Revisiting an old idea:
Factor XIII in Scleroderma
Family Day 2016
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Clinical Research Fellow in Rheumatology

Kindly presented by
Professor Christopher Denton
What is Factor XIII?

Factor XIII (FXIII) is a clotting factor – a natural protein which helps the blood to stick together and form a scab when you cut yourself.

We all have it in our bodies.

However, it also has other roles in tissue repair and wound healing.
What is Factor XIII?
What does Factor XIII have to do with Scleroderma?

The connective tissue and skin in Scleroderma form a dysregulated micro-environment involving the blood vessels, the immune system and its cells, and the fibroblasts which produce scar tissue.
What does Factor XIII have to do with Scleroderma?
What does Factor XIII have to do with Scleroderma?

- Blood vessels
- Immune cells
- Fibroblasts
- Platelets
- Skin cells

Improved interaction with skin cells

Improved cell migration and reduced cell death

Blood vessel

Reduced TSP-1, which stops new blood vessels forming

Reduced collagen (scar tissue) formation

Immune cells
What does Factor XIII have to do with Scleroderma?

Blood vessels

Scleroderma

Fibroblasts

FXII

Immune cells
Around 1 in 2 million people have a deficiency of Factor XIII and are treated with purified human Factor XIII called Fibrogammin.

Therefore we are able to give people more Factor XIII than they naturally have, which is useful for clinical trials.
Factor XIII and Scleroderma: Results from the Past

In the 70s and 80s, researchers in Europe gave systemic sclerosis patients repeated doses of Factor XIII into the vein. They saw good improvements in some areas of the disease including skin softness, Raynaud’s attacks and
Factor XIII and Scleroderma: Results from the Past

This work was paused due to concerns regarding blood products during the BSE/vCJD scare of the 90s.

People with Factor XIII deficiency have required treatment during this time, and we have seen no transmission of vCJD or blood-bourne viruses by this drug.

Former minister for agriculture John Gummer feeds his 4 year old daughter a beefburger to show safety in 1990.
Factor XIII and the Royal Free

We are currently conducting a clinical trial to see if purified Factor XIII (Fibrogammin) will be a good treatment for our patients.

This is in two sections.
Section 1 – Measurement Phase
Completed

8 patients
with limited
or diffuse
scleroderma

1 dose of IV
Factor XIII

Blood samples
and wellbeing
checks every week
for 6 weeks
Section 2 – Treatment Phase

18 patients with limited or diffuse scleroderma

2/3 receive Factor XIII for 6 months

Blood samples and wellbeing checks every 2 weeks for 6 months

1/3 receive Placebo for 6 months
Section 2 – Treatment Phase

How will we know if it has worked?
1. Comparisons before and after
2. Comparisons between Placebo and Treatment groups

Where will we look for changes? “Outcome Measures”
1. Skin thickness
2. Number of digital ulcers
3. Number of Raynaud’s attacks
4. Ability to use hands in day-to-day life
5. Wellbeing questionnaires
6. Lung function
# Outcome Measures

## Table 4: Response Frequencies Regarding Degree of Difficulty in Performing Activities of Daily Living Using the Neth assessment Questionnaire (RAQ) and a Modified RAQ (mRAQ)

<table>
<thead>
<tr>
<th>Degree of difficulty</th>
<th>Without aid</th>
<th>With some aid</th>
<th>Some help</th>
<th>Unable to do</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Dressing and grooming</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>2. Shaving your feet</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>3. Shaking your head</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>4. Getting out of bed</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>5. Getting in/out of chair</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>6. Getting up straight from sitting</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>7. Getting in/out of car</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>8. Stair climbing</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>9. Stair going up straight</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>10. Stair going down straight</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>11. Getting in/out of bath</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>12. Getting out of bed</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>13. Getting up straight from sitting</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>14. Getting in/out of car</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>15. Stair climbing</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>16. Stair going up straight</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>17. Stair going down straight</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>18. Getting in/out of bath</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>19. Getting out of bed</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>20. Getting up straight from sitting</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>21. Getting in/out of car</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>22. Stair climbing</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>23. Stair going up straight</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>24. Stair going down straight</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>25. Getting in/out of bath</td>
<td>0.80</td>
<td>0.30</td>
<td>0.10</td>
<td></td>
</tr>
</tbody>
</table>

*Note: Values are based on a Likert scale of 1-5*
If anyone is interested in learning more or being involved in the Treatment Phase of this study we will be recruiting more patients around Christmas 2016

Please contact the Clinical Trials team or email me on anna.gill@nhs.net

Thanks for listening!
And Finally…

My partner, Iain, and I will be swimming, cycling and running the Blenheim Palace Triathlon on 4th June 2016 to raise funds for Scleroderma and Raynaud’s UK.

All donations will be gratefully received.

You can sponsor us at www.virginmoneygiving.com/AnnaandIain