New insights into the mechanisms of tendon injury
1. What other factors affect onset of tendinopathy?

2. What treatments are best for tendinopathy?
Figure 2 Complex interaction between internal and external risk factors leading to an inciting event and resulting in injury.
What factors predispose a person to tendon injury?

- In some tendons, extrinsic factors (load) make a person susceptible
  - Young active men
  - Patellar tendon in jumping athletes
  - Adductor tendon in kicking athletes

- In some tendons it appears that intrinsic factors have a strong influence
  - Older sedentary women
    - Gluteal tendinopathy (? Long term compressive loads)
    - Supraspinatus
      - Both sexes
Tendinopathy

- Achilles tendon is heterogeneous in prevalence and onset
- Intrinsic and extrinsic factors are evident
  - Presents across a range of ages and activity
  - 11% lifetime incidence (Kujala et al 07)
    - Young high load athletes
    - Middle aged moderate load people
    - Older low load post menopausal women (Maffulli et al)
  - Sedentary people
Tendinopathy is a person disease with a load topping

- Tendinopathy in systemic disease
  - Diabetes, arthridites
- Collagen diseases
  - Marfan’s, Ehlers–Danlos
- Drug induced tendinopathies
  - Statins, fluroquinolones
- What intrinsic factors have been shown to affect tendons?
  - Genes
  - Age
  - Sex
  - Body composition
  - Biomechanics
Genes

Blood group
- Yes (Kannus et al 91, Jarvinen 92)
- No (Maffulli)

Specific polymorphisms for type V collagen and tenascin-C gene are more common in those with chronic Achilles tendon pain
- No difference Type I collagen
  - Mokone et al 05, Collins et al 08
Age

- After the third decade, tendinopathy appears to increase dramatically
  - Evidence for this is lacking
  - Compressed tendons under some load seem vulnerable
    - Gluteus medius
    - Rotator cuff
- They do not become pathological just because they are older

- Tendons lose
  - Proteoglycans
  - Water
- Become stiffer
  - Less capable of absorbing load
Young people

Are also at risk in tensile loaded tendons

<table>
<thead>
<tr>
<th>Number of patellar tendons imaged</th>
<th>US abnormality as relative risk for symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>48 female basketball Khan 1997</td>
<td>Same as past symptoms</td>
</tr>
<tr>
<td>54 young athletes Cook 2000</td>
<td>3 times greater risk in 14-18 yr</td>
</tr>
<tr>
<td>40 male athletes Cook 2001</td>
<td>No greater risk</td>
</tr>
<tr>
<td>54 male athletes Fred berg 2002</td>
<td>No greater risk</td>
</tr>
</tbody>
</table>
Body composition

- BMI in subjects that failed the Achilles eccentric program higher (>28) than in responders (Alfredson et al)
- BMI correlated with pathology score (Mokone et al)
- BMI over 35 increased risk of shoulder tendon surgery by more than 3 times (Wendleboe et al 04)
BMI as a RISK factor for upper extremity tendinitis

Cohort study in 500 workers over 5 years

- No baseline symptoms
- Clinical diagnosis of wrist, elbow or shoulder tendinopathy
- Aside from symptoms and history of other conditions (CTS), BMI was the ONLY significant factor
  - 29.5 UET, 27.7 no UET (no variance reported)
- Age, sex, job, exercise, smoking, support, stress, disease all not significant
  - Werner et al 05
Body composition

- Systematic review identified 41 studies that examined tendons and body fat
  - 19 found a significant association (Gaida et al, submitted)
  - Trends in same direction for all but two of the remaining studies
Waist and pathology

Malliaras et al. 06
How does fat affect tendons?

- **Cytokines**
  - Visceral fat excretes pro-inflammatory cytokines
    - IL-6, IL-1
  - Also factors known to be associated with bone-tendon junction pathology
    - TNF-α

- **Lipid deposition**
  - In arteries
    - Vascular compromise
  - In tendons
    - Tendolipomatosis
      - Seen in familial hypercholesterolaemia
    - Cholesterol levels linked to Achilles tendinopathy
    - 70% of those examined had elevated cholesterol levels
      (Gaida et al 09)
## Lipids

- **= Tot Chol, = LDL**
- **↑ Triglyceride**
- **↓ %HDL–C**
- **↑ TG/HDL–C**
- **↑ APO–B**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Achilles</th>
<th>Control</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chol (mmol/L)</td>
<td>5.47 (1.02)</td>
<td>5.16 (1.00)</td>
<td>0.094</td>
</tr>
<tr>
<td>TG (mmol/L)</td>
<td>1.22 (0.77)</td>
<td>0.96 (0.47)</td>
<td>0.039</td>
</tr>
<tr>
<td>HDL (mmol/L)</td>
<td>1.44 (0.39)</td>
<td>1.58 (0.48)</td>
<td>0.097</td>
</tr>
<tr>
<td>%HDL</td>
<td>27.6 (8.5)</td>
<td>31.9 (10.3)</td>
<td>0.016</td>
</tr>
<tr>
<td>LDL (mmol/L)</td>
<td>3.37 (0.86)</td>
<td>3.14 (0.93)</td>
<td>0.166</td>
</tr>
<tr>
<td>LDL/HDL</td>
<td>2.53 (0.98)</td>
<td>2.18 (0.93)</td>
<td>0.052</td>
</tr>
<tr>
<td>TG/HDL</td>
<td>0.941 (0.746)</td>
<td>0.691 (0.459)</td>
<td>0.036</td>
</tr>
<tr>
<td>ApoB (mg/L)</td>
<td>1005 (230)</td>
<td>896 (231)</td>
<td>0.017</td>
</tr>
</tbody>
</table>
Clinical application

- If you exercise (increased load)
  - With a genetic predisposition to tendon disease and/or central fat storage
  - AND you are fat
- You may have a series of factors that leave you vulnerable to tendon disease
Factors that affect the Achilles

- So how might fat explain other populations with tendinopathy?
  - Sedentary people might have higher fat mass
    - Surgery in athletic and not athletic populations
      - NA were shorter, heavier (higher BMI), higher subcutaneous fat
        - 25/48 good result cf 32/45, VISA 88 cf 74
        - Suffered more wound infection and sensitivity, more hypertrophic scarring, more repeat surgery
          - Maffulli et al 07
  - Middle aged men have higher visceral fat levels
  - Post menopausal women change fat deposition from subcutaneous to visceral
Factors that affect the Achilles

- **Sex**
  - Women get less Achilles mid-tendinopathy than men
    - Is oestrogen a factor?
  - Female hormones may be protective of tendons
  - Non-load related tendinopathy in post-menopausal women
  - Increased incidence in rupture post menopause
Role of female hormones in Achilles tendinopathy

- 95 post-menopausal women
  - Achilles tendon US
  - VISA-A score
  - Golfers and controls
  - Current and never HRT

Results
- Positive effect from HRT
- Negative effect from golf
  - More pathology
  - Larger tendons

Cook et al 2007
Summary

- Tendinopathy has a range of factors that contribute to it.
- Occurs in tendons with a variety of loads:
  - The pathology is likely the same.
  - The aetiology is likely different.
- Understanding and addressing the factors associated with the condition may improve outcomes.
Why do eccentric programs work?

- Decreased eccentric strength?
  - Haglund–Akerlind 93
- Neuroirritant
  - Soft tissue firm tissue interface
- Muscle effects
  - Increased length of MTU
- Effects on matrix structure
- Fluctuating length–force relationship
  - Rees 2008
- Decrease in cross sectional area after eccentric exercise
  - Bryant et al 08
Effects of a single bout of exercise

- A single bout of eccentric exercise
  - decreases cross-sectional area in normal tenons
  - In abnormal tendon increased tendon
    - Signal by 31%
    - Volume by 17%
    - Shalabi 04
Effect of an eccentric exercise program

**PICP (ug/l)**

<table>
<thead>
<tr>
<th>Sick tendon</th>
<th>Healthy tendon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>Before</td>
<td>After</td>
</tr>
</tbody>
</table>

- **Activity related Achilles tendon pain (>3 months)**
- **Elite football players 12 weeks training**
- **Microdialysis Achilles region Sick + healthy side (n=10)**

Langberg, Ellingsgaard & Kjær 07
Benefits and limitations of eccentric recipes

- **Benefits**
  - Easy to apply
  - Known outcomes
  - Both programs are progressive tendon loading

- **Limitations**
  - Population specific
    - Most evidence in middle aged recreational athletes
    - Alfredson program yields very good results in older, pre-surgical cohorts  
      \textit{Alfredson} 1998, 2000, 2001
    - Evidence in elite?
      - Do these athletes need a speed program?
    - Evidence in non athletic cohort
      - Poorer outcome Maffulli 06
Not just eccentric exercise

- Achilles
  - All did general and specific strength
    - Not just eccentrics
  - Randomised 2 groups
    - One allowed to stay active
      - <5/10 pain
      - One rehab only

- No difference in outcome
  - Silbernagel (in press)
Eccentric exercise compared to stretching

- Eccentric vs stretching
  Lateral elbow tendinopathy
  RCT
  - n=38
  - Matched age, symptoms
  - 3 sets of 5 reps with dumbbell
  - Started at 1 kg (M) and 0.5 kg (F)
    - Increased weight 10% weekly
    - Exercises intended to be pain free
  - Svernlov & Adolfsson 01

- 71% vs 39% completely recovered @ 12 mths
  - p = 0.09

- Greater increase in grip strength in exercise group
  - p < 0.05
Eccentric exercise compared to stretching

- Achilles RCT, n=45
  - Eccentric vs 30 s stretch both bent and straight knee
- No difference (?) in outcome
  - 3 and 12 months
- Issues
  - Follow up
  - Outcome measures
    - US, palpation and unvalidated questionnaires
      - Norregaard et al 07
Not just eccentric exercise

- High load resistance training
  - Patellar tendon
    - 3 groups
      - Decline squat, heavy load resistance, control
  - Heavy slow resistance better than decline at 12 weeks
    - Kongsgaard et al (in press)
  - Similar results with Bronstromm machine
    - Frohm et al
Any exercise helps tendons

Odds ratio 13 (3-47)

Holmich, Lancet, 1999
As long as it has an eccentric part

- Randomized controlled trial
- Heel drops
  - n=22
- Heel raises
  - n=22
- Same routine
- 82% success rate in eccentric group
  - VAS from 69 to 12
- 36% success rate in concentric group
  - p<.002

Mafl, Lorentzon, Alfredson, KSSTA, 2001
Eccentric exercise in season

- Unsuccessful in patellar tendon
  - Visnes, Fredberg

- Soccer players
  - Randomised to intervention or control
    - Intervention stretching and eccentric exercise
      - 25 times each leg, 3 sets, 3 times a week
  - No difference in outcome
    - 9% of normals developed US changes both groups
    - RR of developing symptoms 2.8 (1.6, 4.9) in both groups if US abnormal at baseline

- Eccentrics have never been shown to have a preventative role
  - In-season loads are high
Summary of eccentric programs

- Good starting point
  - Especially in the population they have been shown effective
- Will it adapt the muscle-tendon unit to required load capacity?
  - Yes – go right ahead, remember it is NOT a muscle strengthening program
  - No – add more or do different program
- Have strategies and time frames to vary program if necessary
  - Added interventions
  - Altered interventions
Tendon rehabilitation

- The cornerstones of tendon rehabilitation is a good assessment
  - Defining the stage of tendinopathy
    - Patient history
    - Diagnostic ultrasound
    - Quantify tendon symptoms & function
    - Loading tests
- And then providing the right stimulus to the tendon
  - Modify the tendon load
    - Training
    - Biomechanical
  - Progressive loading/exercise program as required
    - Affected by presentation, timing
Define the stage
– Patient history

- Age
- History of onset
  - First episode?
  - Exercise history
    - Periods of down-time
- Person factors
  - General health
    - Diabetes, inflammatory diseases, gout
  - Lipid profile
    - Waist girth
    - Cholesterol
  - Other tendinopathies
  - Biomechanics
Physical assessment

- Confirm pain localisation
  - Include related structures
- Assess load – pain response
  - Progressive load
  - Pain score /10
- Irritability
  - 24 hour response to training load
  - Morning stiffness in Achilles
- Assess kinetic chain
  - Atrophy
  - ROM – Ankle, foot and other m–t units
  - Strength, power, fatigability
  - Dynamic, sports–related function

www.fisiokinesiterapia.biz
What are we trying to achieve with rehab?

- Avoid exacerbation of the tendon cells/matrix
  - Unload the affected tendon
- Remodelling of matrix through graduated and specific loading
  - Is the sub–acute tendinopathy weak? – probably not
- Maintain/improve function of muscle, kinetic chain and athlete
  - Load progression geared towards a return to sport
Tendon unloading and reloading

- Prolonged periods of unloading are not beneficial to the matrix
  - Greater than 2–3 weeks
- Mechano-transduction theory would support slower/lower impulse loading in acute phase
  - Less likely to up-regulate the tenocytes or matrix
- Elastic function loading sessions only every 3rd or 4th day \textit{Langberg 1999, Cook 2003, Silbernagel 2004}
- Structure high, low, medium tendon load day
  - Strength day, power day, energy storage day
What else?

- Prehab in those with known tendinopathy and/or symptoms
  - Maintain strength always
- Monitoring
  - Use provocative tests
- Early intervention
  - Stitch in time approach
- Training planning
  - Ideal vs real
  - Negotiate with coach....
What doesn’t help?

- High load drills/exercises with little recovery
  - Plyometrics
- Painful eccentric programs
  - in acute onset pain, in-season
- Rehab using solely eccentric exercise
- Ultrasound & frictions
  - Tenocyte activation
- Glucosamine compounds
  - Inhibition of breakdown of aggrecan
Current thoughts

- Staging the condition is a key to optimal medical and rehabilitation management
- Latent (24 hr) pain response is probably the most useful guide to load progression
- Early tendinopathies are essentially load management
- High load, painful eccentric programs are not indicated in all tendinopathies
Treating tendinopathy

- Identify if you think compression is a factor
  - If so, limit the compression on the tendon
- Identify factors that might influence outcome
  - Fat is easy
  - Genes, sex a bit harder
- Identify if they are in a population that responds to an eccentric program
  - Middle ages recreational athletes
    - If so, start with that
    - Otherwise consider other factors that might impact on outcome
Summary

- Exercise is the most potent stimulus to maintain and remodel the matrix
- Maintenance and prevention
  - Kinetic chain analysis
  - Off season pre–habilitation
  - In season maintenance of strength
  - Regular monitoring & early intervention
  - Care with programming of change of load

There is no magic bullet!