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DESCRIPTION OF HUMAN DEVELOPMENT: 'IZAM AND LAHM STAGES

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I. Introduction.

Human development from the gamete stage (nuṭfah) throughout pregnancy has been mentioned in the Holy Qur'ān with elegant simplicity and clarity:

«وَلَقَدْ خَلَقْنَا الإِنْسَانَ مِنْ سُلاَلَةٍ مِنْ طِينٍ ، ثُمَّ جَعَلْنَاهُ نُطْفَةً فِي قَرَارٍ مَكِينٍ ، ثُمَّ خَلَقْنَا النُّطْفَةَ عَلَقَةً فَخَلَقْنَا الْعَلَقَةَ مُضْغَةً فَخَلَقْنَا الْمُضْغَةَ عِظَاماً فَكَسَوْنَا الْعِظَامَ لَحْماً ثُمَّ أَنْشَأْنَاهُ خَلْقاً آخَرَ فَتَبَارَكَ اللَّهُ أَحْسَنُ الْخَالِقِينَ» (سُورَةُ الْمؤْمِنُونَ: آيات 12-14)

"We (God) created man from a quintessence of clay. We then placed him as a nuṭfah (drop) in a place of settlement, firmly fixed, then We made the drop into an 'alaqah (leech-like structure), and then We changed the 'alaqah into a muḍghah (chewed-like substance), then We made out of that muḍghah, 'iẓām (skeleton, bones), then We clothed the bones with laḥm (muscles, flesh), then We caused him to grow and come into being and attain the definitive (human) form. So, blessed be God, the best to create." (Surah Al-Mu'minūn, 23: Āyāt 12-14).

In this paper, the processes of embryonic osteogenesis and myogenesis are described in current biological terminology; then the 'iẓām and laḥm developmental stages, which describe the occurrence of these processes, are discussed.

II. Osteogenesis.

Development of both human bone and muscle has been well described and reported in contemporary scientific literature. Bone, of course, does not develop simultaneously throughout the body. Rather, there is a program or timetable of osteogenesis. For example, the ossicles of the inner ear are the first bones to fully ossify (during fetal life) whereas the growth centers in long bones of the leg do not close until 20 or more years after birth.

However, a distinct stage for bone formation is discernible in which cartilaginous skeleton begins to form with the spread of the cartilage in the 7th week.

Bone develops in one of two ways (depending upon its locale), viz., as endochondral bone or as intramembranous bone. Both types of bone formation involve a precursor population of mesenchyme (embryonic connective tissue) cells.

Where intramembranous bone forms (e.g., mandible and maxilla), mesenchyme cells condense (form dense cell aggregates) and differentiate into osteoblasts. The osteoblasts secrete the collagen-rich organic matrix of bone about themselves. Once surrounded by matrix, the cells are referred to as osteocytes. The organic matrix mineralizes as the bone ossifies.

Endochondral bone forms in a similar fashion except that the condensed mesenchymal cells first differentiate into chondroblasts that lay down the organic matrix of cartilage (Figure 5-1). So, a cartilage model of the bone forms initially. Secondarily, the cartilage is replaced by bone. A layer of connective tissue called perichondrium surrounds the cartilage model (or periosteum around bone) and serves as a reservoir of progenitor cells (chondroblasts or osteoblasts) as these tissues grow.

Although precursor cells to muscle and bone may reside quite near one another (in the somites, for example), their histories begin to diverge as cells begin to migrate to various sites in the embryo (Figure 5-2).

The long bones of the body are derived from embryonic mesenchyme. Mesenchymal cells in the limbs condense, i.e., aggregate in

A

B

C

D

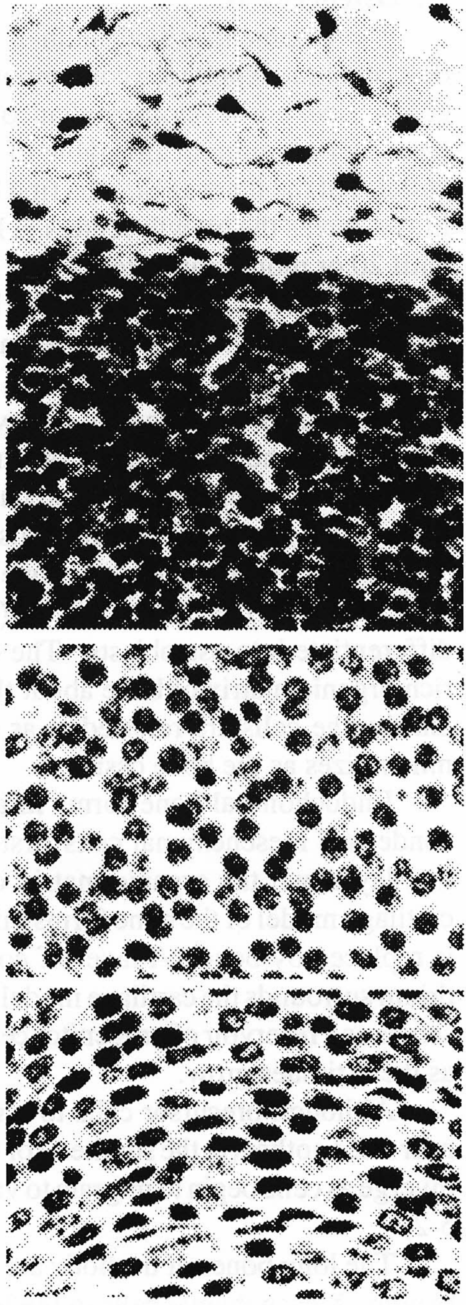

Figure 5-1. In the histogenesis of cartilage, mesenchymal cells (*A*) withdraw their processes and become crowded together to form an area of precartilage (*B*). In newly formed embryonic cartilage (*C*) in the 'izam stage, the densely aggregated cells of the precartilaginous stage have been moved apart by deposition of clear hyaline matrix between them. The cells then become angular (*D*) and isolated in clearly demarcated lacunae. (Reprinted with permission from Fawcett, 1986)

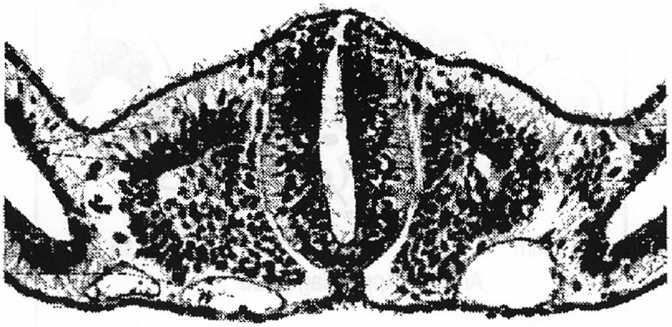

Figure 5-2. Section through 2.9 mm human embryo (in early mudghah stage) showing somite cells prior to migration. (Reprinted with permission from Blechschimdt, 1961)

the region where osteogenesis is going to occur later. From this densely packed mass of cells begins the histogenetic process by which mesenchyme cells differentiate into chondroblasts. The chondroblasts, in turn, secrete around themselves the organic matrix of cartilage. The chondrification process results in the appearance of a cartilage model of the bone that is to form, resulting in a skeleton and human shape for the embryo. From the connective tissue of the perichondrium, cells differentiate and form a bony collar around the shaft of the cartilage model. As a consequence of this, the avascular cartilage is cut off from diffusing nutrients, becomes necrotic, and the chondrocytes die. This is followed by an invasion of connective tissue cells and vascular elements from the adjacent connective tissue. Certain of these invading cells differentiate into osteoblasts, surround themselves with newly secreted bony organic matrix and thereby the osteocytes of newly developing bone (where previously there was a cartilage model).

Formation of bone does not begin uniformly throughout the body. Rather, there is a sequential appearance of bony tissue. However, in the 7th week the spreading development of the skeleton occurs. Bone development in the limbs commences in the limb buds from mesochymal cells. Primary ossification centers appear in the femur during week 7 (Figure 5-3) and in the sternum and the maxilla in weeks 8-9 (Figures 5-4, 5-5).

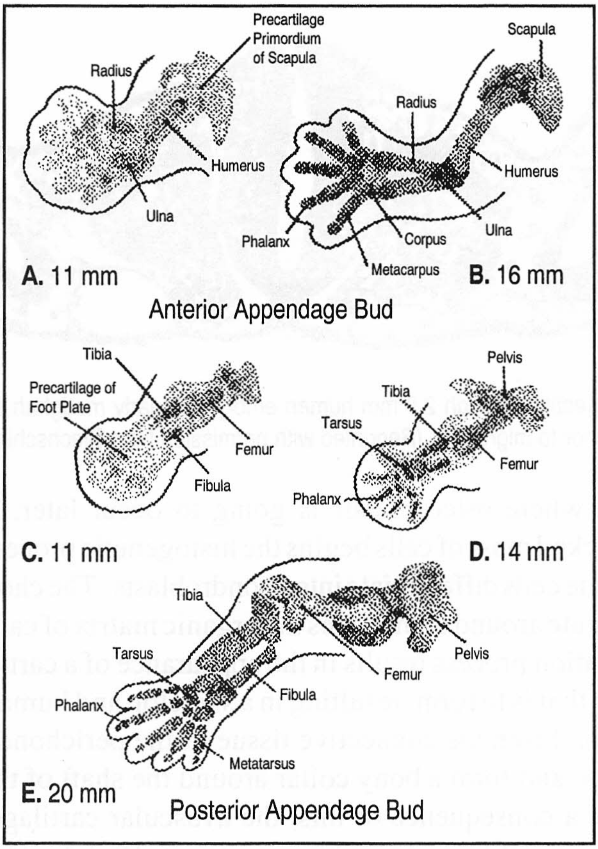

Figure 5-3. Primary ossification centers in the human embryo during the seventh week. (Reprinted with permission from Patten, 1968)

In recent decades, the process of osteogenesis in the human embryo has been reasonably well documented. At the histological level, the role of the mesenchyme, osteoblasts, osteoclasts, and osteocytes has been studied. Staging of cartilage deposition and mineralization in the embryo has been facilitated by the application of staining procedures specific for cartilage and bone.

Although precursor cells (myoblasts) are present adjacent to developing bone, differentiation into skeletal muscle attachments occur after the ossification process in the shaft and ends of the bones has begun (Figure 5-6).

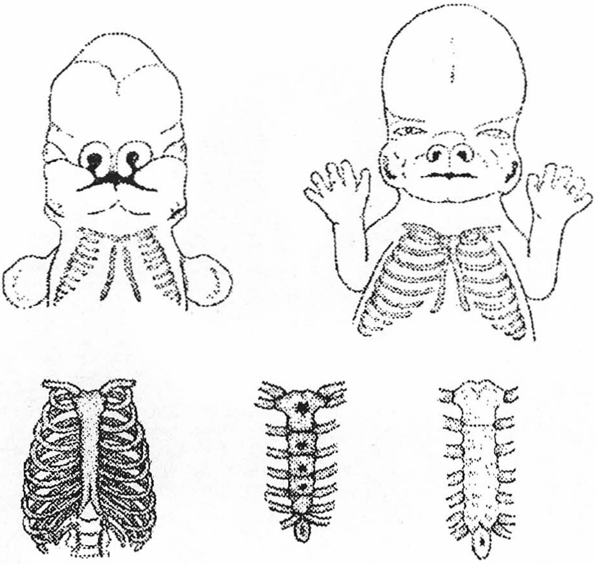

Figure 5-4. Primary ossification centers in the sternum during weeks eight through nine. (Reprinted with permission from Patten, 1968)

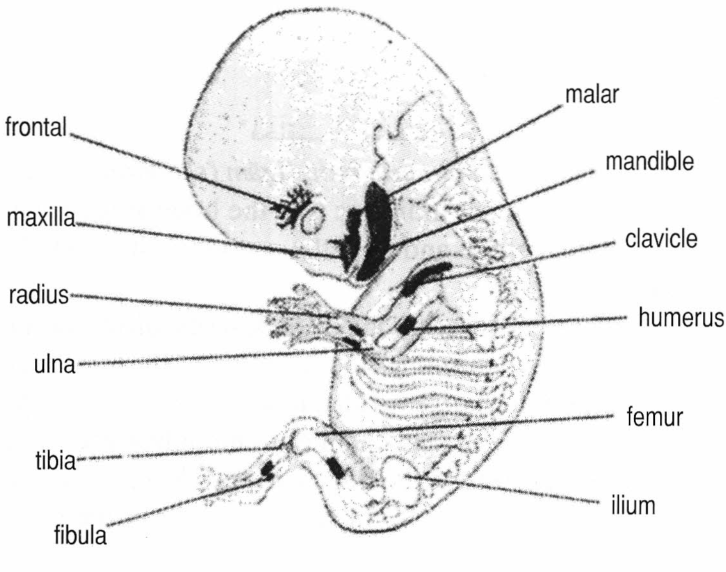

Figure 5-5. Primary ossification centers in the maxilla during weeks eight through nine. (Reprinted with permission from Patten, 1968)

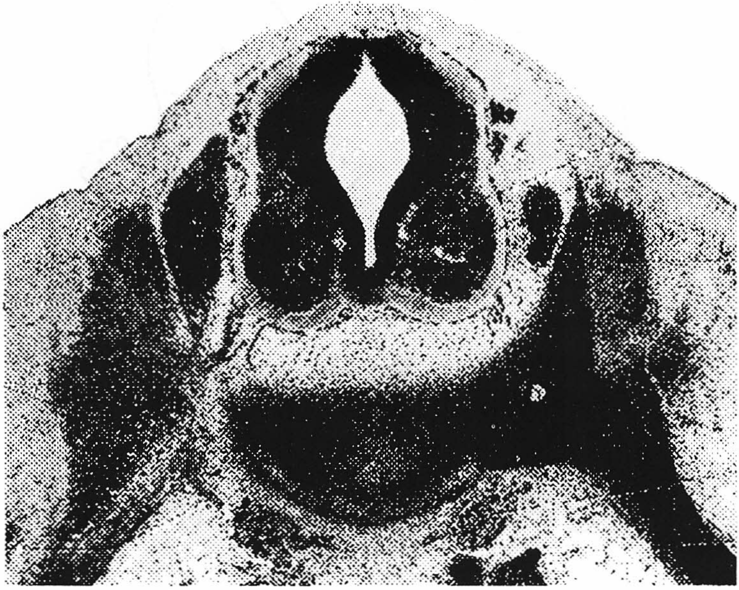

Figure 5-6. Section through 11 mm human embryo. Note precursor musculature forming adjacent to developing bone. (Reprinted with permission from Blechschmidt, 1961)

III. 'Iẓām stage.

"فَخَلَقْنَا الْمُضْغَةَ عِظَاماً"

"Then (fa) We made out of that muḍghah, 'iẓām (skeleton, bones)..."

This Qur'anic statement indicates that the bone stage is subsequent to the muḍghah stage and that the muḍghah has developed skeletal elements.

Specific terms are used in the Qur'ān to describe different stages. The shape of the embryo determines the selection of the term used for each stage, e.g. the nuṭfah changes to alaqah when it loses its drop-like appearance. Similarly, the alaqah changes to muḍghah according to a change in its shape. Therefore, the stage which follows the muḍghah is called the 'iẓām (bone) stage for the development of the skeleton spreads during this stage.

The conjunction *fa* (then) of the Qur'anic āyah indicates that the 'iẓām stage develops after the muḍghah stage without a long delay.

The mudghah stage lasts approximately until the 6th week, and the bones make their appearance by the beginning of the 7th week with the development of the cartilaginous skeleton in accordance with the ḥadīth:

«عن حُذيفة رَضى اللّهُ عَنْهُ أن رَسول اللّه صَلى اللّهُ عليه وسَلّم قال: "إذا مَرَّ بالنطفة ثنْتَان وأربعُون ليلةً بعثَ اللّهُ إليها ملكًا فصوَّرها، وخلقَ سمعَها وبصَرَها، وجلدَها، ولحمَها، وعظامَها"» (صَحيح مُسلم: كتابُ القدر)

"When 42 nights have passed from the time of the nutfah (time of conception), Allah sends an angel to it, who shapes it and makes its hearing, sight, skin, muscles and bones...." (Saḥīḥ Muslim, Kitāb Al-Qadar).

In the early part of the 'iẓām stage, the embryo takes on a human appearance (*taṣwīr ādamī*), and the ḥadīth describes this with the word of "shapes." Before the 42nd day, it is difficult to distinguish the human embryo from the embryos of many animals, but at this time it becomes clearly distinguishable in its appearance (Figure 5-7).

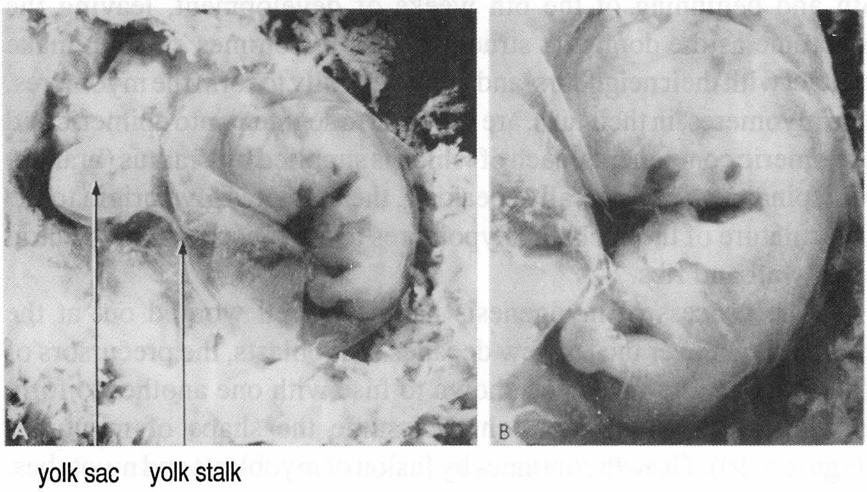

Figure 5-7. *A*, Photograph of an embryo during the 'izam stage (44 to 46 days in age) in its amniotic sac, exposed by opening the chorionic sac (x 2.7). *B*, Higher magnification of the 14 mm (crown-rump length) embryo (x 4.8). Note the human appearance (*taswir adami)* at this age. (Reproduced with permission from Moore, K.L., *The Developing Human, Clinically Oriented Embryology*, 4th ed., Philadelphia, Saunders, 1988)

Also, some of the generalized cells of the embryo begin to differentiate into various lines and modify into different functional moieties. This process results in straightening and the formation of organs necessary for viability. The body surface is becoming more even and attaining a straighter configuration at this stage, as described in the Qur'ān:

«الَّذِي خَلَقَكَ فَسَوَّاكَ فَعَدَلَكَ» (سورة الإنفطار 82: آية 7)

"Who (God) created you, then (fa) made you even and straight (sawwak) and then (fa) modified you ('addalak)" (Surah Al-Infiṭār, 82: Āyah 7).[1]

IV. Myogenesis.

Most skeletal muscle cells take origin in the somites. Hence, the musculature arises in a metameric (segmented) fashion. This segmentation is indicated in the adult body by distribution of the cutaneous nerves (Figure 5-8) and can be related back to the embryonic segments (myotomes, Figure 5-9). The sclerotomal (presumptive skeletal elements) and dermatomal (presumptive dermis of the skin) cells migrate away from the original somite region by the end of the 5th and beginning of the 6th weeks of development, leaving the myotome as the dominant structure. The myotomes expand, make contact with their neighbors, and grow ventrally to form the myomeres. The myomeres, in their turn, are destined to segment into epimeric and hypomeric components, each of which is supplied by a ramus (branch) of a spinal nerve. Generally speaking, the epimeres give origin to the musculature of the back; the hypomeres to the muscles of the ventral body wall and ribs.

The process of myogenesis has been well worked out at the cellular level over the last few decades. Myoblasts, the precursors of the muscle cells, have been shown to fuse with one another to form multinucleated complexes which assume the shape of myotubes (Figure 5-10). Growth continues by fusion of myoblasts and myotubes. During or shortly after fusion, progressive synthesis and organization of the myofilaments (actin, myosin, etc.) occur in the muscle cells (fibers). At first, the arrangement of myofilaments appears random. Gradually, the myofilaments become aligned into the bundles of

[1]See Chapter 10, "The Scientific Significance of the Qur'anic Terms"

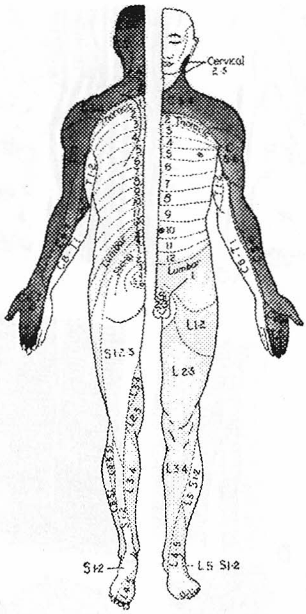

Figure 5-8. Distribution of the cutaneous nerves in the adult body indicating the metameric (segmented) fashion in which musculature formed. (Reprinted with permission from Patten, 1968)

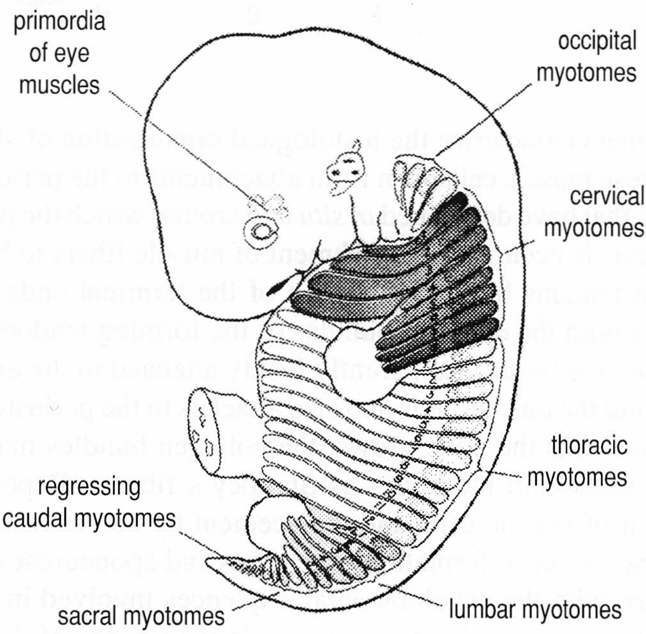

Figure 5-9. Embryonic myotomes, or segments, from which musculature arises, during the lahm stage (51 days). (Reprinted with permission from Patten, 1968)

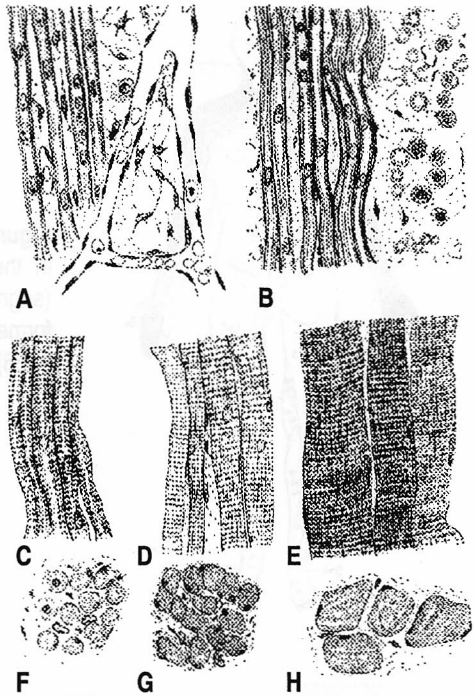

Figure 5-10. Histogenesis of muscle. Samples taken from (*A*) a 32 mm embryo; (*B*) a 45 mm embryo; (*C*) a 200 mm embryo; (*D*) a term fetus; and (*E*) an adult diaphragm. *F, G,* and *H*, Transverse sections through specimens *C, D,* and *E*. (Reprinted with permission from Patten, 1968)

myofibrils that characterize the histological organization of skeletal muscle. These muscle cells then form attachments to the periosteum of the bones that have developed *in situ* and around which the process of myogenesis is occurring. Attachment of muscle fibers to bone is mediated in tendons by interdigitation of the terminal ends of the muscle cells with the collagen bundles of the forming tendon. This dense connective tissue is apparently firmly attached to the external lamina around the muscle cells and also attaches to the periosteum of forming bone. As the bone grows, the collagen bundles may also become embedded in the bones as Sharpey's fibers. Reportedly, degeneration of muscle cells and replacement by connective tissue elements may occur in formation of tendons and aponeuroses.

Concern with the developmental sequences involved in osteogenesis and myogenesis is an occurrence in the science of developmental biology. The general sequential pattern has been summarized as follows:

"As the bones of the appendicular skeleton become differentiated, the mesoderm from which the muscles will take shape tends to aggregate in masses grouped dorsal to, or ventral to, the developing skeletal parts" (Patten, *Human Embryology*, 3rd ed., p 248, 1968).

The Qur'ān stated the fact that the embryonic bones form first, then they are clothed with flesh (muscles):

"فَكَسَوْنَا الْعِظَامَ لَحْماً"

"Then (fa) We clothed the bones with laḥm muscle, flesh)..."

V. The laḥm stage - Al-kisa' bil-laḥm (clothing the bones with flesh).

During the first forty days, the bones and flesh (muscles) do not differentiate (see Chapter 7). As the embryo forms, a new distinct stage begins which is different in appearance and structure from the preceding mudghah stage. The primordia from which the bones and muscles develop are formed before the 7th week, differentiation of the skeleton occurs first in the 7th week and differentiation of the muscles occurs next in the 8th week.

A major developmental landmark during the 8th week is the laḥm stage, which describes the myogenesis period described above, and which marks the development of definitive muscles in the trunk and limbs. Movement also begins. The muscles take their position around the bones ("clothing the bones") and continue the process of straightening and smoothing (*taswiyah*) which began in the 'iẓām stage (Figure 5-11).

During the laḥm stage, the embryo develops human features, and the various organs assume their proper positions and are better proportioned. This stage differs from the 'iẓām stage in structure, congruity, image and the embryo's ability to move. This stage begins from the end of the 7th week to the end of the 8th week and comes immediately after the 'iẓām stage.

The correct timing and sequencing of the embryonic and fetal developments are indicated not only in the order in which they are mentioned in the Qur'ān but also in the uses of the conjunctions *fa* and *thumma*. The Qur'anic text (see Introduction) uses *fa* (then) between the 'iẓām and laḥm stages to indicate a rapid sequence of events with little delay between them. The passage also indicates that the laḥm stage represents the end of the embryonic (takhlīq) stage, which is

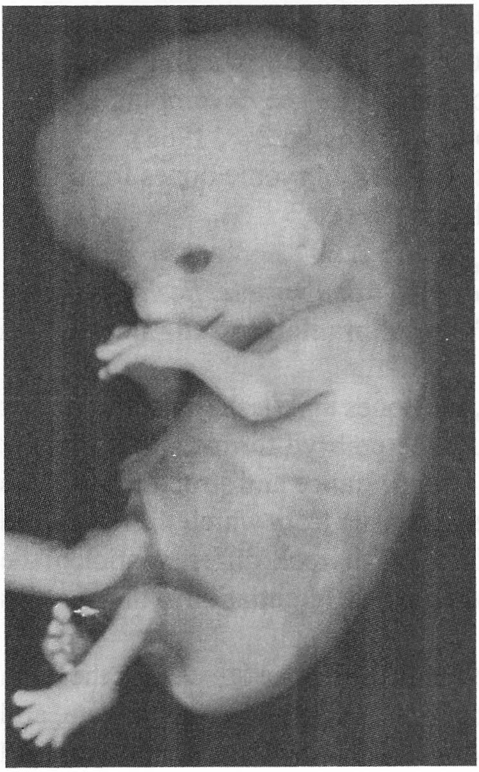

Figure 5-11. Photograph of a 29 mm (crown-rump length) embryo during the lahm stage (56 days) (x2). The intestine is still in the umbilical cord (arrow). The digits are clearly defined. The regions of the limbs are apparent, and the tail has disappeared. The smoothing and straightening (*taswiyah*) which has occurred is a result of the formation of musculature. (From Professor Jean Hay, Department of Anatomy, University of Manitoba, Winnipeg, Canada)

followed by the nash'ah (fetal) stage. The conjunction *thumma* (then) indicates a slow sequence with a time lag between these two major stages.

VI. Summary.

The use of the terms ‘iẓām (skeleton) and laḥm (muscles) clearly indicates major features of the 7th and 8th weeks respectively, which are marked by the periods of osteogenesis and myogenesis, and describe these stages in clear, unambiguous terms.

Although reference to the concept of sequential development was made by Aristotle and some others of the ancients who made many advances in this field, many of their observations were based on the development of chick embryos and did not apply to the very early development of humans. Scientists did not recognize that human development passes through various stages until the second half of the 19th century (see Chapter 1 on the historical progress of embryology).

It is to the Holy Qur'ān that one must turn for the earliest "stage-by-stage" descriptive statements on this topic. Here one can find a description of developmental events antedating by many centuries information only acquired during the lifetime of many of today's developmental biologists, and only after sophisticated instrumentation had been developed.

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BIBLIOGRAPHY

Blechschidt, E., *The Stages of Human Development before Birth*, W.B. Saunders Co., Philadelphia, 1961.

Corliss, C.E., *Patten's Human Embryology*, McGraw Hill, New York, 1976.

Fawcett, D.W., *Bloom and Fawcett's A Textbook of Histology*, 11th ed., W.B. Saunders Co., Philadelphia, 1986.

Hamilton, W.J., Boyd, J.D., and Mossman, H.W., *Human Embryology*, 3rd ed. (rev.), Williams & Wilkins, Baltimore, 1964.

Moore, K.L., *The Developing Human*, 4th ed., W.B. Saunders Co., Philadelphia, 1988.

Patten, B.M., *Human Embryology*, 3rd ed., McGraw Hill, New York, 1968.

Al-Qurṭubī, *Al-Jami' li-Aḥkām al-Qur'ān,* Dār Iḥya' at-Turāth al-'Arabī, Beirut, n.d.

Sadler, T.W., *Langman's Medical Embryology*, 5th ed., Williams & Wilkins, Baltimore, 1985.

Aṭ-Ṭabarī, *Jāmi' al-Bayān fī Tafsīr al-Qur'ān*, 3rd edition, Dār al-Ma'rifah, Beirut, 1398 A.H., 1978 A.D.

Az-Zabīdī, *Tāj al-'Arūs*, 1st edition, n.p., Cairo, 1306 A.H.