Essay title: As the only long bone that lies horizontally, the clavicles are susceptible to damage making them the weakest bone. Describe the development of the clavicle

Abstract

The process of creating bone is initiated early on in development through two unique and specific processes: endochondral and intramembranous ossification. Bone formation can normally persist for up to 25 years where it would follow either technique based on where it is and its function. The clavicles are an exception where they follow both types of formation. The processes are composed of an intricate number of cell types that work closely in unison to create the optimum environment for bone deposition and formation. Through this cycle we can see how bones become longer overtime and the methods they undertake to withstand this increase in pressure and stress. As a result, they also undergo numerous steps to grow thicker to assist further. The unique shape of the clavicle's aids in its function as an important landmark for numerous connections between other bones and points of insertion for the muscles of the upper body.

Bone formation, also known as osteogenesis, begins early on during foetal development between the sixth and seventh week and can continue up until 25 years for some individuals [1]. All of the bones of the body tend to ossify via two processes: endochondral ossification and intramembranous ossification. The location and function of the bone dictates which process to undergo for ossification [1]. The first bone to begin ossification and the last to complete this process is the clavicle [2]. Despite all bones developing through either one of these processes, the clavicle presents an interesting exception, such that its medial end undergoes endochondral ossification while its lateral end develops via intramembranous ossification [2]. Even though the formation of the clavicle has been heavily researched and backed up by evidence, we must consider its development holistically in order to appreciate how this can aid its functions in the upper limb. In light of this, this essay will introduce the types of cells involved in bone ossification and how they cooperate to promote growth to the clavicles through either process. This essay will also cover how the clavicle's grow wider as well as the overall anatomical development and the importance of these developments for the function of the clavicles.

Osteogenesis is a complex process involving the differentiation of mesenchymal stem cells (MSC) or hematopoietic stem cells into specialised cells that function to remodel bone [1]. These specialised cells consist of osteoblasts, osteocytes and osteoclasts which work to resorb old bone and replace it with new bone. Osteoblasts function as bone depositing cells which originate from MSC and form 4-6% of the total bone cells [3]. Osteoblasts release osteoid, a bone matrix which mineralises within a few days and traps osteoblasts within them. At this stage, trapped osteoblasts are able to differentiate into osteocytes, which make up 90-95% of the total bone cells [3]. Osteocytes are sensitive to mechanical strain and act as sensors to detect mechanical pressures and loads. In response, osteocytes relay these signals to osteoblasts and osteoclasts through the canaliculi, thereby regulating their activity to maintain the rate of bone deposition and resorption simultaneously [3]. Osteoclasts originate from hematopoietic stem cells and act to resorb calcified cartilage to allow bone modelling [3]. This is done through the release of protein digesting enzymes which break down the collagen fibres and the release of hydrochloric acid which dissolves bone minerals such as calcium phosphate. Initially during osteogenesis, osteoblasts will form woven bone when the osteoid is produced rapidly, which is immature bone composed of irregular bundles of collagen fibres with large and numerous osteocytes [4]. Woven bone is replaced gradually during bone remodelling into mature lamellar bone which consists of regular parallel rings of collagen fibres with hydroxyapatite crystals added onto them for bone strength [4]. Bone is composed of two different types depending on the location to provide strength as well as a location to store bone marrow. Cortical bone is a thick and dense layer of calcified tissue found on the external parts of the bone, as shown on fig.1. Its thickness and calcification aid with providing mechanical and protective support. Cancellous bone is a thin, porous layer of tissue found internally towards the mid region of bone. It is not as calcified as cortical bone as it carries a differential role of housing bone marrow, blood vessels and connective tissue [4]. As a result, cancellous bone is mainly responsible for metabolic functions such as erythrocyte and leukocyte production [4]. To be able to grasp how these processes occur within the clavicle in greater detail we must consider how the clavicle develops via endochondral ossification.

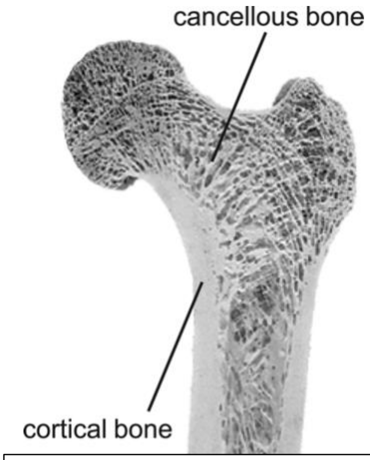

Figure 1 (fig.1): Image of a transverse section of a femur bone, displaying the cortical and cancellous bone [5]

As previously mentioned, bones tend to ossify through endochondral or intramembranous ossification. Both processes are initiated with a mesenchymal tissue precursor, yet they differ when concerning how the precursor transforms into bone [1]. On one end, endochondral ossification utilises a cartilage intermediate which is later replaced by bone while on the other, intramembranous ossification converts the precursor into bone without the need of a cartilage intermediate [1]. In the medial aspect of the clavicle, mesenchymal cells differentiate into chondrocytes which proliferate and secrete an extracellular matrix to create the cartilage model, which is surrounded by the perichondrium [1]. Chondrocytes close to the cartilage model centre undergo hypertrophy adding onto the matrix and altering it to allow calcification [1]. Calcification will prevent nutrients from reaching these chondrocytes resulting in apoptosis. This allows blood vessels to invade the spaces formed from apoptosis, increasing the size of the spaces as a result and eventually forming the medullary cavity [1]. These blood vessels also bring in osteogenic cells and transform the perichondrium to the periosteum, thereby providing the area with osteoblasts which forms the periosteal collar. This region forms the primary ossification centre, where cartilage starts to get replaced with bone [1]. While this process is occurring, chondrocytes continue to proliferate allowing longitudinal growth of the clavicles [1]. The areas that provide longitudinal growth later become the epiphyseal growth plates which continue to provide growth even during adulthood. It is important to note that after birth, endochondral ossification repeats in the epiphyseal region to form the secondary ossification centre which allows for bone growth as we age [1]. While endochondral ossification is forming the medial aspect of the clavicle, the lateral end is undergoing intramembranous ossification to form the remainder of the clavicle and due to this, it is imperative to look into this other process in greater detail to understand the overall development of the clavicles.

During the development of the clavicles, we recognised the steps taken during endochondral ossification and the formation of the medial aspect. In the lateral aspect of the clavicles, mesenchymal cells differentiate into osteoblasts which cluster to form an ossification centre [1]. Osteoblasts will release osteoid which will bind calcium to mineralise and trap osteoblasts within the osteoid. As previously mentioned, at this stage this entrapment results in the formation of osteocytes from these osteoblasts. While this is occurring, osteoid is being continuously secreted by osteoblasts to surround blood vessels in order to produce cancellous bone [1]. These blood vessels will go on to form the red bone marrow that is stored within the cancellous bone [1]. Mesenchymal cells on the bone surface form the periosteum which contains cells on the inner surface that differentiate into osteoblasts to secrete osteoid in multiple layers, parallel to the original existing matrix [1]. This is done in order to produce cortical bone. While the clavicle is growing longitudinally through both types of ossification, it is important to recognise how the clavicle's grow wider and what process is occurring simultaneously to produce thicker clavicles to accommodate for increases in length.

While the clavicles are growing longer, they must also increase in thickness to respond to stress generated from an increase in activity or weight. It is important to consider that this increased thickness must be carefully controlled to prevent bones from becoming too heavy and dense which would impede the effectiveness of bones in performing their protective, supportive and motor functions [6]. The clavicles as well as the bones around the body achieve this growth via appositional growth. During appositional growth, osteogenic cells found in the periosteum differentiate into osteoblasts to form new bone matrix [7]. Bone ridges form on either side of the periosteal vessel and fuse together, enclosing the blood vessels within a haversian canal. Inside the haversian canal, the periosteum is converted to an endosteum and with the help of osteoblasts, lamellar bone is made which fills the haversian canal [7]. While bone is being deposited osteoclasts are working simultaneously to maintain the thickness of cortical bone, and this is done through the removal of old bone lining the medullary cavity [8]. This allows the bone to increase in diameter through an increase in the diameters of the diaphysis and the medullary cavity [8]. The importance of regulating the activity of osteoblasts and osteoclasts during this process becomes apparent since an error can lead to an increase in bone deposition or resorption being made for the bone in question, reducing its overall effectiveness as previously mentioned. During the development of the clavicles, several projections are formed to serve as articulations and important landmarks. Viewing these projections and the clavicle’s overall shape will aid in reinforcing our understanding on the clavicle’s development as well as the functions it serves throughout the body.

Once developed the clavicle is a sigmoid-shaped long bone, as shown on fig.2, that forms the pectoral girdle alongside the scapula [2]. Medially the clavicles articulate with the manubrium of the sternum to form a synovial saddle sternoclavicular (SC) joint [2]. On the lateral end the clavicles articulate with the acromion of the scapula to form a synovial plane acromioclavicular joint [2]. In order to determine the locations for muscle attachment, the shaft of the clavicle is divided into a medial two-thirds and a lateral third. The sternocleidomastoid (SCM) and subclavius muscle attach onto the medial two-thirds superiorly and inferiorly respectively [2]. The subclavius muscle lays along the subclavian groove which can be viewed inferiorly according to fig.2. The anterior aspect of the medial two-thirds provides attachments for the pectoralis major whereas the sternohyoid muscle can be found attached onto the posterior aspect [2]. The costal tuberosity can be seen as an impression for the costoclavicular ligament to insert onto and support the SC joint. Looking at the lateral third, the deltoid and trapezius muscles are found to attach onto the anterior and posterior surfaces respectively [2]. When viewing the clavicles inferiorly on fig.2 you can view the conoid and deltoid tubercles as well as the trapezoid line. The conoid ligament attaches onto the conoid tubercle while the deltoid muscle attaches onto the deltoid tubercle [9]. The trapezoid line serves as a point of attachment for the trapezoid ligament [9]. As a result of the sigmoidal shape of the clavicles as well as all the attachment points it provides for muscles, a great degree of motion is exhibited around the glenohumeral joint which is unimpeded with the assistance of the clavicle’s positioning [2]. It is also important to consider the protective functions the clavicles serve, as their anatomical location protects neurovascular structures which include the brachial plexus, subclavian artery and vein [2]. This emphasises the importance of the clavicle’s positioning as morbidity would increase as a consequence of having one of those structures disrupted.

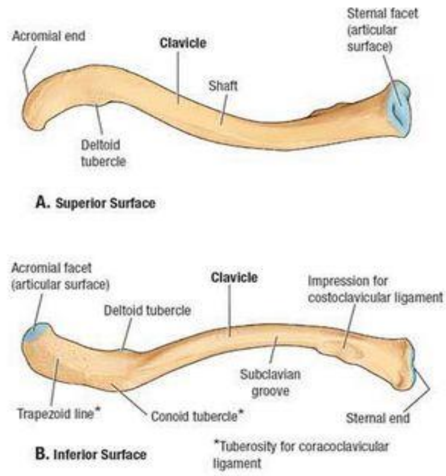

Figure 2 (fig.2) Labelled image of a clavicle viewed from the superior and inferior surfaces [10].

The development of any bone is a long and complex task. It involves numerous processes as well as types of cells working in unison to initiate the formation of immature woven bone, which eventually is replaced with mature lamellar bone. Looking back at the mentioned points, because of the extensive research and evidence already available, our understanding of the development of the clavicles was strengthened and elaborated, in that it stood out from the remaining bones due to its nature of growing through endochondral and intramembranous ossification. Furthermore, the importance of the clavicles as a point of muscle and ligament attachment was shown which is essential for a magnitude of movements in the upper limb, such as humerus and head flexion. Despite the evidence we currently have for the development of the clavicles, it is important to continue the conversation in order to truly appreciate the clavicle’s use in overall mobility and protection in the upper extremities

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