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Editorial

Some thoughts on the true value of ultrasound

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Fetal abnormalities, premature birth and impaired placentation account for more than 90% of perinatal deaths. These problems are as common today as they were more than 30 years ago and our failure to reduce their prevalence is essentially the consequence of inadequate methods of screening and lack of effective strategies for their prevention.

Extensive research in the last 20 years has now established that ultrasonography can identify the majority of affected fetuses and women at high risk for these problems. The remaining challenge is to ensure that this knowledge finds a practical application in a service for the benefit of pregnant women and forms the basis for further research to develop effective therapeutic interventions.

Fetal abnormalities

The ultrasonographic features of all major malformations have been well described for more than 20 years but there is a continuing problem with providing high-level scanning to all pregnant women. How can we explain, for example, the failure to detect prenatally the great majority of major cardiac defects, which are by far the main cause of postnatal death due to congenital abnormalities? Why is it still necessary for women to be subjected to second-trimester serum alpha-fetoprotein screening for diagnosis of neural tube defects, rather than looking for the cranial and cerebellar signs? What could possibly be the reason for obstetricians to willingly engage in producing the 'collateral damage' of fetal death associated with the widespread use of amniocentesis for the sole indication of advanced maternal age?

I now believe that these problems cannot be solved only by improved education of sonographers or quality of machines but rather by ensuring that those undertaking the scans are appropriately trained and accredited to do so. In private healthcare systems it should be the responsibility of professional bodies to put the interests of pregnant women above the economic benefits of their members. In nationalized healthcare systems governments should ensure that care moves on with the times and does not remain entrenched in outdated practices from the 1970s.

It is clear that women want early diagnosis of fetal abnormalities, that chorionic villus sampling is at least as safe as amniocentesis and that termination of pregnancy in the first trimester is safer than in the second trimester. It is now widely accepted that increased nuchal translucency (NT) thickness at $11+0$ to $13+6$ weeks is the single most effective marker of trisomy 21 and all other major chromosomal defects (Figure 1)[1,2]. In screening for trisomy 21 by a combination of maternal age, fetal NT and serum free β-human chorionic gonadotropin and pregnancy associated plasma protein-A, the detection rate can be 90% for a screen-positive rate of 5%, provided the sonographers are competent and the laboratories, reagents and software reliable[3].

There is also extensive evidence that a high proportion of chromosomally abnormal fetuses have nasal bone hypoplasia and a wide frontomaxillary facial angle (both of which can be assessed in the same mid-sagittal plane as for measurement of NT (Figure 2)), and Doppler evidence of tricuspid regurgitation or reversed end-diastolic flow in the ductus venosus[4–7]. Inclusion of these markers in the $11+0$ to $13+6$-week scan, either in all cases or in those with an intermediate risk after NT and serum testing, can improve the detection rate to about 95% with a simultaneous reduction in the screen-positive rate to 2%.

It is likely that research within the next 3 years will, firstly, investigate the effectiveness of prospective first-trimester screening for chromosomal abnormalities by an integrated approach that incorporates the new

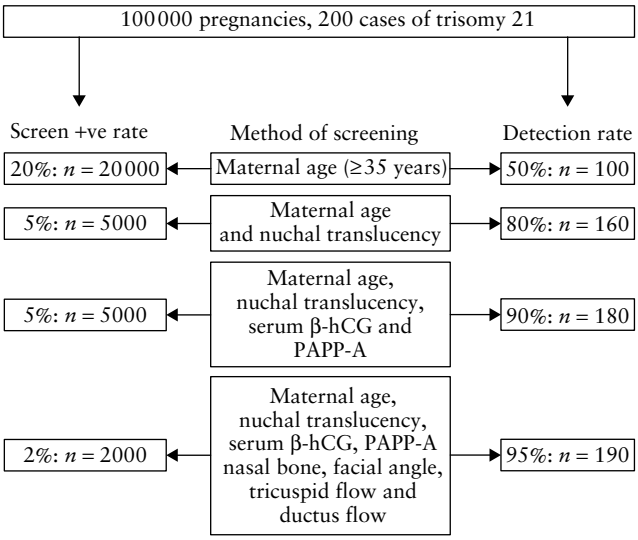

Figure 1 In many developed countries the maternal age is 35 years or more in about 20% of pregnancies. Consequently, screening for trisomy 21 by maternal age could identify 50% of affected fetuses after amniocentesis in 20% of women. The alternative is to screen by a combination of maternal age, serum biochemistry and ultrasound examination at 11 + 0 to 13 + 6 weeks, with a 10-fold reduction in the need for invasive testing and a doubling in detection rate. β-hCG, β-human chorionic gonadotropin; PAPP-A, pregnancy associated plasma protein-A.

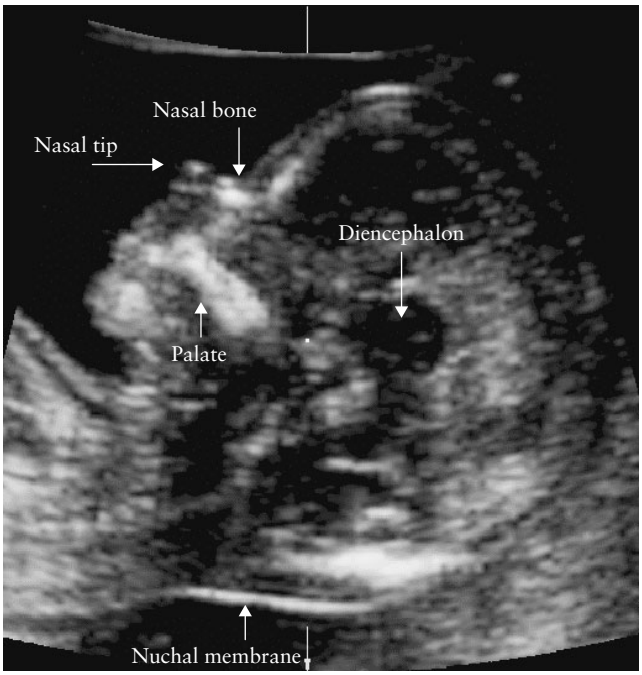

Figure 2 Ultrasound image of the fetal profile in the mid-sagittal plane demonstrating the tip of the nose and nasal bone, the rectangularly shaped palate, the translucent diencephalon and the nuchal membrane. This view is used for assessment of three markers of chromosomal defects at 11 + 0 to 13 + 6 weeks: nuchal translucency thickness, fronto-maxillary facial angle and nasal bone.

sonographic markers; secondly, validate preliminary data that the vast majority of major cardiac defects can be suspected from increased NT, abnormal flow across the tricuspid valve or the ductus venosus and direct examination of the four-chamber view (which will, in any case, be necessary to assess tricuspid flow); and thirdly, confirm that the majority of all clinically significant malformations can be detected at the 11 + 0 to 13 + 6-week scan.

Prematurity

All births before 37 weeks' gestation are defined as premature but the vast majority of morbidity and mortality relates to early delivery before 34 weeks, which occurs in 1.5–2.0% of pregnancies (Figure 3). Two-thirds of such births occur spontaneously and one-third are iatrogenic, mainly for pre-eclampsia and fetal growth restriction. In half of spontaneous early births the women have had previous pregnancies and one-third of such early births are in women who had a previous premature birth. Consequently, screening by obstetric history will detect only 17% of women destined to have early premature birth.

A method that is better than obstetric history at identifying women at high risk is ultrasonographic measurement of cervical length at 22 weeks' gestation. For a screen-positive rate of 10%, an integrated model using cervical length and obstetric history can detect more than 60% of early premature births[8]. The only proven method that can reduce the risk of premature delivery is the prophylactic administration of progesterone from mid-gestation to 34 weeks to women who have previously had a premature birth and those found to have a very short cervix (15 mm or less) at routine ultrasound examination at 22 weeks[9–11]. Measuring

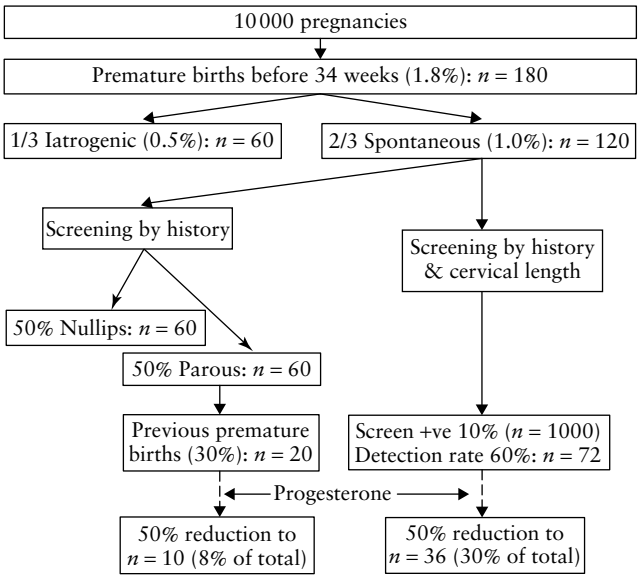

Figure 3 Screening for and prevention of spontaneous early premature birth. Screening by maternal history detects only 17% of cases and if the prophylactic use of progesterone halved the rate of prematurity, the overall impact on premature births would be less than 10%. The reduction could potentially increase to 30% if the method of screening was essentially based on measurement of cervical length at 22 weeks' gestation. +ve, positive; Nullips, nulliparous.

cervical length is a readily learned skill for obstetric sonographers. Furthermore, ultrasound screening is available routinely in maternity units and studies have shown that transvaginal ultrasonography is acceptable to pregnant women and does not cause discomfort in the vast majority[12].

It is likely that the failure to reduce the rate of premature birth during the last 30 years can now be reversed by a strategy of routine screening of pregnant women by ultrasonographic measurement of cervical length and the prophylactic administration of progesterone to those with a short cervix. As mentioned above, progesterone has been shown to be effective in women with a cervical length of 15 mm or less at 22 weeks' gestation; randomized studies within the next 3 years should investigate the potential effectiveness of progesterone in the group of women with a cervical length of 16–25 mm.

Pre-eclampsia

Pre-eclampsia, which affects about 2% of pregnancies, is thought to be the consequence of impaired trophoblastic invasion of the maternal spiral arteries and their conversion from narrow vessels to wide non-muscular channels. However, in women with pre-eclampsia the prevalence of placental lesions is inversely related to the gestational age at delivery[13] and it is early disease requiring delivery before 34 weeks, found in 0.5% of pregnancies, that is associated with fetal growth restriction and increased risk of perinatal mortality and morbidity and both short-term and long-term maternal complications.

Attempts at the prevention of pre-eclampsia by the prophylactic use of drugs from mid-gestation have been largely unsuccessful in the case of calcium and antioxidant vitamins, or they had a small effect (10% reduction) in the case of low-dose aspirin[14–17]. It is now time to determine whether pharmacological interventions starting from the first rather than the second trimester will prove to be more effective in the prevention of pre-eclampsia, but before this can be investigated it is essential to develop a method of effective and early identification of the high-risk group.

The likelihood of developing early pre-eclampsia is increased by a number of factors in the maternal history, including Afro-Caribbean race, nulliparity, high body mass index and personal or family history of pre-eclampsia. However, screening by maternal history has a detection rate of about 50% for a screen-positive rate of 10% (Figure 4).

A better method than maternal history for identifying women at high risk of early pre-eclampsia is Doppler ultrasound measurement of the impedance to flow in the uterine arteries both in the second trimester but also at 11 + 0 to 13 + 6 weeks[18–20]. A model using Doppler and maternal history has a detection rate of about 80% for a screen-positive rate of 10%. It is likely that research within the next 3 years will establish an integrated model based on uterine artery Doppler and maternal history, mean arterial pressure and serum biochemistry,

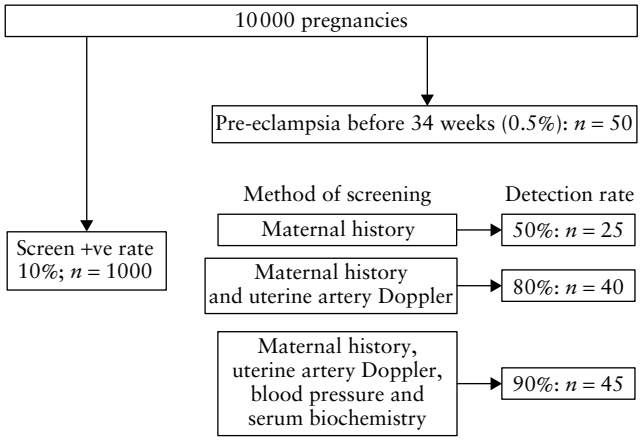

Figure 4 Screening for severe pre-eclampsia requiring delivery before 34 weeks of gestation. An integrated approach combining maternal history with biophysical and biochemical measurements at 11 + 0 to 13 + 6 weeks could potentially detect 90% of pregnancies destined to develop pre-eclampsia for a screen-positive (+ve) rate of 10%.

with a detection rate in excess of 90% for a screen-positive rate of 10%. Essentially, the same methodology as used in screening for chromosomal abnormalities will be applied to derive from factors in the maternal history the *a priori* risk, which will then be multiplied by the likelihood ratio associated with biophysical and biochemical measurements to derive patient-specific risks for pre-eclampsia at 11 + 0 to 13 + 6 weeks.

Conclusion

Two ultrasound examinations in pregnancy, one at 11–13 weeks and another at 20–22 weeks, can identify the majority of women at high risk for each of the three major causes of perinatal death and damage. There is a continuing need for further research to help improve screening and therapeutic interventions. However, in the meantime, it is essential that governments and professional bodies ensure that ultrasonography is appropriately used for the benefit of pregnant women.

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