THE HISTOPATHOLOGICAL CHARACTERISTICS OF THE SKIN IN CONGENITAL IDIOPATHIC CLUBFOOT

BY

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submitted in partial fulfillment of

the requirements for the degree

PhD

in the Department of Orthopaedics

Faculty of Medicine

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This thesis is dedicated to:

All the children who participated in this study

PREFACE

This study was undertaken in the Departments of Orthopaedics and Anatomical Pathology at the King Edward VIII Hospital and Inkosi Albert Luthuli Central Hospital respectively.
The study was supervised by Prof. S. Govender and Prof. P. K. Ramdial.
The study represents the original work of the author and has not been submitted in any other form to another university.

M. N. Rasool

ABSTRACT

Purpose:

To highlight the histopathological characteristics of the skin in congenital clubfoot and correlate the clinical findings in clubfoot with the changes in the dermal layers.

Materials and methods:

One hundred skin specimens, from 77 infants (6 to 12 months), were studied between 2004 and 2008. Using the Pirani scoring system, the clinical severity was recorded. The mobility of the skin and the correctability of the medial ray were assessed clinically. A skin specimen (1cm x 1mm) was taken from the medial side of the foot at surgery following failed plaster treatment. The layers were studied under light microscopy. The thickness of the dermis and the histopathological features of clubfoot skin were compared with 10 normal skin specimens.

Results:

The dermis of clubfoot skin showed significant fibrosis with thick bundles of collagen fibres (P = .001) on Haematoxylin and Eosin staining (H&E). The dermal thickness ranged between 1.0mm and 5.2mm in clubfoot skin, compared with controls (0.64-1.28mm). Fibrosis extended into the subcutis in a septolobular fashion in 95% of the cases. Significant atrophy of eccrine glands was seen in 98% (P = .001). Hair follicles were absent in 78%. The elastic fibres of clubfoot skin, stained with Elastic van Gieson staining (EVG), showed hypertrophy in varying degrees in all skin specimens. They were fragmented, with loss of their parallel arrangement. There was no significant inflammatory reaction in the dermis. The Pirani score was significantly increased (mean 7.8).

Discussion:

Fibrosis and thickening of the dermis were the most significant histopathological features of the clubfoot skin. The elastic fibres were also abnormal. There was atrophy of the skin appendages due to the fibrosis. There was a strong correlation between the Pirani score and the severity of the deformity(P 0.016). The cases with poor outcome had a higher score than those with a satisfactory outcome.Lack of a significant inflammatory reaction suggests that neither the serial manipulations of the foot, nor the repeated plaster cast changes, were responsible for the dermal fibrosis, which is probably present from birth and contributes to the deformity.

PRESENTATIONS AT SCIENTIFIC MEETINGS

1. Foot Deformities and Occult Spinal Abnormalities. South African Orthopaedic Association Congress. Pretoria, September 1989

2. Clubfoot – a Spectrum of Associated Clinical Manifestations. South African Orthopaedic Association Congress. Cape Town, September 1992

3. The Outcome of Surgical Treatment of Congenital Idiopathic Clubfoot. South African Orthopaedic Association Congress. Cape Town, September 2007

4. The Histopathological Characteristics of the Skin in Idiopathic Congenital Clubfoot. South African Orthopaedic Association Congress. Port Elizabeth, September 2010

PUBLICATIONS

1. Foot Deformities and Occult Spinal Abnormalities in Children. J Paed Orthop 1992; 12: 94 - 99

2. Clubfoot – a Spectrum of Associated Clinical Manifestations. (Abstract) J Bone Joint Surg 1993; 75B: P78

3. Foot Deformities and Occult Spinal Abnormalities. (Abstract) J Bone Joint Surg 1993; 75B: P79

4. Foot Abnormalities Associated with Occult Deformities of the Neural Axis in Children. South African Journal of Orthopaedic Surgery 2004; 3: 37 – 46

5. Congenital Clubfoot – Aetiology and Classification. The Specialist Forum 2008; 8: 35 – 38

6. Congenital Clubfoot – Treatment. The Specialist Forum 2010; 10: 12 – 14

ACKNOWLEDGEMENTS

I would like toexpress my sincere thanks and gratitude to the following people for their contribution to this thesis:

My supervisors, Prof. S. Govender (Head of Dept. of Orthopaedics) and Prof. P. K. Ramdial (Head of Dept. of Anatomical Pathology) for their high standard of supervision and invaluable guidance.
Tonya Esterhuisen and Stephan van der Linde from University of KZN, for providing the statistical analysis.
The registrars that rotated through the Paediatric Orthopaedic Unit at King Edward VIII Hospital.
The medical managers of King Edward VIII Hospital.
The technical and secretarial staff of the Dept. of Anatomical Pathology at Inkosi Albert Luthuli Central Hospital.
The secretarial staff of the Dept. of Orthopaedics at University of KZN Medical School.
Rashidah Rasool and Yumna Rasool for preparing the manuscript.

ETHICAL APPROVAL

Ethical approval for the study was obtained from the University of Kwa-Zulu Natal in August 2003. Permission was granted for specimen and data collection by the management of King Edward VIII Hospital.

MEMORANDUM

To : Professor S Govender
Orthopaedic Surgery
Nelson R Mandela School of Medicine

From : Professor J Moodley
Chairman : Research Ethics Committee
Nelson R Mandela School of Medicine

5 August 2003

PROTOCOL : Histopathological characteristics of the skin in severe club foot deformities in children. M N Rasool, Orthopaedic Surgery. Ref.: H181/02.

The Research Ethics Committee and the Higher Degrees Committee considered the abovementioned application and made various recommendations. These recommendations have been addressed and the protocol was approved by consensus at a full sitting of the Research Ethics Committee at its meeting held on 5 August 2003.

PROFESSOR J MOODLEY
Chairman : Research Ethics Committee

c.c. Dr M N Rasool, Orthopaedic Surgery
Mrs L Adendorff, Postgraduate Education

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CHAPTER 1

1.1 INTRODUCTION

Congenital talipes equinovarus (CTEV), or clubfoot, is a complex three dimensional deformity consisting of four components: equinus, varus, adductus and cavus.

Although substantial progress has been made in the understanding of the deformity, there are divergent opinions regarding the aetiology, pathogenesis, treatment and prognosis. This may be attributed to the indiscriminate use of the all-inclusive term “congenital clubfoot” to describe all equinovarus deformities.

Many conditions can produce a clubfoot deformity with similar structural changes. At birth, congenital foot deformities may appear similar to each other, irrespective of the aetiology. A clubfoot deformity may be acquired after birth due to muscle imbalance as in cerebral palsy, poliomyelitis and muscular dystrophy. The presentation of clubfoot is variable, even amongst the so called idiopathic deformities. The treatment of clubfoot continues to provide a significant challenge to the orthopaedic surgeon. The goal of treatment is to ensure a supple, plantigrade and painless foot suitable for comfortable shoe wear and function. Extensive work has been done on the causes of idiopathic clubfoot. There is still debate regarding the aetiology.

1.2 HISTORICAL BACKGROUND OF CLUBFOOT TREATMENT

The earliest documentation of clubfoot comes from the ancient Egyptians. Paintings on the walls of their ancient tombs depict the clubfoot deformity, and a statue of a diastrophic dwarf with a clubfoot can be found in the Tutankhamen collection [1].

Hippocrates first described the clubfoot deformity around 300 BC.
Arcaeus, Pare and Fabrig in the 17th century recommended repeated stretching of the deformity with a turnbuckle [1].
Chelselden in the 18th century utilized repeated stretching and bandaging to maintain the correction. Scarpa, in 1803, described the pathologic anatomy as a "twisting of the scaphoid, os calcis and cuboid around the astragalus" and called it a "congeGuerin nital dislocation of the astragalo scaphoid complex". He devised an apparatus with springs to stretch the contractures [1].

Subcutaneous tenotomy of the tendoachilles was performed by Lorenz in Frankfort in 1782, and in 1823 by Delpech of France. Stromeyer, in 1831, popularized subcutaneous tenotomy in Germany.In 1838, Guerin reported on the use of plaster of Paris in the treatment of clubfoot. Little performed subcutaneous tenotomy in England in 1839 [1].
In 1857, Guerin performed the first bony operation on clubfoot by removing a part of the cuboid. This procedure was a precursor to calcaneocuboid wedge resection in clubfoot [1].
In 1872, Lund performed the first recorded talectomy for clubfoot. Hugh Thomas devised the Thomas' wrench, towards the latter part of the 19th century, to forcibly manipulate and correct the clubfoot deformity. After manipulation a splint was applied to hold the correction. The method was regarded as brutal and was discontinued [1].

Phelps in 1890, described a one stage medial release with lengthening of the tendons. He also added an osteotomy of the neck of the talus with wedge

resection of the calcaneus. Between 1890 and 1937, osteotomy of the neck of the talus was popularized to correct the clubfoot deformity. However, this operation lost popularity due to avascular necrosis of the head of the talus [1].
Hiram Kite popularized non-operative treatment with serial manipulations and plaster cast immobilization [2].
Denis Browne advised forceful manipulations before application of his splint [3]. This method has fallen into disrepute, as it caused joint stiffness and bony deformities. McCauley stressed the radio-graphic evaluation of the results of treatment [4]. Bost emphasized the importance of releasing the contracted plantar structures [5]. The one-stage posteromedial release of clubfoot, popularized by Turco, still remains a standard procedure practised by most surgeons [1].

Currently, there is agreement that non operative treatment should be attempted prior to surgery. In recent years, the Ponseti method of manipulation and casting in the treatment of clubfoot has gained popularity worldwide [6]. The multiplicity of operations and methods of treatment are evidence that the correction of clubfoot is still an unsolved problem.

1.3 INCIDENCE

Worldwide, approximately 100, 000 children are born with clubfoot deformity each year. The reported incidence of idiopathic congenital talipes equinovarus ranges from 0.64 to 6.8 per 1000 live births [7, 8]. The reported incidence in whites generally, is approximately 1 per 1000 [7]. In the United States, the incidence is reported as 2.57 per 1000 live births [7]. In India, it is 0.9 per 1000 [9]. It is higher in the Hungarian Gypsies: 3.41 per 1000 live births [10]. The highest incidence was reported in East and Central Africa and in Polynesia [11]. Ching found that the incidence amongst Hawaiian patients was 6.8 per 1000 live births [12]. The incidence amongst South African Blacks is 3.5 per 1000 [13]. Beals studied 50 Maori families and found an incidence of 6.5 to 7.0 [14]. In Zambia, 500 children are born yearly with clubfoot [15].

1.4 THE NORMAL ANATOMY OF THE CHILD'S FOOT

1.4.1 The skeletal components

The skeletal components of the ankle and foot include the distal tibia and fibula, the tarsal and metatarsal bones, and the phalanges. The tibia contributes to the inferior surface, and the surface of the medial malleolus articulates with the trochlea tali. The enlarged lateral malleolus has a medial facet for articulation with the talus [1, 10, 15, 16].

There are seven tarsal bones which form the heel and the posterior portion of the foot. The calcaneus is the heel bone and is located beneath the talus. The calcaneus is the largest tarsal bone and its superior surface articulates with the talus by posterior and middle talocalcaneal joints which are separated by the sulcus calcanei containing the interosseous ligament (Fig 1(a), Fig 1(b)). The sustentaculum tali bears the middle articular joint. The posterior aspect of the calcaneus has a specially roughened area on its superior surface for the attachment of the tendoachilles. The talus is composed of the body, head and neck (Fig 2). The superior and lateral articular surfaces of the body form the trochlea tali, which articulates with the medial and lateral malleolus, and has a large convex articular surface for articulation with the inferior surface of the tibia. The head of the talus articulates with the navicular bone in front. The cuboid lies in front of the calcaneus. The three cuneiforms lie distal to the navicular and medial to the cuboid. The cuneiforms are wedge-shaped and articulate with the three medial metatarsal bones. The medial surface of the navicular has a tuberosity for the insertion of the major portion of the tibialis posterior tendon.
The cuboid lies between the calcaneus and the fourth and fifth metatarsals. Laterally and inferiorly, the cuboid tuberosity has a sulcus for the tendon of the peroneus longus muscle (Fig. 3a, 3b).

The only tendons attached to the bones of the midfoot are the tibialis posterior to the navicular and medial cuneiform, and the tibialis anterior to the medial cuneiform.

The metatarsals form the skeleton of the anterior part of the foot and consist of a base, shaft and head. The bases are firmly bound to the tarsi by ligaments at the tarsometatarsal joints. The phalanges contribute little to the length of the foot, and represent a miniature long bone.

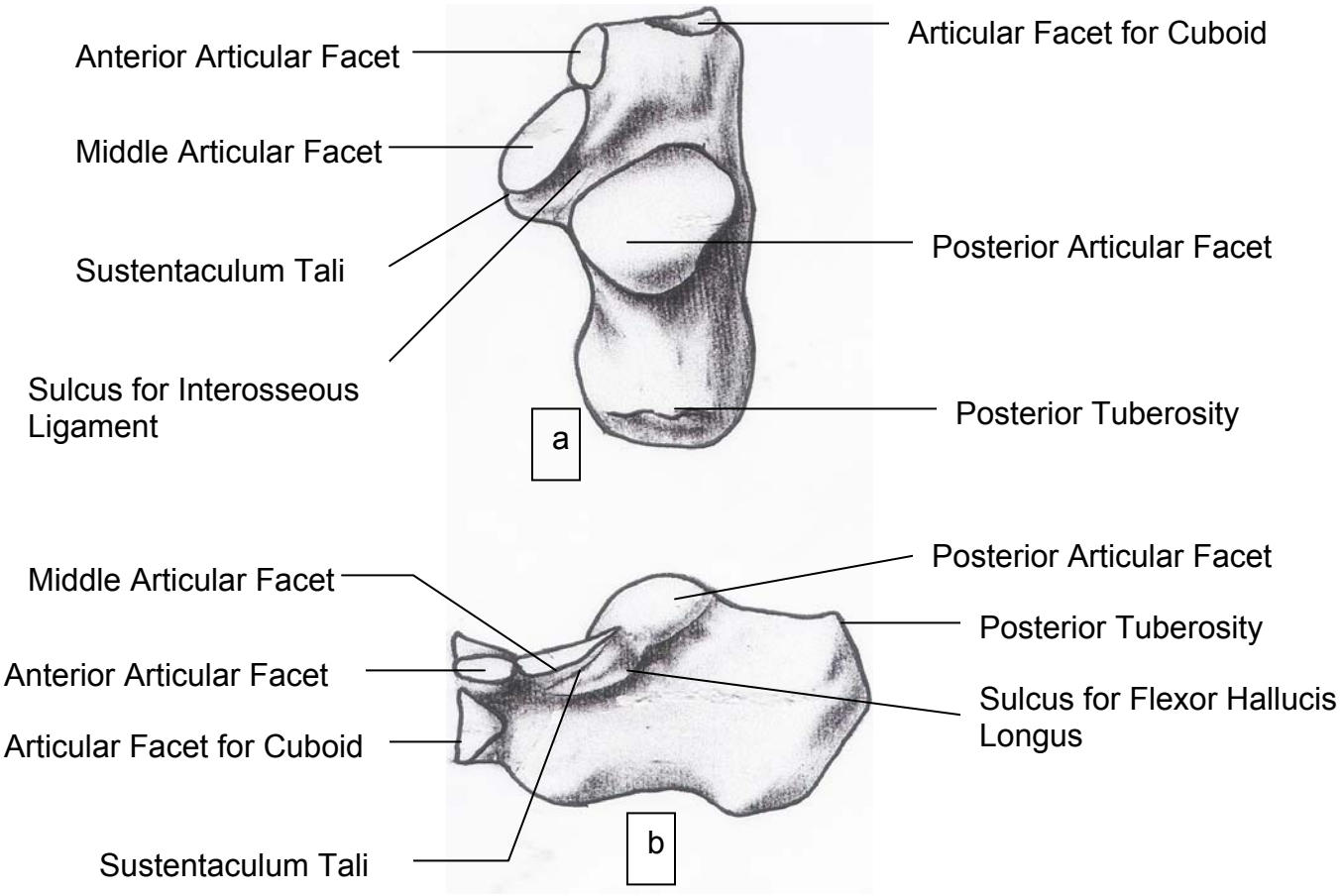


Fig. 1a Right Calcaneus – superior surface showing articular facets for the talus and cuboid
Fig. 1b Right Calcaneus – medial surface showing articular facets for the talus and cuboid

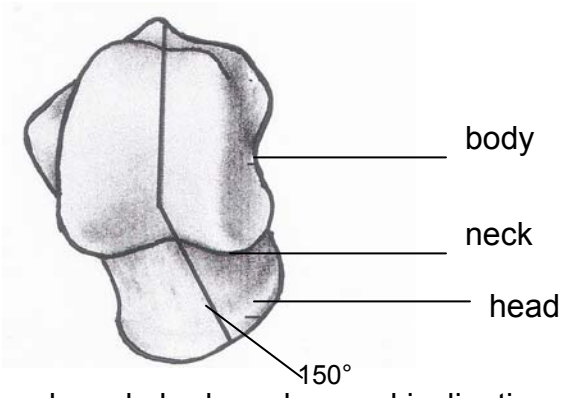


Fig. 2: Right Talus – Showing head, neck, body and normal inclination

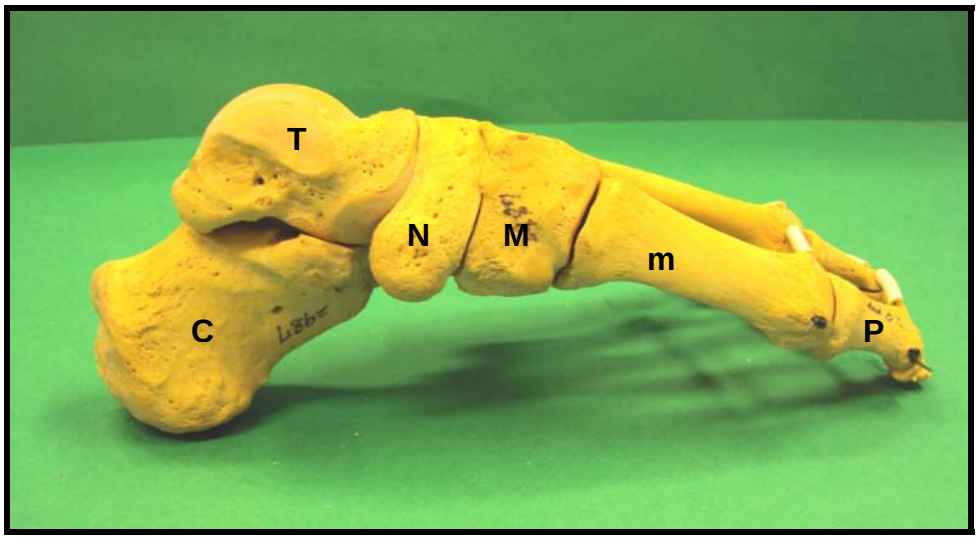


Fig. 3a Medial surface of the articulated foot

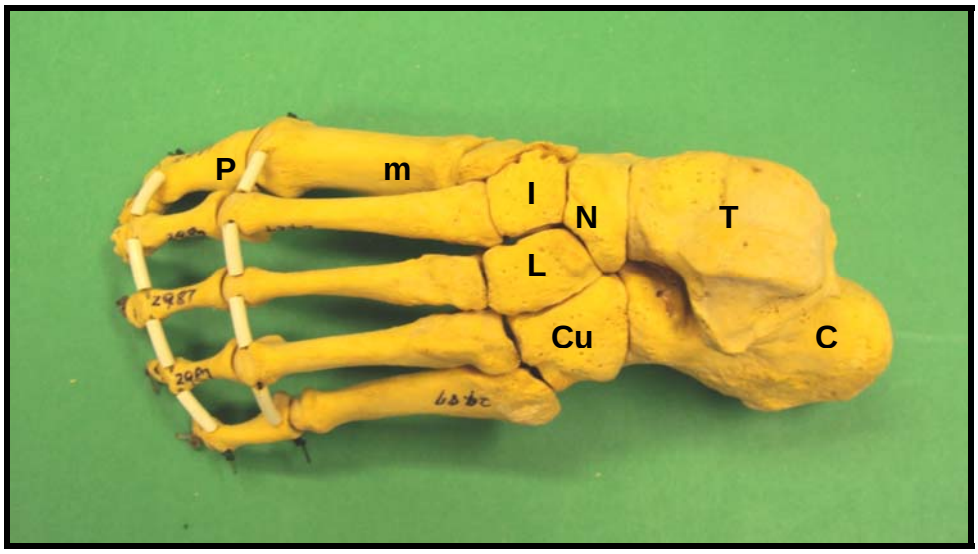


Fig. 3b Dorsal surface of the articulated foot

Key:

T = Talus
C = Calcaneus
N = Navicular
Cu = Cuboid
m = Metatarsal
P = Phalanx
M = Medial Cuneiform
I = Intermediate Cuneiform
L = Lateral Cuneiform

There are two columns in the foot (Fig 3a, 3b):

I. Medial column consisting of the talus, navicular, medial, intermediate and lateral cuneiforms, the 1st, 2nd and 3rd metatarsals.
II. Lateral column consisting of calcaneum, cuboid, 4th and 5th metatarsals.

Both lateral and medial columns are affected in clubfoot – the lateral column is lengthened and the medial is comparatively shortened.

1.4.2 The joints of the foot and ankle

1.4.2.1 The tibiotalar joint (ankle joint)

The trochlea of the talus forms a tenon wedged in a mortise formed by the lower tibia and the medial and lateral malleoli. The tibia and fibula are firmly bound by the tibio-fibular interosseous ligaments. Additional stability to the bony mortise is provided by the medial and lateral ligaments of the ankle joint. Dorsiflexion and plantar flexion occur at this joint.

In plantar flexion, the anterior part of the body of the talus is out of the mortise. Consequently, secondary changes in the shape of the talus can develop in the growing infant when the equinus deformity is severe and prolonged as in clubfoot. The ligaments of the ankle are the deltoid ligament medially and the three lateral ligaments. The deltoid is a strong, dense, fan-shaped ligament which arises from the medial malleolus and consists of a superficial and deep component. The superficial part has three components that each run from the tibia to the navicular, the spring ligament and the calcaneus. The deep part inserts on the neck and the medial surface of the body of the talus. The posterior capsule of the ankle joint can be considered an extension of the deep deltoid.

The three lateral ligaments radiate from the fibula as the anterior talofibular ligament to the neck of the talus, the calcaneofibular ligament runs vertically down to insert on the calcaneus, and the posterior talofibular ligament runs horizontally to insert on the posterior body of the talus.

1.4.2.2 Subtalar joint

The talus articulates with the calcaneus below, forming the talocalcaneal (subtalar) joint. Movements of inversion and eversion occur at this joint. The subtalar joint is divided into two separate compartments. The talocalcaneal interosseous ligament divides the joint into anterior and posterior subtalar joints. The ligament binds the talus and calcaneus together.

The posterior joint is a saddle-shaped facet formed by the concave posterior facet under the body of the talus resting on the convex posterior facet of the calcaneus. The middle and anterior talocalcaneal articulations between the head and neck above and the anterior end of the calcaneus below, are included in the anterior talocalcaneal joint.

1.4.2.3 The midtarsal joints

These consist of two articulations: the talonavicular and the calcaneocuboid joints. The talonavicular is a ball and socket joint and is the most mobile of the midtarsal joints. The calcaneocuboid joint is a gliding joint and has limited motion.

1.4.2.4 The naviculocuneiform joints

Very little gliding motion occurs at these joints. The first metatarsal articulates only with the medial cuneiform, has weak ligamentous attachments and is more mobile than the four lateral metatarsals. They are attached to each other and to the tarsal bones by strong ligaments and interlocking joints allowing minimal gliding.

1.4.2.5 The talocalcaneonavicular joint

This joint is involved in the patho mechanics of all hindfoot and midfoot deformities. It is a complex articulation which involves the talar head, the anterior end of the calcaneus, the navicular, the plantar calcaneonavicular ligament (spring ligament), and the anterior subtalar and midtarsal joints (Fig 4). The talocalcaneonavicular joint has the configuration of a ball and socket joint. The acetabulum for the round head of the talus is formed by the posterior concave surfaces of the navicular, the middle and anterior facets of the anterior part of the

calcaneus, and the spring ligament. The spring ligament bridges the interval between the navicular and the sustentaculum tali. It has a fibrocartilaginous central part that supports the talar head.

The socket of the talar head is supplemented by fibroelastic tissues as follows: dorsomedially, the talonavicular capsule, the deltoid ligament, and the tendon of tibialis posterior; subtalarly, the spring ligament; laterally, the calcaneonavicular portion of the bifurcated or Y ligament; and posteriorly, the talocalcaneal interosseous ligament.

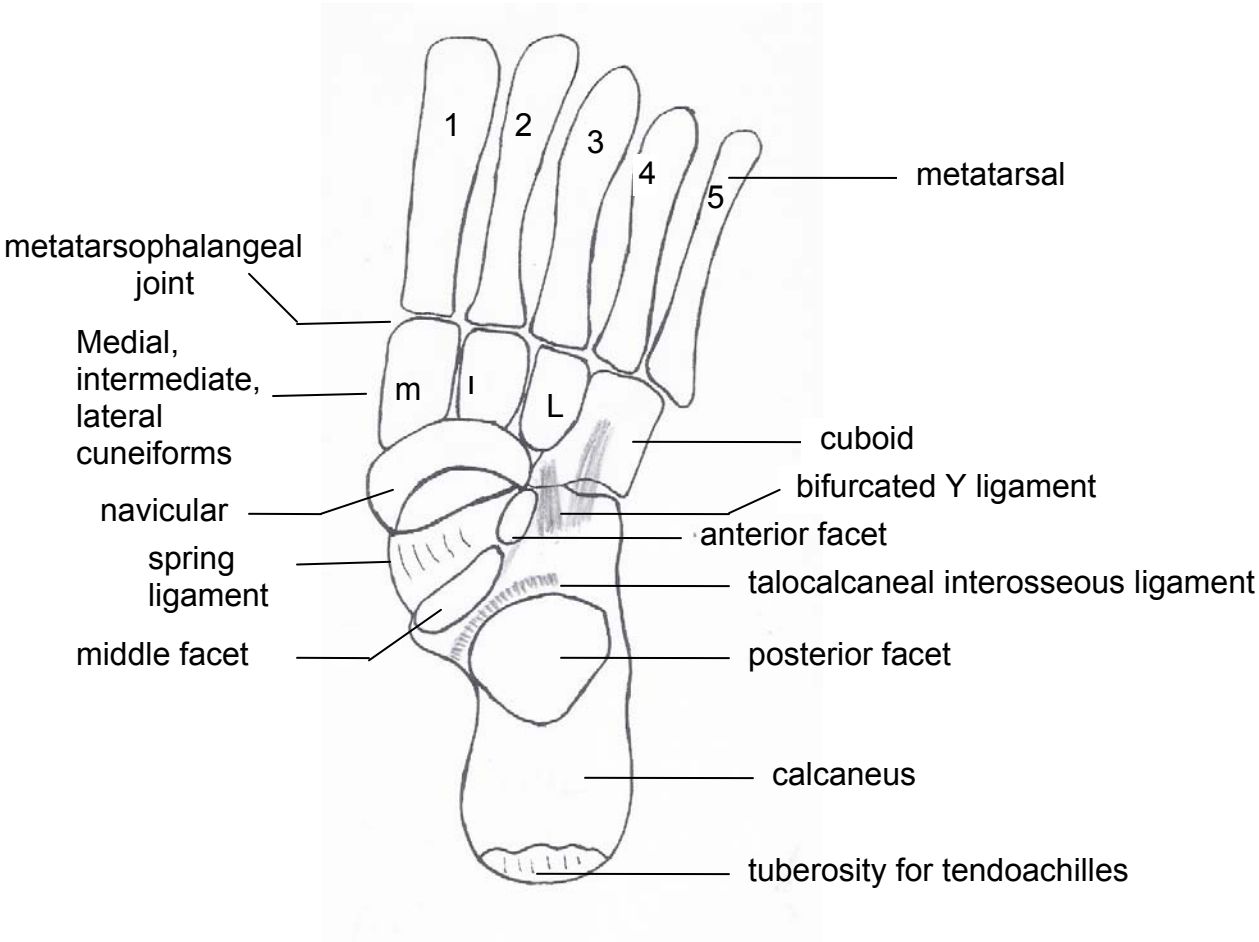


Fig. 4: Diagram showing the arrangements of the tarsal articulations and the talocalcaneonavicular socket - socket for the head of the talus; formed by the navicular, calcaneal facets and the plantar calcaneonavicular (spring) ligament. It has the configuration of a ball and socket joint.

1.4.3 The muscles of the lower leg and foot

These muscles are divided into two groups: extrinsic and intrinsic.

1.4.3.1 The extrinsic muscles

The gastrocnemius and soleus form the triceps surae; the common tendon, the tendoachilles, inserts on the posterior tuberosity of the calcaneus.
The three deep posterior muscles are the flexor digitorum longus, tibialis posterior and flexor hallucis longus. These muscles plantarflex and invert the foot. The tibialis posterior is an important muscle in clubfoot deformity. It is primarily inserted on the tuberosity of the navicular, and also gives off fibrous expansions that insert on the sustentaculum tali of the calcaneus, the adjacent cuneiforms, the firstmetatarsal and the spring ligament. The tibialis anterior muscle inserts on the medial cuneiform and on the base of the first metatarsal. It dorsiflexes and inverts the foot. The extensor digitorum longus and hallucis longus extend the toes.

The peroneus longus and peroneus brevis tendons pass behind the lateral malleolus; the brevis attaches to the base of the fifth metatarsal, and the longus runs across the sole of the foot to attach to the base of the first metatarsal. The peronei evert the foot.

1.4.3.2 The intrinsic muscles

These are the abductor hallucis, flexor digitorum brevis, abductor digiti minimi, interossei and flexor accessorius. The abductor hallucis is the longest muscle in this group and lies along the medial border of the foot. It inserts onto the medial side of the proximal phalanx of the big toe. The plantar aponeurosis is a strong superficial ligament that extends from the os calcis to the toes. The central part of the aponeurosis is stronger and thicker than the medial part which covers the undersurface of the abductor hallucis.

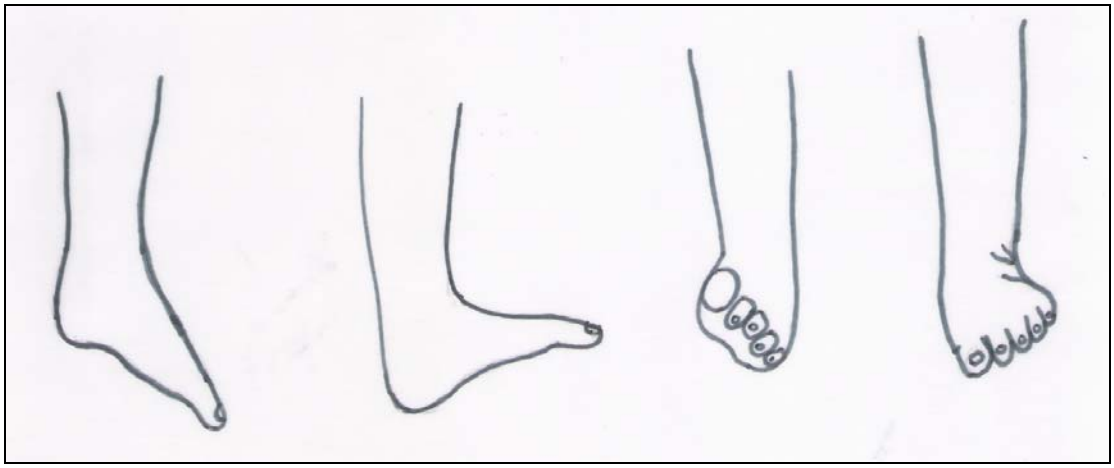
Table 1

DEFINITIONS IN MOVEMENTS OF THE FOOT AND ANKLE	
Adduction	the foot moves towards the median plane of the body
Abduction	the foot moves away from the median plane of the body
Flexion	the foot moves in the plantar direction (plantarflexion)
Extension	the foot moves in a dorsal direction (dorsiflexion)
Inversion	the plantar surface of the foot moves towards the median plane of the body. The sole is directed medially.
Eversion	the plantar surface of the foot moves away from the median plane of the body. The sole is directed laterally.
Supination	the combined movements of adduction, flexion and inversion
Pronation	the combined movements of abduction, extension and eversion
Heel varus	results from movements of inversion and adduction of the calcaneus
Heel valgus	results from movements of eversion and abduction of the calcaneus
Equinus	an increase of the plantar flexion of the foot
Calcaneus	an increase in dorsiflexion of the foot
Cavus	an increase in the height of the medial arch of the foot
Planus	a decrease in the height of the medial arch of the foot (flatfoot)

1.5 MOVEMENTS OF THE FOOT AND ANKLE

Dorsiflexion and plantarflexion are movements of the foot that occur at the tibiotalar joint (Fig. 5). Dorsiflexion (upward movement) is accompanied by pronation and abduction of the foot. In plantarflexion (downward movement), the foot supinates. It is a combination of equinus, inversion and adduction. Full dorsiflexion and plantarflexion are not possible without motion in the talocalcaneonavicular complex. In eversion, the foot is abducted and pronated. In

inversion, the normal foot is adducted and supinated. The movements of inversion and eversion take place in the subtalar joint. Adduction and abduction of the forefoot are horizontal motions which occur at the navicular cuneiformmetatarsal joints.



Plantarflexion Dorsiflexion Inversion Eversion

Figure 5: Movements of the left foot

1.6 NORMAL HISTOLOGY OF THE SKIN

Knowledge of the normal histology of the skin is central to an understanding of cutaneous pathology. The skin has three main layers (Fig. 6): [17, 18, 19]

I. an outer keratinizing stratified squamous epithelium which is self-regenerating – the epidermis
II. an underlying tough, supporting and nourishing layer of fibroelastic tissue – the dermis
III. a variable deep layer, mainly adipose tissue – the hypodermis or subcutis (subcutaneous layer).

In addition, there are specialized epithelial appendages such as sweat glands, hair follicles and sebaceous glands, which arise as downgrowths into the dermis from the epidermis during embryological development. There are variations in structure at different sites on the body surface according to the major function of

the skin at that site. Acral skin demonstrates progressive thickening and contraction of the stratum corneum.

The epidermal layer has an undulant undersurface in two-dimensional sections, with downward invaginations termed rete pegs and interdigitating mesenchymal cones termed dermal papillae. The epidermal retia form a honeycomb of interconnected ridges, with dermal papillae representing rounded conical invaginations resembling the undersurface of an egg carton.
The basement membrane, 1 μm thick, separates the epidermis from the dermis.
The dermis consists of endothelial and neural cells, supporting elements, fibroblasts, dendritic and non-dendritic monocytes, macrophages, and mast cells enveloped within a matrix of collagen and glycosaminoglycan (ground substance).
The subcutaneous tissue is an underlying layer formed by cells engorged with lipid and nourished by vessels that grow within these intervening septae.

1.6.1 The epidermis

Two types of cells constitute the epidermis: keratinocytes and dendritic cells. The keratinocytes differ from the dendritic cells, or clear cells, by possessing intercellular bridges and ample amounts of stainable cytoplasm.
The keratinocytes are arranged in 4 layers
1) Basal Layer - Stratum basalis
2) Squamous Layer – Stratum spinosum
3) Granular Layer – Stratum granulosum
4) Horny Layer – Stratum corneum
The terms ‘stratum malpighii’ and ‘rete malpighii’ are often applied to the three lower layers, which contain the basal, squamous and granular cells and constitute the nucleated, viable epidermis.

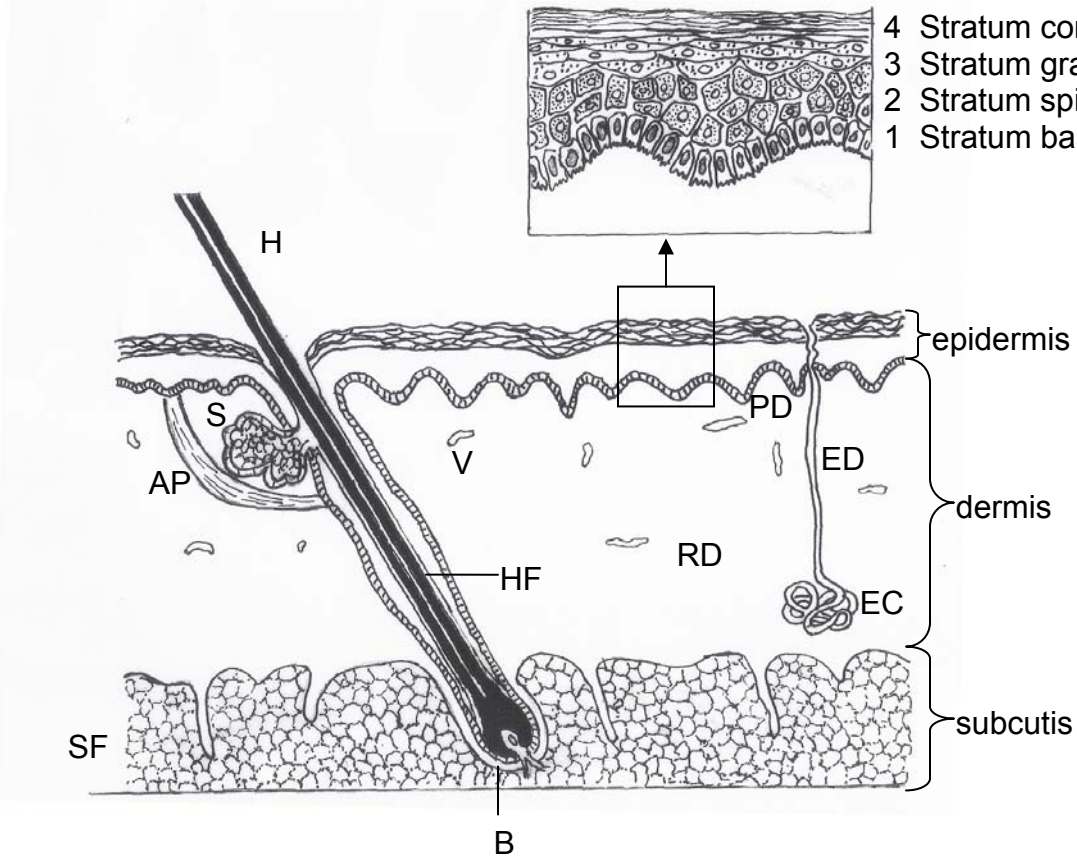


Fig. 6
NORMAL ANATOMY OF HUMAN SKIN

KEY:

PD – papillary dermis
RD – reticular dermis
SF – subcutaneous fat
AP – arrector pili muscle
S – sebaceous gland
EC – eccrine gland
ED – eccrine duct
V – vessel
B – bulb
HF – hair follicle
H – hair

1.6.1.1 Stratum basalis

The basal cells form a single layer, are cuboid or low columnar, and lie with their long axes perpendicular to the dividing line between the epidermis and dermis. They have a more basophilic cytoplasm than cells of the stratum spinosum that parallels the skin colour, and contain a dark-staining oval or elongated nucleus. They often contain melanin pigment transferred from adjacent melanocytes.

1.6.1.2 Stratum spinosum

The cells of the squamous layer are polygonal and form a mosaic of cells usually five to ten layers thick. The so-called ‘prickle cells’ of this zone are relatively large and polyhedral in shape.

They become flattended towards the surface with their long axes parallel to the skin surface.

1.6.1.3 Stratum granulosum

The cells of the granular cell layer are diamond shaped or flattened, and their cytoplasm filled with keratohyaline granules that are deeply basophilic and irregular in size and shape. The thickness of the granular layer is proportional to the thickness of the horny layer. The horny layer is thick in the sole.

1.6.1.4 Stratum corneum

The cells are anucleate and are thus technically dead. The horny layer stains eosinophilic as a result of lack of basophilic nuclei. Most of the horny layer shows a basket weave pattern in formalin-fixed specimens because of the presence of large intercellular spaces. The cells of the horny layer are arranged in orderly vertical stacks.

1.6.1.5 Other cells in the epidermis

Dendritic Cells of the Epidermis

These are of three types. Only the melanocyte can be easily identified in histological sections stained with haematoxylin-eosin. The second type, Langerhans cells, can be identified with immuno-histochemical methods or by electron microscopy. The third type, the indeterminate dendritic cell, can be identified with the electron microscope only. Melanocytes are derived from the neural crest. They are responsible for the synthesis of the brown pigment called melanin. They are found randomly wedged between the basal cells of the epidermis. In light skin, staining with haematoxylin and eosin may reveal few or no melanin granules in the basal cell layer. In dark skin colour, melanin granules are present in the basal cell layer.

Langerhans cells are bone marrow-derived cells that stain as clear cells in the suprabasal epidermis. They are functionally and immunologically related to the

monocyte, macrophage and histiocyte series which constitute 2-4% of the total epidermal cell population. They play an active role in cutaneous immunity.

1.6.1.6 The skin appendages

Skin has a variety of appendages, principally hair follicles, sebaceous glands and sweat glands, derived embryologically from the epidermis.

The distribution and structure of the appendages vary from one part of the skin to another. There is a basic pattern:

Hair follicles

Hair germs, in their earliest stage of development, develop into buds that protrude into the dermis. They develop two or three bulges on their undersurface. These three bulges develop into the sebaceous gland, an apocrine gland, and the attachment for the arrector pili muscle. The hair follicle consists of three parts: the lower portion extending from the base of the follicle to the insertion of the arrector pili muscle; the middle portion, or isthmus, a short section extending from the insertion of the arrector pili to the entrance of the sebaceous duct, and the upper portion, or infundibulum, extending from the entrance of the sebaceous duct to the follicular orifice.

Sebaceous glands (holocrine glands)

One or more sebaceous glands are associated with each hair follicle. These glands secrete an oily substance called sebum onto the hair surface. It may consist of one lobule, but often has several lobules leading to a common excretion duct composed of stratified squamous epithelium. In the skin, the sebaceous duct opens into the pilosebaceous follicle.

Sweat glands (eccrine glands and apocrine glands)

Eccrine glands are composed of three segments: the intra-epidermal duct, the intradermal duct, and the secretory portion. The secretory portion makes up about half the basal coil, the other half being composed of duct. The basal coil lies either at the border between the dermis and the subcutaneous fat, or in the lower third of the dermis. When located in the lower dermis, it is surrounded by fatty tissue that connects with the subcutaneous fat. The intra-epidermal eccrine duct extends from the base of a rete ridge to the surface and follows a spiral course. The eccrine sweat gland is engineered for temperature regulation.

Eccrine glands are present everywhere in the human skin, except in areas of modified skin that lack cutaneous appendages. They are found in greatest abundance on the palms, sole and axilla.

*Apocrine glands*are a different type of sweat gland found in the skin of the axilla and genital regions and external ear. In contrast to the merocrine sweat glands, these glands are believed to secrete by the apocrine process. They produce a viscid secretion which is discharged into the hair follicles. Apocrine glands are tubular, and like eccrine glands, are composed of three segments: intra-epithelial duct, intradermal duct, and the secretory portion.

1.6.2 The dermis

The dermal layer of the skin provides a flexible base for the epidermis and contains a generous vascular supply for the metabolic support of the avascular epidermis and for thermoregulation. The dermis is divided into two zones; a superficial thin papillary dermis, and a more extensive, deeper reticular dermis.

The papillary dermis is loose and contains very fine interlacing collagen fibres. It contains venules, arterioles, capillary loops, lymphatics and fine nerve twigs from sensory nerve endings, the Meissner's corpuscles. The reticular dermis consists of coarse, irregularly situated bundles of collagen, within which are the blood vessels that join the plexus of vessels in the papillary dermis with the larger, deeper vessels at the junction between dermis and subcutis. Elastin is an important component of both layers of the dermis and stains black with the Elastic van Gieson (EVG)stain against the red-stained collagen. The cellular component of the dermis is mainly fibroblasts which are responsible for the production of collagen and elastin, but lymphocytes, mast cells and tissue macrophages involved in non specific defence and immune surveillance are also present.

The extra-cellular matrix of the dermis consists of collagen and elastic fibres embedded into ground substance. All three components are formed by fibroblasts.

1.6.2.1 Ground substance

The ground substance, an extracellular amorphous substance that fills the spaces between collagen fibres and collagen bundles contains glycosaminoglycans or acid mucopolysaccharides.

1.6.2.2 Collagen fibres

Collagen fibres represent, by far, the most abundant constituent of the connective tissue of the dermis. On light microscopy, the collagen consists of fibres 2-15μm in diameter, present either as a finely woven network, or as thick bundles. Collagen, as a finely woven network of fibres, is found in the papillary layer of the dermis. In addition, the pilosebaceous units, and the eccrine and appocrine glands are encircled by a thin meshwork of collagen fibres similar to that present in the papillary dermis. The blood vessels of the dermis are also surrounded by a thin layer of fine collagen fibres. Biochemically, the papillary dermis is composed primarily of Type III collagen.

The rest of the dermis constituting, by far, the largest portion of the dermis, and referred to as the reticular dermis, shows the collagen fibres united into thick bundles. These collagen bundles extend horizontally in various directions and thus, some are cut lengthwise and others across, in histological sections. As a rule collagen fibres cut lengthwise appear wavy.

Their nuclei are pale staining and when cut lengthwise, appear spindle shaped. A small number of fibroblasts are interspaced between the collagen bundles. The only other cell type present in the normal dermis is the mast cell, seen generally in small numbers in a perivascular arrangement. Usually, mast cells can be seen only with special stains, which stain the mast cell granules purple.

Biochemically, reticular dermal collagen is composed primarily of type I collagen.

1.6.2.3 Elastic fibres

On light microscopy sections, elastic fibres are inconspicuous with routine stains. With special stains they are found entwined among the collagen bundles. Because elastic fibres are thin and wavy in comparison with collagen bundles, measuring 1-3 μm, only a small portion of any fibre is seen in microscopic sections, giving even normal elastic fibres a fragmented appearance. The elastic fibres are thickest in the lower portion of the dermis where they are arranged as collagen bundles, chiefly parallel to the surface of the skin. Elastic fibres become thinner as they approach the epidermis.The elastic fibre of the dermis consists of two components: the matrix elastin and the microfibrils.

The elastin that stains with elastic tissue stains is markedly extensible, whereas the microfibrils are the elastic, resilient component of the elastic fibre. Elastin makes up 85% of the elastic fibre.

1.6.2.4 Reticulum fibres

Reticulum fibres are not recognizable with routine stains – they can be impregnated with silver nitrate which stains black. Reticulum fibres are present normally around blood vessels and as a basketlike capsule around each fat cell. They represent a special type of thin collagen fibre 0.2 μm to 1μm in diameter, in contrast to collagen fibres which measure 2μm to 15μm in diameter. Reticulum fibres are associated with increased fibroblastic activity in pathologic conditions such as dermatofibrosis and healing wounds.

1.6.2.5 Dermal microvascular unit

The arrangement of the cutaneous blood vessels consists of a subcutaneous plexus of small arteries from which arterioles ascend into the dermis and are interconnected. The dermal microvasculature is divided into two important strata. The first - a superficial vascular plexus, defines the boundary between the papillary and reticular dermis and extends within an adventitial mantle to envelop adnexal structures around eccrine glands and hair follicles.

This plexus forms a layer of anastomosing arterioles and venules in close approximation to the overlying epidermis and is normally surrounded by other cellular components of the dermal microvascular unit. Small capillary loops from the superficial vascular plexus extend into each dermal papilla.

The second plexus – the deep vascular plexus is connected to the first by vertically orientated reticular dermal vessels, and separates the reticular dermis from the subcutaneous fat. Many of these vessels are of larger caliber and communicate with branches that extend within fibrous septae that separate lobules of underlying subcutaneous fat.

Dermal lymphatics

These are often inconspicuous in normal skin because they do not have well-developed walls, as do blood vessels. They are easily detected when they become slightly ectatic as a result of increased lymphatic drainage.

The *glomus cell*is found mainly in the pads and nail beds within the reticular dermis of the volar aspects of hands and feet. Glomus is concerned with temperature regulation and represents a special arteriovenous shunt.

1.6.2.6 Nerves and end organs of the dermis

Specialized sensory nerve end organs are found in areas of hairless skin on the palms, soles and in areas of modified hairless skin.

There are 3 types: mucocutaneous end organs, Meissner corpuscles, and Vater-Pacini corpuscles.

Mucocutaneous end organs are found in modified hairless skin at the mucocutaneous junctions in the papillary dermis.

Meissner corpuscles are located in the dermal papillae and mediate a sense of touch. They occur in the hands and feet, on the ventral aspects.

Vater-Pacini corpuscles are large nerve end organs that are located in the subcutis and mediate a sense of pressure. They are found in the volar surface of palms and soles.

Neural network

The skin is supplied with sensory and autonomic nerves, which permeate the entire dermis with nerve fibres showing frequent branching. The autonomic

nerves, derived from the sympathetic nervous system, supply the blood vessels, arrectores pilorum, eccrine and apocrine glands. The sebaceous glands possess no autonomic innervation and their functioning depends on endocrine stimuli. All autonomic nerves end in fine arborizations as do the sensory nerves, except in a few areas where they terminate in special nerve organs.

1.6.2.7 Cells of the dermis

Mast cells

Are bone marrow-derived cells that occur in the normal dermis in small numbers as oval to spindle shaped cells, with a centrally located round to oval nucleus. They are generally concentrated around blood vessels, specifically around post capillary venules. They contain numerous granules in their cytoplasm. The granules appear as round, oval or angular-shaped, membrane-bound structures. Degranulation of mast cells occurs after cross-linking of IgE on the cell surface after exposure to neuropeptides, thermal or mechanical stimuli.

Emigrant inflammatory cells

Various types of cells, largely derived from the bone marrow, infiltrate the dermis and occasionally the epidermis during inflammatory conditions. Three groups of cells are derived from bone marrow: granulocytic group, lymphocytic group including plasma cells, and the monocytic or macrophagic group.

Dermal fibroblasts

Fibroblasts are derived from mesenchymal cells. Fibroblasts appear as inconspicuous bipolar spindle cells with elongated ovoid nuclei. Under EM, fibroblasts that actively synthesize collagen have a prominent rough endoplasmic reticulum composed of many membrane-lined cisternae, with large numbers of attached ribosomes.

1.6.2.8 Muscles of the skin

Smooth muscle or involuntary muscle of the skin is the arrectores pilorum. The muscle fibres arise in the connective tissue of the upper dermis and are attached to the hair follicle below the entry of the sebaceous duct. They are situated in the obtuse angle of the hair follicle, and when contracted, they pull the follicle into a vertical position.

1.6.3 The subcutaneous layer

Mature subcutaneous fat consists of lobules of adipocytes, the cytoplasm of which is markedly expanded by non-vacuolated or membrane-bound lipid that displaces the cell nucleus eccentrically.

The lobules that form the subcutis are separated by thin fibrous septae through which small vessels course. The septae provide structural stability to the subcutaneous layer by compartmentalizing it and by connecting the lowermost reticular dermis to the fascial planes that underlie the subcutis.

1.7 CLASSIFICATIONOF CLUBFOOT

Clubfoot can be classified into four major groups [16].

(i) Congenital (ii) Teratologic (iii) Syndrome complex (iv) Positional

The congenital clubfoot is usually an isolated deformity without evidence of other musculoskeletal abnormalities. This type is frequently considered *idiopathic*.

The teratologic form of clubfoot is associated with an identified underlying neuromuscular disorder such as myelodysplasia or arthrogryposis multiplex congenita. Clubfeet, as part of a syndrome, may also be genetic in origin. There are autosomal dominant, autosomal recessive and x-linked recessive disorders that include clubfeet as part of their clinical manifestations. Children with chromosomal abnormalities e.g. Down Syndrome, may also have clubfeet. The pathogenesis, response to treatment and the prognosis of the non idiopathic