

EDITORIAL

Safety first: choices in antenatal screening for Down's syndrome

Reasonably effective methods of antenatal screening for Down's syndrome have been available for about 15 years. Most commonly, effectiveness has been gauged by the detection rate that can be achieved at a 5% false-positive rate, which in practical terms means the proportion of women offered an amniocentesis or chorionic villus sampling (CVS) procedure. During the past 15 years, with improvements in second trimester serum screening and the introduction of first trimester screening markers, test performance has increased the detection rate from about 60% to 85%, all for a 5% false-positive rate.

Relating screening performance to a fixed 5% false-positive rate has been a reasonable way to mark improvements in screening and probably stems from obstetric practice in the 1970s and 1980s, when approximately 5% of pregnant women were of advanced maternal age and were being offered amniocentesis based on their age-related risk of Down's syndrome. Today, an invasive procedure rate of 5% has become an acceptable goal.

But what does a 5% invasive procedure rate mean in terms of the safety of the antenatal screening process? At best, the high-risk group identified through screening at a 5% false-positive rate is at no more than a 20-fold higher risk than the total population; for example, if a population begins with a group risk of one in 1000, the risk in the high-risk group will be one in 50. If the miscarriage rate caused by an invasive procedure is one in 100, then one unaffected pregnancy will be lost for every two Down's syndrome pregnancies identified.

Now that high detection rates have been achieved, screening safety will markedly improve only by reducing the percentage of women needing invasive procedures, i.e. by reducing the false-positive rate. Such a reduction will also relieve many women from the anxiety of being identified as high-risk and having to consider a procedure that risks the viability of the pregnancy.

In 1999, a screening method was described that would substantially reduce the false-positive rate while maintaining a high detection rate.¹ Named the Integrated Test, it uses the best available screening markers from the first and second trimester and calculates a single estimate of risk for the pregnancy. The estimate of performance is an 85% detection rate for a 1% false-positive rate, an 80% reduction in the proportion of women having to consider an invasive diagnostic procedure. The risk in the high-risk group would be one in 10 rather than one in 50, with one wanted pregnancy lost for every 10 Down's syndrome pregnancies identified.

This issue of *Journal of Medical Screening* contains the report of SURUSS (the Serum, Urine and Ultrasound Screening Study), the most comprehensive antenatal Down's syndrome screening study undertaken to date. SURUSS

examined almost all of the currently used and proposed Down's syndrome screening markers, and assessed the performance of the possible marker combinations. SURUSS detailed the performance of the ultrasound marker, nuchal translucency, providing details of the practical aspects of its use, including important information on differences among operators, instruments, and the timing of the measurement.

What clearly emerges from the extensive details of the SURUSS report is the marked gain in performance and hence in safety when screening markers are most effectively combined. The performance estimates for the Integrated Test are remarkably consistent with previously published values, as they are for the more established second trimester and first trimester tests.

There is additional evidence that the SURUSS report is not alone in showing the gain in performance and safety that the Integrated Test provides. At a recent conference at Brown University on introducing the Integrated Test into medical practice, the results of a multi-centre project on implementing the Integrated Test demonstrated its acceptability and showed that the reported performance estimates for the Integrated Test were correct.

With so many choices in the timing and type of antenatal screening available, extensive education for health care providers as well as for pregnant women needs to begin so that priorities are clearly understood. Earlier is not always better when the choice involves a five-fold greater chance of losing a wanted pregnancy. The temptation to retest women at various points in pregnancy is strong, but at what cost? Should we condone the offer of a first trimester screen, followed by a second trimester serum screen, followed by an ultrasound scan looking for soft markers of Down's syndrome, with the unstated effect that as many as 15–20% of pregnant women may be offered invasive diagnostic procedures?

It is our obligation as health care professionals to offer the most effective and safe screening method. There can be little doubt that at the present time the evidence is now strong that the Integrated Test should be the screening method of choice whenever possible. The SURUSS report published in this issue of *Journal of Medical Screening* strongly supports this.

Jacob Canick

Professor, Department of Pathology
Women and Infants Hospital, Brown Medical School
Providence, Rhode Island, USA

Reference

- 1 Wald NJ, Watt HC, Hackshaw AK. Integrated screening for Down's syndrome based on tests performed during the first and second trimesters. *N Engl J Med* 1999;**341**:461–7.