CHAPTER 1

Introduction

> " … find out the cause of this effect,
> Or rather say, the cause of this defect,
> For the effect defective comes by cause."
>
> — *Hamlet,* Act II, Scene II

There is always a need for further knowledge about the growth of bone(s). This is true particularly because an understanding of the normal and abnormal growth of bone(s) forms the basis of early recognition, possible prevention, and appropriate treatment of many deformities. However, it is less well appreciated that findings on the abnormal may be employed to test and extend our knowledge of the normal. The genetic makeup, as well as various types of diseases, and injuries (such as trauma), inflammation, radiation, and chemicals, may affect skeletal growth sites, thereby causing faulty growth of bone(s). The degree of the subsequent deformity will depend not only on the type, intensity, extent, and chronology of the noxious agent but also on the site and its particular susceptibility and growth activity. A growth deformity of bone may be readily produced by interfering with a cartilaginous but not a sutural growth site.[1]

The problem of plastic-surgical treatment for craniofaciodental deformities is a difficult one. The dysplastic pattern of growth continues. In unilateral disturbances, the discrepancy between the two sides becomes greater as the patient becomes older because of limited or no growth of the affected side. Even though the deformity may not be progressive, it is not self-correcting, and there is no totally satisfactory way to compensate for the lost or retarded growth. The disturbance itself is not fully remedied by orthodontic, prosthetic, or surgical procedures. However, these measures do give functional and cosmetic improvement. Consequently, the craniofacial surgeon is called upon to treat and improve both the function and the appearance of these abnormalities.

Alteration of the position of the craniofacial complex by various types of osteotomies is a common surgical procedure. Other surgical approaches are directed toward contributing bulk and increasing length by means of bone, cartilage, and soft-tissue grafts as well as flaps. Autogenous tissues have been transplanted and alloplastic materials implanted as masking procedures to build up the less developed side in asymmetries or to the mental or other regions where there has been a symmetrical arrest. Distraction osteogenesis is a significant recent addition to the surgical armamentarium. If these corrections are made in a patient who has not attained full growth, a later procedure may be necessary in adult life.

As a plastic surgeon with a basic science background, in my practice I saw patients with a variety of both soft- and hard-tissue deformities, which frequently were distributed over many parts of the body. Invariably there were many unanswered questions. In an attempt to find answers, I returned part-time to the laboratory. Over the years I conceived, designed, initiated, and carried out a series of experiments in regard to bone(s), teeth, and cartilage as well as cartilage implants in both young and adult animals (turtles, rats, gophers, lagomorphs, pigs, dogs, monkeys, and humans). Each procedure had its advantages and disadvantages. Although an attempt was made to limit the number of variables and to obtain a definite "yes" or "no" answer, this was not always possible.

My early research interests were in skeletal problems of a systemic nature. Later, one of my concerns was the possible effects of trauma — accidental and intentional (surgical) — on growth of bone(s). Eventually, I directed my efforts principally toward local surgical experimentation as it related to both normal and abnormal gross postnatal craniofaciodental growth. Because of the wide variety of different structures, their interrelated individualities, and the challenges presented in both its richness of sites of growth and its complexity, the skull and particularly the face, proved to be a most unusual source of study.

Many of these investigations were carried out in collaboration and done principally at the University of Chicago, the University of Illinois, the Cedars-Sinai Medical Center, and the University of California at Los Angeles.

BONE GROWTH AND CHANGE

Growth and development of the skeletal system has an important role in determining body form. The dynamics of growth of bone(s) is a complex process. Although significant articles in regard to bone growth appeared in the literature more than 225 years ago,[2] many basic questions are still unanswered. What are some of the problems in need of study? What are the inherent difficulties? Any determination of bone growth must concern itself with one or more of the following questions: What are the centers? The sites? The amounts? The rates? Do they vary? When? What are the directions? What are the changes in size and in shape (Fig. 1.1)? What are the changes in proportion? What is the pattern? What are the mechanisms? What factors are influential?

Some principles of the biology of bone are central to this presentation. The basic blueprint of a bone is inherent. Postnatal bone growth is but a continuation of prenatal bone growth interrupted by the event of birth. *In utero*, the fetus with its genetic beginnings is subjected to the vicissitudes of the maternal environment. After birth, the individual is subjected to the effects of the general environment. Development of body form is related to the synchronous coordination of three-dimensional, multiple, differential skeletal growth sites and centers and associated structure activities (Fig. 1.2).

The following generalizations may be made about normal skeletal growth. Growth of bone(s) occurs essentially in three ways: cartilaginous (endochondral) and sutural (appositional without resorption), representing bone(s) as organs; and remodeling (appositional and resorptive), representing bone as a tissue (Table 1.1). A definition of growth is change over time. A basic physiologic concept is that throughout life, bone, the tissue, is in a continuous state of apposition and resorption. Consequently, skeletal size and shape are always subject to change. When skeletal mass increases, as in children, apposition is more active than resorption.

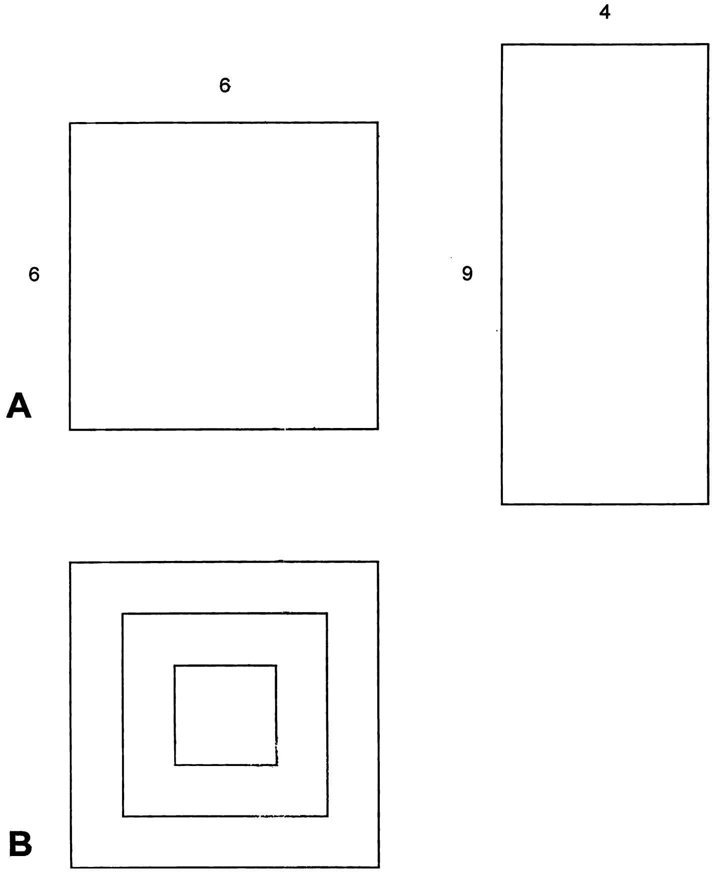

Fig. 1.1 Size plus shape equals form. (**A**) Size is constant but shape is variable; (**B**) shape is constant but size is variable. [From: Sarnat BG (2001). Effect and noneffects of personal environment experimentation on postnatal craniofacial growth. *J Craniofac Surg* **12:** 205–217.]

Cartilaginous and sutural growth are both active (i.e. positive growth). When skeletal mass is constant, as in the adult, apposition and resorption, although active, are in equilibrium (i.e. neutral growth). Cartilaginous and sutural growth have ceased. When skeletal mass decreases, as in old age, resorption is more active than apposition (i.e. negative growth). This concept of growth change is not new[3] and is also evidenced by the following passage from *Alice in Wonderland*, by Lewis Carroll: " … said Alice, 'and if

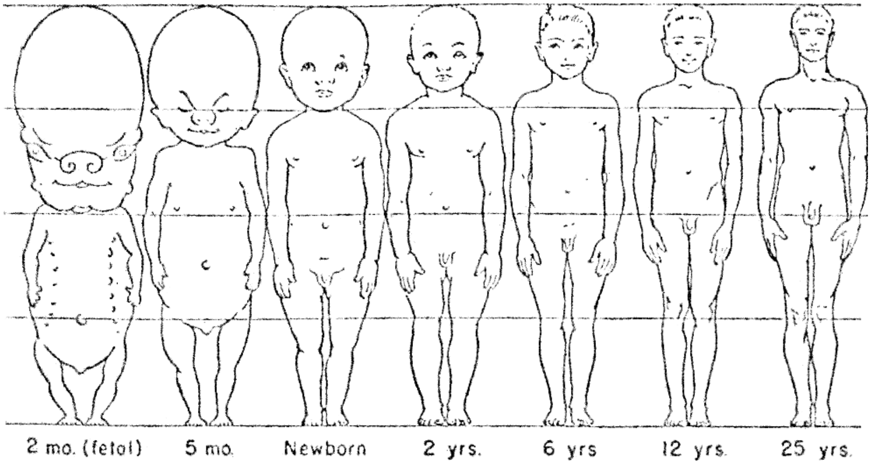

Fig. 1.2 Development of the total human body from *in utero* to adulthood. (From: Scammon, in *Morris Human Anatomy*, 9th ed., edited by C.M. Dodson, 1933.)

it makes me grow *larger*, I can reach the key; and if it makes me grow *smaller* [italics added], I can creep under the door.'"

Various methods have been used in the study and measurement of growth of bone(s) (see Chap. 36). Each, however, has its limitations.[4] One may yield information about the sites of growth, another about the rate, and still another about the direction. However, a combination of methods will potentially yield more information and, in certain instances, more accurately than one method alone. Although some of these methods often lend themselves primarily to experimental work on animals, they nevertheless contribute to our fundamental knowledge of the subject.

The physiologic stability of the bony components is the result of many interrelated factors, normal functional use being a prominent one. Well recognized are the effects of either excessive use, with hypertrophy (i.e. an increase in the mass of bone), or disuse, with atrophy (i.e. a decrease in the mass of bone). Thus modifications in the functions of a part are reflected in alterations in the form of the part.

Despite its hard, semirigid, supporting, mineralized nature, bony tissue, by virtue of the highly sensitive periosteal and endosteal membranes, is

Table 1.1 Bone: Growth, Remodeling and Repair*

	Growth				Repair	Clinical Considerations
	Cartilaginous	Sutural	Remodeling	Skeletal mass		
Infancy and childhood	Active	Active (apposition, no resorption)	Apposition greather than resorption	Increasing (positive growth)	Active	Giantism and other growth deformities Acromegaly
Adulthood	Long or tubular bone, skull base, etc. (epiphysis) Inactive Mandibular condyle (epiphysis-like) Latent (potentially active)	Inactive	Apposition equal to resorption	In equilibrium (neutral growth)	Active	
Old age	Long or tubular bone, skull tissue, etc. (epiphysis) Inactive Mandibular condyle (epiphysis-like) Latent (potentially active)	Inactive	Apposition less than resorption	Decreasing (negative growth)	Active	Senile osteoporosis
Clinical consideration	Conditions affecting cartilage: achondroplasia, rickets, etc.	Conditions affecting sutural growth: synostosis, etc.	Skeletal adjustments to various conditions	Change in size and shape	Fracture, osteotomy, ostectomy, distraction osteogenesis, bone graft	

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dynamic and ever-changing, adaptable to every nuance of tension and pressure. The basic and dual response of resorption and apposition is evident in the reaction of bone to growth, healing of fractures, alteration in muscular balance, orthopedic therapy, change in position of bone(s) after osteotomy and/or ostectomy, distraction osteogenesis, and other intrinsic and extrinsic factors.

NORMAL CRANIOFACIAL GROWTH

The craniofacial skeleton changes in size and shape in all three planes: height, width, and depth. However, it grows in these three dimensions of space differentially in both time and rate (Figs. 1.3–1.5). Many sites contribute to the multidirectional growth. The dynamics and details of normal postnatal growth, simultaneity, coordination, and change and nonchange of the craniofaciodental skeletal system in both the young and the adult are fascinating, complex, and incompletely understood problems in the field of biology.

Fig. 1.3 The aging face: child, adult, old age. (From UCLA–Center on Aging.)

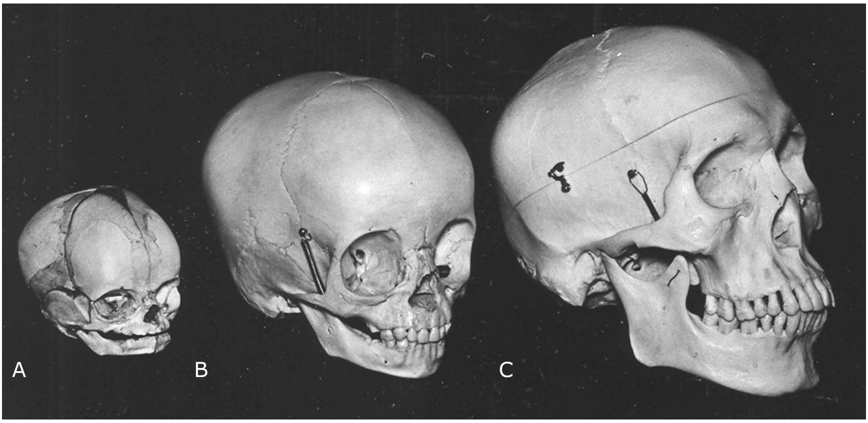

Fig. 1.4 Normal growth of the human skull. (A) clinically edentulous skull at about birth; (B) skull of a child with completely erupted deciduous primary dentition; (C) skull of an adult with completely erupted secondary dentition. Note that in the infant the cranium is prominent, and the face is much less so, representing a smaller part of the total skull size. Also note that the orbit makes up a large part of the face. In the adult, the face is prominent and represents a larger part of the skull size. The orbit makes up a considerably smaller part of the total face in the adult than in the infant. Differential growth takes place at different times and rates in various parts of the skull. [Reprinted with permission from Sarnat BG: Normal and abnormal craniofacial growth: some experimental and clinical considerations. *Angle Orthod* **53:** 263, 1983.]

Craniofacial bones, like bones in general, grow in three principal ways (Table 1.1). One is *cartilaginous* — at the nasal septum — and *endochondral* growth (i.e. the replacement of cartilage by bone) — at the base of the skull, at the spheno-occipital and sphenoethmoidal junctions. These bones are joined by cartilage (synchondroses). In addition, endochondral growth of bone occurs at the septopresphenoid joint and at the mandibular condyle. The second way is *sutural* growth, where bones are united by connective tissue (synarthroses). This is found only in the skull. Sutures grow differentially by apposition without resorption. The amount of growth may vary on either side of the suture, the rate varies for different sutures at a particular time, and the same suture grows differentially at different times. These sites, as well as the endochondral, are of limited growth and usually cease activity as an individual reaches adulthood. The third

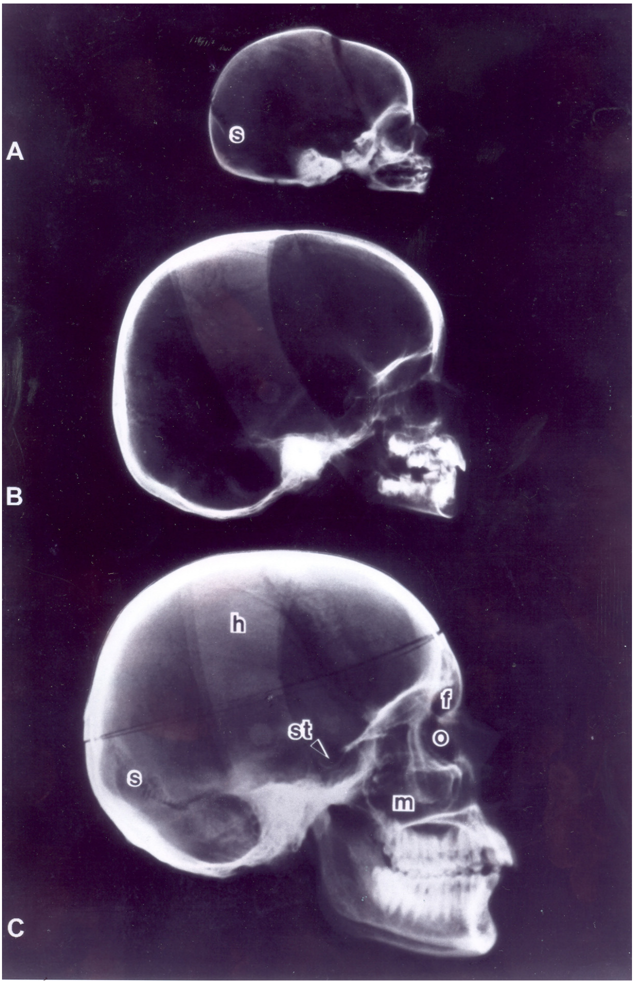

Fig. 1.5 Lateral cephalometric radiographs of skulls shown in Fig. 4. Note in the infant skull the presence of unerupted teeth in the jaws. (**A**) In the child skull, the primary dentition is fully erupted, and the permanent teeth are forming within the jaws. (**B** and **C**) In the adult skull, the permanent teeth are fully erupted. The maxillary (m) and frontal (f) sinuses are not evident in the infant skull, are in early development in the child skull, and are fully developed in the adult skull. Note the open, actively growing suture, S, in the infant cranium, in contrast to the closed inactive suture, S, in the adult cranium. St — sella turcica; o — orbit; h — head holder apparatus. [Reprinted with permission from Sarnat BG: Craniofacial growth, postnatal, in Delbucco R (ed.), *Encyclopedia of Human Biology*, 2nd ed. Academic, San Diego, California, 1997, pp. 71–82.]

Table 1.2 Craniofaciodental Growth

I. bone(s)
  - A. Cartilaginous — bone(s) as organs
    - 1. Endochondral
    - 2. Nasal septal
  - B. Sutural — bone(s) as oggans
  - C. Remodeling (appositional and resorptive) — bone as tissue

II. Cavities
  - A. Matrix
    - 1. Brain and cranium
    - 2. Orbital contents and orbit
  - B. Matrix and air
    - 1. Septum and nasal cavity
    - 2. Tongue and oral cavity
  - C. Air
    - 1. Maxillary sinus
    - 2. Frontal sinus
    - 3. Ethmoid sinus
    - 4. Sphenoid sinus

III. Teeth

type is *appositional* and *resorptive* growth (i.e. remodeling), which occurs on the outer surfaces (periosteal) and inner surfaces (endosteal) of bone throughout life. The differential responses and interrelationships of these processes are important.

The size and shape of the skull are determined not only by the growth of bones but also by its cavities (Table 1.2). Increases in the size of the contents of the cranial and orbital cavities of the skull influence the growth of adjoining bones and sutures. The air-containing maxillary, frontal, ethmoid, and sphenoid sinuses also increase in size and contribute to growth of the skull. This occurs by a combination of resorption and deposition of bone on the surfaces and adjustments at the sutures. An interesting comparison can be made when the infant, child, and adult skulls are modified to about equal size (Fig. 1.6).

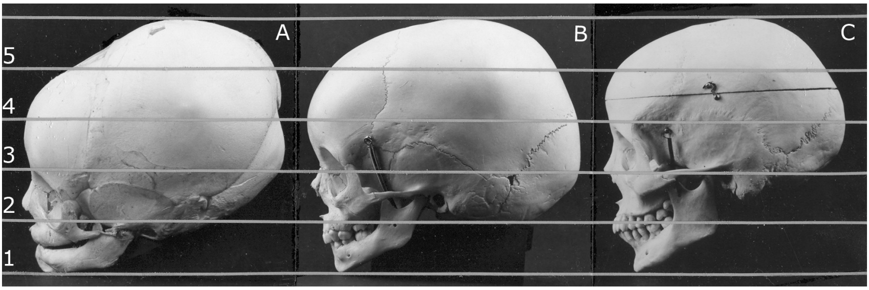

Fig. 1.6 Lateral view photograph of the skulls in Figs. 1–4 enlarged to about the same skull height and oriented in the Frankfurt horizontal plane. Note the differences in form and proportions of the total skull and its components. The distance between the lower border of the mandible and the superior border of the orbit represents about 40% of the skull height in the infant (**A**) and 60% in the adult (**B** and **C**). The orbital height is nearly the same in all three skulls. The cranial height represents about 60% of the skull height in the infant and 40% in the adult. The skull height is divided into fifths.

The cranium and the masticatory facial skeleton are integrated into an anatomic and biologic unit. However, the masticatory skeleton is in part dependent on muscular influences, growth of the tongue, and the dentition. These two parts of the skull follow different paths of development, and the timing of their growth rates is entirely divergent. Nevertheless, the growth of any one part of the skull is coordinated with the growth of the whole.

The more important sites of growth for the maxillary complex are three sutures on each side: the frontomaxillary suture between the frontal bone and the frontal process of the maxilla; the zygomaticomaxillary suture between the maxilla and the zygomatic bone (and, secondarily, the zygomaticotemporal suture in the zygomatic arch); and the pterygopalatine suture between the pterygoid process of the sphenoid bone and the pyramidal process of the palatine bone.[5,6] It is significant that these three sutures are parallel to each other and all are directed from above and anteriorly, downward and posteriorly. Thus growth of these sutures will have the effect of shifting the maxillary complex downward and anteriorly. Transverse growth at the median palatine suture, which is affected by the downward and divergent growth of the pterygoid processes, is both simultaneous and correlated with the widening of the downward-shifting maxillary complex. There is also anteroposterior growth along the maxillary side of the transverse palatine suture between the horizontal plate of the maxilla and the palatine bone, and along the posterior margin of the palatine bone.

The downward, outward, and lateral growth of the subnasal part of the maxillary body is accompanied by eruption of the teeth and apposition of bone at the free borders of the alveolar process. Thus the apposition in this area contributes to the increase in height and width of the upper facial skeleton. At the same time, the downward growth of the alveolar process accounts for the transition from the flatly curved palate of the infant to the highly arched one of the adult. However, the downward shift of the hard palate by resorption on its nasal surface and apposition on its oral surface tends to obscure the downward growth of the alveolar process. Thus the pathogenesis of the high palate seems to start with a deficiency of the modeling resorption at the nasal floor with a failure of the normal downward shift of the hard palate. However, the vertical growth of the alveolar processes at the free borders continues in correlation with the growth of the mandible and accentuates the discrepancy.

The growth of the upper facial skeleton is closely correlated with that of the mandible. However, the mode of mandibular growth is entirely different from that of the maxillary part of the face. In the latter, the growth is primarily sutural. In the mandible, an important site of growth is the hyaline cartilage in its condyle. These differences explain a certain independence and yet dependence of the growth of these two parts of the facial skeleton.

The growth of the mandible is indispensable for the normal vertical growth of the upper face. (See Chap. 2 for details of mandibular growth.) Upward and backward growth at the condyle, which rests against the articular fossa of the temporal bone at the cranial base, results in movement of the entire mandible downward and forward so that the upper and lower teeth and alveolar processes become more distant from each other. Since the teeth maintain occlusion by continued vertical eruption, the alveolar processes grow at their free borders. Disorders of mandibular growth, therefore, lead secondarily to changes in the upper face. They generally involve only the subnasal part of the maxilla.

Thus the skull, a complex of bone(s), has proven to be both a rich and a challenging source of study, particularly since the combination of different types of bone growth and increase in size of various cavities and growth, calcification, and eruption of teeth is not found elsewhere in the body.

Cranial and orbital growth occur predominantly early in life, while facial growth occurs predominantly somewhat later in life, mostly during the periods of growth and eruption of the primary and secondary dentitions and the development of the paranasal sinuses. A number of excellent references are available that describe the anatomic structures and give the details of craniofaciodental growth and movement.[6,7] Every student of growth will delight in becoming acquainted with the seminal works of Thompson[3] and Brash *et al.*[8]

Environment and Growth

A great deal has been learned about the prenatal and postnatal etiology of craniofacial and other abnormalities in the experimental animal. The material of these reports is only part of a series of experiments in which the relationship of injury to postnatal growth has been studied.

Throughout our lives we are constantly reacting to our environment. Variations in temperature, light, humidity, atmospheric pressure, terrestial and extraterrestial radiation and gravity affect us. In addition, the vast number of toxic agents, intentionally or unintentionally ingested through our food (or essential deficiencies) and water and inhaled form the air, determine our destinies. Consider the effect of our environment upon the skeletal growth sites and the resulting changes in size and shape of the jaws, face, cranium, and body.

There are many mechanisms (nervous, hormonal, metabolic, enzymatic) by which the environment directly induces adaptive changes. Environmental stresses can interact either directly — such as through variations in temperature and oxygen — or indirectly with the genetically controlled enzyme-forming system. There is no evidence that environmental stresses can induce genetic change.[9] Rather, those stresses permit such genetic changes as may occur in natural mutations to be realized and fixed.

Young rats exposed to cold stress had a smaller skull, a longer face in relation to the cranial vault, a narrower nose, a rounder cranium, and a shorter femur.[10] Natives living at high altitudes and exposed to the environmental stresses of hypoxia and cold have slower postnatal growth and a lesser adolescent growth spurt than other groups.[11] On earth, gravity is considered normal, or 1.0 g. What skeletal and other changes will occur in environments of hypogravity (moon, 0.18 g) or hypergravity (Jupiter, 2.65 g)? These and other factors are of great interest to the new field of cosmic biology and should be of concern to us.

In a 12-session, 2-hour graduate seminar on bone biology at UCLA, I would ask the following take-home open-book final examination question: Earth man and earth woman decide to live on the moon (or Jupiter). Earth woman gives birth to moon (or Jupiter) child. Describe the growth, development, size, shape, and skeletal and muscular systems of moon (or Jupiter) person.

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