

depression of skeletal function following burn injuries remains to be discovered.

Idiopathic juvenile osteoporosis (IJO) is a term used to describe a severe and rapidly progressive form of osteoporosis seen in the years before puberty.¹⁵ The disease affects both sexes and its cause is unknown. At the onset of puberty, the disease remits and, while residual deformity persists, new growth takes place in the absence of further fractures. IJO is not known to be a familial condition, but the possibility that it is due to an underlying disorder of collagen formation, much like that in OI, cannot be ruled out. **The remission of osteoporosis with puberty is a feature shared by many other types of osteoporosis in adolescents, even those whose causes have nothing to do with gonadal hormone status, such as in corticosteroid-induced osteoporosis and OI.** The natural history of these conditions bears witness to the powerful effect of gonadal hormones on bone.

PEDIATRIC ASPECTS OF ADULT OSTEOPOROSIS

If bone mass increases steadily throughout childhood and the early 20s and is then subject to an inevitable decline, it follows that measures to promote skeletal accretion in youth may limit the effects of bone loss later in life. **The factors contributing to**

the gain in bone mass in childhood include calcium nutrition,¹⁶ the timing of puberty, other hormonal influences, and innate genetic traits. A start in unraveling these genetic factors may have been made by the observation that polymorphisms in the noncoding region of the vitamin D receptor gene are predictors of adult bone mass.¹⁷ Doubtless other genetic influences will be discovered since there is certainly a familial component to postmenopausal osteoporosis.¹⁸

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Abstracts From the Literature

Identification of a Stimulator of Steroid Hormone Synthesis Isolated From Testis

A follicle-stimulating hormone (FSH)-dependent product of the rat Sertoli cell that stimulates Leydig cell function through paracrine mechanisms was identified. A 70-kd protein complex was resolved into 2 proteins of 28 kd and 38 kd. The 28-kd fraction expressed Leydig cell-stimulating activity. The 38-kd protein permitted maximal expression of this activity. The 28-kd fraction also stimulated steroidogenesis in isolated rat granulosa cells and mouse adrenocortical cells. Further studies revealed that the 28-kd fraction was identical to the tissue inhibitor of metalloproteinase-1 (TIMP-1) and the 38-kd fraction to the proenzyme form of cathepsin L/Sertoli cell cyclic protein-2 (CP-2).

TIMP-1 is present in many tissues. Among other functions, it binds to matrix metalloproteinases or interstitial collagenases and influences cell migration, angiogenesis, embryo implantation, and cell growth. The mechanisms by which TIMP-1 stimulates steroidogenesis are as yet unknown. Procathepsin L enters lysosomes through the mannose-6-phosphate receptor (the type II insulin-like growth factor receptor) and is metabolized to cathepsin L, a cysteine proteinase

that is involved in prohormone activation, bone resorption, and sperm maturation. Since TIMP-1 contains 6 disulfide bonds, cathepsin L may be involved in full expression of the steroidogenic activity of TIMP-1 by modifying its 3-dimensional structure.

Boujrad N, et al. *Science* 1995;268:1609-1612.

Editor's comment: *The importance of TIMP-1/cathepsin L in steroidogenesis in humans is uncertain, although human Sertoli cells have been reported to secrete an FSH-responsive factor that stimulates Leydig cell function.¹ Whether this factor may be involved in the physiology of normal adrenarche or in the pathogenesis of such disorders as polycystic ovary syndrome or male limited gonadotropin-independent sexual precocity in some patients remains an issue for future study.*

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