

### What is already known on this topic

Patients with stroke returning home from hospital often encounter unanticipated disability and difficulties in adapting to the home environment

No intervention has been shown to alleviate these problems

### What this study adds

A brief programme of domiciliary occupational therapy can enhance recovery and reduce the risk of deterioration in patients with stroke returning home

Rehabilitation should be extended beyond discharge from hospital

intervention has been observed previously and used to justify a more prolonged therapy input.<sup>4 5</sup> Reducing the longer term impact of stroke remains a major challenge.<sup>9</sup>

### Implications

Our results lend support to the principle of extending routine stroke rehabilitation from the inpatient period to postdischarge period. Our resource analysis shows that the service costs are significant but that one therapist could manage 80-100 patients per year and prevent about 10 deteriorating in function after discharge home. We did not attempt to reduce hospital stay, but two recent British trials of early hospital discharge with a domiciliary multidisciplinary rehabilitation have shown a shortening of the period of inpatient care with no apparent adverse effect on

patient outcomes.<sup>10 11</sup> If confirmed, this potentially offers a way of improving postdischarge rehabilitation without incurring major additional service costs.

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## Six year survey of screening for Down's syndrome by maternal age and mid-trimester ultrasound scans

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### Abstract

**Objective** To assess the effectiveness of antenatal screening for Down's syndrome by maternal age and routine mid-pregnancy ultrasound scanning.

**Design** Retrospective six year survey.

**Setting** Maternity units of a district general hospital.

**Subjects** Pregnant women booked for delivery in hospital between 1 January 1993 and 31 December 1998.

**Main outcome measures** All cases of Down's syndrome occurring in district identified from regional congenital anomaly register and cytogenetic laboratory records. Women's case notes were examined to identify indication for karyotyping, gestation at diagnosis, and outcome of pregnancy.

**Results** 31 259 deliveries occurred during study period, and 57 cases of Down's syndrome were

identified, four in failed pregnancies and 53 in ongoing pregnancies or in neonates. The analysis was confined to ongoing pregnancies or liveborn children. Invasive antenatal tests were performed in 6.6% (2053/31 259), and 68% (95% confidence interval 56% to 80%) of cases of Down's syndrome were detected antenatally, giving a positive predictive value of 1.8%. There were 17 undetected cases, and in seven of these the women had declined an offer of invasive testing. In women aged less than 35 years the detection rate was 53% (30% to 76%). Most of the cases detected in younger women followed identification of ultrasound anomalies.

**Conclusions** The overall detection rate was considerably higher than assumed in demonstration projects for serum screening. As a result, the benefits of serum screening are much less than supposed. Before any new methods to identify Down's syndrome

are introduced, such as nuchal translucency or first trimester serum screening, the techniques should be tested in properly controlled trials.

## Introduction

Down's syndrome is one of the commonest causes of congenital mental handicap, and many parents consider it desirable to diagnose the condition antenatally to allow them the option of terminating an affected pregnancy. The first indicator used to identify pregnancies at high risk was maternal age, but more recently biochemical markers have been used. In 1992, on the basis of their demonstration project of serum screening, Wald et al concluded that its advantages were so great that "the NHS should ensure that antenatal maternal serum screening for Down's syndrome is available throughout Britain."<sup>1</sup> The method gained rapid acceptance, and by 1994 over half of obstetricians in England and Wales were offering it to all women under their care.<sup>2</sup>

The introduction of serum screening was supported by a 1993 report by the Royal College of Obstetricians and Gynaecologists, which considered the evidence for its use.<sup>3</sup> Four advantages were suggested compared with reliance solely on maternal age:

- It could detect twice as many affected pregnancies for the same rate of amniocentesis
- It could identify affected pregnancies in women below the age cut off
- It could reassure older women whose risk was lower than that predicted by age alone so they might avoid the need for amniocentesis
- At detection rates above 40%, it was more cost effective.

This report derived its evidence from four demonstration projects.<sup>1-4-6</sup> Since then, many similar demonstration projects have been published in a wide variety of populations.<sup>7-23</sup> Despite the large number of studies, we have not been able to identify a single one in which there was a contemporaneous control group of women screened by maternal age. The studies all make a similar assumption about the effectiveness of screening by maternal age—that the maximum success rate of this method will inevitably be limited to the proportion of babies with Down's syndrome born to women above the chosen age cut off. This is variously given as between 20% and 30%. In this paper we present data suggesting that these assumptions are not borne out in current practice—hence the advantages of serum screening are less than supposed—and we examine the factors that improve the effectiveness of screening by maternal age.

## Subjects and methods

### Screening procedures

At the Princess Anne Hospital, Southampton, screening for Down's syndrome is based principally on maternal age: amniocentesis is offered routinely to women who will be  $\geq 35$  years old at their estimated date of delivery. All women are also offered an ultrasound scan for anomalies at 19 weeks' gestation, and invasive testing is offered in selected cases where structural anomalies are seen that suggest the fetus is

aneuploid. In these cases the amniocentesis would normally be performed within a day or two of a problem being identified. Some women also have ultrasound scans earlier in pregnancy if there is a clinical indication, such as uncertain dates or vaginal bleeding. Serum screening is not offered, but a small number of women organise this privately.

### Identification of subjects

From the records of the Wessex Regional Genetics Laboratory and from the Wessex Antenatally Detected Anomalies Register, we identified all cases of Down's syndrome detected prenatally or postnatally in women booked for delivery in this hospital during the six years from 1 January 1993 to 31 December 1998 inclusive. As a regional centre, the hospital receives referrals from other units for antenatal diagnosis, but we excluded all cases diagnosed in women living outside the health district. We considered that an affected fetus had been successfully detected if the diagnosis was made before 24 weeks' gestation, at a stage in pregnancy when termination can be offered more easily. We examined the notes of all the affected women to identify their address, the indication for karyotyping, the gestation at diagnosis, and the outcome of the pregnancy. Where possible, we confirmed the prenatal diagnosis by checking the results of chromosome analysis performed after delivery.

We estimated the proportion of pregnancies in which an invasive procedure was performed from the total number of births and the number of antenatal karyotype investigations performed in each year during the study period. The hospital does not have a computerised maternity information system, so the age structure of the population during the whole study period could not be determined. Instead, we estimated it by obtaining the date of birth and estimated date of delivery from laboratory records of women who had  $\alpha$  fetoprotein screening for spina bifida. These were available for a two year period from 1995 to 1997.

## Results

In the six years studied 31 259 babies were delivered in the Princess Anne Hospital or associated community units, and 53 cases of Down's syndrome were detected either during pregnancy or in newborn babies. The overall incidence was 1.7 per 1000 births, consistent with national figures.<sup>3-24</sup> One of the affected children, born to a woman aged 29, had a de novo unbalanced Robertsonian translocation (chromosomes 14 and 21), and the remainder were due to non-disjunction. Down's syndrome was identified in a further four failed pregnancies in which the fetal karyotypes had been checked. Three of these women were found to have had missed abortions (failure to expel a fetus after its intrauterine death) at 13, 15, and 16 weeks' gestation, and the other had had a spontaneous miscarriage at 15 weeks in a pregnancy conceived with an intrauterine contraceptive device in situ. These four cases have not been included in the analysis below since they could not have resulted in a liveborn affected child.

Table 1 shows the number of babies born each year and the number of invasive procedures performed. From the records available in the regional laboratory, it is not possible to differentiate in all years between inva-

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**Table 1** Numbers of deliveries and pregnancies tested by invasive procedures in Southampton during 1993-8

Year	No of deliveries	No (%) of pregnancies tested by karyotyping
1993	5 547	339 (6.1)
1994	5 361	369 (6.9)
1995	5 198	335 (6.4)
1996	5 030	316 (6.3)
1997	5 098	318 (6.2)
1998	5 025	376 (7.5)
Total	31 259	2053 (6.6)

**Table 2** Age distribution of pregnant women in Southampton during 1996-8

Age (years)	No (%) of women
<20	561 (7)
20-24	1508 (20)
25-29	2648 (34)
30-34	2172 (28)
35-39	703 (9)
40-44	102 (1)
≥45	3 (<1)
Total	7697

sive procedures carried out on local women and those carried out on women referred from outside the district, since only the hospital where amniocentesis was performed is recorded. Thus, for consistency, we show the total number of procedures performed throughout. This overestimates the procedure rate for our local population, making it 6.6% (2053/31 259). Since 1996, all invasive procedures performed in Southampton have been recorded on a local database, so we can accurately exclude women referred from elsewhere during 1996-8. In these three years 791 karyotyping procedures were performed and 15 153 babies were delivered, giving an invasive procedure rate for local women of 5.3%. This is an appropriate rate when the age structure of the local population is considered (table 2): the mean age was 28.4 years, and 10% of women were aged ≥35.

#### Antenatal detection of Down's syndrome

Table 3 shows the number of cases of Down's syndrome diagnosed in each year. The number of cases varied considerably from year to year, and this was accompanied by some fluctuation in the rate of antenatal detection, from 54% at its lowest to 87.5% at best. The overall detection rate during the five years was 68% (95% confidence interval 56% to 80%). This gives a positive predictive value where women accepted an amniocentesis of 1.8%. An alternative method of viewing this is that 1 in 57 amniocenteses resulted in a diagnosis of Down's syndrome.

*Detection in women aged ≥35*—Table 4 shows the detection rate in older women and the indications for performing amniocentesis. Invasive testing would be offered to all older women routinely, but in three women fetal anomalies were noted on scans carried out before 16 weeks, when amniocentesis would usually be performed. These early scans were performed because of uncertain dates in two women and in the third because she had developed abdominal pain three weeks after insertion of a Shirodkar suture. In each of these three cases the fetus was noted to have

a cystic hygroma, accompanied by an abnormal heart in one and by generalised oedema in another.

*Detection in women aged <35*—In younger women the detection rate was 53% (95% confidence interval 30% to 76%), and six of the nine cases detected were found after abnormalities were seen on ultrasound scans (table 4). In four of these six cases the scans were routine mid-pregnancy examinations performed at 18-20 weeks, with nuchal pads or cystic hygromas apparent in three and ascites noted in the fourth fetus. The other two cases were detected on earlier scans: one mother had a history of recurrent miscarriage and so was scanned in the first trimester, revealing generalised fetal oedema at 11 weeks' gestation, and in the second case the fetus was noted to have a cystic hygroma on a scan performed at 13 weeks because of uncertain dates. Among the other cases detected in younger women, one was found when a 34 year old woman organised private serum screening, and another was found when a 32 year old woman arranged a private nuchal translucency measurement. If we assume that these two cases would not have been detected for other reasons, the detection rate in younger women would have been 41% (17% to 65%).

*Undiagnosed cases*—In total, 17 cases of Down's syndrome were not diagnosed antenatally, eight in women aged <35 and nine in older women. Seven of these mothers, six aged ≥35 and one younger woman whose fetus was noted to have bilateral pyelectasis and polyhydramnios, had been offered invasive testing but had declined. One of these mothers had privately arranged for nuchal translucency scanning and had received a reassuring result: when the mid-pregnancy anomaly scan suggested the fetal femur was short and the woman was offered amniocentesis for a second time, she again declined. We cannot tell retrospectively whether these mothers declined amniocentesis for fear of miscarriage or for ethical reasons, because they would not have considered termination of pregnancy and would never have accepted an antenatal test. Three of the undiagnosed cases of Down's syndrome occurred in twin pregnancies with a single affected fetus, where serum screening is ineffective: one occurred in a woman aged 33, the second in a woman who required clomiphene to conceive and was just aged 35 at delivery but not offered amniocentesis, and the third in a 41 year old woman who was offered amniocentesis but declined.

In those women in whom Down's syndrome was detected antenatally the mean gestation at diagnosis was 17 completed weeks (range 11-20). We routinely perform amniocenteses for women aged ≥35 at 16 weeks' gestation, and the Wessex Regional Genetics Laboratory reports on these samples in an average of seven days, with the great majority reported within 10 days. The gestation at diagnosis was considered to be the time when the information on which the decision about continuation of the pregnancy was based became available. This was usually when the karyotype result was known, but in two cases the mothers decided on termination on the basis of scan anomalies without waiting for the chromosome analysis.

#### Discussion

In the studies of serum screening it has been assumed, but not shown, that the detection rate for Down's syndrome using screening based on maternal age

would be no higher than 30%. In our population we have shown a much higher detection rate, which results from two factors. The first is the routine use of ultrasound scanning to identify anomalies. This is performed in most units in Britain and was largely responsible for the detection of affected fetuses in women aged less than 35 years. The second is the age structure of the local population, which may have an important influence on the effectiveness of screening by both age and biochemistry. The risk of having an affected pregnancy increases steeply as the mother's age rises above 35 years, so a small increase in the proportion of women over this age produces a disproportionate increase in the percentage of affected pregnancies that occur in the older age group. This was illustrated by a study examining the effects of changing age demographics of women in the United States on the incidence of Down's syndrome.<sup>25</sup> In 1960, when almost 11% of births were to women aged over 35 years, 44% of affected pregnancies occurred in this age group, but by 1978 the proportion of older women fell to only 4.5%, and only 21% of cases of Down's syndrome were born to them. In our study 10% of the women were more than 35 years old, and 66% of the cases of Down's syndrome occurred in this group, and this contributed to the high detection rate. Serum screening may provide more benefit in populations with a younger age structure, but this needs to be demonstrated in practice since its effectiveness is also reduced in younger women.

#### Implications for serum screening

Our findings suggest that the advantages of serum screening are much less in current practice than were suggested in the demonstration projects<sup>1-6</sup> used in the report by the Royal College of Obstetricians and Gynaecologists.<sup>3</sup> Firstly, our detection rate using maternal age and ultrasound scanning is within the range shown by demonstration projects of serum screening. A similar study of the detection of Down's syndrome by maternal age and ultrasonography carried out in Isère county in France showed a detection rate for Down's syndrome of 51%: amniocentesis was offered routinely to women aged over 38, with 46% of those cases found antenatally being detected as a result of ultrasound anomalies.<sup>26</sup> The proportion detected by ultrasonography increased during the study period between 1990 and 1995 from 17% to 58%.<sup>26</sup>

Secondly, the advantage of biochemical screening at detecting Down's syndrome in women under the age of 35 was also lower than supposed. In our population the detection rate in younger women was 53% (or 41% if the cases detected as a result of privately arranged serum or nuchal translucency screening are excluded) with most cases found as a result of ultrasound anomalies. The detection rate was lower than in older women, but this is also true for biochemical screening: in women younger than 35 the detection rate by serum screening ranged between 50%<sup>6</sup> and 57%<sup>12</sup> compared with 100% in older women,<sup>6</sup> while the relative detection rates were 39% and 71% in those below or above 37 years old.<sup>1</sup>

A third proposed advantage of serum screening, that it may allow women over the age of 35 to avoid unnecessary invasive testing, may also be overstated. Our findings and those of others<sup>27</sup> suggest that a normal mid-trimester ultrasound scan reduces the prior risk by a third to a half, and this provides an alter-

**Table 3** Number of cases of Down's syndrome detected in ongoing pregnancies or in newborn infants in Southampton during 1993-8

Year	No (%) of cases		
	Diagnosed antenatally	Diagnosed postnatally	Total
1993	2 (67)	1 (33)	3
1994	7 (54)	6 (46)	13
1995	7 (64)	4 (36)	11
1996	7 (88)	1 (13)	8
1997	5 (83)	1 (17)	6
1998	8 (67)	4 (33)	12
Total	36 (68)	17 (32)	53

**Table 4** Detection rate of Down's syndrome and indication for invasive testing in women above and below the age of 35 in Southampton during 1993-8

Diagnosis and indication for testing	No (%) of cases		
	Women aged <35 years (n=17)	Women aged ≥35 years (n=36)	All women (n=53)
Not diagnosed	8 (47)	9 (25)	17 (32)
Diagnosed:	9 (53)	27 (75)	36 (68)
Ultrasound anomaly	6 (35)	3 (8)	9 (17)
Previous history	1 (6)	2 (6)	3 (6)
Nuchal translucency	1 (6)	0	1 (2)
Serum screening anomaly	1 (6)	0	1 (2)
Maternal age	0	22 (61)	22 (42)

native mechanism to offer reassurance. We are not aware of any studies that have investigated whether ultrasonography or biochemical screening is more effective at such risk adjustment.

The economic arguments for serum screening are valid only if it provides a large increase in the detection rate of Down's syndrome. The Royal College of Obstetricians and Gynaecologists' report suggested that it would be cost effective at detection rates above 40%. The costs of serum screening were examined by Sheldon and Simpson in 1991.<sup>28</sup> They assumed that 80% of women would accept screening and that 75% of those with a positive result would accept amniocentesis, but their calculations did not allow for any additional time spent counselling women about the test.<sup>29</sup> They calculated that, at prevailing prices, the average cost of avoiding each birth of an infant with Down's syndrome was £29 341, whereas the excess cost for caring for an affected child was £90 000. However, if the improvement in the detection of Down's syndrome is small, the marginal cost for each additional affected fetus identified is considerably higher than the average cost per case,<sup>30</sup> and the economic arguments for biochemical screening are invalidated.

The demonstration projects of serum screening have made little mention of the potential disadvantages. One of the greatest problems is with counselling before the test. Health professionals involved in advising women may have limited understanding of the test themselves<sup>31</sup> or feel that they have inadequate facilities to offer full information.<sup>2</sup> Thus, despite clearly defined standards about counselling for serum screening,<sup>3</sup> many women do not understand the test properly before undergoing it: in one study, even after counselling, only 38% of women were aware that the test screened for Down's syndrome, only 32% were aware that most women with a positive result would have a normal child, and only 36% understood that a negative result did not completely exclude aneuploidy.<sup>32</sup> Furthermore, some women whose screening tests were



## Key messages

- Serum screening for Down's syndrome has never been compared with screening by maternal age in a controlled trial
- This study examined the effectiveness of screening by maternal age in combination with mid-trimester ultrasound scanning
- The overall detection rate was 68%, considerably more effective than assumed in demonstration projects of serum screening
- The benefits of serum screening, compared with screening by maternal age in conjunction with routine fetal anomaly scanning, may be much less than supposed
- A higher standard of evidence should be demanded before proposed new screening methods are adopted

positive felt that their local units were unprepared for dealing with such results.<sup>33</sup>

## Conclusions

Our data challenge the assumptions about screening for Down's syndrome based on maternal age that underpinned the introduction of second trimester serum screening. We cannot discount the possibility that the addition of serum screening in our population would raise our detection rate further, but this could only be tested by a properly controlled trial, and the Wessex Antenatally Detected Anomalies Register shows no evidence of higher detection rates of Down's syndrome in districts in Wessex that use serum screening compared with those that do not.<sup>34</sup> The need for such a trial was pointed out as long ago as 1991,<sup>28</sup> but serum screening is now so firmly established in clinical practice that it is unlikely that it will ever be tested properly. We urge that before other new screening methods are introduced—such as first trimester,<sup>35</sup> improved second trimester serum screening, or nuchal translucency measurement<sup>36</sup>—clear evidence be obtained of their effectiveness compared with current practice in properly conducted controlled trials that state the age structure of the populations studied.

**Contributors:** The paper was conceived and produced as a collaboration between the departments of fetal medicine and clinical genetics in Southampton and cytogenetics in Salisbury. Data for analysis was taken from the regional congenital anomaly database maintained by DW and from laboratory records obtained by JB and TB, who also performed the cytogenetic analyses. DTH and RG performed most of the analyses of clinical data. All authors contributed to the final version of the paper. DTH is guarantor for the paper.

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