GROWTH HORMONE AND IGF ABNORMALITIES OF THE AFRICAN PYGMY

Thomas J. Merimee *
Department of Medicine
University of Florida
Gainesville, FL

INTRODUCTION

Since the elucidation of the structures of insulin-like growth factors I and II (IGF I and IGF II) by Humbel\textsuperscript{1,2}, and the development of specific radioimmunoassays for each by Zapf and Froesch\textsuperscript{3}, a number of clinical conditions have been identified that are associated with defects in either the secretion or action of these agents\textsuperscript{4,5}. After 25 years of investigating stature of the African pygmy, data have now been obtained indicating a unique genetic variation in the GH-IGF I axis in these subjects. These data will be presented in this article.

Pygmies themselves are unique: living in the central part of Africa south of the Sahara, they now are one of the few surviving groups that live much as they did in Paleolithic times. In Zaire live the Mbuti of the Ituri forest, considered the smallest of them all, and more to the south, the Kivu Twa. The Binga form a western group. The existence of these groups in Africa can be dated to the earliest known historical records. Monuments in early Egypt depict pygmies, and Greek writers including Homer (900 B.C.) and Strabo (24 B.C.) described accurately their geographical location\textsuperscript{6}.

The cause of short stature in the pygmy was long the subject of speculation prior to our work\textsuperscript{7-10}, but none of these earlier studies provided definitive hormonal and genetic investigations.

EARLY HORMONAL STUDIES

In our earliest studies of short stature in the African Pygmy, we established that African pygmies normally secrete growth hormone (GH) after provocative stimuli but do not respond to the administration of GH with normal changes in nitrogen, calcium, phosphorus and carbohydrate metabolism\textsuperscript{11-14}. When hypopituitary subjects were treated with GH, we demonstrated hypercalsuria, a decrease in serum urea nitrogen and enhanced insulin secretion after glucose\textsuperscript{13}. These responses were never seen in pygmy subjects. The change of plasma free fatty acids in pygmies after infusing growth hormone was particularly informative\textsuperscript{13}. The mean fasting concentration of plasma free fatty acids (FFA) in Pygmies (0.722 ± 0.10 mM/liter) did not differ significantly from that of controls (0.719 ± 0.10 mM/liter). After the intravenous infusion of 4 mg hGH over a 20-minute period, the mean plasma FFA concentration of the controls rose to 150%
and that of hGH-deficient dwarfs to 178% of basal values after 120 minutes. The mean plasma FFA concentration of the Pygmies, however, rose to only 111% of the basal value after GH, a change that was not significantly different from that observed after saline infusion. This reduced lipolytic effect, unlike the absence of GH's other effects, could only represent direct resistance to growth hormone, per se, not a deficiency of IGF I. Growth hormone in vitro and in vivo increases FFA release from adipose tissue, whereas IGF I has the opposite effect. The importance of this observation was only appreciated at a later date.

In 1982 we were able to establish that serum concentrations of IGF I were decreased in adult African pygmies, whereas their IGF II concentrations in serum were normal. We were able to show also that the IGF I concentration in serum did not increase after growth hormone treatment, while such increases were readily demonstrated in other non-pygmy subjects. In 1987, we reported data that added substantially to earlier findings, demonstrating that the major

![Graph 1](attachment:image1.png)

**Figure 1.** Growth in cm is shown for controls and pygmies in the upper panel. For the serum concentrations of IGF I (2nd panel) and testosterone (3rd panel) the open bars indicate controls; hatched bars, pygmies. SEMs are given.