Newborn screening for DMD

195th ENMC workshop, December 14-16 Netherlands

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Duchenne Parent Project NL

United Parent Projects MD

21 participants

neuropediatrics, neurology, genetics, biochemistry, psychology, ethics, sociology, parent representatives

7 countries

UK, Netherlands, Germany, Italy, Canada, USA, Australia

DMD NBS was last discussed at the 14th ENMC workshop in 1992, justification to screen for DMD ‘is to provide optimal and specific information to the parents in time, so they can make the decisions which are the most appropriate for their family’.

Ommen G.J.B., Scheuerbrandt G.: Workshop Report, Neonatal screening for muscular dystrophy. Consensus recommendation of the 14th workshop sponsored by the European Neuromuscular Center (ENMC), Journal Neuromuscular Disorders, 1993, 3: 231--239

NBS programs

At least 17 pilot programs

Breitnau - Dr Gunther Scheuerbrandt 1974-2011

Wales (UK) 1990-2011

Manitoba (CA) 1986-2007

Ohio (USA)

Technique used

Serum Creatine Kinase (CK)

Treshold 600-750 U/L

Bloodspot collected as part of the heel prick test taken shortly after birth

Ideal test

High sensitivity and specifity

Unequivocal predictive value

Low false positive or negative rate

New programs

Australia 2013
In Sydney instead of Perth
Difference in the implementation of W and J criteria

Recently Taiwan

Soon Yucatan Mexico

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Wilson and Jungner criteria

1962

Criteria adult screening

Not created for children nor rare diseases

Wilson and Jungner

Wilson and Jungner attempted to define screening criteria to guide the selection of conditions that would be suitable for screening, based, among other factors, on the capacity to detect the condition at an early stage and the **availability of an acceptable treatment**

Wilson and Jungner

The original Wilson and Jungner criteria for mandatory, state funded screenings acknowledged that '**there should be a recognisable latent or early symptomatic stage**'

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DMD

Perception there is an associated long pre-symptomatic or ‘carefree’ period, because affected children are frequently not seen by a health care professional until they are at least 2 years old.

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DMD

Reality it is only the first few months following birth, that a true pre-symptomatic period exists.

Pane et al 2013 report that in 45% of boys with a mean age of 27 months were found to have a suboptimal developmental quotient, with the motor function and speech and language domain more frequently affected after the age of one year, compared to their peers.

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Eurordiscare survey

PARTICIPANTS IN THE SURVEY

Responses from 913 families of DMD patients from 13 countries were analysed

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Eurordiscare survey

Due to the age of onset of the disease, neonatal diagnoses were rare (5.2%)

Resulting from other cases in the family in 50% cases, but also from neonatal testing (one in three).

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Eurordiscare survey

During the quest for diagnosis, 88% of families consulted one to five physicians, and 10% of families consulted six to ten physicians.

A significant number of various examinations and tests (biological testing, 76%; genetic testing, 39%; X-rays, 22%; and functional testing, 40%) were then performed.

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Eurordiscare survey

Inappropriate treatments resulting from misdiagnoses occurred in 54% of patients (medical, 12%; surgical, 5%; or psychiatric, 10%).

For 55% of the families, a delay in diagnosis was considered responsible for deleterious consequences.

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Eurordiscare survey

The more frequent consequences included maladapted family behaviour (18%) (e.g. complaint or punishment for a boy ‘medically diagnosed’ as lazy) and a lack of confidence in medicine.

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Eurordiscare survey

When provided, the sources were

medical in 66% of cases, but also patient organisations 20% of the time.

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Eurordiscare survey

Psychological support accompanied 32% of the announcements of the diagnosis and was provided by a psychologist (9%), another health professional (12%) or a patient organisation member (6%).

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Eurordiscare survey

Neonatal diagnosis is possible, simple and inexpensive and can prevent the consequences of a delayed diagnosis.

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Am J Med Genet A. 2003 Jul 15;120A(2):209-14.
Parental attitudes regarding newborn screening of PKU and DMD.
Campbell F Ross LF

Citing a variety of psychosocial concerns, respondents believe that parents should have access to predictive genetic testing for childhood onset conditions, even when there are no proven treatments. Respondents want this information to make reproductive and non-reproductive plans and decisions. Although respondents varied in their personal interest in testing, **overwhelmingly they believed that the decisions belong to the parents**. Professional guidelines that proscribe predictive testing for untreatable childhood onset conditions should be re-examined in light of consumer attitudes.

Neonatal screening for treatable and untreatable disorders: prospective parents' opinions.

Plass AM, van El CG, Cornel MC

Pediatrics. 2010 Jan;125(1):e99-106. doi: 10.1542/peds.2009-0269. Epub 2009 Dec 21.

Prospective parents in the Dutch population seem interested in newborn screening for untreatable childhood-onset disorders; therefore, we argue that additional debate of pros and cons is needed among policy makers, health care professionals, and consumers

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Valueing the Carefree Period Retrospectively

"It was of course a somewhat more carefree period...That's the only positive thing about not knowing it ..".

"But we never had a true carefree period"

"I would not have been so hard on him when he was three years old, saying 'we are not going to carry you.' I would have treated him more caution. You really feel guilty afterwards,.."

"Well, there has been a period that the physiotherapist was busy doing the wrong things. Therefore, it would be better knowing this earlier"

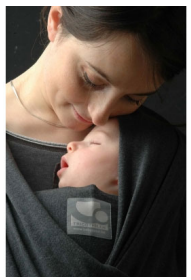
Good Parenting vs Carefree Period

A true carefree period does not exist.

Early diagnosis would have enabled parents to treat their child in the best possible way, adjusted to their child's condition: '**good parenting**'.

This emerging need for '**good parenting**', parents expressed, by far outweighed the possibility of enjoying a carefree period in the child.






Quantitatively assessing the Carefree Period and Good Parenting

The argument of 'good parenting' regarding early diagnosis parents mentioned cannot be found in literature

How do other, and larger groups of parents feel about this?

- Other and more parents of children with DMD
- Parents of children that did not suffer from any developmental backlog during the first year
- Parents of a child affected with another heriditary x-linked early onset childhood disorder: the Fragile X syndrome (FXS)

Online Questionnaire

Asking all parents the same questions about:

The desireability of early diagnosis of childhood onset disorders: i.e. DMD & FXS, for which a treatment that prevents irreversible damage in the child does not exist yet

The (developmental) worries they had during the first year of life of their child

Good parenthood

Parents in favour of DMD and FXS NBS

Nearly 1,000 parents filled out the online questionnaire (77 DMD parents and 107 FXS)

Respondents were very positive about testing newborns in the newborn screening program for both DMD and FXS.

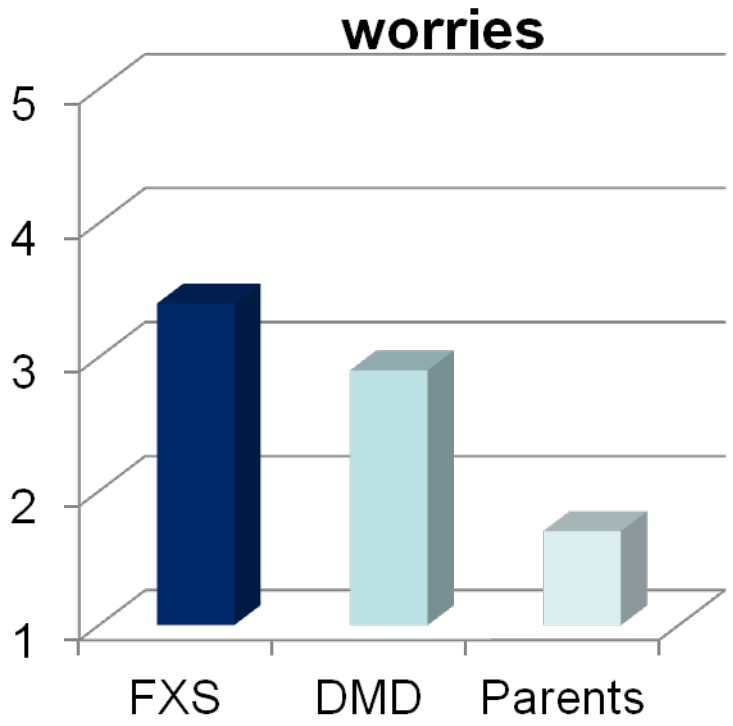
There was no difference between the DMD parents, the FXS parents and the general parent group

Parents favoured newborn screening as best timing for testing

Carefree period

- DMD-parents had significantly had more worries about the child's development during the first year compared to the general population.
- FXS parents worried the most

- Good parenting by far overweighed enjoying a carefree period



Good Parenting needs attention

It is essential for (all) parents to be able to take the best possible care for their child (good parenting)

Early diagnosis can effectuate this

The argument of the need for good parenting needs to be highlighted

In Conclusion

A true carefree period does not exist

All parents are in favour of addition of childhood onset untreatable disorders to NBS, despite the health status (healthy, DMD, FXS) of their child

From the perspective of the parent's early diagnosis adds to being able giving the best possible care




Pediatricians' attitudes toward expanding newborn screening.

Pediatrics Oct 2005

Willingness to expand newborn screening does not correlate with professional characteristics but rather with personal interest in testing of their own children.

Be a better parent!

99% of DMD care is done by parents

Time for adjustment

School, building - learning difficulties

Housing

Support and understanding

Not blaming him for things he cannot do

Preventing from bad falls

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What are the arguments of DMD parents?

Be a better parent for your child

The alternative is a long diagnostic delay 2,5 yr

There is no good moment for such diagnosis

Family planning

New treatments in the pipeline

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Access to treatments

Catch 22: Young children not diagnosed, no natural history data of young children, no access to trials, no market approval for this group, no access to new drugs.

Setting up NBS when drugs are on the market, will skip a large cohort of children from opportunities

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New treatment option in the pipeline

‘In the past, the only real benefit of early screening for DMD would have been in preparing parents for the hardships that lay ahead. Now, the potential benefits include being able to take part in clinical trials, which may delay the onset of the disease before obvious symptoms arise, and in doing so, help the child live a healthier and longer life. If you don't know your child is affected, that opportunity will be lost, because most of the treatments being trialed are unlikely to help replace muscle that has already wasted away.’

Klair Bayley *is a research student at the University of Western Australia, mother of a child with DMD, and hospital clinical manager.*

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Conclusions

Yes : NBS for DMD is a good thing.

Good parenting being one of the reasons.

Avoiding diagnostic odyssee

Early detection allows for early intervention.

Treatment in the pipeline, need for natural history

No delay in access when treatments are available

Under which conditions?

Reliable test (low false pos/neg rate)

A rigorous consent process will be necessary to ensure that the decision whether or not to test is a voluntary and informed choice.

Good support and coaching of parents after the diagnosis

Competent psychologists with knowledge of genetic diseases with serious prognoses should systematically propose psychological support.

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Reliable test

Two–tiered CK/DNA NBS test for DMD NBS should be developed for use by other screening centres.

(Jerry Mendell Ohio)

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When?

Birth?

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1 year?

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We need

More data on interventions at an early age

For example effect of Steroid treament, physiotherapy, learning etc.