# Introduction

Bone densitometry is a widely used and universally accepted tool for the assessment of bone mass in adults. In the last two decades, however, interest in bone densitometry in children has increased. This can be explained firstly by the introduction of more effective treatment regimens aimed at increasing and maintaining bone density in a variety of diseases influencing bone development and or growth and secondly, by the fact that several reports have indicated the importance of peak bone mass in relation to future development of osteoporosis **(Van Rijn et al., 2006).**

There are 2 main reasons for measuring bone mineral content (BMC) in children : to quantify the deficits in bone mineral associated with the various disorders that cause osteopenia in children and to improve our understanding of the childhood antecedents of osteoporosis, a condition that happens to manifest itself in elderly subjects. Available data suggest that the genetic susceptibility to osteoporosis may be detectable in early childhood **(Gilsanz and Wren, 2007).**

Measurement of bone mineral density (BMD) by dual – energy x-ray absorptiometry (DEXA) is viewed widely as the preferred method for clinical use in children because of its speed, precision, safety, and wide spread availability. The radiation exposure is comparable to that received during a round trip transcontinental airplane flight **(Bachrach, 2005).**

DEXA is an attractive option for clinical use that gives estimates of bone mineral mass, fat free mass (FFM), which is approximately equivalent to lean body mass (LBM), and total fat mass (TFM). DEXA exploits the fact that the energy dependency of the strength of interaction between X-rays and bone mineral differs from that for soft tissue. At low energies, bone dominates the attenuation process while, at higher energies, X-rays interact to about the same extent with bone and soft tissue **(Sala et al., 2006).**

The 3 main limitations of DEXA measurement in children are: (1) the current lack of a standardized pediatric normative database, (2) the lack of a meaningful clinical outcome measure related to DEXA values in children, and (3) inaccuracies resulting from growth -related variations in bone and body size and composition **(Gilsanz and Wren, 2007).**

# Aim of the Work

The aim of this work is to set a standardized pediatric normative database for BMD and body composition in a representative sample of healthy Egyptian female children aged 7-8 years by DEXA scanning.

*Chapter (1)*

# Normal Bone Anatomy and Physiology

Bone is a specialized mineralized connective tissue that is built by various types of metabolically active cells during embryonic and postnatal development. In the adult, the same cells contribute to the maintenance of structural and functional integrity, and accomplish the healing process following injury ***(Gruber et al., 2008).***

## The Skeleton:

The adult human skeleton has a total of 213 bones (Fig. 1), excluding the sesamoid bone. The appendicular skeleton has 126, axial skeleton 74 bones, and auditory ossicles six bones ***(Clarke, 2008).***

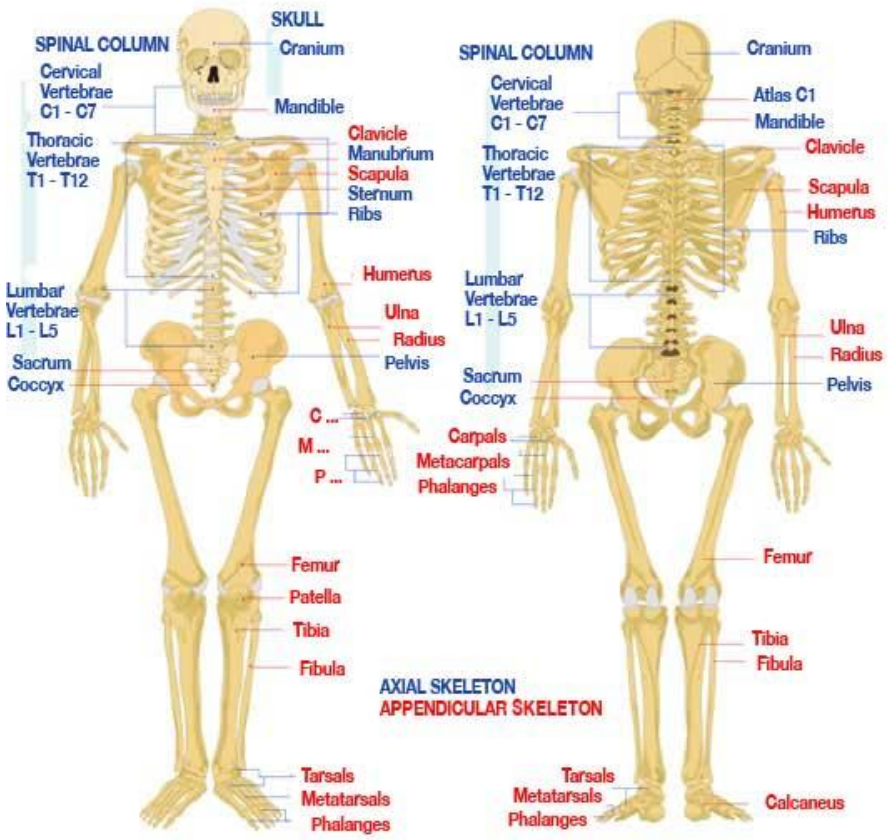


**Fig. (1):** Skeletal anatomy**.**

# Bone function:

The skeleton conducts a number of essential functions for maintenance of life. Some of which involve the obvious rigid structure provided by bone and others that result from the dynamic organization of bone at the microscopic level. Bone provides both mechanical support of the body, including both attachment of locomotor muscles and protection of portions of soft tissue, such as brain, spinal cord, heart and lungs. In addition, all blood

cell formation or hematopoiesis takes place in the bone marrow. A less obvious function of bone is that it serves as a metabolic reservoir for calcium and other minerals. A constant exchange of ions of calcium, phosphate (inorganic phosphorus or pi), and other mineral elements occurs between bone mineral surfaces and extracellular fluid in bone tissue. This constant ebb and flow of Ca and Pi is the result primarily of the active exchange of these minerals that occurs at the interface of bone mineral surfaces with the extracellular fluid and secondarily of remodeling processes within bone that renew bone microstructure throughout life .as described by Talmage and others ,the control of free calcium ion concentration in the extracellular fluids is primarily regulated at the mineralized bone surfaces **(Talmage and Talmage, 2006, 2007) and (Talmage and Mobely, 2008, 2009).**

## Gross anatomy:

The four general categories of bones are long bones, short bones, flat bones, and irregular bones (fig. 2). Long bones include the clavicles, humeri, radii, ulnae, metacarpals, femurs, tibiae, fibulae, metatarsals, and phalanges. Short bones include the carpal and tarsal bones, patellae, and sesamoid bones. Flat bones include the skull, mandible, scapulae, sternum, and ribs. Irregular bones include the vertebrae, sacrum, coccyx, and hyoid bone. Flat

bones form by membranous bone formation, whereas long bones are formed by a combination of endochondral and membranous bone formation **(Clarke, 2008).**

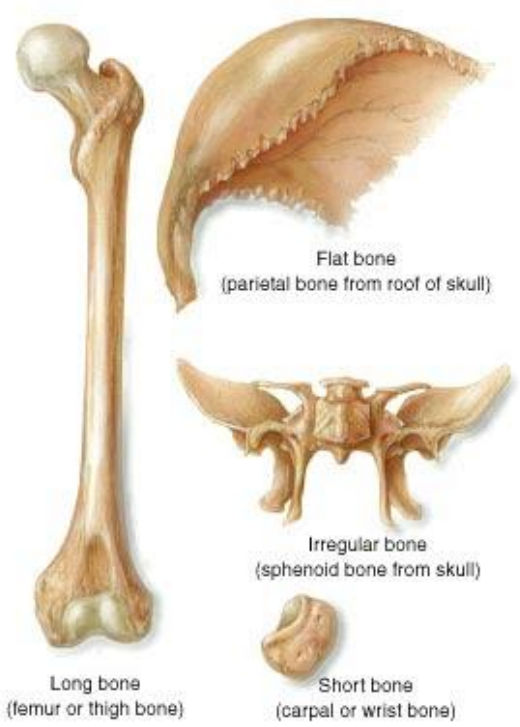


**Fig. (2):** The four general categories of bones.

The long bones are composed of a hollow shaft, or diaphysis; flared, cone shaped metaphyses below the growth plates; and rounded epiphyses above the growth plates. The diaphysis is composed primarily of dense cortical bone, whereas the metaphysic and epiphysis are composed of trabecular meshwork bone surrounded by a relatively thin shell of dense cortical bone (fig. 3) (**Clarke, 2008)**.

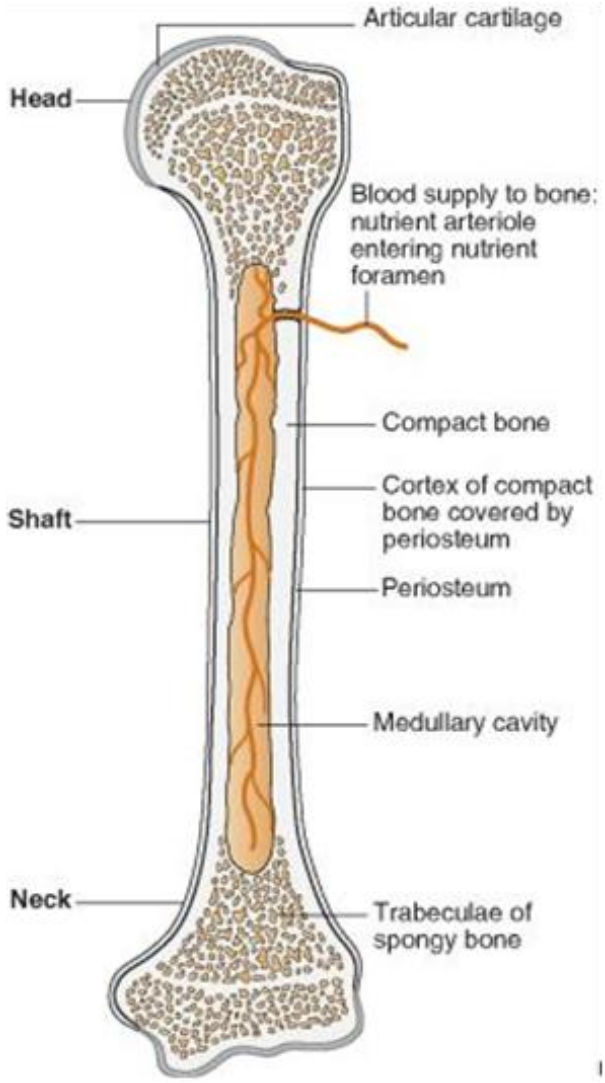


**Fig. (3):** Structure of long bone **(Aspinall and O'Reilly, 2004)**

## Structural organization of bone:

Bone is organized into two types of structure that are intermixed within each bone **(Clarke, 2008).** These structures are compact (cortical ) bone, which forms the shafts of the long bones and the outer surface of almost all

bones and trabecular bone ,also called cancellous or spongy bone, which fills the ends of the shafts of the long bones as well as forming most of the structure of the vertebrae (**Fawcett, 1994**). (fig. 4).

Cortical and cancellous bone can consist of either woven (primary) or lamellar (secondary) bone. Comparison of cortical and cancellous bone demonstrates a similar matrix structure and composition, but vastly different masses, with cortical bone having a greater mass-to-volume ratio **(Downey and Siegel, 2006).**

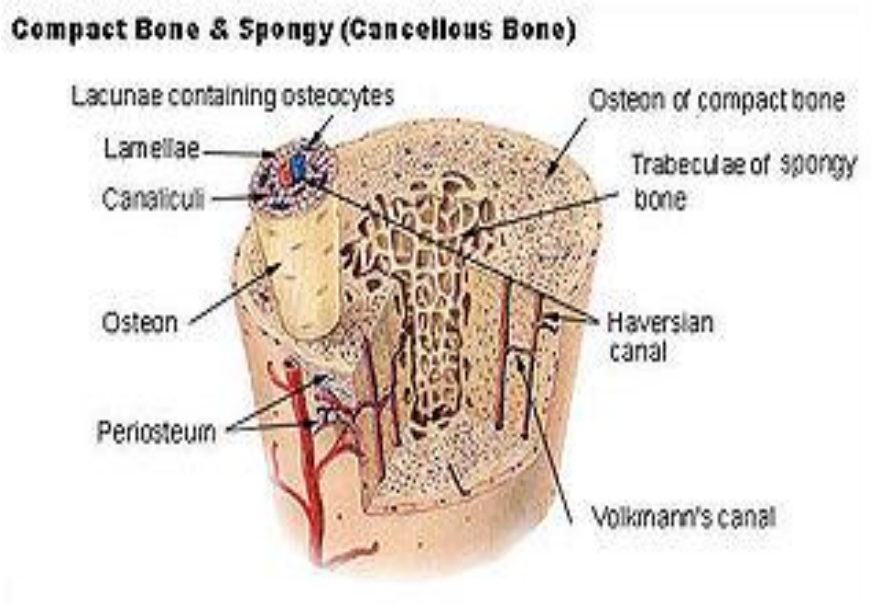


**Fig. (4):** Compact bone & spongy (cancellous) bone **(Katja et al., 2007**)

## Woven and lamellar bone:

Both types of bone are formed by two different tissues: woven and lamellar bone. The skeletal embryo consists of woven bone, which is later replaced by lamellar bone. Normally, there is no woven bone in the skeleton after four or five years but it reappears during the healing process after fracture. The two types of bone have many differences in composition, organization, growth and mechanical properties. Woven bone is quickly formed and poorly organized with a more or less random arrangement of collagen fibers and mineral crystals. Lamellar bone is slowly formed, highly organized and has parallel layers or lamellae that make it stronger than woven bone (**Doblar'e, 2004**).

## Bone Envelops:

### *Periosteum:*

The periosteum is a fibrous connective tissue sheath that surrounds the outer cortical surface of bone, except at joints where bone is lined by articular cartilage, which contains blood vessels, nerve fibers, and osteoblasts and osteoclasts. The periosteum is tightly attached to the outer cortical surface of bone by thick collagenous fibers, called

Sharpey's fibers, which extend into underlying bone tissue ***(Clarke, 2008).***

***Endosteum:***

The endosteum is a membranous structure covering the inner surface of cortical bone, trabecular bone, and the blood vessel canals (Volkman's canals) present in bone. The endosteum is in contact with the bone marrow space, trabecular bone, and blood vessel canals and contains blood vessels, osteoblasts, and osteoclasts **(Clarke, 2008).**

# Bone Composition:

## *Extracellular Composition (Bone Matrix):*

The extracellular makeup of bone comprises approximately 90% of its volume compared with the remaining 10% comprising cells and blood vessels. This extracellular matrix is composed of both an organic component and an inorganic component. The organic matrix accounts for approximately 35% of the total weight of bone tissue compared with 65% for the inorganic part **(Downey and Siegel, 2006).**

## *Inorganic Matrix:*

The inorganic (mineral) component comprises of calcium and phosphate in the form of needle-like or thin

plates of hydroxyapatite crystals [$Ca_{10}$ (PO4)6$(OH)_2$]. These are conjugated to a small proportion of magnesium carbonate, sodium and potassium ions **(Mohamed, 2008).**

## *Organic Matrix:*

The organic matrix is composed of collagen type I fibers (approximately 95%) and of proteoglycans and numerous non-collagenous proteins (5%). This organic matrix, calcified by calcium phosphate minerals, embeds bone cells, which participate in the maintenance and organization of bone, namely osteoprogenitor cells, osteoblasts, osteocytes, and osteoclasts **(Barrère et al., 2006).**

## *Cellular composition of bone:*

### *Osteoclasts:*

Osteoclasts are the only cells that are known to be capable of resorbing bone. Activated multinucleated osteoclasts are derived from mononuclear precursor cells of the monocyte macrophage lineage. Mononuclear monocyte macrophage precursor cells have been identified in various tissues, but bone marrow monocyte-macrophage precursor cells are thought to give rise to most osteoclasts (fig 5) (**Clarke, 2008).**

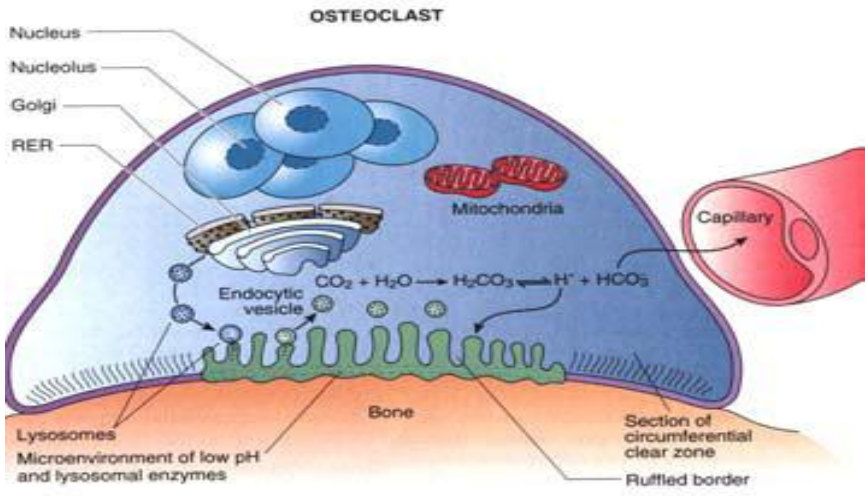


**Fig (5):** Osteclast cell **(Gartner and Hiatt, 2006).**

*Function:*

Bone resorption depends on osteoclast secretion of hydrogen ions and cathepsin K enzyme. H + ions acidify the resorption compartment beneath osteoclasts to dissolve the mineral component of bone matrix, whereas cathepsin K digests the proteinaceous matrix resulting in formation of saucer shaped Howship's lacunae on the surface of trabecular bone and haversian canals in cortical bone **(Clarke, 2008**).

## ii) Osteoblasts

Osteoblasts are mononucleated bone-forming cells derived from bone marrow stromal cells or connective tissue mesenchymal cells **(Ducy, 2000).**

***Function:***

They are located on the surface of osteoid seams and make a protein mixture known as osteoid, which mineralizes to become bone. Osteoid is primarily composed of Type I collagen. Osteoblasts also manufacture hormones, such as prostaglandins, to act on the bone itself. They produce alkaline phosphatase, an enzyme that has a role in the mineralisation of bone, as well as many matrix proteins. Osteoblasts are the immature bone cells, and eventually become entrapped in the bone matrix to become osteocytes- the mature bone cell. The bone lining cells is essentially inactive osteoblasts. They cover all of the available bone surface and function as a barrier for certain ions **(Ducy, 2000).**

***Osteocyte:***

The osteocyte is an osteoblast that has been incorporated into the cortical bone. It survives in single cell-sized hole in the bone known as a lacuna. Although its function as an osteoblast has ceased, it still plays a vital role in bone homoestasis. It's also the most abundant of the bone cells. Ninety percent of all bone cells are osteocytes, and they can survive for decades (fig. 6) (**Einhorn, 2007**).

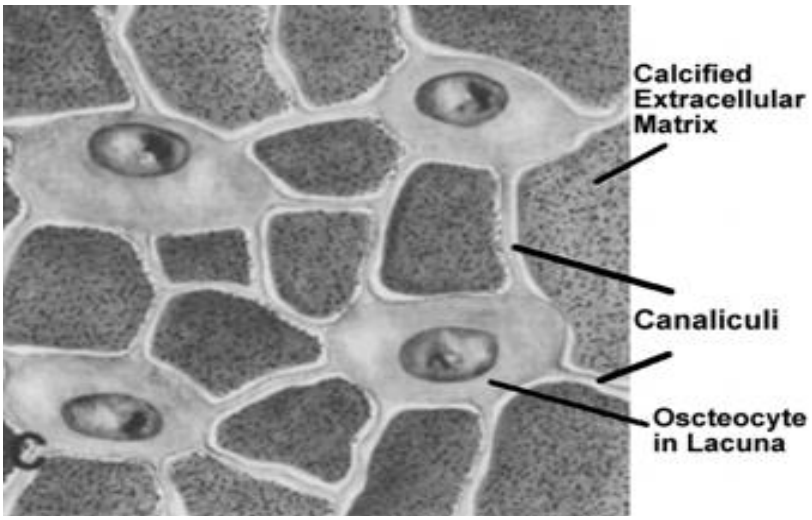


**Fig. (6):** Osteocyte cells **(Gartner and Hiatt, 2006**).

Osteocytes have long dendrite like processes that extend throughout canaliculi (tunnels) within the mineralized matrix. These dendrite like processes interact with other osteocytes within mineralized bone and also interact with osteoblasts on bone surface (**Raggatt and Partridge, 2010).**

***Function:***

Osteocytes probably act as mechanosensors that signal the need for bone modeling to adapt the bone to functional loading and remodeling to repair micro-structural changes within the bone matrix. Osteocytes can detect changes in the levels of hormones, such as oestrogen and glucocorticoids that influence their survival rate. Since osteocytes form a network spanning the skeletal system,