SHORT REPORT

Diagnosis of Down's syndrome in neonates

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Arch Dis Child Fetal Neonatal Ed 2002;**87**:F220–F221

The results of karyotyping for Down's syndrome in neonates were surveyed. From local data 36%, and from a national questionnaire, 32% of such samples were negative for Down's syndrome. To examine this, a subset of notes was reviewed for documentation of clinical signs of Down's syndrome. Some characteristics were often recorded, but other common discriminatory characteristics were noted less often or not at all.

The clinical diagnosis of Down's syndrome in the neonatal period has been described as "seldom a problem to the neonatologist",[1] but the variable nature of the presenting features is such that the diagnosis can be uncertain.[2] When the diagnosis is suspected, it is good practice to inform the parents and await confirmation of the karyotype, which can take two or three days. This wait for confirmation of a life changing diagnosis is one of great anxiety for parents. Maximising clinical diagnostic accuracy is therefore important, and several studies documenting the most characteristic physical features including diagnostic indices have been published, but only two of these have looked specifically at the diagnosis of Down's syndrome in the newborn.[3 4]

The purpose of this study was to survey the results of karyotyping for Down's syndrome in neonates locally and nationally, and to investigate which criteria are being used to reach a diagnostic suspicion of Down's syndrome.

METHOD

Two cytogenetic laboratories in Greater Manchester (Royal Manchester Children's Hospital and St Mary's Hospital) performed database searches to identify all samples of babies aged 0–4 weeks analysed for a diagnostic query of Down's syndrome for the period 1 January 1999 to 30 December 2000. These laboratories process samples from several paediatric departments in Greater Manchester and North West England. These data were then used to determine those infants with karyotypes not compatible with Down's syndrome (Down's syndrome negative, DSN) and those who had a karyotype consistent with Down's syndrome (Down's syndrome positive, DSP).

A questionnaire was then sent to 25 other cytogenetic laboratories in the United Kingdom asking for information about the number of requests processed in the last two years for a clinical suspicion of Down's syndrome in the neonatal period and the number of those requests proving positive or negative.

Two equal groups of notes for DSP and DSN babies identified from the Manchester data were then analysed for recording of 29 dermatoglyphic, physical, and clinical traits. It was also noted whether parents had been informed of the suspicion of Down's syndrome before samples were sent for karyotyping and whether reference was made in the notes of a diagnostic index being used.

RESULTS

The two Manchester centres processed 174 cases that met the above criteria. These requests were received from 27 hospitals. Of these, 109 were DSP and 63 were DSN. Thus 36% of the cases referred for cytogenetic testing were not Down's syndrome.

The questionnaire was sent to 25 other regional centres in Britain and Ireland. Completed questionnaires were received from 17 (68% response rate). In two years, these 17 centres had processed 962 requests for a diagnostic query of Down's syndrome, of which 307 (32%) were negative and 655 (68%) were positive for Down's syndrome. For the 12 centres that process more than 10 such requests a year, the proportion found to be DSN ranged from 19% to 44% (median 32.25%).

A total of 36 DSP and 36 DSN case notes were reviewed from the Manchester data. All 36 of the DSP babies had trisomy 21. In 35 of the DSN cases, the karyotype was normal, and one was 49 XXXXY. In none of the reviewed cases had an antenatal diagnosis of Down's syndrome been made. Parents were informed of the clinical suspicion of Down's syndrome and the need for karyotype testing in 71/72 cases reviewed.

Of the 29 factors included on the proforma, five are routinely available from a standard newborn examination (maternal age, birth weight, presence or absence of jaundice, admission to special care, feeding difficulties), and were documented for all 72 babies. The head circumference was noted in 57 (79%) and supine length in 36 (50%) of the 72 babies.

With regard to physical characteristics other than routinely gathered information, the presence or absence of hypotonia and slanting palpebral fissures was recorded in all 72 cases, and of a simian palmar crease in 71/72. Other commonly recorded criteria were the presence or absence of low set ears in 89% of the 72 babies, a wide gap between 1st and 2nd toes in 80%, and a flat nasal bridge in 57%. Reference was made less often to the presence or absence of a prominent neck fat pad (47%), brachycephaly (29%), Brushfield spots (25%), or a protruding tongue (24%). The least commonly noted criteria were internipple distance/chest circumference ratio and short, broad hands, which were recorded in four (6%) and six (8%) patients respectively. Nine factors were not documented at all in any of the cases. Eight of these nine were dermatoglyphic traits, and the other was ear length. No sets of notes examined recorded evidence that a diagnostic index had been used.

DISCUSSION

Midwifery staff usually express the initial concern that a baby has Down's syndrome. Clinical examination can often confirm or refute this with confidence. If there are no clinical grounds for making the diagnosis, the parents can reasonably be kept unaware of the initial suspicion; this study has not been able to determine how often, if ever, this situation arises. When the diagnosis is considered possible, the threshold for performing karyotype testing and informing the parents is reached. Our results suggest that, where this threshold is reached, there is about a two thirds chance of the baby having Down's

Abbreviations: DSN, Down's syndrome negative; DSP, Down's syndrome positive

Table 1 Frequency of recording of Fried's[3] most discriminatory characteristics in current study notes review

Characteristic	Percentage recorded in current study (n=72)	Most discriminatory characteristic 1–8 (Fried[3])
Excess neck skin	47	1
Mouth corners turned down	0	2
Hypotonia	100	3
Flat face	57	4
Dysplastic ear	89	5
Epicanthic fold	Data not collected	6
Gap 1st/2nd toes	80	7
Protruding tongue	24	8

Table 2 Fried's diagnostic index[3]

Number of characteristics	0–2	3–5	6–8
Conclusion	DSN	Unclear	DSP
Error	No false –ves (<1/100 DSP babies)		No false +ves (<1/100000 DSN babies)

DSN, Down's syndrome negative; DSP, Down's syndrome positive.

syndrome. Part of the reason for this high DSN rate may be that some samples are sent after delivery to allay parental anxiety following antenatal serum screening results in the absence of significant dysmorphism (10/41 DSN cases from one centre, although this reason was not apparent in the 72 sets of notes we reviewed locally).

We found no recent studies detailing the clinical diagnostic accuracy of Down's syndrome in the newborn. Fried,[3] using a diagnostic index, was able to accurately identify the diagnosis on clinical grounds for 22 of 30 (73%) newborn babies suspected of having Down's syndrome. This value is by no means directly comparable with the results of our study because the Fried study used a prescribed set of physical characteristics in babies examined prospectively by a single interested clinician. Our study reflects a current working view of the issue, with data coming from a broad cohort of paediatricians.

The retrospective study of notes has limitations because what is recorded may not accurately reflect how decisions were reached. Nevertheless, the review indicates that diagnostic indices do not appear to have been adopted. Also it appears that many important traits are not often recorded as contributing to a diagnostic decision, whereas well known but relatively poorly discriminating characteristics commonly figure. Of the three physical features most often recorded in the notes review—that is, hypotonia, slanting palpebral fissures, and Simian crease—the latter two are relatively non-specific. Excess neck fat pad, an easily noted and more specific feature, was recorded much less often, as were other important signs (table 1). Other less well known but useful diagnostic features such as dermatoglyphics, ear length, the pursed eyelids, and vertical wrinkling sign,[5] and the Smithells hypotonia test[6] were not recorded.

There have been, to our knowledge, no studies looking at the effects of a false positive diagnosis of Down's syndrome on parents, but common sense suggests that such a suspected diagnosis should be discussed on as informed a basis as possible. (One of the authors has direct experience of such a scenario where the parents still felt resentful one year later about the false diagnosis and did feel that it had marred their early enjoyment of their newborn daughter.) A targeted and systematic examination of the baby using simply observed external physical characteristics (table 2) may allow a more informed discussion to take place with parents, including a more accurate weighting of the likelihood or otherwise of a positive diagnosis.

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Accepted 12 April 2002

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