

Paediatric muscle disease- moving into adulthood



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The "paediatric" NMD diseases

- Duchenne muscular dystrophy (2-40 years)
- SMA type 1/2 (1-52 years)
- Congenital muscular dystrophy (3-33 years)
 - The management strategies which have made this difference
 - The challenges for the future

Current Paediatrics 2005

Vol 15, 292-300 Bushby et al

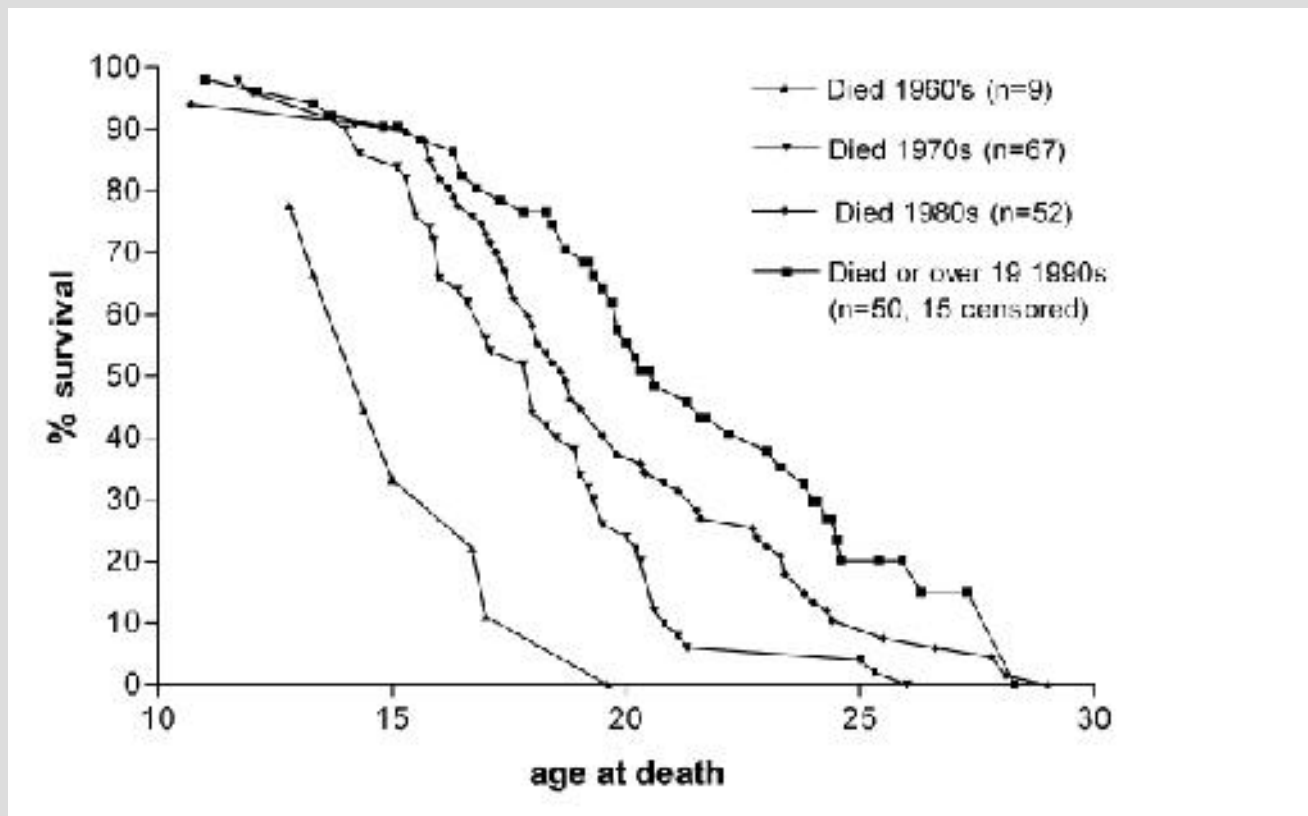
- Multidisciplinary management of DMD allows treatment of complications
- Steroid treatment prolongs ambulation, reduces scoliosis and improves respiratory and possibly cardiac function
- Cardiac surveillance and treatment is likely to have major benefits
- Respiratory support is proven to improve life expectancy with maintenance of a good quality of life
- Spinal surgery for scoliosis can also enhance life expectancy and quality of life
- A nihilistic attitude to the disease is no longer tenable

What has made the difference?

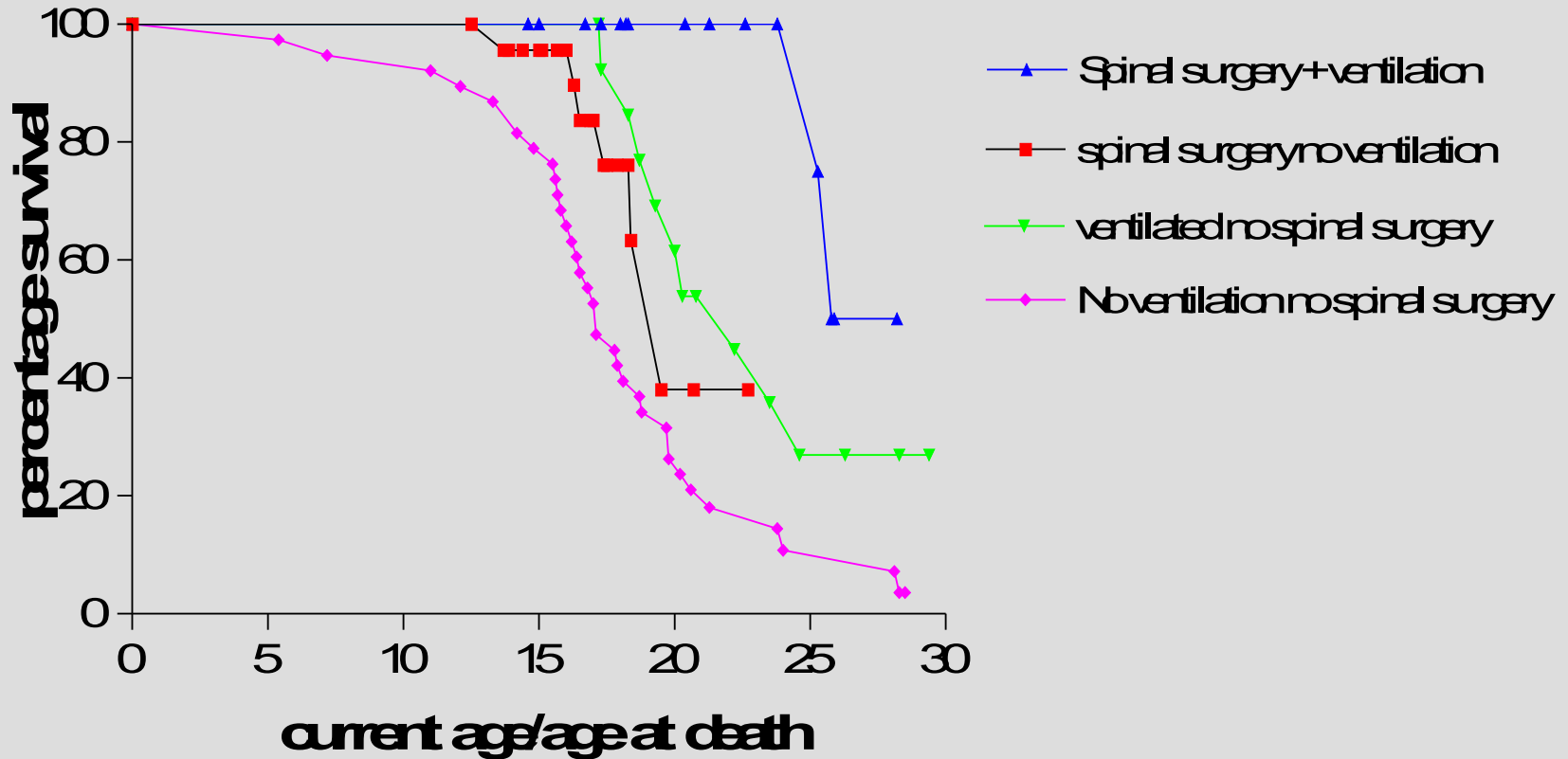
- DMD and survival (M Eagle)
- Studied the notes of 197 boys with DMD looked after in Newcastle since 1967
- Mean age at death in 1960s was 14 years
- 1970s, 80s and 90s it was 19 years

SPECIALIST CARE +5 YEARS

Better co-ordinated care probably led to improved survival across decades, but without treatment of respiratory failure survival beyond 25 is unlikely



Analysis of the impact of spinal surgery and ventilation in patients born since 1970



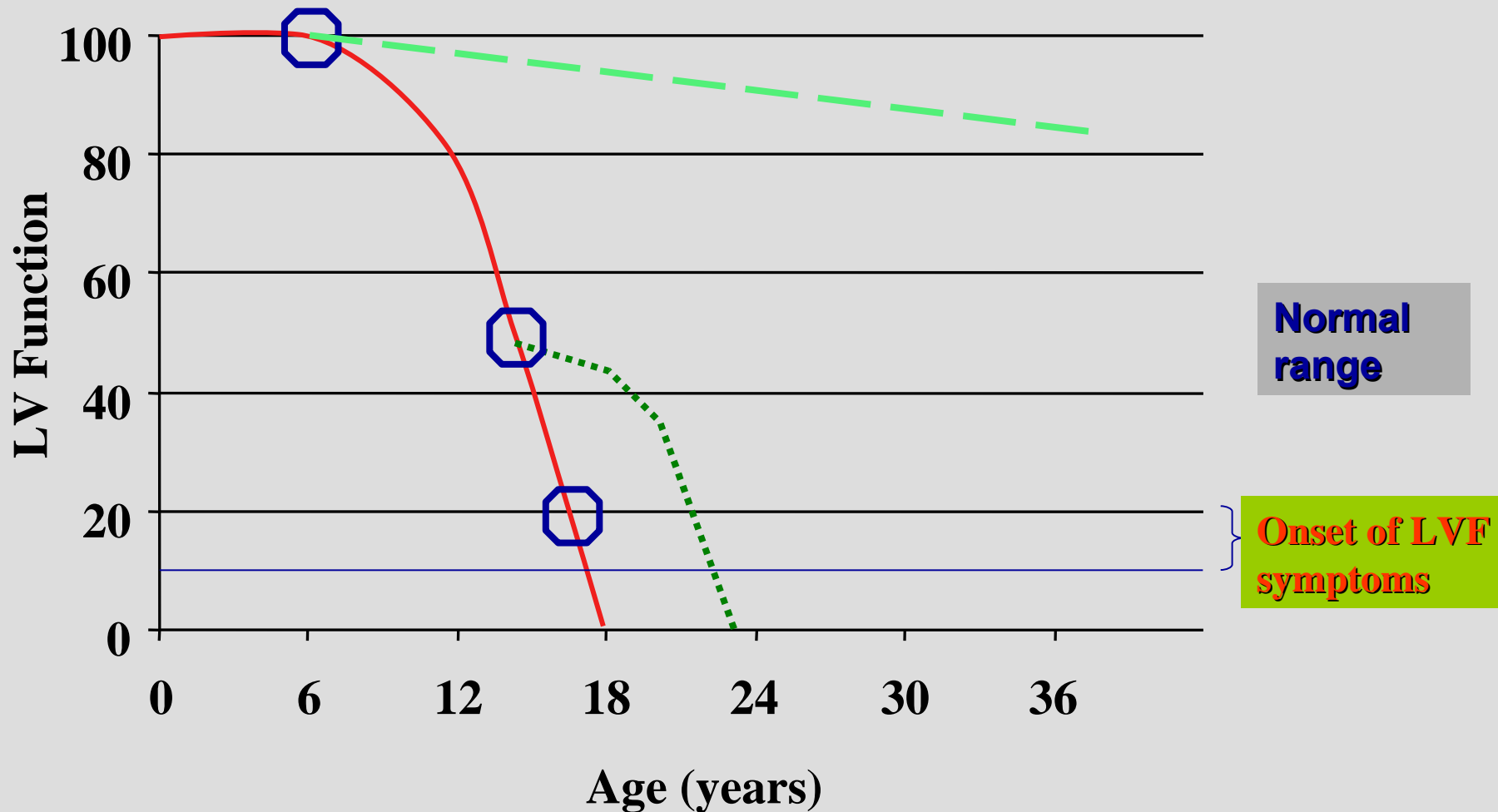
HOME NIV AND SS + 9 YEARS

Respiratory management: prevention, surveillance and treatment (Finder et al 2004)

- “Although respiratory disease in DMD is a major problem there is inadequate awareness of its *treatable* nature”
 - ATS guidelines
- Prevention: flu immunisation, chest physio, assisted insufflation
- Surveillance: forced vital capacity, overnight home oximetry
- Treatment: prompt treatment of infections, nocturnal ventilation

Cardiac involvement in DMD / BMD

What is the real goal of intervention?



Cardiology

- ENMC guidelines on cardiac follow up
 - Echo and ECG annually at least from age 10
 - Early intervention (ACE inhibition, beta blockers)
 - Rationale: improve systolic, diastolic function, myocardial oxygen balance, anti arrhythmic and reduce adrenergic stimulus especially as respiratory insufficiency is a further drive to myocardial stress
- Duboc, Towbin studies support importance of prophylactic intervention
- When to start?- UK heart protection study
- Alternative interventions- Santhera study

Treatment modalities in a complex disease are additive

- Specialist care + 5 years
- Home nocturnal ventilation + 7 years(+)
- HNV plus spinal surgery + 9 years
- Management of cardiac failure
- Long term steroid treatment
- Still progress to be made: dissemination, improved tools, regimes for managing complications

Future therapies are also likely to be additive

- Read-through of stop mutations.
- Increasing muscle bulk
- Viral vector delivery of dystrophin cDNA
- Cell transplantation
- Upregulation of utrophin
- Modification of the mutated mRNA

As our paediatric DMD patients approach adulthood....

- The majority are on non-invasive nocturnal ventilation (mean age 17 years)
- The majority are on ACE inhibition and beta blockade
- Most have had scoliosis surgery
- Most are still at home with no plans for tertiary education or employment

Transition

- The medical context
 - The planned movement from child centred to adult centred care
 - Complexity of relationships
 - The paediatric vs adult care approach
- The social context
 - Moving from dependency to independence and autonomy



The Newcastle Muscle Centre Model

- Single team for NMD from childhood to adulthood
- Multidisciplinary input from cardiology, respiratory support, orthopaedics etc
- Central transition issues can be addressed smoothly with a team the young person knows and trusts
- Community issues are still highly variable



The continuing challenges for adult patients with DMD

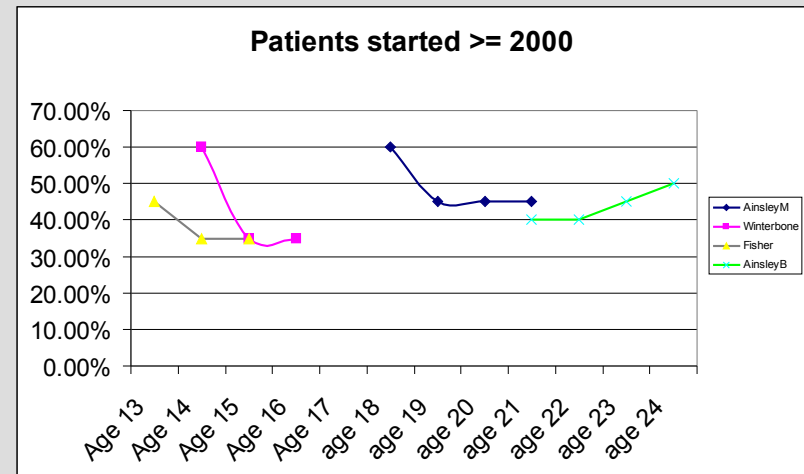
- Medical care
 - Ventilation- may use GPB/ some increasing requirement with age
 - The role of steroids
 - Cardiac support- risk of arrhythmia?
 - Nutrition- ng tube/ gastrostomy?
 - GI and GU
 - Osteoporosis
 - Weakness/ contractures (upper limb function)
- End of life issues
 - Cause of death?
 - High risk group

Continuing medical care

- Ventilation/ respiratory support
 - Trend to increasing requirement with age
 - May adopt glossopharyngeal breathing
 - Need to move from mask to tracheostomy ventilation?
 - Continued need for vigilance with chest infections, cough assist etc
 - The role of steroids?

Continuing medical care

- Cardiology
 - "uncharted waters"
 - How long can stabilisation of cardiac function be maintained?
 - What is the risk of ventricular arrhythmias?
 - High risk with even mildly invasive procedures

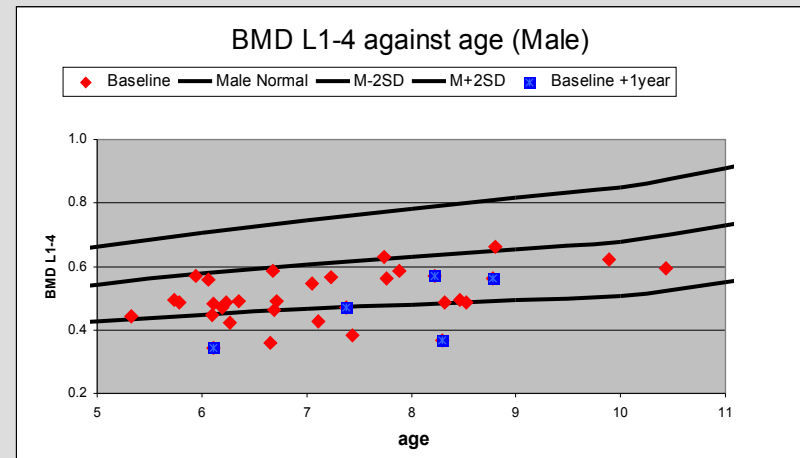


Continuing medical care

- GI and GU problems
 - Feeding difficulties, gastrostomy
 - Reflux, oesophagitis (proton pump inhibitors)
 - Constipation (diet, hydration, senna, docusate)
 - Urinary retention/ incontinence (assessment, anticholinergics, physical help)

Continuing medical care

- Bones, mobility, joints
 - Osteoporosis
 - Continued need for physio, postural support
 - Maintenance of function
 - Addressing new contractures (neck)
 - Late complications of scoliosis/ surgery



End of life issues

- Need to address with sensitivity and care
 - Family issues
- Cause and timing of death difficult to predict

Adults with DMD- the social context

- Major period of readjustment for today's parents
 - "the goalposts have moved"
 - Schools and social services not geared towards adult life
 - Uniform agreement in QOL studies that patients are positive and do not regard themselves as "ill"
 - Family and technology are major determinants of wellbeing
 - Families may be dissatisfied with lack of social opportunities

Ensuring more consensus in the future for uptake of therapies

- Define the pathway from lab to clinic
- Identification of promising therapies
- Assessment of models and patients
- Registries, databases, standards of care
- Clinical trials support
- Information, education, communication



Partners: clinical centres, researchers, industry, patient organisations