THE JOINTS OF CHILDREN WITH HAEMOPHILIA:

CAN WE PRESERVE THEM?

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synovitis, cartilage destruction, epiphyseal overgrowth and articular, chronic haemophilic fibrosis and joint destruction. In particular, chronic haemophilic arthropathy of the knee is the most disabling of all the haemophilic joint problems in the paediatric age group and is now to be focused on. While the management of this complication is important, aspects to be considered in the prevention of all these important aspects to be considered in the haemophilic arthropathy of the knee.
**JOINT DAMAGE**

- In 1992: prophylactic F-VIII not available: 93% 13-16y had joint damage
- Prophylactic F-VIII from 1990’s:
  - 66% FEWER BLEEDS
- Only 10% of world’s 650,000 P’s: access F-VIII
- Joint bleeds still occur frequently

Economic challenges in haemophilia: 2005 Haemophilia; Brown et al
HOW MANY BLEEDS FOR THE VICIOUS CYCLE OF JOINT DESTRUCTION TO START?
1998 GERMAN STUDY

MRI NOT AVAILABLE

21 patients:

Grp I: F-VIII aet <2Y; no more than one jt bleed

COMMENCED F-VIII; NO FURTHER BLEEDS; NO JOINT DAMAGE IN LONG TERM
Grp II: F-VIII aet 3-6Y

Had 6 joint bleeds (median)
No XR changes on plain films
Commenced on F-VIII
No further bleeds

But joint damage appeared & progressed relentlessly
Grp III: F-VIII@ >6y;

>10 jt bleeds (median)

Plain XR changes seen if >5 jt bleeds

Damage continued relentlessly
IN SUMMARY:

• One joint bleed probably OK
• Lots of joint bleeds not OK
• Few joint bleeds not OK tho’ XR probably OK progressive damage already on the way, despite use of F-VIII
PROCESS STARTS WITH ONLY SECOND HAEMARTHROSIS

- Human in vitro studies
- 4 days of exposure to whole blood irreversible damage
- 16 days: synovial inflammation evident

GAME OVER!
NOT CLEAR HOW LONG THESE CHANGES TAKE;
BUT THE VICTIOUS CYCLE STARTS EARLY

MRI: WOULD BE MUCH MORE REVEALING, EARLIER
MECHANISMS OF JOINT DAMAGE
2 Processes sequential & parallel:

• Iron in cartilage → damage → break down products → inflammation → synovium & fluid → break down cartilage

• Iron in synovium → damage → inflammation → cytokines, enzymes → break down cartilage

• **Whole blood found more inflammatory than iron (Hb) alone:**

• **WCC: Produce enzymes or cytokines**
Capacity for removal of blood ↓ each bleed → chronic synovitis (overgrowth synovium, neovascularisation)
WHY NOT GET WHOLE BLOOD & IRON OUT?

THAT’S WHAT WE DO

ASAP:

BLOOD OUT!

IRON OUT!

CORTICOSTEROID IN!
• Wash out haemarthroses of large joints ASAP
  – Avert direct damage to cartilage from iron, blood
  – Prevent accumulation hemosiderin and continuation of inflammatory cycle

• Instil semi-soluble corticosteroids to
  – Prevent chronic inflammation of synovium and continuation of inflammatory cycle
  – Prevent hypervascularity of joint bleeding
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35 JOINT INJECTIONS
16 CHILDREN
1 R KNEE
20 L KNEE
2 R ANKLE
11 L ANKLE
1 SHOULDER
1 ELBOW
1 WRIST
RESULTS

No extra bleeding in joints

No infection from injections

Virtually all: “normal” joints, except Peet

No target joints according to strict definition

No plans for synovectomies!

No plans for joint replacements!
STEROID INJECTIONS SAFETY ISSUES
There have been concerns that intra-articular injection may damage intra-articular structures. Objective evidence of safety of intra-articular steroid injection into joints in JIA was reported by Huppertz et al, by means of MR scans pre and post-procedure.\(^{32}\) In this study at 13 months follow-up, cartilage integrity was well preserved in all joints treated with intra-articular steroids. Prior to intra-articular steroid injection, pannus was noted in seven joints, and at 13 months follow-up pannus was only present in two of these joints. By means of MR scan, Eich et al reported resolution of pannus that had replaced articular cartilage in the knee one month
### Table III. Main side effects of IAC therapy.

<table>
<thead>
<tr>
<th>Side Effect</th>
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<tr>
<td>Subcutaneous atrophy</td>
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<td>Periarticular calcification</td>
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<td>Crystal-induced synovitis</td>
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<td>Avascular necrosis of bone</td>
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<td>Cushingoid syndrome</td>
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<td>Septic arthritis</td>
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<td>Anaphylactic reaction</td>
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SEPSIS WITH I/A STEROIDS

• NO REPORTS IN CHILDREN
• ONE REPORT 48hrs POST INJECTION, ? FROM BACTERIAL RESPIRATORY INFECTION
TASH

- Presented 10 mths with acute swollen L knee
- No FH haemophilia
- Presumed infection; washed out; no infection, old blood; diagnosis
- @ 11 M wash out and steroid injection & casting (fixed flexn)
- @ 13 M wash out and injection
- @ 5 Y wash out and injection
TASH

- DOING FINE
- THEN 2 YEARS LATER
- SWOLLEN PAINFUL LEFT KNEE
ACUTE INFECTION: DELAY AVOIDED
KNEE WITH 4 BLEEDS AND SEPTIC ARTHRITIS

MRI: VIRTUALLY NORMAL

With conservative Rx: serious damage
OUR MOST DIFFICULT CASE
FIRST BLEED L KNEE @ 10 W
WASHED OUT 1 WEEK LATER

2\textsuperscript{ND} BLEED @ 14 W; WASHED OUT.

UNIQUE AND UNKOWN PATHOLOGY: F-VIII DISAPPEARS <24H

BY THE AGE OF 8 YEARS

• 12 LEFT KNEE INJECTIONS AND WASHOUTS
• 4 LEFT ANKLE INJECTIONS AND WASHOUTS
JOINTS WITH RECURRENT BLEEDS ARE DESTROYED

AND PEET’S JOINTS?
8 YEARS

12 BLEEDS INTO THE KNEE
• Our worst case

• Despite
  – tenuous cover with FVIII
  – bleeds as a baby with surgery not covered c F-VIII
  – 12 bleeds in knee

• Washouts and steroid have contained damage & XR would still show no damage

• Some capacity for healing, with cartilage replaced by fibrocartilage if inflammation can be controlled with I/A steroids
Quality of life is associated to the orthopaedic status

1. GET BLOOD AND IRON OUT OF THE JOINTS ASAP

2. STEROIDS ARE SAFE AND HELPFUL

3. PLAIN XRAYS DO NOT GIVE THE TRUE PICTURE

4. ADD A PAEDIATRIC RHEUMATOLOGIST TO THE TEAM
HAEMOPHILIAC CHILDREN’S JOINTS:
CAN WE PRESERVE THEM?

Yes, We Can!

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Table I. Type and dose of corticosteroids currently used for intra-articular corticosteroid injections at the corresponding author’s centre.

<table>
<thead>
<tr>
<th>Joint</th>
<th>Corticosteroid</th>
<th>Dose</th>
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<tr>
<td>Shoulder</td>
<td>TH</td>
<td>1 mg/kg (max 40 mg)</td>
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<tr>
<td>Elbow</td>
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<td>0.75 mg/kg (max 30 mg)</td>
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<td>Wrist</td>
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<td>5–10 mg $^\S$</td>
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<td>Hip</td>
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<td>1 mg/kg (max 40 mg)</td>
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<td>Knee</td>
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TH: triamcinolone hexacetonide; MP: methylprednisolone acetate.
$^\S$: Depending on the child’s size.