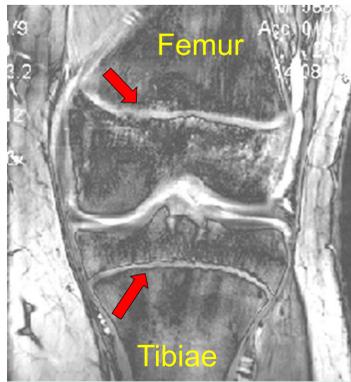


Altered gene-expression in human growth plate cartilage tissue exposed to dexamethasone

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Conclusions:

- In growth plate tissue samples from a male patient, the expression of collagen-2, osterix, and TGF- β , important genes in chondrogenesis, were clearly affected when exposed to dexamethasone in vitro
- In contrast, in a female patient the expression of these genes were only marginally altered
- More samples are needed to rule out if the difference between the two patients is linked to gender or any other reason

Figure 1: Magnetic resonance imaging of human femur and tibiae. The arrows point at the epiphyseal growth plate cartilage.

All authors declare no conflict of interest.

Background:

Synthetic glucocorticoids (GCs) are widely used drugs but their suppression of growth in paediatric patients is a well-known problem. Collagen-2, osterix (Osx), and transforming growth factor β 1 (TGF- β) are crucial genes in the growth plate, involved in chondrocyte differentiation and migration. We for the first time exposed human growth plate cartilage directly to GCs to analyse the effect on gene-expression level.

Aim:

Our aim was to study the expression of collagen-2, Osx and TGF- β in human growth plate cartilage when exposed to GCs.



Figure 2: Fold change in RNA-expression in dexamethasone treated compared to vehicle treated cartilage from two different patients.

Results:

In tissue from patient 1, we found that dexamethasone suppressed collagen-2 expression by 88%, compared to vehicle. Interestingly, dexamethasone also suppressed TGF- β by 79%. There was also a slight increase in Osx expression in the dexamethasone treated cartilage. In patient 2, there were only marginal changes in gene expression between dexamethasone and vehicle treated cartilage tissue samples.



Figure 3: Epiphyseal surgery in order to arrest further leg growth in an extremely tall patient.

Method:

Tissues of human growth plate cartilage were obtained during epiphyseal surgery in order to arrest further leg growth. Biopsies were collected from one boy (patient 1), 17 years old, pubertal stage GH; PH4 (Tanner), and one girl (patient 2), 16 years old, pubertal stage B2; PH2. Slices of the cartilage were cultured in vitro and treated for 24 hours with 10 μ M dexamethasone, and snap-frozen in liquid nitrogen. RNA was extracted with Trizol® and qPCR was performed with primers for human collagen-2A1, Osx, and TGF- β 1. The study was preapproved by the local ethics committee at Karolinska University Hospital, Stockholm, Sweden, and informed consent was obtained from the patient and both parents.

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