

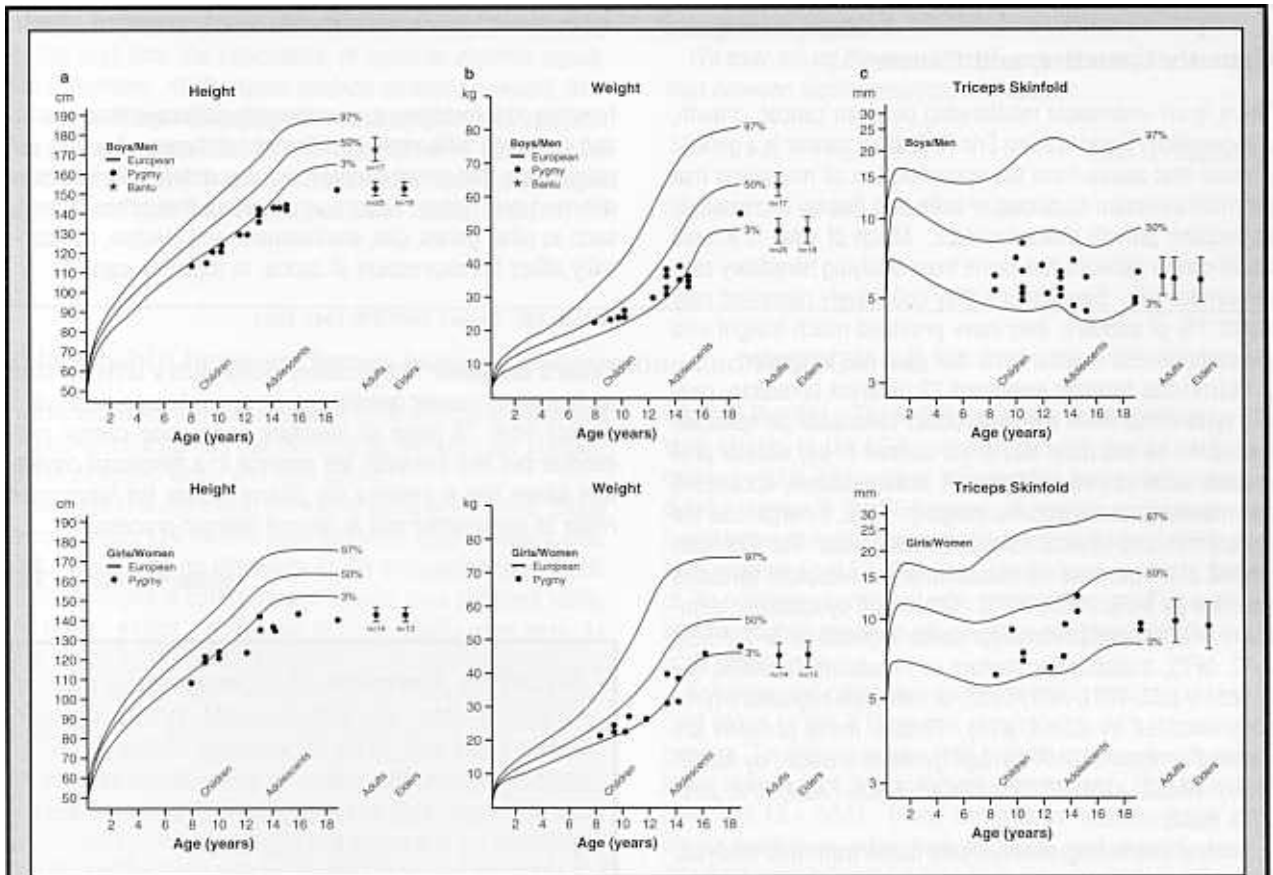
Dissociation of Systemic GH-IGF-1 Axis From a Genetic Basis for Short Stature in African Pygmies

The investigators tested the hypothesis that the primary cause of short stature in African Pygmies resides in low levels of insulin-like growth factor 1 (IGF-1) and evaluated whether any observed alterations in their systemic IGF-1 status could be associated with malnutrition and/or altered immune status. Extensive serum assays and auxologic measurements were done for purposes of evaluating the hormonal and immune status versus the phenotypes of children, adolescents, and young and old adults. None had overt clinical or biochemical signs of malnutrition. Bantus living in the same equatorial rain forest of eastern Cameroon were used as controls.

Pygmies did not differ from Europeans or Bantus in mean serum IGF-1 or IGF-binding protein 3 (IGFBP-3) levels. How-

ever, in both African groups, IgG, IgM, IgE, C-reactive protein, and ceruloplasmin were above normal for Europeans, but the Pygmies had much higher IgG and IgM levels than the Bantus. Low IGF-1 levels were inversely associated with serum levels of IgG and IgM.

The authors concluded that in growing and adult African Pygmies without evidence of clinical or biochemical signs of nutritional deficiency, serum IGF-1 and IGFBP-3 are essentially normal. They believe that these studies disprove the previous hypothesis that there is a defect in IGF-1 production or growth hormone insensitivity, and that the short stature of African Pygmies is unrelated to a genetically determined lesion that becomes unmasked at puberty to suppress the surge in circulatory IGF-1 levels. They suggest that much of the



Height (panel a), weight (panel b), and triceps skinfold thickness (panel c) plotted against age for African Pygmies are shown with a reference European (British) population (Tanner et al, 1966 a,b; Tanner & Whitehouse, 1975). Data for boys/men and for girls/women are shown on top and bottom part of the figure, respectively. For each anthropometric measurement, individual values are shown for children and adolescents, while mean and SD are shown for adults and elders; in addition the mean and SD values for the Bantu men are indicated using an asterisk symbol. Note that the heights of all Pygmies are below or close to the 3rd percentile of the European standard.

Reprinted with permission from Dulloo AG, et al. Dissociation of systemic GH-IGF-I axis from a genetic basis for short stature in African Pygmies. *Eur J Clin Nutr* 1996;50(6):371-380.

growth retardation of Pygmies may be due to excessive exposure to infections with resultant elevation of immunoglobulins, in spite of absent gross nutritional deficiency secondary to infection.

Dulloo AG, et al. *Eur J Clin Nutr* 1996;50(6):371-380.

Editor's comment: This study is very nicely executed, and extensive data are presented to raise much skepticism about the

previous hypothesis that an increase in IGF-1, which is normally associated with the adolescent growth spurt, does not occur in Pygmies. The data not only negate the former hypotheses but also reveal a new biochemical alteration (elevated immunoglobulins) that, in my opinion, may or may not be associated with growth retardation. This article was kindly brought to my attention by Dr. Guy Van Vliet.

Robert M. Blizzard, MD

Nonadipose Tissue Production of Leptin: Leptin as a Novel Placenta-Derived Hormone in Humans

The authors report that leptin, the appetite-regulating polypeptide hormone secreted by adipocytes, also is synthesized and secreted by human placental chorionic villi and amnion cells. They demonstrated that plasma leptin concentrations were higher in pregnant women than in nonpregnant women of comparable body mass index (BMI), a finding made by other investigators. Whereas in nonpregnant women plasma leptin concentrations and BMI were directly related, this relationship was not demonstrable in pregnant subjects. Leptin values

declined rapidly after birth. Umbilical vein leptin concentrations were slightly higher than umbilical artery values. Leptin was detectable in amniotic fluid. Plasma leptin values were elevated in patients with hydatidiform moles and choriocarcinoma and fell rapidly with surgical removal or chemotherapeutic ablation of the tumor.

Expression of *ob*, the leptin gene, was demonstrated in placental chorionic villi and amnion. Immunoreactive leptin was present in trophoblasts of first trimester chorionic villi and syncytiotrophoblasts and amnion cells in the third trimester. The investigators suggest that placental leptin may be of physiologic importance in modulating the metabolic relationship between mother and fetus. Plasma leptin values may serve as a marker of tumors of placental origin.

Masuzaki H, et al. *Nat Med* 1997;3:1029-1033.

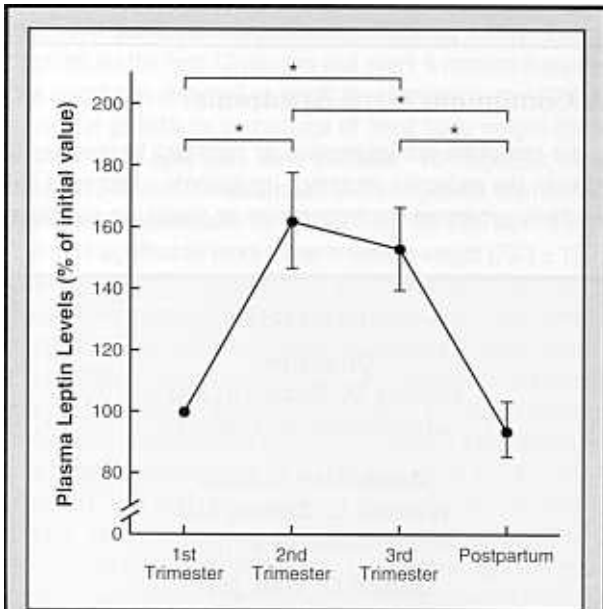
Editor's comment: This paper reports that leptin may be secreted by nonadipose placental cells, namely, placental trophoblasts and syncytiotrophoblasts, and secreted into amniotic fluid and the maternal circulation. Thus, leptin is another of the many protein hormones that are secreted not only by their primary tissue but also by the placenta. Placental leptin may modulate metabolic homeostasis in the pregnant woman and fetus. One wonders if, in the pregnancy complicated by placental insufficiency and intrauterine growth retardation, leptin deficiency may permanently alter hypothalamic appetite regulatory mechanisms that influence the postnatal growth of that individual.

Chehab points out that the elevated leptin concentrations in pregnant women imply an element of leptin resistance because appetite is not suppressed by pregnancy. Although these investigators did not note correlation between BMI and serum leptin concentrations in pregnant women, Hartmann et al reported that the 2 were highly correlated.

Allen W. Root, MD

Chehab FF. *Nat Med* 1997;3:952-953.

Hartmann BW, et al. *N Engl J Med* 1997;337:863.



Elevated plasma leptin levels during pregnancy. Time course of plasma leptin levels determined consecutively during pregnancy and postpartum ($n=40$). The plasma leptin levels in the first trimester are defined as 100%.

* $P<0.005$ versus the values in the first trimester or postpartum.

Reprinted with permission from Masuzaki H, et al. Nonadipose tissue production of leptin: leptin as a novel placenta-derived hormone in humans. *Nat Med* 1997;3:1029-1033.