects survive, usually with major lifelong physical disabilities and sometimes intellectual impairment as well
- Most lesions (all anencephaly and about 80% of spina bifida and encephalocele) are open and lead to leakage of  $\alpha$  foeto-protein (AFP) into amniotic fluid and therefore into maternal serum
- Most neural tube defects can be prevented by increasing maternal folic acid intake around the time of conception<sup>1</sup>

#### Prevalence

- Before the advent of screening the birth prevalence of neural tube defects varied in different populations from less than 1 per 1000 to over 4 per 1000<sup>2</sup>
- In England and Wales the birth prevalence of neural tube defects decreased from about 2800 per year in 1965 to about 80 per year in 1996 (about 1 in 10 000 births),<sup>3-5</sup> mostly owing to antenatal screening and selective termination

#### Spina bifida: screening

- Biochemical: Maternal serum AFP screening for open spina bifida at 16–18 weeks of pregnancy. At 17 weeks using an AFP cut off level of 2.5 multiples of the median (MoM), corrected for maternal weight, and a biparietal diameter measurement to estimate gestational age yields a detection rate of 85% for a 1.4% false positive rate,<sup>6</sup> based on data from the UK collaborative AFP study<sup>7</sup>
- Ultrasound: Three ultrasonographic signs of spina bifida are recognised from secondary changes in the cranium: (a) pinched frontal region of the skull (so-called “lemon” sign)<sup>8</sup>; (b) reduced transverse diameter of the cerebellum (leading to the so-called “banana” sign)<sup>8</sup>; (c) diminished thickness of the cerebellum.<sup>9</sup> A fourth sign, small biparietal diameter,<sup>10</sup> is used indirectly with serum AFP measurement. A meta analysis of studies yields an 87% detection rate and a 0.9% false positive rate for the lemon sign; screening performance may have been enhanced by directly seeking a spinal lesion on the same scan<sup>11</sup>

#### Spina bifida: diagnosis

- Ultrasound scan visualisation of the spinal defect; detection rate about 87%, false positive rate 0.5% (detecting the defect is time consuming and inappropriate as a screening test)<sup>11</sup>
- Amniotic fluid AFP and acetylcholinesterase (AChE) measurement if AFP  $\geq 2$  MoM: detection rates 99% for open spina bifida for a 0.3% false positive rate<sup>12</sup>
- The greatest diagnostic accuracy is achieved using both ultrasound visualisation and amniocentesis and repeating the scan if the two are discrepant; because of the risk of fetal loss from amniocentesis (0.9%)<sup>13 14</sup> a negative ultrasound is, in certain centres, accepted on its own

#### Encephalocele: screening and diagnosis

- For open lesions the performance of AFP screening and biochemical diagnostic tests is similar to that for open spina bifida lesions

#### Anencephaly: screening and diagnosis

- Maternal serum AFP is raised ( $\geq 2.5$  MOM) in nearly all cases<sup>7</sup> and ultrasound makes the diagnosis in nearly all cases

#### Practical issues

- Ultrasound to date pregnancy should be routine
- Specialist ultrasound units may abandon AFP screening if audit on sufficient numbers shows a high detection of past cases from ultrasound alone

#### Conclusions

- The performance of ultrasound screening, though not reliably known, is high. The need to continue AFP screening at centres where an ultrasound scan examination is routinely offered is uncertain. However, AFP screening is simple, does not rely on operator skills and training, as does ultrasound, and has an additional use in identifying Down's syndrome and other disorders, such as trisomy 18

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