Steroids-
Speaking the same language

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What are corticosteroids?

- Synthetic relatives of naturally occurring hormones
- Show complex effects which are anti-inflammatory and influence the immune response
  - Inhibit migration of inflammatory cells
  - Suppress production/release of other inflammatory factors
Effects relating to hormonal role

• **Mineralocorticoid**  
  - Hypertension, fluid retention (minimal with glucocorticoids)

• **Glucocorticoid**  
  - Diabetes, osteoporosis, change in behaviour, growth suppression, Cushingoid appearance

• **Glucocorticoids are used in DMD**  
  (prednisolone, prednisone, deflazacort)
Steroids are widely used in medicine

- Rheumatoid arthritis
  - Many other rheumatological conditions
- Asthma
  - Chronic obstructive airways disease
- Following organ transplantation
  - Etc
- Trials in DMD have consistently shown an increase in strength
How do steroids work in DMD?

- Many suggested mechanisms of action
  - Positive effect on muscle development
  - Anabolic effect on muscle mass
  - Stabilisation of muscle membrane
  - Reduction in muscle necrosis
  - Effect on intracellular calcium concentrations
  - Immunosuppressive effect, though other immunosuppressive drugs do not seem to be beneficial
Different regimes

• Hypothesis
  - Reducing the steroid dose should reduce the incidence of side effects
  - Reduced by having lower total dose
  - Or allowing steroid “holidays”
  - While allowing reasonable efficacy
Alternative regimes

• No steroids at all
• Alternate days
• Low dose daily
• 10 days on/ 10 days off
• 10 days on/ 20 days off
• Weekend only high dose
• Weekend only low dose
• .........................
No randomised controlled trials completed to date have tested alternative regimes against daily steroids.

So there are no data on the relative risks/benefits.....
Time to start speaking the same language

- Cochrane review of steroids (Manzur et al)
- International US/ENMC meeting April 2004
  - Daily corticosteroids do improve strength and functional outcomes (deflazacort and prednisolone)
  - Evidence from randomised controlled trials and cohort studies of significant long term benefits
Long term prednisolone

- Starting dose of 0.75mg/kg/day
- In longer term “natural attrition” to ~0.5mg/kg/day
- Prolonged ambulation to mean of 14.5 years
- Reduced need for scoliosis surgery
- FVC extraordinarily improved
Long term deflazacort

- 0.9mg/kg/day as starting dose
- ~0.7mg/kg/day with time
- Ambulation to mid teens
- Scoliosis surgery reduced from 90-10%
- FVC preserved to 80%
- Protection versus cardiomyopathy (preliminary data)
Long term side effects

- Weight gain (probably less with deflazacort)
- Growth suppression (benefit?)
- Pubertal delay (reversible with testosterone)
- Cataracts (deflazacort > prednisolone)
- Vertebral fractures
Consensus

- Use of corticosteroids is in the mainstream of treatment for DMD
- Any other treatments would need to be tested against this gold standard
- Corticosteroids are likely to be a part of the treatment of DMD for many years to come
- Long term trials of different regimes are needed but should not delay treatment
Information

• For families and medical practitioners
• Q and As to be made internationally referable and accessible
• Further information to be generated and disseminated through family organisations
• Information to be gathered from regimes already used
  - standardisation of data collection, best practice monitoring of efficacy
frequency of jumping ability
pre and post steroids

% frequency of jumping ability
pre and post steroid use
Best practise monitoring

• Side effect monitoring and prophylaxis need to go hand in hand
  - Weight, height
  - Blood pressure
  - Urinalysis
  - Osteoporosis
  - Cataracts
weight gain before and after strict dietary advice prior to starting steroids

weight gain over time starting steroids between Sept 02 and March 03 (n=20)

weight gain over time starting steroids between April 03 and April 04 (n=12)
Osteoporosis

- People with DMD have low bone density without steroids.
- Steroids increase this tendency (especially in the back).
- The best way to keep bones healthy is by maintaining a good diet, getting sunshine and maintaining mobility.
- DEXA scores should not be used to dictate treatment plans (steroids or bisphosphonates).
Trials of different regimes

• The ONLY way to give the answer
  - Regime A gives ....% efficacy versus ...% of side effects compared to ......
  - These trials need to be done
    • The alternative regimes need to be tested
    • There is lack of consistency in treatments offered
  - Will require long term commitment to randomisation, follow up
  - Joint international project planned
Lessons for other trials

• “Why has it taken so long for use of steroids to be universally accepted? Perhaps the answer lies in the designs, outcomes and dissemination of the various trials”
Lessons for other trials

• “Why has it taken so long for use of steroids to be universally accepted? Perhaps the answer lies in the designs, outcomes and dissemination of the various trials”

• Rheumatoid arthritis
Further information

- www.enmc.org/workshops/reports
- www.cochrane.org/