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The effect of hormones on bone growth is mediated through mechanical stress

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Abstract

Mechanical stresses play a key role in regulating cell growth and cell differentiation. Using mechanical and physiological data available in the literature, we are able to construct a growth curve of a child, which we compare to the standard curve. It appears likely that the impact of hormones on pubertal growth rate sprout followed by growth arrest can be solely explained by increased mechanical stresses. The uptake of hormones by the muscles results in increased mechanical stress on the chondrocyte before and at the puberty, resulting in a peak in growth followed by growth cessation. ***To cite this article: X. Wertz et al., C. R. Biologies 329 (2006).***

Résumé

La croissance osseuse est régulée par les hormones via les contraintes mécaniques. Les contraintes mécaniques jouent un rôle prépondérant dans la croissance et la différenciation cellulaire. À partir des données mécaniques et physiologiques colligées dans la littérature, nous construisons une courbe de croissance d'un enfant, que nous comparons à la courbe standard. Il est vraisemblable que l'action des hormones sur le pic de croissance et la fin de l'ossification puisse être expliquée par la variation des contraintes mécaniques. Les hormones induisent un anabolisme musculaire, responsable d'une augmentation de la contrainte exercée sur le cartilage de conjugaison. Ceci explique vraisemblablement le pic de croissance prépubertaire suivi de l'arrêt de la croissance. ***Pour citer cet article : X. Wertz et al., C. R. Biologies 329 (2006).***

Keywords: Bone growth; Cartilage; Growth rate; Hormones; Mechanical stresses

Mots-clés : Ossification ; Cartilage ; Taux de croissance ; Hormones ; Contraintes mécaniques

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1. Introduction

Growth and maturation of bones is a highly predictable phenomenon [1]. Growth is fast (about 20 cm per year) during early childhood and then slows down. A peak in growth is followed by growth cessation at puberty (Fig. 1, after [2]). The reason for this highly reproducible pattern is unknown. This paper aims at suggesting that this pattern can be explained by the mechanical constraints exerted on the chondrocyte.

During embryogenesis, bones are formed on an initial cartilaginous model. Cartilage is later replaced by bone; this process is called 'enchondral ossification' [3]. Long bones end near the joint in a separate epiphysis, which is ossified later. During childhood, epiphyses undergo a characteristic series of events: central calcification, absorption of cartilage and enchondral ossification [3]. At puberty, epiphysis becomes fused with the shaft of the bone (diaphysis), resulting in growth arrest [3].

Cartilage and bone are subjected to mechanical stresses; the greatest load comes from the muscle [4]. Collagen secretion is not isotropic, but directional [5]. Its direction is ruled by main loading directions [6]. These constraints appear to play a key role in the growth and the transformation of cartilage into bone. In the embryo and later in life, ossification of the cartilage starts in parallel with active movement of the feet by muscle contraction [7,8]. Mechanical stress resulting from the contraction of the muscles seems to guide enchondral ossification patterns [7,9–11].

Extensive mechanical constraints, like the use of rigid fixation for fracture, can result in growth arrest. For example, epiphyses plated for a year show increased bone differentiation, premature closure, and growth arrest [12]. Similarly, heavily trained gymnasts [13] or swimmers [14] experience attenuated growth during their years of training, followed by catch-up growth during reduced training schedule or the months following the end of extensive training.

Hormones have a well-known effect on cartilage growth and on the differentiation of cartilage into bone. They induce prepubertal bone growth followed by a subsequent bone arrest. The question is whether the effect of hormones are mediated by the androgen receptor located at the surface of the chondrocyte or by changes in mechanical constraints.

The effect of hormones on the development of muscles is well known. The muscle load increases around puberty. The most intense force development occurs between 12 and 15 years of age in boys [15]. Treatment with testosterone of young boys prior to puberty increases both muscle mass and bone growth [16].

Common measurement made in order to predict children's final height are built on the evolution of growth speed with time (Fig. 1a$_2$). An example of such a curve is given by Despert [2]. The question is about phenomena taking place, leading to such a behaviour of growth speed.

This paper aims at suggesting that a peak in growth followed by growth cessation at puberty is mediated at least in part by increased mechanical constraints.

We will show that the height velocity (the derivative function on time of a height curve) can be calculated (Fig. 1b) using mechanical sollicitations and physiological data on cartilage.

We use the following experimental data:

- the evolution of muscle strength with age;
- a growth curve allowing to calculate the evolution of long-bone section with age;
- the evolution of chondrocyte synthesis according to mechanical loadings;
- the evolution of cartilage volume with age (measured from a bone age atlas);

and we construct the curve of the evolution of collagen synthesis by cartilage with age, which is an equivalent to a height-velocity curve.

2. Material and methods

We have retrieved data on human growth [17], bone cells [11], and muscles [18] from the literature, as well as informations on the effects of mechanical constraints on cartilage and the anabolic effects of hormones on muscles [18].

2.1. Correlation between muscle strength and time

The evolution of the relationship between muscle strength and time is given in the curve in Fig. 2a (from Clarke, cited in [18]). In this work, a correlation between the strength of leg muscles and time among young boys is observed.

2.2. Correlation between bone section, cartilage volume and time

Bone section increases during childhood. We have calculated the normalized bone section versus time (homothetic growth, see [5]). This curve is thus qualitatively identical to the square of the growth curve, in function of time (growth curve after Kumar and Clark [19]). Normalization is done: *normalized section*