The camel is a multipurpose animal providing milk, meat and transport power, in addition to social culture functions. According to FAO, 2013 the general estimate of the camel world population may probably be around 30 million head. About 88% of the camels are found in Africa, while Asia has 12%. There are an increased interest in the camel as a multipurpose animal that encourage more researchers into the etiology and pathology of camel diseases, but very few published reference books were directed towards dermatology. The first edition of "dermatology of camelids" has been completely, particularly in the areas of functions and structure of skin of the camelids, diagnostic approach of camelids skin diseases viral, bacterial, fungal and parasitic diseases. This book is intended to facilitate the initial stages of diagnosis of camelids skin diseases and to serve as a refresher to those in the profession who may have had little experience on skin of the camelids. It is the authors' hope that those studying to be veterinarians will find this book to be a helpful complement to their education and that graduate veterinarians will find this book to be valuable in postgraduate studies.

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DERMATOLOGY OF CAMELIDS

Karima Akool Al Salihi

Dermatology of Camelids

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KARIMA AKOOL ALSALIHI

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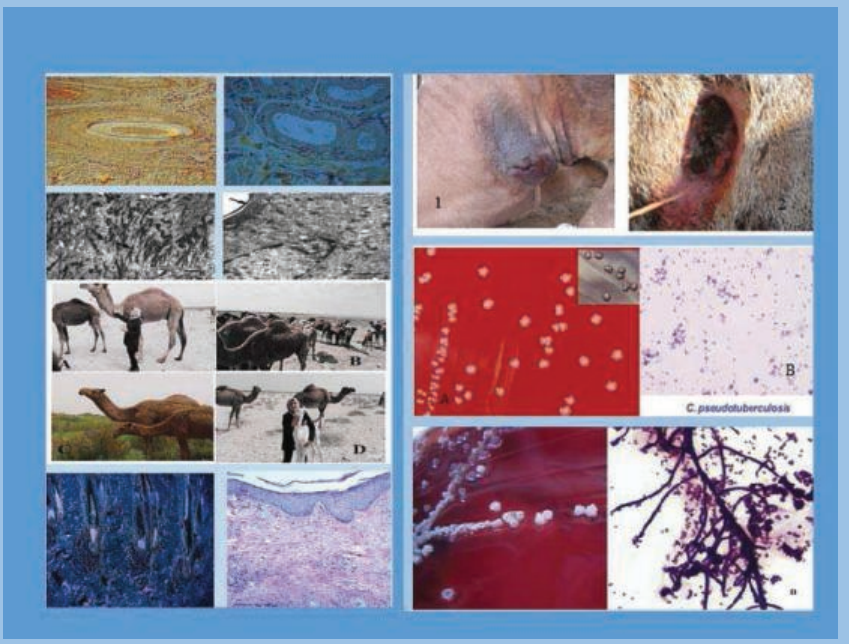
DERMATOLOGY OF CAMELIDS



Preface

The camel is a multipurpose animal providing milk, meat and transport power, in addition to social culture functions. The total number of camels is probably underestimated because camels are migrant animals. Moreover, it is difficult to conduct a census for camels such as the wild Australian camel population. However according to FAO, 2013 the general estimate of the camel world population may probably be around 30 million head. About 88% of the camels are found in Africa, while Asia has 12%. There are an increased interest in the camel as a multipurpose animal that encourage more researchers into the etiology and pathology of camel diseases, but very few published reference books were directed towards dermatology. Camels were formerly thought to be resistant to most of the diseases commonly affecting livestock, but new data confirmed that camels are susceptible to a large number of pathogenic agents. The camel is also indicated for the transmission of several transboundary animal diseases like Bluetongue, PPR, Rift Valley and West Nile Fever and zoonotic diseases.
Considering the importance of camelids and the lack of knowledge of camelids dermatology, this first book edition ″dermatology of camelids″ is published to help improve diagnosis capacity and to illuminate the role of some pathogens in epidemiology and pathogenesis of skin diseases in camelids. The first edition of ″dermatology of camelids″ has been completely, particularly in the areas of functions and structure of skin of the camelids, diagnostic approach of camelids skin diseases viral, bacterial, fungal and parasitic diseases. The book is divided into six chapters the first chapter is dealing with normal structures (macroscopic and microscopic) appearance of camelids skin, in addition to ultra-structures. The second chapter is dealing with a guide for diagnosis of camelids skin diseases. Meanwhile, the third , fourth , fifth and sixth chapters are containing details information on etiology, epidemiology, clinical signs, pathology, diagnosis, treatment and prevention of viral , bacterial, fungal and parasitic skin diseases. Treatment and control has been given special emphasis in this book.

This book is intended to facilitate the initial stages of diagnosis of camelids skin diseases and to serve as a refresher to those in the profession who may have had little experience on skin of the camelids. It is the authors' hope that those studying to be veterinarians will find this book to be a helpful complement to their education and that graduate veterinarians will find this book to be valuable in postgraduate studies.

Congratulations to the author for her dedication and willingness to share her experiences with colleagues around the world.

Karima Akool AL Salihi

Author

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Structure and Function of the Skin

Chapter 1: Structure and Function of the Skin

Structure and Function of the Skin

1.1 Introduction

The skin is the largest organ of the animal body, representing approximately one-tenth of the body mass, and is necessary for animal survival [1, 2, 3]. It serves several important functions, including a physical barrier to the external environment, thermal regulation, and retention of normal hydration [4]. It provides protection from physical, chemical and biological injury. Skin sensory components perceive heat, cold, pain, pruritus and pressure. In addition, the skin is synergistic with internal organ systems and, thus, reflects pathologic processes that either is primary elsewhere or are shared with other tissues. The skin also works as a mirror reflecting the milieu interior. The skin is an exclusive evolutionary acquirement of vertebrates, and it should be distinguished from the integuments of other animals [5]. The skin consists of two tissues differing in origin, namely, the epithelial and connective tissue layers separated by a basal membrane. The surface epidermis is of ectodermal origin, while the underlying derma is a mesodermal derivative developing on account of the somite dermatome. These layers exert reciprocal influences on each other when forming different derivatives during ontogeny [6, 7, 8, 9, 10, 11, 12]. The emergence of vertebrates on land, the main historical event in their phylogeny, is reflected in the development of two basic types of the cover epithelium, essentially aquatic and terrestrial, with the transitional amphibiotic or ichthyoid type [13]. Histological, histochemical and ultrastructural information on the skin of different large animals has shown that significant species differences exist [14].
Theoretical considerations suggest that desert animals exposed to high levels of solar radiation and high temperatures should possess smooth reflective coats and black skins. In addition, the coat should not be so thick as to prevent evaporation at the skin surface, but not so thin as to allow too much heat to strike the body surface. High albedo values are achieved if the coat is light in color while the black skin absorbs much of the ultraviolet light that penetrates the coat, preventing damage to tissue proteins. The data indicate that while the camel is clearly adapted for a desert lifestyle, these adaptations do not include significant specializations at the cellular or subcellular level in the integument [15, 16, 17, 18, 19].

1.2 General Functions of the skin

The skin has essential vital functions for keeping the physiological and biochemical conditions of the body in its optimum state. The skin has three main functions:

protection, regulation, and sensation. Wounding affects all the functions of the skin [20, 21, 22]. The skin serves the following important functions:

1. The skin is an organ of protection. The primary function of the skin is to act as a barrier. It provides protection from: mechanical impacts and pressure, variations in temperature, micro-organisms, radiation and chemicals. The skin surface has antibacterial and antifungal properties.
2. The skin is an organ of regulation. It regulates several aspects of physiology, including: body temperature via sweat and hair, and changes in peripheral circulation and fluid balance via sweat. It also acts as a reservoir for the synthesis of Vitamin D.
3. The skin is an organ of sensation. It contains an extensive network of nerve cells that detect and relay changes in the environment. There are separate receptors for heat, cold, and pain. Damage to these nerve cells is known as neuropathy, which results in a loss of sensation in the affected areas. Sick animal with neuropathy may not feel pain when they suffer injury, increasing the risk of severe wounding or the worsening of an existing wound.
4. Immunological functions: Keratinocytes, Langerhans's cells and lymphocytes together provide the skin with an immune surveillance capability that effectively prejudices against the development of cutaneous neoplasm and persistent infections.
5. The skin plays an important indicator of general health and the effects of medicine taken internally.
6. The flexibility, elasticity and toughness of the skin allow motion and provide shape and form.
7. The skin produce keratinized structures such as hair, hooves horn, and horny layer of the epidermis (adnexa production).
8. The skin has additional active job in the camel, which is energy conversation. A camel in its natural summer coat has fur about 30 mm thickness on the flanks and straight short hair about 15 to 20 mm long on the belly and legs. Such animal can maintain a lower body temperature than a camel with its fur shorn to 5-10 mm and since there is less heat to be dissipated requires expending less energy [15, 16, 17, 18]. If the coat is too thick, it may reduce evaporative heat loss at the body surface. The coolest point in a water/water vapor chain is at the point of change. If evaporation occurs at the skin surface while the fur remains dry, the heat flow from the environment, through the fur to the body is reduced. If the fur is too thick to allow evaporation at the skin surface the water from the skin wets the fur. Evaporation then occurs at the fur/air interface, not at the skin surface. The resulting accumulation of heat has then to be dissipated by the expenditure of energy. Via sweating through the skin, camels avoid the energy expenditure, since the nature of the coat allows efficient heat loss by this mean. The pH of the camel sweats is 8.2- 8.5 [17] and is high in potassium (about four times as much as sodium) and hydrogen carbonate ions.

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1.3 Ontogeny

Zoologists are still facing a challenge about the problem of origination and diversification of skin derivatives in vertebrates. Several studies in different animal's species have been included the subject on embryology of the skin [1, 2, 3]. Following fertilization, of ova, the zygote undergoes a series of mitotic cell divisions resulting in a ball of cells called the blastula. This undifferentiated embryonic structure then

undergoes a phase of major cell migration called gastrulation, producing a gastrula with three separate germ layers: the endoderm, mesoderm, and ectoderm. The skin rises from mesoderm and ectoderm germ layers [2]. Since ectoderm is the outermost layer found during gastrulation, the ectoderm is said to develop first. The ectoderm is actually comprised of three separate layers: the external ectoderm, the neural crest, and the neural tube. The ectoderm is noted for giving rise to the epidermis of skin and its derivatives (i.e. hair, nails, sweat glands, sensory receptors). Initially, the embryonic skin consists of a single layer of ectodermal cells. The ectodermal covering progressively develops into two layers (the basal cell layers, or stratum germinativum, and the outer periderm), three layers (the stratum intermedium forms between the outer layers), and then into an adult-like structure. Melanocytes and Langerhans's cell become identifiable during this period of ectodermal maturation [3, 4, 5, 6, 7, 8, 9, 10]. The mesoderm is formed during gastrulation from cells that migrate inward and stop between the inner layer (endoderm) and the outer layer (ectoderm). The evolutionary significance of the mesoderm is that it led to the development of the coelom. Coelom is another term for body cavity, and refers to the region between an animal's outer covering, and the outer covering of the gut cavity. The mesoderm gives rise to many of the "middle tissues," but is dynamic in its ability to differentiate in atypical directions. That is to say, cells originally found in the mesoderm might end up migrating and differentiate into an endoderm tissue. Cells that stay in the mesoderm most notably give rise to the dermis (middle layer of the skin) [3, 4]. A dermis containing loosely arranged mesenchymal cells embedded in ground (interstitial) substance. Dermal development is characterized by increasing thickness and numbers of fibers, decreasing ground substance, and the transition of mesenchymal cells into fibroblasts. Elastin fibers appear later than collagen fibers. Histiocytes, Schwann's cells, and dermal melanocytes also become recognizable. Fetal skin contains a large percentage of Type III collagen, in humans, in contrast with adult skin, it contains a large proportion of Type I collagen. Fat cells begin to develop in the subcutis from spindle-shaped mesenchymal precursor cells in the second half of gestation. The embryonal stratum germinativum differentiates into hair primary epithelial germs, which give rise to hair follicles, sebaceous glands, and apocrine sweat glands. Hair germs initially consist of an area of crowding of deeply basophilic cells in the basal later of the epidermis. Subsequently, the areas of the crowding become buds that protrude into the dermis. Beneath each bud lies a group of mesenchymal cells, from which the dermal hair papilla is later formed. As the hair germ lengthens and develops into hair follicle and hair, three bulges appear [5, 6, 7]. The lowest of the bulges develops into the attachment for the arrector pili muscle, the middle bulge differentiates into the sebaceous gland, and the uppermost bulge evolves into the apocrine sweat gland. These appendages develop on the ental side of primary hair follicles, while secondary hair follicles develop on the opposite or ectal side [8, 9]. Eccrine gland germs also begin as areas of crowding of deeply basophilic cells in the basal layer of the epidermis. They initially differ from hair germs only slightly, by being narrower and by showing fewer mesenchymal cells at their base [11, 12].

In camels, the skin consists of 2 main layers: epidermis and dermis [13, 14]. The hypodermis is clearly seen only in the mid-side position. The epidermis begins to appear as a single row of cells at 90 days. Both the epidermis and dermis are fully developed at 147 days of fetal life at which time the epidermis is differentiated into its 4 strata (corneum, granulosum, spinosum and basale or germinativum). The dermis is differentiated into papillary and reticular sub-layers. The plugs which will form the hair follicles begins to appear at 147 days, while the hair fibers begin to appear in its follicles at 268 days of fetal life. The follicles are clearly differentiated into primary and secondary follicles at

268 days of fetal life. The hair follicles are arranged in groups and are clearly seen at 375 days of fetal life [13, 15, 16]. Each group consists of 3 primary-follicles (1 central and 2 laterals) and several secondary follicles (on the ectal side of the primary follicles). The thickest secondary follicles (early secondary follicles) are situated near the primary follicles, while more thin secondary follicles (late secondary follicles) are far away from primary follicles. The primary follicle is associated with a sebaceous gland, a sweat gland and an arrector pili muscle, while each secondary follicle is associated only with a sebaceous gland. The sebaceous glands that are attached to the primary follicles has large lobules, while those attach to the secondary follicles are small. The several lobules of the sebaceous glands open into a common short excretory duct. The sebaceous glands begin to appear at 229 days of fetal life [17, 18, 19, 20, 21, 22]. The apocrine sweat gland is formed of a glandular tortuous part, their uppermost straight ducts passes between or beside the sebaceous glands lobules. It enlarges then into a sac before it opens near the follicle opening at the skin surface. The glandular tortuous distal part is situated either at or lower than the level of the hair follicle bulb, and is formed of 1 layer of cuboidal epithelium. The sweat glands begin to appear at 229 days of fetal life. The arrector pili muscle is formed of smooth muscle fibers. It ran from the lower part of the follicle to the area below the epidermis. The arrector pili muscles first appears at 229 days of fetal life (Table.1.1).

Table 1.1 The morphological events during the fetal skin development of the camel.

Table .1. 1 Morphological events during fetal skin development.	
Event	gestation period
Epidermis began to appear as a single row of cells	90 days
Both the epidermis and dermis were fully developed	147 days
The plugs which would form the hair follicles began to appear	147 days
sebaceous glands began to appear	229 days
sweat glands began to appear	229 days
The arrector pili muscles first appeared at	229 days
hair fibres began to appear in its follicles	268 days
follicles were arranged in groups and were clearly seen	375 days

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1.4 Gross anatomy of the skin

Skin is the general covering of the entire external surface of the body, including the external auditory meatus and the outer surface of tympanic membrane. The skin is continuous with the mucous membrane at the orifices of the body (digestive, respiratory, ocular urogenital) .Skin is considered a very important organ of the body [1, 2]. The skin and hair coat vary in quantity and quality between species, breeds within a species, and individuals within a breed, from one area to another on the body, and according to age and sex [3]. Generally, skin thickness decreases dorsally and to ventrally on the trunk and proximally to distally on the limbs. The thickest areas of the skin appear on the forehead, dorsal neck, dorsal thorax, and base of the tail, while the thinnest areas are on the pinnae and the axillary, inguinal, and perianal. In an adult human, the surface area of the skin is 1.5-2 square meters. The proportion of skin covering various parts of human body can be explained in percentages as: Head and Neck = 9%, each upper limb = 9%, Front of the trunk = 18%, Back of the trunk (including buttocks) = 18%, each lower limb = 18% and Perineum =1%. In addition the appearance of skin varies across different regions of the body. This is because the physio-anatomical characteristics of the lower-level components can differ significantly from one region of the body to another. For example, the nose and the forehead have greater amounts of skin surface lipid compared to the cheek. As a result, the nose and the forehead tend to appear glossier than the cheek [4]. The reported average thickness of the general body skin of adult large animal is as follow: horse, 3.8 mm, cow, 6.0 mm, sheep, 2.6mm, goat, 2.9mm and pig, 2.2mm [3]. The average skin size of a six-year old camel ranges between 1.6 and 2.8 m^2. Skin thickness varies from 2.5 mm at the belly to 6 mm at the ridge [5, 6,7,8,9]. Llama skin thickness decreases dorsally to ventrally on the trunk. The average skin thickness, from the top of the stratum corneum to the bottom of the dermis, averages about 3.9 mm and is best exemplified by that of the lateral thorax. The thickest haired skin is present on the dorsal and lateral aspects of the neck (13-14 mm), followed by the dorsal thorax (5.8 mm). The skin also is exceptionally thick near mucocutaneous junctions (chin = 6.9 mm, upper lip = 8.3 mm, anus = 4.1 mm, nipple = 6.3) and in many of the specialized areas (interdigital scent gland = 8.5 mm). The thinnest haired skin is found on the concave surface of the pinnae (1.2 mm), followed by the perianal region (2.4 mm), axillae (3.4 mm), and caudal abdomen (3.7 mm) [10]. Hair is characteristic of mammals and is important in thermal insulation and sensory perception and as a barrier against chemical and physical injury to the skin. The ability of the hair coat to regulates closely with length, thickness, and medullation of individual hair fibers. In general, hair cats compose of short, thick and medullated fibers are most efficient at high environmental temperatures. Conversely, hair coats composed of long, fine, poorly medullated fibers, with coat depth increased by piloerection, are most efficient for thermal insulation at low environment temperatures. In addition, coat color is of some importance in thermal regulation, with light-colored coats being more efficient in hot, sunny weather. Primary (guard, outercoat, Kemp) and larger secondary (undercoat) hairs are medullated. Smaller secondary hairs in goats are non medullated (lanugos' hairs). Secondary hairs are more numerous than primary hairs in the goat and sheep [3, 4]. The Skin of the camelidae family is considered thick and non-pliable. Generally, mature males have the thickest cervical skin, a feature which may provide protection against potential trauma. The tough, thick skin in the cervical area of the camel and llama often creates difficulty in performing jugular venepuncture. The camel leather has a high tensile strength [11]. The skin of camel is supply over the most part of the body with short fine hairs, which may be longer in

cooler climates or during the cool season in hot areas. The longer hair is usually confined to the hump and the shoulder but this varies between individuals. The hair color is generally brown, varying from color of Debs (syrups of dates) almost black color, through reds, rusts, fawns to almost white in some types. Some two-colored animals particularly is found in the western Sudan and Chad [12, 13, 14] (Figure. 1.1.A, B, C, D) anatomically, the skin of camel is attached rather tightly to the underlying tissue and is relatively immobile. This is a disadvantage when the animal is attacked by biting and flying insects, particularly in view of its short and ineffectual tail. The animal is thus reduces to stamping, kicking and throwing its head about in the effort to remain comfortable, apparently often without much success [14].

Figure. 1. 1. A, B, C, D: Show the different colors of camel

The skin is thicker over the back than elsewhere and particularly over the hump when this is in decline. The epidermis is well developed and dermis is compact and hard and is rich in elastic fibers which have long papillae; the sub-epidermal tissue is very hard. Sweat glands occur sparsely all over the body but sweating is restricted to very hot periods and to times when the animal is excessively tired [15, 16, 17]. The pads are modified skin and occur at the points where the camel is in contact with the ground when couched. The dark horny membrane of which they consist is generally about 7 mm secreting membrane beneath which there is a foundation of fibro-cartilaginous tissue. The largest pad is generally referred to as the pedestal and is on the chest below the sternum; there are in addition pads on the elbows and stifles and less important ones on the knees and outside the hocks. In young animals the pads are less developed and covered with short hair which wears away after a few months [5]. The fleece of camel contains two distinct population of fiber; a short and fine non-modulated insulating fiber and long coarse medullated guard hair which are produced by secondary and primary follicles respectively. Seasonal fibre shedding is common in camel; thus considerable amount of fibre is lost annually. There is a scarcity of information in the scientific literature on the fibre shedding and follicle cycle in the camel. Efforts need to be made to define the annual pattern of camel fibre growth manipulating the growth cycle to increase production or allow shearing at a more favourable time to prevent fibre loss.

Examination of the state of activity of follicles is required for a full understanding of pelage cycles. Without such information it is difficult to develop systems of management of fibre harvesting strategies which will optimize the efficiency of fibre production [16, 17, 18, 19, 20, 21].

1.5 Hair cycle

The mammalian hair follicle is a dynamic structure that generates a hair shaft through a tightly controlled cycle of growth, remodeling, and loss. Once a hair follicle is made, it can undergo many of these cycles, continually making, growing, and losing the hair shaft. In mammals, the cycle of hair growth includes three stages: anagen (follicle generation and hair production), catagen (follicle regression), and telogen (resting phase). The production of the follicle is an extremely complicated event, and literally dozens of genes are known to play roles in its formation. Like the kidney, tooth, and the eye, there are reciprocal inductions. In this case, the developmental dialogue involves the epidermal cells of the skin (an ectodermal epithelium) and the dermal cells beneath it (a mesodermal mesenchyme). The progression of the developmental dialogue for hair formation has been summarized as in the following [22, 23, 24].

1.5.1 Initial inductive events

- The first signal is probably from the dermis, telling the epidermis to "make an appendage." Regions of epidermal cells proliferate and form local thickenings (placodes) of the epidermis. The signal here may be TGF-b molecules. The epidermis thickens in these regions and expresses particular adhesion molecules such as NCAM. These adhesion molecules are thought to separate the presumptive follicle cells from the remainder of the epidermis.
- The epidermal placodes then respond by sending a message into the mesenchyme, telling the mesenchyme cells to "aggregate beneath the epidermal placodes." This signal appears to be a series of paracrine factors including fibroblast growth factors, sonic hedgehog, and BMP2.
- Once aggregated, these mesenchyme cells now form the dermal papilla. The papilla sends a second message to the epidermis: "make a hair placode."
- The epidermis responds to this signal by proliferating further into the mesenchyme. As it does so, it sends a signal to the mesenchyme, signaling the mesenchyme to condense into the definitive dermal papilla that will become surrounded by the proliferating epidermal placode. The epidermal placode has now become a primitive hair shaft. Camel hair fibers have specialty hair fibers that are different from other mammal's hair. Production of fiber from various world dromedaries (one humped) and Bactrians (two humped) camels has been reported [25]. The fleece of double coated animals such as camels consists of two major fiber types the guard hair and down fibre [26]. The Guard hairs grow from primary follicles. It is coarse, medulated fibers, which typically form a protective coat over the underlying fiber. The Down fiber grows from secondary follicles in the skin [27, 28] and is finer (19–24 μm) than the guard hair (20–120μm) and medulated fiber [26]. There is a scarcity of information in the scientific literature on fiber shedding and follicle cycle in the camel. However the information which is presented in this chapter about the description of camel hair follicles characteristics were taken from few studies that have been done in some areas, may be not meet the camel hair follicle cycle in another areas in the world because the hair cycle and thus the hair coat, are controlled by photoperiod, ambient temperature, nutrition,

hormones, general state of health, genetics, and poorly understood intrinsic factors. The process of seasonal hair follicle cycle and fibre shedding in dromedarian camel was described by Ansari-Renani [21]. Camel hair follicle cycle is composed of anagen (active), catagen (quiescent) and telogen (inactive) phases. Follicle cycle studies of camel hair indicated that most secondary follicles lost activity in February and March and remained in telogen for 3–4 months before returning to anagen. Thus for many camels, the significant new growth of down does not occur until April and May. The date of shearing should be late enough to obtain maximum fibre yield, but early enough to avoid significant down losses from shedding. Since the value of down fibre is determined by weight and diameter [29]. The extent of follicle inactivity during shedding season which contributes to down weight will influence the financial return from each camel. The activity and characteristics of hair follicle was studied in offspring, young and adult of one and two humped camels. (Tables1.2 and 1.3). The camel's hair follicle group composed of more than 3 primary follicles and several secondaries depending on the locations [15, 16, 17, 18, 19, 20]. There is differences in the consistency of camel's hair follicle group between the Indian camel and South American camelids, Bolivian Llamas and Peruvian Vicuna [29, 30] because of differences in the breeds and the place of origin. The average number of hair follicles per square millimeter of skin of dromedaries and bactrianus camels has variability between different records in the same species of camels [15, 16, 17, 18, 19, 20].

Table 1.2: Least square means and standard errors of sex, age, groups and region of dromedarian camels for secondary to primary (S/P) ratio, primary (P) follicle density, secondary (S) follicle density, primary plus secondary (P + S) follicle density and percentage of secondary (S) inactive follicles. (Ansari-Renani HR *et al*., 2010).

	No		Follicle characteristics			
S/P			P density	S density	P + S density	S inactive %
Sex		NS	NS	NS	NS	Ns
Male	31	6.4±0.2	4.4±0.2	27.3±1.1	31.7±1.2	31.2±3.8
female	159	6.3±0.1	4.1±0.1	25.8±0.4	29.8±0.4	28.9±1.3
Age group		NS	*	*	*	**
Offspring	6	6.5±0.6	5.4±0.9a	31.7±4.6a	37.1±5.4a	9.1±2.4c
Young	31	6.7±0.2	4.1±0.1b	26.5±0.8b	30.5±1.0b	21.8±2.8b
Adult	99	6.2±0.1	4.2±0.1b	25.7±0.5b	29.9±0.5b	31.0±1.7a
Aged	54	6.2±0.1	4.0±0.1b	25.6±0.7b	29.4±0.8b	32.6±2.1a
Region			*	NS	NS	*
Golestan	30	6.1±0.2^{bc}	4.4±0.2a	27.5±1.2	31.6±1.3	37.2±2.6a
S and B1	38	6.3±0.1^{b}	4.3±0.1a	26.5±0.7	30.8±0.7	25.2±2.2b
Boushehr	36	6.0±0.2^{bc}	4.0±0.1a	24.8±0.5	28.9±0.5	26.9±2.2b
N. Khorasan	19	7.0±0.2^{a}	4.4±0.2a	27.2±1.4	31.2±1.7	6.2±0.9c
S. Khorasan	35	6.9±0.1^{a}	3.6±0.1b	24.3±0.7	27.9±0.7	31.1±2.4ab
Yazd	32	5.8±0.2^{c}	4.4±0.2a	26.5±1.2	30.9±1.4	40.9±3.4a
R-Square		0.3	0.3	0.3	0.3	0.6
CV (%)		13.9	19.8	18.4	17.6	16.1

NS: not significant. 1 Sistan and Baluchestan province.
* Significant at $P < 0.01$

Table 1. 3: Least square means and standard errors of sex and aged groups of bactrian camels from Ardebil province for secondary to primary (S/P) ratio, primary (P) follicle density, secondary (S) follicle density, primary plus secondary (P + S) follicle density and percentage of secondary (S) inactive follicles. (Ansari-Renani HR *et al*., 2010).

No		S/P(Secondary/ primary)	Follicle characteristics			
			P density	S density	P + S density	S inactive %
Sex		NS	NS	NS	NS	Ns
Male	8	8.3±0.5	4.0±0.3	29.2±1.6	33.1±1.4	30.8±5.9
female	3	9.1±1.0	3.3±0.3	28.8±3.9	32.1±3.6	32.3±9.0
Age group		NS	NS	NS	NS	*
Young	3	8.0±0.9	3.7±0.4	27.3±2.2	30.9±1.9	20.4^{b}±3.7
Adult	2	9.5±0.5	3.2±0.2	31.7±1.7	34.9±1.9	35.7^{a}±10.1
Aged	6	8.5±0.6	4.0±0.4	29.1±2.4	33.1±2.2	35.1^{a}±7.4
R-Square		0.2	0.3	0.1	0.2	0.4
CV (%)	11	19	19.6	17.2	15.6	50.2

NS: not significant.

* Significant at $P < 0.05$.

Criteria for estimating camel (Secondary/ Primary) S/P ratio was different from that in cattle [31] buffaloes and rabbits [32], since all hair follicles in such species are primaries, i.e. each follicle is associated with a holocrine sebaceous gland, and apocrine sweat gland and an arrector pilli muscle with no discernible follicle group. There was a tendency for young camels to have higher percentage of anagen follicles and lower inactive secondary follicles followed by adult and aged camels. The main reason behind this appears to be the physiological status such as lactation and pregnancy of the older camels and the protection provided by nature to the young animals. However large variations existed between individual camels in the number of inactive follicles ranging from 7% to 74% indicating large genetic variation in susceptibility to follicle shutdown. Seasonal changing plays important role on the camel's hair cycle. The follicle activity declined and about 30–40% of fibre shed over winter and spring seasons. In February and March about 30–40% is at the peak of inactivity and the secondary follicles stop producing fibre and remain in telogen for 3–4 months before returning to anagen. Only about 31% of follicles remain in telogen and the remaining secondary follicles continue producing fibre at anagen stage over shedding season to provide some late winter coat and continuous hair cover. The mechanism by which some follicles are in anagen and some others transfer into telogen during shedding season remains unknown. The susceptibility of individual follicle types with different characteristics (size, volume, depth, blood flow and etc.) to shut down in response to changes in photoperiod and neuro-secretory rhythms via the pineal gland and associated hormones need to be elucidated. The shedding is commenced on the neck, chest and shoulders and spread to the back and rump. The sequential, bilaterally symmetric pattern is also seen in cashmere goats and double coated Wiltshire sheep. Unlike natural shedding, cortisol injected Merino sheep, shedding of fibre starts from rump and belly areas extending to shoulders.

Follicle culture is also shown similarities of inactivity in vitro in response to different concentrations of EGF and suppra physiological doses of cortisol [16, 17].

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1.6 Microscopically appearance of the skin

The skin of camel is unique among domestic animals [1]. It has similar epidermis and dermis layers to that of other hairy mammals, but it differs in the arrangement of the hairs and the morphology of the hair follicles from that of other domestic mammals [2]. The distribution and morphology of sebaceous glands is similar to other animals, but each branch of the compound follicles which contain the wool hair has their individual ring of sebaceous glands [3]. No tarsal glands occur in the eyelids [4]. Information about the microanatomy of the skin has been the subject of only few studies in camel [1, 2, 3, 4, 5, 6] .The unfortunate statement that the skin of the camel has no sweat glands [7] has been rejected by many scientists and finally approved by the scientists, who stated that sweat glands are present [8, 9, 10]. Sweat glands were found to be distributed over the general body surface, one in association with each cover hair, but none are found in the skin of

the upper lip, external nares and perianal region [4]. Their ducts open into the necks of the follicles of the cover hairs, and their structure conforms to that of other domestic mammals. No sweat glands are seen associated with the compound follicles of the wool hairs [4, 5, 6]. Epidermis and dermis attach between them by a special manner in the camel [11], in addition there are differences in the structure and distribution of glands in some respects from that described for domestic mammals. The arrangement of hairs and their follicles also differs from that described for other mammals [4].

1.6.1 Epidermis

Epidermis or the outer layer of the skin is composed of multiple layers of cells ranging from columnar to flat. These are of four distinct types: keratinocytes, melanocytes, langerhan·s cell, and Merkel·s cells. The epidermis of the camel has the same structure as described by Krolling and Grau [12] for domestic mammals. But there is variation in the thickness of the epidermal layers in various areas of the body. Also, the degree of vascularity and mononuclear infiltration may also vary. The hypodermis (subcutis) is composed of loose connective tissue, which attaches skin to the underlying bones or muscles. Some sweat glands extend into the hypodermis.
The epidermis of the camel is comprised of a relatively thin keratinized stratified squamous epithelium (Figure.1. 2). Under light microscopy, cells of the stratum basale, stratum spinosum and stratum granulosum combined to form a band of dark staining cells along the surface of the skin [13]. Cells of the most superficial stratum of the epidermis, the stratum corneum, are extremely flattened. Frequent separations between individual cell layers of this stratum may be apparent (Figure.1. 3).

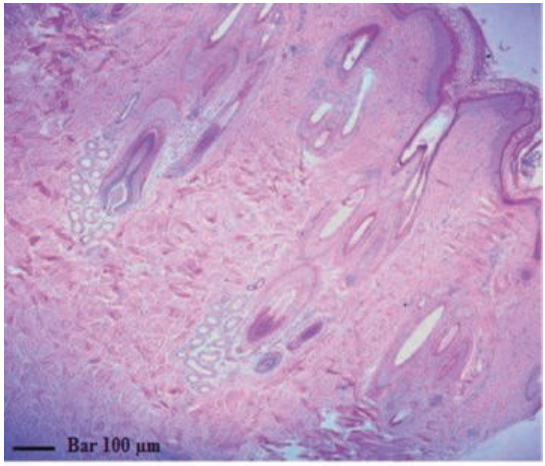

Figure .1. 2: Section of the skin of the camel shows all layers of the skin (X 10, H&E).

In most body regions, the viable epidermis is three to five cells thick and lacks rete ridges. Rete ridges are present in most hairless areas and in haired areas near mucocutaneous junctions. Rete ridges also occur in some of the specialized areas of skin such as the metatarsal glands, interdigital glands and footpads. The thickness of the

camel dermis layer is different over the body surface. The average thickness of the epidermis in each examined area is obtained by measuring the thickest and thinnest zones in the sections. Lee and Schmidt-Nielsen, 1962 found that a general average of all areas studied gives a value of 0.76 mm[4].

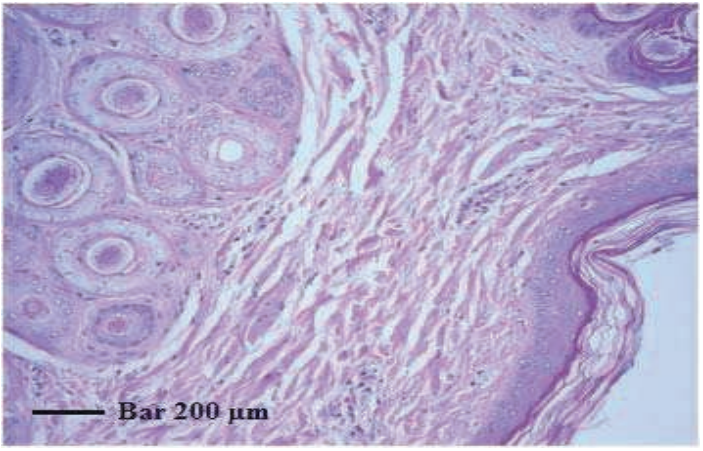

Figure. 1. 3: Illustrates the three distinct zones typically present as well as the fairly even contour of the basal cell layer and the absence of epidermal "pegging" in hairy areas, the stratum the cells of the corneum layer is very clear (X 20, H&E).

The thickness of the llama epidermis seems to be greatest where hair is most sparse. The average thickness of the llama epidermis in haired skin was determined to be 80 mm. This is slightly thicker than the camel epidermis, which is reported to average 60 mm [14]. This is also generally thicker than the total epidermal thickness in haired skin of sheep (range = 27 ± 42 mm) and goats (range = 20 ± 40 mm), but it lies within the normal range reported for horses (30 ± 95 mm) and cattle (16 ± 145 mm) [15]. As other camelidae skin, llama skin shows epidermal rete ridges only in hairless regions, near mucocutaneous junctions, and in some of the specialized areas (i.e. metatarsal glands, interdigital glands, footpads), all other large animals, except pigs have generalized rete ridges [15].

For purpose of identification, certain areas of the camlidae, epidermis are classified as layers and are named from within inward , as follows [1].

1. The stratum corneum (horny layer) is constantly being shed. It is the outer layer of completely keratinized tissue. It is consisting of flattened anuclear, eosinophilic cells. This layer is thicker in lightly haired or glabrous skin. Its gradual desquamation normally is balanced by proliferation of the basal cells, which maintains a constant epidermal thickness [15] (Figure.1. 4). The Stratum corneum (horny layer) represents 1/2 - 3/4 of the total epidermal thickness [2]. This layer consists of fully keratinized cells pushed up from basal layers. In llama skin, the typical stratum corneum (horny layer) has a basket weave appearance, but regional variation exists. Mucocutaneous junctions have either non-existent or extremely thin compact stratum corneum. At the mucocutaneous junction of the eyelid, the stratum corneum becomes laminar, with retained attended nuclei. An extremely thick compact stratum corneum protects the

footpads, while a thick modified stratum corneum with retained cellular outlines is seen over the metatarsal and interdigital glands [17]. The typical stratum corneum in haired skin generally represents 1/ 2-3/4 of the total epidermal thickness and is one to three times the thickness of the viable epidermis. The thickness of the stratum corneum in haired skin ranges from 28 mm over the caudal abdomen to 167 mm over the dorsal thorax [2]. The stratum corneum in haired llama skin appears to be thickest over the dorsal thorax [18]. llama footpads have a structure of the massive compact laminar stratum corneum which seems to be similar to that of the equine frog, equine chestnuts, equine ergots and the footpads of carnivores [19].

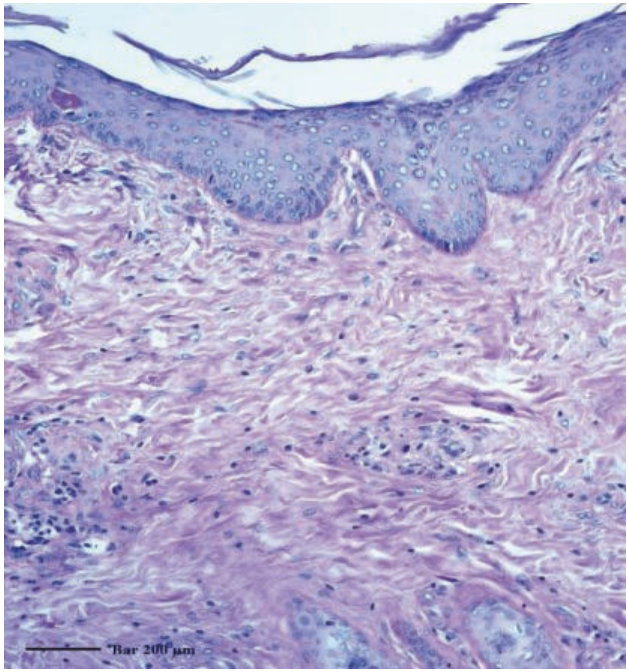

Figure.1.4. Shows the normal gradual desquamation of the stratum corneum (horny layer) (X 20, H&E)

2. The stratum lucidum (Clear layer), is a thin homogenous eosinophilic band along the base of the stratum corneum. It is seen in areas that are sparsely haired, glabrous or near mucocutaneous junctions such as the smooth surface of the lip. The stratum lucidium is a fully keratinized compact thin layer of dead cells [4, 20, 21]. The clear layer is anuclear, homogenous, and hyaline-like and contains retractile droplets (eleidin) [15]. A stratum lucidum has been identified in similar locations in glabrous or sparsely haired llama skin and in skin located near mucocutaneous junctions [17]. A stratum lucidum rarely is present in haired skin of large domestic herbivores, except over the muzzle, coronet, and perianal regions [15]. A stratum lucidum has been described only in the footpads of domestic carnivores [19].

3. Stratum granulosum (granular cell layer) is consistently present in haired skin and discontinuous in others. In most locations it is composed of a single layer of thin flattened cells with compressed nuclei (parallel to the surface) and small basophilic kerato- hyaline granules (Figure.1.5). The function of keratohyalin granules is incompletely understood but is thought to be concerned with keratinization and barrier function [22, 23]. Mucous membranes and some mucocutaneous junctions lack a stratum granulosum. A thick stratum granulosum with dark granules is present in areas of thick stratum corneum and sparse hair, such as the teat, haired area adjacent to the lips, dorsal muzzle, chin, metatarsal glands, interdigital glands and footpads [14].

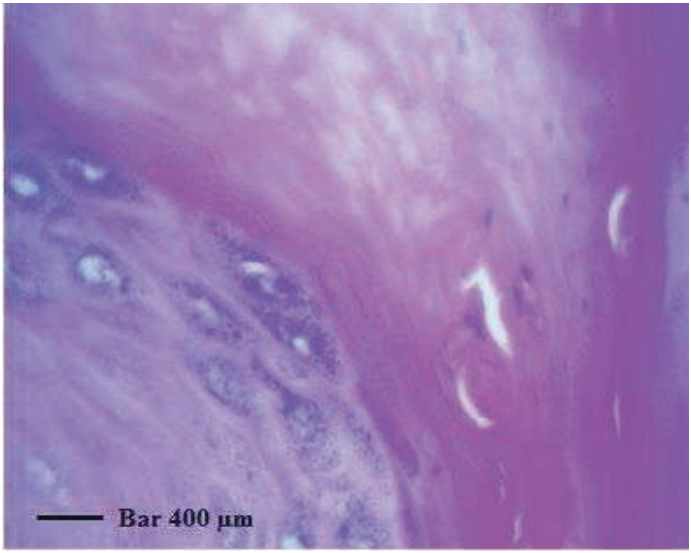

Figure. 1.5: Shows the Kerato-hyalin Granules in the Stratum granulosum layer (granular cell layer) (X 40, H&E).

4. The stratum spinosum (prickle layer) of haired skin tends to be thin, but it is composed of daughter cells of the basal layer averaging one to three cell layers. These cells are viable and nucleated and actively synthesize keratin. This layer is correspondingly thicker, and has more prominent intercellular bridges, in areas of thicker epidermis and thinner hair coat [2]. In the llama, as in other large animals, a direct correlation exists between the thickness of the stratum spinosum and the thickness of the epidermis, while an inverse relationship existed between the thickness of this layer and the density of the hair coat. In llama, the stratum spinosum of haired skin tends to be thin, averaging one to three cell layers. This layer is correspondingly thicker, and has more prominent intercellular bridges, in areas of thicker epidermis and thinner hair coat. The stratum spinosum cell membranes are extremely dense in some of the specialized areas, such as the metatarsal gland and interdigital gland, and probably give rise to the vacuolated stratum corneum in these areas [17]. In other large animals, the stratum spinosum has been reported to average two to four cell layers[15]. The stratum basale (stratum germinativum, basal cell layer) is the deepest layer of the epidermis and

consists of a single layer of cuboidal or columnar cells most of which are keratinocytes with a few melanocytes. Melanocytes contain melanin pigment in pseudopods distributed between epidermal cells of the skin and hair [8, 24].
In IIama, the stratum basale (stratum germinativum, basal cell layer) consists of a single layer of cells resting on a prominent eosinophilic basement membrane. The basal keratinocytes vary from cuboidal to columnar and have basophilic cytoplasm. The basal cells of the nail epithelium are elongated columnar cells with vacuolated cytoplasm. With the exception of the eyelids, melanocytes are rare at most mucocutaneous junctions. They are absent in most mucous membranes and in many of the specialized areas such as the `interdigital gland' and `metatarsal gland'. But, they are prominent in the footpads [17].
Melanocytes are interspersed between basal cells of the epidermis and the ratio of melanocytes to basal keratinocytes ranged from 1: 3 to 1: 14. In other domestic herbivores, the ratio of melanocytes to basal keratinocytes has been reported to range from 1: 10 to 1: 20 [15]. The melanin content of the llama eyelid epidermis, especially near the muco-cutaneous junction, is quite high. Heavy black pigmentation also is present around the eye of the camel and other desert animals, where it is suspected to play a role in photo protection [14].

1.6.3 Dermis

The dermis (corium) is an integral part of the body's connective tissue system and is of mesodermal origin. In areas of thick haired skin, the dermis accounts for most of the depth, whereas the epidermis is thin. In very thin skin, the decreased thickness results from the thinness of the dermis. The dermis is composed of fibers, ground substance, and cells. It also contains the epidermal appendages, arrector pili muscles, blood and lymph vessels, and nerves [15]. True papillary and reticular dermis, as described in humans, was not approved previously in large animals (except swine) because researchers didn't recognized epidermal rete ridges and dermal papillae in the normal haired skin of large animals [15]. In camel the dermis (Corium) is relatively thick [5] (Figure. 1.6). The dermis of the dorsal cervical and caudal tibial regions is markedly thicker than that of other areas (up to 1 cm in the cervical region of a mature male camel), and consists of a superficial layer composed of loose connective tissue interdigitating with undulations in the epidermis and deep dermis, which is composed of dense fibrous tissue. The dermis contains hair follicles, blood and lymph vessels, nerves, and sebaceous and sweat glands. The mid-dermis is characterized by a proliferation of blood vessels, in contrast to that in other domestic animals. Vessel walls are hyalinized. Papillae are prominent in non-hairy areas such as the lip and perianal areas, but are not present in hairy areas [4]. However, a thin superficial zone of delicate, closely woven fibers (stratum papillary) and a thick deeper zone of larger fibers (stratum reticular) are clearly evident in all areas. In the llama, the average dermal thickness as typified by that of the lateral thorax, is 3.1 mm. Most dorsal and lateral body areas have a relatively thick dermis. The thickest dermis is present on the dorsal aspect of the neck (4.6 mm) and lateral aspect of the neck (5.1 mm). Ventral areas have a much thinner dermis (2-3 mm). The thinnest dermis (0.3 mm) is found on the concave surface of the proximal pinna. The superficial dermis consists of fine collagen fibres with abundant oval fibrocyte nuclei. The deep dermis is composed of large, dense collagen fibres with few fibrocyte nuclei. In the teat, the collagen fibres have an especially undulating appearance. In the teat and chin, the deeper collagen bundles are arranged loosely. In

the ear canal (Fig 10), there is no apparent distinction between the superficial and deep collagen [17].

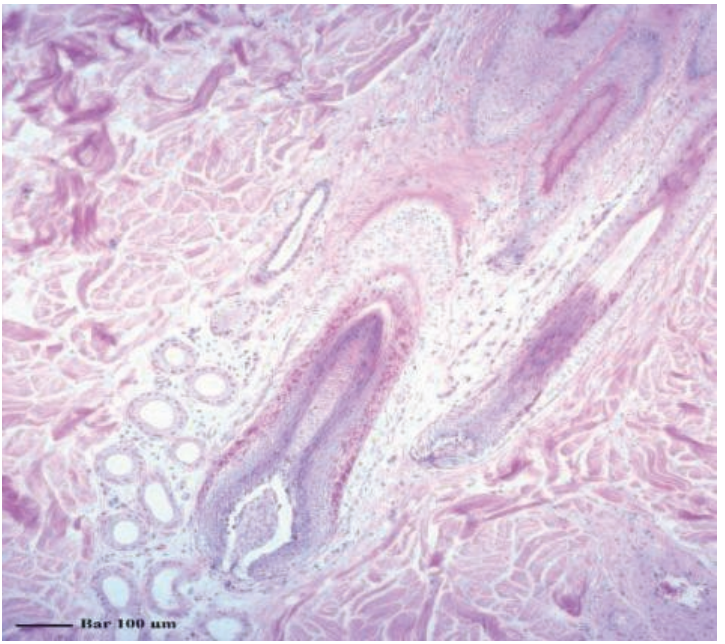

Figure.1.6: Shows Deep dermal layers show the hair follicles, sweat glands and collagenous fibers. (X 10, H&E).

1.6.4 Dermal fibers

The dermal fibers are formed by fibroblasts and are collagenous, reticula (R), and elastic (Figure. 1.7). Collagenous fibers (collagen) have great tensile strength and are the largest and most numerous (approximately 90 percent of all dermal fibers are collagen). They are thick bands composed of multiple protein fibrils and are differentially stained by Masson's trichrome stain. Reticular fibers (Reticulin) are fine-branching structures that become closely approximated to collagen with age. They can be detected best with special silver stains. Elastics fibers (elastin) are composed of single, fine branches that possess great elasticity. They are well visualized by Verhoeff's and van Gieson's elastin stains [15]. There are at least seven and possible ten genetically and structurally different types of collagen molecules in the body. Type I collagen predominates in the dermis, and Type IV collagen is present in the epidermal basement membrane zone. The biosynthesis of collagen is a complex process of gene transposition and translation, intracellular modifications, packaging and secretion, extracellular modifications, and fibril assembly and cross linking. Collagen abnormalities may result from genetic defects, deficiencies of vitamin C, iron, and copper, and ß-amino-proprio-nitrite poisoning (Iathyrism) [25]. In general, the superficial dermis contains fine loosely arranged collagen fibers that are irregular distributed and a network of fine elastin fibers.

The deep dermis contains thick, densely arranged collagen fibers that tend to parallel the skin surface and elastin fibers that are thicker and less numerous than those in the superficial dermis. Small amounts of mucin (a blue –staining, granular to stringy appearing substance) may be seen in the interstitial areas of the dermis, especially around vessels and appendages. In llama, the superficial dermis consists of fine collagen fibers with abundant oval fibrocyte nuclei. The deep dermis is composed of large, dense collagen fibers with few fibrocyte nuclei. In the teat, the collagen fibers have an especially undulating appearance. In the teat and chin, the deeper collagen bundles are arranged loosely. In the ear canal, there is no apparent distinction between the superficial and deep collagen [17].

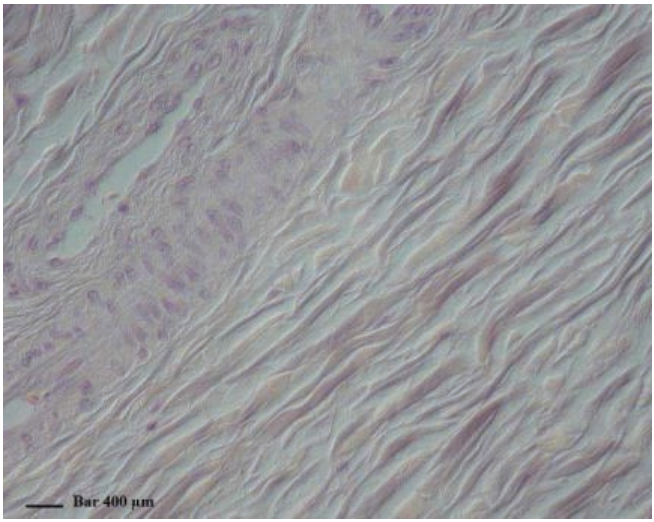

Figure. 1.7: Shows dermal fibers in the skin of the camels (X 40, H&E).

1.6.5 Dermal and ground Substance

The ground (interstitial) substances, the main component of the dermis, is a mucoid gel-sol of fibroblast origin composed of proteoglycans, principally hyaluronic acid, dermatan sulfate (chondrotin sulfate B), chontroitin -4 sulfate (chondrotin sulfate A), and chondrotin -6-sulfate(chondrotin sulfate C). It fills the space and surrounds other structures of the dermis but allows electrolytes, nutrients, and cells to traverse it in passing from the dermal vessels to the avascular epidermis [15, 26]. The proteoglycans function in water storage and homeostasis; selective screening of substances (e.g., protein and electrolytes); and supporting dermal structure, lubrication, and collagen fibrillogenesis, orientation, growth, and differentiation. As animals age, the ground substance decreases in amount. Cell surface fibronectin is an adhesive glycoprotein that mediates cell to-cell interaction and cell adhesion to substratum and modulates microvascular integrity, vascular permeability, and wound healing. Fibronectin is synthesized by fibroblasts, macrophages and endothelial cells [27].

1.6.6 Dermal Cellular Elements

The dermis is usually sparsely populated with cells. Fibroblasts are present throughout. Melanocytes may be seen near the superficial dermal blood vessels. Horses and ruminants tend to have a mild perivascular accumulation of small (lymphoid) and large (histiocytic) mononuclear cells in the superficial dermis.

Mast cells most abundant around superficial dermal blood vessels and appendages, especially in the pinna, eyelid, face, ventral abdomen, scrotum, and interdigital areas. They are best visualized with special stains such as toluidine blue or acid orcein-Giemsa .In goats, there are two morphological forms of mast cells seen in skin: One is small and spindle-shaped resembling a fibroblast; the other is large and ovoid. Healthy, parasite free swine were shown to have an average of 32 mast cells\ mm ^{2} of skin, and the numbers decreased markedly when the swine were stressed. Eosinophils are frequently seen in small numbers in the normal dermis of large animals. It has been reported that the number of eosinophils in the skin of normal cattle approximately doubles in the summer as compared with winter. Presumably, this reflects exposure to biting insects and arthropods and would be expected to happen in all large animals [10]. The histological examination of IIama skin identified the presence of unusual vascular plexuses within the dermis layer (Figure.1.8). These unique vascular structures also have been described in the skin of guanacos and alpacas where they are sometimes misinterpreted as a pathological change (angiomatosis) [28]. Although their role remains uncertain, the close proximity of the vessels to each other suggests a possible countercurrent exchange mechanism, perhaps functioning in the prevention of water loss from the intravascular compartment. Water conservation is thought to be an important function of the cutaneous vasculature of the camel [29]. The vascular plexuses also may represent arteriovenous anastomoses similar to the `glomus', a specialized complex vascular structure in the skin of certain animal species, which functions in thermoregulation [15, 28]. The exact identity of the different cell types present within the perivascular stroma of llama skin has yet to be determined. Some of the mononuclear cells may represent `glomus cells', thought to be modified smooth muscle cells, typically found in high concentration between the vessels of the glomus [15]. The absence of identifiable mast cells is unusual because most animals have abundant perivascular accumulations of mast cells in the superficial dermis, where they play an important role in the skin immune system. In the perivascular areas, we noted the presence of unique cells with eosinophilic cytoplasmic granules. The classification of these unusual cells is uncertain. Other investigators have called these cells `eosinophils' [18]. These cells may be true eosinophils, as small numbers of eosinophils are frequently seen in the normal dermis of large animals, presumably in relation to biting arthropod exposure [15, 30]. However, these llama perivascular cells differ from typical llama eosinophils in that their nuclei appear round to oval instead of multi-lobulated. Perhaps these cells represent mast cells or mast-cell derivatives, such as globule leucocytes. Globule leucocytes, mononuclear cells with eosinophilic granules, contain immunoglobulins and are thought to play a role in immune reactions to parasites. They occur between the epithelial cells of various mucous membranes in a variety of mammals[31]. Similar mononuclear cells with eosinophilic granules have been noted in the mucosa of the gastrointestinal tract of llamas necropsied at the University of California Davis Veterinary Medical Teaching Hospital (personal observations).

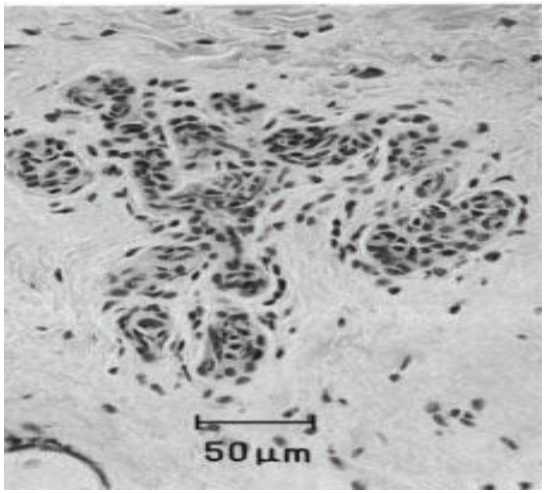

Figure. 1.8: shows capillary plexus from abdomen (x100). (B. A. Atlee *et al.,* 1997) Focal small blood vessel plexuses are present in the superficial to mid dermis in almost all parts of the body. They are large and prominent in areas of long dense hair coat and smaller in some sparsely haired areas and near many mucocutaneous junctions. The vessel walls are thick with a hyaline appearance and have large round endothelial nuclei. Erythrocytes are seen within vessel lumens. A loose fibrous connective tissue stroma surrounds the entire vascular plexus. Numerous cells (fibroblasts, small mononuclear cells) are evident within the surrounding stroma. Rare cells with small eosinophilic cytoplasmic granules also are present within this stroma [17].

1.6.7 Hair follicles

Details on the production of camel hair are very limited. Camel has both simple and compound hair follicles, and the proportion and structure of each varies with body location. The simple hair follicles vary greatly in size and structure, depending upon body location and specialized function. There are differences in the distribution of the hair follicles over the body of the camel. The camel hair follicles over the area near the margin of the lip, external nares and lower eyelid are spaced and singly. The hair follicles over the dorsal and lateral aspects of the body are present in relatively high density and are orientated at a sharp oblique angle [4, 11, 32]. The clipped camel skin surface reveals hair cluster consisted of two or three larger cover hairs, emerging singly, and close to these are from two to five groups of smaller wool hairs, when examine by means of the stereoscopic microscope [5, 12]. Hair follicles are observed to be in various stages (anagen, catagen, telogen). The fibrous root sheath surrounding the larger solitary hair follicles, especially those in catagen, is especially thick. The majority of hair shafts appear to have a small discontinuous medulla. Most primary hairs, especially the giant guard hairs, contain a prominent eosinophilic medulla, while the secondary hairs have variable medullation. Hair follicles are grouped into distinct clusters. Each cluster is projecting from an irregular depressed area or groove and is separated from adjacent clusters by elevated ridges [4, 33, 34]. These groups consisted from two to nine hairs

emerging from a common orifice. Majority of hair follicle groups consist of 3 primary follicles associated with secondary follicles, but some follicle groups contained more than 3 primary follicles (Figure. 1.9). The basic criterion for distinguishing a primary follicle from a secondary follicle is the presence of sweat gland in primary follicle. Secondary follicles do not bear sweat glands. When hair follicles became inactive the morphology of these follicles are undergoing substantial changes which can be observe by histological examinations. The smaller secondary follicles are regressed earlier than larger secondary follicles. In an inactive follicle the structure of fibre, the inner root sheath and outer root sheath cells is disrupted. In such follicles the outer root sheath cells are often columnar and radially or spirally arranged in contrast to the randomly arranged cells in normal follicles [34]. As in camel the llama compound hair follicle consists of one or two primary follicles surrounded by multiple (two to nine) smaller secondary follicles, all fusing together near the entrance of the sebaceous ducts and sharing a common follicular infundibulum. The entire compound follicle is surrounded by a continuous fibrous root sheath. The areas of short sparse hair coat have rare compound follicles, and the ratio of primary to secondary hairs averages 1: 2. The areas of long dense hair coat have the largest and most abundant compound follicles, and the ratio of secondary to primary hairs (S/P ratio) averages 9: 1[17].

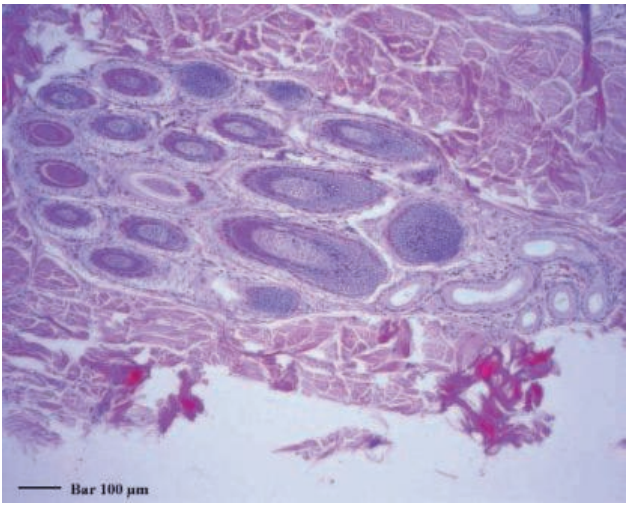

Figure.1.9: Shows the transverse section through the skin sample (at the sebaceous gland level) from an adult dromedaries camel indicating follicle groups consisting of more than 3 primary follicles associated with secondary follicles in telogen stage.

1.6.8 Hair Anatomy

Pilosebaceous unit is a mini-organ build of sebaceous gland and the arrrector pili muscle and the hair follicles. However, different hair follicle types may contain these components in varying proportions. A single hair follicle is composed of multiple mesenchymal and epithelial cell layers - all of them comprise more than twenty different

cell populations. The basic hair follicle structure can be divided into different regions on the basis of:

1. Morphology - whether the structure is ectoderm- or mesoderm-derived
2. The hair cycling characteristics of each structural unit.

At the most basic level, the difference is made between the permanent, superficial structure and the transient cycling component of the hair follicle, which includes the hair bulb [35, 36, 37]. The physical dividing line, between these two components lies a little below the bulge region and the insertion of the arrector pili muscle. The hair follicle may be divided anatomically into four parts:

1.The bulb consisting of the dermal papilla and matrix
2.The suprabulbar area from the matrix to the insertion of the arrector pili muscle
3.The isthmus that extends from the insertion of the arrector pili muscle to the sebaceous gland
4.The infundibulum that extends from the sebaceous gland to the follicular orifice.

The superficial part of the hair follicle infundibulum is called the acro-infundibulum. It is lined by epidermis including a well-developed stratum corneum and a stratum granulosum layer. The lower part of the infundibulum, called the infra- infundibulum, may experience a continuous loss of epidermal differentiation occurring towards this isthmus.

The infundibulum layer of the hair follicle consists of five major portions*:*

1.The dermal papilla
2.The matrix
3.The hair shaft, consisting from inward to outward the medulla, cortex, and cuticle
4.The inner root sheath (IRS) consisting of the inner root sheath cuticle, Huxley's layer, and Henle's layer
5.The outer root sheath (ORS).

The isthmus is the part that lies between the sebaceous gland duct opening and the bulge. The isthmus provides a border zone that is relatively devoid of distinctive features. Though the thick vitreous membrane between ectoderm and mesoderm visible elsewhere in anagen stage hair follicles becomes noticeably thinner here. The wall of hair follicle isthmus consists of two or three rows of flattened cells. The angle of orientation of these cells can be observed to change along the length of the isthmus as the outer root sheath merges with the skin epithelium. There is a bulge region below the isthmus - it provides the insertion site of the arrector pili muscle. Additionally, it harbors the so called bulge region, which is a specialized compartment of the outer root sheath. It in turn forms a niche for epithelial and neurectodermal stem cells as well as various immature cell populations including immature Langerhans cells and mast cells. The part that extends from the skin surface down to lower end of the bulge region forms the permanent portion of the hair follicle; no significant cyclic changes are observed in this area. However, the presence of hair follicles, and also their size and their density, affects the enlargement of the skin surface to a considerable extent (Figure. 1.10,). Alternatively, the inferior unit extends from the bulge to the base of the hair follicle bulb; it can be further subdivided into the bulb and suprabulbar region. The epithelial compartments of the hair follicle include the outer root sheath and the inner root sheath. Both of them are composed of different cell sub layers, and the matrix cells. The outer root sheath that starts from the matrix cells in the hair bulb extends up to the entry level of the sebaceous duct. Outer root sheath cells contain clear vacuolated cytoplasm - they are filled with large amounts of glycogen. The outer root sheath below the isthmus does not contain keratins. The inner root sheath disintegrates at the level of the isthmus and the outer root sheath keratinizes without forming granules.

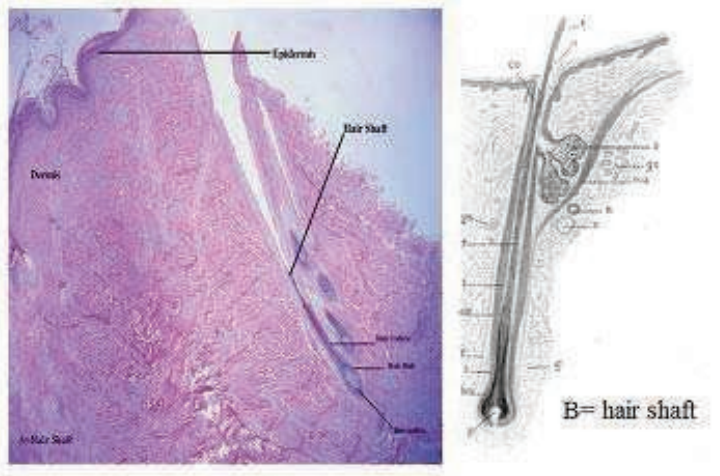

Figure. 1.10: t = hair shaft, 0 = hair follicle opening, mu = arrector pili muscle, s = sebaceous gland, r = radicular portion of hair shaft, f = connective tissue sheath of hair follicle, ex = outer root sheath, i = inner root sheath, bc = bulb of hair follicle, p = dermal papilla, g = adipose tissue, a = arteriole in cross section, n = nerve, gs = coils of sweat gland.

The outer root sheath cells are characterized by the presence of a large diversity of mediators, hormones and receptors. All of them are keratinized. Because it hardens before the presumptive hair fiber does, hence, it is believed to control the cross sectional and longitudinal shape of the hair produced. A vitreous or basal membrane separates the mesenchymal sheath from the epithelial root sheaths. A dense vascular network surrounds this whole complex. A cuff is formed with free nerve endings; it provides the basis for intensive piloneural interactions. Proliferative activity of matrix keratinocytes gives rise to the hair shaft and the inner root sheath - the hair growth is the result of this entire process. The hair shaft and the inner root sheath are localized in the bulb where they sit on top of the dermal papilla. The dermal papillae are clusters of specialized mesenchymal cells with important hair growth inductive properties. The fact that surgical removal of the dermal papilla and the lower dermal sheath prevents hair growth indicates the importance of these specialized mesenchymal cells - they act as the key signaling center in hair follicles. A blood capillary loop is located within the dermal papilla of terminal hair follicles - the nutrition to the papilla and the overlying matrix cells is supplied through this. Dermal papillae at the root of vellus hair follicles typically do not have capillaries – their nutrition diffuses in, from blood vessels around the outside of the vellus hair follicles. The llama compound hair follicle observes to consist of one or two primary follicles surrounded by multiple (two to nine) smaller secondary follicles, all fusing together near the entrance of the sebaceous ducts and sharing a common follicular infundibulum. These typical compound follicles have been previously referred to as `follicular nests' [38]. Camel compound follicles also have been reported to consist of two to nine small secondary follicles but to lack the primary hair follicles seen in llamas [4]. Areas of llama skin with a short sparse hair coat appears to have rare compound follicles under microscope. The average ratio of primary to

secondary hairs follicles in these areas is 1: 2. The areas of long dense hair coat appear to have the largest and most abundant compound follicles. The ratio of secondary to primary hairs (S/P ratio) are 9: 1, while sheep have S/P ratios which are range from 3 : 1 to 20 : 1, depending upon the breed [39]. Most llama hair shafts appear to have a discontinuous medulla as in other domestic animal hair, which also identified a discontinuous medullary space [38, 18, 39]. Most llama primary hairs have a prominent eosinophilic medulla, while the secondary hairs have variable medullation. Although sheep also have medullated primary hairs, smaller secondary `wool' hairs lack a medulla [39]. The medullary diameter of alpaca hair has been reported to be smaller than that of llama hair [38].

1.6.9 Sebaceous glands

Sebaceous (holocrine) glands are simple or branched alveolar glands distributed throughout all haired skin. The glands usually open through a duct into the pilary canal in the infundibulum (pilosebaceous follicle). Low density hair follicle areas have largest sebaceous glands. They are largest an most numerous near mucocutaneous junctions, the coronet, and over the dorsal neck and rump. Sebaceous glands have an abundant blood supply and appear to be innervated. Their secretion is thought to be under hormonal control, with androgens causing hypertrophy and hyperplasia, but with estrogens and glucocorticoids causing involution. In general, the composition of surface lipids consists of varying percentages of triglycerides, phospholipids, cholesterol, cholesteryl esters, and unesterified fatty acids [15]. The sebaceous gland of camel is presented in all skin regions. The sebaceous gland is consisted of several lobes which are not subdivided into lobules. The connective tissue sheath around the gland showed blood vessels and nerve fibers. The general disposition of the sebaceous gland in this species appeared to resemble that of other domestic animals studied by Jenkinson *et al.,* (1985) [40]. Cells at different stages of development and maturation could easily be identified in the sebaceous gland. It appears to consist of three types of cells; the first type is found at the periphery of the gland. These cells are flat and stain more darkly than the rest of the cells in the gland. The second type of cell is present next to the peripheral cells and the cells are spherical in shape with rounded nuclei. These cells occupied about two thirds of the gland. The third type consists of cells which are spherical but looks paler than the second type of the cells and their nuclei are either absent or pyknotic. Since these types of cell in the sebaceous gland of the camel conform to the general scheme suggested by Jenkinson *et al.,* (1985) [40] for the sebaceous gland of the cow, sheep, goat and horse, same terminology, namely peripheral, maturing and necrotic cells, was decided to adopt (The sebaceous gland supply with nerve fibres). The nerve fibers are appeared in the vicinity of the gland and appeared to innervate the peripheral cells. However the nerve fibres in the camel were not confined to the connective tissue around the gland but penetrated the basal lamina and innervated the gland as has been demonstrated by silver impregnation and confirmed by electron microscope. The sweat gland demonstrated to be innervated by a plexus of AChE-positive nerve fibers. In the papillary layer, the nerve breaks to form a plexus supplying the blood vessels, from this plexus fibers end in the deep interface of the epidermis. End bulbs and free intra epidermal nerve ending are reactive for AChE [41] in the horse, cow, sheep and goat, the nerves are confined to the connective tissue sheath [40]. Nevertheless, Rollinson *et al.,* (1972) [42] have tentatively suggested that the cholinergic nerve fibres found in the vicinity of the sebaceous gland of the camel apparently end on them. The electron microscopic evidence of the innervation of the sebaceous gland has been

published by Dugan (1974) [43]; he believed that the presence of nerve endings among the peripheral cells in the rat suggests a possible role in holocrine differentiation or elaboration. In the camel, the sebaceous glands are found in all the regions of skin. Camel sebaceous glands are lobed and surrounded by a connective tissue sheath. Each covered hair follicle in the camel is surrounded by a ring of typical simple or branched saccular glands of the holocrine type. In the compound follicles of the wool hairs, each branch has its own independent ring of such glands. Camel sebaceous glands appear to consist of three types of cells; the first type is found at the periphery of the gland. These cells are flat and they stained more darkly than the rest of the cells in the gland. The second type of cell is present next to the peripheral cells and the cells are spherical in shape with rounded nuclei. They can occupy about two thirds of the gland. The third type consist of cells which are spherical but look paler than the previous ones and their nuclei are either absent or pyknotic (Figure 1.11 A&B)..

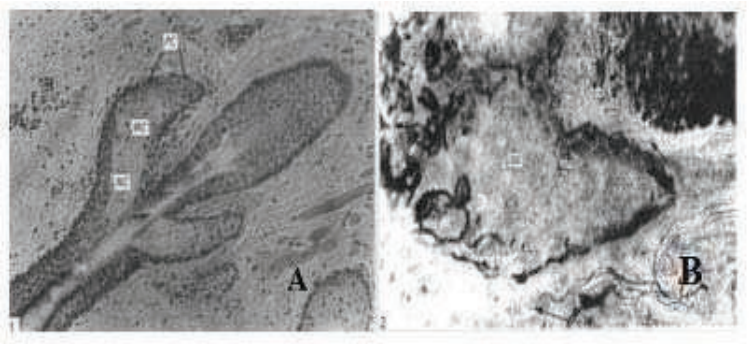

Figure. 1.11 (A&B): A. lobed sebaceous gland showing three types of cells; peripheral flattened cells (PC), mature spherical cells with rounded nuclei (MC), and necrotic cells with pyknotic nuclei (NC). Each lobe opens into the hair follicle by a short duct. x 160. ; B. Nerve fibres around the sebaceous gland (SG). Note that some of the nerves appear to end on the peripheral cells (arrows). x 700. (TAHA, 1988)

Since these types of cell in the sebaceous gland of the camel conform to the general scheme suggested by Jenkinson *et al.,* (1985) for the sebaceous gland of the cow, sheep, goat and horse, it is also decided to adopt the same terminology, namely peripheral, maturing and necrotic cells. Nerve fibres are observed in the vicinity of the sebaceous gland and they appear to innervate the peripheral cells. No sebaceous glands are observed in skin areas without hair follicles. Sections of the eyelid are revealed no tarsal glands and this can be confirmed by direct examination of the skin specimens with the stereoscopic microscope [3]. Most areas of llama skin that show only one or two small sebaceous glands are associated with each hair follicle. The basic structure, abundance, and regional size variation of the llama sebaceous glands is similar to those of most other mammals, including camels [15, 40]. The llama sebaceous glands are generally smaller and less numerous than the well-developed multilobulated sebaceous glands of sheep, which probably explains the presence of less oil (lanolin) in the coats of llamas than in sheep [38]. The size and number of sebaceous glands increase near mucocutaneous junctions and in the ear canal. Several large sebaceous glands (glands of Zeiss) are associated with each eyelash follicle. All sebaceous glands are associated with hair follicles. Because the footpad lacks hair follicles, sebaceous glands are absent in this

area. In the ear canal and perianal skin, although the prominent sebaceous glands at first may appear to open directly on to the skin surface, each actually is associated with a rudimentary hair follicle (`sebaceous follicle'). Most sebaceous ducts are short and wide, but some are longer and narrower. The sebaceous duct is composed of two cell layers of non-keratinized stratified squamous epithelium [17]. Sebaceous lobules are bordered by a basement membrane zone, upon which sits a single layer of deeply basophilic basal cells (reserve cells). The cells become progressively more lipidized and eventually disintegrate to form sebum toward the center of the lobule. Sebaceous ducts are lined with squamous epithelium. The oily secretion (sebum) produced by sebaceous glands tends to keep the skin soft and pliable by forming a surface emulsion that spreads over the surface of the stratum over the hair shafts and gives them a glossy sheen. During periods of illness or malnutrition, the hair coat may become dull and dry as a result of inadequate sebaceous gland function. In addition to its action as a physical barrier, the sebum-sweat surface emulsion forms a chemical barrier against potential pathogens. Many of sebum's fatty acid constituents (linoleic, muristic, oleic, and palmitic acids) are known to have antimicrobial actions.

1.6.10 Sweat glands

Previous information in the literature concerning the presence of sweat glands in the skin of the camel has been conflicting [7], claim being made that sweat glands are totally absent. But, laterally similar sweat glands are approved widely distributed in the skin over the body surface of the camel. Furthermore, the orifices are macroscopically visible, and if an area of the skin is covered in hot weather it will become wet. Usually the rate of sweat secretion is so low that the camel's skin seems dry even though the amount of water actually evaporated may be quiet high as shown by the cup method. Finally actual prints of the sweating pattern were obtained by using ferric nitrate and tannic acid impregnated filter paper, and permanent records of the distribution of active sweat gland orifices were obtained. Such prints showed a rather high density of the orifices. From that time, it has been demonstrated that camels do, in fact, have sweat glands which are deeply embedded in the skin and distributed over the body surface, and these glands are of importance in heat regulation [4]. There is an average of 200 sweat glands per square centimeter on camels, about one-quarter of the number found on cattle. Structural changes have shown that they are more active in hot summer temperatures than in winter ones [4]. Apocrine sweat glands are generally coiled and saccular or tubular and are distributed throughout all haired skin. The glands are localized below the sebaceous glands and usually open through a duct into the pilary canal in the infundibulum, above the sebaceous duct opening. The sweat glands of camel are found in all the body areas except the lips, the external nares and the perianal region. The glands are always associated with the large cover hair, clustered around the hair bulb in the reticular layer of the dermis. The secretory tubules varied greatly in size. In some regions, e. g. the scrotum, medial aspect of the arm, the tubules are large, whereas in other regions, e. g. ventral aspect of the neck, the glands are relatively small. Their ducts are observed to open into the neck of the cover hair follicles above the level of the sebaceous gland ducts. The duct is narrow and is lined by a two-layered cuboidal epithelium. The expanded secretory portion is at first spiraled but the terminal end coils into a loose elongated, serpentine net. It is lined by a low columnar epithelium which is separated from the surrounding basement membrane by numerous myoepithelial cells. Occasionally tubules lined with flat epithelium are seen. Secretory granules can be seen in the apices of the epithelial cells and the bleb like protrusions on some of them indicate

the possibility of an apocrine mode of secretion [4]. Adjacent tubules might show one or the other type of epithelium. The secretory cells possess oval, basally situated nuclei, and rest on myoepithelial cells. The lumen of the tubule is filled with globular material in which nuclei are often seen. The gland duct is narrower than the secretory tubule. It has a lining of two layers of cuboidal cells, although sometimes, as in the interdigital region, more than two layers of cuboidal cells might be seen. The secretory cells are intensely and uniformly reactive to P.A.S. test (Figure.1.12 A, B, C, D). The granular reaction, which is resistant to diastase digestion, is confined to the supranuclear region. The lumina of the tubules and the ducts are consistently unreactive [45]. The tubular skin glands of animals classifies as consisting of two functional types [46], merocrine and apocrine. In primates, the merocrine glands open on the surface of the epidermis at a sweat pore and are distributed over the general surface of the body, while the apocrine glands are confined to certain body regions such as the axilla. In domestic animals, Schaffer [46] describes the apocrine type as being the generally distributed type, these possessing ducts which open into the neck of hair follicles, whereas the merocrine type is confined to certain body regions such as the foot pad of the dog and the frog of the capsula ungulae of the horse. The ducts of the latter are opening on the surface of the epidermis. In llama, sweat glands are well described by Barbara *et al.,* 1997 [17]. Llamas sweat significantly in response to high ambient temperatures, and this may be an important mechanism of thermoregulation [47]. Sweating is apparently one of the major cooling mechanisms in camels [14]. This differs from goats and sheep, in which sweating is minimal [14, 48]. The glandular portion of the llama sweat gland is tubular and usually coiled. The secretory epithelium of the sweat glands varies from flattened to columnar. Myoepithelial cells are present between the secretory epithelium and basement membrane. The sweat gland duct is either coiled or straight and consists of two or three layers of squamous or cuboidal cells, and continuous with, the external root sheath of the hair follicle. A thin single layer of flattened epithelial cells containing keratohyalin granules lines the opening of the duct, and keratin is present within the lumen. In haired skin, the duct empties into the follicular infundibulum of primary hairs near the follicular ostium in an epitrichial fashion. The size and distribution of llama sweat glands vary with body location. Epitrichial sweat glands are well-developed and extend deeply into the dermis in the ventral sparsely haired areas, muzzle and teat. Several large sweat glands (glands of Moll) are associated with each eyelash follicle. Well-developed sweat glands (ceruminous glands) are associated with rudimentary hair follicles in the ear canal. Small, relatively straight glands with narrow lumens are found in the superficial to mid dermis of the concave surface of the pinnae, chin and most densely haired areas. Sweat glands are sparse over the chin and absent near mucocutaneous junctions of the lips, vulva and anus. Large, discrete, well-circumscribed atrichial (eccrine) tubular glands, with keratinized ducts emptying directly on to the footpad surface, are present within the dermis of the llama footpad. Tortuous keratinized stratified squamous epithelial ducts extend from these glands, through the epidermis and stratum corneum, to the footpad surface. A few large well-circumscribed tubular glands are present in the deep dermis of the metatarsal and interdigital gland region. The glandular epithelium consist of a single layer of cuboidal to columnar cells resting on a prominent eosinophilic basement membrane. Some of these cells have luminal buds (`caps'). The glandular epithelial cells have eosinophilic to amphophilic cytoplasm and round, oval or flattened central basophilic nuclei with homogenous chromatin. Spindled myoepithelial cells with elongate nuclei are located between the acinar cells and the basement membrane. A tortuous duct extends from each gland to the surface of the stratum corneum. The duct is formed of stratified squamous keratinized epithelium. A

granular cell layer (1-3 cells thick) is present, and the ductal lumen is filled with keratin. The acini and the dermal portion of the duct are surrounded by a loose vascular connective tissue stroma [17]. Previously, sweat gland nomenclature was based on erroneous interpretation of differences in the mode of secretion (`apocrine' versus `eccrine'), now, the new nomenclature classifies sweat glands based on the anatomic location of the duct. Thus, the term `epitrichial' is now used to describe sweat glands that open into the hair follicle (formerly `apocrine' glands), while the term `atrichial' describes those sweat glands which empty on to the skin surface in an interfollicular location. Most domestic mammals also have epitrichial sweat glands[49]. The activity of the camel sweat gland has been said to be regulated by environmental temperature and hydration state[44]. The larger sweat glands in the relatively hairless ventral areas of the llama have been hypothesized to play a role in evaporative cooling [18]. The llama may be able to prevent loss of body heat by simply lying down and covering these areas. The hyperthermia often experienced by debilitated recumbent animals may be explained by the inability to lose body heat from these occluded ventral areas [17]. The distribution of sweat glands in guanaco, shows no significant differences between areas, season or sex. However, the same number of active sweat glands in the areas covered with short hair may represent an important avenue of heat loss by evaporation if body temperature is stable. Radiative heat loss was shown that postural changes by the guanaco modify the exposed surface area of the almost bare areas [50] . Axillar and flank regions are potentially more effective in evaporative cooling because these areas are covered with short hair [51]. Guanaco sweat glands are simple and glomerular. The secretory portion is extremely curled in areas where hair is short and the epithelium is of the simple cubic type. The secretion is apocrine and the high P.A.S. (+) reaction indicates the high glycogen content. The secretory ducts are straight; the lumen is small and characterized by a cubic simple epithelium. The mouth of the ducts surface is close to the hair follicle. In areas where the hair follicles are grouped, only one sweat gland per group is present. In other areas where hair follicles are sparser, sweat glands are associated to the big hair follicles where a single tube may be folded into a ball-like shape. The average count was 925 and 750 glands/ cm2 in the axillar and flank regions, respectively. In both areas the glands are epitrichial, with their secretory portion deep in the dermis and beneath the hair follicles. The adenomers are extremely curled and surrounded by myoepithelial tissue. No difference in distribution or number of sweat glands can be found between males and females in different times of the year (summer-winter) [52].

1.6.11 Sweating and thermoregulation in camel

The camel is able to save considerable amounts of energy by allowing its body temperature to rise during the day, thus absorbing heat which would otherwise have to be dissipated by some form of cooling. The variations in the camel's temperature were formerly thought to be an indication of poor thermoregulation. It is now realized, however, that the rise in temperature indicates a sophisticated control mechanism rather than poor regulation. Sweating is important for cooling in many species. Sweating is the secretion of water plus some salts from special sweat glands in the skin, which occurs as a response to an increase in T^{b}. The glands are of two types. Atrichial (without hair) glands are found in primates and also on the pads of cats and dogs. They develop from the epidermis independently of the hairs and open on the free surface of the skin. Atrichial sweats glands are at their densest on human palms and soles, and elsewhere on the body they are at a density of 100-300cm^{-2}. Epitrichial (around hair) sweat glands

develop only in association with hair follicles. They are found in many mammalian species including cattle, sheep, horses and camels (Figure.1.13. A&B).

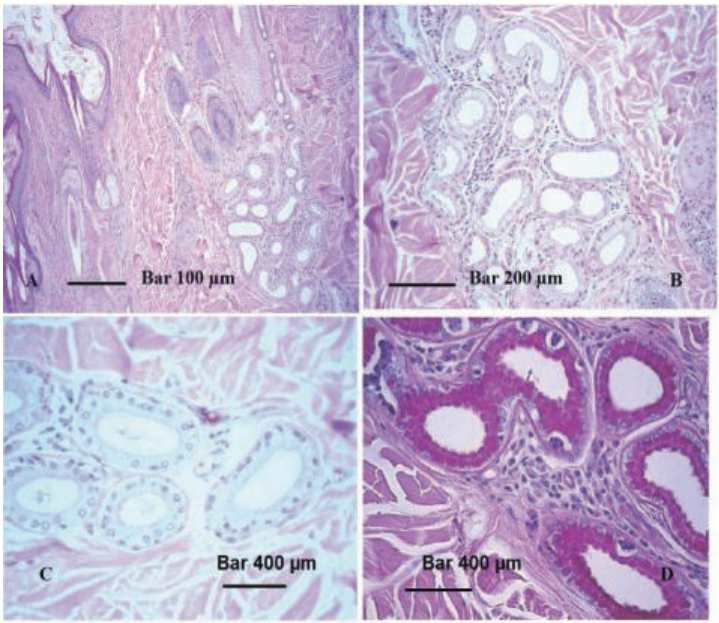

Figure. 1.12 A. B. C. D: Shows camel sweat gland: A, B & C different magnification of sweat glands tubules (X 10, X 20 and X40 respectively H&E). D. The secretory cells are intensely and uniformly reactive to P.A.S. test (X 40 PAS stain)

Epitrichial sweat glands play an important role in thermoregulation in these species. In cattle there are about 1800 cm^{-2} and in sheep, about 300^{-2}. Sweat is an ultra-filtrate of plasma, containing sodium chloride and other salts, lactic acid and urea. As sweat glands absorb much of the electrolytes, sweat is hypotonic to plasma; the salt content of sweat falls with acclimatization. Evaporation of sweat, promoted by input of heat energy from the skin, cools the body, one problem for thermoregulation by sweating in furry mammals is that water evaporating from a fur coat takes a significant proportion of its heat from the air rather than from the skin, and is therefore less effective in cooling the body. Sweating has a physiological cost in that it involves loss of salts and organic molecules as well as water from the body.

The camel handles its water balance problems more effectively than humans. In man at high sweating rates daily loss of sodium chloride may go up to 10-30 g. During sweating the effect of salt loss may not be apparent, but when water is replenished the body fluids become suddenly diluted and this may lead to serious consequences known as cheat cramps sometimes ending in death. In a camel watered daily (hydrated) the diurnal temperature variation is of the order of 2 ^{0} C which implies heat storage of $4.2X10^{6}$J, if the camel weighs 500kg. In the dehydrated camel, however when energy

conservation becomes important, the temperature can fluctuate over a range of more than 6 ^{0} C. The camel is able to store 1,26X10^{7} J of energy in this way.

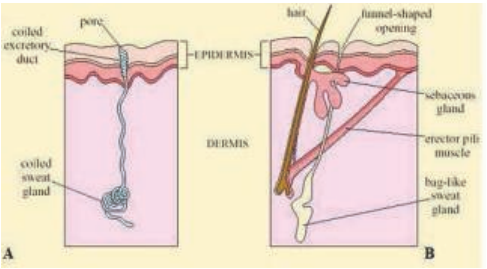

Figure.1.13. A&B: The main structural features of sweat glands known to function in temperature regulation. (a) A human atrichial gland. (b) An epitrichial gland of the ox with its accompanying structures.

To dissipate this energy the camel would require to sweat 6 liters of water compares the temperature fluctuations of camels, donkey and humans in the same environment. In Lama Guanaco, where sweat glands are present all over the skin and where sweat production varies from 4.98 to 73.36 gm^{-2}h^{-1} of skin. Ambient temperatures between 20 and 33 ^{0} C are the main stimuli for activation of sweat glands, generating a heat loss ranging from 11.9 to 37% of standing basal metabolic rate. Respiratory water loss is not an important mechanism for heat dissipation. Water loss is controlled by postural changes in the guanaco [52].

1.6.12 Arrector pili muscles

The Arrector Pili (AP) muscle is a smooth muscle that rises from the uppermost part of the dermis, just beneath the epidermis, and inserts into the hair follicle [53]. They are present in all haired skin and are largest in the dorsal neck and rump. The distal end of the AP muscle shows multiple muscle fibers splaying into multiple branches at the level of the papillary dermis [54]. AP muscles are of mesenchymal origin and consist of smooth muscle with intra and extracellular vacuoles. The zone of the AP muscle follicular attachment, the bulge, is thought to contain epithelial stem cells responsible for regenerating follicles, playing a critical role in the hair growth cycle [55, 56]. The evidence of the anatomy of follicular units (FUs) in horizontal sections, shows that fascicles of the AP muscle may surround the entire circumference of some hair follicles at the bulge area [57, 58]. They have reported [59] that the AP muscle displays a clear relationship to the follicular unit, forming a common thick bundle which is always oriented towards the same pole in different follicular units (FUs). Based on these findings, they hypothesized that the AP muscles form a single structure that is shared by the follicles contained in each follicular unit. Recently, researchers introduced the anatomical concept of a follicular unit served by a muscular unit, which can be identified in horizontal sections made at the upper level of the isthmus. This muscular unit results from the merging of the arrector pili muscles that originate from the hair follicles contained in that particular follicular unit. This anatomical disposition suggests that the arrector pili muscles could play an important role in the integrity of the follicular unit as well as in the secretion of the sebum contents [60]. These anatomical relationships between the sebaceous glands,

arrector pili muscles, and hair follicles as components of the follicular unit played important role in the integrity of the follicular unit as well as in the secretion of the sebum contents. Smooth muscle cells are characterized ultrastructurally by central nuclei, peripheral basement memberane, and intracytoplasmic myofilaments [61]. Little information has been written concerning the function of arrector pili muscle in camelidae as well as in other large animal species. In horses, cattle and sheep, these muscles are known to contract in response to epinephrine or norepinephrine, producing piloerection, which may be helpful for thermoregulation [62]. In camel and IIama, the arrector pili muscles consist of thin smooth muscle bundles with regional size variation. Well-developed arrector pili muscles are associated with larger hair follicles in the areas of long dense hair coat. The arrector pili muscles are small and vestigial in areas with short sparse hair coat and are absent on the chin, teat, vulva, anus, ear canal, footpad, metatarsal glands and interdigital glands[17]. It has also been theorized that arrector pili muscles play a role in the emptying of sebaceous glands[63].

1.6.13 Blood vessels (Vasculature)

Cutaneous vessels ultimately arise from underlying named source vessels. Each source vessel supplies a 3-dimensional vascular territory from bone to skin termed an angiosome. Adjacent angiosomes have vascular connections via reduced caliber (choke) vessels or similar caliber (true) anastomotic vessels. The cutaneous vessels originate either directly from the source arteries or as terminal branches of muscular vessels. During their course to the skin, the cutaneous vessels travel within or adjacent to the connective tissue framework and supply branches to each tissue, which they come into close contact (bone, muscle, fascia, nerve, fat). They emerge from the deep fascia in the vicinity of the intermuscular or intramuscular septa or near tendons and travel toward the skin, where they form extensive subdermal and dermal plexuses. The dermis contains horizontally arranged superficial and deep plexuses, which are interconnected via communicating vessels oriented perpendicular to the skin surface. Cutaneous vessels ultimately anastomose with other cutaneous vessels to form a continuous vascular network within the skin [64, 65, 66]. In the skin of the camel and IIama, unusual vascular large thick-walled blood vessels forming plexuses are present in the deep dermis and are especially abundant in glabrous areas. Lymphatic vessels occasionally are seen in the superficial dermis. Focal small blood vessel plexuses are present in the superficial to mid dermis in almost all parts of the body. Their size is directly proportional to the length and density of the hair coat. These vascular plexuses are large in areas of long dense hair coat and in the eyelid and smaller in sparsely haired areas and near many mucocutaneous junctions. The vessel walls are thick with a hyaline appearance and have large round endothelial nuclei. Elliptical erythrocytes are seen within vessel lumens. A loose fibrous connective tissue stroma surrounds the entire vascular plexus. Numerous fibroblasts, small mononuclear cells, and cells with small eosinophilic granules are present within the stroma surrounding the vascular plexuses. No typical mast cells are recognized [17].These unique vascular structures also have been described in the skin of guanacos and alpacas where they are sometimes misinterpreted as a pathological change (angiomatosis) [28]. Although their role remains uncertain, the close proximity of the vessels to each other suggests a possible counter-current exchange mechanism, perhaps functioning in the prevention of water loss from the intravascular compartment. Water conservation is thought to be an important function of the cutaneous vasculature of the camel [29]. The vascular plexuses also may represent arteriovenous anastomoses similar

to the `glomus', a specialized complex vascular structure in the skin of certain animal species, which functions in thermo- regulation [28, 15].

1.6.14 Lymph vessels

The mechanisms of angiogenesis have been studied extensively over the past years. The focus, however, has been almost exclusively on blood vessels, whereas little effort has been directed toward understanding lymphangiogenesis and the role of lymphatic vessels in physiology and pathology. The lymphatic system, acting in concert with the blood vascular system, is of fundamental importance in maintaining tissue homeostasis, and disorders of the lymphatic system are common, often resulting in chronic, disabling conditions. The cutaneous blood microvasculature is organized into upper and lower horizontal plexuses with the dermal capillary loops arising from the upper plexus [67]. Likewise, the lymphatic vessels of human skin form two plexuses [67, 68, 69]. The superficial plexus extends into the dermal papillae and is found near the subpapillary arterial network. It consists of thin vessels without valves. Whereas the bulk of the blood microcirculation resides immediately below the epidermis, lymphatic vessels are situated somewhat more distant. From the superficial plexus, branches drain vertically into a series of larger lymphatic vessels in the lower dermis and the superficial zone of the subcutaneous tissue. The deep lymphatic plexus is situated below the second arterial network. Similar to the collecting venules of the lower dermis, the deep lymphatic vessels contain numerous valves. Whereas blood vessels are found at the junction of the fat layer and the dermis and within the fat lobules, lymphatic vessels are not contained within the subcutaneous adipose tissue. Although blood and lymphatic capillaries may lie immediately adjacent to each other they never anastomose. The described cutaneous lymph vessel configuration is similar throughout the body; however, certain areas such as the fingers, the palm of the hand, the sole of the foot, and the scrotum appear to have a more abundant lymphatic network. The structure of the cutaneous lymphatics is dependent on the structure of the skin at the particular site and can thus vary in different areas. Generally, lymphatic vessels have a regular, uniform shape in the areas where the skin is firm and thick, whereas the shapes are more variable in regions, where the skin is thin and loose [70]. Blood and lymphatic vessels are similar in that they form a system of tubes with a continuous endothelial lining; however, reflecting differences in their function, the structure of lymphatic capillaries is different from that of blood capillaries in several important aspects [71]:

(1) The lymphatics generally possess a wider and more irregular lumen than blood capillaries. In the papillary dermis, the outside diameters of blood vessels are generally in the 17 ± 22 mm range [67], whereas lymphatic vessels can reach up to 60 mm in diameter.

(2) Lymphatic capillaries are characterized by an endothelium with extremely attenuated cytoplasm, except in the perinuclear region. Whereas post-capillary venules in the horizontal dermal plexus that are comparable in size with the lymphatic vessels of the area possess a vessel wall thickness of 3.5±5 mm, the vessel walls of lymphatic capillaries measure 50-100 nm, except in the nuclear region where the vessel wall thickness can reach up to 6 mm.

(3) Lymphatic endothelial cells contain numerous fine cytoplasmic filaments whose longitudinal orientation implicates their contractile function.

(4) In contrast to blood vessels, lymphatic capillaries have either no or only a poorly developed basal lamina and they are not encircled by pericytes.

(5) Tight junctions and adherence junctions, which are major types of intercellular junctions in blood vessels, are not as frequently seen in lymphatics. Nevertheless, they are implicated in maintaining firm cell-cell adhesion along the lymphatic vessel. In lymphatic vessels these adhesive molecules represent focal points of adhesion instead of connecting adjacent endothelial cells over entire cell boundaries as in blood vessels. The fact that skin blood and lymphatic capillaries do not anastomose suggests the possible existence of lymphatic endothelium specific cell adhesion molecules.
(6) One of the most striking characteristics of lymphatic capillaries is that they come into an intimate association with the adjacent interstitial areas. The end of the lymphatic capillary is open for free passage of fluid and particles into the vessel, and lymphatic endothelial cells are closely connected to the surrounding tissue by fine strands of reticular fibers and collagen [70]. These anchoring filaments are attached to the abluminal surface of the cells and extend deeply into the connective tissue, thereby firmly attaching lymphatic endothelium to interstitial collagen fibers and to the network of elastic fibers. Elastic fibers represent a low resistance path for the transinterstitial transport of fluid and are thus regarded as pre-lymphatic pathways. In the skin, they are ideally arranged for directing fluid into the lymphatics; in the upper dermis fibers are oriented perpendicularly whereas they are oriented horizontally in the lower dermis. Lymphatic capillaries respond to increased demands for fluid transport by widening their lumen. An increase in the interstitial fluid volume stretches the connective tissue fibers and pulls the lymphatic vessels open, despite an increase in the interstitial pressure. Greater demand for fluid uptake is also accommodated by opening of intercellular junctions.
(8) Overlapping intercellular junctions formed by extensive superimposing of adjacent endothelial cells are a property unique to lymphatic vessels. By being loosely apposed to each other over long distances, lymphatic endothelial cells cast intercellular clefts. When interstitial fluid pressure rises and exceeds the pressure within the lymphatic vessel, anchoring filaments open the intercellular channels by pulling adjacent endothelial cells apart, thus permitting easy passage of fluids and particles into the vessel. Under normal circumstances, lymphatic capillaries are generally collapsed. An elevation of interstitial pressure from values of ±7 to +2mmHg distends lymphatic vessels and increases lymph flow. When the interstitial fluid pressure is raised to more positive values, however, there is no further increase in flow. Thus, the inability of the lymphatic system to accommodate excess fluids leads to edematous conditions as the interstitial fluid pressure approaches +2mm Hg [70]. The concept of anchoring filaments explains why venules are compressed in inflammatory reactions and other conditions associated with increased fluid accumulation, whereas lymphatic are greatly dilated. The functional state of lymphatic vessels, however, cannot be determined by their morphology, as lymphatics can be dysfunctional when over distended, but also when they are collapsed. Extensive degradation of the extracellular matrix, e.g., by hyaluronidase, induces a collapse of lymphatic vessels and renders them nonresponsive to the changes in the interstitium. Hence, the functioning of lymphatic vessels is critically dependent on the extracellular matrix composition, geometry, and integrity.

1.6.15 Nerves

One of the important functions of the skin is to receive stimuli from the environments and surroundings. So skin of instance is the most extensive sensory receptor. It is richly supplied by myelinated and non-myelinated sensory nerve fibers through cerebrospinal and autonomic nerves. The nerves vary widely in number in different parts of the skin. The terminal fibers either end free in the epidermis and in certain parts of the corium or

form special microscopic corpuscles of several kinds [72]. Cutaneous nerve fibers have sensory functions, control the vasomotor tonus, and regulate the secretory activities of glands. They also exert a number of important functions, including the modulation of multiple inflammatory, proliferative, and reparative cutaneous processes. Cutaneous nerves are in close contact with dermal vessels, mast cells, fibroblasts, keratinocytes, and langerhans cells. Neuropeptides released by cutaneous nerves can activate a number of target cells such as keratinocytes (inducing release of cytokines such as IL-1), mast cells (producing potent proinflammatory cytokines such as TNT-α) and endothelial cells (upregulating VCAM-1 expression and causing secretion of IL-8). Such neuropeptides include substance P, neurokinin A. calcitonin gene-related peptide, vasoactive intestinal peptide, neuropeptide Y, somatostain and pituitary adenylate cyclase activity peptide. In addition skin epithelium can generate neurotrophins, thus influencing the development, sprouting and survival of nerve fibers. In general, cutaneous nerve fibers are associated with blood vessels. Peripheral sensory nerves include small unmyelinated nerve fibres which mediate sensations of itching and pain and nerve fibers which encircle hair follicles and make unmyelinated sensory endings within them to enable even slight bending of hair detectable by those endings. In addition, there are a several types of specialized encapsulated nerve endings present in skin: Paccinian corpuscles are receptors, found in deeper dermis and also in hypodermis, of sites that are sensitive to pressure (e.g., in the fingers and toes). Nerve impulses from the skin (the sensations of pain, touch and generally, feelings) are particularly associated with the Paccinian corpuscles and free nerve endings. Meissner's corpuscles are other touch receptors present in the tips of dermal papillae, particularly numerous in hairless skin (e.g., palms and fingers, soles and toes, nipples and lips). Under the light microscope, small cutaneous nerves and free nerve endings can be demonstrated satisfactorily only by methylene blue staining, metallic impregnation, or histochemical techniques. In addition to the important function of sensory perception (touch, heat, cold, pressure, pain, and itch), the dermal nerves promote the survival and proper functioning of the epidermis (so- called trophic influences). In the papillary layer of the camel's skin, the nerve breaks to form a plexus supplying the blood vessels, from this plexus fibers end in the deep interface of the epidermis. The End bulbs and free intra-epidermal nerve ending show positive reaction for AChE enzyme [41, 73, 74, 75.]

1.6.16 Subcutis

Usually, the dermis overlies a subcutis consisting of loose connective tissue containing a small amount of adipose tissue. This loose connective tissue is especially abundant in the specialized subcutis of the footpad (`digital cushion'). Occasion- ally, the dermis rests directly on hyaline cartilage (ear canal) or on underlying muscle (lateral thorax, forehead, ventral tail, dorsal muzzle, anus). In perioral areas, such as the chin and lips, abundant skeletal muscle extends up into the dermis almost to the dermal-epidermal junction. In the eyelid, numerous strands of skeletal muscle (orbicularis palpebrae) are interspersed among the dermal collagen [15, 17]. The specialized loose wavy connective tissue identified in the llama footpad subcutis (`digital cushion') is thought to function as a shock-absorber [19, 47]. The structure of the llama nail and the underlying dermis appeared to resemble that of the equine hoof [19]. The nail plate, resting on the underlying nail bed epithelium, extends into the dermis as large parallel ridges of keratin and corresponds to the primary laminae of the equine hoof. The germinal epithelium forms numerous small rete ridges orientated perpendicular to the larger ridges and corresponds to the secondary laminae of the equine hoof.

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1.7 Ultrastructure of camel's skin

The skin consists of an outer epidermis, the dermis, and the hypodermis. It includes nerves, blood vessels, glands and hair follicles. Epidermis is a continually renewing, stratified squamous epithelium. It is populated by keratinocytes (80 %) and dendritic cells (20 %): melanocytes, Langerhans and Merkel cells. The ultrastructure of the skin of man has received more attention than that of other species [1, 2, 3, 4, 5, 6]. Although many electron microscopical studies of the human skin are now available, such studies on the camel appear to be lacking. Only limited studies on the ultrastructure of integument of the camel have been done.

1.7.1 Epidermal Ultrastructural

The germinative layer (stratum basale) of the camel's epidermis consisted mainly of a single layer of cuboidal to columnar cells, along with some suprabasal cells which also may contribute to proliferation. Basal cells rested upon a distinct basement membrane that separated the stratum basale from the subjacent, dermal collagenous connective tissue [7] (Figure. 1.14.). In this region both the outer lamina rara and the deeper lamina densa of the basement membrane could be discerned, as well as numerous hemidesmosomes in the basal aspect of the epithelial cells. Large ovoid nuclei with numerous indentations, cytoplasmic melanin granules, and many tonofilaments are

found in camel stratum basale cells (Figure. 1.15). Three types of melanin granules can be recognized: electron dense granules, electron lucent dense granules, and mixed granules containing electron dense and electron lucent particles . Some melanin granules may be surrounded by a halo of ribosomes. Sometimes melanin granules can be observed among tonofilaments of keratinocytes, and a few of them are enclosed by a membrane. Free ribosomes and some rough endoplasmic reticulum can be observed in the cytoplasm of melanocytes (Fig. 2119). The thin cytoplasmic processes have Lateral inter-digitations in addition to desmosomes between adjacent stratum basale cells (Figure.1.16).

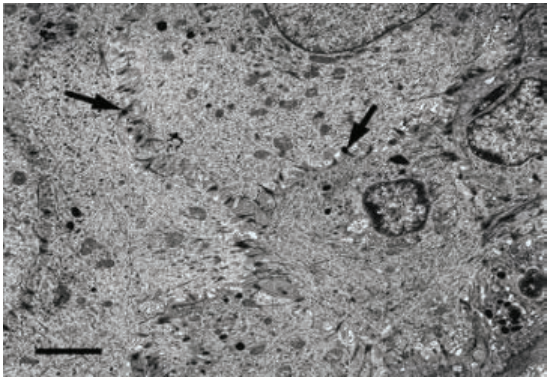

Figure.1.14. Epidermal cells within the stratum spinosum were tightly connected by inter-digitating boundaries with numerous desmosomes (arrows). ·6800; scale bar ¼ 2 lm. (Pfeiffer *et al.,* 2006).

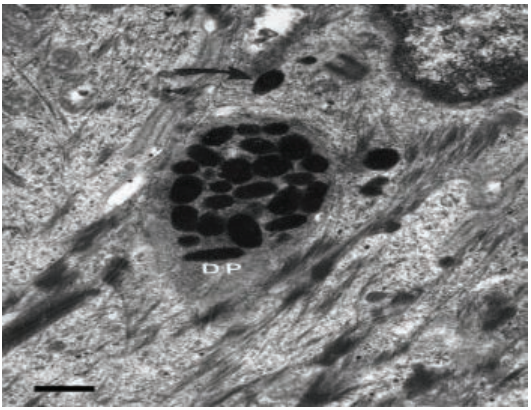

Figure.1.15: Cross-section of a dendritic process (DP) of a wandering melanocyte in the stratum granulosum. Note that melanin granules are seen both in the cytoplasm of the stratum granulosum keratinocyte (arrow), as well as in the dendritic process. ·19 200; scale bar ¼ 1 lm. (Pfeiffer *et al.,* 2006).

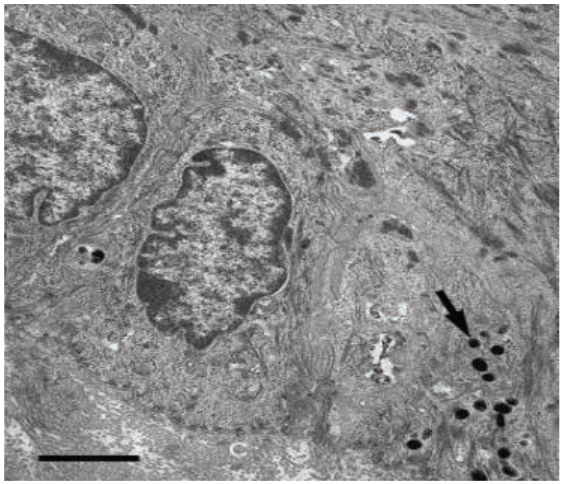

Figure.1.16: Cuboidal cells of the camel stratum basale, resting upon collagenous connective tissue (C) of the dermis. Note melanin granules (arrow). ·7900; scale bar ¼ 2 lm.(Pfeiffer *et al.*, 2006).

Some cells of the stratum basale have a relatively flat non-serrated base, and fewer cytoplasmic tonofilaments (Figure.1.17), some others may show a highly serrated base with deep projections extending into the underlying dermis, and larger congregations of tonofilaments. In the serrated cells the tonofilaments extended into the basal cytoplasmic projections and connected to the hemidesmosomes. Melanin granules appear in the cytoplasm. A stratum spinosum rest upon the proliferating stratum basale and consisted of a layer of irregular-shaped keratinocytes two to four cells deep. The cells become increasingly flattened in the outermost layers. These cells have large spherical nuclei with sparse chromatin, electron lucent cytoplasm containing small mitochondria, a few small (0.5 lm) electron dense granules and sparsely scattered short tonofilaments.

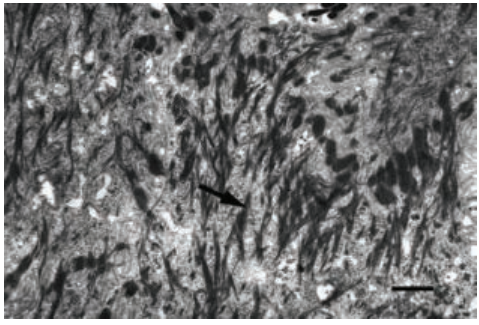

Figure. 1.17: Stratum granulosum epidermal cells in the camel, as in other species, displayed a greater concentration of tonofilaments (arrow), than were seen in underlying stratum spinosum cells. ·9800; scale bar ¼ 1 lm. .(Pfeiffer *et al.,* 2006).

Other organelles and melanin granules are seldom observed. Cells of the stratum spinosum are joined by numerous desmosomes. The most striking changes that occurred in the camel stratum granulosum keratinocytes (Figure. 1.18.) compared with the subjacent stratum spinosum are (a) increased flattening of the cells, (b) greater electron density of the cytoplasm because of aggregation of tonofilaments into dense filament groups, (c) nuclear changes, and (d) increased numbers of melanin granules. The changes in nuclear morphology consisted of flattening and evidence of peripherally placed heterochromatin.

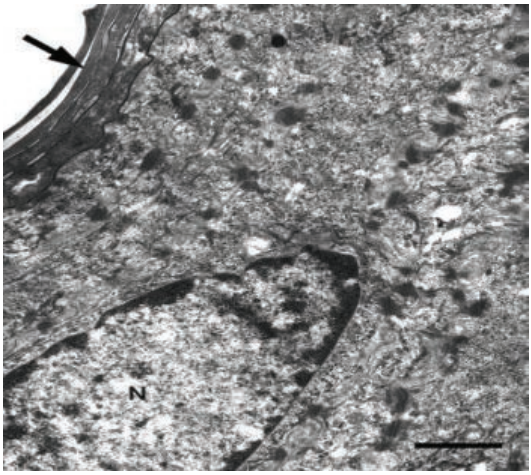

Figure. 1.18: . Flattened, electron dense stratum corneal cells (arrow) comprised a thin outer layer to the camel epidermis. Note the large nucleus (N) and granular cytoplasm of the underlying stratum granulosum keratinocytes in this section, and the dense plasma membrane separating the basal corneocyte from the stratum granulosum cell. ·14 100; scale bar ¼ 1 lm. (Pfeiffer *et al.,* 2006)

Tonofilaments are connected to desmosomes at inter-cellular boundaries Melanin granules are frequently seen in the keratinocyte cytoplasm and are also observed in migrating dendritic melanocytes, the processes of which might be seen interspersed between keratinocytes. The stratum corneum of the camel epidermis consists of six to 10 layers of flattened corneocytes. The first layer is firmly attached to the outermost layer of the stratum granulosum cells but successive layers of corneocytes become separated by increasingly larger inter-cellular spaces. The outermost layer of stratum granulosum cells, which are considerably thicker than the corneocytes they anchored, has a variable cytoplasm, likely reflecting their transitional status. The cytoplasm is granulated or vacuolated. The vacuoles may have resulted from artifactual disappearance of small keratohyalin granules. Vestigial remnants of organelles, such as melanin granules and other less dense cytoplasmic granules, are evident in the detaching cornified layers. Although desmosomes are no longer distinguishable at corneocyte boundaries, a continuous electron dense band (in two dimensions) is observed at the corneocyte surfaces, including the intact attachment surface with the transitional cell layer of the stratum spinosum. The loosely attached outer layers of corneocytes are

going to display some cytoplasmic, degraded remnants of keratohyalin fibrils as well as some granulated inter-cellular debris [7]. The Merkel cells cannot be clearly identified in standard histology, but electron microscope, give a more details possibility to view the Merkel cells. Ultrastructurally, camel's Merkel cells are oval or rounded and mainly located in the basal layer of the epidermis. The Merkel cells are found unstained with light cytoplasm (Figure.1.19). Some free ribosomes, mitochondria, lysosomes and vacuoles can be seen in the cytoplasm of Merkel cell. Occasionally, melanin granules are found in Merkel cell mainly in adult camels (Figure.1.20). The nuclei are ovoid with some lobulations and clearer in the adult animals. Merkel cell has electron dense cored granules that are bounded by membrane and relatively uniform and mainly concentrate at the periphery of the cytoplasm. These electron dense granules are few in young aged skin and numerous in aged ones. The Intranuclear rodlets can be seen mainly in young camel skin. Cytoplasmic extensions of Merkel cells are short. The cytoplasm contained dense-cored granules mainly concentrated in the cytoplasmic processes. Round perinuclear aggregates of cytoplasmic intermediate filaments and microfilaments may be seen.

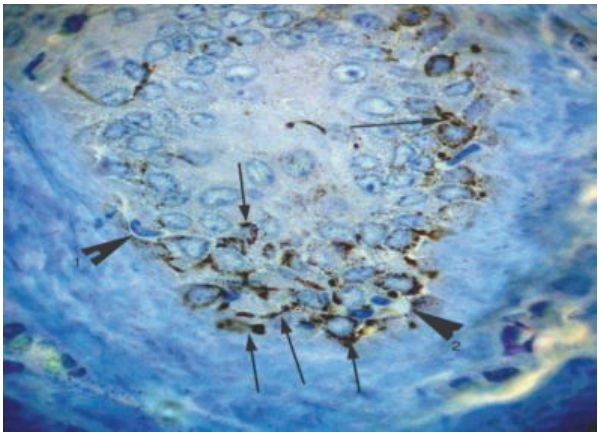

Figure. 1.19**:** A photomicrograph showing the high amount of melanin granules (arrows) in the epidermis of adult skin camel, the Merkel cell (arrow head 1) and the Langerhans cell (arrow head 2). (Toludene blue stain, semithin section. Mic.Mag. X 1000). (Doaa Zaghloul & Amira Derbalah, 2011).

Langerhans cells are located basally and suprabasally in the epidermis. The cytoplasm of Langerhans cells are electron lucent, lacked tonofilaments and no desmosomes can be seen along the cell membrane (Figure.1.21). The cytoplasm contains specific granules with a trilaminar membrane. These granules are mainly seen in cross section and sometimes in longitudinal section. The cytoplasm contains the usual cell organelles such as mitochondria, Golgi apparatus, lysosomes, rough endoplasmic reticulum and free ribosomes. Langerhans cell granules are mainly found in the periphery of the cells. No melanin granules can be seen in the cytoplasm. Cytoplasmic processes are observed in the intercellular spaces between keratinocytes and recognized by the light cytoplasm. The nuclei of Langerhans cells are ovoid, indented or kidney-shaped and sometimes lobulated.

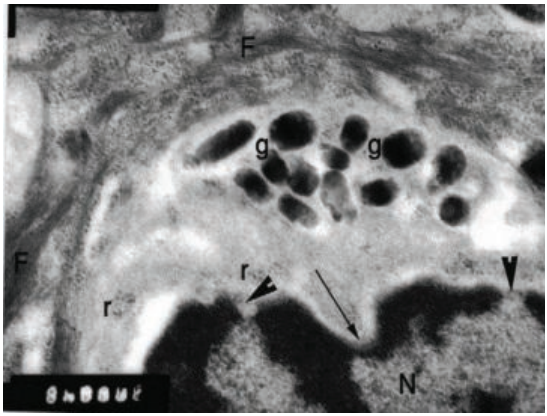

Figure.1.20: High magnification transmission electron micrograph of Merkel cell of adult camel epidermis, showing part of its nucleus (N) with clear indentation (arrow), light cytoplasm with electron dense cored granules (g) and free ribosomes (r). Note the nuclear pores (arrow heads) and the filaments (F) of keratinocytes. (Mic. Mag. X 13000). (Doaa Zaghloul & Amira Derbalah, 2011)

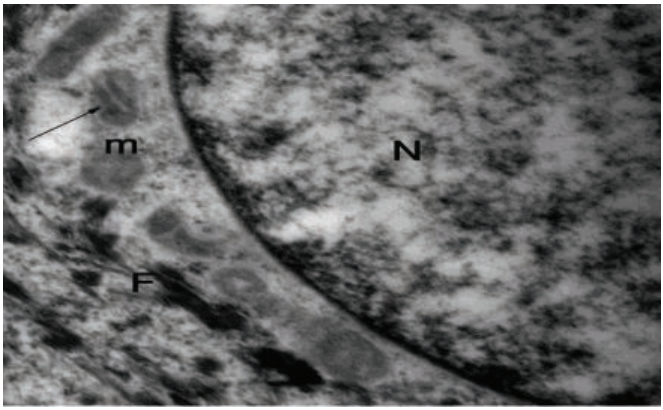

Figure.1.21 : Transmission electron micrograph of Langerhans cell in young camel epidermis, showing an oblique section in its specific granules (arrow), mitochondria (m), part of the nucleus (N), and cytoplasmic filaments (F) from the neighboring cell. (Mic. Mag. X 13000). (Doaa Zaghloul & Amira Derbalah, 2011)

The cells of adult epidermis did not differ too much from those in the young animals, but the number of cells in adult skin was greater than that in young ones, and the oval or some-times round nuclei were seen only in adult skin. There is also no difference in the shape and structure of melanocytes in young and adult camel skin except the higher number of cells in the adult camel skin compared to young camel skin and the more numerous melanin granules in the adult melanocytes [8].

Ultrastructure of sweat gland

The secretory cells of the camel's sweat gland are polyhedral in shape, with rounded or oval nuclei situated towards the base and sometimes clefted and are in close proximity to small mitochondria with densely packed cristae. The adjacent cells may make contact in an almost straight line with no infoldings; desmosomes are seen at these contacts. The luminal cell membrane presented microvilli which protruded into the lumen of the tubule. Most of the microvilli of one cell might be cut along their long axis, while those of an adjacent cell might be cut transversely. The secretory cell is characterized by a paucity of cell organelles, but mitochondria are numerous. Occasionally a portion of a mitochondrion structure is seen almost enclosed in the secretory granule. Most of the cytoplasm is filled with closely packed, electron lucent, spherical or ovoid secretory granules. Occasional inclusions resembling lipid granules are electron dense and has a granular content. Some contain single, small (0.37 lm), spherical. The apical surface is covered with long (1.7 lm), closely packed microvilli. In some instances the large apical granules could be observed being individually released into the lumen of the gland by exocytosis. At the base of the secretory cells, circular smooth muscle cells, i.e. myoepithelial cells, are often observed encompassing the gland. Increased folding of the basal plasma membranes is observed at the basolateral, inter-cellular region between the secretory cells of the camelid tubular gland. Ducts of the apocrine glands are comprised of basal myoepithelial-like cells and luminal epithelial cells. The latter cells are covered with short (0.3 lm) microvilli that may project into the lumen of the duct[9] (Figure. 1.22).

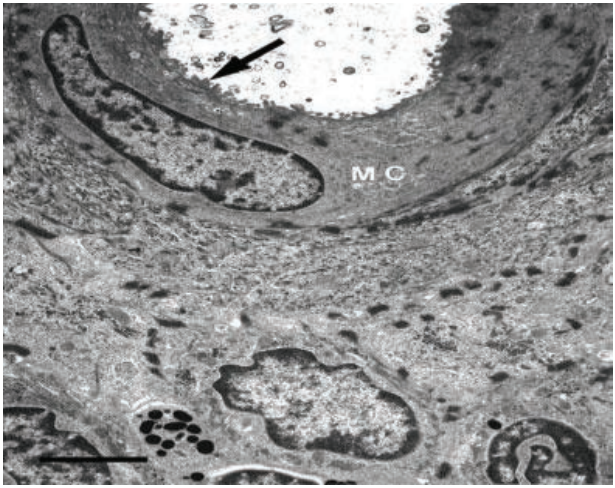

Figure.1.22. A tubular gland duct, present in the dermis of the camel integument, shows the presence of short microvilli (arrow) projecting into the lumen and myoepithelial cells (MC) encircling the duct. ·7800; scale bar ¼ 2 lm. (Pfeiffer *et al.,* 2006).

1.6.2 Ultrastructure of sebaceous gland

The sebaceous gland is surrounded by a connective tissue sheath which consists mainly of collagenous fibres and fibroblasts. Occasionally, blood vessels and myelinated axons are seen in the connective tissue. Encapsulated nerve endings are infrequently found in the connective tissue (Figure. 1.23). They are evidently spindle shaped and each one consisted of a central axon, an outer capsule and a subcapsular region. The Schwann cell supporting the central axon showed few processes. The subcapsular region contains fine collagenous fibrils. The capsule consists of three capsular cells with long and slender processes arranged in concentric lamellae. In between the lamellae collagenous fibrils are present. The unmyelinated axons detect in the connective tissue around the gland appeared to penetrate the basal lamina and innervate the cells at the periphery (Fig. 44 42). These axons show numerous microfilaments and very few clear vesicles. Axons and the cells might show no specializations between them [10].

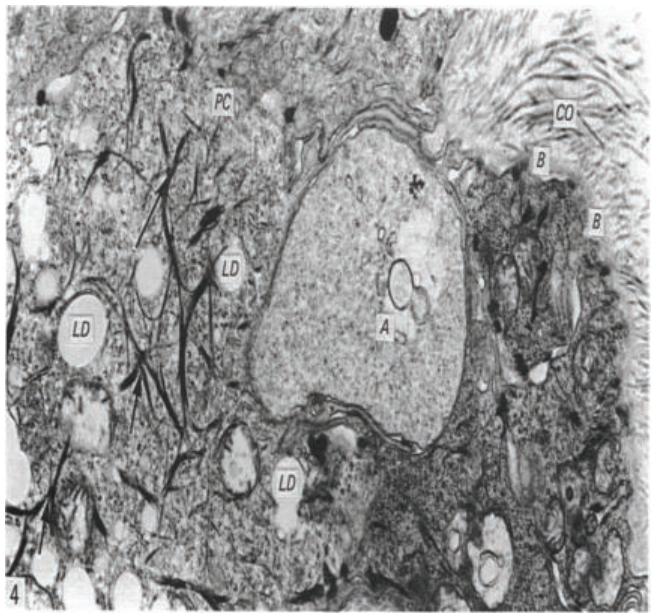

Figure.1.23: . An axonal ending (A) innervating the peripheral cell (PC). Note the many microfilaments and the small number of clear vesicles in the axoplasm. The peripheral cell (PC) shows numerous tonofilaments (arrows) and lipid droplets (LD). B, basal lamina; CO, collagen fibrils. x 12300.(TAHA, 1988).

1.6.2.1 Peripheral cells

These cells are clearly separated from the connective tissue by a basal lamina and show many hemidesmosomes. The peripheral cells are elongated in shape and the cell membrane adjacent to the mature cells displayed many desmosomes and enfolding. Their nuclei are oval and had one or two nucleoli. The cytoplasm of the majority of the

peripheral cells contains tonofilaments which appeared to be inserted to the desmosomes. Other cytoplasmic components are a few mitochondria, rough endoplasmic reticulum and free ribosomes. Lipid droplets are sometimes present in the peripheral cells. Some of these cells look quite pale and contained few organelles. Langerhans cells are consistently observ between the peripheral cells.

1.6.2.2 Mature cells

These cells lay next to the peripheral cells and they constitute the majority of the sebaceous gland cells. The most striking features of these cells are the numerous lipid droplets and the smooth endoplasmic reticulum. The lipid droplets varies greatly (Figure. 23.1) in size and number between different maturing cells and within the same cell. While some of the lipid droplets fuse with each other, others fuse with the mitochondria, and in some instances; they appear to indent the nucleus. Lipid droplets seem to have developed from the mitochondria. The smooth endoplasmic reticulum is abundant and it took the form of a grid lattice, membranous whorls, or parallel cisterns . The smooth endoplasmic reticulum is commonly associated with lipid droplets, often encircling them. Other organelles which are present in the mature cells are a few mitochondria, rough endoplasmic reticulum, coated vesicles, and a Golgi apparatus. The cell membrane of the mature cells shows many enfolding and desmosomes. Moreover, microvilli are consistently observe in the intercellular spaces. The above-mentioned ultrastructural features are mainly found in the mature cells that 1ay immediately next to the peripheral cells. However, as these cells developed and moved upwards, there was a marked reduction in their cytoplasm and smooth endoplasmic reticulum and a marked increase in the number of lipid droplets. Several lipid droplets fuse together and become more pronounced which lead to indent the nucleus.

1.6.2.3 Necrotic cells droplets

These cells are completely filled with fusing lipid droplets with no identifiable organelles and pyknotic nucleus (Figure. 1. 24).

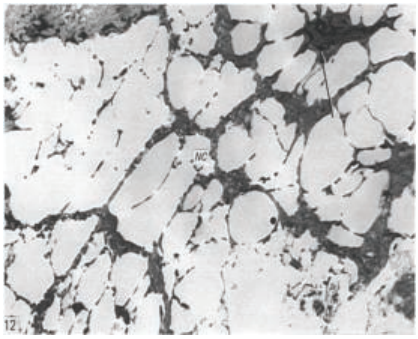

Fig. 1. 24:A necrotic cell (NC). The cytoplasm is completely filled with a conglomeration of lipids leaving wisps of cytoplasm. Note that the nucleus (arrow) is pyknotic. x 6800.(TAHA, 1988).

1.6.2.4 Other cell types

A variety of other cell types are observed in the camel dermis, including eosinophils, mast cells, and fibroblasts. Numerous capillaries, small arterioles, veins and small neurons near the vasculature can also seen in the dermis. Smooth muscle cells, appear mainly in arrector pili muscles, attach to hair follicles or in arteriolar walls, are seen in the dermis. The ultrastructure of arrector pili myocytes contains numerous fusiform densities, centrally placed nuclei and/or mitochondria, and pinocytotic vesicles as typically appear in smooth muscle. A thick (0.3 lm) basement membrane encircles the myocytes, and collagenous fibres are observed between the cells.

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1.8 Specialized skin structures

1.8.1 Poll gland in camel's male

Behind the ears of the male camel there are two symmetrical tubular glands (Figure.1.25).

Figure.1.25: the Poll glands of a rutting male in secretion

It are called poll bodies and situated subcutaneously on the back of the neck. Their name was derived from their position in the poll region [1] and are present in male camels at birth, they remain inactive up to the time of' pubescence, and then become active only during the rutting season. No visible glands are observed in female camels at any age [2]. Poll bodies are known to undergo cyclic activity, yielding a yellowish watery secretion with a characteristic offensive odour during the rutting season [2, 3, 4, 5, 6]. However relatively little is known about this glands and their function is not well known, though they are play a role during the rutting season. The opinion of Purohit & Singh (1958) [2] are the poll glands secrete unknown substances of a male character. The morphological details of the glands have been described and there are conflicting reports with regard to the morphological features of the active and inactive glands [2, 3, 5, 7]. However, Yagil & Etzion (1980) [6] have reported the presence of androgen in the secretions of the poll glands of the rutting male. Preliminary finding have been reported elsewhere [8]. Several investigations have studied the histological and histochemical characteristics of the poll glands in camels as well as ultrastructural studies [7,8,9,10,11]. More recently, Ebada et al 2012 [12] have studied the histology and immunohistochemical findings of poll glands of the dromedary camel (*Camelus dromedarius*) during the rutting season. Poll glands described as tubuloalveolar sweat glands of modified apocrine type. These glands are first to be functionally active at puberty [2] as in the case of apocrine sweat glands [13]. The immunohistochemical reactions of poll glands to Cks, SMA and S100 protein are similar to a large degree to the apocrine sweat glands [12]. Grossly, poll glands appears as paired and composes of two parts located on either side of the ligamentum nuchae behind the ears, about 7 cm below the occipital crest, in the male camel. Each part is broad at the

base, and caudally the two parts become narrow and lay close together. The skin overlying the glands become thin, slightly elevated with less hair, and the hair itself is stained dark brown during the period between September and March. In aged animals, the area occupied by the poll glands appeared bald. A profuse yellowish watery secretion with a characteristic foetid odour is exuded; following exposure to air, it change to dark brown or even black. The amount of secretion has been noted to be minimal during the months of September/October and February/March. Such secretion is also observed when the animal is subjected to stress, regardless of the time of the year. On removal of the skin, the bilobed gland is exposing as a subcutaneous structure closely adherent to the skin. Each lobe is enclosed within a capsule and divided into numerous macroscopic lobules, which varies from the size of grain to that of a pea with a diameter ranging from 1-5-3-5 mm. During the period between April and August, and in the castrate male, the glands are markedly smaller and so are the lobules; they are non-secretory [7, 9]. No reference is made as to whether these are apocrine or merocrine in their mode of secretion.

1.8.2 Histology of poll gland

Earlier poll glands are described as consisting of an aggregation of a number of compound tubulo-alveolar glands resembling the mammary glands in microscopic appearance [4]. Poll glands are enclosed within a connective tissue capsule consisting mainly of collagenous fibers, a few elastic fibers and smooth muscle together with blood vessels, lymphatics and nerve fibers. Trabeculae attaches to the capsule dividing the gland into numerous lobules with tortuous excretory ducts which opened into hair follicles. Poll gland shows a wide variations in the amount of interlobular and intralocular connective tissue and its structure of the gland in correlation with its functional state. Gland shows two main stages, the active (secretory stage) and the inactive (resting stage) in which may be included the structure observed in the castrate animal [7]. The active glands have lobules which are sharply demarcated and crowded, with the interlobular connective tissue reduced to thin strands. Average lobular diameter amount to 6-0 mm. The different lobules are not in the same functional state; some of the alveoli are lined by flat or simple cuboidal epithelium and possesses wide lumine, while others have tall cells with round basally located nuclei and distal protruding tips which almost occlude the lumen. The apical cytoplasm of the tall cells is granular and stains more deeply. The predominance of one over the other type of cell seems to indicate the extent of activity; in active alveoli, the narrow lumen communicates with secretory canaliculi between the lining cells. The eosinophilic homogeneous material containing leukocytes, mainly neutrophils are seen occasionally in the luminal content of the alveoli. Elongated cells with slender nuclei are seen frequently between the alveoli and the basement membrane; these cells are probably myoepithelial cells. Closely applied to them are connective tissue elements consisting predominantly of reticular fibers, together with collagenous and elastic fibers. Intra-lobular excretory ducts are seen amongst the secretory alveoli. They are round or oval in transverse section and are lined by simple columnar epithelium; this gradually changes to two layers of columnar cells, especially in the interlobular ducts. Luminal bleb-like projections can also be observe in these ducts. Examination of serial sections reveals that the lobules are drained by several excretory ducts which pursue a tortuous course towards the surface, and ultimately opened into the upper portions of hair follicles. The extra parenchymatous segment of the duct, especially its most distal portion, is line by stratified squamous epithelium [7]. The lining epithelium of the alveoli and intralobular ducts fail to stain with

alcian blue, but it shows mild to strong PAS-positive apical blebs in the secretory cells [12]. The inactive glands show reversion in the glandular elements to a resting stage. The lobular size diminishes and there are an apparent increase in the stroma with massive deposition of collagenous fibres. The secretory alveoli become of somewhat smaller in diameter (about 40 /tm), with wider lumina and comparatively thinner walls lined by simple squamous to low columnar epithelium. Luminal cytoplasmic protrusions encounter rarely and they become much shorter than those of the active gland. The inactive glands occur in the castrate animal, with a remarkable amount of interlobular connective tissue. This is sometimes so abundant as to predominate over the inactive alveoli. It is constituted mainly if not entirely of collagenous fibers. The secretory units become few in number and greatly reduced in size. They are either in the form of alveoli with wide lumen and simple squamous epithelial lining, or of mere clusters or cords of cells; possibly the latter feature represented a tangential section through part of the wall of an alveolus. Only intra-lobular excretory ducts are seen and line by simple squamous epithelium; the more distal parts are probably occluded [7]. The luminal surface of secretory cells appears to cover with microvilli in scanning electron microscopy. The secretory cells pinch off smooth surfaced apocrine blebs. After pinching off, crater-like pits remain on the luminal surface of secretory cells [14].

1.8.3 The Female camel and llama teats

The female of all members of the Camelidae has four teats located in the caudal abdominal area [15]. The camel udder consists of four quarters, each with two, sometimes three separated glandular complexes leading into one teat. So in each teat there are two (or three) milk canals [16, 17]. The left and right halves of the camel udder are separated by a groove as the udder is suspended by fibro-elastic tissue, leading from the linea alba to the prepubic tendon[18]. As one-humped camels are not systematically bred for milk production, there is a great variety in different udder and teat shapes and sizes. Additionally the shape can vary according to age and stage of lactation [19, 20, 21]. A thick hairless scaly elongate area of skin is present on the medial and lateral surface of each metatarsal region. These unique structures have been referred to as metatarsal glands or `scent glands' due to their strong odour. Although the function of these regions is uncertain, it has been suggested that they may be involved in pheromone secretion and perhaps are associated with individual and group identification[15]. These structures are sometimes called `chestnuts', but debate exists regarding the relationship between these structures and the equine chestnut.11-13 elongate hairless patches, referred to as interdigital glands, are distributed along the entire length of the dorsal interdigital space of each foot. Grossly, they resemble the metatarsal glands and may have a similar function. Each foot has two digits with one nail, similar to the human nail, at the distal end of each digit. This non-weight-bearing nail is a feature of Camelidae and is unusual among animal species. Footpads are present in llamas and other Camelidae, but they are unusual among other herbivores. A separate footpad (`slipper') covers the plantar weight-bearing surface of each digit in llamas, in contrast to the single footpad which covers the entire weight-bearing surface of the foot in camels [15].

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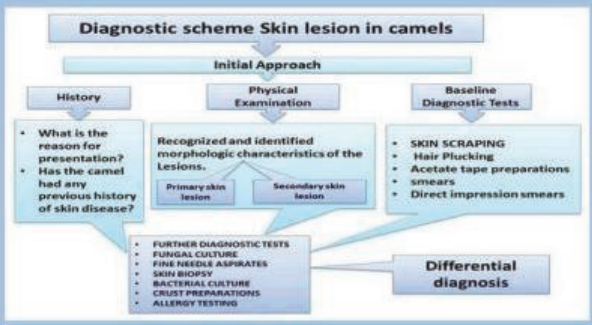
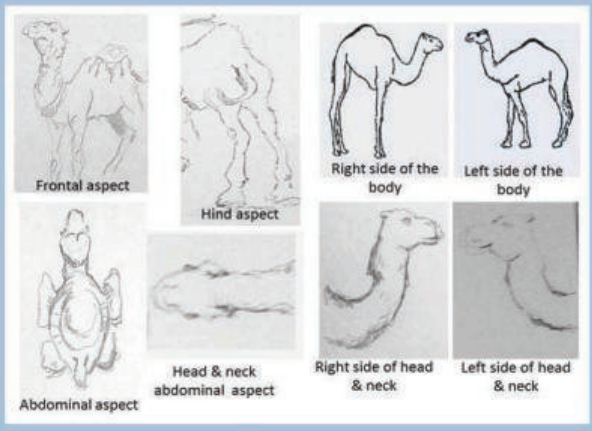
Chapter. 2

Diagnostic approach of camelids skin diseases





Chapter 2: Diagnostic approach of camelids skin diseases

2.1 Introduction

Effective treatment of skin disease requires accurate diagnosis of its cause. Skin abnormalities might result from, specific, causes but can also reflect the general health of the camel. A careful examination of the whole sick camel and a methodical examination of its skin are essential parts of the clinical examination. Further investigation is required to confirm the diagnosis in some cases. The zoonotic nature of some camel skin diseases and restrictions on drug therapy in milk and meat producing animals are important considerations when planning treatment.

The veterinarian is commonly faced with camel or herd of camel with skin disease, the management of which requires a thorough clinical investigations and diagnostic work-up. This chapter outlines the general approach to the diagnosis of such skin diseases in camels and describes the approaches which might aid diagnosis. It also discusses the diagnostic tests to a specific dermatological cases (Figure. 2.1).

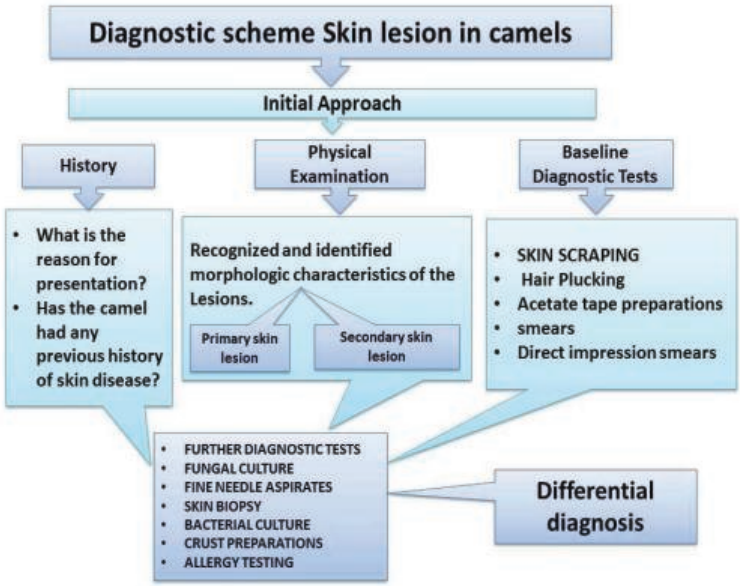


Figure. 2.1: Diagnostic procedure for skin diseases in camel.

2.2 Diagnostic methods in dermatology

The steps of Initial diagnostic tests procedures for an accurate diagnosis in the camel skin diseases are:

1. Case history
2. Physical examination.
3. Differential diagnosis.
4. Baseline diagnostic tests

1. History

Always veterinarian tries to collect detailed history from the owner or nomads having most contact with the camels. A good case history provides assistance in diagnosis and treatment. The history must not be limited to cutaneous symptoms but should include information on other systems. Accurate clinical history is an essential first diagnostic step in the investigation of skin disease in the camels. The method of history taking is very much a matter of personal preference. Many clinicians use a special printed history sheet when questioning owners and asking questions to each individual case are preferred (Figure. 2.2). Important questions which should be included in each case are listed down. A detailed history is obtained from the owner or person having most contact with the camels.

A. **General history taking**

1. Age of camel: Age might be important, some skin diseases are associated with specific age group as for example mange both very young and very old camels are particularly susceptible and Camel contagious ecthyma is a highly contagious viral disease, which primarily affects young camels exhibiting most regularly localized lesions and frequently generalized changes that resemble camel pox [1].
2. Sex: There are differences between male and female skin disorders resulting from hormonal imbalance frequently develop in female. Specific skin lesions also occur in male.
3. Environment: Including climate and geographical conditions which effect on the skin, such as distribution of trace elements in the soil may lead to many of skin lesions in rainy periods. Also allergic skin disorder as in photosensitization may be related to environmental condition.
4. Nutritional conditions: Some skin lesions are developed from deficient nutrient in some vitamins, minerals and tract elements.
5. Hypersensitivity reaction to normally innocuous environmental allergens [2].

B. **Principals of History taking in relation to skin only**

1- Has the camel previously suffered a disease? If so, what is the diagnosis?
2- Do of other camels of herd have a similar skin disease?
3- Have the lesions been localized or generalized in many areas?
4- What has the duration of the lesions?
5- What is the usual behavior of the camel?
6- What is type of the sick camel nutrient and source of water?
7- What is the sick camel history concerning external and internal parasite?

A

History sheet

Date.....

Owner name .....

Area's or Field's name: .....
Sex:..... Age:.....

General History

1. *Age and origin:*.....
2. *Geographical area of population:*.....
3. *Way of life and Diet:*.....
4. *Reproduction:*.....
5. *Previous history of diseases:*.....
6. *Previous dermatoses & dermatophytosis:*.....
7. *Current non skin-related problems:*.....
8. *Behavioural changes:*.....

Dermatological History

1. *Chief compliant:*.....
2. *Date of onset:*.....
3. Pruritus, severity and time of onset (before or after lesions):.....
4. Specific clinical signs :.....
   related behavior (Itching in different body regions: Head, Legs, trunk...ect)
   .....
   .....
   .....
5. Skin changes and fleece lost.....
6. *First cutaneous lesions observed and their development:*.....
   .....
7. *Seasonal influences:*.....
   .....
8. *Numbers of other affected animals or human beings in contact:*.....
   .....
9. *Presence of external parasites(Ticks ,Flea, ect...)*
10. *Anti-parasitic treatments given:*.....
    .....
    .....
11. *Previous treatments (date, products, dosage and duration) and responses:*.....
    .....
    .....
    .....

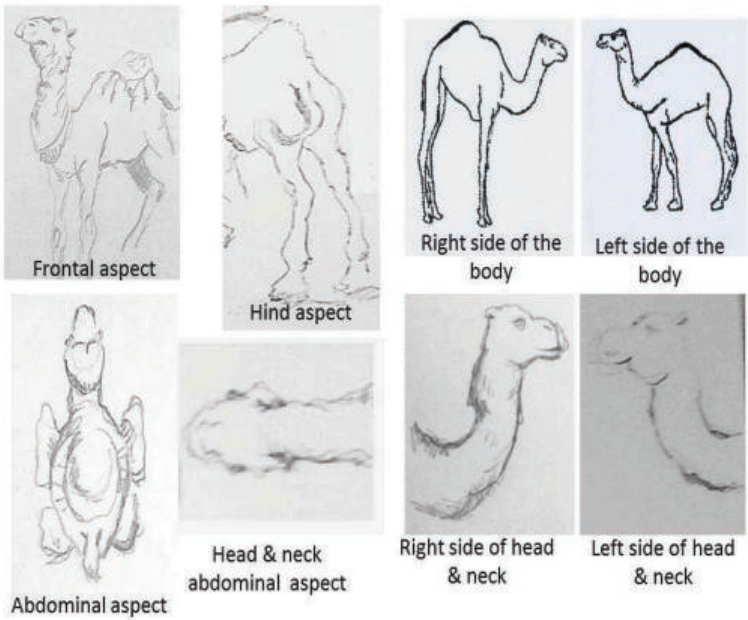


Figure. 2.2. A. Dermatological examination sheet and B. Some camel silhouette and camel image to mark the location of the lesion.

C. **General questions about the environment**

1. Has the camel had any contact with other camels, farm animals, wild animals or domestic pets?
2. Does the owner have any skin lesions?
3. The clinician should also ask questions relating to:

The Pastoral areas (eg, location, construction, and feeding arrangements eg, type of pasture if there is any change in the grazing area and local water sources). And any changes in routine.

D. **Previous therapy**

1. Has the camel had any topical therapy (eg, insect repellents)?
2. Is the camel undergoing any current systemic therapy?
3. Has the camel had any previous therapy for skin disease? If so, what was the response to it?

E. **Dermatological history**

1. What is the reason for presentation?

2. Has the camel had any previous history of skin disease?
3. When did the current disease start?
4. How has it progressed? Here, the clinician should obtain information about:
    i. The types of lesion and their progression
    ii. The distribution of the lesions
    iii. Any associated pruritus
    iv. Any seasonal pattern to the disease

F. **Any other history**

The owner should also be given the opportunity to disclose any other pertinent information which the clinician may have omitted to ask.

2. Physical Examination

A complete physical examination is carried out and the status of all body system evaluated and noted. All parts of the skin are examined; the camel fleece being parted and skin palpated where necessary. Good lighting and use of the magnifying lens are essential. The condition of the fleece and the nature and distribution of any lesions are noted and it is important to recognize the different types of skin lesions and to describe them accurately (Figure.2.3).

Figure: 2.3: The physical examination of the skin lesion in camel.

3. Differential diagnosis considerations and selection of diagnostic tests:

Case history of the lesions must be consider carefully and combined with the results of the physical examination in order to be able to suggest a number of possible causes of condition. The proper diagnostic procedures must be selected, which will confirm or eliminate these possibilities. It is important to differentiate primary and secondary skin diseases and lesions.

4. Baseline diagnostic tests

The investigator should perform skin scraping; hair plucking and take acetate tape impression smears of the skin, as a minimum, in addition to the direct impression smears of any lesions. The site for sample collection should be selected according

to the locations of the lesions (Figure. 2.2 B). Both normal and lesional skin should be sampled (Figure. 2.4 A&B).

Figure 2.4. Skin samples should be collected from both normal and lesional skin.

The diagnostic tests include the following tests (Table. 2.1):

Table.2.1: Shows the diagnostic tests in dermatology

Procedure	Causative agent demonstrated
1-Wood's lamp illumination.	Some of Microsporum species.
2- Skin scrapings.	Ectoparasites, dermatophytes, helminthes.
3- Hair plucking.	Ectoparasites, dermatophytes, hair morphology.
4- Coat brushings.	Ectoparasites, dermatophytes.
5- Swab / crust samples.	Fungi, bacteria, virus.
6- Smear / wet preparation.	Bacteria, fungi, protozoa, cytology.
7- Biopsy.	Bacteria, fungi, virus, histopathology, histochemistry.
8-Blood.	Cytology, Biochemistry, hormonal status, and serology.

1. Wood's lamp illumination:

The Wood's lamp is an important part of any dermatology investigations. The Wood's lamp produces invisible long-wave ultraviolet light (340-450 nm wavelength) [3]. This UV light can help to detect medications that are taken systemically (tetracycline) or that are applied to the skin as well as help diagnose skin disease inducing infectious agents that have a characteristic fluorescence (*Microsporum* species, Pseudomonas infections and pigmentary alterations). The test is simple, the UV light from the Wood's lamp is directed over the area of the suspected infection and the dermatologist looks to see if there is any fluorescence/visible light reflected back. It is seen only in infection of actively – growing fibre. The disadvantages of this method are, it may give + ve result with other chemical agents as tetracycline, and failure to demonstrate such fluorescence does not rule out dermatophytosis [4] .

2. Skin Scrapings

Skin scrapes are one of the most common dermatologic diagnostic tests. This relatively simple and quick test can identify many types of parasitic infections. Although not always diagnostic, the relative ease and low cost makes it an essential test in a dermatological minimum data base [5] . The skin scraping is one of the most valuable and commonly used tests in veterinary dermatology, confirming the diagnosis of the ectoparasites and dermatophytosis [6]. Superficial skin scrapings are particularly useful for identifying surface-living parasites. Samples should be taken from predilection sites (eg, areas of crusting and scaling on the lower limbs to check for the presence of mange mites). Other parasites that may be identified using this method include lice and the larval stage of harvest mites and free-living mites.

Technique

Skin scraping technique requires pervious experiences in camels due to the hardness of the skin lesions of the camels (Figure 3.4). There are different kinds of skin scrapings depend on the purpose of the diagnosis [3]. These are including :

I. Superficial skin scrapes: Skin scraping are collected dry or moistened with water or liquid paraffin. The area of scraping with great care to the predilection sites for the disease either ectoparasites or dermatophytes, should be selected. The selected skin should be moisten with liquid paraffin. A dulled scalpel blade is held perpendicular to the skin and used with moderate pressure to scrape in the direction of hair growth. If the area is haired it may be necessary to clip a small window to access the skin. In an attempt to find the relatively few mites that may be present on a camel, large areas are scraped (1-2 inches). Applying mineral oil directly to the skin to be scraped helps dislodge debris and makes it easier to collect the scraped material. Since these mites do not live deep in the skin, it is not necessary to visualize capillary oozing or blood. Usually several slides are needed to spread the collected material thinly enough for microscopic examination. Initially view slides under a low-power microscope lens, moving to a higher power objective, if necessary.

II. Deep skin scrapes are collected dry and suspended on slide in 20% potassium hydroxide. A dulled scalpel blade is held perpendicular to the skin and used with moderate pressure to scrape in the direction of hair growth. If the area is haired (usually alopecic areas caused by folliculitis are selected) it may be necessary to clip a small window to access the skin. After several scrapes, the skin should become pink with the capillaries becoming visible and oozing blood (Scraping is continued until the first signs of bleeding appear). This assures that the material collected is from deep enough within the skin to collect the follicular mites. Most veterinarians also squeeze (pinch) the skin to express the mites from deep in the follicles into a more superficial area so that they are more easily collected. If the scraping failed to collect a small amount of blood, then the mites may have been left in the follicle resulting in a false negative. In some situations (deep inflammation with scarring) it may be impossible to scrape deep enough to harvest the mites. These cases are few in number but require biopsy to identify the mites in the hair follicles. Hair-plucks from a area of lesional skin may be used to

help find mites but the accuracy of this technique compared to skin scrapes is unknown. The deep scraping samples process as follow:

1. Suspension is warmed to accelerate clearing.
2. Cover slip is applied and the preparation is examined under the x10 and x 40 objective.
3. Scrapings are collected in test tube or small beaker and add 4-10% sodium or potassium hydroxide.
4. Heat gently, but not boil, until the hair is dissolved for about 5 minutes. “If the sample is boiled the parasite will be transparent and difficult to diagnosis”.
5. Maceration overnight without heat may be sufficient.
6. Allow the tube to stand for minutes and cooling.
7. Centrifuge the sample and examine the sediment.
8. Sample from the sediment transfers to slide with cover glass and examined microscopically under the low power.
9. Scrapings can be collected dry in sealed paper envelope and then cultured directly for isolation of dermatophytes on specific media.

Figure 2.5. Diffuse camel skin lesion on the neck region

3. ACETATE TAPE PREPARATIONS

Tape preps are used to evaluate a variety of different conditions [6]. The basic technique involves using crystal clear tape (single or double sided) to collect a sample of fiber or superficial skin debris. Acetate tape impression smears can be taken from skin lesion of both haired and alopecic areas. On haired skin, this technique is useful also for the detection of superficial parasites. On alopecic areas, surface bacteria, such as Staphylococcus species, yeasts, and Candida species, may be identified.

Technique

Adhesive tape, such as 3M Scotch tape, is particularly useful for this technique as it picks up organisms well and retains its shape when stained. On haired skin, press the tape firmly onto the fiber several times. Mount directly onto a microscope slide

and observe under low power initially and then under high power, if required. On hairless areas, press the tape onto the skin and rub gently with the thumb to pick up microorganisms. Stain with a rapid stain, such as Diff Quik (Wardle Chemicals) or Rapi Diff (Diachem International). Mount and observe

4. Fiber plucking

Fiber plucks can be used to visualize the fiber tips, shafts and bulbs. In pruritic conditions, the fiber tips may be frayed and split, indicating self-inflicted trauma. Dermatophyte arthrospores and parasite eggs may also be seen on shafts. Hair bulbs may be in anagen, suggesting active hair growth, or in telogen, the resting phase of the hair cycle [6].

Technique

Fibers from the chosen site should be gently grasped with forceps so as not to damage the fiber shafts and firmly pulled out. Fiber plucks taken between finger and thumb tends not to be representative as only telogen fibers are epilated. Sample may be inoculated directly onto specific media for mycological isolation and identification. Samples may be mounted in liquid paraffin to examine fiber structure or in potassium hydroxide to detect fungal elements. Where dermatophyte infections are suspected, blue black ink may be added to potassium hydroxide to stain any fungal elements. View under a low power objective x 10 microscope lens and then at high power under x 40 objective and fiber held with mineral oil gives better resolution.

5. Further diagnostic tests

Depending on the case history further diagnostic tests can be selected, in addition to the physical and clinical findings. For example, the presence of skin nodules would indicate that fine needle aspirates, skin biopsies and/or tissue cultures may be necessary. Where camel's fiber can be easily epilated from the coat, the presence of a follicular disease is suggested and, in such cases, fungal culture, tissue culture, skin biopsy and endocrine function tests, as well as routine health screens, may be indicated.

6. FINE NEEDLE ASPIRATES

Fine needle aspirates are useful for sampling large lesions, such as infected bacterial or fungal nodules. Aspirates of hyperplastic lesions may yield useful information. However, neoplastic lesions, such as sarcoids, should be sampled with care as occult and nodular sarcoids may develop into fibroblastic lesions after sample collection [6].

Technique

- Aspirates can usually be taken from an un-sedated camel. Sedation is recommended, where a fractious animal is to be sampled or where the lesion is in a sensitive or inaccessible area.

- The lesion may be swabbed with spirit. The nodule can then be aspirated using an 18 to 21 gauge needle attached to a 5 or 10 ml plastic syringe.
- Once the sample has been aspirated, the needle is detached from the syringe and the plunger drawn back on the syringe to fill it with air. The needle is then reattached and the contents of the needle expelled onto a clean glass slide.
- The aspirate can be air-dried and stained directly. Alternatively, where large quantities of material are obtained, the aspirate can be smeared and then air-dried. Samples can be examined in-house with a rapid stain or submitted unstained to an external laboratory.

7. SKIN BIOPSY

In general, there are no definitive indications for a skin biopsy. The diagnostic reliability of skin biopsies can be improved through the proper selection of lesions for biopsy, the use of a dermatopathologist, and by providing the pathologist with a complete clinical differential diagnosis list [7]. Cutaneous biopsy has the potential to provide the most information in the shortest period of time. Biopsies should be considered for any dermatosis that has not responded to rational therapy, cannot be diagnosed with a routine diagnostic test, could potentially be neoplastic [8], or is severe enough to be associated with systemic disease. The more chronic the disease process, the less likely it is that the histopathologist will be able to make a useful histological interpretation. Ideally, therefore, the biopsy should be obtained from a lesion within the first two to three weeks of the onset of the skin disease. Multiple biopsies should always be taken. Where possible, primary lesions, such as macules, papules, plaques, nodules, tumours, pustules, wheals or vesicles, should be biopsied. Where alopecia is present, samples should be taken from a variety of lesions, including completely alopecic area, a partially alopecic area and an area of apparently normal skin. The three most common methods of skin biopsy are punch biopsy, wedge biopsy and shave biopsy. In the majority of cases, a punch biopsy is indicated. Wedge biopsies are most useful in transitional zones and for large lesions, while shave biopsy is the technique of choice for exophytic lesions, such as warts, but can also be used to sample areas such as the coronary bands.

Technique

- The area may be prepared by gentle clipping of the fiber. The site should not be prepared aseptically as this can destroy vital pathological features.
- The selected site may be circled with an indelible felt-tip marker before being anaesthetised. Local anaesthetic (without adrenaline) can be infiltrated into the site.
- When, the sensitive areas are to be biopsied, a general sedative or local nerve block may be employed. The latter is particularly useful when biopsies are to be collected from the camel's leg. Care should be taken when biopsies are taken from skin overlying important structures such as nerves blood, vessels and Ligaments.
- Punch biopsies can be taken using a disposable 8 or 10 mm diameter biopsy punch.
- The technique for wedge biopsies is essentially the same as for punch biopsies except the sample is taken in a wedge using a scalpel blade.

- Where a shave biopsy is taken, the skin is raised as a fold and cut with a scalpel blade parallel to the skin surface. The area can be sutured, bandaged or left to heal if minimal hemorrhage occurs.
- The sample should be fixed in 10 percent formal saline and submitted to a pathologist who is experienced in looking, at camel skin samples for detailed pathologic, histochemistry and electron microscopy assessment. Biopsies should always be accompanied by a history, description at the clinical lesions and, where possible a list of differential diagnoses.
- Immunodiagnosis is necessary in diagnosis of skin diseases and based on the histopathologic impression.

8. FUNGAL CULTURE

Fungal culture is important where there is a history of hair loss or crusting and scaling lesions, especially where more than one animal is affected. Dermatophyte test media (DTM) are used to isolate and identify dermatophyte organisms. DTM is made with special ingredients that inhibit bacterial growth and turn red when dermatophytes grow [3].

Technique

The infected area usually cleans gently by applying alcohol to the fiber and skin, prior to specimen collecting. The alcohol must dry before samples of fiber, crust or scale are collected from lesional skin using a sterile forceps. Using a Wood's lamp to collect fluorescing fibers may increase the diagnostic accuracy. DTM media should be keeping at room temperature before inoculated with the collected material to help hasten fungal growth. The sample should be gently applied to DTM media and being careful not to bury the sample within the media. Fungal culture plates with a large removable or flip-up lid make sample deposition much easier (standard Petri dish). For animals without lesions (resolving infections or subclinical carriers) a new tooth brush can be used to brush the entire hair coat. The collected sample is then distributed onto the culture plate. The DTM culture plates should be examined daily for 2-3 weeks. With dermatophytes, the medium will change color as soon as a white/buff colored fluffy colony is visible on the medium. Some contaminants (usually black, grey, and green) will be able to change the medium to red but only after growing for several days. If the culture plate has not been evaluated daily, then it will be impossible to determine when the color change occurred in relationship to the appearance of the fungal colony growth. Once the fungal colony has been growing for several days it will begin to produce macroconidia. Keeping the culture warm and in a humid environment facilitates conidia formation. The macroconidia should be sampled and microscopically examined to determine the dermatophyte species.

9. BACTERIAL CULTURE

Bacterial cultures are an important part of dermatological diagnostics path. Any deep cellulitis-like lesions, especially with draining tracts, should be cultured for bacterial and fungal organisms [3]. Nodules and tumors should be cultured if infectious etiologies are on the differential list. Where bacterial infection is suspected, samples may be submitted for culture. Swabs taken from the surface of

the skin rarely reveal the pathogenic organisms involved. Where primary pustules are present, the pustule can be gently perforated with a fine 25 gauge needle and the pus absorbed onto a swab and submitted for culture. Where crusts are present, swabs can be taken from the underside of a moist crust. However, in many chronic lesions, especially where there is a folliculitis of more than two to three weeks duration, the causative organism can be difficult to isolate except by tissue culture. Tissue culture is the preferred method of culture. Tissue samples are collected as for punch biopsy and submitted for culture in a sterile container.

10. CRUST PREPARATIONS

Primary lesions may be difficult to find on the skin. Maceration of the crust may give useful information about the underlying pathology [6]. This technique is particularly useful to the identification of bacteria such as *Dermatophilus* species, and may reveal evidence of acanthocytes suggestive of an immune-mediated disease.

Technique

- The crust is mixed on a slide with 0.9 per cent saline.
- The sample is carefully macerated to form an emulsion and left to dry.
- After drying, any large pieces of residual crust arc removed and the sample stained with Diff Quik or Rapi Diff.
- The sample is examined under a microscope, initially at low power and then at a higher power, if necessary.

11. PCR Assays

PCR (polymerase chain reaction) assays use laboratory methods to amplify DNA within a sample. PCR is many times more sensitive and specific than other diagnostic tests for the identification of viral, bacterial and fungal organisms. Among the molecular biological techniques, polymerase chain reaction (PCR) is most employed in the diagnosis of various infectious diseases as an alternative to conventional diagnostic assays. Recently a specific diagnostic PCR for the detection of *Camelpox virus* (*CMLV)* has been reported [9]. They described the C18L gene–based single PCR or duplex PCR based on the C18L and DNA polymerase (DNA pol) genes for specific and rapid detection and quantitation of CMLV. PCR techniques are also used in diagnosis of other camels skin diseases (will be explained in details in each individual disease).

12. Blood samples

• Changes in the cellular or biochemical composition of the blood are useful in confirming or ruling out differential diagnosis in dermatology.
• Specialized tests as hormonal assays, and serological tests may be used to identify specific conditions.

Collection of blood samples in camelidae

The site of blood collection in camelidae is the jugular vein. Head restraint is a minimum requirement in conditioned animals but wild camels will require anaesthesia or sedation. Needle 19-21G is usually used to bleeding camel [10, 11].

(A) Clotted blood or serum

• Cleaning the site of vein puncture.
• Obtaining the blood in the containers as centrifuge tubes vials.
• The container is left to clot in sunlight in sleep manner to give large surface area for oozing of serum.
• Then centrifuge the sample for obtaining maximum amount of serum.
• Transfer the serum into other tubes or vials and closed then preserved in deep freezer.
• Serum is collected for demonstration of biochemical composition such as minerals including: Copper, Zinc, Manganese, Sulfur and other elements such as Iron and calcium.

(B) Whole Blood sample

Blood samples are obtained by vein puncture using sterile needle and adding anticoagulants as heparin and EDTA. Whole blood samples are obtained for detection the cellular changes, which may resulted of the skin disease. This changes to be detected necessitate the following:-
• Erythrocytic count.
• Total leucocytic count.
• Differential leucocytic count.
• Haematocrite value.

2.3 Special dermato-pathology

Dermatopathology means histopathology of the skin and subcutis, and study of the causes of skin disease. The reaction of the skin to noxious stimuli varies with the severity and depth of injury. In the corium or dermis the reaction is the same as that of other tissues due to presence of blood vessels, nerve fibres, lymphatic vessels and connective tissues.

1. Classification of skin diseases according of its origin:

1- Primary skin diseases

In this type of diseases initially at least the lesions are restricted to skin and its associated structures, spread to other tissues may occurs later as secondary complications. It is evidenced by the clinical examination, which reveals that the lesions are restricted to skin without systemic reactions.

2- Secondary skin diseases

In this type the lesions occur as the result of extension of the disease process from another organ or tissues other than the skin, system reactions are present with cutaneous lesions.

2. Some macroscopical and microscopical Terminology

A. Macroscopical Skin lesions and their terminology (Scott,1988)

Nodules
Nodule is a circumscribed, solid elevation greater then l cm in diameter that does not deform when palpated.
Nodule extends into the deeper layers of the skin, and it results from cellular infiltrates into the dermis and subcutis.
Ulcers
An ulcer is a cutaneous defect resulting from a complete loss of the epidermis and usually part of the underlying tissues.
Erosion
An erosion is a cutaneous defect resulting from partial loss of the epidermis that does not penetrate beneath the basal laminar zone.
Papules
A papule is a solid, circumscribed, elevated lesion up to l cm in diameter. Papules are essentially small nodules that do not extend beneath the dermis.
Pustules
A pustule is a pas-fined, fluctuant, circumscribed, elevated accumulation of pus up to l cm in diameter.
Vesicles
A Vesicle is a fluid-filled, a cellular, circumscribed, elevated lesion up to l cm in diameter. While, a bulla is a vesicle that is greater than l cm in diameter.
Scaling
Scale is a visible accumulation of fragments of the horny layer of the skin (stratum corneum). It represents the final product of epidermal keratinization.
Histologically, scale is recognized as hyperkeratosis, which may be either parakeratosis or orthokeratosis. Grossly, it varies in appearance (color), consistency, and adherence.
Crusts
Crusts are dried exudate that adheres to the skin surface and hair. Crusts often cover erosions or ulcer; crusts are composed of serum, cells, fibrin and infectious agents.

B. Microscopical Skin lesions and their terminology

Epidermal changes

Hyperplasia	Increase in the number of cells
Hyperkeratosis	Thickening of the stratum corneum
Orthokeratosis	Hyperkeratosis without parakeratosis
Parakeratosis	Flattened keratinocyte nuclei within the stratum corneum

Follicular plugging	Hyperkeratosis within hair follicle
Hypergranulosis	Thickened granular layer (may have associated hyperkeratosis)
Hypogranulosis	Decreased thickness of granular layer (may have associated parakeratosis)
Acanthosis	Thickened squamous cell layer
Psoriasiform hyperplasia	Regular acanthosis, with elongation of rete ridges, as seen in chronic plaque psoriasis
Papillomatosis	Elevation of adjacent dermal papillae above the surrounding epidermal surface
Pseudoepitheliomatous hyperplasia	Extensive acanthosis simulating well-differentiated squamous cell carcinoma
Epidermal atrophy	Decreased thickness of epidermis
Cellular vacuolisation	Intracellular clear rounded spaces
Spongiosis	Intercellular oedema between keratinocytes (sometimes associated with exocytosis)
Exocytosis	Inflammatory cells within epidermis (usually refers to lymphocytes, and implies a benign process)
Acantholysis	Separation & rounding up of keratinocytes because of loss of intercellular adhesions
Dyskeratosis	Abnormally or prematurely keratinised eosinophilic keratinocytes, identified by prominent eosinophilic (red-staining) cytoplasm
Colloid bodies	Non-nucleated eosinophilic deposits in lower epidermis or upper dermis formed from the intracellular filaments of dead keratinocytes, and may entrap immunoglobulin or fibrin
Corps ronds & grains	Acantholytic dyskeratotic cells
Apoptosis	'Programmed cell death' of individual cells. Produces colloid bodies (which initially may contain shrunken dark nuclei).
Vacuolar degeneration	Damage to the basal layer, with intracellular oedema and vacuoles. May be associated with colloid body formation and clear spaces at the dermal-epidermal junction, sometimes resulting in a subepidermal blister.

Dermal changes

Melanin incontinence	Melanin in the upper dermis following damage to basal cells
Dermal atrophy	Decreased thickness of the dermis

Oedema	Accumulation of interstitial fluid (may be difficult to identify and can have a similar appearance to mucin)
Hyalinisation	Accumulation of dense 'hard looking' eosinophilic acellular material (stains red/pink)
Solar elastosis	Accumulation of basophilic material (grey/blue) in the upper dermis of photo-aged skin
Sclerosis	Hyalinised collagen with decreased fibroblasts
Mucin	Pale blue threadlike or granular staining. Larger amounts 'myxomatous' (washed-out), resemble oedema
Calcification	Dark blue brittle deposits: Metastatic – may involve blood vessels; Dystrophic – affects damaged tissue
Haemosiderin	Brown iron-containing pigment from disintegrated red blood cells. Must be differentiated from melanin.
Cleft	Empty space that previously contained material that has been dissolved in tissue processing such as fluid, crystals or lipid
Cells	
Neutrophils	Often referred to as 'polymorphs'. Hypersegmented nuclei; cells clustered into abscesses or scattered in epidermis. In large numbers in the dermis in 'neutrophilic' dermatoses.
Eosinophils	Segmented nuclei. Obvious numerous red (eosinophilic) granules in the cytoplasm. Associated with bullous disease, allergies, drug reactions and insect bites, but not specific. May be found in the epidermis or dermis.
Plasma cells	Clock face nuclei, paranuclear clearing. Characteristic of chronic inflammation near mucous membranes and often seen around invasive tumours.
Lymphocytes & histiocytes	The predominant cell type in most inflammatory skin diseases. Histiocytes are macrophages, and may be seen to have engulfed debris.
Multinucleated giant cells	Large cells containing multiple nuclei, which are usually formed from histiocytes, but there are several different types, which may suggest particular infections or tumours.
Granulomas	Nodular aggregate of histiocytes and other inflammatory cells. There are several subtypes, which may suggest specific infectious or non-infectious causes.
Red cells	Extravasated into epidermis (rare) or dermis
Mast cells	Classically have a 'fried-egg' appearance, but may be spindle or stellate shaped and very hard to identify without special stains.

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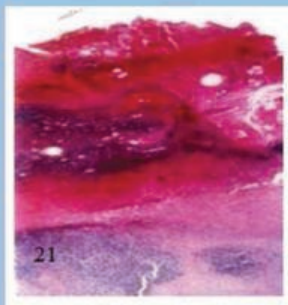
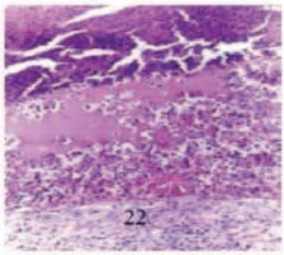
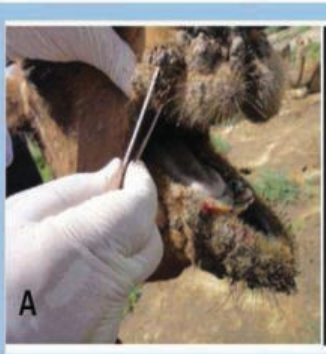
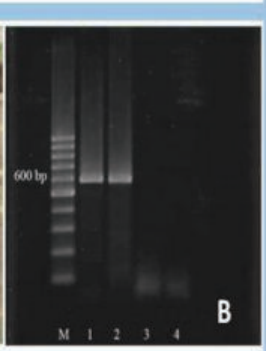
Chapter. 3

Viral diseases









Chapter 3: Viral diseases

3.1 Introduction

Only a few viruses appear to cause diseases in camels. They include rabies, camelpox, contagious ecthyma, papillomatosis, influenza, rotavirus diarrhoea, equine herpes virus infection and bovine viral diarrhoea. The camel seems to be minimally susceptible to foot-and mouth disease and rinderpest and immune to most of the other bovine viral diseases. Viral skin diseases, which occur in the camel, are discussed in detail in this chapter.

3.2 CAMELPOX (Poxvirus infections)

3.2.1 Definition

Camelpox is a wide-spread infectious viral disease of Old World camelids. New World camelids are also susceptible. This highly contagious viral disease of camels related to Poxviridae family, genus *Orthopox* virus characterized by fever, pox lesion on skin, and lesion on mucous membrane of respiratory and Gastrointestinal Tract (GIT). It is an economically important disease that restricted to camels. It is enzootic in almost every region where camel breeding is practiced with the exception of Australia [1]. Camelpox occurs throughout the camel-breeding areas of Africa, north of the equator, the Middle East and Asia and leading to loss of production and sometimes death. Diagnosis is usually based on characteristic clinical signs and lesions. An attenuated strain of vaccinia virus has been used as a vaccine [2].

3.2.2 Cause

The camelpox is caused by *Orthopoxvirus cameli* virus, which belongs to genus *Orthopoxvirus* (Figure.3.1) within family Poxviridae. It is one of the genera of the subfamily Chordopoxvirinae (Figure.3.2). *Orthopoxvirus*, is much more homogeneous, as befits its lower taxonomic status. The names, host ranges and geographical distribution on the basis of their biological properties are presented in Table.1. The genome structure has 9 distinct species of *Orthopoxvirus*. All these species show extensive serological cross-reactivity, by both in vitro test including i. serological tests (gel diffusion, complement fixation and haemagglutination inhibition), in addition to neutralization tests, ii. gross-protection in laboratory animals; indeed the last two tests form the basis for the tentative allocation of a poxvirus isolate to the genus *Orthopoxvirus* [3]. Traditionally, species of *Orthopoxvirus* have been named primarily on the basis of the host animal from which they were derived, and identified on the basis of a range of biological characteristics in laboratory animals [4, 5, 6, 7]. The most important indicators were the host range; the morphology of the pock and the ceiling temperature at which it was produced on the chorioallantoic membrane of the developing chick embryo. The situation

was changed by the discovery of Muller *et al.,* (1978) [8] and Esposito *et al.,* (2001) [9] that the DNAs of representative strains of each of several different species of *Orthopoxvirus* showed distinctive patterns after digestion with restriction endonucleases. With a larger number of strains of several different species, researcher [10] showed that all species of *Orthopoxvirus* shared a large conserved central part of their genomes. Analysis of the DNA structure now provides an alternative and more fundamental primary criterion for the classification of orthopoxviruses.

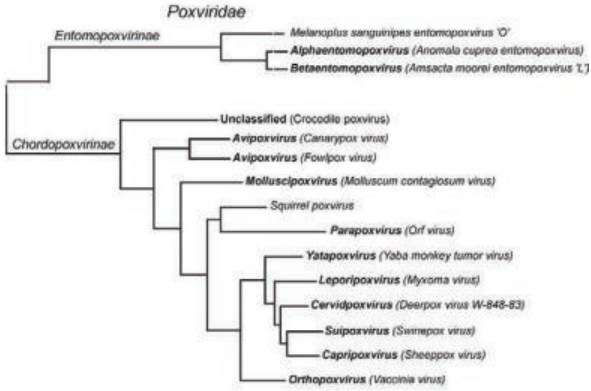


Figure. 3.1: Phylogenetic trees of (A) the poxviruses. The phylogenetic prediction is based upon aligned amino acid sequences from 19 conserved genes of representative virus strains for each genus (Duraffour *et al.,* (2011) [1].

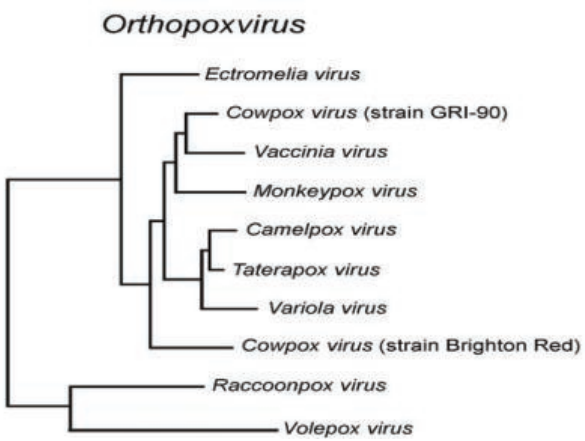


Figure.3.2: Codon-aligned nucleic acid sequences from nine conserved genes of the representative strains were used. The phylogenetic predictions were inferred using Bayesian analysis, as implemented by the program Mr Bayes (Duraffour *et al.,* 2011)[1].

Table 3. 1. Species of the genus *Orthopoxvirus*

Species	Animals found naturally infected	Host range In laboratory animals	Geographical range: natural infections
Variola	Man (Infection now eradicated)	Narrow	Formerly world-wide
Vaccinia virus (smallpox vaccine virus)	Numerous: man, cow, buffaloe [s] , pig [a], rabbit [a]	Broad	World-wide
Cowpox	Numerous: cow, man, rats, cats, gerbils, large felines, elephants, rhinoceroses, okapls	Broad	Europe (and Turkmenian SSR)
Monkeypox	Numerous: monkeys, great apes, anteaters, squirrels, man	Broad	Western and central Africa
Ectromelia	Mice, ?voles	Narrow	Europe
Camelpox	Camels	Narrow	Africa and Asia
Taterapox	Tatera kempl (a gerbil)	Narrow	Western Africa
Raccoonpox	Raccoons	?Broad	USA
Uasln Glshu dlsease	Horses (from a wildlife reservoir host)	Medium	Eastern Africa

a, Human infection

Based on sequence analysis, camelpox virus shares several biological properties with variola virus the aetiological agent for small pox and was originally described as being "extremely closely related" to variola virus [4]. However, it behaves differently in cultured cells [5] and has a distinctive genome structure. The camel appears to be the only natural host. It was first isolated in tissue culture by Ramyar & Hessami, (1972) [11] and its affinities with the genus *Ortbopoxvirus* were recognized by Baxby, (1972) [4]. In vivo experiments performed in the seventies on camels, additionally supported these findings: infection of camels with VARV strain EA8 protected against subsequent challenge with a pathogenic dose of CMLV [6]. Twenty years later, HindIII restriction fragment length polymorphisms further sustained that CMLV was clearly a separate OPV species [12, 13]. Similar methods using HindIII and XhoI restriction endonuclease analysis additionally allowed the partial differentiation between CMLV clinical isolates from different geographic regions [13, 14]. Extensive studies in Somalia during the Intensified Smallpox Eradication Program confirmed that camelpox virus did not cause disease in man. Conversely, the first definite approve of camelpox zoonotic infections in unvaccinated smallpox human connected with epidemics in dromedarian camels has been reported in India by Bera *et al.,* (2011) [16]. They confirmed the zoonotic nature of camelpox for the first occasion by laboratory investigations. They described three human cases that suffered from papules, vesicles, ulceration and finally scabs over the fingers and hands (Figure.3. 3). Molecular characterization of the causative agent accompanied with clinical, epidemiological and serological tests were the basis for confirmation CMLV zoonosis in human cases.

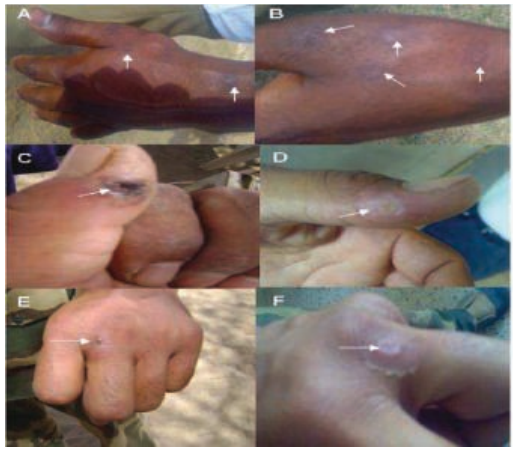


Figure.3.3: Skin lesions of camelpox in human cases. Case 1: (A&B) revealed disseminated cured scabs over the hand. Case 2: (C&D) Pock lesion displayed as ulcerated open wound with central necrosis that surrounded by a sharp hemorrhagic edge on the thumb. Case 3: (E&F) Typical pock-like lesions appeared as eruption at the base of the middle finger (Bera *et al.,* 2011) [16].

Camels have been successfully vaccinated against camelpox with vaccinia virus strains. Serological studies demonstrated also the cross-antigenicity between VACV, VARV, CPXV and CMLV, but not with viruses belonging to the *Parapoxvirus* and *Avipoxvirus* genera [4, 17]. The average size of the virion is 250 nm- 350 nm. Orthopoxviruses are enveloped, brick-shaped [18, 19] (Figure.3.4) and the outer membrane is covered with irregularly arranged tubular proteins.

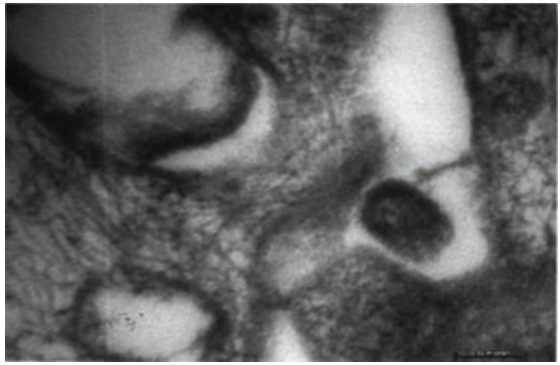


Figure. 3.4: The CPV has a typical brick-shaped appearance with irregularly tubular surface proteins appear in the cytoplasm of infected cells (X 100.000) *(*Salem *et al.,*2008) [20] .

A virion consists of an envelope, outer membrane, two lateral bodies and a core. The nucleic acid is a double-stranded linear DNA. The genome has cross links that join the two DNA strands at both ends. The end of each DNA strand has long inverted tandemly repeated nucleotide sequences that form single- stranded loops; the central region of the genome contains genes that are highly conserved in all sequenced *orthopoxvirus* [21]. CPV is indistinguishable from the prototypic vaccinia virus with respect to size, shape, structure, physico-chemical properties and replication [22]. The full-genome sequences of two CMLV strains from Iran and Kazakhstan, i.e., CMLV-CMS and CMLV-M96 respectively, have been published [22, 23]. The Camel pox virus genome is AT-rich (66.9%) and, in line with the genomic organization of other Orthopoxviruses, it contains a central region of genes that are highly conserved. Among these, 87 are conserved in all sequenced members of the subfamily Chordopoxvirinae [22, 23]. The central region encodes proteins required for RNA transcription, DNA replication, and virion assembly. In contrast, genes located within the terminal regions are non-essential and encode proteins involved in host range, virulence and immunomodulation. For these reasons, the sequences of the terminal regions and the organization of the open reading frames (ORFs) are more variable between OPVs. However, the arrangement of ORFs close to and within the inverted terminal repeat (ITR) of CMLV and VARV showed a higher degree of similarity in comparison with other OPVs [22, 23]. Camelpox virus may be propagated on the chorioallantoic membrane (CAM) of embryonated chicken eggs (Figure.3.5). After 5 days, characteristic lesions can be observed on the CAM. Camelpox virus shows typical cytopathic effect on a wide variety of cell cultures (Figure.3.6). Intracytoplasmic eosinophilic inclusion bodies, characteristic of poxvirus infection, may be demonstrated in infected cells using haematoxylin and eosin staining [20].

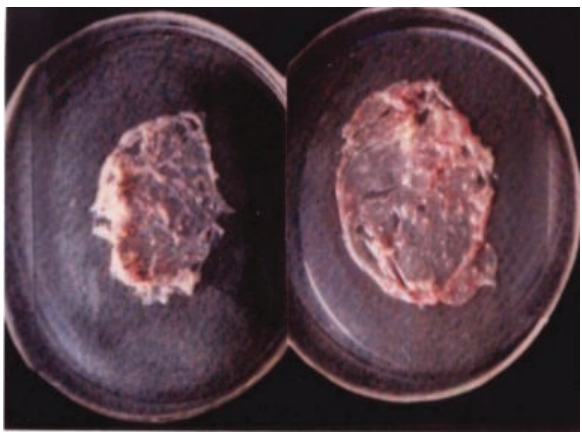


Figure. 3.5: Chorioallantoic membrane showing pock lesions characteristic for CPV (Salem *et al.,* 2008) [20].

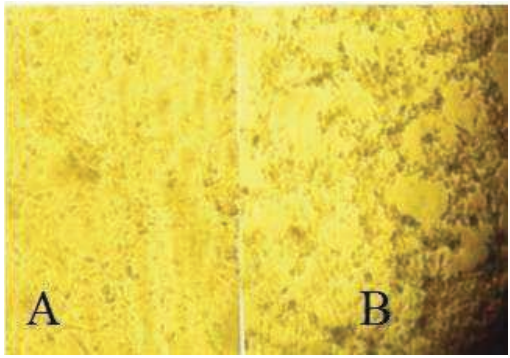


Fig.3.6: A- Non infected Vero cells. B- Infected Vero cells showing CPE characterized by cell rounding, aggregation and detachment of cell sheet. (Salem *et al.,* 2008) [20].

Many authors have compared the behavior of numerous CMLV strains in cell cultures. In general, cells derived from camel, lamb, calf, pig, monkey, chicken, hamster and mouse enable the propagation of CMLV strains. Both, transformed and primary human cells are permissive for CMLV replication. In contrast, cell monolayers derived from horse, rabbit and dog lead to a poor replication of CMLV for most of the strains tested and repeated sub cultivations were required [13].

Virus replicates in the cytoplasm of the host cell, in so-called inclusion bodies. Poxviruses, including CMLV, encode multiple genes that antagonize or affect the antiviral host immune response by interfering with the interferon (IFN) response, key proinflammatory cytokines (IL-1b, IL-18 and tumor necrosis factors [TNFs], chemokines and the complement system. CMLV has been shown to encode secreted proteins that bind to, and subsequently inhibit the biological activity of IFN-c, CC chemokines and tumor necrosis factor [24, 25, 26, 27]. It has been demonstrated that CMLV expressed a novel protein inhibiting apoptosis (v-GAAP) and a novel virulence factor and the schlafen-like protein 176R [28, 29]. In the case of IFN-a/b inhibition CMLV secrete a protein with IFN-a binding activity (CMLVCMS- 252 with similarity to VACV B19R), but its inhibitory potency might be low as shown by Symons and colleagues [27, 30, 31].

Camelpox virus is ether resistant and chloroform sensitive [32, 33]. The virus is sensitive to pH 3–5 and pH 8.5–10 [32]. Poxviruses are susceptible to various disinfectants including 1% sodium hypochlorite, 1% sodium hydroxide, 1% peracetic acid, formaldehyde, 0.5–1% formalin and 0.5% quaternary ammonium compounds. The virus can be destroyed by autoclaving, boiling for 10 minutes and is killed by ultraviolet rays (245 nm wave length) in a few minutes.

3.2.3 Geographic distribution

Although camelpox has presumably existed for millennia, its causative agent was not isolated until the early 1970s, during the opening phase of the global smallpox eradication campaign [34, 35].

Disease occurrence is accompanied with morbidity, mortality, and case fatality rates respectively of 30–90%, 1– 15%, and 25% [36]. As mentioned above, the causative agent, camel pox virus (CMLV), was earlier thought as a zoonotic agent reported initially in Punjab, India, since 1909 [37, 38], but so far a little evidence has been documented from

Somalia in smallpox unvaccinated individuals [39]. Subsequently, outbreaks have been reported in many countries of the Middle East, Asia, Africa and southern Russia, where the disease is enzootic (Figure. 3.7 &Table. 3. 2). The disease is endemic in these countries and a pattern of sporadic outbreaks occurs with a rise in the seasonal incidence usually during the rainy season. Of note, camelpox has never been reported in Australia, even though camel farming is practiced [38]. It has been suggested that different strains of camelpox virus may show some variation in their virulence [38]. As a general pattern, young camels under the age of four years (Figure. 3.8 &9) and pregnant females appear more susceptible to camelpox. Abortion rates can reach 87%, as observed in Syria [36] albeit, this high percentage might be explained by the absence of immunity as CMLV circulation had never been reported in this country before. Furthermore, mean morbidity rates can be as high as 92%, while the mean mortality rates may vary from 0% to 15% and the case fatality rates may range from 0% to 25%. The circulation of CMLV infections in herds has also been confirmed by sero-epidemiologic studies which showed the presence of neutralizing antibodies in 9.8% of the animals in Libya [40] and in 9.14% in Saudi Arabia [41]. In these two studies, it was mentioned that camelpox vaccinations were not practiced. In contrast, a prevalence of neutralizing antibodies of 72.5% was measured in Sudan in an unvaccinated population following the outbreak of 1992–1994 [42]. The disease is economically important in all camel rearing countries [43].

Figure.3.7: Geographical distribution of camelpox in the world 1. Kazakhstan,2. Iran, 3. Turkmenistan, 4. India , 5. Saudi Arabia, 6. United Arab Emirate, 7. Iraq, 8. Syria, 9. Egypt, 10. Sudan, 11.Ethiopia, 12.Somalia, 13. Kenya, 14. Libya, 15. Niger, 16. Mauritania, 17. Morocco.

Figure.3.8: Camel pox: A three year-old female camel showing pox eruptions on the groin and inner thighs. (A. I. Khalafalla Epizootiology of Camel Pox, Camel Contagious Ecthyma and Camel Papillomatosis in the Sudan Proceedings of the Third Annual Meeting for Animal Production Under Arid Conditions, Vol. 2: 115-131 © 1998 United Arab Emirates University.

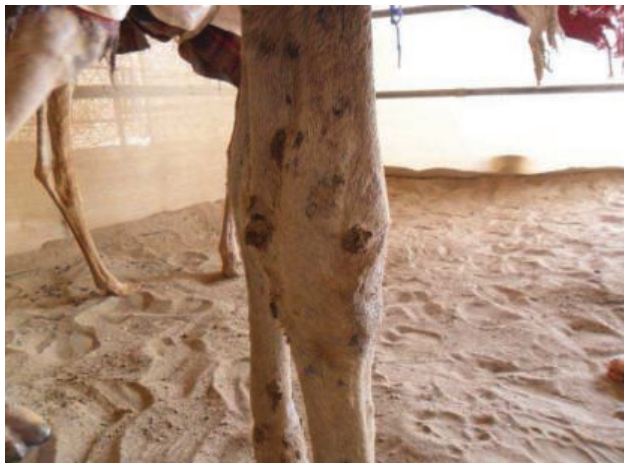


Figure. 3.9: Skin lesion in limbs (one year old female racing camel) (Qatar – 28/12/2010) Dr.Medhat Abdelkader Elshemy – veterinary surgeon.

Table. 3.2. Camelpox and Geographical distribution.

Country and years	Clinical appearance and Strain	References
1.India Punjab and Rajputana (1909)	Initial report	Lesse, S., 1909. Two diseases of young camels, Journal of Tropical Veterinary Science, 4, 1.
1.India, Rajasthan, Bikaner (1997)	Isolated from an outbreak with considerable morbidity , CMLV1	Chauhan and Kaushik (1987), Bhanuprakash et al. (2010a,b)
1.India,Rajasthan, Bikaner (1997)	CMLV2, Isolated from an outbreak with considerable morbidity	Chauhan and Kaushik (1987), Bhanuprakash et al. (2010a,b)
1.India,Rajasthan, Bikaner (2002)	Isolated from a male camel aged 10 years with eruptions on cheeks, nostrils, limbs, scrotum and sheath/ CMLV-Raj-4 06	Chauhan and Kaushik (1987), Bhanuprakash et al. (2010a,b)
1.Russia/Kazakhstan	CMLV-Guerevski (1967)	Tantawi, H.H., El Dahaby, H., Fahmy, L.S., 1978. Comparative studies on poxvirus strains isolated from camels. Acta Virol. 22, 451–457.
2.Russia/Turkmenia (1967)	CMLV-Turkmenskii	S. Duraffour et al. / Antiviral Research 92 (2011) 167–186
3.Russia/Turkmenia (1972)	CMLV-T72	S. Duraffour et al. / Antiviral Research 92 (2011) 167–186
4.Kazakhstan (Mangistauskiy area)	Isolated from a sick camels CMLV-M96	Afonso, C.L., Tulman, E.R., Lu, Z., Zsak, L., Sandybaev, N.T., Kerembekova, U.Z., Zaitsev, V.L., Kutish, G.F., Rock, D.L., 2002. The genome of camelpox virus. Virology 295, 1–9.
1. Iran (Teheran, 1970)	Obtained from vesicles and crusts harvested from natural outbreaks of camelpox/ CMLV-Teheran or CP-1 or CML1	Ramyar and Hesvami (1972), Baxby et al. (1975), Tantawi et al. (1978), Resnier-Muller et al. (1988), Pfeffer et al. (1990), Duraffour et al. (2007a,b)
1. Iran (Gorgan area, 1970)	Obtained from vesicles and crusts harvested from natural outbreaks of camelpox/ CM-G1	Baxby (1972), Ramyar and Hesami (1972), Baxby (1974), Baxby et al. (1975)
1. Iran (Gorgan area, 1970)	Obtained from vesicles and crusts harvested from natural outbreaks of camelpox/ CM-G2	S. Duraffour et al. / Antiviral Research 92 (2011) 167–186
4.Iran (Shiraz area, 1970)	Obtained from vesicles and crusts harvested from natural outbreaks of camelpox /CM-S	S. Duraffour et al. / Antiviral Research 92 (2011) 167–186
Iraqi in Al-Ethi area near Iranian-Iraqi border	Isolated from camel skin lesions at different stages of development /CMLV-Eth78 (1978)	Fathi et al. (1979)
Syria (Dama and Homs regions, 2005)	Isolated from specimens of vesicles, pustules, crusts and scabs from affected camels / CP Syria CP-SA	Al Zi'Abi et al. (2007)
1. Saudi Arabia (1986)		Resnier-Muller et al. (1988), Pfeffer et al. (1990)
1. Saudi Arabia, Northern region, Al Jouf.	Pathogenic field strain isolated from skin scabs collected during an outbreak of camelpox at the Experimental Camel Farm of the Range and Animal Development Research Center /CMLV- Jouf	Hafez et al. (1992)
1. Jouf, Saudi Arabia	Derived from CMLV-Jouf, and passaged 80 times in CKCC / Jouf 78 (vaccinal strain) Vaccine strain used in field testing	Hafez et al. (1992)
1. Saudi Arabia (Eastern Saudi Arabia (1997)	Isolated from a camel with a slow spreading mild form of camelpox/ CMLV-GabCE3	Alkeedi et al. (1994)
1. Saudi Arabia (1987)	Field strain isolated from the lung of a dromedary which died from generalized and internal camelpox / 262-95 (or 262-Skin and 262-Lung)	Wernery and Zachariah (1999), Pfeffer et al. (1996)
1. Saudi Arabia (Al-Ahsa region, 1990).	Isolated from skin biopsies from camels with a moderate form of camelpox CMLV-Al-Ahsa	Abu Elein et al. (1990)
7.Saudi Arabia / Jazan region	An outbreak of camelpox in December 2003 to July 2004. 25 camel herds 10(76%) clinically affected , different ages especially under one year of age. Morbidity 41% and 3.6% mortality.	M.A.Ommer Dafalla and A.M Abdelhamid Elhadil . Epidemiologic and clinical of Camelpox in Jazan Region, Saudi Arabia. Veterinary research 1(3): 68-67, 2007. ISSN: 1993-5412. Medwell Journals, 2007.
1. United Arab Emirates (Dubai, December 1993–March 1994).	CP-1	Resnier-Muller et al. (1988), Pfeffer et al. (1990)
1. United Arab Emirates (Dubai, December 1993–March 1994).	Isolated from scabs of camels with localized and generalized lesions CP-14 (CMLL14) to CP-29 (various CP strains)	Pfeffer et al. (1996), Duraffour et al. (2007b)
1. United Arab Emirates (winter 1993–1994).	Field strains isolated during camelpox outbreaks in winter 1993–1994 from camels that developed localized or generalized lesions. Various strains (813-93,864-93,...)	Wernery et al. (1997a, b)
4.United Arab Emirates (winter 1995–1996)	Field strains isolated during camelpox outbreaks in winter 1995–1996 from camels that developed localized or generalized lesions. Various strains (1230-95, 1251-95)	
8. United Arab Emirates (Dubai) Derived from O. Cameli strain passaged 90 times in Vero	Isolated from severe pox-lesions in a young camel Used for camelpox vaccine production (Dubai camelpox vaccine) / O. Cameli Dumpox 298/89 (vaccinal strain)	Arzoni et al. (1996)
1. Kenya.	Isolated from pox-like vesicular eruptions of camels / CMLV-H520	Davies et al. (1975)
2.Kenya (1992)	Various strains not named Isolated from sick camels	Gitao (1997)
1. Sudan (Butana area, 1992–1994)	Isolated from skin samples of sick camels CP/Sd2/93/1	Khalafalla and Mohamed (1998)
1. Sudan (Butana area, 1992–1994)	Isolated from skin samples of a two year old male dromedary in 1992 /CP/Nu-92/2	Khalafalla and El Dirdiri (2003); Sheikh Ali et al. (2008)
3. Sudan (Butana area, 1992–1994)	Isolated from skin samples of sick camels /CP/Bbg/92/3	
1. Sudan (Butana area, 1992–1994)	Isolated from skin samples of sick camels / CP/Sh/92/4	
1. Sudan (Butana area, 1992–1994)	Isolated from skin samples of sick camels / CP/Ak/93/5	
1. Sudan (Butana area, 1992–1994)	Isolated from skin samples of sick camels / CP/Tu/93/6	
Egypt (1970)	Isolated from a skin pox-like disease in a camel/ CMLV-Fayoum 71	Tantawi et al. (1978)
Niger	Isolated from camels with generalized skin lesions/ CP-NIG (or VD49)	Ortcheiu et al. (1996)
Niger	Isolated from camels with generalized skin lesions and this strain gives strong cytopathic effect in cell cultures/ VD47; VD48.	Ngeyen et al. (1989), Sheikh Ali et al. (2009)
Niger	Derived from VD47, and passaged 90 times in two cell types Used for camelpox vaccine production / VD47/39 (vaccinal strain)	Ngeyen et al. (1996)
Morocco (1984)	TR (vaccinal strain) Passaged on Vero cells and inactivated with formol, vaccine strain	El Harrak and Lourfi (2000)
Mauritania (1984)	Isolated from camels with generalized skin lesions/ CP-MAU	Ngeyen et al. (1989); Resnier-Muller et al., 1988, Ortcheiu et al. (1996), Pfeffer et al. (1999a).
Mauritania,	Derived from CP-MAU, and passaged 114 times in Vero Selection of an attenuated CMLV strain/ CP-MAU #114	Ortcheiu et al. (1996)
Mauritania (1987)	Isolated from camels with camelpox / VDR-A2	Ngeyen et al. (1996)
Obtained from München, West Germany (1980)	CMLV-München	Sehgal and Ray (1980)
Not mentioned	CMLV-66	Khgeiri et al. (1995)
Not mentioned	CMLV-208/2	

3.2.4 Economic importance

Camels are very important animal in the arid regions; provide transport and maintenance to both nomadic and non-nomadic populations. Camels are also used for racing and as a source of wool, milk and meat. Therefore, camelpox outbreaks have serious economic consequences in herds as affected camels may suffer from loss of condition and reduction in milk production and weight. In addition, the appearance of camelpox in herds may favor secondary infections from other circulating diseases from which camels might die. Prevention from participation in racing competitions and affect the performance of racing camel for long time may be over 2 to 3 months.

3.2.5 Susceptibility

Both Old World camelids and New World camelids are susceptible to the disease. Young animals are more susceptible than elder ages because of diseased animal acquired long immunity. Males are more susceptible than females.

3.2.6 Pathogenesis

Infection is usually acquired by cutaneous or respiratory routes. Camelpox virus commonly gains access to the systemic circulation via the lymphatic system, although multiplication at the site of inoculation in the skin may lead to direct entry into the blood and a primary viremia. A secondary viremia disseminates the virus back to the skin and to other target organs.

CMLV has certain strategies used to circumvent the immune response of the host. CMLV, encode multiple genes that antagonize or affect the antiviral host immune response by interfering with the interferon (IFN) response, key pro-inflammatory cytokines (IL-1b, IL-18 and tumor necrosis factors [TNFs]), chemokines and the complement system 44, 45. (Nazarian and McFadden, 2007; Perdiguero and Esteban, 2009). Only few articles have been identified the immune-modulations mechanisms in CMLV [24, 25, 26, 27, 28, 29]. So far, CMLV was restricted to camelids but, recently, three human cases of camelpox have been described in India, highlighting the need to pursue research on its pathogenesis and the characterization of CMLV immune-escape pathways, which has been hampered by the lack of small animal models. CMLV replication in tissues and body fluids was confirmed in the two models. The sequencing of two CMLV strains has brought additional knowledge on potential immunomodulatory proteins encoded by CMLV. NMRI immunocompetent mice are resistant to intranasal (i.n.) CMLV infection. However, CMLV induced a severe disease following i.n. challenge of athymic nude mice, which was accompanied with a failure in gaining weight, leading to euthanasia of the animals. On the other hand, intracutaneous (i.c.) infection resulted in disease development without impacting the body weight evolution. CMLV has been shown to encode secreted proteins that bind to and subsequently inhibit the biological activity of IFN-c, CC chemokines and tumor necrosis factor [24, 25, 26, 27, 28]. Recently, it has been demonstrated that CMLV expressed a novel protein inhibiting apoptosis (v-GAAP) and a novel virulence factor, the schlafen-like protein 176R [28, 29]. In the case of IFN-a/b inhibition CMLV secrete a protein with IFN-a binding activity (CMLVCMS- 252 with similarity to VACV B19R), but its inhibitory potency might be low [27, 30, 31]. CMLV uses other proteins to modulate interactions with the host, but whether or not these identified ORFs produce a functional protein is not known. From bioinformatics analysis, CMLV-resistance to IFN could be also mediated by the CMLV097 gene, homolog of the VACV H1L gene, which

has been shown to encode an intracellular protein that dephosphorylates STAT1 and thus prevents the action of IFN-c on infected cells [46]. Also, the 32L and 55L genes may encode proteins which, in VACV, have been shown to prevent the activation of PKR (dsRNA dependent protein kinase) and the production of IFN [47]. IL-1b is a potent pro-inflammatory cytokine involved in inflammation. To inhibit it, CMLV could produce a viral soluble receptor encoded by three genes CMLV193, 194 and 196 which are seen as separate parts of the VACV B16R IL-1 binding protein [23]. However, Symons and colleagues demonstrated that CMLV inhibits IL-12-induced production of IFN-c by mouse splenocytes [31]. Symons *et al.,* (2002) [31], suggested that CMLV produces an active caspase 1 inhibitor, which, by inhibiting the cleavage of IL-18, significantly contributes to reduce IFN-c production by IL-12 [31]. CMLV may utilize several ways to alter or shut down the host immune response and, though these mechanisms have been described in vitro, they may reflect the in vivo situation and explain the pathogenicity of CMLV in its host, the camel. Immunodeficient mice are found a permissive for CMLV propagation and can provide a basis for studying the pathogenesis of CMLV, as well as for evaluating potential antiviral therapies in an immunodeficiency context [1].

3.2.7 Clinical signs

Camelpox is recognized as one of the most important viral disease in camels. Transmission of camelpox occurs by direct contacts with sick animals through skin abrasions or via aerosols [38] or indirect by contaminated environment (virus excreted in milk, nasal, eye and mouth discharge), the role of insects suspected because of the disease observed after rainfall. Risk factors associated with higher incidence of camelpox have been defined and include the average age of the animals (less than four years old), the rainy season of the year, the introduction of new camels in a herd and the common watering [48].

The clinical features of camelpox have been extensively described by several groups [38, 43]. The incubation period is usually 9–13 days (varying between 3 and 15 days). Clinical manifestations of camelpox range from unapparent and mild local infections, confined to the skin, to moderate and severe systemic infections, possibly reflecting differences between the strains of camelpox [38]. The disease is characterized by fever, enlarged lymph nodes and skin lesions. Skin lesions appear 1–3 days after the onset of fever, starting as erythematous macules, developing into papules and vesicles, and later turning into pustules. Crusts develop on the ruptured pustules. These lesions first appear on the head, eyelids, nostrils and the margins of the ears. In severe cases the whole head may be swollen. Later, skin lesions may extend to the neck, limbs, genitalia, mammary glands and perineum. In the generalized form, pox lesions may cover the entire body. Skin lesions may take up to 4–6 weeks to heal. In the systemic form of the disease, pox lesions can be found in the mucous membranes of the mouth, respiratory and digestive tracts [39] (Figure. 3. 10). The animals may show salivation, lacrimation and a mucopurulent nasal discharge. Diarrhoea and anorexia may occur in the systemic form of the disease. Pregnant females may abort. Death is usually due to secondary infections and septicaemia.

Figure.3.10: Shows the clinical signs of camelpox A. Nasal discharge, B. Severe skin lesions on the head and face of the infected camel.

3.2.8 Histopathology of camelpox

Generally poxviruses induce lesions by a variety of mechanisms. Degenerative changes in epithelium are caused by virus replication and lead to vesicular lesions typical for many poxvirus infections. Degenerative changes in the dermis or subcutis may result from ischemia secondary to vascular damage. Poxvirus infection may also induce proliferative lesions via epithelial hyperplasia. The host -cell DNA synthesis is stimulated before the onset of cytoplasmic virus-related DNA replication.

Grossly camelpox lesions in the skin have a typical clinical evolution, beginning as erythematous macules and becoming popular, and then vesicular. The vesicular stage is well developed in some pox infections and transient or nonexistent in others. Vesicles evolve into umbilicated pustules with a depressed center and raised, often erythematous, border. This lesion is the so called pock. The pustules rupture and form a crust. Eruptions are mainly localized on the head, nostrils and eyelids, as well as on the mucous membranes of the lips and the nose and also in the oral cavity. Later, lesions may extend to the limbs, mammary glands or scrotum. Healed lesions often leave a scar. Histopathological examination of the early skin nodules reveals characteristic cytoplasmic swelling, vacuolation and ballooning of the keratinocytes of the outer stratum spinosum (Figure.3.11). The rupture of these cells produces vesicles and localised oedema. Perivascular infiltration of mononuclear cells and variable infiltration of neutrophils and eosinophils occurs. Marked epithelial hyperplasia may occur in the borders of the skin lesions [49]. There are only a few details pathological descriptions of internal camelpox lesions. Multiple pox-like lesions on the mucous membranes of the mouth, respiratory and digestive tract are the most common lesions observed on post-mortem examination of camels died from severe infection camelpox. The size of the lesions in the lungs may vary in diameter between 0.5 and 1.3 cm, occasionally up to 4–5 cm. smaller lesions may have a hemorrhagic center. The lung lesions are characterized by hydropic degeneration, proliferation of bronchial epithelial cells, and infiltration of the affected areas by macrophages, necrosis and fibrosis [14, 50, 51, 52, 53].

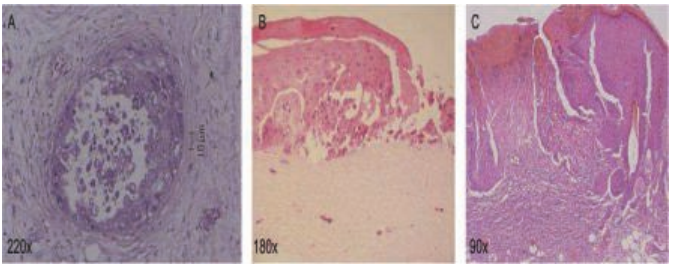


Figure.3.11: Histopathology of skin biopsies. (A) Skin biopsy collected during a camelpox outbreak in Dubai in 1994–1995 on a dromedary exhibiting camelpox dermatitis with epithelial proliferation. Note the intracellular edema of keratinocytes and cellular debris in the center. This picture was kindly provided by Prof. Wernery U., Central Veterinary Research Laboratory, Dubai, United Arab Emirates. (B) Histology of human skin-equivalent cultures infected with CMLV (strain CML1), as observed at day 12 postinfection. Note the cytoplasmic swelling and the ballooning of the keratinocytes, as well as destruction of the epithelium. (C) Histology of back skin of an athymic nude mouse infected with CMLV (strain CML1) by scarification at the lumbosacral region. Note the exophytic lesion covered with hyperplastic squamous epithelium, which centrally invaginates to form a crater filled with parakeratin and inflammatory cells. (B) and (C), our data. All images: hematoxylin and eosin staining.

3.2.9 Diagnostic methods

Camelpox in camels can be confused with other viral diseases, such as contagious ecthyma (parapoxvirus) and papillomatosis (papillomavirus), differential diagnosis may be needed [38]. Several diagnostic methods are available and, where possible, more than one should be used to make a confirmatory diagnosis of disease. Camelpox is routinely diagnosed based on clinical signs, pathological findings and cellular and molecular assays. Five complementary techniques might be advised for camelpox diagnosis: transmission electron microscopy (TEM), cell culture isolation, standard PCR assays, immunohistochemistry and demonstration of neutralizing antibodies. TEM is a reliable and rapid method to demonstrate the presence of OPVs in scabs or tissue samples, although a relative high concentration of the virus in the sample is required. This technique enables the differentiation between OPVs, which are brick-shaped, and parapoxviruses, which are ovoid-shaped [18]. Chorioallantoic membranes (CAMs) used for the growth of CMLV [54], but it is important to consider that the pocks produced by VARV and CMLV in this system are indistinguishable [4]. Virus isolation in cell culture must be initiated, in parallel to TEM [55, 56]. Blood, serum and homogenized tissue samples can be used to infect cell cultures. Cultures should be monitored for 10–12 days. However, depending on the virus concentration, cytopathic effects, including the formation of multinucleated syncytia, can already appear at one day post-infection. CMLV identification must be confirmed by TEM, PCR and/or sequencing [57]. Numerous commercial kits use to extract DNA from cell culture samples and clinical material. Recently, a reliable and low-cost two-step extraction procedure has been developed for isolating CMLV DNA from skin samples [58]. The PCR assays available to identify CMLV are based on the detection of sequences encoding for the A-type inclusion body (ATI), the hemagglutinin (HA), the ankyrin repeat protein (C18L) or the DNA polymerase (DNA

pol) [59, 60, 61, 62]. ATI gene-based PCR is performed with a single set of primer which enables the differentiation of OPV species by producing amplicons of different sizes. An extra step consisting of a BglII or XbaI restriction digestion allows then an unequivocal identification of the virus species [59, 60]. The HA-PCR amplicon TaqI restriction fragment length polymorphism (RFLP) permits to differentiate between OPV species, but species-specific primers within the HA open reading frame of OPVs have also been described [62]. Recently, a single-plex C18L and a duplex C18L-DNA pol PCR have been developed to specifically identify CMLV and to differentiate it from other OPVs, capripoxviruses and parapoxviruses [61]. Venkatesan *et al.,* (2012) [63] reported the development of loop-mediated isothermal amplification (LAMP) assay based on ankyrin repeat protein gene (C18L) for specific and rapid detection of camelpox virus (CMLV). They found that LAMP assay is a simple, specific, sensitive, rapid and economical diagnostic tool for detection of CMLV from clinical materials. The assay was optimized using viral genomic DNA (gDNA) extracted from density gradient purified CMLV and standard control recombinant DNA plasmid containing the target, which resulted in reliable amplification at 62 ◦C for 60 min. The amplified LAMP product was identified by agarose gel electrophoresis and subsequent direct visualization under UV light or observation by naked-eye for the presence of turbidity and color change following the addition of SYBR Green I dye and hydroxy naphthol blue (HNB). The analytical specificity of LAMP and conventional PCR assays was evaluated using other related poxviruses namely buffalopox, goatpox, sheeppox, and orf viruses, which revealed only a specific amplification of CMLV. The LAMP assay was 10-fold more sensitive than the conventional PCR. Further, the assay was evaluated with DNA extracted from the cell culture isolates of CMLV (n = 11) and clinical samples (n = 23). Before 2011, no real-time quantitative PCR has been described for the specific diagnosis of CMLV. In 2011, indoor Real/time polymerase chain reaction was innovated of for diagnosis of camel pox virus [64] in clinical filed. The samples are performed using primer site belongs to Capripoxvirus. A total of 15 specimens from camels suspected of being infected with CPV were collected from Riyadh province during 2009, and submitted for virological investigation at the central veterinary laboratory diagnostic Lab (CVDL) , Riyadh, Ministry of Agriculture , KSA. Camel pox virus was achieved in 10 samples by conventional polymerase chain reaction (PCR). A trial for development of simple and rapid qualitative real/time polymerase chain reaction (RT-PCR) was applied using primer site belongs to Capripoxvirus to detect CPV load in prepared tissue samples comparing to inoculated Chorio-allantoic membranes (CAMs) and Vero cells were (reveals pocks or CPE) using SYBR green I chemistry. They found that RT-PCR assay was rapid, accurate and effective for the direct and qualitative detection of camel pox virus (viral DNA) in both necropsy specimens and inoculated egg or tissue culture samples.

3.2.10 Control and treatment

Like smallpox, camelpox meets the basic requirements to be a candidate for eradication: the disease affects a single host; its causative agent has no wildlife reservoir; and diagnostic tests and vaccines are available to diagnose the disease and block its transmission [65, 66]. As for other potentially eradicable diseases, a cost-benefit analysis could be performed to determine the priority of its elimination versus other health needs [67, 68]. To eradicate camelpox, it would not be necessary to vaccinate all of the world's camels. Instead, veterinarians could employ the ''ring vaccination'' strategy that was so successful in the final phase of the smallpox campaign, in which intensive surveillance was used to detect cases of disease, followed by vaccination of all surrounding contacts

and continued monitoring to ensure that no more cases occurred. For camelpox, such a strategy would have to include testing to differentiate it from a clinically similar disease, contagious ecthyma, caused by a parapoxvirus. Polymerase chain reaction (PCR) and other diagnostic assays have been evaluated in a number of countries [16, 61] and are delineated in the OIE's Manual of Diagnostic Tests and Vaccines for Terrestrial Animals [2].

3.2.10.1 Immunity and vaccination

Immunity against camelpox is both humoral and cell mediated. The relative importance of these two mechanisms is not fully understood, but it is believed that circulating antibodies do not reflect the immune status of the animal). Life-long immunity follows after natural infection. Live, attenuated vaccine provides protection against the disease for at least 6 years, probably longer [52]. Inactivated vaccine provides protection for 1 year only. The camelpox virus is very host specific and does not infect other animal species, including cattle, sheep and goats. Field reports of mild skin lesions in humans associated with camel pox have been made [69], but it appears that only one suspected case of human camelpox has been described [39], underlining that camelpox is of no public health importance. Further analyzed to innate immune and B cell responses induced in the spleen and draining lymph nodes after exposure to CMLV has been done by investigators. In both models, strong increases in CD11b (+) F4/80(+) macrophages were seen in the spleen, while neutrophils, NK and B cell responses varied between the routes of infection. In the lymph nodes, the magnitude of CD11c (+) CD8α(+) lymphoid and CD11c (+)CD11b (+) myeloid dendritic cell responses increased in intra nasal challenged animals. Analysis of cytokine profiles revealed significant increases of interleukin (IL)-6 and IL-18 in the sera of infected animals, while those of other cytokines were similar to uninfected controls. Different commercial CMLV vaccines are available to be used to protect camels against camel poxvirus. For example, a live attenuated vaccine, Ducapox, is manufactured by Highveld Biologicals, Onderstepoort, South Africa and an inactivated vaccine by Biopharma, Rabat, Morocco. A live attenuated vaccine gives long-term protection against camelpox [52]. However, a booster vaccination is recommended for young animals vaccinated before the age of 6–9 months. When inactivated vaccine is used, the animals must be vaccinated annually (Table.3.3).

Table 3.3 CMLV vaccines currently in commercial production. (Duraffour *et al.,* 2011/ Antiviral Research 92 167–186)

CMLV vaccine strain/ commercial name	Manufacturing company	Market places	Notes	References
Jouf-78	-	Saudi Arabia	Attenuated CMLV strain, passaged in cell cultures	Nguyen et al. (1996)
VD47/25	-	Mauritania	Attenuated CMLV strain, passaged in cell cultures	
Ducapox (298/89)/ Ducapox®	Highveld Biological, South Africa	United Arab Emirates and other countries	Attenuated CMLV strain, second injection for young calves, immunity lifelong	El Harrak and Loutfi (2000); Khalafalla and El Dirdiri (2003)
CMLV-T8/CAMELPOX®	Biopharma, Morocco	Morocco and other countries	Inactivated CMLV strain, second injection required, repeat injection annually	

3.2.10.2 Treatment

No successful treatment but isolation of infected cases and supportive treatment are necessary procedure in the outbreaks of the disease. Supportive treatment include: (vitamin C) for increase body immunity against the virus and some antibiotic to avoid secondary bacterial infection for example (oxytetracycline) and antipyretics (NSAIDs) (R/ Vita-c-vetiquinol. R/Alamycin300LA, R/pen&strep, R/novasul, R/phenylarathrite, R/vetalgen). In case of facial edema or edema of limbs we can use dexamethasone, R/diurizone, R/dexaphenylarathrite. Over the last years, potent antiviral molecules active in vitro and in vivo against poxviruses, including OPVs, have been developed and could be envisaged for the treatment of camelpox disease [70, 71, 72]. They include in particular (i) the molecules belonging to the acyclic nucleoside phosphonate (ANP) family, i.e., cidofovir (Gilead, CA, USA) and its lipid derivative CMX001 (Chimerix Inc, NC, USA) [73,74], and (ii) the compound ST-246 (SIGA Inc, OR, USA) [75]. These three drugs have gained Investigational New Drug (IND) status, allowing their emergency use for the treatment of life-threatening VACV infections [76, 77, 78, 79]. Cidofovir, CMX001 and ST-246 are potent inhibitors of CMLV replication in vitro. In mouse models of camelpox infection, cidofovir either formulated as cream or for systemic use protected animals from disease development and/or death. Nevertheless, CMX001 and ST-246 offer the advantage of being orally available which may render them more attractive for veterinary use [101].

References

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3.3 Camel Contagious ecthyma ((Auzdyk)

3.3.1 Definition

Camel Contagious ecthyma (CCE), (contagious viral pustular dermatitis, contagious pustular dermatitis, soremouth, orf) is caused by *Parapoxvirus*. Both the one-humped and two-humped camels are prone to this disease. Pox-like lesions are produced by the affected animals. However, camel herders in many countries regard CCE as a separate disease and give it local names such as *Auzdic* in Kazakhstan [11] and *Abu Shalambo* and *Al Kolate* in Sudan [1, 27]. Modes of transmission are similar to those described in camel pox. The virus is morphologically different from *Orthopoxvirus* and can easily be identified by electron microscopy. Clinical symptoms are similar to those caused by the

Orthopoxvirus, but a diagnosis based on these lesions can only be presumptive. The main practical differences between camel pox and camel contagious ecthyma are that, the latter disease is more severe and affects camels of all ages. In immature camels the lesions are mainly found around the mouth and nostrils and occasionally on the eyelids. The mandibular lymph nodes are enlarged. Due to intensive pruritus animals spend a lot of time scratching and rubbing the affected area, resulting in haemorrhages and skin excoriations. Grazing and suckling ability is impaired. Both localized and generalized skin lesions have been observed. Whether recovered animals have a lasting immunity is not clear, but according to field observations, recovered animals were not affected during new disease outbreaks. Control and care are similar to those for camel pox.

3.3.2 Cause

Parapoxviruses (*PPV*) belong to the family *Poxviridae*, which consists of over 80 known or tentative species that infect both animal (subfamily *Chordopoxvirinae*) and insect (subfamily *Entomopoxvirinae*) hosts. The viruses within the family have large, brick shaped (220-450 nm x 140-260 nm) or ovoid (250-300 nm x 160-190 nm) particles with genomes of linear double-stranded DNA (dsDNA) varying in size from 130 kbp to 375 kbp. The subfamily *Chordopoxvirinae* consists of nine genera on the basis of their natural host-range, morphology and their genetic and antigenic relatedness. In addition, the *Chordopoxvirinae* includes several unclassified poxviruses, which might form additional genera once their phylogenetic relationships have been established. The classified genera are *Avipoxvirus*, *Capripoxvirus*, *Leporipoxvirus*, *Molluscipoxvirus*, *Orthopoxvirus*, *Parapoxvirus*, *Yatapoxvirus*, *Suipoxvirus* and most recently *Cervidpoxvirus* [45]. All chordopoxviruses cause disease characterized by cutaneous lesions, but the severity of the disease varies from localized self-limiting infection (for example contagious ecthyma caused by PPV *Orf virus*) to systemic disease with high mortality (for example smallpox caused by *Variola virus* of the genus *Orthopoxvirus*). The orf virus is the prototype of the parapoxvirus genus. It can cause contagious ecthyma in goats, sheep, camels and other ruminants worldwide. The viruses are sometimes transmissible to humans due to direct contact [20]. Most infections in humans are localized and heal spontaneously; however, large, poorly healing lesions can occur in people who are immunosuppressed. The International Committee on Taxonomy of Viruses (ICTV) currently recognizes four species in the genus *Parapoxvirus*. These are Orf virus (*ORFV*) (synonyms contagious pustular dermatitis virus and contagious ecthyma virus), Bovine popular stomatitis virus (BPSV), Pseudocowpox virus (PCPV) (synonyms Milker's nodule virus and Paravaccinia virus) and Parapoxvirus of red deer in New Zealand (PVNZ). ORFV, the prototype member of the genus, infects mainly sheep and goats, whereas BPSV and PCPV infect cattle. Tentative species of the genus include Auzduk disease virus, Camel contagious ecthyma virus, Chamois contagious ecthyma virus and Sealpox virus [12, 45]. The major criteria for classifying parapoxvirus species are the distinctive virion morphology and affected host, combined with restriction fragment length polymorphism (RFLP) and cross-hybridization analyses of the genome. Parapoxviruses are ovoid particles of 220–300 x 140–170 nm in size, with a single thread-like surface tubule surrounding the particle in a spiral fashion. Inside the surface membrane is the enveloped core containing genomic DNA together with several proteins, and lateral bodies between the core and the surface membrane [45]. Cryoelectron microscopy of ORFV infected cells has shown that ORFV produces two forms of virions: intracellular mature virions (MVs) and wrapped virions (WVs), which differ that the WV is a MV particle surrounded by two additional membranes derived from the trans-Golgi network [46]. During virus egress, the WV loses

its outermost membrane and becomes an extracellular enveloped virion (EV). In *Vaccinia* virus (VACV), MV and EV are the two main infectious forms that are produced during the virus replication cycle [34]. The demonstration of ORFV MV, WV and EV [46, 48], in addition to the fact that ORFV has homologues of most VACV genes encoding proteins associated with structure and morphogenesis, as well as genes involved in replication and transcription of the genome [15, 35], suggests that the morphogenesis and replication cycle of ORFV and VACV are likely to be similar. Studies with ORFV and PCPV have shown that PPV DNA replication begins 4-8 h post infection (p.i.) and continues to 25-36 h p.i., and that the first virus-induced polypeptides can be detected starting at 10 h p.i. Both ORFV and PCPV viral particles appear at 12-18 h p.i. and they are produced until at least 48 h p.i. [13, 49]. The PPV genome is a linear dsDNA molecule of 130-140 kbp with inverted terminal repeats (ITR) and cross-linked ends [19, 36]. PPV ITRs, which are identical but oppositely oriented sequences at the two ends of the genome, are between 1.2 and 4.0 kbp in length [15, 19, 36, 38]. Studies with ORFV strain NZ2 have revealed that the two strands of DNA are covalently closed with hairpin loops of about 100 bp [36], and the regions adjacent to the hairpin loops contain a conserved motif that is required for the resolution of replicating concatemeric forms of poxvirus DNA [37].

The nucleotide composition of PPV genomes are unusually guanine and cytosine G+C rich (on average 63-64%) [15, 38, 53] compared to other poxviruses (30-40%) with the exception of *Molluscum contagiosum virus* (MOCV) (64%) [45]. However, analysis of three isolates of ORFV and one isolate of BPSV have shown that their G+C content differs from the average in the terminal regions of the genome, and is especially low (approximately 42-47%) in parts of the right end of the genome. The pattern of genome G+C variation is so similar among ORFV and BPSV and distinct from that of the other poxviruses including MOCV as to form a signature. This signature might represent a genus-specific feature of the PPVs [37]. The ORFV and BPSV genomes have only recently been sequenced and are predicted to contain 132 and 133 genes, respectively [15, 38]. The majority of the genes are non-overlapping but closely spaced, there are no introns, and the transcription is directed generally towards the nearest end. The central parts of the sequenced PPV genomes contain genes that predominantly have orthologues to VACV and other poxvirus genes essential for virus replication, transcription and morphogenesis. This central core region lacks two (D9R and F15R in VACV strain Copenhagen; VAC_Cop) of the 90 conserved genes present in all other vertebrate poxviruses, and thus reduce the minimum essential chordopoxvirus genome to 88 genes [15, 38, 51]. In contrast, the genes located at the ends of the genome have important roles in virulence and virus-host interaction. The terminal regions of PPV genomes, primarily the right end of the genome, contain genes that are not found in other poxviruses [15, 38]. The terminal regions of PPV genomes vary considerably, and do not cross hybridize between species [22, 43].

Camel *Parapox* virions are ovoid particles that range in size from 230 to 360 x 131 to 160 nm, their axis ratio is about 1:1.56 and their surface shows a regular crisscross pattern of filaments [16] (Figure. 3.12). The viral genome consists of the linear double-stranded DNA (134- 139 kb). Essential genes are located in the conserved central part of the genome, and variability is observed in the terminal ends. Genes in near-terminal regions of the genome encode factors with important roles in viral-host interactions such as modulating host responses to infection and determining host range, but often not essential for growth in cultured cells. The B2L gene resides in the BamHI B fragment of NZ-2 strain and encodes a major envelope protein of 42 kDa. The B2L gene has been used for detection of orf virus by PCR [16]. The virus is extremely resistant to environmental factors. On concentrates and coarse fodder stored under the usual conditions, it remains viable for 270-300 days, and in various soils, as well as in manure not subjected to biothermal

treatment, it survives for up to 120 days. It is very resistant to various disinfectants, the most effective of which are caustic soda, phenol and potassium permanganate. In double concentrations, these can kill the virus in 10-20 minutes at 60°C. It is destroyed practically instantaneously in boiling water (96-98 °C). The virus is very resistant to the action of antibiotics. It takes two hours for penicillin and tetracycline in concentrations of 150-200 thousand units per ml to inactivate it, and 4 hours at a tetracycline concentration of 10,000 units/ml [11].

Like many poxviruses PPV encode virulence factors that can subvert their host's defense mechanisms by inhibiting or modifying the early stages of the host response during viral replication. The genes that involved in PPV virulence and immunomodulation are the ankyrin-like repeat (ANK)/F-box proteins (ORFs 008, in ORFV, and in addition ORFs 003 and 004 in BPSV), the interferon (IFN) resistance protein (ORF020), the chemokine-binding protein (ORF112), viral vascular endothelial growth factor (vVEGF; ORF132), viral interleukin 10 (vIL- 10; ORF127), the GM-CSF inhibitory factor (ORF117), an inhibitor of apoptosis (ORF125) and an NF-κB inhibitor (ORF121). Apoptosis, a regulated form of cell death, is an important host defense mechanism against virus infection. Poxviruses have been shown to encode several anti-apoptotic proteins that function to prevent apoptosis in an effort to prolong their own survival (Taylor and Barry, 2006), but so far only one has been identified in ORFV. The ORFV ORF125 encodes a Bcl-2-like protein that localizes to mitochondria and blocks UV-induced apoptosis [54]. Members of the Bcl-2 protein family are regulators that either inhibit or promote mitochondrial apoptosis. The ORFV Bcl-2-like protein has been shown to bind to pro-apoptotic Bcl-2 family members and prevent them for triggering apoptosis when irradiated with UV-light [54, 55]. Orthologs of ORFV125 are present in PCPV, BPSV and PVNZ and they display similar features to the ORFV Bcl-2-like protein [55].

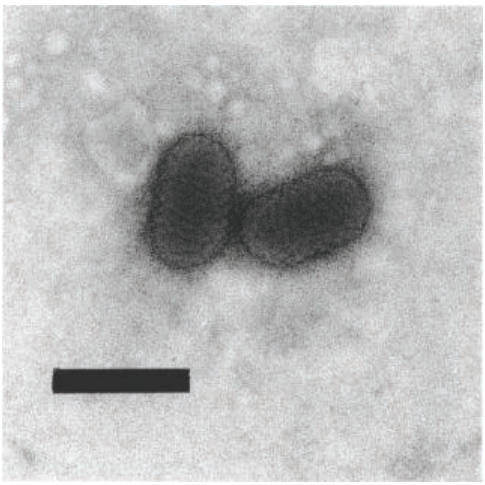

Figure. 3.12: Parapoxvirus particles with a typical arrangement of the filaments. Negative stain. Bar = 300 nm (Tryland TD, Josefsen A, Oksanen A. Aschfalk. (2001). Parapoxvirus infection in Norwegian semi-domesticated reindeer (Rangifer tarandus tarandus Veterinary Record M. 149, 394-395) [60].

3.3.3 Geographic distribution

Contagious Ecthyma, is a globally distributed contagious disease of sheep [1, 3, 5, 16, 23]. Camel contagious ecthyma virus (CCEV) produces a disease in camels (Auzdyk), closely resembling contagious ecthyma in other ruminants [10] and humans. Although the disease has been known since the early twentieth century, clinical and serological records are relatively recent [10]. The disease CCEV is widely recognized in camel-rearing regions of the world [1, 2, 3, 4, 5, 21, 30, 39, 40].

Contagious ecthyma virus can cause a disease in old world camel and new world camel [1, 18, 24, 57]. Camel contagious ecthyma was first described in Kazakhstan in 1968 [11]. CCE has also been reported in Mongolia [16], Kenya [40], Kazakhstan and Turkemania [11], Somalia [39] and in western Sudan [1, 26, 27, 28, 29]. The disease also reported in Saudi Arabia, Bahrain in 2005, Iran, and Israel (Figure. 3.13). There are few studies on this disease and the description of its causal agent in the literature (Table .3.4). In 2018, the CCE was diagnosed for the first time in Nigeria based on clinical signs and molecular detection using PCR results [59]. In these outbreaks, suspected cases of CCE were reported in a farm, live animal market and abattoir, in three different states (Bauchi, Plateau and Zamfara) in Northern Nigeria. Skin scabs, lungs, liver and intestine samples were collected. Polymerase chain reaction (PCR) was carried out using the primers which targets the RPO30 gene fragment of the genus PPV. The clinical signs observed from the suspected cases of CCE were proliferative skin lesions, papules, scabs on the lips and nares (Figure. 3. 14). CPPV was detected in 80.0% (4/5) of the samples collected by PCR [59] (Figure. 3.15).

Figure.3.13: Geographical distribution of Contagious ecthyma in camel. 1. Kazakhstan, 2. Mongolia, 3. Kenya, 4. Somalia, 5. Saudi Arabia , 6.UAE. 7. Iran, 8. Kingdom of Bahrain, 9. Israel, 10.India, 11.Libya, 12. Sudan.

Figure. 3. 14: Representative clinical signs of contagious ecthyma in camels observed in Nigeria. (A): Proliferative scabby skin lesion on the lips and nose of a camel in a camel farm in Bauchi, Nigeria. (B): Contagious ecthyma lesions around oral commissures in a camel in a live animal market in Jos, Nigeria. (C and D): Severe bloody and multiple scab lesions of contagious ecthyma in a camel in the Bauchi camel farm (Adeyinka *et al.,* 2018) [59].

3.3.4 Economic importance

Camel contagious ecthyma is a highly contagious viral disease. It primarily affects young animals exhibiting most regularly localized lesions and frequently generalized changes that resemble camel pox [40]. It is difficult to accurately assess actual annual losses due to CCE owing to the nomadic nature of camel production. The disease is not only a cause of calf mortality, but also affects camel performance with weight loss and severe reduction in milk production, since she-camels cease to lactate when their calves die [26]. There is scarcity about the information dealing with economic importance of CCE. In Sudan, which is considered the second most densely populated country in the world by camels, following Somalia with estimated number of camels 3.1 million , was more than about 98% of CCE cases occur in calves less than one year old with 60-100% morbidity and 9-38% mortality rates. The disease is endemic in most parts of Sudan where camels are raised with variations in intensity of infection and mortality rates.

The disease re-appears regularly every year in the early rainy season (July-August) affecting camel calves in their first autumn of grazing. The disease is characterized by localized lesions, although generalized forms have also been observed, resembling true camel pox [41]. The disease, which is caused by a parapoxvirus, affects young animals producing lesions around the lips and nostrils. It rarely takes the generalized form that resembles camel pox (CP), and differentiation from camel pox can be achieved by electron microscopy [40].

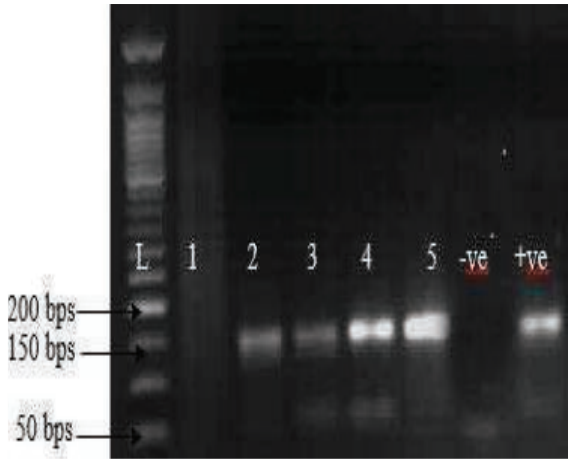

Figure. 3.15: Agar gel electrophoresis of PCR product of RPO132 gene of camel parapoxvirus. (Lanes 1-5): Samples collected from suspected cases. The positive samples were amplified at 140 bp fragment. (L): DNA marker (New England BioLab®). (+ve) Positive control. (–ve): Negative control (Adeyinka *et al.,* 2018) [59].

3.3.5 Susceptibility

New and old world camelids are susceptible to the disease. Contagious ecthyma affects camels of all ages, particularly young stock in their first autumn of grazing (young calves under one years old about 98% of total cases), but may be some adult camel show sign of infection and also adult camels especially those which are coming from disease-free herds. Sheep, goats, and other wild animals are also susceptible. There is no doubt that the eating of prickly plants does damage the lips, opening the way for infection while grazing.

3.3.6 Pathogenesis

Direct contact between animals and indirect contact with dry scabs in pens are the method of transmission of the disease. The virus is resistant to drying and may be viable in scabs for months and years in empty feedlots and pens. Farm workers may disseminate the virus among animals of different pens with contaminated equipment, feed and farm vehicles. Skin abrasion of the lips caused by browsing *acacia* trees seems to represent the major predisposing factor to CCE [11] argue that the thorny plants damage the lips allowing transmission of the parapoxvirus. Movements of camels during the rainy season have a significant role in the spread of CCE in Eastern Sudan, and insects have also been incriminated in the spread of the disease [26, 28]. Skin is the main site of predilection and essential for establishment and development of lesions. Initially PPVs replicates in the epidermal keratinocytes and localized lesions progress. At the time of grazing, the dried stemmy and spiny feed may abrade the tissues of lips, nostrils, mouth as well as fore stomach.

Table 3. 4: Camel Contagious ecthyma epidemiological information of (Country & year, affected age, Morbidity % and Mortality %)

Epidemiological information (Country & year, affected age, Morbidity % and Mortality %)	Reference
Kazakhstan in calves	TULEPBAEV S.ZH. (1971). - Postlike disease ("suzdyk") of the camels in Kazakhstan (in Russian). Diss. Kand., Alma-Ata.
Mongolia, 1979, in adults with morbidity 10-80% and 0% mortality 2 to 3-month-old suckling camels with morbidity 50-70% and 0% mortality 1-year-old animals with morbidity 100 and 0% mortality	Dashtseren T, Solovyev BV, Varejka F, Khokhoo A. Camel contagious ecthyma (pustular dermatitis) Acta Virol. 1984 Mar;28(2):122-7
Kenya, Young camels	Munze., Schillingerd., Reimann M & Mahnelh. (1986). Electron microscopical diagnosis of Ecthyma contagiosum in camels (Camelus dromedarius). First report of the disease in Kenya. J. vet. Med., B, 33, 73-77.
Turkana district of Kenya, 8 months old Calves, with morbidity 100 and 0% mortality	C.G. Gitao (1994). Outbreaks of contagious ecthyma in camels (Camelus dromedarius) in the Turkana district of Kenya. Rev. sci. tech. Off. int. Epiz., 1994,13 (3), 939-945
central Somalia in 1986, young dromedaries about two years old and of both sexes.	Ahmed S M, Moallin and K. H. Zessin (1988) Outbreak of camel contagious ecthyma in central Somalia Trop. Anita. Hlth Prod. 20, 185-186
Sudan, 1991, 14 months old with morbidity 6 % and 0% mortality	Ali O A, SAM Kheir, H Abu Damir and MES Barri. (1991). Camel (Camelus dromedaries) contagious ecthyma in Sudan. A case report. Rev Elev Med vet Pays trop. 44, (2): 143.145.
Sudan,1991, total animals number were165, and 29 sick calves, morbidity 17.3%, mortality rate of 6.6% and the case fatality rate of 37.9%	Khalafalla A.I., Agab H., Abbas B. (1994). An outbreak of contagious ecthyma in camels (Camelus dromedarius) in Eastern Sudan. Trop. Anim. Health Prod., 26: 253-254.
United Arab Emirate 1997, 16 months old calves with morbidity 20 % and 0% mortality	Wernery U, OR Kaaden and M Ali, (1997). Orthopoxvirus infections in dromedary camels in United Arab Emirates (UAE) during winter season. J.Camel.Prac.and Res.4. (1): 51-55.
Sudan,1998, 12 months old calves with morbidity 60.2 % and 8.8% mortality	Khalafalla, A.I., 1998. Epizootiology of camel pox camel contagious ecthyma and camel papillomatosis in the Sudan., Proceedings of the Third Annual Meeting for Animal production Under Arid Conditions, vol. 2, pp. 115–131.
Saudia Arabia 1998, young and adults with morbidity 24 % and 0% mortality	Abu Elzein, E M E, Coloyan A A Gameel, R.O. Ramadan and AI. Al-Faleq. (1998) Camel contagious ecthyma in Saudi Arabia. J.Camel.Prac.and Res.5. (2): 225-228.
Saudia Arabia ,2004, one month old calves , morbidity 50 % and 0% mortality	Fadhel Housawi, ElTayeb Abu-Elzein, Ahmed Gameel, Mohamed Mustafa1, Adel Al-Afaleq, Janice Gilray, Abdulwahab Al-Hulaibi, and Peter Nettleton(2004) Severe Auzdyk infection in one-month-old camel calves (Camelus dromedarius) VETERINARSKI ARHIV 74 (6), 467-474, 2004
Libya , 320 camels both sexes, 37.9% morbidity with 0% mortality.	S.M. Azwai, S.D. Carter,Z. Woldehiwet(1993) Immune responses of the camel (Camelus dromedurius) to contagious ecthyma (Orf) virus infection ,Veterinary Microbiology 47 (1995) 119-131.
Israel in June 1998, morbidity reached 90 %. The disease primarily affected the adult camels and only later spread to the young stock., mortality 0%.	M VAN STRATEN, O. FRIEDGUT, B. EVEN-TOV(2001) Outbreak of contagious ecthyma in camels in Israel. Veterinary Record ,148, 150-151
Kingdom of Bahrain2005, camels (n=150), female camels 2-3 years old ,morbidity rate was 100%, with 0% mortality	Abubakr, MI; Gould, EA; Moss, S; Abdelrahman, AO; Fadlallah, ME; Nayel, MN; Adam, AS.(2007) An outbreak of contagious ecthyma in the Kingdom of Bahrain. In: Gahlot, TK (Editor). Proceedings of the International Camel Conference "Recent Trends in Camelids Research and Future Strategies for Saving Camels", Rajasthan, India, 16-17 February. 42-43.
Iran. In May 2009 a pox like disease was investigated in Karaj province of Iran	Taghipour Bazargani, T., Nikjou, D., Taffy, A., Varshovi, H.R., Nazari-Naslaji, A. A regional outbreak of contagious camel echtyma in Iran. Journal of Camel Practice and Research , Volume 17, Issue 2, December 2010, Pages 221-224
NRC on Camel, Bikaner, Rajasthan, India, 2010, September, camel calves of below one year 2010, a total number of 15 severely affected animals.	Nagarajan, G., Ghorui, S.K., Kumar, S.K., Pathak, M.L., 2010. Complete nucleotide sequence of the envelope gene of pseudocowpoxvirus isolates from Indian dromedaries (Camelus dromedarius). Arch. Virol. 155, 1725–1728.
Nigeria, In these outbreaks, suspected cases of CCE were reported in a farm, live animal market and abattoir, in three different states (Bauchi, Plateau and Zamfara) in Northern Nigeria.	Adeyinka Jeremy Adedeji, Ahmed Abdulkadir Gamawa, Nneka Chineze Chima, Ahmed Isah Ahmed, Victoria Isioma Ifende, Jolly Amoche Adole, Ibrahim Ahmad, Timothy Yusufu Woma and Pam Dachung Luka. (2018). First report of camel contagious ecthyma in Nigeria. Open Veterinary Journal, (2018), Vol. 8(2): 208-211.

Through such abrasions virus penetrates the skin of mucosa and leads to formation of acanthosis, ballooning degeneration of spinose cells, hyperplasia of basal cells and edematous and granulomatous inflammation of dermal cells. The virus produces the characteristic lesions in a sequence of papules, vesicles, pustules, scabs and resolution. The pustules develop within a few days. The rupture of pustules results into ulcer formation followed by thick overlaying crust or scab, which is shed within 3–4 weeks leaving no scar. The disease is self-limiting in uncomplicated cases, and the scabs peel off the skin usually leaving no scar. Primary lesions can be severe and proliferative, and sometimes continued proliferation of the epithelium leads to dense wart-like outgrowth. Secondary complications cause lesions to become ulcerative and necrotic without scab formation, which delays healing [20, 44]. The most frequent invaders are *Staphylococci*, alpha hemolytic *Streptococci* and *Corynebacteria*. Sometimes the proper diagnosis of orf is difficult due to invasion by *Dermatophillus congolensis*. Usually scabs develop within one week and resolve in 4-6 weeks, but there have been cases of persistent long lasting ORFV infections in goat kids that lasted three [25] and six months [5]. However, the immune response to virus infection is predominantly accompanied by humoral immunity, cell-mediated immune mechanism plays an important role in the process of recovery [32, 33].

3.3.7 Clinical signs

The main clinical signs of contagious ecthyma are swelling of the lips, cheeks, nasal skin and eyelids, with a slight rise in body temperature (38.5-39 °C) and some depression [47, 50]. After 1-2 days small nodules the size of a millet grain develop on the inflamed areas of skin, rapidly changing to vesicles containing lymph which is clear at first, and then becomes turbid. The lesions consisted of papulae and pustulae which, in some cases, coalesced to form scabs. In some cases, secondary bacterial infection of the lesions occurred. When the vesicles rupture spontaneously, or as a result of being rubbed, the exudate contained in them becomes spread over the skin, leading to the formation of fissured crusts, through which an inflammatory exudate emerges and soon dries upon exposure to air. The formation of a grayish firm crust conceals inflamed skin. In many cases, submandibular lymph nodes were much enlarged and some camels suffered from perioccular lesions (Figure. 3.16, 17, 18).

Figure. 3.16: Contagious ecthyma lesions on the lips and the periocular lesions of a 14 month-old dromedary camel, Sudan (Khalafalla *et al.,* 2015) [60].

Figure. 4.17: Camel parapox scab on the lips of an affected one-month old camel calf (Housawi *et al.,* 2004 / Severe Auzdyk infection in one-month old camel calves (*Camelus dromedarius*). Veterinary Archives. 74:467–474.)

Figure.3. 18: Camel calf of six months of age exhibiting typical symptoms of contagious ecthyma. (Nagarajan *et al.,* 2010/ complete nucleotide sequence of the envelope gene of pseudocowpox virus isolates from Indian dromedaries (*Camelus dromedarius*). Arch. Virol. 155, 1725–1728).

Some camel contagious ecthyma outbreaks were so severe like the Outbreak of contagious ecthyma in camels in Israel in 1998, the severe Auzdyk infection in one-month-old camel calves (*Camelus dromedarius*) in Saudi Arabia (SA) in March 2002, and mid-September 2010 outbreak in India (Bikaner and Rajasthan 2011).

Straten, *et al.,* (2001) [52] described an outbreak of a skin disease emerged in a herd of 150 camels of different ages grazing in the semi-arid northern Negev region of Israel in June 1998. The lesions were initially noticed in two adult female camels, one nursing a four-month-old calf. Rectal temperatures of the affected camels were 38.3°C and 38.9°C, respectively. The lesions spread very rapidly to other animals in the herd and within two weeks morbidity reached 90 per cent. The disease primarily affected the adult camels and

only later spread to the young stock. Although morbidity was very high, mortality was zero. In nearly all cases, lesions were located on and around the lips and around the nostrils. The lesions consisted of papulae and pustulae which, in some cases, coalesced to form scabs. In some cases, secondary bacterial infection of the lesions occurred. In many cases, submandibular lymph nodes were much enlarged and some camels suffered from perioccular lesions. A few camels exhibited a generalised form of the disease with papulae in the neck area, on the lateral aspects of the thorax and abdomen, and on the thighs. No pustulae were observed in these areas. Two weeks after the start of the outbreak, the first affected camels started to improve; the lymph node swelling and swelling of the lips was markedly reduced and scabs started healing.

Housawi *et al.,* (2004) [21] reported an outbreak of CCE which occurred on 11 March 2002, two approximately one-month-old, one-humped camel calves (*C. dromedarius*) were presented to the University Veterinary Teaching Hospital, King Faisal University, Al-Hasa, Saudi Arabia (SA), suffering from severe lesions on the lips and hard palates. On examination, temperature was 39 °C. The calves were panting and showed restlessness and pain. They were weak and had not suckled since the appearance of the lesions three days before. The involved herd consisted of eighty camels of different age groups. Although the morbidity rate was 50%, the calves were the worst affected. No mortality was recorded. The herd was kept in the desert to graze freely but was also supplemented with concentrate feed.

Abubakr *et al.,* (2007) [6] described an outbreak of contagious ecthyma in camels (n=150) from Bahrain. The affected animals showed severe papules and pustules on the lips, muzzles and eyelids, increase in body temperature, profuse salivation, foul mouth smell and facial oedema. The morbidity rate was 100%, but no mortality was recorded. The infected camels were given supportive treatment. Bazargani *et al.,* (2010) [14] described an outbreak of contagious camel echtyma in Iran.

In May 2009, a pox like disease was investigated in Karaj province of Iran. At the time of investigation, cutaneous lesions (scabs) were prominent and mostly confined on the lips. Nagarajan *et al.,* (2011) [42] described the outbreak that occurred in the mid-September 2010, in the camel herd of NRC on Camel, Bikaner, Rajasthan, India. The camel calves of below one year of age of either sex were showing symptoms of contagious ecthyma. The disease was characterized by papules and then pustules on the lips-muzzle and eye lids of infected camels. Profuse salivation, foul mouth odour and facial edema were also observed. The pustules on the lips ruptured and became ulcerated. Those lesions in the muzzle dried and became covered by grey or brown scabs. Infected animals were showing pruritis and intermittent rubbing against the wall of the corrals, which eventually led to the sloughing of the skin at the affected areas.

3.3.8 Histopathology of camel contagious ecthyma

Macroscopically, numerous multifocal papulae and pustulae which, in some cases, coalesced to form scabs , broad based, hairless, greasy, malodorous, ulcerated and papillary nodules are characteristic of skin lesions. At necropsy of malignant form of orf, irregular shaped lesions with congestion of oral cavity and respiratory tract are revealed. Histological changes depend on the stage of lesion development. Initially, affected skin tissues reveal epidermal hyperplasia with hyperkeratosis, ballooning and degeneration of keratinocytes with infiltration of eosinophilic cytoplasmic inclusion bodies. The histopathological section from the lip lesions showed epidermal hyperplasia with acanthosis and epitheliomatous hyperplasia. The dermis was densely cellular, exhibiting fibroplasia and infiltration mainly of macrophages and lymphocytes, which greatly

obscured the dermo-epidermal junction. Some infected animals may show advanced epidermal necrosis with neutrophil infiltrations, presence of bacterial colonies and hyperkeratosis. The dermis show intense infiltration with neutrophils, indicating secondary bacterial infection. Specific fluorescence was seen intracytoplasmic in the sections, which were collected from the lips of the affected camel calves [21]. The inoculated cell culture showed no discernible cytopathic effect (CPE), in spite of two blind passages. No pathological changes were observed in the inoculated CAMs of the inoculated chicken embryos and none of the inoculated embryos died until they were collected seven days post- inoculation (Figures.3.19, 20, 21, 22).

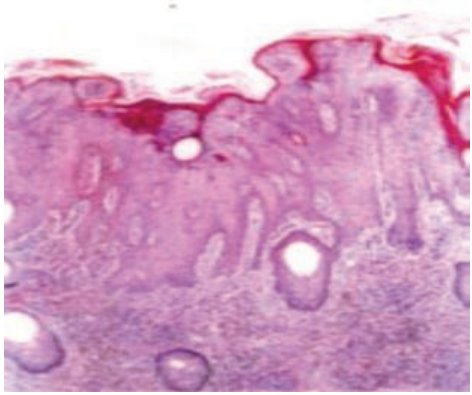

Figure. 3.19: Thickened epidermis with acanthosis, epitheliomatous hyperplasia and dermal infiltration by mainly mononuclear cells. H&E, ×100 (Housawi *et al.,* 2004/ Severe Auzdyk infection in one-month old camel calves (*Camelus dromedarius*). Veterinary Archives.74:467–474.)

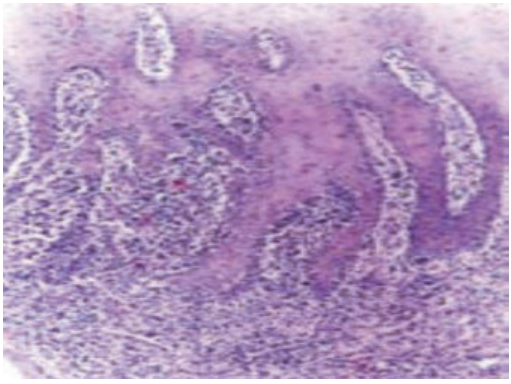

Figure.3.20: Epitheliomatous hyperplasia and dermal infiltration by mainly lymphocytes and macrophages which partly obliterate the dermo-epidermal junction. H&E, ×200 (Housawi *et al.,* 2004/ Severe Auzdyk infection in one-month old camel calves (*Camelus dromedarius*). Veterinary Archives.74:467–474.)

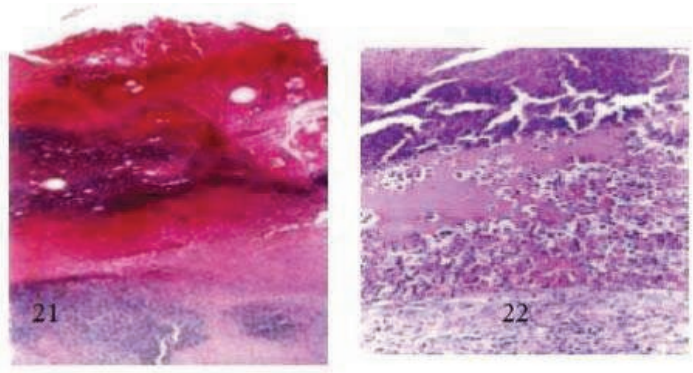

Figure.3.21: Advanced epidermal necrosis and hyperkeratosis with infiltration of neutrophils. H&E, ×100. (Housawi *et al.,* 2004/ Severe Auzdyk infection in one-month old camel calves (*Camelus dromedarius*). Veterinary Archives.74:467–474.)
Figure. 3.22. Advanced epidermal necrosis with edema and neutrophil infiltration. H&E, ×400 ((Housawi *et al.,* 2004/ Severe Auzdyk infection in one-month old camel calves (*Camelus dromedarius*). Veterinary Archives.74:467–474.)

3.3.9 Diagnostic methods

The contagious ecthyma can be detected on the basis of characteristic lesions on the anatomic areas of predilection and it should be differentially diagnosed from true camelpox, mange or dermatophilosis. Specific laboratory diagnosis is achieved by one or a combination of the following methods: 1) isolation and characterization of the virus in cell culture, 2) direct demonstration of virions, viral antigens, or viral nucleic acids and 3) detection and measurement of antibodies [12]. Laboratory tests used in PPV diagnostics are described in (Figure. 3.23)

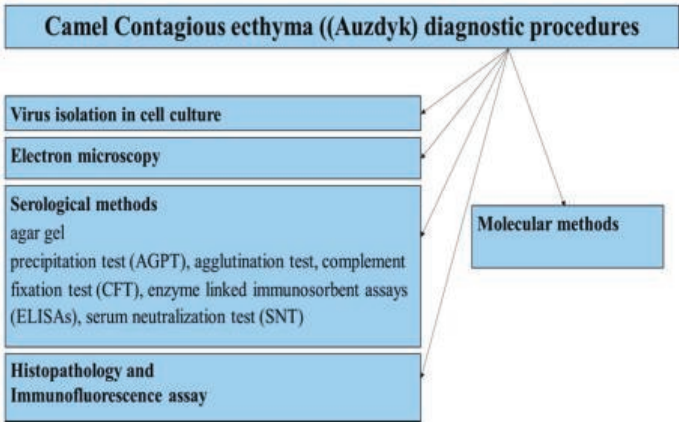

Figure.3.23: The Camel contagious ecthyma diagnostic procedures

1. Virus isolation in cell culture

Although the isolation method does not provide fast diagnosis of infectious agent, it is important in detection of unknown viruses, and it is the only method for generating stock of live virus for further studies. Various primary and continuous cell lines including primary lamb testis, kidney, turbinate and muscle [15, 25, 31], bovine fetal spleen and muscle , primary bovine testis and lung, Madin-Darby ovine kidney (MDOK) [25] and Madin-Darby bovine kidney (MDBK), cells have been reported to be suitable for cultivation of parapoxviruses. Cytopathic effect (CPE) is commonly seen as cell rounding, clumping and detachment, but it may take several blind passages to appear [31]. Generally, parapoxvirus cultivation in cell culture is regarded difficult because of many unsuccessful attempts to isolate virus, but the reasons for this are unknown. Moallin and Zessin, (1988) [39] reported that it has not been possible to grow the camel contagious ecthyma (CCE) virus in cell cultures, except in the case of the isolate from Mongolia, which has been grown in the chorion-allantoic membrane of embryonated chicken eggs[16] . Meanwhile, Van Straten *et al.,* (2001) [61] collected scab material from infected camels and used to inoculate chorioallantoic membranes (cAM) of 10-day old embryonated chicken eggs (ECE) and Vero cell culture in 25 cm2 plastic flasks. No cytopathic effects (CPE) were observed in two seven-day passages in Vero cell culture, death did not occur in ECE, and CAM lesions were not apparent. Virus isolation trials were also suggestive of CCE, as camel parapoxvirus is known not to cause CPE in cell cultures [3]. Housawi *et al.,* (2004) [21] collected lip biopsy in PBS pH 7.4 from CCE to inoculate the CAM of chicken embryos, and Vero, primary lamb kidney cell culture and primary lamb's cell testicles. The inoculated cell culture showed no discernible cytopathic effect (CPE), in spite of two blind passages. No pathological changes were observed in the inoculated CAMs of the inoculated chicken embryos and none of the inoculated embryos died until they were collected seven days post- inoculation.

2. Electron microscopy

Electron microscopy is the most rapid method of diagnosis and differentiation of camel contagious ecthyma virus. It is a direct and rapid method for visualization of parapoxviruses in clinical specimens. In 1994, Khalafalla *et al.,* [27] were collected nodules and scabs from 5 affected animals for virus identification. Negative contrast electron microscopy of homogenates of scabs revealed particles suggestive of parapoxvirus measuring approximately 131 × 230 nm in 4 out of 5 samples. Moreover, camel contagious ecthyma virus *Parapoxvirus* particles were identified by FM from the scab material in most outbreaks of the disease. EM view of parapox appears as negatively stained oval-shaped virus particles with the arrangement of the outer protein filaments and the size of the virus particles is approximately 260nm×130nm. Disadvantages of the method, besides the inability to differentiate viruses at the species level, include low sensitivity (requires a minimum of 10^6 particles per ml), high cost and low availability of the EM facilities with experienced personnel. EM examination is usually performed on scabs or biopsy specimens. After initial preparation of the samples virions are released from the cells e.g. by ultrasonic disruption, concentrated by centrifugation and examined by electron microscopy with phosphotungstate as a contrasting agent [25].

3. Serological methods

Parapoxviruses have been revealed to elicit detectable antibody responses in the host [32, 33]. The viruses are immunologically closely related and exhibit serological cross reactivity [53], although a panel of monoclonal antibodies has been shown to be capable of discriminating between different parapoxvirus species [21.] Various serological methods have been used to measure parapoxvirus antibodies in different animal species, but most of the conventional serological methods are difficult and time consuming, which makes them not well suited for primary diagnosis. However, serological methods are valuable in confirmatory testing and in epidemiological studies. *Parapoxvirus* antibodies have commonly been detected with agar gel immunodiffusion tests (AGID), enzyme-linked immunosorbent assays (ELISA), and to a lesser extent with serum neutralisation tests. AGID is a simple method that detects parapoxvirus antibodies on the basis of a precipitation reaction between a serum sample and the virus antigen. The test is performed in agar gel, where the serum sample is placed in a round well cut into the agar opposite a similar well containing virus antigen. The liquid in different wells diffuse towards each other, and if the sample contains antibodies against the test virus, a visible line of precipitation will form. Housawi *et al.,* (2004) [21] was designed in such a way AGID test to detect the precipitin antibodies in camels infected with CCE , the results revealed that a precipitation line was produced between the suspect material and the reference orf antiserum. This line completely merged with a line produced between the known sheep orf virus and the reference antiserum, making a line of complete identity. The negative controls did not react in the test. AGID cannot discriminate between different parapoxvirus species nor between ORFV and the capripoxviruses, and it is a less sensitive test than the ELISA [21]. The method has been used for parapoxvirus surveys and for confirmation of positive ELISA results. ELISA is a rapid method that enables screening of large number of samples at the same time. In an ELISA test, serum samples are incubated in 96-well microtiter plates coated with purified virus antigens with antibodies being detected with alkaline-phosphatase conjugated secondary antibodies [33], peroxidase conjugated protein A or protein AG. Although ELISA does not discriminate between different parapoxvirus species either, it has been applied successfully in the diagnosis of ORFV in humans and parapoxvirus infections in California sea lions. Azwai *et al.,* (1995) [9] was developed enzyme-linked immunosorbent assay (ELISA) together with a western blotting technique for the detection of total and specific IgG and IgM antibodies to the contagious ecthyma (orf) virus in camel (*Camelus dromedarius)* sera and for identifying the seroreactive antigens of the virus. It is considered that the ELISA technique is valid for orf serodiagnosis in the camel and could be usefully applied to other species at risk of orf infection. ELISA was conducted on outbreak of generalised contagious ecthyma in camels, which was diagnosed for the first time in Libya [9]; the seropositivity rate in a herd with clinically affected camels was 37.9% (and was related to clinical signs) and in apparently normal herds was 0% to 6.8%. Two viral antigenic determinants (22 and 40 kDa) were shared by the western blotting patterns of all the positive camel sera tested, another viral antigenic component of 28 kDa was shared by the positive sera with high ELISA titres. Very close similarity was seen with the western blot of orf-positive sheep sera. The serum neutralization test measures neutralizing antibodies in a serum sample against a known titer of the test virus in cell culture. If a fourfold rise in the antibody titer between acute and convalescent-phase serum is observed, the test is considered to confirm serological diagnosis. The method has been applied in detection of ORFV in domestic and wild ruminants in Alaska, but because immunity to ORFV infection is predominantly cell-mediated and virus neutralizing antibodies are usually undetectable or develop only

at low level [20], the test is not reliable for primary diagnostic purposes. El Hassan *et al.,* (2004) [17], detected antibodies against camel contagious ecthyma virus (CCEV) in camel sera by passive hemagglutination test (PHT) with a mean antibody prevalence of 35%. PHT revealed that the infection is widespread in all parts of the Sudan where camels are raised with variable prevalence rate. The antibody prevalence was 42% in Butana, 41% in Darfor and 19 % in Blue Nile areas. The antibody prevalence was higher post rainy season (87.5%) compared to post rainy season (2.8%) confirming seasonality associated with the rainy season (Jun-october). The prevalence in age group 1-4 years was relatively higher (41%) in comparison with calves less than one year (32%) and adults (35%). Those researchers are recommended PHT, they developed for routine serological surveys and immune response of PPV infections in camels as they claimed that Elisa is much expensive and it requires expertise and special equipment if compared with PHT [17].

4. Histopathology and immunofluorescence assay

Camel contagious ecthyma virus affected skin tissues reveal epidermal hyperplasia with hyperkeratosis, vacuolation and ballooning and degeneration of keratinocytes. Hyperkeratosis, parakeratosis and acanthosis of the epidermis, degenerative changes in stratum spinosum and infiltration of mononuclear cells including macrophages, lymphocytes and neutrophils are evident. Eosinophilic inclusion bodies are demonstrable in the cytoplasm of the infected cells but may not be a consistent feature [3, 21]. The presence of immune and inflammatory cells underneath and adjacent to virus-infected cells and marked capillary dilation and proliferation of the dermal lesions have been described [33]. These virus-induced morphological changes can be seen with the light microscope using haematoxylin and eosin staining of thin sections of the affected skin, and have been used in parapoxvirus diagnostics [25]. Immunofluorescence assays (IFA) are based on detection of virus antigen with fluorophore-labelled primary antibody (direct method) or secondary antibody (indirect IFA): the fluorophore-labelled antibody fluoresces under UV illumination indicating the presence of virus antigen when viewed with a microscope. IFA is a useful and sensitive method because the diagnosis can be made on the basis of only few cells containing fluorescence of the right color and expected antigen distribution. In detection and characterization of parapoxviruses, both polyclonal convalescent sera from parapoxvirus-immunized animals and a panel of monoclonal antibodies against ORFV have been used in indirect IFA. The results of this test indicated significant antigenic overlap between ORFV, PCPV and BPSV although six monoclonal antibodies against ORFV were found capable of differentiating ORFV from PCPV, BPSV and PVNZ confirming the ORFV diagnosis.

5. Molecular methods

Molecular methods that have generally been used in parapoxvirus diagnostics include restriction fragment length polymorphism (RFLP), nucleic acid hybridization and especially conventional and real-time PCR. These nucleic acid based methods, particularly PCR, offer fast, sensitive and specific identification of the target virus and are thus the preferred diagnostic methods used today [6, 42, 61].

A. Restriction fragment length polymorphism (RFLP)

RFLP, or restriction fragment length polymorphism, is a molecular biological technique used to compare DNA from two samples. Special enzymes that cleave the DNA in

specific locations are used to digest strands of DNA and the resulting restriction fragments are separated according to their size, by agarose gel electrophoresis, to generate distinct restriction fragment profiles. The RFLP analyses of parapoxvirus genomes revealed genetic heterogeneity that has enabled species and even strain differentiation. In RFLP variations in genomes of even closely related virus species are exploit [22, 53]. No previous records have been found regarding application of RFLP in camel, however RFLP profiles generated by *Kpn*I, *Eco*RI, *Hin*dIII and *Bam*HI have been used to investigate parapoxviruses in various animal species including sheep, bovine, red deer, reindeer, musk ox, Japanese serow and Sichuan takin [25]. Nuclecic acid hybridization has been used together with RFLP analysis to confirm virus classification. Digested DNA samples are hybridized with labeled probes derived from the central and terminal regions of parapoxvirus genomes, and although the results indicate that a strong inter-species homology exists between regions within the central parts of the genomes, terminal regions hybridize only to the same virus species [22, 53].

B. PCR

PCR is well recognized to be a stable, fast, and sensitive diagnostic method for the detection of nucleic acids. It is one of the most powerful and applied methods in virus diagnostics [61]. It is based on the ability of thermostable DNA polymerase to synthesize a new strand of DNA during repeated cycles of heat denaturation, annealing and extension. The target sequence is defined by specific oligonucleotide primers complementary to the target DNA which in turn allow the amplification of the desired region. The identity of the amplified product can be verified using DNA hybridization or more commonly by direct sequencing [21, 25, 31]. The benefit of sequencing is that it allows comparison of the amplified sequence with existing data and thus enables molecular epidemiological and evolutionary studies. In parapoxvirus diagnostics, PCR methods detecting a number of target genes have been developed. These include the most widely used PCR for the major envelope protein B2L and PCRs for the interferon resistant protein (VIR) [31], ATPase (A32L), dsRNA-binding protein (E3L) and GM-CSF/ interleukin-2 inhibitory factor (GIF) genes [21]. The efficacy of PCR was comparable (85–87%) to the cell culture/neutralization methods. Aduplex PCR assay using A29 gene (413 bp) and H3L gene (708 bp) has considerable potential as a diagnostic approach for detection and differentiation of CPV and ORFV [58]. The determination of the nucleotide sequence of virus DNA extracted from pustules, saliva, and blood of camels presenting with contagious ecthyma, in Bahrain was done [6] and also from a sample (SACamel) of infected tissue from a camel that had presented with contagious ecthyma in 1998 in Saudi Arabia [3]. Sequence homologies and phylogenetic analysis showed that this extracted DNA was more closely related to Pseudocowpox virus (PCPV) than *Orf virus* (ORFV), which infects sheep, goats, and other animal species. The phylogeny also demonstrated that PCPV in Arabian camels was phylogenetically distinct from, and circulates independently of, ruminant-associated PCPV from Europe. Nagarajan *et al.,* (2011) [42] were amplified Topoisomerase gene of pseudocowpox virus from Indian dromedarian camel by PCR using the primers of PCPV (pseudocowposvirus) from Finnish reindeer and cloned into pGEM-T for sequence analysis. Analysis of amino acid identity revealed that Indian PCPV of camel shared 95.9–96.8 with PCPV of reindeer, 96.2–96.5 with ORFV and 87.5 with BPSV. A minor groove binder–based quantitative real-time PCR assay targeting the B2L gene of parapoxviruses on the ABI Prism and the Light- Cycler platforms are also developed. RT-PCR appeared as suitable assay for the detection of parapoxvirus infections in clinical material of human and animal origin. Nucleic acid hybridization

techniques based on PCR was used for the detection of camel parapoxvirus infections Southwest Iran [61] (Figure. 3.24. A& B).

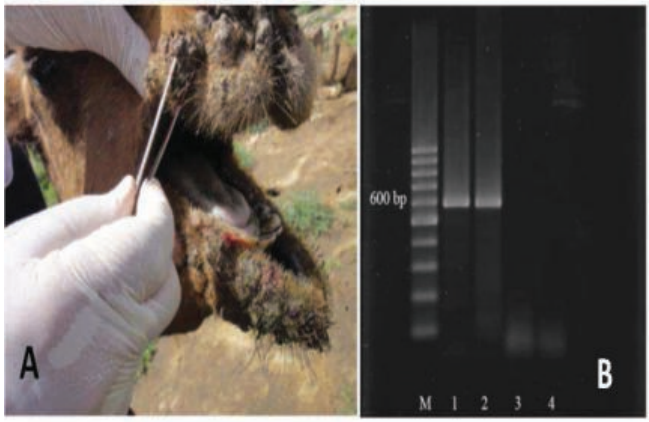

Figure. 3.24 A& B: A. Samples collection from Papules on the lips and nostrils of a camel due to contagious ecthyma disease.B. Identification of camel contagious ecthyma virus. Lane M: 100 bp marker; Lane 1: Amplification of genomic lamb testis (LT) cell DNA infected with contagious ecthyma virus (CEV) Kerman/2000 strain; Lane 2: Amplification performed on skin biopsy of camel infected with CEV; Lane 3: Amplification performed on normal skin biopsy; Lane 4: Amplification performed on uninfected LT cell DNA (E. Gharib Mombeni *et al.,* 2013). Outbreak of contagious ecthyma in camels (*Camelus dromedaries* and *Camelus bactrianus*) in Southwest IranRevue d'élevage et de médecine vétérinaire des pays tropicaux. 66 ;(4):113-115.

3. 3. 10 Control and treatment

There is no specific treatment for CCE. As most nomads deny the infectious nature of CCE, the disease is either allowed to take its natural course or traditional treatments are applied. Traditional treatments include cauterization of regional lymph nodes, application of sesame oil and hot milk and sometimes plant tar. Antibiotics given for 3-5 days prevent a secondary bacterial infection and reduce the severity of the infection. The effective control programs of CCE are required to apply in the area with outbreaks history. The sanitary measures for infectious diseases are important. These must include quarantine of infected areas, restriction of camel movements, and management of drinking water and avoidance of skin abrasions. These measures are difficult to implement owing to the migratory pattern of camel production in different region and the difficulty to reach camels especially during the rainy season. Like all other viral diseases, CCE is better prevented than treated. Attention should therefore be directed towards vaccine production. Virus isolates propagated in cell culture is expected to lay the ground for the production of a cell culture attenuated or inactivated vaccine. The implementation of a nationally approved program for CCE control is much needed.

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3.4 Camel papillomatosis

(Warts, Mucocutaneous fibropapillomas)

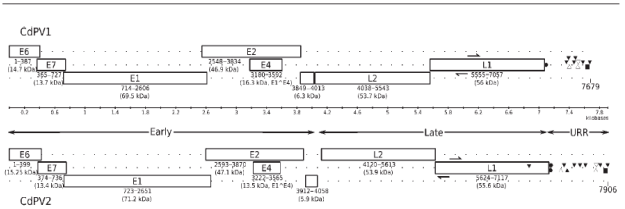
3.4.1 Definition

Papillomatosis (warts) are dry, rough surfaced protruding growths usually white, grey or light tan colored. The most commonly affected areas are the nose, chin, lips, neck, shoulder and brisket. *Camelus dromedarius papillomavirus types 1* (*CdPV1*) and *2* (*CdPV2*), are the causative agent [6]. Papillomaviruses induce hyperproliferation of epithelial cells of the skin or mucosa and certain types can also infect fibroblasts. They are a very heterogeneous group of viruses, and individual types are associated with specific lesions. The papillomas are mostly benign but some tumors may eventually undergo malignant conversion when genetic or environmental factors are involved [20, 21, 22, 23, 35, 36]. Camel papillomatosis is the fourth most widespread viral disease of camels, along with camel pox, camel contagious echthyma, and rabies [2]. Reports on camel papillomatosis are rare. The disease affects mostly young camels and causes nodular lesions, mostly around the mouth. The disease was reported in Sudan, Iraq, Syria, India, United Arab Emirate, Iran and Somalia [4, 6, 3, 7, 14, 10, 11, 12, 8, 9]. The warts are generally self-limiting and disappear between 8–12 weeks [11, 4]. Khalafalla *et al.,* (1998) reported morbidity rates of 3.3%, in Sudan, but the mortality rate reached to 77.5%, however, no mortality has been reported in Iraq [3].

3.4.2 Cause

Animal Papillomaviruses were first identified in the early 20th century. Studies showed that skin warts or papillomas could be transmitted between individuals by a filterable infectious agent. The first *Papillomavirus* was isolated from rabbits by Richard Shope in 1933 [16]. In 1935 Francis Peyton Rous, previously demonstrating the existence of a cancer-causing sarcoma virus in chickens, went on to prove papilloma

virus could cause skin cancer in infected rabbits. This condition may have led to the infamous "jackelope" myth, a cross-mating between a jackrabbit and an antelope. This was the first demonstration of a virus inducing cancer in mammals [1]. Much of knowledge about papilloma virus comes from Bovine Papillomavirus (BPV) for which animal host systems exist [20, 35, 36]. Papilloma viruses are epithelioltropic DNA tumor virus capable of inducing lesions in human and different species of animals [36].
Papillomaviruses are small, double-stranded DNA viruses, Naked, non-enveloped icosahedral particles ~52-55nm diameter. There are 72 capsomers (60 hexameric + 12 pentameric) arranged on a T = 7 lattice. There are 2 capsid proteins, 1 major (encoded by the L1 gene) and 1 minor (L2). The papillomavirus genome consists of circular, d/s DNA ~8kbp in size, associated with cellular histones to form a chromatin-like substance. At least 12 different HPV genomes have been sequenced, and the genetic organization of all is similar (Figure. 3.25).



Genomic organization of CdPV1 and CdPV2. The three main regions of the genome are depicted below the ruler. Numbers below each ORF (open boxes) indicate nucleotide position from the start to the stop codon and the molecular mass for the corresponding putative protein. The E4 ORF does not contain a start codon (ATG), but an ATG is probably added by splicing of E4 mRNA to E1 mRNA generating an E4 protein that starts with 5 aa from E1 (E1^E4). Putative binding sites for viral proteins and cellular factors are shown as follows: ▼, E2-binding site; △, E1-binding site; ■, TATA box; ●, polyadenylation signal. The position of primers used for amplification of the genome and further cloning are indicated with half arrows.

Figure.3.25: Papillomaviruses genome (Ure *et al.,* 2011) [6].

The individual isolates are highly species specific. All are tropic for squamous epithelial cells (receptors unknown) [17]. The virus infects the basal cells of the dermal layer, and early gene expression can be detected in these cells (in situ hybridization). However, late gene expression, the expression of structural proteins and vegetative DNA synthesis is restricted to terminally differentiated cells of the epidermis, which implies a link between cellular differentiation and viral gene expression. Genome is functionally divided into Early 1-8 (expressed immediately after initial infection of a host cell) and Late (capsid genes L1 and L2) regions in order of gene expression [18], those are:

E1– Viral replication and helicase activity
E2– Regulation of transcription and chromosome attachment
E3– Function as of yet unknown
E4– Coding of cytoplasmic protein in BPV-induced warts, facilitates replication and viral release
E5, E6, E7– Transformation
E8– Function as of yet unknown
L1– Major Capsid protein (pentameric capsomers), includes receptor
L2– Minor capsid protein, disrupts endosomic vesicle after entry [19].

Some mammals have several distinct papilloma viruses—humans have >20; cattle, 6; dogs, 3; rabbits, 2and camel 2. Different papilloma viruses often have considerable species, site, and histologic specificity (Figure.3.26) (Table.3. 5) .

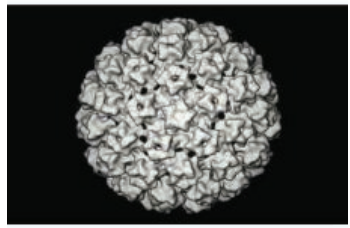


Figure.3. 26 : Papillomavirus Capsid. (http://en.wikipedia.org/wiki/Image) [18]

Table. 3.5: Papillomavirus/ Virus Taxanomy

Family; Subfamily	Genus Name	Type Species Name
Papillomaviridae	Alphapapillomavirus	Human papillomavirus-32
	Betapapillomavirus	Human papillomavirus-5
	Gammapapillomavirus	Human Papillomavirus -4
	Deltapapillomavirus	European elk Papillomavirus
	Epsilonpapillomavirus	Bovine papillomavirus-5
	Zetapapillomavirus	Equine papillomavirus-1
	Etapapillomavirus	Fringilla coelebs papillomavirus
	Thetapapillomavirus	Psittacus erithacus timmeh papillomavirus
	Iotapapillomavirus	Mastomys natalensis papillomavirus
	Kappapapillomavirus	Cottontail rabbit papllomavirus
	Lambdapapillomavirus	Canine oral papillomavirus
	Mupapillomavirus	Human papillomavirus-1
	Nupapillomavirus	Human papillomavirus – 41
	Xipapillomavirus	Bovine papillomavirus – 3
	Omicronpapillomavirus	Phocoena spinipinnis papillomavirus
	Pipapillomavirus	Hamster oral papillomavirus

The characterization of the complete genomes of *Camelus dromedarius papillomavirus types 1 and 2* was reported by Ure *et al.,* (2011) [6]. DNA was extracted from a cauliflower-like nodule, from the lip of a camel male calf and from a round oval raised nodule from the lip of another male calf. In this study specific primers were then designed for each PV in a back-to-back orientation to clone the genomes. They found that each of the samples contained a unique complete PV sequence (Figure.3. 27) and comparisons of their L1 open reading frames (ORF) revealed that they had 69.2% nucleotide identity to each other. The closest related PV of the first isolate was bovine

papillomavirus type 1 (BPV1; 66.3 %), whilst the closest of the second isolate were BPV1 and BPV2 (both 64.6%), justifying the naming of the viruses as *Camelus dromedarius papillomavirus* types 1 and 2 (*CdPV1 and CdPV2*) (Table. 3. 6). The complete genomes of CdPV1 and CdPV2 contained 7679 and 7906 bp with a G+C content of 45.8 and 47.2mol%, respectively.

Table.3.6: CdPV1 and CdPV2 nucleotide (and amino acid) identities with members of the genera Deltapapillomavirus (δ) and Epsilonpapillomavirus (ε)

Upper and lower parts of the table show sequence identities compared with CdPV1 and CdPV2, respectively.

Virus*	Genus	E6	E7	E1	E2	E4	L2	L1	GenBank accession no.
CdPV2	δ	52.6 (39.8)	56.9 (47.2)	66.3 (62.4)	62.1 (51.6)	52.2 (45.3)	58.7 (50.5)	69.2 (72.8)	HQ912791
BPV1	δ	53.9 (39.1)	49.0 (30.8)	60.0 (52.0)	44.6 (32.3)	49.9 (25.2)	52.7 (38.4)	66.3 (65.0)	NC_001522
BPV2	δ	51.8 (38.4)	48.9 (31.6)	59.3 (51.8)	54.4 (40.6)	46.8 (32.4)	51.3 (37.9)	65.5 (64.6)	M20219
CcaPV1	δ	52.8 (42.0)	47.8 (33.3)	59.8 (52.3)	55.4 (43.3)	43.9 (29.0)	53.9 (38.8)	65.3 (65.6)	EF680235
RtPV1	δ	51.4 (38.6)	49.2 (29.8)	60.0 (50.7)	53.2 (43.8)	48.5 (27.3)	53.1 (39.4)	64.1 (64.9)	AF443292
AaPV1	δ	51.4 (38.1)	51.1 (34.4)	59.8 (52.4)	54.2 (39.1)	43.8 (29.4)	51.9 (38.6)	64.5 (64.7)	NC_001524
OvPV1	δ	53.4 (41.3)	49.6 (29.4)	60.5 (50.8)	53.7 (41.2)	47.3 (27.1)	53.2 (37.3)	62.7 (59.3)	NC_001523
OaPV1	δ	50.3 (40.8)	47.7 (31.5)	59.0 (52.0)	52.8 (42.5)	48.4 (31.2)	48.6 (31.3)	63.2 (62.9)	NC_001789
OaPV2	δ	49.7 (40.0)	47.2 (31.7)	59.2 (51.4)	54.7 (45.4)	48.1 (33.3)	52.2 (36.1)	65.2 (64.9)	U83595
BPV5	ε	52.4 (38.7)	48.5 (29.9)	57.3 (48.6)	52.6 (37.3)	48.3 (24.3)	54.1 (38.8)	62.2 (59.6)	NC_004195
BPV8	ε	50.7 (38.5)	49.1 (30.4)	58.2 (48.1)	53.4 (40.6)	48.6 (24.3)	53.5 (40.7)	62.1 (60.6)	NC_009752
CdPV1	δ	52.6 (39.8)	56.9 (47.2)	66.3 (62.4)	62.1 (51.6)	52.2 (45.3)	58.7 (50.5)	69.2 (72.8)	HQ912790
BPV1	δ	55.7 (44.9)	51.0 (31.9)	59.6 (48.9)	46.9 (31.7)	51.2 (27.2)	50.3 (38.3)	64.6 (64.1)	NC_001522
BPV2	δ	55.8 (44.2)	47.5 (29.0)	59.1 (48.1)	58.2 (42.3)	54.9 (32.2)	52.1 (37.4)	64.6 (64.2)	M20219
CcaPV1	δ	49.4 (32.4)	50.7 (30.7)	59.9 (51.7)	55.0 (41.8)	51.4 (33.3)	53.9 (39.1)	64.0 (64.0)	EF680235
RtPV1	δ	51.4 (36.4)	44.7 (31.1)	57.9 (47.9)	55.3 (40.8)	49.6 (27.1)	53.3 (41.4)	63.3 (62.5)	AF443292
AaPV1	δ	49.8 (35.7)	48.9 (31.4)	59.6 (50.3)	54.7 (38.4)	53.2 (29.3)	53.0 (41.1)	63.0 (62.1)	NC_001524
OvPV1	δ	48.8 (35.5)	50.4 (30.5)	58.2 (48.8)	54.2 (39.2)	48.7 (29.9)	51.6 (37.0)	61.4 (58.8)	NC_001523
OaPV1	δ	51.0 (41.9)	46.7 (29.0)	59.4 (52.8)	52.5 (41.2)	54.4 (34.2)	49.2 (34.7)	62.6 (62.3)	NC_001789
OaPV2	δ	50.6 (39.7)	48.6 (28.2)	59.9 (52.5)	55.1 (42.6)	55.1 (34.7)	51.7 (41.1)	62.8 (63.7)	U83595
BPV5	ε	56.2 (39.4)	49.0 (29.3)	58.4 (47.3)	53.9 (39.3)	48.3 (22.6)	53.4 (40.1)	62.5 (59.8)	NC_004195
BPV8	ε	55.6 (40.1)	50.0 (27.8)	58.0 (49.7)	54.2 (38.9)	49.1 (24.0)	54.2 (40.1)	62.0 (60.0)	NC_009752

*CcaPV1, *Capreolus capreolus* papillomavirus 1; RtPV1, *Rangifer tarandus* papillomavirus 1 [Reindeer papillomavirus (RPV)]; AaPV1, *Alces alces* papillomavirus 1 [European elk papillomavirus (EEPV)]; OvPV1, *Odocoileus virginianus* papillomavirus 1 [deer papillomavirus (DPV)]; OaPV, *Ovis aries* papillomavirus.

Seven ORFs were identified in both genomes. The putative E6 protein from both dromedary PVs manifested two zinc-finger domains [24], which are conserved among PVs and are present in all artiodactyls (even-toed ungulates) PVs currently known [25, 26, 27]. Similarly, there was one zinc-finger domain in the E7 proteins but no retinoblastoma tumour suppressor (pRB)-binding domain (L-X-C-X-E) [28]. In the E1 protein, the superfamily 3 ATP-dependent helicase domain [29, 30] was found in both viruses. The E2 proteins had the typical C-terminal DNA-binding domain and the N-terminal transactivation domain [31, 32]. The research approved also that for both CdPV1 and CdPV2, the E4 ORF did not contain a start codon. The derived E4 protein is known to be generated by RNA splicing, generating an E1‘E4 fusion product with approximately 5 aa from the E1 N-terminal end [33]. Based on BPV1 sequence information about donor and acceptor splicing sites [34, 35], corresponding sites were identified in E4 for both dromedary PVs. No obvious E5 ORF could be identified in the region between E2 and L2, although a short ORF was present in both CdPVs.

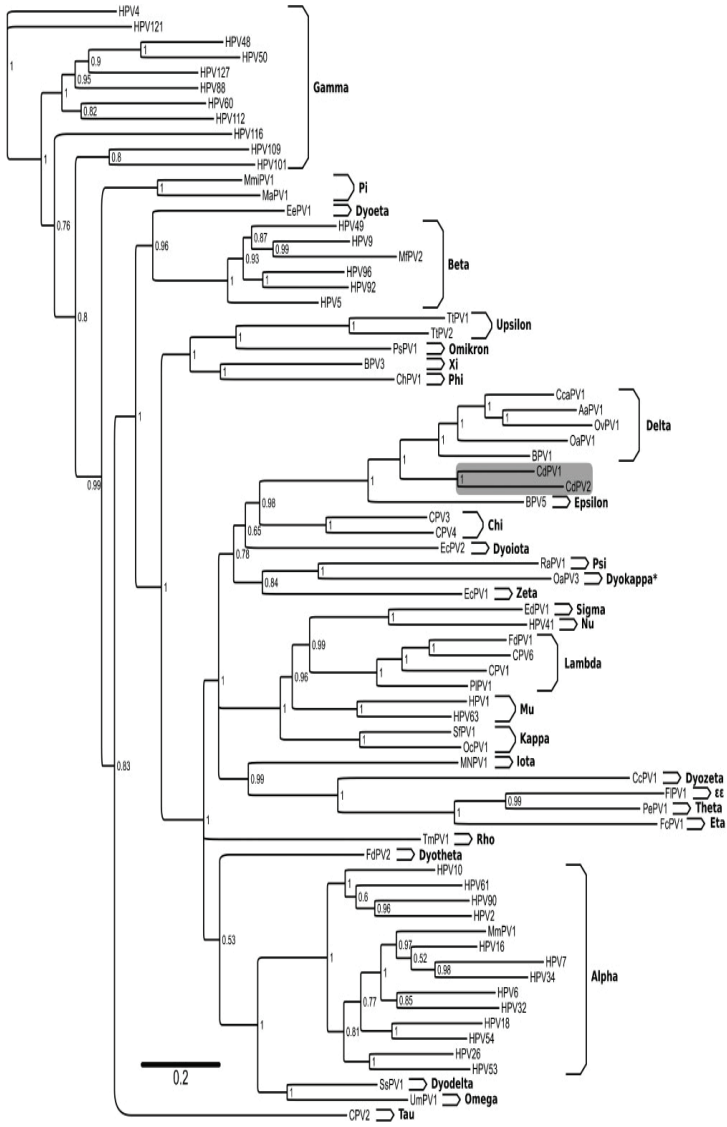


Figure. 3. 27: Bayesian phylogenetic tree inferred from the L1 nucleotide sequence of CdPV1 and CdPV2 and 71 representative papillomaviruses. Acronyms are according to Bernard et al. (2010) [39] and PV genera are indicated in bold [37] (Fauquet et al., 2005). CdPV1 and CdPV2 are located in a separate branch between delta- and epsilon papilloma viruses. Numbers on nodes are the supporting posterior probability of the split. Bar, 0.2 nucleotide substitutions per site. *, Genus Dyokappa suggested by the authors of the paper describing the virus but not yet officially recognized by the ICTV; ee, Dyoepsilon. CcaPV, Capreolus capreolus papillomavirus; CcPV, Caretta caretta papillomavirus; ChPV,

Capra hircus papillomavirus; CPV, Canis familiaris papillomavirus; EcPV, Equus caballus papillomavirus; EdPV, Erethizon dorsatum papillomavirus; EePV, Erinaceus europaeus papillomavirus; FcPV, Fringilla coelebs papillomavirus; FdPV, Felis domesticus papillomavirus; FlPV, Francolinus leucoscepus papillomavirus; HPV, human papillomavirus; MaPV, Mesocricetus auratus papillomavirus; MfPV, Macaca fascicularis papillomavirus; MmiPV, Micromys minutus papillomavirus; MmPV, Macaca mulata papillomavirus; MNPV, Mastomys natalensis papillomavirus; OcPV, Oryctolagus cuniculus papillomavirus; PePV, Psittacus erithacus papillomavirus; PlPV, Procyon lotor papillomavirus; PsPV, Phocoena spinipinnis papillomavirus; RaPV, Rousettus aegyptiacus papillomavirus; SfPV, Sylvilagus floridanus papillomavirus; SsPV, Sus scrofa papillomavirus; TmPV, Trichechus manatus latirostris papillomavirus; TtPV,
Tursiops truncatus papillomavirus; UmPV, Ursus maritimus papillomavirus. (Ure *et al.,* 2011) [6].

Additional analysis of the conceptual translation of the short ORFs revealed in both cases a hydrophobic protein of 54 and 48 aa, with grand average values of hydropathy (GRAVY) of 1.498 and 1.077 for CdPV1 and CdPV2, respectively. In addition, transmembrane regions were predicted to be present in the putative protein from this short ORF of both CdPV1 and CdPV2. During the sequencing of CdPV1, it was observed that the L2 ORF contained a region of 11 consecutive adenines (at nt 5502). This was confirmed by additional sequencing of two different clones as well as amplicons from the original DNA sample (in both orientations). Nevertheless, it must be noted that the original clone contained only ten adenines, which caused a frame shift and a consequent overlap between the L2 and L1 ORF. In the putative L1 protein, a nuclear localization signal ubiquitous for PVs [36] was found in both CdPVs (aa 481–497 in CdPV1 and aa 480–495 in CdPV2). Immediately downstream of the L1 ORF, a polyadenylation site (AATAAA) was identified in the CdPV1 genome (at nt 7085), whereas a double polyadenylation site (AATAAATAAA) was found in the CdPV2 genome (at nt 7145). The phylogenetic analysis demonstrated that CdPV1 and CdPV2 were positioned on a separate branch between the genera Delta papilloma virus and Epsilon papilloma virus (Figure. 3.27). Both of these genera contain PVs that infect mammals of the order Artiodactyla (even-toed ungulates), including dromedaries, cervids, cows, bison and sheep. CdPV1 and CdPV2 shared similar values of nucleotide identity of L1 with members of the genera Delta papillomavirus and Epsilon papillomavirus, with mean values of 64.0 and 62.2% respectively. In addition, pairwise comparisons of the L1 ORF of the PVs within these genera demonstrated nucleotide identities of .60%. Both clones were deposited in the new International Reference Centre for Animal Papillomavirus at the American Museum of Natural History (New York, USA).

3.4.3 Geographic distribution

The disease are observed worldwide in humans and a variety of mammals. Camel papillomatosis is the fourth most widespread viral disease of camels, and is most commonly seen on younger animals [4, 6, 13]. Although the disease has been known since the early twentieth century, clinical and histopathological records are relatively recent. The disease is recognized in camel-rearing regions of the world, however, published articles mentioned that camel Papillomatosis has only reported in old world camel [4, 6, 11]. Meanwhile, disease has also been reported in new world camel [5]. Sadana *et al.,* (1980) [14], reported a rare case of papillomatosis in a dromedary in India. The Wart, located on the fetlock of a 15-year-old dromedary and weighting 2 Kg, was removed surgically without complications. It is believed that this growth was not papillomatous , but rather a tumor(fibropapilloma). The first report of papillomatosis in dromedaries was published in 1990 [8]. The disease has also been reported in kenya [38] and they found that there are a relationship between camelpox and papillomatosis; in Sudan [13, 6], United Arab Emirates [10,11,12], Syria

in AMazareb [8] , Iran in 18- and 24-month-old camels [9] and in Iraq [3]. Papillomatosis has also been shown in South American camelids (llamas and alpacas) [5].

3.4.5 Economic importance

As camel papillomatosis does not result in mortality, it is of little interest as a potential form of biological control.

3.4.6 Susceptibility

Depending on the age of the animal, it may take anywhere from 1 to 12 months after being exposed to the virus for warts to develop. Papillomas, or warts, are most commonly seen on younger camels 3–14 months old [13]. The disease reported in young animals aged about 3–7 months in Sudan 2009 [6], however five mucocutaneous fibropapillomas from two llamas and three alpacas were reported in 6 years old and in 18- and 24-month-old camels in Iran [9]. In Iraq, the papillomatosis was diagnosed in 77.5% of camels ranged in 5-10 years old and 22.5% of camels more than 10 years old and 0% in camels less than 5 years old and disease was diagnosed histologically in 102 affected camels and 4.2% of the 2412 total inspected camels in different locations in Iraq [3].
Ure *et al.,* (2011) [6] explained an interesting feature of the outbreak in their study, they found that only young animals (8 months old) were affected. This is in agreement with a survey of camel papillomatosis carried out between 1992 and 1994 in eastern Sudan [13]. That work revealed a 3.3% morbidity rate predominantly in young animals aged 3–14 months. This suggests that the immune system of adults is capable of controlling these papillomaviruses and that CdPV1 and CdPV2 are immunogenic. Nevertheless, the study approved that the cumulative incidence was about 20% for the herd and 44% for the young animals. The variation of the morbidity rate could be due to differences in the number of young animals studied or the time of year in which the animals were examined, as not only papillomatosis but also camel contagious ecthyma and camel pox have been associated with the rainy season [13]. Also, the time point for examination of animals could influence the prevalence of papillomatosis, as it has been reported that within 3 weeks virtually all young animals in a herd are infected [8]. Even though papillomatosis is a mild disease in dromedaries and recurrence has not been reported, the high morbidity shown in this and previous studies highlights the importance of understanding the viral genomic sequences for surveillance of the disease, as new outbreaks with a higher severity might occur.

3.4.7 Pathogenesis

Papilloma viruses are known to infect the epithelial tissues of reptiles, birds and mammals, and almost all Papillomaviruses are strictly specific to their natural host and do not infect even closely related species [39, 40]. Due to the species specificity of papilloma viruses, infection of experimental animals with human papillomavirus (HPV) is not possible. However, understanding the natural history and carcinogenic potential of HPVs is assisted by the study of several animal papilloma viruses. Whereas cancer is the end-point to assess carcinogenicity in the study of HPV, benign tumours (warts and papillomas) are often used as the end-point in the analysis of the association of papillomavirus with naturally occurring or experimentally induced neoplasia in animals. This is based on the grounds that: (a) the incidence of warts is higher than that of cancer and is therefore easier to monitor; (b) it is difficult to follow the course of disease in wild animals; (c) domestic

animals, such as cattle, are usually killed before the onset of malignancy; and (d) papillomavirus-associated cancer ultimately derives from warts, and thus the presence of warts can be considered as an indication of possible incipient neoplastic progression [41]. Previously, there is no experimental reproduction of warts by camel papillomaviruses and tumour production in transgenic animals. The disease is spread through direct contact between affected and susceptible animals. However, there seems to be a close relationship with cases of CCE. Most cases of camel papillomatosis were observed in late rainy season coinciding with outbreaks of CCE. The virus accesses basal cells via wounds or abrasions in animals. Intraspecies transmission of the disease is of yet unclear. Lack of a suitable tissue culture makes it difficult to isolate the virus. Interactions between the virus and host cells in vitro, without any variable host/environmental influences can only be guessed. Camels may spread cutaneous papillomas via fly which may act as a vector moving amongst wound sites on different camels. Papillomavirus infections usually regress, but occasionally they develop to cancer. Papillomavirus infection starts in epithelial basal layers (Figure. 3. 28), with the virus undergoing differentiation throughout the activation of E (early) and L (late) genes to produce virions on the superior external layers. The penetration of a non-enveloped virus into the target cell involves two steps: i) attachment and interaction with the cell membrane through binding to a surface receptor molecule and ii) penetration of the viral particle. Papillomavirus probably attaches to a conserved receptor widely expressed on the cell surface. The studies have suggested that the entrance of papillomavirus involves interaction with cell surface molecules that act as receptors, such as integrins α6β4 or α6β1 or heparan sulfate, or mechanisms such as endocytosis via a clathrin-dependent pathway [42].

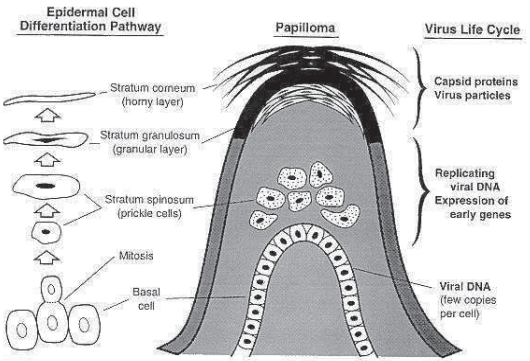


Figure. 3. 28: Papillomavirus life cycle

3.4.8 Clinical signs

The major concern with camel papillomatosis is that the clinical signs are often indistinguishable from camel pox, and that the disease can often occur with or follow Camel Contagious Ecthyma. Ure *et al.,* (2011) [6] described an outbreak of skin tumors occurred in a camel farm of 55 animals in Al Qutaynah locality, about 83 km south of Khartoum, Sudan, during August 2009. The disease occurred in young animals aged about 3–7 months, of which 44% (11/25) were affected with warty lesions. The lesions were located mainly on the lips and lower jaw. Two types of skin lesion were identified. Only

one animal demonstrated a cauliflower-like nodule (Figure. 3.29), whereas the majority of animals exhibited fissured round or oval raised nodules. The lesions were dark grey and were approximately 0.5–1 cm in length and 1–2 cm in width. The disease appears usually as round cauliflower like horny masses mainly on the skin on the lips and submandibular area. The warts are generally self-limiting and disappear between 8–12 weeks [15]. In Sudan, the disease reported with 3.3% morbidity rates but no mortality [13]. The lesions of the camel papillomatosis, firstly appear as small flat elevations, rosy in color or hyperemic. Later, and within 1-2 weeks, they develop into round fissured or cauliflower-like horny masses taking the normal color of the skin [13].

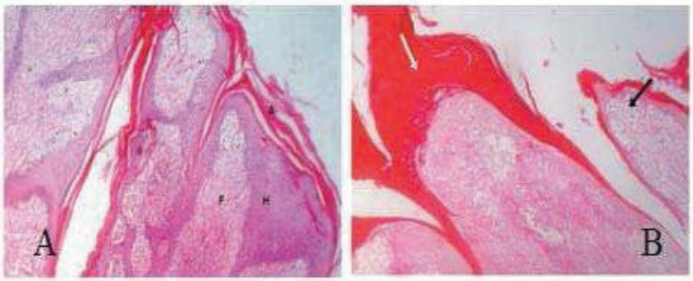
Figure. 3.29: Papillomavrus lesions in the affected camels (Khalafalla *et al.,*1998) Proceedings of the Third Annual Meeting for Animal Production Under Arid Conditions, Vol. 2: 115-131 © 1998 United Arab Emirates University)

3.4.9 Histopathology of camel papillomatosis

Only few reports on the pathology of camel papillomatosis have been published in the literature. Grossly, the lesions appear as gray nodular hyperkeratotic masses around the nostrils, on the lips, or on the cheek mucosa. Histologically, the cutaneous tumors were characterized by spindloid to stellate fibroblastic cells in a moderate amount of collagenous matrix that infiltrated and expanded the dermis and subcutis, surrounded and widely separated adnexa, and abutted overlying hyperplastic epithelium which had long, thin rete ridges (Figures. 3.30 A&B). Neoplastic cells were arranged haphazardly and in vague streams and had oval to fusiform nuclei, finely stippled chromatin, small nucleoli,

a small amount of eosinophilic cytoplasm, and indistinct cell margins. The mitotic index was less than one per ten high-power fields. Mild anisokaryosis and moderate orthokeratotic hyperkeratosis can also recognized. The oral mass reveals a similar neoplasm that expanded the mucosa and submucosa [5].

Similar histopathological lesions were also described by Ure *et al.,* (2011) [6] about camel papillomatosis in sudan outbreak, the lesions revealed multiple papillary proliferations covered with keratinized epithelium and down growth of rete ridges for both types of lesion. There was acanthosis with karyopyknosis and cytoplasmic vacuolations in the stratum spinosum cells, and hyperkeratosis in the upper layers. In addition, subepithelial fibrosis was also observed in dromedaries sections. No inclusions could be detected in squamous cells. Accordingly, the lesions were diagnosed as fibropapillomas. Some case revealed extreme neoplastic proliferation of the connective tissue so that the lesion may be primarily suspected as fibroma [9]. Histopathologically, the epidermis over the mass shows acanthosis and the stratified squamous epithelium is covered with a thick layer of orthokeratotic parakeratosis stratum corneum. The epidermis-dermis junction show finger like projections of epidermal pegs extending deep into the fibromatous tissue of the dermis. The dermis consists of irregular collagenous connective tissue with many fibroblasts, koilocytes including variably sized keratohyalin granules and a few intranuclear inclusion bodies. Hair follicle, sebaceous glands and other adenexae are not present in the dermis of these areas. Both these morphological patterns are defined as fibropapillomas (Figure.3.31).



Figures. 3.30 A&B: The histopathological changes in the skin sections of camel papillomatosis A. shows hyperkeratosis, B. shows multiple papillary proliferations

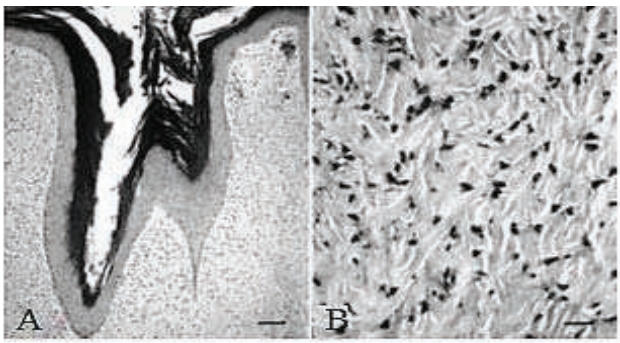


Figure.3.31, A& B: A. Fibropapilloma; llama. Moderate epithelial hyperplasia and orthokeratotic hyperkeratosis. Bar 5 100 mm, B. Fibropapilloma; llama. The

fibropapilloma is moderately cellular and composed of spindloid to stellate fibroblastic cells in a small to moderate amount of collagneous matrix. Bar 5 25 mm. (Schulman *et al.,* 2003) [5].

3.4.10 Diagnostic methods

Viral-induced PV particles can only be found in the keratinized layers of the tumor due to the strong relationship between viral and cellular DNA in proliferating viral-induced papillomas in cells [10]. Although the appearance of sarcoids are relatively easy to identify, further diagnosis is recommended for confirmation against other skin lesions. Diagnostic techniques in the past have included electron microscopy, retrospective analysis on paraffin blocks (lacking sample history and clinical detail), Southern Blot, sarcoid excisional biopsy, DNA probe and PCR. Non-invasive swabs or scrapings can be used on sarcoids with an intact epidermal surface. However, care must be taken to obtain sufficient cellular material without damaging the intact surface as it may lead to transformation of a quiescent sarcoid into an active form. PCR or hybridization with a PD DNA probe is most often recommended. It is of importance to note that Papillomaviruses are very difficult to propagate in tissue culture. The standard method of growing and isolating viruses in a controlled tissue line to infect naive animals and compare similarities is unfortunately absent. As a result, there are no current tissue culture systems available and the virus can't to be grown/studied in vivo. In many cases they replicate so poorly that there isn't enough antigen present in an animal for detection.

3.4.11 Control and treatment

Old-timers say that leaving warts alone is about the best solution. As the animal ages it builds immunity to the virus and in time the warts will disappear on their own. The warts are generally self-limiting and disappear between 8–12 weeks. Currently, there isn't any effective therapy developed for the treatment of papillomatosis[43]. Commonly practiced treatments include cryotherapy, excision, and local immune modulation [43].
Some nomads traditionally want to speed up the process and get rid of the warts quicker, removing them with either a very sharp pair of scissors or a razor blade. Removal should only be done on mature growths, since removing warts too soon can stimulate the growth and spread the virus. Large pedunculated warts can be removed slowly by tying a ligature around the base. The wart will dry up and fall off within a month. As in bovine calves , If most of the camels in a herd are infected and removing the warts from all the animals is not possible, then an autogenous vaccine can be made from warts removed from a few of the camels . The serotype vaccine produced from these warts will contain the same set of antigens of the virus strain that has infected the herd.

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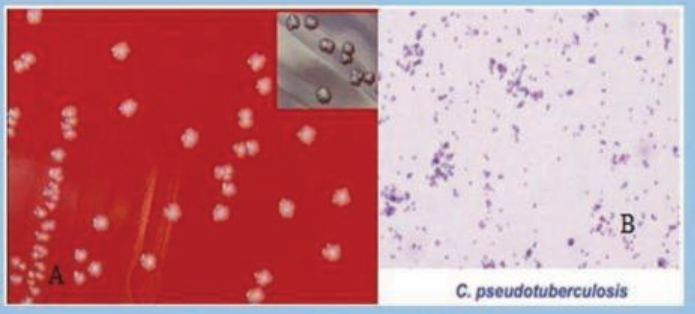
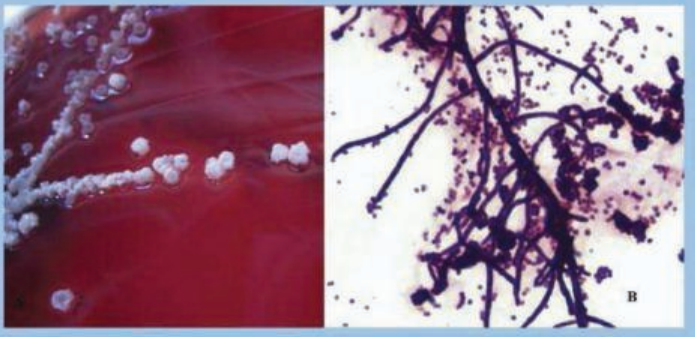
Chapter. 4
Bacterial diseases





Chapter 4: Bacterial diseases

4. Bacterial diseases

4.1. Introduction

Bacterial skin diseases are important in the *Camelidae*, however there is paucity of literature regarding bacterial skin diseases and microbiology of the skin wounds and abscesses in camels [1, 2]. Non-serious bacterial skin diseases are most often caused by *Corynebacterium pyogenes, Streptococcus spp., Nocardia asteroides, Actinobacillus lignieresi, E. coli, and Fusobacterium necropherum* [3]. The most important economic bacterial skin diseases in camelids are most often caused by *Staphylococcus* species, *Corynebacterium pseudotuberculosis* or *Dermatophilus congolensis*. The most common clinical signs associated with bacterial skin infections are crusts, papules, abscesses, and draining tracts; the latter two lesions are more commonly associated with *C. pseudotuberculosis*.

There are different considerations regarding susceptibility of the camel to the diseases. Previously, they thought that camels are less susceptibility to disease but at the same time they believed that skin wound healing is slower than in other animals [4]. Recently, the research regarding camel diseases are boosted and led to change this believe [5, 6]. There are a constant skin infections problem in camel such as contagious skin necrosis, dermatitis, wounds, abscesses or similar skin lesions [7, 8, 9, 10]. These infection are usually chronic and difficult to treat medically and all the ages of camel are susceptible. Pretending these infection are not always fatal but may cause economic losses due to reduced working efficiency [1, 2]. At many circumstance wounds infection or abscesses spread rapidly over the body surface and it becomes very difficult to manage it. In some cases, the pathogenic microorganisms invade into the blood or lymphatic system from the abscesses or cutaneous wounds and lead to internal abscesses, septic polyarthritis and sometimes life threating septicaemia [11]. The following chapter is dealing with camelidae skin diseases that caused by bacterial including the diagnosis approaches for these diseases and the general principles for treatment.

4.2. Contagious Skin Necrosis (CSN) or Pyoderma

4.2.1. Definition

Contagious Skin Necrosis (CSN) or pyoderma are conditions characterised by the formation of hot, painful swellings, which is suppurate and slough, leaving a raw circumscribed skin lesion. The infection is chronic inflammation and suppurative in nature and difficult to treat medically, which is depending on qualities of the causative *staphylococcal* strain and other pathogenic factors [12]. The disease is highly prevalence

during summer season [13]. The disease was first described by Cross, (1917) [14], who rated it second to sarcoptic mange in terms of importance as a camel skin disease. *Staphylococcus sp.* considers the main causative agents of the disease because it constitute the majority of the isolates, although different workers have isolated different kind of organisms from these lesions.

4.2.2. Causes

There is conflict about the causative agent of CSN disease in camels and no single bacterial agent has been suggested to be the main cause of the disease. The aetiology of this disease was largely unknown until Sadykov and Dadabaev, (1976) [15] identified *staphylococcus sp* as the causative agent. Different microorganisms isolated from the disease lesions. In 1917, Cross found *streptococci* in pus collected from the lesions of CSN, while Curasson, (1936) [16] isolated a *streptothrix* which was related closely to *Nocardia farcinica*. He was able to reproduce the disease by scarifying the skin of camels with pure cultures of this isolate. Moreover, Peck, (1939) [17] was able to prevent and in conjunction with local treatment cure affected camels by increasing their intake of dietary salt from the standard one ounce to five ounces per day; he did not investigate the disease bacteriologically. Several *Staphylococcus* strains have been isolated from Bactrians from different areas. The isolated strains named *St. cameli* and possessed identical properties [18]. Another different workers have isolated many organisms (*Streptococcus agalactiae, Staphylococcus aureus, Corynebacterium spp. and Dermatophilus spp*) from skin lesions [19, 20, 16, 21, 10, 22, 23].

In Ethiopia, the pyogenic affections caused two well-defined diseases. These diseases are "mala" or lymphadenitis and "maha" or "doula" or cutaneous necrosis caused after ulceration of skin abscesses [16]. Different microorganisms have been incriminated in the aetiology of the disease, but *Staphylococcus aureus*, *Streptococcus spp*, *Corynebacterium pyogenes*, *Nocardia cameli*, *Actinomyces sp.* and *Erysipelothrix sp.* were the agents most commonly isolated from typical lesions [16, 24, 25, 26]. In Pakistan, cutaneous abscess (other than prescapular adenitis) was also reported in 26 cart pulling camels in Faisalabad metropolis [27]. In India, *Staphylococcus aureus* was also isolated from wounds and abscesses in camels [1,2, 28], whereas *Pseudomonas aeruginosa* was less frequently encountered, while Kalka-Moll *et al.,* (2008) isolated *S. aureus* from subcutaneous abscesses [29].

In Emirates, young dromedaries also infected with different species of pyogenic microorganisms that cause pyogenic dermatitis. Bacteriological examination of abscesses contents collected from wounds, ulcers and other skin lesions, during 15 years, showed the following microorganisms: *Staphylococcus aureus, Staphylococcus spp, Actinornyces pyogenes, C. pseudotuberculosis, Derrnatophilus congolensis, Streptococcus spp., Pseudornonas spp., Proteus spp. and E. coli* [18].

In Egypt, different microorganisms spp isolated from non-draining abscesses of the head, shoulder, chest, leg and abdomen of the camels in Egypt [30]. The isolated organisms are: *Staphylococcus aureus, Actinomyces pyogenes, C. pseudotuberculosis, Streptococcus pyogenes, E. coli, Klebsiella spp., Proteus vulgaris, Proteus mirabilis, Pseudomonas aeruginosa, Clostridium perfringens, Fusobacterium necrophorum*. The same species isolated by El-Seedy *et al.,* (1990) [31] from wither fistulae in 93 pack camels in Egypt also.

Meanwhile, in Egypt, the effect of contagious skin necrosis and trypanosomosis on health status of camels was studied in fifteen camels, out of them 10 camels were suffered from CSN [32]. They found also five camels infected with *Trypanosoma evansi*

and CSN and showed increased in the lipid peroxidation products of the blood. They found that *Staphylococcus aureus* was the predominant bacterial alone in 6 cases and coupled with other bacteria in the remained 4 cases, the latter was coupled with coagulase negative Staphylococci in 3 cases and coupled with *Streptococcus agalactiae* in one case. In Sudan, *Staphylococcus aureus* was the dominant bacterial species that isolated from Contagious Skin Necrosis in the One-humped Camel. It found either as a single isolate or mixed, in variable frequencies, with other bacterial species that belonged to the genera, *Actinomyces, Bacillus, Corynebacterium, Enterobacter, Escherichia, Pseudomonas, Salmonella and Staphylococcus* [3].
Staphylococcus aureus was also identified as the main cause of skin lesion in India. Fifteen isolates were identified from skin lesion of camel and confirmed genotypically by Ribo-typing for 23S rRNA using the sequences for the two primers, Primer 1 – 5' ACGGAGTTACAAAGGACGAC 3' and Primer 2 – 5' AGCTCAGCCTTAACGAGTAC 3' [6] . Staphylococcus aureus has also been isolated from abscesses of an alpaca [34] (Fowler, 1998) that was diagnosed with botryomycosis, a purulent granulomatous lesion.

4.2.3. Geographic distribution

Peck (1938 and 1939) [17] was the first who reported the diseases in northern Somalia. Then, in 1974 Edelstein and Pegram [9] found that affected camels were seen in all areas of the northern regions of Somalia but the prevalence was low. However, the disease was also found in Central Asia among Bactrian camels [15]. CSN disease is widespread among Bactrian camels in Central Asian republics of the USSR, giving rise to various names in the different local languages. In Kazakhstan it is called 'ksaga' or 'ak bas', which means 'white head'. In Turkmenia it is called 'sychagpychak'. [8, 35]. The disease has also been reported in Sudan which is locally known as El-Naeita or El Naria [22, 24], Egypt [5, 30, 31], India [1, 2, 6], Ethiopia [11], Bahrain [36], Pakistan [37] and Emirates [18].

4.2.4. Economic importance

Contagious skin necrosis is not always fatal but causes economic losses due to reduced working efficiency. However, CSN diseases is life threating when the pathogenic organisms from abscesses and cutaneous wounds invade into the blood or lymphatic system that can resulted in internal abscesses, septic polyarthritis and septicaemia [11].

4.2.5. Susceptibility

The disease spreads rapidly, Semushkin, (1968) [8] called this condition "contagious skin abscesses" which can affect 5 - 20% of the camel population and induce a mortality of 10-15%. The pus exudate is considered to be the source of infection to the rest of the herd. Contagious skin necrosis is a common disease in all camel-raising herds [38]. It is highly contagious and all camels in different ages are susceptible [24,39]. However, young camels less than 5 years old are more susceptible to infection than those over 5 years [22, 33]. In Ethiopia, CSN was found to affect mostly young animals, while adults seemed to be relatively resistant, owing perhaps to previous exposure [40]. Both female and male camels were susceptible to CSN [33]. Camel herders put forward a suggested association of contagious skin necrosis with salt deficiencies. Similarly, some earlier researchers speculated that contagious skin necrosis arises as a result of salt deprivation and noted

that the disease was rare among free ranging camels with ready access to salty bushes [41]. Although there is no controlled study conducted to disprove this speculation, recent evidence may not support this assumption, as the disease was reported to affect pastoralist camels, with some herds showing up to a 55% prevalence [24]. Camel herders put forward a suggested association of contagious skin necrosis with salt deficiencies.

4.2.6. Mode of transmission

Contagious skin necrosis lesions characterized by pruritic itching. The affected animals can observed rubbing themselves with any standing post. This may contribute to the transmission of infectious agents to susceptible animals. Ticks infestation consider also as possible transmitting agents as highest disease incidence corresponded with high tick infestation in affected herds but the location of the lesions were not typical tick feeding sites in camels. The mixed bacterial infection characteristic of the disease may indicate soil as the source of infection, animals becoming infected when they lie down or sand-bathe on contaminated ground.

4.2.7. Clinical signs

CSN is appeared in different clinical features in the outbreaks that reported by the researcher in different countries. Contagious skin necrosis is a specific dermatitis of camels characterized by necrosis, abscessation and sinus formation in different parts of the skin (Figure. 4.1&2). Body temperature of affected camels is increased by 0.5-1 °C. The lesions usually begin as a folliculitis that develop to small nodular and swollen painful area and increased in size over 2 to 3 weeks. The lesion then develops a well demarcated necrotic centre which sloughs off exposing an ulcerated, purulent or hemorrhagic layer underneath. The lesion sometimes healed spontaneously over a period of two months, but lesions that have remained open with a streak of pus expressible upon manipulation.

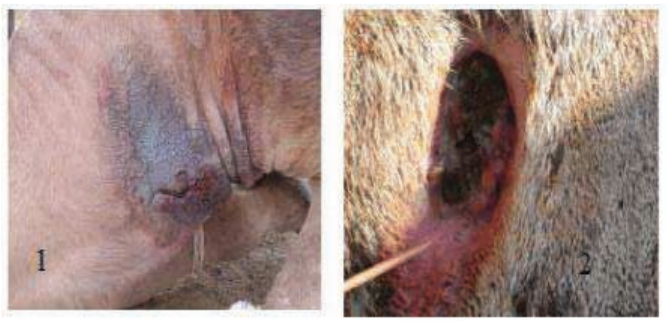


Figure. 4,1 &2: 1, Camel with CSN, skin looked black in color and hairless.
2, Camel with CSN showing ulcer filled with larg amounts of whitis pus material tinged with blood. (Hamed I Maha and Abd Ellah R Mahmoud. (2012). Effect of contagious skin necrosis and trypanosomosis on health status of camels. Journal of Animal and Veterinary Advances 11 (2); 284-288. © Medwell Journals, 2012) [32]

In some cases individual nodule be 3-5 mm big abscesses (Figure.4.2). The pus is covered with easily removable scab. Removing of the pus from this lesion reveals a crater. Large abscesses can also be seen and when lanced, yield a whitish green pus.

The lesions were mostly located on the neck, shoulders or legs, but other sites such as the flank region or ventral abdomen are also affected. The Larger abscesses are frequently encountered between the forelegs of the animal. The lesion further characterized by pruritic itching when affected animals were observed rubbing themselves with any standing post. This may contribute to the transmission of infectious agents to susceptible animals.

Edelsten, and Pegram, (1974) [9], described the clinical appearance of CSN disease in camels during a survey that carried out on the diseases of livestock in the northern regions of the Somalia during the years 1970-72. The lesions found in the centre of the gluteal region as a single sinus on either leg. Less frequently the lesions were more numerous, affecting the skin of the inguinal, perineal and lower cervical regions. A firm swelling appeared first, which burst after 5 to 10 days, leaving a circular discharging sinus 5-15 mm across. Small quantities of pus could be squeezed out of the sinus until the scab formed. Following evacuation, there was little swelling and apparently no pain. Under-running in the subcutaneous tissue was observed in some cases. Spontaneous resolution of the sinus with scab and then scar formation took place in approximately half of the cases within a month; in the others, sinuses discharged intermittently for many months.

Lymphadenitis lesions have also been described by Bornstein (1995) [42] in camel calves less than 4 months old. These lesions have similar clinical appearance of large abscesses formation. These abscesses were warm and painful as big as an orange contained 500ml of creamy yellow pus. Several calves can be affected in the herds and most affected animals are disturbed and can lose condition or might succumb. *Streptococcus spp.* and *Staphylococcus spp.* have been isolated from these lesions.

In some cases, generalized abscesses formation appeared in different body areas of the animal due to pyogenic septicaemia. The affected camels can died from generalized skin disease infection. Post-mortem examination of camels which have died recently reveals purulent lymphangitis. And purulent inflammation of superficial lymph nodes, particularly those of the neck, prescapular and head regions. Microscopic examination of sections of purulent foci and parenchymatous organs reveals cocci isolated or in clumps (like bunches of grapes) [35].

4.2.8. Diagnostic methods

Pus samples from camels that showed lesions of contagious skin necrosis should be collected aseptically with absorbent swabs from the abscesses and labelled with date of collection, sex, age and location. The samples are immediately send to laboratory in proper transportation method for further processing. In the laboratory the swabs submit for direct Gram-stained smear and for bacterial isolation, identification, and their sensitivity to different antibiotics. The organism can be isolated by sowing ordinary meat-peptone broth or agar and incubating for 1-2 days. *Staphylococcus* grows in nutrient medium containing 10% sodium chloride. Previous studies confirmed that colonies on agar are white and rounded, and difficult to remove from the surface of the agar. In broth, the bacterium forms flakes which settle to the bottom of the tube, while the supernatant fluid remains clear. The bacterium, which has been named *Staphylococcus cameli*, readily takes up aniline dyes and is Gram-positive. Antigen (extract of bacterial mass) gives a clear precipitation line in agar gel with blood serum

from naturally infected camels and experimentally infected guinea pigs, which are susceptible to infection with the *camel staphylococcus* (although rabbits, hamsters and mice are insusceptible) [35]. Six strains of the *staphylococcus*, obtained from camels which died from naturally acquired infection in Kazakhstan and the Tuva ASSR, have been studied. All strains had identical properties in various tests: plasma coagulase reaction, haemolysis reaction, dermatonecrotic test, pigment formation, fermentation of mannite, phage typing, catalase formation, carbohydrate medium with Andrade's indicator, pathogenicity for camels and laboratory animals; and also similar survival in the environment, feed, soil and manure [35].

4.2.9. Treatment

Although the disease is highly contagious, it is not fatal, and responds well to treatment with parenteral antibiotics and local iodine tincture. It is important to start treatment during early course of the disease. *St. aureus* strains develop resistance to antibiotic easily and sensitivity test should be performed on the isolated strain before starting treatment of the infected camel. Both local and systematic antibiotic should be prescribed to the infected animals. Skin lesion should be cleaned daily with antiseptic solution. Ripe abscesses lanced and pus drained and wash with *iodine tincture*. Local antibiotic apply to the lesions and in severe cases parenteral antibiotic administration should be tried. Rathore and Kataria (2012) [43] studied the antimicrobial susceptibility profiling of *Staphylococcus aureus* of camel (*Camelus dromedarius*) skin origin. They studied the efficacy of 25 different antibiotics against 15 S. aureus organisms isolated from camel skin wounds. They found that the most effective antibiotic was linizolid against, which all the isolates were sensitive, followed by azithromycin and gentamicin against which 93.33% of the isolates were sensitive; 80.00% isolates were sensitive to methicillin, levofloxacin, rifampicin, ofloxacin and vancomycin, 73.33% to azlocillin, 60.00% to bacitracin and norfloxacin and other antibiotics were still less effective. Four of the antibiotics viz. ampicillin, cefexime, metronidazole and nalidixic acid were found completely ineffective as resistance to these antibiotics was shown by all the isolates. Antibiotic therapy is highly effective, curing 75-100% of cases if given sufficiently early. Hamed and Abd Ellah, (2012) [32] recommended to supply camels suffering from CSN with antioxidants to overcome the deterioration of blood oxidative status.

4.2.10. Control

General precautionary measures should be implemented on infected farms and farms at risk. It is including the isolation and treatment of affected animals, disinfection of paddocks and buildings, and restricting trade in camels. *St. aureus ,* the causes of CSN is difficult to treat with antibiotics if not treated earlier. Most researcher have regularly produced auto-vaccines for the afflicted dromedaries. The auto-vaccines were developed for the individual animal or for a small group of animals from the same herd. The production of an individual auto vaccine is necessary as there are many different immunological and virulence factors present in *St. aureus* strains. This also prevents the industrial production of a vaccine. Dromedaries suffering from *St. aureus* dermatitis were given 5 to 8 mL of a formalin-inactivated vaccine subcutaneously. Sixty percent of the dromedaries vaccinated showed initial improvement within the first few days; the abscesses underwent exsiccation and reduced in size. Only a few animals required a booster injection after 14 days. All cases of *St. aureus* dermatitis were successfully treated in this manner. It was also possible to inoculate the unaffected animals

prophylactically and so inhibit the spread of the disease. The remarkable success of the *St. aureus* vaccine is based on a general non-specific stimulation of the immune system, a para-immunization, as well as a specific immunization against all of the antigenic exotoxins and other virulence factors of the dermatopathogenic strains of *St. aureus.* Phagocytosis resumes following neutralization of anti-phagocytosis virulence factors of the pathogenic *Staphylococci.* The major problem in the treatment of pyoderma is being able to adequately increasing the body's own defence mechanisms [44].

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4.3. Pseudotuberculosis (Caseous Lymphadenitis)

4.3.1. Definition

Corynebacterium pseudotuberculosis (*C. pseudotuberculosis*) causes granulomatous lymphadenitis in old world camelids and severe chronic granulomatous lymphadenitis in South American camelids. The organism has also been isolated from abscesses in alpacas [1, 2, 3, 4]. The organism well known as a causative agent of caseous lymphadenitis in sheep and goats, ulcerative lymphangitis in cattle and horses, and also external and internal abscesses in horses.

4.3.2. Causes

C. pseudotuberculosis is the specific cause of the disease. It is a soil-born organism. It is a short, irregular ovoid, Gram-positive rod almost resembling a coccus (Figure. 4. 3. A&B) . The bacteria show a marked pleomorphism in smears made from abscesses contents. *C. pseudotuberculosis* is a pyogenic, facultative intracellular bacterium. The organism has ability to penetrate the tissue and produce filterable toxins. *C. pseudotuberculosis* possesses a cytotoxic surface lipid coat that facilitate intracellular survival of the organism and abscess formation. *C. pseudotuberculosis* produces also a phospholipase exotoxin (hemolysin) that causes hemorrhages, increases vascular permeability and has an inhibitory effect on phagocytes which help in spread of infection in the host body. There are two proposed biotypes, of *C. pseudotuberculosis*, ovine/caprine and equine/bovine according to serological reaction. Right now, researcher has only found the first strain in camels. *C. pseudotuberculosis* strains have different pathogenicity which led to variation in toxin production [5]. The toxic lipid cell

wall is the virulence factor of *C. pseudotuberculosis* that mediates resistance to killing by phagocytes.

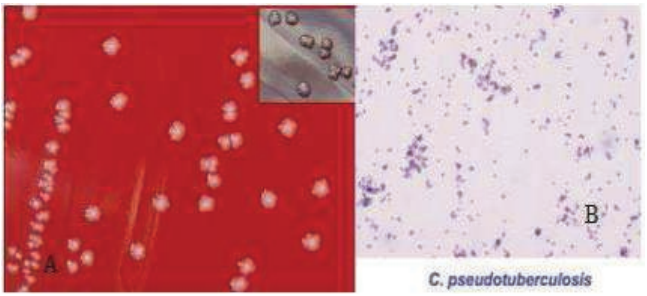

Figure.4.3: Small colonies of *C. Pseudotuberculosis* on blood agar (2 mm in diameter). Cultivation 72 hours, 37°C. B. Gram-positive, asporogenous, nonmotile rods. "Coryneforms".

4.3.3. Geographic distribution

Camel pseudotuberculosis occurs in the major camel-producing countries in the world including feral camel in Australia, Saudi Arabia, India, Russia, Iran, China, Egypt, Ethiopia, Kenya, East Africa and UAE [6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21].

In camels caseous lypmadenitis, *C. pseudotuberculosis* is not always the only bacteria that isolated from the abscesses. Radwan *et al.,* (1989) [7], isolated *Staphylococcus aureus, C. renale, C. equi, Shigella spp. and E. coli* in 15% of 2500 dromedaries suffered from caseous lymphadenitis and abscessation in Saudi Arabia. Musculature and subdermis abscess formation over the neck, tail and joints had also reported in this study. There was a generalized lymphadenopathy without abscess formation in the lymph nodes. Simultaneously, the afflicted animals found being suffered from a severe infestation of ticks (*Hyalomma*) from which the authors were able to isolate *C. pseudotuberculosis*. Intraperitoneally *injection of C. pseudotuberculosis* cultures in Guinea pigs led to die these animals 3 weeks later with multiple abscesses.

From Ethiopian dromedaries, Domenech *et al.,* (1977) [17] were also isolated the following bacterial species: *Streptococcus* 57% (Lancefield Group B), C. *pseudotuberculosis* 37%, *staphylococcus spp.* 10% , *C. pyogenes* 6.7%.

In the Soviet Union different microorganisms were isolated as a causative agents of pseudotuberculosis. *Actinomyces pyogenes* considers important in the pathogenesis of pseudotuberculosis as *C. pseudotuberculosis* [18]. Histoplasma furciminosum consider also as the causative agents of pseudotuberculosis among Bactrian camels outbreak [9, 23]. The clinical signs of the disease were seen in pre-shoulder lymph nodes in camels, when camels were walked from Central Asia to several farms near Moscow in 1958 . Mycelium and *Cryptococcus* like organisms were also detected in the draining lymph nodes. While *Cryptococci* were observed in macrophages.

In Egypt, *C. pseudotuberculosis* outbreak was reported in 21 dromedaries in 6 Egyptian villages that characterised primarily by edema of the elbows, the chest and enlargement of the external lymph nodes. Ulceration of some superficial lymph nodes associated with a bloody exudate were also seen (Ismail et al. 1985). *C. pseudotuberculosis* alone was isolated from the non-ulcerative lymph nodes, though C. *pseudotuberculosis*, while

Staphylococcus aureus were isolated from the ulcerated lymph nodes. Lymphadenitis detected in 10.9% (37/339) dromedaries from Egypt [22]. The affected adult camels revealed enlargement and abscess formation in the superficial lymph nodes. A thick, caseated creamy pus and/or calcified material released from the lymph nodes. *C. pseudotuberculosis* ovis was isolated in pure culture from 62.1% cases and associated with *Staphylococcus aureus* and *Streptococcus spp.* from the rest. In UAE, Afzal *et al.,* (1996) [23] isolated pure cultures of *C. pseudotuberculosis* from 11 racing camels suffering from lymphadenitis. Experimental camels was inoculated at the base of the ear with one of each camel's isolate (with and without dermonecrosis) and sheep strain. Camels infected with the sheep strain and the dermonecrotic isolate produced lymph node swelling only, whereas the strain without dermonecrosis produced multiple abscesses in the experimental camels 40 days after infection. Re-infection of the experimentally infected dromedaries after they had recovered from the disease did not produce any lesions. The infected camels in UAE seldom develop abscessation in lymph nodes, pseudotuberculosis is more of an aesthetic problem than a health problem. And staphylococcal dermatitis consider of greater importance.

4.3.4. Economic importance

Visible abscessation is the only the effects of the *C. pseudotuberculosis* in most infected camels. There is no overt clinical diseases or impairment of health. *C. pseudotuberculosis* pathological changes in the internal organs are rare in camels [7]. The generalized cutaneous form is also seldom observed [23, 25]. The disease is important economically in alpacas because of the internal Localization of the abscesses and absence the opportunity to treat each abscess under natural conditions of extensive management in South America. This localization of abscesses was described also for young alpacas under extensive management in the Andes [26]. In intensive production of alpacas in USA, most of the abscesses in young alpacas are localized in the head, cervical or thoracic area [27].

4.3.5. Susceptibility

The occurrence of abscesses was described also for young alpacas under extensive management in the Andes [26]. Pseudotuberculosis occurs primarily in camels more than 3 years old [28]. However, all camelids in different ages are susceptible to the diseases and there is also no preference of the sex in the incidence of the disease. Both male and female camels are susceptible to pseudotuberculosis. Pseudotuberculosis remains one of the most important bacterial diseases in camelids [15, 17, 22] with an infection rate between 10% and 60%. The disease is seen much more frequently in breeding than in racing dromedaries.

4.3.6. Sources and transmission of infection

Discharges from ruptured abscessed superficial lymph nodes are the sources of infection. Skin or mucous membrane are the portal of entry. Several factors act to damage skin and thus create portals of entry for *Corynebacteria*. These factors include ticks infestation, nodular worms and contaminated injection needles. Acacia thorns and hard stems from desert plants have ability to create injuries in the skin and mucous membranes of the oral cavity and act as entry of the *Coryneybacterium*.

4.3.7. Pathogenesis

After the entry of C. *pseudotuberculosis* through the skin or mucous membrane, the bacteria are then transported via the afferent lymphatics to the regional lymph nodes in which lesions may develop. Lymphogenous and hematogenous distribution of the infection from the primary site to internal organs and tissues may occur latently. Different scientists conclude that *C. pseudotuberculosis* may not always be the sole cause of lymphadenitis in camelids. However, there is some confusion whether the samples were obtained from closed or open abscesses. Stowe, (1984) [29] reported that in open abscesses, secondary infection with coccal organisms can be expected.

4.3.8. Clinical signs

Multiple abscess formation in camels experimentally infected with *C. pseudotuberculosis* occurred 40 days after infection [24]. Pathological changes in the internal organs such as extensive caseous necrosis in internal lymph nodes and other organs (especially lung), are rarely developed in camels [7]. The generalized cutaneous form is also seldom observed [23, 25]. The clinical signs of the disease are cold, closed, painless abscesses up to the size of a lemon or orange in the external lymph nodes, especially at the base of the neck and in the pre scapular lymph nodes [30]. Thick yellow cream-like pus extrudes, when the abscess open. Most abscesses are enveloped by well-developed connective tissue capsules. Previously, these pathological changes have never been described in camelids. However, Braga *et al.,* (2007) [4] described clinical responses of primary infection in experimentally infected alpacas with *C. pseudotuberculosis* groups A, B and C. Fever, swelling and abscess formation were the predominant clinical signs. *C. pseudotuberculosis* was isolated from the pus that flowed through fistulae. The initial lesion progressed to scars 2 weeks post infection, of approximately one inch in diameter in all experimental alpacas. Tumefaction of the draining left inguinal lymph nodes was observed as early as 1 week post infection. Infected alpacas did not show any behaviour change and appetite was considered normal. Post mortem examination of the alpacas that died after experimental challenge inoculation showed subcutaneous edema in the abdomen and perineal area, with a yellowish liquid that coagulated upon exposure to air. Enlargement of the regional lymph nodes from the prepuce and inguinal area without pus on cut surface were also seen. A necrotic area of 5 cm, with purulent discharge were observed at the inoculation site. Abscess formation were seen internally in the renal lymph node. Abscessation were also observed in other internal organs in the infected alpacas such as the regional and inguinal lymph node. The primary sham inoculated alpacas had abscesses in the regional and internal lymph nodes from the right, challenged side.

A few cases have been seen in dromedaries whereby the abscesses break through the ribs and the organism enters the lung, producing severe bronchopneumonia with pulmonary caverns. Histopathological examinations of the affected lymph nodes by Abou-Zaid *et al.,* (1994) [22] revealed acute serous, acute suppurative and chronic suppurative lymphadenitis. A rare case of arthritis, peri-arthiritis and pleurits associated with Corynebacterium pseudotuberculosis infection and Salmonella enterica in a dromedary camel is also reported [33] (Figure. 4. 4).

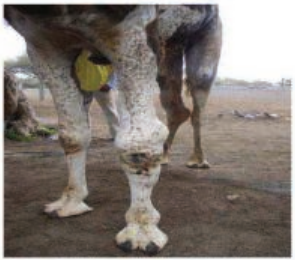

Figure. 4. 4: Articular and periarticular enlargements of the affected Joints due to mixed infection of *Salmonella enterica* and *Corynebacterium pseudotuberculosis*. (María T. Tejedor-Junco & Pablo Lupiola & María J. Caballero & Juan A. Corbera & Carlos Gutierrez. (2009). Multiple abscesses caused by *Salmonella enterica* and *Corynebacterium pseudotuberculosis* in a dromedary camel. Trop Anim Health Prod. 41:711–714) [33].

4.3.9. Diagnostic methods

The isolation of *C. pseudotuberculosis* from discharging lesions is necessary to confirm the diagnosis. The isolation of C. *pseudotuberculosis* from abscesses poses certain difficulties as the colonies resemble *streptococcal* colonies and are frequently overgrown by accompanying bacteria. In contrast to pseudotuberculosis in sheep and goats, *C. pseudotuberculosis* is not always the only bacteria isolated from the abscesses in camels [17]. Indirect ELISA test was used to detect antibody to cell wall antigens in alpacas [4]. A primary infected alpacas had a robust antibody response against *C. pseudotuberculosis* cell wall antigen with significant differences with respect the naïve challenged alpacas.

4.3.10. Treatment

Treatment of individual cases are possible. The superficial abscesses can be treated with surgical drainage, in strict aseptic procedures. The infected material must be destroyed and contaminated equipment disinfected. *C. pseudotuberculosis* is susceptible to antibiotics such as penicillin, tetracyclines other than the aminoglycoside group. However, treatment is not usually attempted because the abscess is encapsulated and pus prevents the medication from reaching the bacteria, the organism is intracellular and response is poor. Braga *et al.,* (2007) [4] mentioned that under natural conditions of extensive management of alpacas, in the Andes, there is no opportunity to treat each abscess case, especially if it is localized internally. A combination of penicillin and erythromycin has been suggested by Bergin (1986) [6], to treat pseudotuberculosis in camels since erythromycin is the more able to penetrate the tissues. Intravenous injection of 20 mL dimethyl sulfoxide (DMSO) and 20mL Baytril@ for **12** days is also one option for treating of camel pseudotuberculosis. The abscess will eventually subside with no relapse.

4.3.11. Control

Separation of healthy camels from affected animals that serve as reservoirs of infection, should be the first step in the control of camel pseudotuberculosis. Vaccination of the camel herd that show past incidence does not provide complete protection against the development of abscesses but controlled field trials show a significant reduction in the number of camels that develop abscesses and lymphadenitis in infected camels. This vaccine might be developed based on a sheep strain of *C. pseudotuberculosis* [24]. The production of a trial vaccine against camel's pseudotuberculosis has been studied by scientists [31, 32]. In sheep, vaccines formulated from concentrated, formalin-inactivated *C. pseudotuberculosis* Culture supernatants containing phospholipase D have considerable efficacy and are available in many countries. This vaccine is also intended for trials in camels [6]. The attenuated mutant vaccines also show promise [31].

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4. *Dermatophilus congolensis* infection in camels

4.1 Definition

Dermatophilosis (cutaneous streptotrichosis, lumpy wool) is an acute, subacute, or chronic superficial exudative skin disease caused by a Gram-positive pleomorphic bacterium called *Dermatophilus congolensis* [1]. It is a typical epidemic in the humid tropics and subtropics regions. The disease has a wide host range [2, 3] and affects many species of domestic and wild animals and occasionally, humans. Endemic and epidemic infections are most commonly reported in cattle, sheep, goats, and horses [4, 5, 6, 7, 8, 9, 10, 11, 12]. Camel dermatophilosis is recognised as widespread, and incidence may be related to the presence of ticks which cause initial skin damage. The lesions are characterized by an exudative dermatitis with scab formation. The disease causes severe skin matting resulting in hide depreciation, overall decrease in animal productivity and, in severe cases, mortality in susceptible weak animals may be as high as 50% in the absence of treatment. Camel dermatophilosis is recognised as widespread in several camel rearing countries in the tropics. Natural *D. congolensis* infection of camels was first reported in Kenya in semi-arid conditions [13]. The most effective control measure of this disease was thought to be through control of tick infestations. Several treatment regimens were tried in other animal species but with varying degrees of success. The only control method of this disease practiced in dromedary camels was the regular washing with 1% potassium aluminium sulphate solution.

4.4. Causes

The infective agent is *Dermatophilus congolensis,* but requires damage to the skin from other causes to establish infection. The organism is dimorphic and grows as branched filamentous mycelia containing dormant zoospores which are transformed by moisture to the infective stage of motile isolated cocci (zoospores) (Figure.4.5 A&B). Genetic diversity is considerable between isolates. Isolates from the same geographic region are not necessarily closely genetically related [14]. However, a recent study found that genotypic variation between isolates did correlate with host species [15].

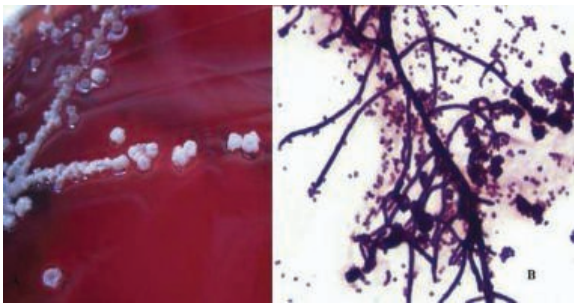


Figure.4.5 A&B: A. Colonies of *Dermatophilus congolensis* on blood agar incubated at 37°C in 5% CO2, appears as 0.5–1 mm in diameter after 24 h. Colonies are β-haemolytic, greyish white, elevated, wrinkled, hard and adherent. After 2–5days they sometimes obtain an orange colour. B. The filamentous structures with transversal and

longitudinal segmentation of *Dermatophilus congolensis* that finally evolving to coccoid forms.

4.5. Geographic distribution

No recorded of natural dermatophilosis cases in camels noted in Abu-Samra and Imbabi literature review in (1976) [17]. Other researcher indicated similar cases that called a contagious condition. These conditions caused by streptothrix-like organisms associated with other genera is common in Egypt, Sudan, India and Somalia, especially in the rainy seasons [17]. No details &clinical manifestation or bacteriological isolation were given. Currason, (1918) [18] identified a fungus in pus and later (1947) [19] named it *Actinomyces* (*Nocardia cameli*).The disease was diagnosed as contagious skin necrosis affecting mostly the back or rump and occasionally the base of the neck [17]. Dermatophilosis was first described in dromedary camels in the Ol-Maisor farm in Laikipia, Kenya [20, 21]. The disease also reported in Sudan [21, 22, 23]. The disease fatality rate among infected dromedary calves in the Butana region of Sudan was found to be ranging between 10% to 30% [2]. However, no mortality was noticed among affected adult camels. The disease was the most common disease among growing calves in Butana region of eastern Sudan [23]. There is a strong debate about the role of ticks, particularly the Bont tick *Amblyomma variegatum*, on the epidemiology of this disease in camels since this tick species was not found in camels among which several other tick species were recovered [24].
In Saudi Arabia, Dermatophilosis was described in a dromedary herd of 559 animals for the first time as a mixed infection of *Dermatophilus congolensis* and *Microsporum gypseum*. The morbidity rate was 23.4% [22]. The disease found to be affected with discrete circumscribed crusty hairless lesions. The disease was also more prevalent among young and growing calves than older ages. *D. congolensis* and *M. gypseum* were diagnosed by direct microscopy, isolation and histopathology. However, it is worth to mention that during this outbreak in Saudi Arabia, affected camels were not infested with ticks. This observation is contrary the situation in Sudan and Kenya, where the affected camel herds had very high tick loads. This finding is consistent with other conclusions which suggested that agents, other than tick infestation, are involved in the pathogenesis of *D. congolensis* in camels as well as in bovines [20, 24].
Dermatophilosis in dromedaries has also reported in UAE [25], in Ethiopia [26] and in Kenya [27]. Joseph *et al*., (1998) [28] isolated a non-hemolytic *D. congolensis* strain from dromedaries' skin lesions in the UAE. A similar strain was identified from scab originating from limbs of dromedaries in the UAE suffering from skin necrosis. From these results it may be assumed that contagious skin necrosis and streptothricosis are identical to dermatophilosis. The susceptibility of dromedary to experimental infection with *D. congolensis* was approved by Abu Samra *et al.,* (1976) [16].
In Iran, dermatophilosis has recently reported in 14 (13.6%) of 103 camels (*Camelus dromedarius*) slaughtered in Yazd Province. All affected camels presented with a heavy infestation with brown hard ticks on the lesions that, identified as *Hyalomma spp* on parasitology examination [29, 30].

4.6. Economic importance

Outbreaks of dermatophilosis have resulted in serious economic losses in many countries, primarily in the livestock and leather industries. *D. congolensis* has been the

most important infectious skin disease of ruminants in the Caribbean Islands, Ethiopia, and in many West, Central, and East African countries [31,32] . In man, the disease causes skin and nail infection, and its clinical spectrum ranges from an asymptomatic infection to a pustular eruption of the skin [33]. The disease results in gradual loss of condition, impaired reproductive performance, decreased milk production, and a marked increase in the somatic cell counts in milk [8, 34]. *D. congolensis* infection is reported as one of the conditions that impede camel production in the Kenya, Sudan, and Saudi Arabia [21, 22].

4.7. Susceptibility

Animals of all ages are susceptible, including suckling a few weeks old. In Kenya, the disease was more prevalent in the wet season (21.2%) compared with its prevalence in the dry season (14.5%), and the calves were found to be more susceptible (23.1%) compared with the adults (19%) [13, 20]. In Butana region in Eastern Sudan, the disease were first found in two herds of adult camels, of which 50%-75% of the animals were affected. However, the disease in other thirteen herds examined, camel calves were more likely to be infected (34%) than adults (8.9%), and lesions were more severe and involved most parts of the body.

4.8. Sources and transmission of infection

Clinically normal carrier animals and crusts from infected animals probably serve as sources of infection [1]. Zoospores are transmitted either by direct contact or by vectors (external parasites) such as ticks, lice, mites, flies, and mosquitoes that act as mechanical vectors [1]. Supposedly the thorns of the acacia and grain awns are also able to transmit the spores [35]. Khodakaram-Tafti *et al.,* (2012) [29], found that dermatophilosis lesions were mostly associated with tick infestation (*Hyalomma spp.*) in Iran. They found that Hyalomma tick species may have an important role in the pathogenesis of dermatophilosis in the camels of Iran. In cattle, severe outbreaks of the disease have been closely associated with the presence of the tropical bont tick *Amblyomma variegatum* (Figure.4.6) [36]. This has been shown to be associated with immunomodulation of the host by *A. variegatum* [37, 38].

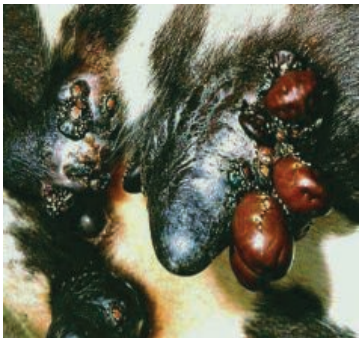


Figure. 4.6: The presence of the tropical Bont tick *Amblyomma variegatum* on the udder of the dermatophilosis infected animal.

4.9. Pathogenesis

Briefly, dermatophilosis pathogenesis sequence of events involves physical damage to the skin, bacterial multiplication in the epidermis, repeated cycles of invasion by hyphae, infiltration by neutrophils and exudate, regeneration of epidermis and reinvasion (Figure.4.7). Multiple known and unknown factors appear to be involved in the pathogenesis of natural dermatophilosis.

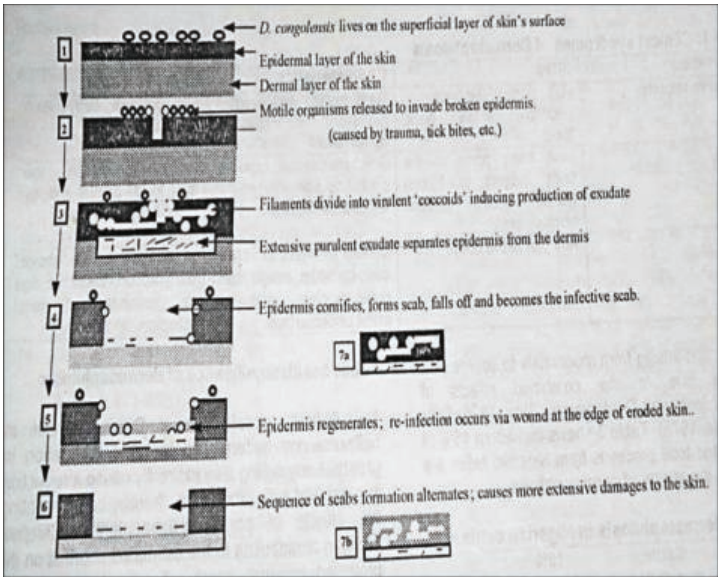


Figure.4.7: Shows the transmission of zoospores from the crusts of infected animals that serve as sources of infection.

Trauma to the skin and prolonged wetting appear to be the two most important factors. The protective barriers of the hair, surface lipid film, and stratum corneum agent of the skin resist invading the organism and unable it to overcome. Trauma from ectoparasites, shearing, dipping, barb wire injuries, sharp stones, and scratches from sharp vegetation may therefore act as portals of entry for the organisms and allows establishment of infection. The organism multiply then in the epidermis. The hyphae developing from the spores in the epidermis attack the hair sheath. This causes an exudative inflammatory reaction, resulting in a bulging of the slow growing epidermis away from the corium, thereby allowing growth of a new layer of epidermal cells [39]. Drying of the serous exudate forms pyramidal-shaped crust that is a distinguishing characteristic of this disease. The rapid infiltration of inflammatory cells such as neutrophils, and regeneration of the epidermis play important roles in the formation of the crusts. The crusts can be removed, revealing a wet reddish area that secretes a thick, blood contaminated exudate (exudative dermatitis) [40]. The organism in the scab is the source for repeated and expanding invasion which occurs until immunity develops and healing of the lesions. Severe tick infestation suppresses immune function and promotes spread

of the lesion. Extensive suppuration and severe toxaemia may occur due to secondary bacterial invasion.

4.10. Clinical Signs

Dermatophilosis is described to be occurred in two stages, early or acute and chronic or late stages (Figure. 4. 8. A&B) [13] . The early lesions appear as matting together of hair into small tufts forming a characteristic “paint brush” effect in the long hairs. The lesions appear on the rump, flanks, neck and some parts of the lower abdomen. The removing or sloughing of the tufted hair, a raw hyperaemic lesion with serum exudation is appear. Some lesions can exude thick yellowish pus (Figure.4.9). Chronic lesions occur on most parts of the body especially the flanks and rump (Figure. 4.10). The lesions extend to legs and ventral abdomen. Commonly the affected areas are regular or irregular in shape and vary from 3 - 10 cm or more in diameter, in addition to loss of hair and thickening of skin, with an uneven surface. Thick brownish palpable crust is characteristic diagnostic feature that raise above the surface [13].

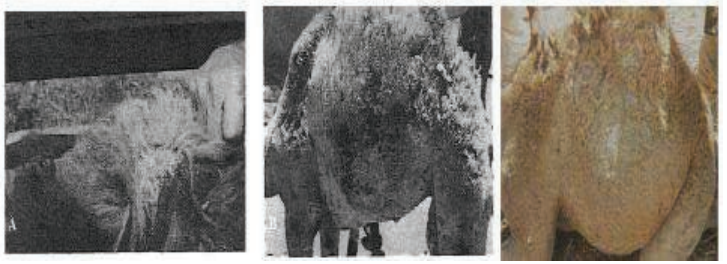


Figure. 4.8. A&B&C: A. Hyperaemie raw necrotic lesion with areas of 'pus exudation, left, after removing matted hair, B&C. Widespread lesions of necrotic hard crusts in a chronically infected camel calf. (Gitao *et al.,* 1990/ Natural *Dermatophilus congolensis* infection in camels (*Camelus dromedarius*) from Kenya. J. comp. Path. 103: 307-312) [13].

Figure.4.9: Camel skin. Thick brownish crusts and alopecia with a heavy infestation with Hyalomma spp. on the flank. (Khodakaram-Tafti *et al.,* 2012/ Prevalence and pathology of dermatophilosis in camels (*Camelus dromedaries*) in Iran.

Trop Anim Health Prod. 2012 Jan; 44(1):145-8. doi: 10.1007/s11250-011-9901-6. Epub 2011 Jun 11) [29].

This different forms of the disease have also been seen by the authors in dromedaries in the UAE. They found distinct differences between infections involving short or long hair. Matted of the long hairs in the vicinity of the exudate giving the characteristic "paint-brush affect. Detach of the matted hair tufts can leave a wettish pink, hyperemic wound surface. The affected areas become covered with a suppurative exudate in severe infection. Urination of the female the dromedaries leading chronic wetness and high humidity of the hindquarters that have been implicated in the aetiology of skin necrosis [41]. Short-haired areas dermatophilosis occurring on almost all areas of the camel body was also described in UAE [25]. The lesions ranged from nodules to thickened, raised areas covered with thick scabs. Upon removal of the scabs, a raw area with a serosanguinous exudate is exposed. *D. congolensis* has produced severe cases of wool rot in llamas. Heavy wool cover over the back in high moisture climates predisposes lamoids to this disease. Lesions consist mostly of crusting, particularly over the dorsum of the back [42].

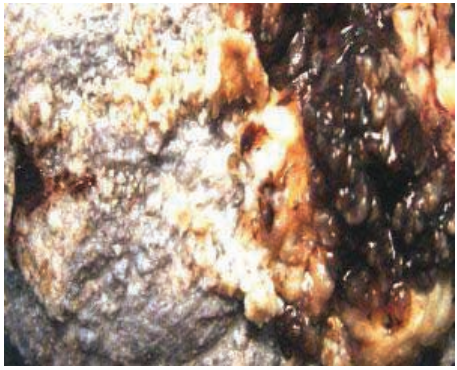


Figure.4.10: Camel skin. Patchy thickening of the skin with dark brown crusts on the rump. (Khodakaram-Tafti *et al.,* 2012/ Prevalence and pathology of dermatophilosis in camels (*Camelus dromedaries*) in Iran. Trop Anim Health Prod. 2012 Jan; 44(1):145-8. doi: 10.1007/s11250-011-9901-6. Epub 2011 Jun 11) [29].

4.11. Histopathology

The histological lesions of camelidae dermatophilosis were described by several authors [21, 22, 29]. Epidermal proliferation, congestion, oedema and infiltration of the epidermis and dermal papillae by neutrophils are the characteristic features of acute dermatophilosis (Figure. 4.11). While, the degenerative changes in the stratum spinosum, alternating layers of hyperkeratosis, degenerate neutrophils and mononuclear cell infiltration are seen in chronic dermatophilosis. Transverse and longitudinal divided filamentous forms of *D. congolensis* is seen invading the keratinised layers and sebaceous glands. The hyphae of the organism stain positively with PAS stain and can recognise in the epidermis of infected skin (Figure.4.12).

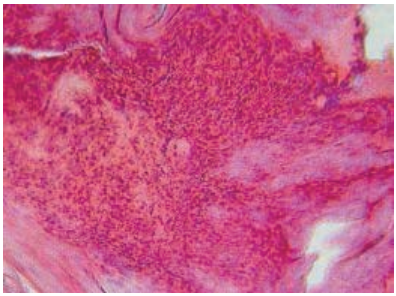


Figure. 4.11: Camel dermatophilosis. Epidermis that include of degenerating neutrophils, serous fluid, and bacterial filaments (H&E, ×450) (Khodakaram-Tafti *et al.,* 2012/ Prevalence and pathology of dermatophilosis in camels (*Camelus dromedaries*) in Iran. Trop Anim Health Prod. 2012 Jan; 44(1):145-8. doi: 10.1007/s11250-011-9901-6. Epub 2011 Jun 11) [29].

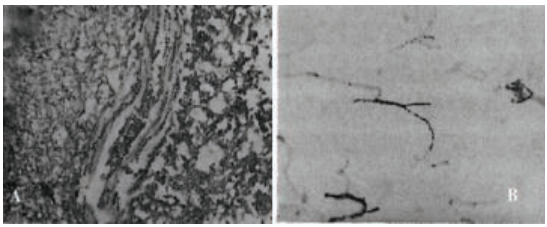
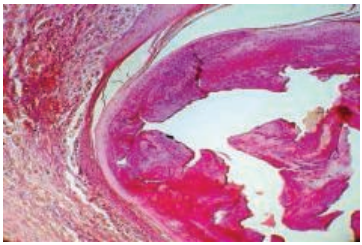


Figure.4.12. A&B: A. Beaded Dermatophilus congolensis from a skin scab. HE x 670, B. Gram-positive filaments with transverse and longitudinal divisions and free cocci, x 670. (Gitao *et al.,* 1990/ Natural *Dermatophilus congolensis* infection in camels (*Camelus dromedarius*) from Kenya. J. comp. Path. 103: 307-312) [13].

Khodakaram-Tafti *et al.,* (2012) [29], described the gross and histopathologic features in 14 infected camels in Iran. Grossly, extensive hair matting and patchy thickening with dark brown scabs or crusts were observed on the affected areas of rump, flanks, abdomen, shoulders and neck. The histopathologic examination of the affected skins revealed prominent superficial thickening of the epidermis composed of orthokeratotic and parakeratotic, hyperkeratosis, degenerating neutrophils, serous fluid, and bacterial filaments (Figures.4.13.). A lot of keratinaceous debris associated with an exudate rich in neutrophils was seen as a remarkable feature of the lesions on the superficial epidermis. Dermal inflammation was mild with infiltration of mononuclear inflammatory cells, particularly lymphocytes, around superficial vessels. A Gram-positive filamentous organism which was divided into parallel rows of cocci was observed in the crusts by Brown and Brenn Gram stain.



Figures.4.13: Camel dermatophilosis. Epidermis composed of orthokeratotic and parakeratotic hyperkeratosis, degenerating neutrophils, serous fluid (H&E, ×280). (Khodakaram-Tafti *et al.,* 2012/ Prevalence and pathology of dermatophilosis in camels (*Camelus dromedaries*) in Iran. Trop Anim Health Prod. 2012 Jan; 44(1):145-8. doi: 10.1007/s11250-011-9901-6. Epub 2011 Jun 11) [29].

4.12. Diagnostic methods

Direct smears from scab material reveal branched Gram-positive filaments. These filaments is showing division along transverse and longitudinal planes to form 2 to 4 rows of coccoid bodies. The organism can also be demonstrated by fluorescent antibody. *D. congolensis* may be isolated from scrapings or a biopsy section and is much easier to isolate from an acute case than a chronic one. The organism is easy to culture and grows well on sheep and ox blood agar. The plates should be incubated at 37°C for up to 5 days in a CO2 atmosphere. Polymyxin B sulfate can be used to suppress contaminants. An enzyme-linked immunosorbent assay (ELISA) use also to detect the antibodies against dermatophilosis in camels. The test detected antibodies to dermatophilosis 21 days after the experimental infection with D. congolensis. ELISA can be use in the epidemiological studies in the field [43]. Counter immune-electrophoresis have also been used to detect serological evidence of infection with *D. congolensis*.

4.13. Treatment

Different treatment directions are used to treat the dermatophilosis in camel. Limited efficacy appears in topical bacterial dips due to its inability to penetrate the scab to the active lesions. However, application of bacterial dips are more appropriate to control. Long acting antibiotic reported as a successful method in the treatment of camel dermatophilosis. Awad *et al.,* (2008) [44] found that topical application of povidone-iodine and parental injection of long-acting oxytetracycline revealed 100% and 66.7% cure rates (respectively) in equines. Another treatment options have also been reported [45]. They reported the use of phytotherapy for the treatment of animal dermatophilosis by applying ointments prepared with ethanolic. They reported the effects of leaves extracts of Senna alata, Lantana camara and Mitracarpus scaber as topical treatments on dermatophilosis lesions. It was observed that the lesions healed completely in all the affected animals without recurrence unlike the results observed by using oxytetracycline, terramycin long-acting or procaine-penicillin antibiotics commonly used parenterally for the treatment of dermatophilosis in many African countries [46]. These phytotherapies, when applied once a day for 8 – 15 days, provoked the falling off of the crusts after 3 – 4 days of treatments and hair growth was noticed on the treated

areas with complete healing without scarring within 3 – 4 weeks after the end of the treatment. Dromedaries dermatophilosis treated successfully with terramycin or procaine penicillin and streptomycin. Terramycin LA is used twice, intravenously to treat infected camels. The affected areas cleansed daily with an iodine solution for 7 days after removing of the scabs. The lesions should be fully healed within 4 weeks [21]. In the Llama, it is recommended to use topical antibiotics only or to use disinfectants and/or systemic penicillin or trimethoprim-sulfadiazine for the treatment of dermatophilosis [47].

4.14. Control

The regular washing with 1% potassium aluminium sulphate solution is one control method of camel's dermatophilosis [20]. However, this method was not efficient when applied on camels in Saudi Arabia. Animal breeders have observed that dermatophilosis susceptibility seems to be determined genetically. Therefore, the control methods based on the identification of molecular genetic markers of resistance or susceptibility to dermatophilosis in cattle were developed. A functional candidate gene approach was used to analyze the DNA polymorphisms of targeted genes encoding molecules implicated in known mechanisms of both non-specific and specific immune responses existing in the pathogen/host interface mechanisms. A haplotype marker of susceptibility was found and validated and used for selection and elimination of susceptible animals. This technique resulted in reducing the prevalence rate of dermatophilosis from 0.76% to 0.02% over five years. However, a cross-breeding plan was suggested to study the genetic transmission of the genotypic and phenotypic characters of susceptibility to dermatophilosis and those individuals at highest risk of contracting the disease will be eliminated [50]. The properties of this system are now under study, including the heterozygote advantage and the frequency dependence theories and their involvement in the biological mechanisms at the host /pathogen interface [50]. Research is still in progress regarding the understanding of the immunological mechanisms involved in the development and the resolution of dermatophilosis at the skin level in order to develop efficient vaccines. Efforts to identify markers correlating with resistance or susceptibility to the disease through analysis of polymorphic systems at the DNA level were on progress.

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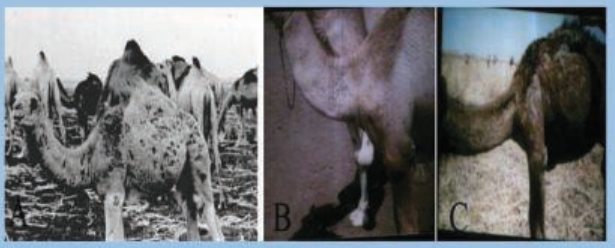
Chapter. 5
Fungal diseases



Chapter 5: Fungal skin lesions of camelidae

5. Fungal skin lesions of camelidae

5.1 Introduction

As a result of environmental alterations, the number of fungal and fungal-like diseases of animals and plants in both natural and controlled systems has increased, over the last two decades[1]. Camelids are like other mammals, may be affected by several fungal diseases. , however, only some are well described. These diseases are dermatophytosis (ringworm) [2,3,4,5,6], *Aspergillosis spp* [7,8,9,10,11], Candidiasis (moniliasis)[12,13,14], Coccidioidomycosis and Mucormycosis [15, 16, 17],Cryptococcosis [18], Histoplasmosis [19], Phycomycosis [20] and Zygomycosis [21].

5.2 Dermatophytosis

5.2.1 Introduction

Ringworm occurs in camelids—dromedaries and Bactrian camels, but also in domestic llamas, and wild ruminants. Mycotic dermatitis is among diseases of camelids caused by fungi. *Trichophyton verrucosum* is the main responsible dermatophyte although *T. mentagrophytes*, *Micosporium canis* or *M. gypseum* are sometimes involved [22, 23, 24, 25]. Dermatophytosis and candidiasis are of particular concern, due their worldwide diffusion and, for some of them, zoonotic potential. In all cases, early diagnosis is essential in order to accomplish an encouraging prognosis. Understanding of the epidemiology, clinical signs, and diagnosis of fungal diseases is important for the launch of effective therapeutic strategies. There are few published articles regarding mycotic dermatitis of camelids. This chapter is discussed fungal skin lesions of camelids, in detail.

5.2.2 Definition

Ringworm, or dermatophytosis, is a highly contagious infection of the keratinized tissue of domestic animals and man. It is one of the three common diseases caused by genera of fungi collectively called *dermatophytes*. There are few published records documenting dermatomycosis of the camel [26]. However, Falah, 2004, defined the dermatophytosis in camelids as a group of closely related fungi that utilize keratin for growth and its classical lesion are circular and known as "ringworm [27]. Previously, there are poor understanding about the susceptibility of camels to dermatophytosis. There is a misconception that camels are not infected by dermatophytes, as their keratin differs from the keratin of other animals. However, Kuttin *et al.,* (1986) [28] approved the contrary. Their survey on ringworm in camels, showed over 25% of young animals suffered from *T. verrucosum* infection, and less

than 0.5% of the camels had *T. mentagrophytes*. They also found that analyses of the amino acid of hair samples taken from human, camel and cow, showed 11% similarity in the compositions.

5.2.3 Causes

Based on the location of the infection, fungal diseases are classified into:
(I) Superficial mycoses, caused by pathogens confined to the stratum corneum except hairs.
(II) Cutaneous mycoses, caused by pathogens invading keratinized tissues (including hairs, horns and skin).
(III) Subcutaneous mycoses.
(IV) Deep mycoses which affect the upper and/or lower respiratory tracts
, as well as internal organs [29].
Approximately 30 species cause skin infections in various mammals and birds and relatively few species are routinely isolated. There are significant differences in the species of a relative importance among different animal hosts. There are also important geographic differences in the dermatophytes encountered and the prevalence of the disease. Dermatophytes, a group of keratinophilic fungi thriving on the keratin substrate, are the etiological agents responsible for causing cutaneous infections. These organisms belong to the three genera namely *Trichophyton*, *Microsporum* and *Epidermophyton* [30]. Infection may also be caused rarely by the members of the genus *Candida* and non-dermatophytic moulds belonging to the genera *Fusarium*, *Scopulariopsis* and *Aspergillus* [31, 32].
Several pathogenic dermatophytes (ringworm) infections have been described in OWC and NWC but they are scarce. Several dermatophytes spp have been isolated from camelid's skin lesions worldwide. The most common dermatophytes isolated from camelids are *Trichophyton verrucosum* [3, 22, 23, 24, 33, 34, 35, 36, 37, 38, 39, 103,104.], *Trichophyton mentagrophytes* [23, 28, 40, 103, 104], *Trichophyton schoenleinii* [5, 41, 42,103, 104, 105], *Trichophvton sarkisovii* (*Trichophyton sarkisovii* was isolated from herds of camels in Kasakhstan and was claimed to be specific of camelids, but this species is now synonymised with *T. mentagrophytes* [43, 44, 45] , *T. equinum , T. concentricum, T.tonsurans, T.violaceum, T. soudanense* and *T. rubrum* were also reported in India[103, 104.] *Microsporum gypseum* [6, 41, 46, 47, 48] , *Microsporum canis* [3, 22, 39, 103]. *M. audouinii*, *M. canis, M. nanum, M. ferrugineum* [103], Human pathogenic fungi (*Epidermatophyton floccosum* and *Scopulariopsis brevicaulis*) were also isolated from camels in India [103]. Moreover, *T. schoenlenii, T. verrucosum, T. mentagrophytes, T. tonsurans, M. audouinii* and *M. canis.* were isolated from 165 suspected camels in Dhamar area, Yemen, where almost half of the study animals were infected with T. schoenlenii (49.6%, $\chi 2 = 102$, $P < 0.05$). In addition, these *dermatophytes* occurs as zoonotic a prevalent skin disease in humans [105].
The other fungi rather than dermatophytes are also isolated. These fungi are *Sporothrix schenckii* [33]*; Candida albicans* [14]*; Penicillium vinaceum, Pseudorotium, spp., Pseudoarachniotus spp., Allescheria spp., Mycelia sterile* [49]*, Cryptococcus neoformans* [50], *Chrysosporium* [23]. Some fungal flora genera are also isolated from camel healthy skin. These flora are *Aspergillus, Penicillium, Mucor, Alternaria alternate, Rhizopus, Chrysosporium, Acremonium , Scoupolariopsis , Cladosporium, Fusarium, Psuedallescheria boydii* and *stachybotrys atra* [51]. The frequently isolated Yeasts are *Candida,Geotrichum candidum and Malassezia* [52].

5.2.4 Geographic distribution

The researcher reported ringworm of camels in different geographical areas around the world. Ainsworth and Austwick, 1959 [53], reviewed critically dermatophytosis in animals. They stated that ringworm in the camel is briefly reviewed by Curasson (1947) [33]. They also mentioned, "This condition is not well understood and the status of *Trichophyton langeroni* (*Grubyella langeroni Baudet*) and *Aleurisma lugdunense* VUil" (from dromedaries "from Algeria in the Hague zoological gardens") and *T. dankaliense* (from a piece of camel skin) is uncertain [28, 54, 55].

A few reported cases of camel ringworm led to consider the disease as a rare conditions [56]. Later on, several dermatophytes cases have been reported in different area in the world. *T. dankaliense* has been reported in Northern Somalia and the Ogaden area, it was affected camels and humans. However, *T. mentagrophytes*, *T. verrucosum* and *Microsporum gypseum* were isolated from camel ringworm in Australia and Israel [26, 28, 53].

In India ringworm due to *T. schoenleinii* was recorded [42]. In 2006, Ghoke *et al.,*[56], studied the prevalence of dermatophytosis in Indian dromedary (*Camelus dromedarius*) belonging to an organized farm located in Kutch area of Gujarat. *Trichophyton verrucosum* was only isolated from 2 camels with cutaneous lesions between totally 18 camels of both sexes. The different age groups were showing skin lesions on several body sites. However, no epidemiological investigation was conducted to establish the source of infection and they were suggested that *T. verrucosum* infection should be considered in the differential diagnosis of dermatitis. Tuteja *et al.,* (2013) [103], was isolated *Epidermatophyton floccosum* and *Scopulariopsis brevicaulis* as a causative agents of skin infections in two camel herds. Sporadic cases of skin infection in individually maintained camels caused by species of common dermatophytes were also reported in India in 2013 [104].

In Egypt, Mahmoud, (1993) [23] diagnosed the fungal infection between camels. The percentage of positive skin lesions with fungal infection were 48%. In addition, the younger individuals were more susceptible to this infection. *Trichophyton, Microsporum* and *Chrysosporium* were the most common genera. *T. verrucosum* appeared to be the main cause of ringworm in small camels while *T. mentagrophytes* infected older ones. El-Timawy *et al*., (1988) [22], also reported *T. verrucosum, T. mentagrophytes*, *Microsporum canis* and *Microsporum gypseum* in camels. In 2006, Amin *et al*., [57] examined a total of 47 skin scrapings from 27 local and 20 imported dromedary camels that showed skin lesions during summer and winter seasons. They found that ringworm infection rate was 14.81% and 12.5% in local camels in summer and winter, respectively, however, no cases of ringworm were observed in imported camels. Dewal *et al.,* (2017) [107] conducted a study on dermatophyosis in the village adjacent to Bikaner, Rajasthan. The examined a total of 16 dermal mycoses infected camels of either sex or different age groups. The found four cases out of 16 infected cases, were infected with dermatophytes which were *Trichophyton rubrum, T. verrucosum, T. schoenleinii* and *Microsporam canis*. They also mentioned that the dermal mycoses occur in majority of the camels during post rainy season and the major clinical manifestations were itching, alopecia, crusty circular lesions specially concentrated over neck, chest, axillaries, legs and abdomen.

In Saudia Arabia, mycotic dermatitis due *Cryptococcus neoformans* is reported in camels [50]. In addition, dermatophytosis due to *Microsporum gypseum* mixed with *Dermatophilus congolensis* in camels (Camelus dromedarius) was also reported [6].

In Iraq, dermatomycosis caused by *T. schoenleinii* was reported [5]. Whereas, Hussain (2009) [58], isolated *Tricophyton verrucosum, Microsporum canis,* and four non dermatophytes *"Penicillium brevicompactum, Ulocladium chartarum, Aspergillus fumigates*, and *Scopulariopsis bainier* from skin affections of camels in three different Iraqi Governorates. Two type of dermatophytes were isolated from 10 cases from 40 camels showed "dry scaly lesion" in one survey study between 2012-2013 in Al-Najaf slaughter house. The isolated fungus were *T. verrucosum* 60% and *T. tonsurans* 40% and non-dermatophytes (*Penicillium spp*., *Aspergillus niger*, *Aspergillus ochraceous*, *Geotricum spp*) (Master student theses unpublished, 2012, 2014). Mixed dermatomycosis and mange infection in camels accompanied with chronic granulomatous hidradinitis was also reported in camels in Iraq by Al-Salihi *et al.,* (2013) [2].

In Iran, 11 (77%) *Trichophyton verrucosum* and 3 (21%) *Trichophyton mentagrophytes* isolates were isolated from camel [59]. A mixed infection of *Trichophyton verrucosum* and *Nocardia asteroides* was also reported [52]. Whereas, Ebrahimi, *et al.,* (2007) [60], also reported the incidence of dermatophytes in 143 hair coat / skin scraping sample of healthy camels from Najafabad slaughter house.

In Sudan Dermatophytosis also reported in Eastern Sudan [24]. Mycotic dermatitis was also reported in camel in Alshowak, in Eastern Sudan and in Alobied in North Kordofan, Sudan [61].

In Oman, dermatomycosis is also reported in camels by Kumar *et al.,* (2012) [62]. They found ringworm the most frequent occurring conditions (95%) encountered throughout the year.

In Morocco, Driot *et al.,* (2011) [106] has been studied the epidemiology and histopathology of sarcoptic mange and ringworm in the one-humped camel at the slaughterhouses in the southern Moroccan towns. The mean prevalence of the disease was 16% among all animals, 44% among animals with skin lesions. Most of the concerned camels were young.

In Yemen, Najla *et al.,* (2016) [105] Isolated and Identified a potential zoonotic Dermatophytes from domestic camels in Dhamar area/ Yemen. They found that a total of 159 (96.4%) of the suspected camels were found to be infected with fungal infection during the direct KOH examination. The infection was significantly higher among young animals of ≤ 12 months (94.3%, $\chi 2 = 73$, $P < 0.05$). Majority of the cultured specimens showed positive growth (93.1%, $\chi 2 = 118$, $P < 0.05$), with high overall rate of dermatophyte infection that reach 83.11%.

5.2.5 Economic importance

Dermatophytes consider as a major public and veterinary health problem reported from different parts of the world. It causes a great economic loss in the camels industry. It has mainly severe effects on Leather Industry from the camel. It effects the quality of the hide due to the ability of dermatophytes organisms to break down the keratin in tissues such as the epidermis, hair, nails, feathers, horns and hooves [63, 64]. The hide of the dromedary in camel producer countries is mainly used for making whips and saddles [64] and to make a gourd-like container for water and milk [65]. Many countries have commercial tanning of camel leather such as Egypt, which is pioneered in this industry. Camel's leather is very versatile and has two unique properties. These are its exceptional tensile strength and an attractive grain pattern on the tanned product. These features ensure its demand for the manufacture of a

wide range of products such as; shoes and boot uppers, hats, fashion accessories, briefcases, garments, harness and sporting goods [64].
The disease has also zoonotic potential impact. In living hosts, dermatophytes usually remain in superficial tissues such as the epidermis, hair and nails. Serious consequences are uncommon and infections can be self-limiting. However, the illness may be disfiguring and uncomfortable, especially when the lesions are widespread. Infrequently, dermatophytes may invade subcutaneous tissues and (very rarely) other sites, especially in immunocompromised hosts.

5.2.6 Susceptibility

In general, younger animals are most susceptible for dermatophytosis [66, 67]. Animal less than one year of age are at greater risk for dermatomycosis and may reflect a lack of specific immunity acquired after first exposure, but also innate immune mechanisms, such as the quantity and nature of sebaceous lipids in the epidermis [68]. Older animals with decreased immune function also may be at increased risk for generalized dermatomycosis [24, 61, 69, 70, 71]. Dermatophytosis is a common skin disease in OWC under 3 years of age with a peak incidence age of 3 to 12 months. In NWC it is, however, very rare disease [17] and only *T. verrucosum* and *T. mentagrophytes* have been isolated from NWC so far. The skin lesions caused by *T. verrucosum* in the camels were very similar to those found in cattle. In both animal species, cows and camels, the younger individuals are more susceptible to the fungus. The infected suckling offspring did not infect lactating camels. There is no significant difference in the susceptibility of male and female camels to ringworm infection [24, 61]. However, contrast were recorded with a higher prevalence of ringworm infection in she camel (77%) than the males (23%) [37, 38].

5.2.7 Transmission of the disease and predisposing factors

Direct and indirect contact with infected animals (or asymptomatic carriers/or from the environment) and fomites are the modes of transmission of dermatophytes. However, the whole epidemiological features of ringworm in camelids, are yet unexplored. Outbreaks of dermatophytosis can persist due to the contamination of reservoir and fomites, such as tack and grooming equipment, and loans of equipment may spread infection between barns. Asymptomatic carrier camels are especially risky for the spread of infection to humans, because no precautions are taken to prevent potential transfer; however, such camels may progress to develop overt infection and more abundant arthrospore shedding. Khamiev, (1982) [37] examined 200 camels with skin lesions, of which 90 were positive for *T. verrucosum*, which named *T. camelius*. Of these 90 animals, 90% were younger than 2 years.The chlamydiospores of *T. verrucosum* and *T. mentagrophytes* may remain viable for up to 4.5 years in hair and cellular debris scraped off animals and left attached to fomites [17]. Infected camels have been shown to cause substantial environmental contamination and a significant airborne load of viable fungal elements. Al-Ani *et al.,* (1995) [5] discussed extensively the source of infection of *Trichophyton schoenleinii*, that occurred in 80 younger camels (6months-3 years), in Iraq. They mentioned several suggestions and stated that the source of infection was not established but could have been from human attendant, introduction of new camel calves into the herd and perpetuated infection within adult camels and spread to susceptible camel calves.

There are several predisposing factors in dermatophytosis. These factors include environment (high humidity, contamination and overcrowding), poor condition (nutritional imbalance, most probably Vitamin A and zinc deficiency and debilitating diseases), age (young) and immunity (prior exposure or immunosuppression. Studies in camels have showed that the prevalence of dermatophytosis to be higher in cold and rainy seasons than in hot and dry seasons [24, 72, 73].

5.2.8 Pathogenesis

There are different possibilities, when dermatophytes contact the skin of the camels (Figure.5.1). The fungi may be:

- Rebuff mechanically
- Failure to initiate residency because of its inadequacy to compete with skin normal flora
- Initiate residency but doesn't show clinical lesions and become as asymptomatic carrier
- Initiate residency and show clinical manifestation of the diseases.

The injured skins, lesion scars, are the possible route of entry for the dermatophytes. Arthrospores or conidia cause infection. Resting hairs lack the essential nutrient required for the growth of the organism. The hair invasion by dermatophytes has been studied extensively [74, 75, 76, 77, 78]. Commonly, dermatophytes do not invade living tissue. The sole pathogen mechanism is the invading the uppermost, non-living, keratinized layer of the skin namely the stratum corneum and produces exo-enzyme keratinase (irritants toxins or allergens). These substance penetrate the living epidermis and enter the dermis, where blood vessels are capable of responding to the threat of toxic or allergenic material and induces the inflammatory reaction at the site of infection [79, 80, 81, 82].

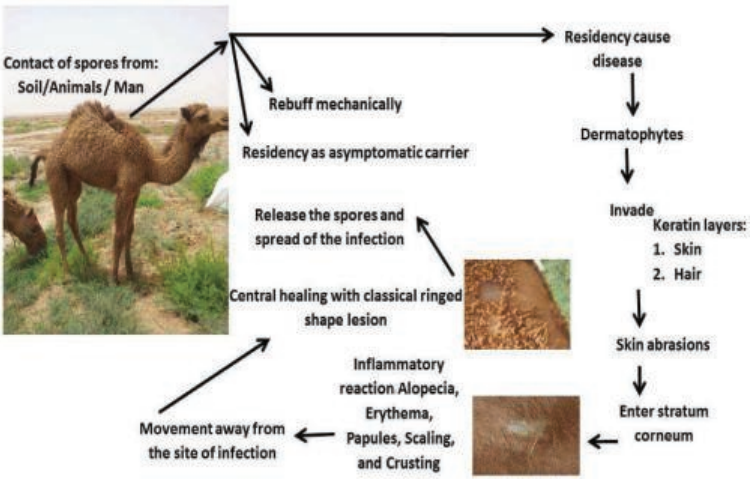


Figure.5.1: The pathogenesis of dermatophytosis in camelids.

The traditional signs of inflammatory reactions such as Alopecia, Erythema, papules, scaling, crusting and alopecia (loss of fur) are seen at the infection site. Inflammation causes the pathogen to move away from the site of infection and take residence at a new site. This movement of the organism away from the infection site produces the classical ringed lesion [83] (Figure.5.2.A, B&C). The infections caused by dermatophytes are commonly introduced to as "tinea" or "ring-worm" infections due to the characteristic ringed lesions [84].

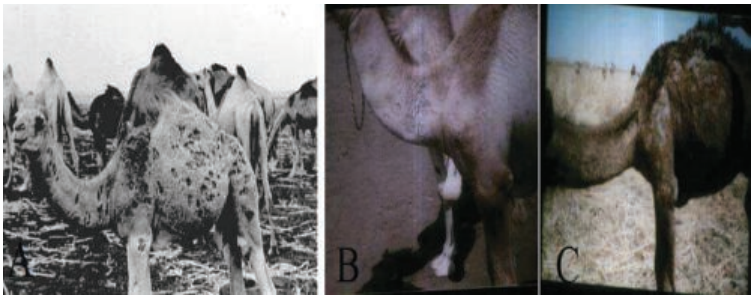


Figure.5.2. A,B &C: Classic dermatophytosis ringed lesions in the skin of camelids

The initial residency of dermatophytes led some researcher to describe it as a biological contact dermatitis [85]. The dermatophytes cope to maintain their existence on the skin, their survival largely depends on not evoking a severe inflammatory reaction. It manages a long-term evolutionary process and adapt itself to survive on the skin of a particular host and, under ideal parasitic conditions, elaborate minimal amounts of toxins or allergens. Dermatophytosis is a self-limited disease in large animals. The duration of clinical infection is one to four months. Reinfection is uncommon. With animals suffering from severe, chronic, or recurrent dermatophytosis, significant environmental (filth, moisture, or crowding) or immunosuppressive (underlying diseases or deficiency) factors should be suspected.

5.2.9 Clinical signs

The clinical signs of camel dermatophytosis infections are extremely variable in their clinical presentation. There are two clinical types the mild (local lesions) and severe (generalize lesions). The severity of the lesions depends on the several factors such as the age of the camels, the species of the pathogens and immunity of the animals. The classic lesions in most cases in camels are alopecia associated with erythema, Papules, Scaling, and Crusting.

The mild infection is well demarcated as grey-white lesion with active inflammation at the periphery, that is well occurred commonly on the face, legs, neck and head of the animals. Small round alopecic areas are surrounded the lesions. Depending on the size and duration of the lesion, there may be central crusting or central healing. These lesions may also coalesce and make large lesions. The severe type is a more generalized. The infection occurs as extensive areas of scarring on head, neck, limbs and flanks. The lesions appear initially as slight scaling of the skin on different parts of the body and head (more common around the mouth and eyes). Two to three weeks later, heavy incrustation on different parts of the body develops, and multiple large

lesions may appear in flanks, neck, chest and legs. The lesion typically consists of an area of alopecia and a prominent encrustation accumulation and scale formation (Figure.5.3.A&B).

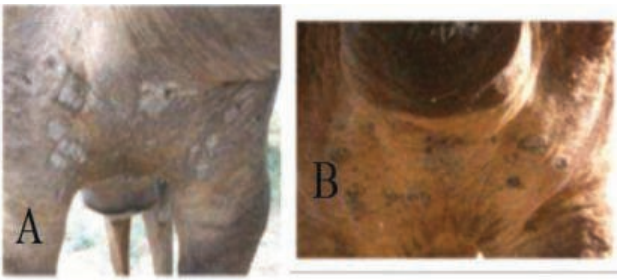


Figure.5.3. A& B: Camels dermatophytosis with typical lesions consists of an area of alopecia and a prominent encrustation accumulation and scale formation

Camel suffering from severe dermatophytosis type develops signs of emaciation and weakness. This lesion may initially be confused with mange; however the diagnostic tools will differentiate the diseases [86].

Most camel dermatophytosis occurs in cold season (winter) and spontaneous recovery appears in affected camels, where the lesions are starting to regress in size and fibre growth resume after 8-16 weeks in early spring. Meanwhile, the treatment of the camels will speed the recovery. There are several studies that described the clinical appearance of dermatophytosis in camels.

In Sudan, Fadlelmula, (1994) [24], presented the survey on camel ringworm. The diseases diagnosed in 217 out of 498 young camel calves under two years old with a peak incidence in autumn and winter. The prevalence among male and female was similar and the lesions were observed mainly on the head, neck and shoulder with frequent extension to the flanks and limbs. In this study, the researcher stated the isolation of *Trichophyton verrucosum* in pure culture for the first time from camel ringworm in the Sudan. Wisal, and Salim, (2010) [61] presented also dermatophytes outbreak in one Hundred thirty six camels in Sudan. They isolated seventy seven *Trichophyton verrucosum*, 47 *Trichophyton mentagrophytes*, 9 *Trichophyton schoenlenii* and 3 *Trichophyton tonsurans*. Both female and male camels were susceptible and camels less than 3 year old were more susceptible to infection. The skin lesions were extremely variable in distribution from multifocal to generalized lesions. The typical lesions were circular with peripheral expansion and central-like covered by grey powdery crust. Occasionally, lesions may spread to the periphery, become confluence and produce a moth- eaten appearance of the fur.

In Saudi Arabia, Gitao *et al.,* (1998) [6], described mixed infection of *Microsporum gypseum* and *Dermatophilus congolensis* in camels reared on a dairy farm. Severe lesions demonstrated in both calves and young camels. The discrete, circumscribed, crusty and hairless lesions were observed on the neck and forelegs of the calves. However, camels of varying ages showed extensive hair matting with crusty, hairless lesions, especially on the flanks. In Iraq, the clinical signs of dermatophytosis of natural and experimental *T. schoenleinii* was described by Al-Ani *et al*. 1995 [5], in one-humped camels in the desert near Baghdad. Slight scaling of the skin on the head and around the mouth and eyes was the initial clinical signs that appeared on the

camels in this outbreak. Heavy incrustation on different parts of the body appeared later. Within 2-4 weeks, new multiple lesions of 5-12 cm in diameter were developed in other areas including the neck, chest, and legs. The lesions typically consisted of an area of alopecia and a prominent whitish asbestos-like accumulation of scales. Emaciation and weakness were appeared on the affected camels. Same clinical features appeared on the experimentally infected camels. Spontaneously recovery was also observed in some affected camels. The lesions regressed in size and hair growth resumed after 8-16 weeks in early spring.

In India, Tuteja *et al.,* (2013) [103], described skin infections in camel caused by *Epidermatophyton floccosum and Scopulariopsis brevicaulis* , which occurred particularly due to high rainfall and high humidity in the environment along with diurnal temperature variations. The camel infected with *Epidermatophyton floccosum showed* fast spreading lesions and peculiar as if hairs were burnt with fire leaving behind ash deposit over the skin. The lesion were observed throughout the body. All ages of the camel were affected but calves were more severely affected. The pronounced dryness of the skin coat was observed and alopecia was seen after lesion necrosis. The affected camels suffered from itching, uneasiness and resulted in weakness and debility of the animals. Whereas the camels infected with *Scopulariopsis brevicaulis* showed several large (5cm in diameter) hyperkeratotic nodules on the abdomen. The lesions more observed under the hairy portion of the skin. Incrustation of the nodules occurred after 15 days which gave appearance of patchy skin necrosis.

5.2.10 Diagnosis

The contagious and zoonotic nature of dermatophytosis obliges veterinarians to maintain a high index of suspicion of this disease. Dermatophytosis should be suspected in any camels showing lesions comprising combinations of alopecia, erythema, papules, scaling, and crusting [87]. The length, complexity, potential toxicity, and cost of treatment required depend on accurate and early diagnosis. Different methods have used to make a confirmed diagnosis of dermatophytosis. In addition to conventional methods [87], molecular [88, 89] methods have been used extensively in recent years.

The World Organization for Animal Health (OIE), (2008) [90], set up an Ad Hoc Group on diseases of Camelids to determine the OIE-listed diseases that should be considered significant in camelids. In addition to the diseases of other domestic animals for which camelids could potentially be pathogen carriers. Camel diseases divide into three groups according to OIE Ad Hoc Group:

1) Significant diseases
2) Diseases for which camelids are potential pathogen carriers
3) Minor or non-significant diseases

Fungal diseases classified as one of the significant diseases.

The difficulty in the diagnosis of dermatophytosis in the camels depends primarily on two factors. First is the absence of standardization of the collection of clinical specimens, because of the hardness of the skin of the camels. Second, is related to the mycological techniques, and the lack of commercial availability for most of the diagnostic reagents needed in camels.

The intention in diagnosing dermatophytosis is to investigate the infiltration of the epidermis or hair shaft by a dermatophyte. Wood's lamp examination, direct

microscopy, culture, and biopsy, consider as the principal complementary diagnostic methods (conventional methods), which should be routinely performed. A biopsy specimen can be useful in unusual presentations, and the results may surprise the clinician when symptoms suggest another diagnosis. None of these is always reliable. However, histopathology is required in some cases for optimum sensitivity and specificity [66].

A. Specimen Collection

A sufficient amount of skin samples should be taken correctly from the edge of the infected area, which coincide to the active zone of the lesion. Hair is also collected for the isolation of dermatophytes. The suspected ringworm lesion and hair samples should be collected by the specialist veterinarian and experienced staff. The samples should be collected before any local or systemic antifungal treatment, to ensure the efficiency of mycological examination. The samples should be submitted with a filled history sheet including all the information concerning the sick animal.
A stubble and broken hair at the advancing periphery of an active lesion should be collected using forceps. Whereas, skin scraping from the lesion must be taken by sterile scalpel blade or skin Plucking. The skin should be disinfected with 70% ethanol before sampling for mycological culture.

B. Direct microscopic examination

Clearing technique is necessary for human's ringworm because of the endothirx infection patterns, however, most animal fungal infection are dominated by ectothrix arthrospore patterns, and can be examined by simply suspending the specimens in mineral oil. However, most diagnostic laboratory still use clearing method. Simply, 20% potassium hydroxide (KOH) add to the hair and keratin in small test tube. The test tube is heated for 15-20 seconds (avoid boiling) or allowed to stand for 30 minutes at room temperature. Then few drops of precipitate are placed on slide and cover slide is gently placed and then examine under microscope. Characteristic hyphae and/or arthrospores might be seen (Figure.5.4.A&B). This test is required considerable skill, and failure to observe hyphae or spores does not exclude the diagnosis; however, the rapid diagnosis from microscope enables treatment and control methods to be initiated without the delay associated with fungal culture.

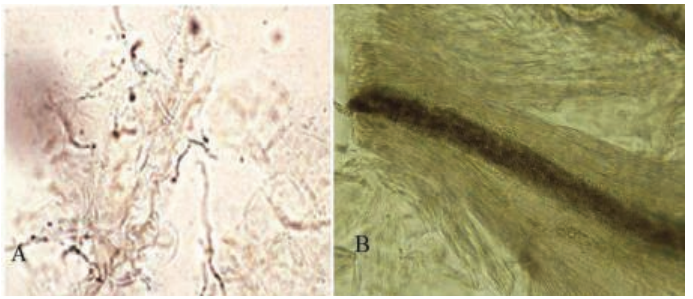


Figure.5.4.A&B: Direct smear from dermatophytosis infected skin using Potassium hydroxide (KOH) preparation. A. arthrospores and hyphae, B. chains of arthroconidia

C. Fungal culture

Identify the species of dermatophyte is done by fungal cultures, which, can be useful in understanding the source of the infection and targeting preventive measures appropriately. Fungal culture is necessary for uncertain, diagnosis in direct microscopic examination, or the infection is resistant to standard treatment. All fungi require several specific selective medium for growth and reproduction. The requirements for growth are less stringent than for sporulation, so it is often necessary to try various types of media when attempting to identify a fungus in culture. Sabouraud's dextrose agar containing antibiotic(s) (chloramphenicol ± gentamicine) and cycloheximide (Actidione) and brain-heart infusion agar, Dermatophyte Test Medium (DTM), either in petri dishes or screw top tubes are commonly used in veterinary mycology as a primary isolation media. The media may be enriched with 5% to 10% sheep blood to support the growth of certain fungi. The incorporation of cycloheximide in the culture medium will prevent the growth of a majority of moulds, but also of some yeast that could restrain the recovery of dermatophytes.

Ready-to-use Sabouraud's agar plates or slants are commercially available under various names from several laboratories (such as Himedia, bioMe´rieux, Bio-Rad, AES, Oxoid or Becton-Dickinson). However, great variations may be observed from one manufacturer to another in composition and pH of their culture medium, and, therefore, in performances of the medium regarding its ability to support fungal growth [91]. Most fungi also thrive on Potato Dextrose Agar (PDA), but this can be too rich for many fungi, so that excessive mycelial growth is obtained at the expense of sporulation. Some dermatophytes that cause disease in camelids have special nutritional or incubation requirements.

Fungal cultures should be examined daily for the first five days. Colonies appear in 5 days to 4 weeks, depending on the organism. Colony morphology can differ with the medium. Descriptions are usually based on Sabouraud agar or other fungal culture media that also be used for isolation. Dermatophyte species can be identified by the colony morphology; the appearance of microconidia, macroconidia and other microscopic structures (Figure.5.5); biochemical characteristics such as urease production; and nutritional requirements. Specialized tests such as the ability to penetrate hairs in vitro, or mating tests (that are usually available only at reference laboratories) may be used occasionally. Differential media (e.g., bromocresol purple - milk solids glucose) can be helpful during differentiation. A slide prepares from the fungal culture overflow with water containing Tween 80, bromocresol purple or lactophenol cotton blue stains can be used to examine the fungal structures. Hyphae and conidia from mature fungal colony can be seen intertwined with each other's on a microscope slide.

Cultural characteristics of dermatophytes spp that have been isolated from camelid's skin lesions worldwide are described briefly in text book and literature (Table.5.1). *Trichophyton verrucosum* isolated from skin and hair taken from the younger camels was described by Kuten, (1986) [28]. The fungus showed slow-growing, glabrous, white to ochraceous colonies with abundant chlamydospores and antler-like branching hyphae. Stimulation of growth and microconidia was seen on the enriched basal medium with thiamine hydrochloride and inositol. However, older infected camels revealed *T. mentagrophytes* colonies. These colonies were white-yellowish powdery colonies with dark red pigment on the reverse side of the colonies. Microscopically, fungus showed clusters and lateral spherical microconidia and club-shaped to spindle shaped macroconidia with 4 or more cells, as well as many spirals.

Mohammod, (1993) [23] were recovered and described sixteen species belonging to nine genera of keratinophilic and cycloheximide-resistant fungi from diseased camels. Al-Ani et al., (1995) [5] was also described the colony morphology of T. schoenleinii isolated from a typical lesion area of alopecia and prominent whitish asbestos-like accumulation of scales. Inoculated plates that incubated at 25 ^{o} C showed growth after 10 days. The colonies were similar to those described for *T. schoenleinii* in human and other species. The colonies appeared as small raised white, leathery types and in time the colour became tan to brown with folded surfaces. *T. schoenleinii* hyphae appeared in the microscopic examination as septate hyphae with very few microconidia while the macroconidia were absent. Gitao *et al.,* (1998) [6] described the *Microsporum gypsium* isolated from camels in Saudi Arabia. While full description and identification of dermatophytes from infected Camels also presented by Wisal *et al.,* (2010) [61].

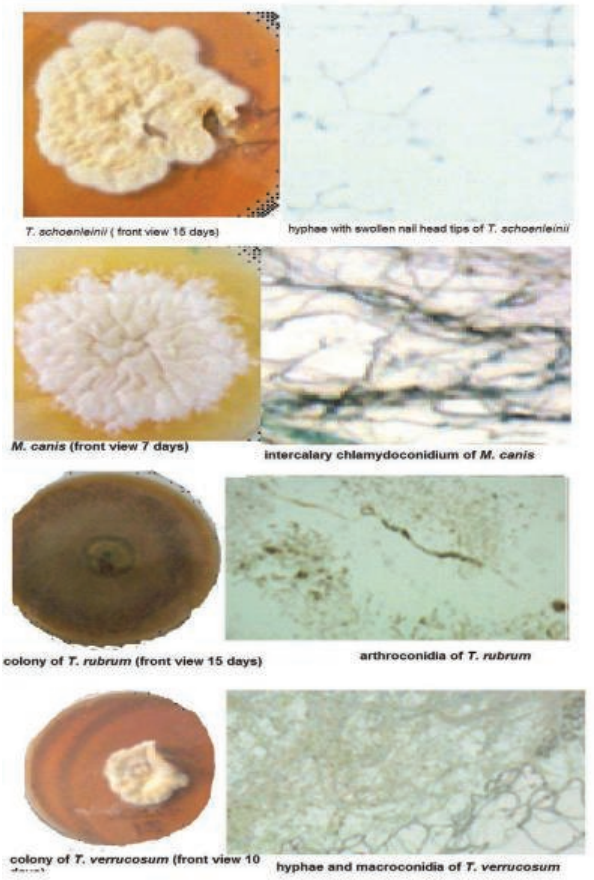


Figure. 5.5: Colonies features and microscopical appearance of some dermatophyes isolated from camelids.

(Table.5.1). Isolation and identification of Dermatophytes from infected Camels. Sudan J. Vet Res. (2010).25: 94-53).

Species	Direct examination	Macroscopic appearance	Microscopic Features	Urease test
T. verrucosum	Ectothrix	Cream, folded, heaped, button like and waxy	Chains of chlamydospores	*Negative*
T. mentagrophyte	Ectothrix	Ggranular, white in the obverse and brown in the reverse, hard in texture	*Coiled spiral hyphae and numerous microconidia*	Positive
T. schoenlenii	Favic hyphae	Glaborus, cream to grey and yellow to light brown in the reverse	Antler hyphae	*Positive*
Trichophyton tonsurans	*Endothrix*	Velvety, folded, heaped, pale yellow obverse and dark yellow on the reverse	Numerous microconidia different size and shape	*Positive*

Tuteja *et al.,* (2013) [103] was isolated and described *Epidermatophyton floccosum* and *Scopulariopsis brevicaulis* from 2 camel herd infection in India. The *Epidermatophyton floccosum* grew moderately rapidly and became mature within 10 days following incubation at 28 °C. The colour of the lesions was brownish yellow to olive grey or Khaki from the front and orange to brown with an occasional yellow border from the reverse. Surface was flat and grainy initially and became radically grooved and velvety by aging. Microscopically septate, hyaline hyphae, thin walled macroconidia, 3-5 celled, smooth and clavate shaped with rounded ends, single or in clusters. Chlamydoconidium like cells, as well as arthroconidia, are common in older cultures. The *Scopulariopsis brevicaulis* grew also moderately rapidly and were granular to powdery. Front colour was white initially and became light brown or buff tan in time. Reverse colour is usually tan with brownish centre. Microscopically septate hyphae, conidiophores are hyphae-like and simple or branched. Lemon-shaped, roughened conidia with truncated bases produced from the tips of annellidic conidiogenous cells. The annellides were produced songly or in penicillate heads. These were cylindrical and slightly swollen as has been reported by De-hoog *et al.,* (2000) [29]. Full description of the growth characteristic of species dermatophytes that caused camel dermal mycoses was made by (Tuteja *et al.,* 2013) [103, 104]. The samples were collected during five years from camel rearing villages in the Rajasthan state in India. Out of the total 207 fungal isolates from camel skin infections included 33 isolates of *Microsporum* spp. and 35 of *Trichophyton* spp. (Table.5.2)

Table.5.2: Macroscopic appearance and microscopic features of some dermatophytes sp. Isolated from camelids

Species		Macroscopic appearance	Microscopic Features
Microsporum Spp. In general, colonies are glabrous, downy, wooly or powdery. Colonies growth on SDCA at °28C may be slow or rapid , colonies size and colour depending on species. Septate hyphae, microconidia and macroconidia are produced. Conidiophores are hyphae are produced in some species.	*M. audouinii*	Flat, spreading, greyish-white to light tan-white colonies having a dense suede-like to downy surface (mouse fur in texture), reverse (yellow-brown to reddish- brown) some strains showed no reverse pigment.	Rarely produced Macroconidia and Microconidia. Sterile culture or thick-walled terminal or intercalary chlamydoconidia are produced.
	M.Canis	Flat, spreading, white-creamy, dense cottony surface (some showing radial grooves), reverse (bright-golden yellow to brownish yellow but non - pigmented also occurred).	Typically, spindle-shaped with 5-15 cells Macroconidia, verrucose,thick-walled with terminal knob. Few pyriform to clavate microconidia were also observed.
	M. ranum	Powdery, cottony, thin, moderately fast growing , spreading, velvety or flat some showing radial or shallow furrows, white to dark beige from front, reddish-brown from reverse.	Septate hyphae, 1-4 celled (usually 2), thin walled and oval-elliptical Macroconidia, club-shaped vay abundance Microconidia.
	M. ferrugineum	Slow growing, waxy, glabrous, convoluted thallus , cream-buff surface, rapidly becoming downy and pleomorphic.	Irregular branching hyphae, prominent cross walls "bamboo hyphae", chlamydoconidia.
Trichophyton Spp. In general, colonies grow slowly to moderately rapid. Septate hyaline hyphae, conidiophores are poorly differentiated from the hyphae , predominant microconidia are one-celled and round or pyriform in shape and numerous, solitary or arranged in clusters , very few macroconidia are multicellular (2-or more- celled), smooth, thin or thick-walled and cylindrical, clavate or cigar- shaped, arthroconidia are observed.	*T. verrucosum*	Slow-growing, small, button- or- disc-shaped, white-cream, suede-like-velvety surface, raised centre with some merged growth, reverse (non-pigmented to yellow)	Irregular hyphae with many terminal and intercalary chlamydospores (often chains). Some hyphae have broad –club- shaped – occasionally divided tips called "antler" effect. Rarely produced Macroconidia with characteristic tail-or- string bean shape.
	T. mentagrophytes	Flat, white-cream, powdery-granular surface, central folding-or- raised central tufts or pleomorphic suede - like-to- downy areas, reverse (yellow-brown to reddish-brown)	Microconidia appears as dense clusters, numerous single-celled , hyaline, smooth-walled and predominantly spherical to sub-spherical in shape, clavate to pyriform forms occasionally occurs. Varying numbers of spherical chlamydoconidia, spiral hyphae and smooth, thin-walled, clavate shaped, multicelled macroconidia may also be present.
	T.schoenleinii	Slow growing, waxy- or- suede-like with a deeply folded honey- comb-like cream to orange brown thallus and some subsurface growth, difficulties to maintain typical convoluted form and rapidly become flat and downy, No reverse pigmentation is present.	No Macroconidia and Microconidia are seen in routine culture , numerous chlamydoconidia, characteristic antler"nail head"hyphae also known as favic chandeliers may be present in older cultures.
	T. equinum	Flat, some may develop white-buff, gentle folds-or- radial grooves, suede-like-downy in texture, deep- yellow submerged fringe and reveres dark red.	Abundant Microconidia which may be clavate to pyriform and sessile or spherical and stalked are formed laterally along the hyphae. Macroconidia are only rarely produced, clavate , smooth, thin-walled and variable size. Nodular organs might be present and Microconidia often undergo a transformation to produce a bundant chlamydoconidia in old cultures.
	T. concentricum	Slow-growing, raised, folded, glabrous becoming suede-like, white-cream, reverse(buff-yellow-brown to brown)	Broad, much-branched, irregular, often segmented, septate hyphae (having "antler" tips, chlamydoconidia presents in older culture, Microconidia and Macroconidia are not usually present produced , some isolates occasionally produce clavate to pyriform microconidia, hyphal segments may artificially resemble macroconidia.
	T. tonsurans	Moderately slow growth, highly variable suede-like, powdery or velvety, flat with a raised centre or folded, often with radial grooves. White, beige, greyish, pale or sulphur yellow, roseor brownish on surface , reverse (varies from yellow-brown to reddish-brown to deep mahogany.	Broad , irregular, much branched with numerous septa hyphae , numerous various shapes and sizes (pyriform, tear drop, club shaped or balloon shaped) Microconidia, intercalary and terminal chlamydospores found in old culture, rare and smooth walled distorted macroconidia .
	T. violaceum	Slow growing, glabrous or waxy, heaped, folded, deep violet ,cultures often become pleomorphic.	Hyphae are relatively broad, tortuous, much branched and distorted. Young hyphae stain well in lactophenol cotton blue and show small central fat globules and granules. Numerous chlamydoconidia are usually present, in older cultures.
	T. Soudanense	Slow-growing, flat-folded, suede-like surface, broad fringe of submerged growth, reverse(deep apricot-orange).	Hyphae often show reflexive or right-angle branching, pyriform microconidia and numerous chlamydoconidia are often found in older cultures.
	T. rubrum	Slow, hyper-pigmented growth, showing a violet to red-violet-red glabrous surface with radial furrows, reverse (deep violet to red-violet)	Few pyriform lateral microconidia, pencil shaped macroconidia, arthroconidia produced from hyphae and macroconidia.

Histopathology

Histology may be useful and has been proposed by some authors as a simple diagnostic for fungal infection in camels. Indeed, histological examination of skin biopsies stain with periodic acid Schiff (PAS) and Gomori's methenamine silver special stains, Acid Orcein-Giemsa (AOG), in addition to haematoxylin and eosin (HE) stain ,seems to be the more sensitive method for the of diagnosis of dermatophytes.
The histopathologic features of dermatophytosis are as variable as the clinical lesions. There is no diagnostic characteristic histopathological appearance for dermatophytosis. However, the most histopathological features seen in dermatophytosis are classified as [69]:

- Perifollicullitis, folliculitis and furunculosis.
- Superficial perivascular dermatitis (spongiotic or hyperplastic) with orthokeratotic or parakeratotic hyperkeratosis of the epidermis and hair follicles.
- Intraepidermal vesicular (sponigiotic) or pustular dermatitis.

Some research article described the histopathological features of the skin biopsies from camels infected with dermatophytosis. Skin sections showed hyperkeratotic areas with sub-acute inflammation, a severe invasion of fungal hyphae and many hairs with ectothrix spores [28].
Sections of skin with a mixed infection of *D. congolensis* and *M. gypseum* [6] revealed congestion, hyperkeratosis with abundant keratinaceous debris. The epidermis was thickened, and the dermis diffusely infiltrated with polymorphonuclear leucocytes. The keratinised layers were invaded by abundant *D. congolensis* filaments and coccoid forms featuring transverse and longitudinal divisions. Sections stained with PAS revealed abundant mycotic filaments in the epidermis. Histopathological changes of mixed dermatomycosis and mange infection in camels accompanied with chronic granulomatous hidradenitis also described [2]. An examination of the skin sections revealed dermatitis characterised by acanthosis with marked parakeratosis, hyperkeratosis and crust formation, rete-pegs, hyperplastic changes in sebaceous glands and hair follicles cells, granulomatous hidradenitis and infiltration with eosinophils, lymphocytes, macrophages and neutrophils. Sections stained with periodic acid-Schiff (PAS) and Gomori's Methenamine silver (GMS) stain, revealed large numbers of fungal arthrospores and hyphae coloured bright magenta with PAS and black with GMS.

D. Molecular biological technology in the Diagnosis of Dermatophytosis

Conventional method in the identification of dermatophyte species is complicated and laborious due to the morphological similarity, variability, and polymorphism shown by dermatophytes. It is based on macroscopic and microscopic observations of their morphological features. Thus, accurate identification is time consuming and requires a significant level of knowledge and technological expertise. Some laboratory use of the mating test as a means of identification, however, it is not practical because many of the anamorphic species lack a teleomorph. The scientists focused on molecular analyses dermatophyte genomes in the diagnosis that is the simple and accurate identification techniques and would clear several problems in the traditional morphology based taxonomy. With these expectations, many investigators have focused their research on the nucleic acids of dermatophytes.

Davidson *et al.,* [92] analysed the G + C content of chromosomal DNA isolated from 34 dermatophyte species. It was belonging to the three genera, *Trichophyton*, *Microsporum*, and *Epidermophyton* and reported that it ranged from 48.7% to 50.3% and is narrow when compared with the range of 48–61% reported in a single genus, *Aspergillus*. This observation indicates a genetic homogeneity among the dermatophytes in contrast to their phenotypic and ecological variation. Subsequently many investigators have focused on mitochondrial DNA (mtDNA) and ribosomal DNA (rDNA) of dermatophytes and gradually determined the phylogenetic relationships among dermatophyte species. These data have widely contributed to the development of techniques for the identification and epidemiology of dermatophytes based on molecular technology, as reviewed by Blanz *et al.,* [93] and Kac, [94]. Further development of molecular diagnosis of dermatophytosis requires the investigation of additional molecular markers for diagnostic tools targeting multiple loci as well as the improvement of techniques [95]. Rapid molecular diagnosis techniques of dermatophytes have been used successfully in horses. Some investigators used a rapid DNA extraction method directly from the hair samples and the total 30 DNA extracts were subjected to PCR using specific primers for dermatophytes group. This PCR resulted in 22 (73.3%) positive samples within 8 hours [96]. Another investigators compared between molecular and traditional diagnostic methods in the diagnosis of dermatophytosis thirty-eight racehorses. PCR is fingerprinting profiles using simple repetitive (GACA) 4 primers showed that all diagnosed horses had the same pattern profile. Oligonucleotide sequencing of CHS1 gene PCR products confirmed *Trichophyton mentagrophytes* as the infectious agent [97]. The PCR-based molecular diagnostic method is an accurate, sensitive and specific and offers very rapid precise diagnosis of dermatophytosis in horses [96, 97] and rabbits [98] as well as in human [99]. Camel dermatophytosis is still needed for the development of more promising diagnostic methods, including molecular techniques that, can be detected directly in clinical samples. Rapid field diagnosis of camel dermatophytosis is very essential. Camels are always lived out of reach of the diagnostic laboratory and rapid and appropriate identification of the causative species will be helpful in the treatment as well as in control by establishing the source of infection and thereby plans to manage and control it.

5.2.11 Differential diagnosis

The diagnosis of ringworm depends on evidence of infection, the appearance of the characteristic lesions and the presence of fungal mycelia and spores. Diagnostic confirmation is made by demonstration of fungal elements in a scraping or biopsy. The owner's camel well knows ringworm and they are able to differentiate this dermatitis from other skin infections. The differential diagnosis list of ringworm, which may be confused with diseases having similar clinical profiles are:

- Zn deficiency (parakeratosis) by tenacious thick crusts and response to treatment with minerals.
- Sarcoptic and Psoroptic mange, in which mites can be demonstrated in scrapings.

5.2.12 Treatment

Dermatophytosis considers as self-limiting disease, with spontaneous remission occurring within four months. The successful treatment of the disease requires always proper diagnosis. Many topical treatments have been reported to be successful in camels, but because spontaneous recovery is common, claims of efficacy are difficult to substantiate. Fungi are eukaryotic and have a mechanism

similar to mammalian cell that's why the development of novel and efficient antifungal drugs is still lagging behind. Hence it becomes very difficult to develop an antifungal agent that is more specific in targeting the fungi alone without any damage to infected patients. A variety of topical and oral antifungal drugs are used to treat dermatophyte infections. The contagious and zoonotic nature of this disease makes treatment highly desirable for Valuable individual farm animals and camels, because this may well limit both progression of existing lesions and spread to others in the herd. A combination of topical and systemic therapy, along with clipping of the fur, is the optimal approach in animals. Clipping the fur from affected areas may assist with the mechanical removal of infected furs and aid the penetration of the topical antifungal drug onto the skin surface, although care should be taken to limit abrasions that might promote new lesions in the shorter term. Thick crusts should be removed gently with a brush, and the material burned or disinfected with hypochlorite solution. Before the treatment, lesions should also be clean with warm soapy water. The topical antifungal agents are available and approved by drug regulatory authorities for veterinary use vary markedly between countries. Topical application is of particular value in targeting fungal elements.A variety of common fungicidal and fungistatic agents such as iodine, 5% sulfur in sesame oil (w/v), 5% salicylic acid, coal tar phenols (3.25%) with copper acetate (0.58%) and hydroxyquinolines may be applied topically as ringworm ointments onto the affected areas. Treatment options depend on the limitations on the use of some agents in animals meant for slaughter. Individual lesions can be treated with miconazole or clotrimazole lotions. These topical treatments are probably of greater value in the early stages of an outbreak when the lesions are small and few. Ainsworth and Austwick, 1973 [53]used Captan@, in the treatment of camels dermatophytosis. It is a fungicide for ornamental plants. They sprayed on infected animals as a solution of 1:200. Captan@ mixture is stable for one week after mixing and the solution should be applied to the lesions and surrounding areas for 2 weeks.

Systemic therapy is recommended for use in farm animals and should give for the infected animals as a complementary step of therapy in most cases. In cattle, it includes the intravenous injection of sodium iodide (1 g/14 kg body weight) as a 10% solution repeated on several occasions. There are pertaining reports of beneficial effects of griseofulvin in ruminants and horses. However, griseofulvin is not recommended in camel because of its side effects such as nausea and diarrhea [100]. Griseofulvin is also teratogenic and should not be given to pregnant animals. Owners should wear gloves when handling the tablets. In addition, this drug does not have a minimum meat residue level under European Union legislation and cannot be used in food producing animals, in this area.

5.2. 13 CONTROL

A. Hygiene

Infected animal acts to widespread of the causative agent in the area as well as to the healthy animals and failure to control on ringworm outbreak. Early diagnosis and isolation and treatment of infected animals are necessary if the disease is to be controlled. Cleaning and disinfection of infected areas, stables and equipment with a commercial detergent or a strong solution (2.5-5 %) of the phenolic disinfectant, 5% lime sulfur, 5% formalin, 3% captan or 5% sodium hypochlorite is advisable to avoid recurrence of infection.

B. Vaccination

The immunoprophylaxis of dermatophytosis in animals has recently been the subject of a detailed review[101]. Most European countries and Scandinavia have achieved a great deal of success in preventing ringworm infection in cattle and horses. Live attenuated but virulent strains of *T verrucosum* that produce abundant microconidia have been used in extraordinarily successful mass vaccination campaigns, in cattle herds in former Eastern block countries and Norway. Vaccines include those containing highly immunogenic, non-virulent strains, or attenuated [102]strains of fungi, or those killed vaccines containing specific fractions of mycelia. Vaccination of all animals in the group is recommended, and isolation and treatment of infected animals and disinfection of premises and gear must be carried out at the same time. In camel vaccination programs against *Trichophyton* spp. and *Microsporum* spp. have been reported from Kazakhstan (Toleutajewa, 1994). Commercial Camelvac Tricho@ (IDT Dessau-Tornau ,Germany), has been successful used in the Republic of Kazakhstan. Before vaccination, ringworm was contagious in Bactrians and reached to 60.1% in less than one year Bactrians, after vaccination no ringworm cases reoccurred for several years. This vaccine is used also for prophylactic purpose with very good success. The Camelvac Tricho@ has also recently been successfully used in several camel herds in the UAE. Young dromedaries with ringworm lesions were vaccinated once. The lesions receded within 14 days and disappeared after 4 weeks.

C. Nutrition

Supplementation of the diet, particularly with vitamin A and zinc to young housed animals, should be encouraged as a preventive measure, because the disease to be a tendency for the poorly fed animals. Although ringworm can also occurred in well-nourished animal.

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5.3 Skin Candidiasis and miscellaneous fungal infection

Candida albicans is a common microbial inhabitant of the respiratory, alimentary, and genital tracts [1, 2]. In a variety of species, *C albicans* can be associated with cutaneous, systemic, and localized infections 1. It is usually sporadic infections and cause non-specific syndromes because of variation in the organs in which they localize. Candidiasis (moniliasis) is a common sporadic disease of the digestive tract caused by the yeast Candida spp. (most commonly *C. albicans*). In domestic mammals and humans, cutaneous infection with *Candida spp* is often associated with underlying immune suppression [3, 4, 5].

There is only few report of infection with a *Candida sp* in camelids. One case of gastric candidiasis had been reported in a neonatal llama, in Europe [6]. Skin lesion caused by *C. albicans* has also been diagnosed in young dromedary calves in the UAE after prolonged treatment with antibiotics [7]. The lesions caused *C. albicans* are resembled *D. congolensis* infections. The camel calves (6-week-old) had developed thick crusts near the hump in which hyphae were demonstrated with PAS stain.

Fungal dermatitis due to *candida albicans* have also been reported in an 8-year-old castrated male llama [8]. The llama were present with large, locally extensive areas of thick, coalescing crusts in sparsely haired areas of the axillary, inguinal, and perineal areas and around the muzzle. The crusts were firm and moist and could be manipulated away from the skin. Removing of the crusts revealed moist and red accompanied with a foul odor underlying skin. Scattered small pustules were also recognized in the affected areas. A pure culture of *Candida albicans* was obtained from the submitted fresh skin samples (Figure.5.6. A& B).

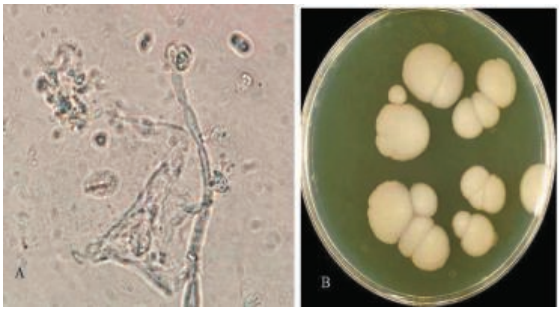

Figure. 5.6: A. Direct smear from dermatophytosis infected skin using Potassium hydroxide (KOH) preparation. Note the hyphae with buds and individual yeast cells, many with buds(40 X), B.Colonies of a pure culture of *Candida albicans* obtained from the submitted fresh skin samples.

The histological features of the punch biopsy specimens obtained from the axillary region were also described. There were marked orthokeratotic to parakeratotic hyperkeratosis with thick serocellular crusts composed of layered degenerate neutrophils, small numbers of RBCs, and myriad yeast organisms. The yeast organisms were 5 to 7 µm in diameter; approximately 5- to 7-µm-diameter pseudo-hyphae with nonparallel walls were also evident. The underlying epidermis was

moderately to markedly hyperplastic with multifocal areas of spongiosis, neutrophil exocytosis, and large intra-epidermal pustules composed of degenerate neutrophils. Within the underlying dermis, there was a marked, multifocal perivascular infiltrate of neutrophils, macrophages, lymphocytes, and plasma cells. According to histological features, the case was diagnosed as "severe, diffuse suppurative dermatitis with serocellular crusting, epidermal hyperplasia, and intralesional yeast and pseudohyphae in haired skin of the axilla." The llama was treated with daily topical application of nystatinc and chlorhexidine acetated ointments to the affected skin regions. Following treatment for 60 days, the llama fully recovered with regrowth of hair within the affected regions. Another female llama in the herd with similar, albeit less severe, clinical signs was treated similarly and responded completely to treatment.

Naturally skin candidiasis reported in dromedary calves, in India 2012 [9]. These cases of skin candidiasis in camel calves were treated topically with three formulations consisting of 2% potassium iodide; 6% sulphur in mustard oil; and 6% sulphur and 3% salicylic acid in mustard oil. All treatments showed ability to relief and minimise the morbidity in young camel calves due to skin candidiasis. Infections with *Coccidioides immitis* and *Conidiobolus coronatus* in camelids have also been reported [10, 11, 12].

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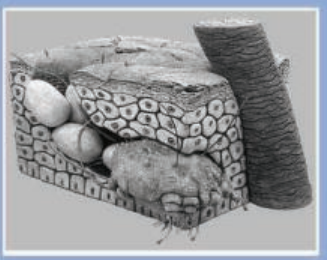
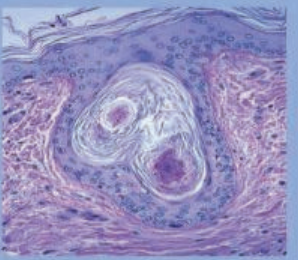
Chapter. 6
Parasitic diseases





Shows *Hylomma dromedarii*

Shows adult *Boophilus spp.*

Shows the infested ticks (larvae, nymph and adult stages)

Chapter 6: Parasitic skin lesions of camelidae

6. Parasitic skin Infestations of camelids

6.1. Introduction

Camelids are a very sturdy animal and well adapted anatomically as well as physiologically to stark climatic conditions of desert. Regardless, camel suffers from various endo and ecto-parasitic diseases, which are major constraints in improvement of camel health. These diseases cause substantial economic losses in terms of decrease in working capacity, growth and productivity. A wide range of parasitic infections can involve the skin and subcutaneous tissues of the camelids. The skin involvement may be transient, the parasite passing through the skin on its migration to the blood stream and so to a specific target organ, or the infection may be localised to the skin, depending on the species of parasite. In the tardy infections, the skin may be the primary site of infection or there may be a secondary invasion of the skin. All parasitic groups (protozoa, trematodes, cestodes, nematodes and arthropods) have species which can involve the skin or subcutaneous tissues. Ecto-parasites dermatoses are the most common skin disorders of large animals including camelids. It is a major health concern throughout the world problem as it may led to death of the animal. Clinical disease has been noted as causing severe economic losses; subclinical issues have yet to be addressed.
The infected camels suffering through-pruritus disfigurement, irritability, annoyance, secondary infection and myiasis is often great [1, 2, 3, 4]. Many of the ecto-parasites are important in the transmission of various viral, protozoal, helminthic, fungal and bacterial diseases. This chapter deals in details with camelids different parasitic skin diseases.

6.2. Skin parasitic infestation

6.2.1. **Protozoan infections** (Besnoitiosis or globidiosis)

Besnoitiosis is an acute or chronic disease caused by a coccidian protozoon of the genus *Besnoitia*. It affects a wide range of domestic (cattle, goats and horses) and wildlife hosts [5]. The characteristic feature of besnoitiosis is the formation of cysts (Figure.6.1) in the connective tissues of the skin, muscles and other organs [6]. The disease is of economic importance, where it occurs in Africa and other parts of the

world [7] and causes of reduction of the qualities of hides and skins for the leather industry.

Besnoitia is an obligate intracellular coccidian protozoon. The disease is transmitted mechanically by biting flies through sporozoites of the parasite on the mouth parts of the flies [8] or by ingestion of mature isosporan-type oocyst shed in the faeces of members of the cat family presumed to be the final host [9]. The sporozoites enter the blood circulation after the fly bite and invade endothelial cells of blood vessels of superficial tissues in which they multiply by endodyogeny [9, 10]. Subsequently, the tachyzoites that are merozoite-like endozoites released from the infected cells invade more endothelial cells and fibroblasts to produce large spherical cysts containing merozoite-like cystozoites or bradyzoites after an initial cycle of proliferation as endozoites [9, 11]. Lesions associated with the infection may be found in blood vessels, scleroconjunctiva, mucosae of the alimentary and upper respiratory tracts, testis, lymph node, endocardium, skeletal muscle and skin [12, 13, 14, 15, 16, 17].

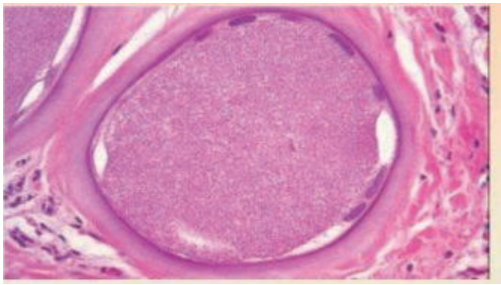


Figure.6.1: A high magnification of a cyst of Benoitia besnoiti in dermis (Benoititiosis or globidiosis). H&E.

In Camelids Besnoitia cysts have been reported in India by Kharole et al., (1981) [18], and Iran, by Tafti et al., (2001) [19] in the intestine of a dromedary. Fazil and Hofmann (1981) [20] stated that the besnoitiosis (which they called globidiosis) often occurred in camels with typical skin lesions on the distal part of the legs. The infection often became generalized with high fever and diarrhea indicating involvement of the intestines. Morbidity rate was low, but the mortality could reach 10% of clinically affected animals.The pathogenesis of the *Besnoitia* species occurring in the skin is still unknown [4]. *Besnoitia* is reported to affect cattle in Africa, Asia, Southern Europe, and south of America [8, 21]. After an incubation period of 6 to 10 days, affected cattle develop pyrexia, anorexia, photophobia, generalized lymphoadenopathy and warm, painfull swelling on the distal extremities and ventrum. The skin then becomes markedly thickened, lichenfied and alopecic and may fissure and ooze. However, in chronic cases, the skin is markedly scaly and crusty. The late-stage cysts of Cutaneous Besnoitia in pachydermatous (abnormally thickened) skin lesions of the cattle population has been well described in cattle in Nigeria. The infected cattle had suffered from pachydermatous skins with rough surfaces, scabs and various degrees of hair loss. Histopathologically, the skin sections showed evidence of hyperkeratosis, parakeratosis, comedones, acanthosis and acantholysis, as well as acute to chronic dermatitis with focal to locally extensive neutrophilic or lymphocytic infiltration into

the dermis and epidermis, empty cysts and cysts containing Various unidentified parasites or Besnoitia cysts in the dermis [22, 23].

6.2.2. Ecto-parasites infection

6.2.2.1 Introduction

Skin of the camels can be infected by different external parasites such as, ticks and mites. It also suffers from fly maggots feeding on wounds and in the nose. Skin parasites are a big problem in camels, because for example, untreated mange (mite infection) can lead to the death of a camel and some ecto-parasites result in the loss of valuable wool and qualities of hides and skins from camels, llamas and alpacas. Ecto-parasites effects on the animal health directly or indirectly and play a significant role in many disturbances. Many of the ecto-parasites are important in the transmission of various viral, protozoal, helminthic, fungal and bacterial diseases. The classification of camelids ecto-parasites are presented in (Figure.6.2 &3) (Table.6.1&2)

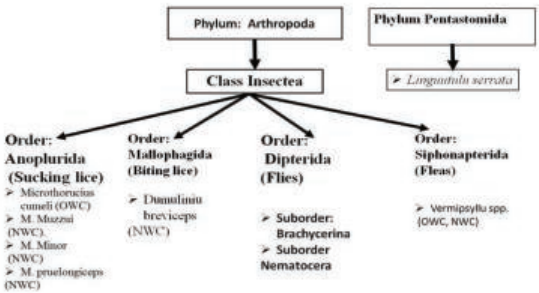


Figure. 6. 2: Classification of of camelids ecto-parasites

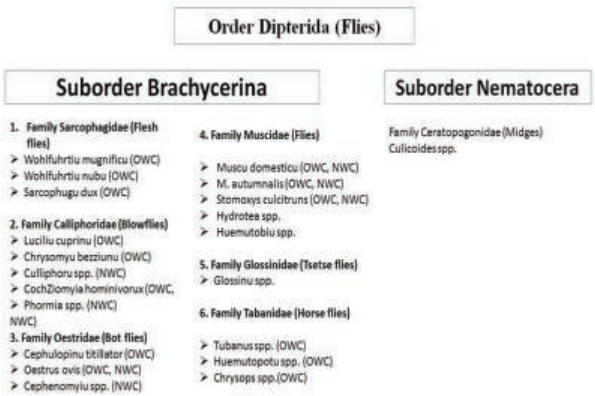


Figure. 6. 3: Classification of camelids ecto-parasites

Table.6.1: Ecto-parasites of camelids (OWC)

OWC ecto-parasites			
Kingdom: Animalia			
Phylum Arthropoda			
Class Arachnea			
Subclass Acaria			
Order	Family	Species	Disease
Astigmata (Mites)	Sarcoptidae	Sarcoptes scabiei	Sarcoptic mange
	Psoroptidae	Psoroptes sp.	Psoroptic mange
		Chorioptes sp	Choriopic mange
Prostigmata	Demodicidae	Demodex	demodectic mange
Metastigmata (Ticks)	Argasidae (Soft ticks)	Ornithodoros savigny O. lahorensis O. tholozani	
	Ixodidae (Hard ticks)	**Hyalomma spp.** H. asiaticum H. dromedarii H. scupense H. franchini H. rufpes H. anatolicum H. detritum H. impressum	
		Amblyomma spp. A. lepidum A. gemma A.variegaturn	
		Boophilus spp. B. Decoloratus Dermacentor spp.	
		Rhipicephalus spp. R. pulchellus R. appendiculatus R. sanguineus	
		Ixodes spp. I. Holocyclus	
Sucking lice	Microthoracius spp.		
Biting lice	Damalinia breviceps		
Fleas	Vermimvlla SDD.		
Flies	Sarcophagidae Calliphoridae Oestridae Glossinidae Tabanidae	Wound orifices Skin perineum Nose pharynx Skin Skin	
Biting midges	Culicoides	Skin	
Tongue worm	Linguatula serrata	Lymph nodes	

Table.6.2: Ecto-parasites of camelids (NWC)

NWC Ecto-parasites			
Kingdom: Animalia			
Phylum Arthropoda			
Class Arachnea			
Subclass Acaria			
Order	**Family**	**Species**	**Disease**
Astigmata (Mites)	Sarcoptidae Sarcoptes mange	Sarcoptes scabiei	sarcoptic mange
	Psoroptidae	Psoroptes spp. Chorioptes sp.	Psoroptic mange Chorioptic mange
Prostigmata	Demodicidae	Demodex sp.	demodectic mange
Metastigmata (Ticks)	Argasida (Soft ticks)	Otobius mengnini	otitis
	Ixodidae (Hard ticks)	Ixodes holocyclus Dermacentor spp	Tick paralysis Tick toxicosis
Phthiraptera	Sucking lice2	Microthoracius spp	
	Biting lice3	Bovicola (Damalinia) brevis	
Siphonaptera	Flees	Vermipsylla sp	
Diptera (flies)	Culicidae (mosquitos) Simulidae (black flies)		
	Tabanidae	Tabanus spp (horse flies, deer fly)	
	Muscidae	Musca domestica (house fly)	
		M autumnalis (face fly)	
		Stomoxys calcitrans (biting stable fly)	
		Hydrotea spp	
	Sarcophagidae Calliphoridae (blowflies)	Calliphora sp	
		Cochliomyia hominivorax (primary screw worm)	
		Phaenicia spp (green blow fly)	
		Phormia spp (black blow fly)	
	Oestridae (Bot flies)	Oestrus sp	
		Cephenomyia sp	

6.2.2.2 Mites

Mites is a causative agent of mange (ectoparasitosis). There are six genera of mites found on animals: *Cnemidocoptes, Chorioptes, Psoroptes, Notoedres, Otodectes*, and *Sarcoptes* [24]. This disease considers as one of the most important and commonest disease of dromedaries after trypanosomiasis [25]. Mange is a highly contagious disease

which can spread to herdsmen or others associated with infected animals. The mite may be transmitted directly by contact or indirectly through objects such as saddles, harnesses, utensils, bedding and even tree trunks. It tends to spread more quickly during cold weather, when animal coats usually grow long and the animals huddle together more often. Mange of camels is one of the important zoonotic disease, before 1950, because camels were important for civil and military transport (Figure.6.4).

Figure.6.4: lesions of camelids mites in human (zoonotic nature of the disease)

The disease can usually transmitted from camel to man during milking. Pseudoscabies is therefore seen mainly in the interdigital spaces of the hands, the flexor surface of the wrists, the forearms, the elbows and axillary folds. In the case of camel riders, the lesions occur between the thighs [26]. Previously, they believed that camel mange has only one causal agent, a mite of the family Sarcoptidae, *Sarcoptes scabiei var. cameli* [27, 28]. However, different types of mites and accordingly different diseases are investigated later. The commonest parasites which affected dromedary camels are *sarcoptic* and *psoroptic* mites [29, 30, 31, 32], whereas *sarcoptic* and *chorioptes* mites affected Llamas [33, 34]. Camelids are subject to a range of dermatological and parasitic problems, of which mange may be particularly severe, occasionally fatal and, in the case of sarcoptic mange, zoonotic [35, 36, 37, 36, 37, 38, 39, 40].

6.2.2.3 Sarcoptes scabiei var. cameli Mange

I. Definition

Scabies is an ancient disease. Based on archaeological evidence from Egypt and the Middle East, scabies is estimated to date back over 2,500 years [41]. Scabies is a major global health problem in human and animal populations [42]. The disease is also called barn itch, scabies and head mange. It is a common cause of pruritic dermatitis in camel, swine, cattle, goats and rarely, sheep and horses. Sarcoptic mange has been reported from 10 orders, 27 families and 104 species of domestic, free-ranging and wild mammals [43]. Sarcoptic mange caused by Sarcoptes scabiei var cameli is a widespread, contagious and debilitating skin disease, ranking among the most serious, zoonotic and economically important diseases of the camel [25, 44].

II. Causes

Originally, *Sarcoptes scabiei* has been described by Gerlach in 1857 and found in humans [45]. *Sarcoptes scabiei*, is a submacroscopic burroing mite, in which male and

female adults, larvae, protonymphs, tritonymphs, and eggs occur in the mammal's epidermis to the level of the stratum granslosum (Figure. 6.5).

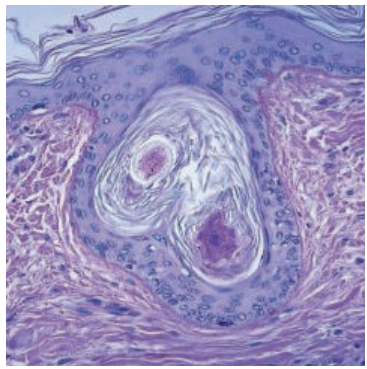


Figure.6.5: Invading mites of camelids epidermis

The burrowing mites consume living cells and tissue fluid. *Sarcoptes scabiei* has a number of varieties each generally specific to a particular host species. The close relationship among the varieties has been confirmed in morphological, immunological and molecular research. However, biological differences, particularly with respect to host specificity haven't yet been explained. Because host specificity is not strict and transference from one host species to another can occur [46], there is some concern when attempting to control the disease. Thus, one may find in the literature both *Sarcoptes scabiei var. cameli* and *Sarcoptes cameli*. This mite is practically confined to the genus *Camelus*; human beings are infected occasionally. The morphology of adult *Sarcoptes scabiei var. cameli* is eyeless spherical, with four pairs of legs (two pairs in front and two pairs behind) (Figure. 6.6. A& B).

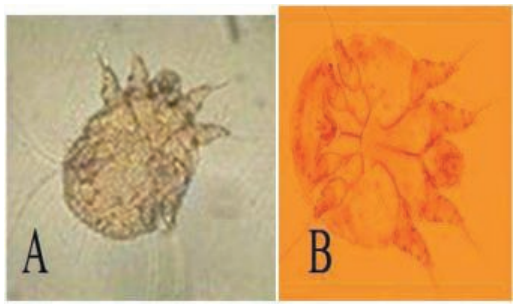


Figure.6.6: *Sarcoptes scabiei var. cameli,* A. from *camelus dromedaries* (Saber Kotb and Ahmed Abdel-Rady, 2015). Sarcoptic mange of camel in upper Egypt: Prevalence, risk assessment, and control measures. J. Adv. Vet. Anim. Res., 2(4): 410-417) [47] , B. from dead alpaca (Twomey, ES Birch, A Schock. (2008). Outbreak of sarcoptic mange

in alpacas (Vicugna pacos) and control with repeated subcutaneous ivermectin injections. Veterinary Parasitology. 159 ;(2):186-91) [40].

It has multiple cuticular spines and its body is flattened ventrally and convex tortoise-like bodies dorsally. Its body also reveals no demarcation into cephalothorax or abdomens. In addition, there are short bristles covering the Mite's surface folds. The front legs end in long, tubular processes known as suckers, and the hind legs end in long bristles. All male legs have a sucker except the third pair legs which, distinguishes it from the female. Females are 0.3–0.45 mm long and 0.25–0.35 mm wide, and males are just over half that size.

III. The life cycle

The life-cycle of *S. scabiei var . cameli* is essentially the same as for other sarcoptic mites and lasts two or three weeks .The life cycle of the *Sarcoptes scabiei var.cameli* lasts for 4-5 weeks . It goes through four stages in its lifecycle: egg, larva, nymph, and adult. Immediately, after infesting camelids host, the fertilised (adult) females dig burrows into the stratum corneum (shallow burrows), where she deposits her eggs (forty to 50 eggs may be laid in the tunnels) and then dies at the end of a burrow. These oval eggs are 0.1–0.15 mm long and hatch as larvae in three to four days (Figure.6.7).

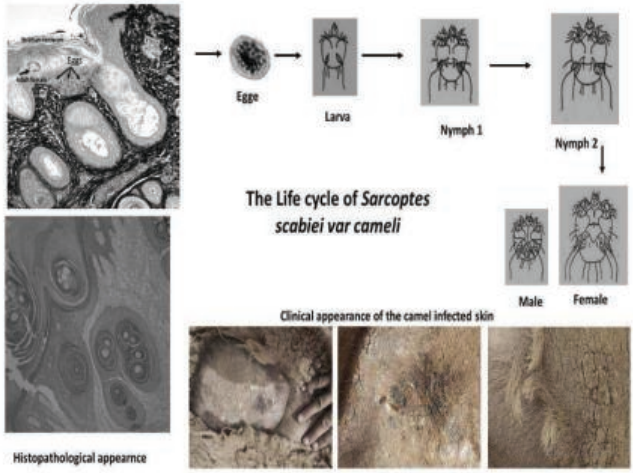


Figure.6.7: Life cycle of *Sarcoptes scabiei var. cameli.*

Development for both sexes includes a larval stage, two nymphal stages prior to molting to the adult. Upon hatching, the six-legged larvae migrate to the skin surface, all life cycle stages, except the eggs, can be found moving on the skin surface and are thus easily transferred to other hosts. After three to four days, the larvae molt, turning into eight-legged nymphs. This form molts a second time into slightly larger nymphs, then the second nymph stage burrow into molting pouches, usually into hair follicles, before a final molt into adult mites. Adult mites then mate, when the male penetrates the molting pouch of the female. Mating occurs only once, as that one event leaves the female fertile for the rest of her life (one to two months). The impregnated female then leaves the molting pouch in search of a suitable location for a permanent burrow. Once

a site is found, the female creates her characteristic S-shaped burrow, laying eggs in the process. The female will continue lengthening her burrow and laying eggs for the duration of her life (Figure.6.8). Significant scratching does not occur until a hypersensitivity develops some 8-10 weeks later.

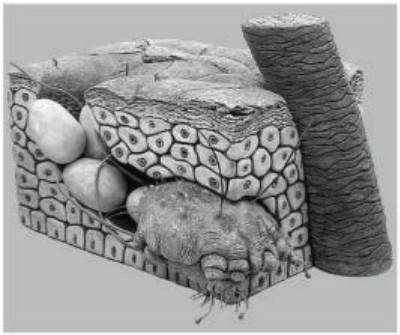


Figure.6.8: *S. scabiei* fertile female continue lengthening her burrow and laying eggs for the duration of her life

IV. Geographic distribution

Sarcoptic mange infection is a serious problem in many parts of the world posing a serious threat to animal health [48, 49, 50, 51, 52, 53]. Literature indicates the widespread prevalence of Sarcoptic mange in all camel rearing country meanwhile, Richard, (1987) [28] stated that Sarcoptic mange occurs wherever dromedaries are kept.

In Saudi Arabia Sarcoptic mange is the most commonly prevalent disease [54]. The disease considers as one of the most important camel diseases because the difficulties with dipping or spraying of large numbers of infected camels may contribute to the failure of controlling mites in some places in the desert [55, 56]. El-Bahy *et al.,* (2008) [57] reported the Sarcoptic mange in camel at Qassim region during spring and summer. They found that the infection was abundant during May to July. *Sarcoptic scabiei var cameli* in one farm also, reported in Western Riyadh, in 14 cases, divided into 10 dromedaries (*Camelus dromedarius*) and 4 llamas (*Lama glama*) [1] . Their observation indicated that the dromedary camels (20.00%) was more sensitively to the sarcoptic mange than llama camelidae (6.66 %.).

In India, Sarcoptic mange in camels is common in different states such as Rajasthan [58] and Punjab [59]. Datt *et al.,* (1978) [60] studied mange in livestock at Hisar (Haryana) and reported its incidence as 19.02% in camels. Orchitis in a camel (camelus dromedarius) due to sarcoptes cameli infection was also reported [61]. While Parsani *et al.,* (2008) [62] considered the *Sarcoptes scabiei var. cameli* is an emerging and serious problem in camels.

Sarcoptic mange in camel is reported in eastern Ethiopia [63, 64, 65, 66] and also in northern part [67]. *Sarcoptes scabiei var auchinae* is reported as the most common causes of parasitic skin disease in camelids in South American camelids [68, 69]. In Jordan, the Sarcoptic mange is reported as a contagious parasitic skin disease [29]. The disease is also reported in libya [30], kenya Onderstepoort [31], in Pakistan (faisalabad metropolis) [32], British llama (*Lama glama*) [33].

In Iraq, *Sarcoptic scabiei var cameli* has been report as endemic diseases in Al-Najaf governorate with 25.9% percentage [70, 71]. *Sarcoptes scabiei* have been reported to be common infestations on NWC (alpacas) also in North and south American and countries outside of South America [43, 72]. Problems with mange are reported frequently from several countries [39] in Europe; UK [73, 74], Belgian [75], Switzerland [76]. Mange mite infection is also common among NWC [72]. In Morocco, sarcoptic mange has been reported in one humped camel at the slaughterhouses of three Southern Moroccan towns [77].
In Borana, Sarcoptes scabei var cameli is one of the most commonly camel diseases with severe clinical manifestations. The infections are more prevalent and severe during the dry periods. Moreover, the disease is more severe in young animals with prevalence over 50% as well as breeding females [78].

V. Economic importance

Sarcoptic mange caused by *Sarcoptes scabiei var. cameli* is the most common, extremely contagious and serious problem in camels. It is chronic debilitating skin disease, with high morbidity and low mortality. However, the World Assembly of Delegates of the OIE in May 2013 considered Sarcoptic mange in dromedaries as a particularly debilitating chronic condition with high morbidity, and it may predispose afflicted hosts to other infections. The disease is ranking among the most serious and economically important diseases of the camel [44]. Once a herd has been infected, continuous reinfections occur. Mange is second to Surra in causing problems and losses in camels. If it is not treated, mange (mite infection) can lead to the death of a camel [79, 80]. The disease has also zoonotic potential impact. The herdsmen are always in an intimate and continuous contact with their camels, which enable the direct transmission of scabies from camel to man .This condition, is termed pseudoscabies in man [81, 82, 83, 84, 85.] Transmission from camel to man usually occurs during milking. Pseudoscabies is therefore seen mainly in the interdigital spaces of the hands, the flexor surface of the wrists, the forearms, the elbows and axillary folds. In the case of camel riders, the lesions occur between the thighs. Once a herd has been infected, continuous reinfections occur. This makes it difficult to assess whether the disease in man is self-limiting, as described for sarcoptic mange transmitted from other animals to man [86,87,88,89].

VI. Susceptibility

Sarcoptic mange is the most prevalent cause of camel morbidity according to Brown (2004) [90]. The disease affects mainly camels reared under poor nutrition, management and hygienic Conditions [91]. The age might be important - both very young and very old camels are particularly susceptible. The season as well considers as one of the important factor, and the disease being most acute and particularly severe during the cold season and in rainy periods [28, 92, 93, 94, 95]. It tends to spread more quickly during cold weather when animal coats usually grow long and the animals huddle together more often [78]. The maximum incidence of acute course mange in the Bactrian camels of Mongolia has been reported by Tsehdehv (1974) [94], during the period November to January (cold weather). This report also confirmed that in the summer the disease was subacute (quiescent) or chronic with focal lesions mainly in the groin and submaxillary regions where the skin was not exposed to the sun. A like seasonality for camel mange has been reported from India by Lodha (1966). The highest incidence for clinically-

observed cases of mange 64% in the winter and the lowest (17. 5%) in the summer has been reported by Rathore & Lodha (1973) [93]. The incidence of disease has been reported to be different in parts of Arab countries. It appears to peak during the hot weather (May, June to September) and in the cooler winter months the activity of the mite seems to decline or the disease becomes chronic [96]. Such a high incidence during periods of high ambient temperature may be an adaptation of the mite's life-cycle to cope with unfavourable conditions for survival and reproduction [82]. The very hot weather, desert watering points are fewer and lower, and camel to camel contact within a nomadic herd is much more concentrated. The nutritional status and dietary intake is an important factor in mange and the nomadic camels on a low plane of nutrition, probably carrying a worm burden [97], in hot arid desert conditions are likely, therefore, to be highly prone to the mange at this time. During such periods of greatest activity, the mites are readily transmissible from animal to animal.

Any camelid regardless of sex and age may be affected by *S. scabiei* [98], however, some reports state that the infection is more prevalent in younger animals [58]. It is often cited that the principal factor favouring mite infestation is poor condition, which make these animals more prone to infection [93, 82, 96]. However, this is controversial as others report that animals in very good condition can also become infected [98].

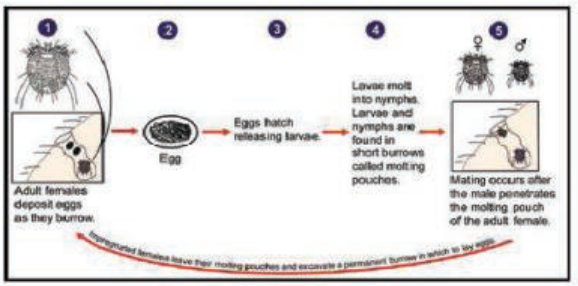
One study in northern part of Ethiopia, found a significant difference in the susceptibility of male and female camels, as well as in different body regions to Sarcoptic mange [67]. They found that the head of the camel becomes affected rapidly in every case because the animal uses its teeth to scratch the affected areas. They found 64 (16.70%) of camels had mange and mite infestation out of the 384 examined camels. Lesions of mange and mite infestation were observed most commonly on the face (72.75%), neck region (58.30%), abdominal region (47.30%), inner surface of the thighs (32.10%) and inguinal region (29.50%) of infected camels. They found also that the prevalence was of 24.20% in female and 14.20% in male camels but no significance difference was observed among the age groups and body condition score of camels ($p > 0.05$). Numerous studies have also been conducted on camel mange mite infestation worldwide and a prevalence ranging from 3.54% to 83.00% have been recorded by various investigators [64, 66].. Variation in the prevalence of camel mange mite due to different management systems and environmental condition has been reported from different countries as follow: 10.68% in eastern Ethiopia [63, 66], 13.40% in Pakistan [32], 27.80% and 32.20% reported from eastern Ethiopia, 31.50% from Borana [78], south Ethiopia,[76], 83.00% from Jordan [99] and 31.60% from Sudan [79]. Iraq 25.9% percentage [70].

In Morocco, Driot *et al.,* (2011) [77] has been studied the epidemiology and histopathology of Sarcoptic mange at the slaughterhouses in the southern Moroccan towns. The disease has been found more frequent in older animals and 33% of animals with skin lesions suffered from mange.

VII. Transmission of the disease and predisposing factors

Direct transmission takes place by contact between animals, when larvae, nymphs or adults are transferred from an infected camel to a healthy one. Infestation can also be contracted indirectly from objects which have come into contact with an affected camel, such as harnesses, tents and tree trunks, and may also be acquired through contact with soil (Figure.6.9). The parasite survives off the host for a maximum of 2 weeks. Transmission may occur by direct animal to animal contact or via fomites such as blankets or baggage tack. Sarcoptic mites can survive outside their host for several

days and remain infective [100], if the microclimate is sufficiently moist and cool. However, Sarcoptic mites rarely survive long off the host under natural conditions or during the dry season in the tropics, but can be transmitted to man [92]. *S. scabiei* of camels found to be remained viable away from their host for 4 days [98]. And other observations indicate that when dislodged from their host, *S. scabiei* mites may remain infective between one half and two-thirds of their survival time [100].
Transmission of Sarcoptes scabiei isolated from naturally infected sheep and goats have been successfully transferred to dromedaries [98].



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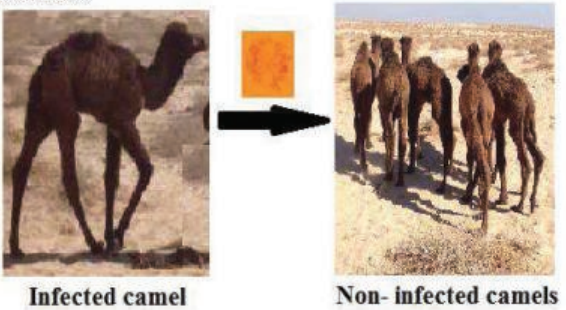

Figure.6.9: Transmission of *Sarcoptes scabiei var. cameli between camels herd*

VIII. Pathogenesis

Sarcoptes is a burrowing mite (Figure.6.10). It penetrates and burrows deeply through the skin surface of the infected camel, usually to the level of the stratum germativium. The burrowing is accomplished by two mechanisms, the first is the action of the cutting mouthparts chelicerae and gnathosoma [100], and cutting of hooks on the legs [101] (Figure. 6.11. A&B), the second is secretion of the digestion substances by the mites that might aid in the digestion of the host tissue and subsequent feeding beneath the skin causes an intense pruritus.

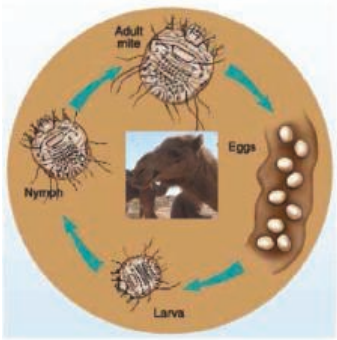

Figure.6.10: pathogenesis of *Sarcoptes scabiei* in camelids

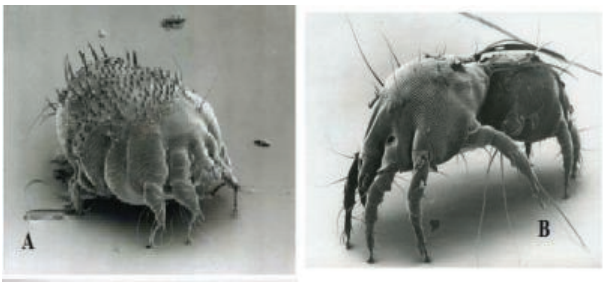

Figure.6.11.A&B: A. Sarcoptes scabiei SEM image of a female adult mite (photo: T. Nikkilä/S. Bornstein).B. Mating pair of Chorioptes sp. (SEM, photo: T. Nikkilä/S. Bornstein). (Bornstein Set and Kerstin de Verdier (2010). Some important Ectoparasites of Alpaca (*Vicugna pacos*) and Llama (*Lama glama*). Journal of Camelid Science 3 (2010) 49-61. http://www.isocard.org) [102]

The mechanical disruption and ingestion of cells and tissue fluid by the mites in the skin certainly contribute to the pathogenesis of sarcoptic mange. The excretion and secretions of living mites may have an irritant and allergic effect. A massive amount of antigenic material is released in the skin, including dead mites, molted skins of living adult and immature mites, and eggshells. Thus, a large part of the pathogenesis of sarcoptic mange is undoubtedly a manifestation of hypersensitivity to the mites. Both types I and type IV hypersensitivity have been demonstrated in some domestic animals such as the dog, pig and camel [103].

Small papule elevations are felt as evidence of early inflammatory reactions to the mite's invasion and injury to the skin. Hairless areas form and serous exudate dries forming scabs. Severe hypersensitivity lesions can occur in the infected camels and often lead to death. The pruritus increases as the mites penetrate deeper .Camels can be seriously disturbed by sarcoptic infestation and the allergic phase lasts for 8-9 months and during this time affected animals are constantly itchy. The disease, if untreated, progress to a localized crust formation characteristic of a chronic

hyperkeratotic state. Severe hypersensitivity lesions can occurred in camels and often lead to death. The effector key in the pathogenesis of scabies is the pro-inflammatory cytokine production [100,104]. The *S. scabiei* extract have been found to stimulate interleukin-1α (IL-1α) and IL-1β, tumor necrosis factor-α (TNFα) and interferon-γ (IFNγ) secretion from keratinocytes, spleen, lymph node and peripheral blood mononuclear cells [100]. These cytokines can also be generated from the inflammation of the skin itself caused by physical stimulation of the burrowing mites. Triggering of this proinflammatory cascade can lead to excessive generation of the reactive oxidants, free radicals which include reactive oxygen species (ROS) such as hydroperoxide radical ($OH^{\bullet}$), superoxide anion radical ($O2^{\bullet-}$) and reactive nitrogen species (RNS) such as nitric oxide radical ($NO^{\bullet}$) in the biological system. Dromedary sarcoptosis has been approved to be accompanied by a state of oxidative stress process, which increased by increasing the area of infestation, and may contribute to the pathogenesis of the disease [103].

IX. Clinical signs

In general, sarcoptic mange in camels shows intense pruritis, exudative dermatitis, parakeratotic scaly crust formation, alopecia and dark thickened skin (Figure. 6.12). The lesions become more aggravated and the camel continues gnawing and rubbing its body against inanimate objects to alleviate the itching, and eventually develop into raw wounds on the skin. Fissures develop in the crust and underlying epidermis resulting in haemorrhages. Emaciation, debilitation, anaemia and subcutaneous oedema are common signs in mangy camels [91]. Severe hypersensitivity lesions in camels infested with *S. cameli* may be also developed (Figure. 6.13.A, B & C).

Infestation arises at any areas of the skin, however, it is more common on thin skin such as the head, base of the neck, mammary gland, prepuce and flank. The head becomes affected rapidly in every case, the animal use its teeth to scratch affected areas. The humps and dorsal aspects of the neck are usually free of any signs of mange [44, 49, 58, 82, 93, 96]. However, mangy lesions on the dorsum (including the hump) have been reported both in naturally and experimentally infected camels. Nayel and Abu-Samra, (1986)[98] and Parmar and Singh, (2005) [105] described the clinically affected camels exhibited pruritis, alopecia with thick, wrinkled skin over the neck, medial aspect of thigh and brisket region. However, Mouchira, and khalid (2009) [1] revealed pruritis characteristics, suggest that, it induced by an immune allergic response to infestation of the skin by the mite *Sarcoptes scabiei* and typical itchy and scratching lesion were observed. The location of lesion involved fore and hind limb, ventral of abdomen, inguinal region and chest were the most severely affected, whereas the head and neck were not included. The incubation period of *Sarcoptes scabiei* mange is 2-3 weeks. The first signs of invasive phase is characterised by numerous small hyperemic papules, accompanied by intense pruritus. About two weeks after the first sign, the affected area of skin has lost their hair forming irregular alopecic areas and scab formation. The lesions may become generalised after 20-30 days. The specific lesions are confined to the integument and comprise hyperkeratosis with areas of keratosis. Later, the hyperkeratotic stage occurs which characterize by dry and hard, with folds forming in the neck, around joints and on the thighs. During the development of mange, itchiness distracts the animals from eating, so that they often become emaciated. Decubitus sores may develop, as well as secondary infections, particularly with pyogenic bacteria. In mild infested camels, skin lesions are confined to patchy areas in the head, neck, flank, thighs, abdomen and inguinal region. Moderate infestation is

characterized by wide alopecic areas covering less than 25% of the body especially in the flank, abdomen and extremities.

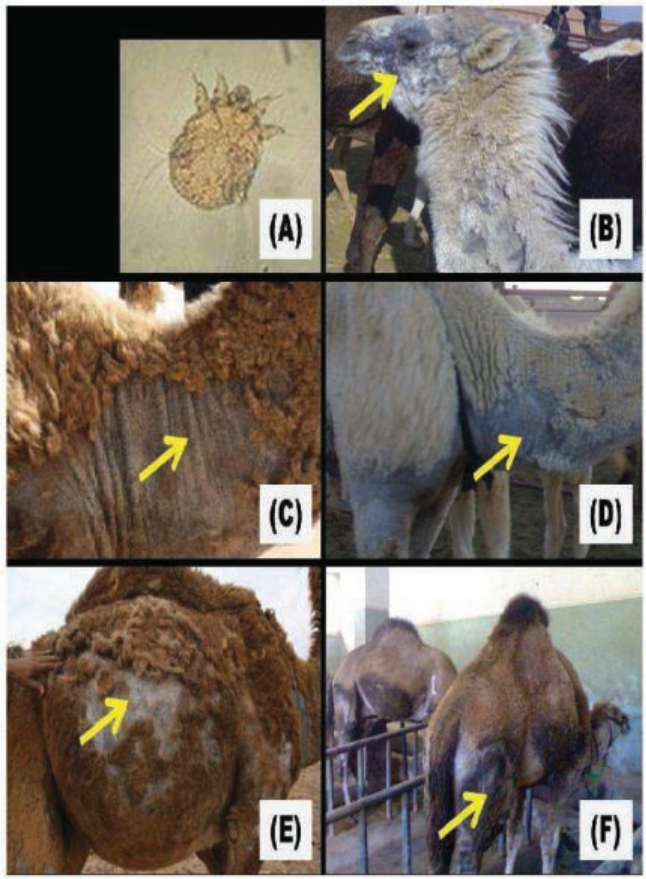

Figure. 6.12: Sarcoptic mite and clinical signs caused by them in camel. (A) Skin scraping showing Sarcoptes scabiei mites, (B) camel is showing hairless area in the head and neck due to Sarcoptic mange, (C) camel is showing hairless area in the neck due to Sarcoptic mange, (D) camel is showing hairless area in the hind and fore limbs due to Sarcoptic mange, (E) camel is showing hairless area in the body due to Sarcoptic mange, (F) camel reared with buffaloes showing hairless area in the hind and fore limbs due to Sarcoptic mange. (Saber Kotb and Ahmed Abdel-Rady. (2015). Sarcoptic mange of camel in upper Egypt: Prevalence, risk assessment, and control measures. J. Adv. Vet. Anim. Res., 2(4): 410-417) [47].

Figure. 6.13. A, B&C: A . Dead alpaca shows severe and extensive thickening of the skin with crust formation, B. Severe skin lesions affecting the face of an alpaca(DF Twomey, ES Birch, A Schock,(2008). Outbreak of sarcoptic mange in alpacas (Vicugna pacos) and control with repeated subcutaneous ivermectin injections. Veterinary Parasitology. 159 ;(2):186-91) [40]. C. Extensive lesions on the abdomen including the scrotum of an alpaca with skin disease of unknown cause. Erythema, papules, pustules, alopecia, crusting, lichenification and thickening of the skin (hyperkeratosis) are seen. Skin lesions as these are often seen in infections by Sarcoptes scabiei and infestations with Chorioptes sp, respectively. No mites were found. The diagnosis supported by histology was `ìdiopathic hyperkeratosis` (Photo AP Foster, case material from the Univ. of Bristol, UK) [68].

The infected skin is roughened, corrugated and covers with grayish chalky scabs and cracked into deep fissures oozing sero-hemorrhagic exudates. In the severely affected camel, the lesions cover more than 25% of the skin and more than 50% of the skin surface becomes affected however, any part of the body may be affected. In the moderate and severely affected cases, varying degrees of anaemia (pale mucus membranes) become prominent accompany with poor body condition (weight loss, small hump, and projection of the ribs, leg oedema, loss of appetite and debilitation. Grazing and even milk production may show a rapid decrease. Orchitis associated with a case of sarcoptic mange has been recorded in a camel suffering from severe mange in India. A large number of mites identified as *S. cameli*, which are morphologically identical to *Sarcoptes scabiei*, is recognized on microscopic examination of skin scrapings taken from the scrotum. *Corynebacterium pyogenes* infection, which caused the orchitis, was believed to be a secondary infection occurring in the tunnels formed in the skin of the scrotum by the mites, *S. cameli*. It is not known whether the orchitis was caused primarily by *C. pyogenes* infection or following the development of extensive mange. Within a few weeks, the untreated, camels with severe acute sarcoptic mange may develop to the chronic stage, which is the stage most often encountered in the field. Hyperkeratosis and proliferation of the dermis leads to the skin becoming thicker, fissured, and corrugated-appearing like a dried cracked field of clay. Arlian *et al.,* (1989) [100], demonstrated a partial immunity or protection against challenge infections in experimentally infected dogs and rabbits. However, absolute protective immunity following recovery after treatment is not known. Antibodies to *S. scabiei* has been demonstrated by an ELISA in naturally infected dromedaries [43, 102].

X. Diagnosis

Diagnosis of the sarcoptic mange in camels is based on the following (Figure. 6.14):

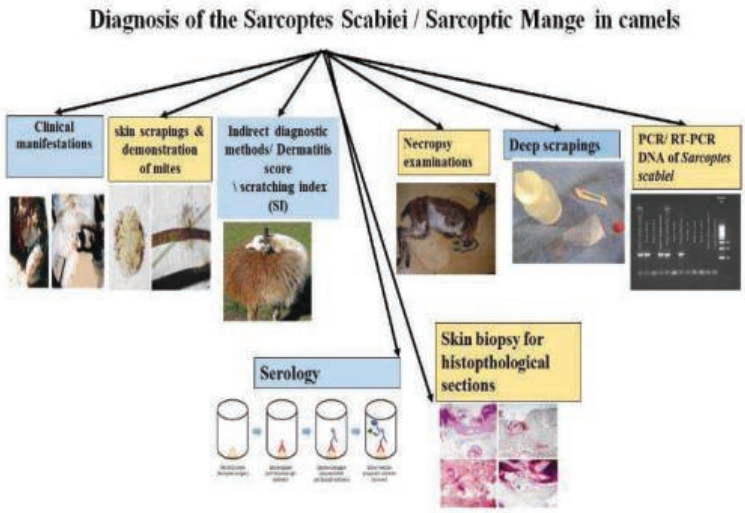

Figure. 6.14: Steps and different methods in diagnosis of *S. scabiei* scabies mange

A. Clinical manifestations and the demonstration of mites or their developmental stages in host skin scrapings [106]. Sarcoptic mange is characherized by hair loss, crusty or scaly skin lesions, dermatitis, thickened skin, scurf, and pruritus. The earliest lesions are often unnoticed, however any pruritic skin disease may be caused by *S. scabiei*. The invasive stage also may be difficult to diagnose, but the intense pruritus is characteristic of this infection. The hyperkeratotic stage is easy to recognise by large areas devoid of hair, with thickened skin and folds around the joints, affecting the hind limbs and neck.

B. The indirect diagnostic methods are also used to estimate mite levels, one is related to the presence of an allergic reaction: dermatitis score, and the other to the presence of pruritus: scratching index (SI). Dermatitis score has been used in several studies [107] and is based on the severity of papular dermatitis at slaughter using a simple scale for classifying carcasses (0–3) [108].

C. Necropsy examinations are not usually undertaken.

D. Deep scrapings which draw blood are required for accurate diagnosis and must be taken from the edges of any evident lesions (scrapings taken from the central portions of lesions are very often negative). There is an importance of taking proper and adequate numbers of skin scrapings from the individual mangy animal. Care should be taken to scrape at least 1 cm^2 area of the mangy skin (about 10% of the total area). The scrapings should be done by parallel strokes of a sharp scalpel blade at the margins of the mange lesions. This is to be followed by taking deeper scrapings until capillary oozing occurs on the whole scraped surface. The skin scrapings should be taken from different lesions area per animal. A drop of mineral oil or glycerol may be placed on

the blade to help hold the skin scrapings during the procedure. Skin scrapings should be placed in sealed containers (e.g. clean, empty salve tins; stoppered glass/plastic test tubes; small, sealable plastic bags) and promptly taken or sent to a laboratory for more thorough examination. An even more effective method of collecting mites from the skin surface and hair is by using a vacuum cleaner fitted with an in-line filter [109]. The material collected, along with the filter, is then examined as a skin scraping also. All deep skin scrapings until bleeding of any skin lesion should be processed further. Place the skin scraping (up to several grams of skin and hair) in a suitably sized beaker, then add sufficient 10% potassium hydroxide to immerse the sample. Cautiously bring the solution to a gentle boil, stirring frequently (a laboratory hot-plate with a magnetic stirrer works well for this), for 5–10 minutes or long enough to digest most of the hair and skin. This step should be performed under a chemical fume hood to limit exposure to caustic fumes. Do not boil for an extended period of time, or the mites may disintegrate. Transfer the digested material to suitable test tubes, and centrifuge at 600 g for 10 minutes. Decant the supernatant. Resuspend the pellet in a small amount of flotation medium (e.g. Sheather's solution or a mixture of 50% corn syrup and 50% water); then, fill the tube completely with flotation medium, and place a cover-slip on top of the tube, assuring that it makes contact with the flotation medium. Let stand for 1 hour, or centrifuge for 10 minutes. Carefully remove the cover-slip by lifting straight up, so that a drop of fluid remains on the underside of the coverslip, and place on a glass slide. Any mites in the sample will have floated to the top and will be found in the drop of fluid attached to the cover-slip. Another simpler but satisfactory technique, that is used in many laboratories, is to re-suspend the pellet in a small amount of distilled water, drop onto a large (76 × 51 × 1 mm) glass slide andcover with a 40 × 50 mm cover-slip. This is examined under a dissecting microscope (×40 or ×100) with understage lighting. The slide then may be examined under a compound microscope for the presence of mites. *Sarcoptes scabiei var cameli* mite is identified on the basis of their characteristic morphological features [110].

E. DNA of *Sarcoptes scabiei* has been successfully amplified and detected by polymerase chain reaction (PCR) from human cutaneous scales. This technique holds promise as an additional procedure for detecting specific, hard-to-find mange mites in skin scrapings [111, 112].

F. Histopathological changes: The chances of making a correct diagnosis by skin biopsies are less likely because *S. scubiei* mites are rarely seen in biopsies. The histologically, lesions of acute sarcoptic mange often suggest a S. scabiei infection due to hypersensitivity reactions seen in the skin. However, these findings alone are not conclusive because other conditions may cause similar skin lesions [93, 98]. In mange, varying degrees of superficial dermatitis, epidermal spongiosis, hyperplasia and para- and hyperkeratosis may be observed [71] (Figure.6.15) Eosinophils and mast cells are sometimes intermingled with neutrophils and macrophages. The papillary layer and dermis often show proliferation of connective tissue and infiltration with lymphocytes, macrophages, some eosinophils and giant cells [98]. Epidermal erosions and crusting are often seen due to self-trauma. Full pathological features of 14 mange cases, divided into 10 dromedaries (*Camelus dromedarius*) and 4 llamas (*Lama glama*), diagnosed as scabies, caused by sarcoptic scabiei var cameli in one farm, Western Riyadh, Kingdom of Saudi Arabia, has been described by Mouchira and khalid, (2009) (Figure.6.16) [1]. Histological examination of the crusts revealed a generalized, mild to marked hyperkeratosis, parakeratosis and acanthosis in focal areas in most of infested

camelidae. Moreover, the larvae formed tunnels to live after destructed and deforming to the epidermis. Gross section of mite occupied the tunnels with crusted scabies and marked hyperkeratosis in the epidermis can be observed. An eosinophilic or dense calcified material surrounded the larvae embedded within the parakeratotic epidermis also recognized in scabies sections. In some infected camelidae, a histopathological features are represented congestion with hemorrhage deep dermal plexus.

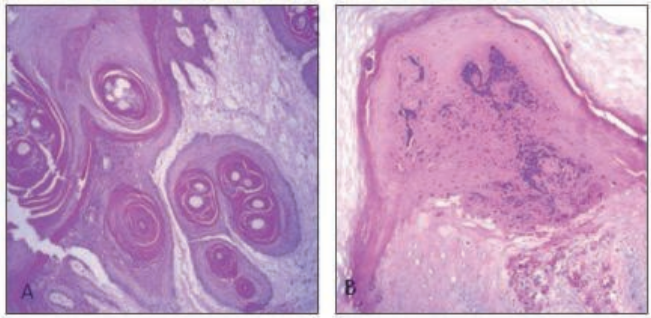

Figure.6.15. A&B: A. The epidermal hyperkeratosis, acanthosis, and rete ridge formation, deep reaction in the dermis layer, formation of keratin cysts, congestion and serocellular exudation (H& E) X10. B. Crust formation composed of degenerating neutrophils appeared in superficial keratin and spongiosis. (H& E) X10. (Al-Salihi, K.A., Abdoalmir, AbdHatem., Ekman,Elisabet., 2013. Pathological studies on mixed dermatomycosis and mange infection in camels accompanied with chronic granulomatous hidradenitis. Journal of Camel Practice and Research. 20 (2), 309-315309-315) [71].

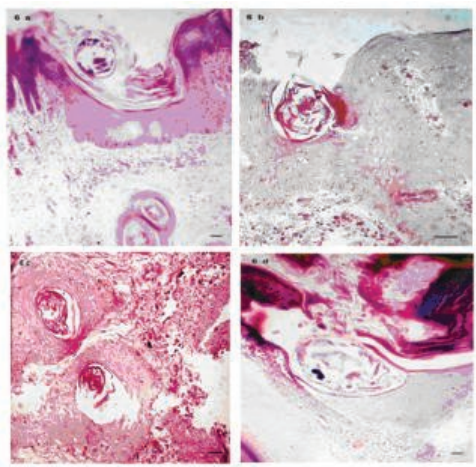

Figure.6.16: camel skin. H&E stain (a) Case 1. Mite occupying the tunnels with crusted scabies in hyperkeratotic epidermis. (b) Case 13. Eosinophilic material surrounding the larvae within the tunnels. (c) Case 13. Multiple tunnels with larvae embedded. (d) Case 6. Larvae burrowing deeply in the epidermis. All scale bar = 100 μm. (Mouchira

M M, Khalid A K. (2009) .Pathological Studies on Acariasis in Dromedary (Camelus Dromedarius) and Llama (Lama glama) Camelidae European Journal of Scientific Research. ISSN 1450-216X Vol.38 No.2, pp.159-171 © EuroJournals Publishing, Inc. 2009. http://www.eurojournals.com/ejsr.htm) [1].

G. Blood samples are collected from jugular vein in vacutainers containing EDTA for haemogram and without EDTA for biochemical assay. Researchers have shown that Sarcoptes scabiei infestations cause measurable specific antibody responses in hosts, namely pigs, sheep, dogs, and camels [113, 114, 115] , this makes possible serological detection of sarcoptic and psoroptic manges. Enzyme linked immunosorbent assays (ELISA) that detect antibodies to *Sarcoptes* in pigs and dogs are commercially available in some countries and have been used for serodiagnosis of scabies [115] in Sweden and Switzerland to support scabies eradication programs in swine. Recombinant antibodies for *S. scabies* and *P. ovis* are commercially available, and they seem to give more consistent test results than whole mite preparations. Although the only unequivocal proof of mange is finding and identifying the offending mites this traditional (direct) method is being augmented by better and better biochemical (indirect) methods. In naturally infected dromedaries Bornstein et al. (1997) also demonstrated antibodies to *S. scubiei* by an ELISA.

XI. Differential diagnosis

Sarcoptic mange can be confused with the following skin diseases:

1. Depilation with thickening of the skin caused by massive tick infestation, eczema (rare in camels).
2. Non-pruriginous depilation occurring in certain camels in very poor condition
3. Following camelpox in young camels, particularly the papule and scab formation stages.
4. Ringworm mixed infection with mange infection has been reported by Al-Salihi *et al.,* (2013) [71].
5. Dermatophilus congolensis(contagious skin necrosis).
6. Staphylococcus aureus dermatitis
7. Endocrinal dermatopathy
8. Inhalant or food allergies
9. Idiopathic hyperkertosis (associated with zinc responsive dermtoses recognized in NWC).

XII. Public Health Considerations

Information indicates that humans and earlier protohumans were most likely the source of animal scabies, first of dogs, and later of other species with subsequent spread to wildlife [104]. Human scabies occurs most frequently in elderly nursing homes and children's day-care centres. Some other mange mites may cause transient disease in humans, but infestations seldom persist. *S. scabiei* can transmit to human from camel, horse, pig, goat, sheep, chamois, ferret, fox and llama, [92, 116, 81, 26, 91] and alpacas [116]. Pseudoscabies occur in humans occasionally due to direct transmission of *Sarcoptes scabiei var cameli* from camel to man due the direct contact between the herdsmen and their camels. The transmission usually occurs during milking. Pseudoscabies is therefore seen mainly in the interdigital spaces of the hands, the flexor surface of the wrists, the forearms, the elbows and axillary folds. In the case of camel riders, the

lesions occur between the thighs. Once a herd has been infected, continuous reinfections occur. This makes it difficult to assess whether the disease in man is self-limiting, as described for sarcoptic mange transmitted from other animals to man (Figure.6.17).

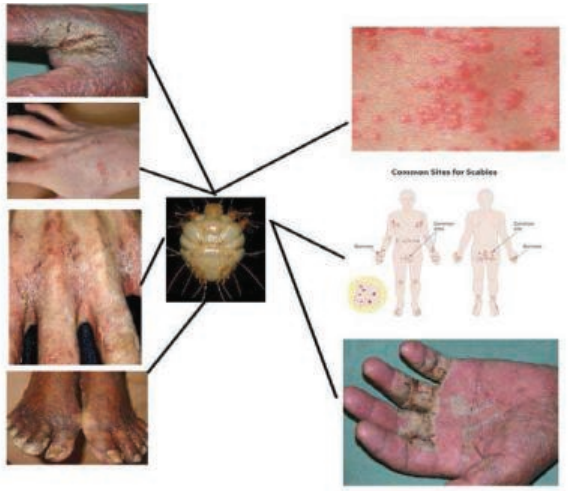

Figure. 6.17: clinical presention of *Sarcoptes scabiei* in human

Delafond and Bouguinon in 1895 were the first scientists to discover *S. scabiei* in llamas at the MusCum National d'Histoire Naturelle in Paris. Two students were accidentally infected by the affected llamas [116]. Cross-infections by *S. scabiei* from animals to humans are called pseudo-scabies, distinguished from true human scabies (infections by *S. scabiei var horninis*). Humans infected by the itch mite *S. scabiei* from camels exhibit signs similar to those of classical scabies: pronounced intensive itching during the night. Erythema and papule formation are seen mainly in the interdigital spaces of the hands, the flexor surface of the wrists, the forearms, elbows and axillary folds (of milkers) and between the thighs (in riders). Secondary infections can occur leading to pyoderma. As long as there is continuous contact with mangy animals, the clinical signs will continue in the contact person. Pseudo-scabies is usually self-limiting. The clinical signs will gradually wane and disappear within about two weeks when contact with the infected animal/s is interrupted or the animals are treated, preventing a reinfection. One of the authors accidentally became infected with *S. scabiei var. cameli* when a mangy camel was walked for 6 h to a different location. The first red spots were detected on the right forearm 24 h later. It is believed that the mites had crawled over the lead rope onto the arm. Eight days later severe erythema and papules were observed on both legs and both arms with severe itching. There were no lesions on the head and very few papules on the body. Skin scrapings were taken from the leg and *S. scabiei* identified. After treatment with Jacutin B emulsion (lindane 0.3g) or PriodermB (malathion 0.5% w/v) for 3 consecutive days and StromectoF 6mg (ivermectin) orally, the lesions receded within 72 h.

XIII. Treatment

Various compounds such as conventional preparations and synthetic pyrethrins have been used to treat mange, with varying success. However, the history of mange treatment goes back a long way, starting with tars prepared from trees and shrubs and a number of plants used in such preparations have been described by Curasson, (1947) [25]. Different acaricides products are applied parenterally as well as topically since many decades to treat mange effectively. Some of these products have been applied trials on camels, and are used in certain countries for controlling the disease. The most commonly used preparation is lindane (the gamma isomer of HCH), an organochlorine parasiticide used in a concentration of 0.05% or 0.02% [86.] It is applied by brushing or as a spray, although brushing is used only on the worst and least accessible lesions. Spray treatment must be applied thoroughly to all parts of the body in order to reach mites within galleries burrowed into the epidermis. Treatment should be repeated after an interval of 8-15 days. The objects the affected animal may have been in contact with, particularly saddles should also necessary to treat with acaricide. Moving of camels away from an infested place for 2 weeks is advisable for free-living mites to die off. Among the organophosphorus compounds, malathion at 0.75% does not seem to be very effective [25]. Some researchers mentioned that topically applied acaricides has not been universally successful due to difficulties with dipping or spraying of large number of camels [56]. Due to these reasons, some investigators suggested an efficacious ectoparasitic control with particular reference to new available chemical technologies, which can be adapted to camels [102]. Other reports about different effective compounds of acaricide trials have been reported in the literature.

A broad-spectrum parasiticide, ivermectin, has been used effectively against mange in camel by several researcher. A trial was conducted on camels by Hashim& Wasfi, (1986) [27], who obtained good results with two subcutaneous injections, 2 weeks apart. This is an interesting observation, for ivermectin is easy to administer, and is also effective against certain nematodes, one of which (*Haemonchus longistipes*) is pathogenic for dromedaries. It would be worth testing the efficacy of a single injection. However, the use of ivermectin on lactating females requires further investigation, for it would be hard to convince camel keepers not to drink the milk during the excretion phase of the product. Nayei and Abu-Samra (1986) [98], has been successfully treated the experimental lesions with salicylic acid followed by Gammatox (hexachlorocyclohexane) and produced rapid and complete cure. In Iraq, Two formulations were used for the application of the insecticide diazinon: in one case it was diluted in 1/100 ml water and in the other in 1.25/1 000 ml liquid paraffin.

The effectiveness of the first formulation was not satisfactory as examination of a deep skin scraping revealed the presence of living mites even after the treatment had been repeated four times at 15-day intervals. The second formulation, on the other hand, gave good results after just one application, following which examination of a deep skin scraping revealed only dead mites or no mites at all. This indicates the effectiveness of using liquid paraffin as a diluter and softener to break down the keratinized area of the skin and as a means of enhancing the deeper and more effective penetration of the insecticide used. In Sudan, Sarcoptic mange is treated by spraying or dousing the camel all over with a freshly prepared solution of Gamatox (lindane) or diazinon. It may be necessary to repeat the applications several times to effect a cure. Ivermectin seems to have a remarkable effect, and may be used in future to control mange in camels and other animals. In India ,Ivermectin has been used for treatment

of Sarcoptic mange at a dose rate of 200 µg / kg body weight against Scabies in camels was reported by Parmar and Singh (2005) [105].

The taramera oil with sulphur, kerosene oil and coaltar are widely used in India. But, these are time and labour consuming and give unsatisfactory result. Some workers reported diazinon, amitraz, deltamethrin, and fenvalerate as 100% effective after three application. Recently, introduction of ivermectin therapy has shown excellent results in the treatment of mangy camels, but this drug is very expensive [62].

The efficacy of Ivermectin based treatment has been assessed at the dose rate of 200 µg / kg body weight by subcutaneous route at the base of the neck at fortnightly intervals until sixty days of infestation along with parenteral administration of 10 ml Vitamin E care Se injections for eight weeks. Benzyl benzoate paint was applied topically for the first week and it was followed by tetmasol soap bath sprays and oral administration of zinc containing tonics. This strategic treatment of scabies in captive camels (*camelus dromedarius*) has shown a marked clinical improvement in appearance with reference to skin texture, healing of skin lesions (i.e.,) disappearance of crusts, wrinkling, falling of scabs, skin folds becoming less and subsequent appearance of fresh shiny skin with glossy hair 1-3 mm long prior to second treatment absence of tissue swelling because of injections, disappearance of clinical signs of itching with parasitological cure noticed by 56 days. The researcher also concluded that Clinical recovery was apparent in all the treated camels, which proved Ivermectin along with hygienic management of farm premises was 100% efficient [117].

Camel mange has been treated with endectocide compound. Acaricidal activities of Ivomec (Ivermectin) and Dectomax (Doramectin) were evaluated in camels infested with sarcoptic mange mites. The study showed that the activity of Dectomax was stronger and last longer than Ivomax as it reduced the number of mites on the tested animals four weeks after treatment. The Ivomec (1% ivermectin) dose of 0.2 mg kg^{-1} on body weight basis is not effective in killing the mite infestation in a short period of time. Whereas, the Dectomax (1% doramectin) dose of 0.2 mg Kg^{-1} on body weight basis killed all the mite infestation quickly and was effective for a longer period of time. They concluded that doramectin is more comfortable and docile besides its high performance rate, efficacy of long protection period and quick relief of infested animals. However, the researchers suggested further studies on Dectomax (Doramectin) due to its acute effect on liver and other organs of camels.

XIV. Control

The control program of camel mange is involve treatment of infected animals with effective external acaracide and or with an injectable ivermectin. The prophylactic standpoint, it would be desirable to treat the entire herd. The attention of camel keepers should be drawn to the indirect transmission of mange, and thus to the need to treat with acaricide the harness and other equipment, observing the necessary precautions for curative and prophylactic application. It is necessary to bear in mind that camel keepers know little of the toxicity of parasiticides. It would also prove valuable to limit the deterioration in bodily condition which occurs during the dry season, but this would not be easy in regions where camel breeding takes place under natural conditions. However, agricultural by-products are available in certain countries, and their use as dietary supplements would help to overcome the physiological conditions which predispose an animal to mange. Camel mange is one of the zoonotic diseases, and in order to control this zoonosis, it is essential to treat both camels and man. The treatment to be preferred in man is hexachlorcyclohexane, Lindane lotion, Premethrin cream,

Ivermectin, Benzyl benzoate and Ivermectin. There are no commercial vaccines for mange.

6.2.2.4 Psoroptic Mange

i. Introduction

Psoropitc mange is the disease caused by the non-burrowing mite, *Psoroptes spp*. It affects a variety of species including sheep, cattle, goats, horse, rabbit and camelids. All *Psoroptes spp.* mites are host specific. Psoroptes mange reportedly infest camelids, but are less commonly found on camelids than *S. scabiei*. It is responsible for body mange in Cattle and horses and ear mange in horses, sheep, goats, and rabbits. The disease is a major animal welfare concern. Chronic infestation with *Psoroptes* mites have all been observed in alpacas in the UK [118,119, 38] and in North America [120].

ii. Morphology and lifecycle

Psoroptes is an oval shaped, astigmatic, with legs longer than those seen in burrowing mites (Figure.6.18). It is of the family Psoroptidae. Mite is larger than *S. scabiei*, about 0.75 mm long with all four legs projecting beyond the body. The males have a pair of copulatory suckers. Psoroptes are confined to the skin surface, and feed on serous exudate by a siphoning process. They cause the formation of scabs, under which they live. The Adult female is capable of laying up to 100 eggs during her life time, which is usually just one month. The eggs are laid on the skin at the edge of a scab and hatch in 1-3 days, although this is prolonged if eggs are not in contact with the skin. There are the usual larval and nymphal stages and the whole life cycle is complete in 10-11 days. All stages are capable of survival away from the host for up to 10 days and under optimum conditions adult females may survive for 3 weeks.

Figure.6.18: Morphological appearance of Psoroptes mite

iii. Pathogenesis

The pathology of infestation varies between hosts and between populations of mite. The mite has abrasive mouthparts and it is active in the keratin layer of the skin. Mites feed on exudate of lymph, lipid exudate, skin cells and bacteria caused by a hypersensitivity reaction to antigenic mite faeces by the host. This causes intense pruritus, leading to self-trauma, crust and scale formation and inflammation. The mite migrates to all parts of the skin and prefers areas covered with hair or wool. Salivary secretions and mite excreta contain proteinases that result in a severe allergic pruritis. The exudation of serum accumulates to form a crust. Psoroptic mange is a disease of considerable economic and welfare importance, particularly in sheep flocks, in many areas of the world [121,122]. The disease is most prevalent in autumn and winter months, however does still occur in the summer, especially in sheep that have not been shorn.

iv. Clinical signs

Pruritus evidence of self-trauma and fibre loss is particularly associated with the pinnae and ear canal are the main signs to notice from within the herd. However, the shoulders, back, sides, tail head, perineum, nares, axillae, groin, neck and legs can also be affected. Once a closer inspection is made, inflammation and an exudate will be noticed on the skin and areas of yellow crust will also be present. In on-going cases, weight loss in adults, or reduced weight gain in growing animals, will be seen due to the irritation causing them to have a reduced feed intake. However, camelids might be a potential reservoir for sheep scab mites. In South American Camelids (SACs), particularly alpaca (*Vicugna pacos*) and llama (*Lama glama*), Psoroptic mange is often seen at predilection sites; pinnae and external ear canals, as erythema, crusting, papules, serum exudates and alopecia. Pruritus is evident emanating from these lesions. Typical lesions seen in the external ear canals are big flakes. Exudate occasionally appears, which is most likely due to secondary infections. Ears and parotid regions may sometimes become grossly swollen [116]. However, lesions as well as pruritus may be generalised with or without involvement of the external ear canal. Other sites with lesions reported include nares, axillae, groin, neck, legs, abdomen, perineum, shoulders, back and its sides and the base of the tail [38]. Intermittent bilateral ear twitching and head shaking may indicate otitis due to *Psoroptes sp.* infestations. The *Psoroptes sp.* of alpacas and llamas has previously been referred to as *P. auchenia* or *P. communis auchinae*, but adequate identifications of the different isolates of the mites have not yet been done [121]. The first report of psoroptic mange in llamas outside of South America was in the US in 1992 [120], and in alpacas a decade later in UK [116]. Psoroptic mange in dromedaries recorded by Gabaj *et al.,* (1992) [30] and the only documented case. In addition, Werner *et al.,* (1989) [4] reported Psoroptic mange in Bactrians in Mongolia. In many countries sarcoptic and psoroptic mange are reportable diseases.

v. Diagnosis

History and clinical signs are often enough to make presumptive diagnosis. Skin scraping to microscopically identify mites (low magnification) should be performed. Mites are found under scabs at the edges of the lesions and in skin folds.

vi. Treatment/ Control

Infestations are difficult to eliminate from a flock so a key factor in control is to not allow it to enter - new stock should be isolated for at least three weeks before mixing with the main flock. Psoroptes can be treated with avermectins or milbemycins by injection, but only moxidectin has any prophylactic effect. Two injections 7 days apart or one single dose (doramectin only) are needed.

6.2.2.5 Chorioptic Mange

Ectoparasites of the genus *Chorioptes* (Acari: Psoroptidae) are distributed worldwide, infesting domestic as well as wild herbivores [123, 124]. These non-burrowing mites are commonly found on cattle, sheep, goats, horses and the New World camelids, where they are a common cause of mange and have considerable veterinary importance. Infestation with Chorioptes is most probably rare in camels. The affected skin areas vary with host and degree of infestation, but the extremities or tail regions are commonly involved. The entire life cycle, from egg-laying through larval and nymphal stages to mature mites, takes place on the same host, and spans approximately three weeks [125]. At present, the taxonomy of Chorioptes is unclear. Two species, *Chorioptes bovis* and *Chorioptes texanus* are generally accepted [123, 126], based on morphology and genetic differentiation, while the existence of three further species, *Chorioptes crewei*, *Chorioptes mydaus* and *Chorioptes panda*, is still questionable [124, 127]. Both *C. bovis* and *C. texanus* are ubiquitous mites with a low degree of host specificity. These mites are mostly found to infest the skin surface of the body, and are rarely found in the ears of the hosts [126, 121]. One exception is reindeer (*Rangifer tarandus*), in which *C. texanus* has been considered to be a primarily auricular mite [126]. *C. texanus* has also been isolated from cattle (*Bos taurus*), goats (*Capra hircus*), roe deer (Capreolus capreolus), sika deer (Cervus nippon) and moose (Alces alces) [123,127, 128, 129]. Reported hosts of *C. bovis* include wild and domestic Bovidae, Cervidae, Equidae and Camelidae [126], however, chorioptic mange reported most frequently in alpacas, llamas and goats in the UK [130]. Chronic infestation with Chorioptes mites have been observed in alpacas in the UK [38, 118, 119] and in North America [120]. Some animals may have concurrent infestations with *Chorioptes* and either *Psoroptes* or *Sarcoptes*, or even all three genera, although *Chorioptes* appear to be the most common [119]. Chorioptic mange in South American camelids is usually assumed to occur on the lower legs and belly and to involve *Chorioptes bovis* [38].

Chorioptes' mouthparts do not pierce the skin and they feed on skin debris and exudate, meaning its pathogenic significance is mild. In cattle, economic significance is the main factor as infestation can cause damage to the hide by self-trauma. The mites cause an allergic, exudative dermatitis; the yellowish serous exudate coagulates and breaks as the hair grows so that small scabby lesions are seen on the hair.

It has been reported on a Bactrian camel and in the Netherlands on one llama, three alpacas and two camels, one of which had ”foot mange”. An infestation of Chorioptes sp. was also responsible for mange in a herd of alpacas from Chile recently imported into France. Previously Chorioptes sp. infestations is considered relatively rare in SACs [35, 72]. *Chorioptic* mange is a very common condition in many herds worldwide, particularly among alpacas [118,119]. Clinical signs of chorioptic mange may mimic sarcoptic mange, but animals affected usually exhibit a milder pruritus and sometimes none at all (subclinical). Individuals with a heavy infestation may be free of any clinical signs of mange although others in the same herd with lower infestations may show severe extensive skin lesions. Often alopecia and scaling are seen on the feet. Often, as in sarcoptic mange, it is found between the toes (Figure. 6.19) and the base of the

tail. Lesions may spread to the ventral abdomen, medial limbs and often the ears. Lichenification and hyperpigmentation (greying of the skin) develop in chronic cases.

Figure. 6.19: Mange between the front toes (interdigital area) of an alpaca infested with *Chorioptes sp.,* exhibiting alopecia, scaling, heavy crusting (hyperkeratosis). Similar lesions may be seen in *S. scabiei* infections (Photo AP Foster, Univ. of Bristol, UK)

Treatment

All the acaricides used topically are effective against the Psoroptes and Chorioptes. It has been shown that pourons may be used. Bayticol, Pour-on 1% (flumethrin), 1 mL/10 kg applied on Bactrian camels with psoroptic mange proved to be effective. Five days after the single topical treatment was applied, no more living mites were found and the healing process of the skin lesions began a few days later.

6.2.2.6 Demodectic Mange

Mites of *Demodex spp.* infest hair follicles of all species of domestic animals. The disease causes little concern but in cattle and goats there may be significant damage to the hide and, rarely, death that may result from gross secondary bacterial invasion.
The demodecids comprise more than 150 species of parasitic mites in seven genera from hosts in 11 mammalian orders. Demodex is the only genus of importance for domestic hosts, and it contains at least 70 named species plus many more that are unnamed and undescribed. The adult Demodex are elongate, spindle-shaped (cigar-shaped), or vermiform mites, 250–850 μm long, that live in the host hair follicles, sebaceous glands, Meibomian glands, and occasionally in epidermal pits (Figure.6.20).

Figure.6.20: Morphological appearance of *Demodex spp* mite

These mites have short anterior mouthparts with two-segmented palps and retractable needle-like stylets used to puncture surrounding host tissues and feed on predigested cellular fluids. The normally four pairs of legs are usually short, stumpy, composed of three segments each, and terminate distally in paired pretarsal claws, usually with a linear empodium. Coxal fields occupy much of the anteroventral surface of the body where the legs attach. The palps or one pair of legs of some stages of some species may be greatly elongated or otherwise modified, primarily as holdfast organs. The very thin cuticle of the body and appendages is all but devoid of setae, but the opisthosoma is usually transversely striate. Befitting the confines of their narrow follicular or glandular habitats, the immature stages, including the eggs, of Demodex spp. are usually spindle-shaped or elongate oval, sometimes extremely so. The Lifecycle is only partially known. It includes eggs (70-90pm x 19-25pm), one larval stage and two nymphal stages, and lasts 3 weeks.

Demodex species are very host specific, only rarely inhabiting more than one species of congeneric mammal host. However, it is not uncommon for a host species to harbour two to four different species of parasitic Demodex. Transfer between hosts occurs only by very close contact between individuals (most probably mother to neonate), making transmission between animal species or from animals to humans very unlikely. Their very thin cuticles mean that demodecids cannot survive away from their hosts for more than a few hours.

The burrowing mite of the genus *Demodex* is preferred site of the hair follicles and sebaceous glands of the skin. Transmission of mites from dam to the offspring is most probably occurred during the nursing. All domestic mammals and humans worldwide is habituated by *Demodex sp* and mainly live as commensals in the skin. Most of the species are named after their hosts, i.e. *D. canis, D. bo*vis etc. In some animals, these mites may cause mange, of particular severity in dogs. In bovines, the most significant sequela to infestation is the damage to the hide, causing economic loss.

Demodex sp. has been reported on dromedaries in Iran where the eyelids of 15% of the camels were infested [131]. The demodex mange has also been reported in Iraqi camels [3]. The study survey began in December 2008 & finished in June 2009 in three governorates; Al-Qadissiya, Al-Najaf & Al-Muthanna in different locations inspecting 2412 dromedaries. They found that 55 of the mangy camels are infected with demodectic mange. The Demodectic mange was diagnosed in 58.2% of camels ranged in 5-10 years old & 16.4% of camels more than 10 years old & 25.4% in camels less than 5 years old and the authors believed that the infection transmitted to the camels

transmitted from the dogs that already domesticated with camels herd. The study indicated the high incidence of Demodectic mange in camels aged group 5-10 years and the infected camels showed thickening of the shin and, white to grey heavy crusts with moist dermis beneath, complete hair loss and itching(Hussain et al 2012). The infection with Demodex mange in camels, reveal neither evidence of any secondary bacterial infection, nor any significant histological changes. The dominant feature was the distention of the hair follicles. *Demodex sp.* was also isolated from camels exhibiting mange on a ranch in. *Demodex sp.* commonly occurs in llamas and alpacas in Bolivia [132]. The mite most probably also infests other NWC in other countries.

Treatment

Spraying the infected camels with the acaricides recommended to prevent spread than cure existing lesions. Ivermectin which does not eradicate the infection in dogs, possibly because of the difficulty in getting the acaricide to the mite, has been reported to cure 98% of beef bulls when used at 0.3 mg/kg [133]. Ivermectin in a premix, fed for 7 consecutive days has been reported to clear the infestation in pigs [134].

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6.3 Ticks Infestations in camel (Metastigmata)

a. Introduction

Ticks (Acari: Ixodida) are parasitic acari that suck blood from their vertebrate hosts [1]. Among external parasites, ticks are undoubtedly the most important economically obligate haematophagous ectoparasites of livestock on global scale [2, 3]. Ticks are distributed worldwide and are responsible for a great variety of livestock and public health problem. Ticks cause direct damage to their hosts and, especially, because they are vectors of a large variety of human and animal pathogens [4, 5, 6, 7, 8, 9, 10, 11]. Ticks are important vectors of protozoal, bacterial, viral and rickettsia1 diseases in many animal species. Ticks infestation lead to reduce milk, meat production and increase susceptibility to other diseases [7, 8].

In camels, several previous reports mentioned that the role of ticks as disease vectors are considered to be less important than in other animals [12, 13, 14]. However, the opposite are approved recently. Many studies are considered the ticks as the most important to the health of camels and cause higher calf mortality [15, 16]. There is no tick-free animal. However, and based on rough counts, only animals with more than 10 ticks were considered positive. The burden has been progressively increased during the subsequent wet seasons and peaked in the minor wet season (October to November) [17]. Ticks infestation causes debility and anemia because its blood-feeders nature. Each tick completing its blood meal, consume a significant amount of blood about 1 to 3 mL. Thousands of ticks may be found on the same infested animal. Steward, (1950) [18] mentioned that, a *Hyalomma sp.* appeared to cause the death of a camel that had been infested by 100 nymphs and adults per 2.5cm 2 skin surface. Rutagwenda, (1984) [19], found the high calf mortality rate of 20% encountered in some camel herds in Kenya due to"tick-anemia". There are more than 900 species of ticks have been recorded globally [20], with two major families, namely Ixodidae and Argasidae, the former generally referred to as hard ticks and the later also known as soft ticks [21]. The most common tick affecting camel belongs to the genera: Ambylomma, Hyalomma, Dermacentor and Rhipicephalus (all hard ticks) or family Ixodidae [22].

b. Morphology and lifecycle

Species of ticks are classified into 2 main families (Figure.6.21, 22 & Table.6.3):

- Argasidae: argasids or soft ticks, with a tough, leathery skin and a concealed ventrally projecting capitulum (± 170 species). There is no scutum in adult animals. A scutum is a dorsal shield. It tends to be endophilic/nidicolous parasites that colonize the nests and burrows of their hosts and feed when the host arrives.
- Ixodidae: ixodids or hard ticks have a rigid scutum and a capitulum with mouthparts projecting forwards (± 670 species). This capitulum is visible when viewed from dorsal. They are mostly exophilic ticks that actively seek hosts when the seasons are suitable, although examples of nidicolous ixodid ticks also exist, especially among species of the genus Ixodes.
- A third tick family, Nuttalliellidae, only has one species, Nuttalliella namaqua.

These three families share common basic properties that are modified distinctively inside each family according to their particular behaviour patterns and life-style [23].
Ticks are small animals related to mites, scorpions and spiders. Ticks are also known as Metastigmata. They derive this name from the large caudal respiratory openings in the post-larval stage. This opening or stigma is located behind the 4th legs in hard ticks, just in front of the 4th legs in argasids. Ticks differ from insects. Their bodies are divided into two parts rather than three. Ticks do not have antennae nor wings. The adults have eight legs instead of six. Ticks have 6 legs in the larval stage (nymphs and adult ticks gain a pair of hind legs). Nymphs have no genital opening. The body of a tick consists of a front section (gnathostoma, capitulum) containing the mouthparts (palps, hypostome and chelicerae) and a leg-bearing hindbody (idiosoma). Some tick species have eyes on this hindbody. On the front legs are found Haller's sensory organs. These structures contain chemoreceptors and are used for scanning the environment. Ticks that have climbed onto grass or other plants become aware of their potential host by vibration, warmth, CO2, moisture and smell (all mammals secrete

butyric acid). They remain attached to feathers, fur, skin or clothing, after which they seek a suitable place to suck blood.

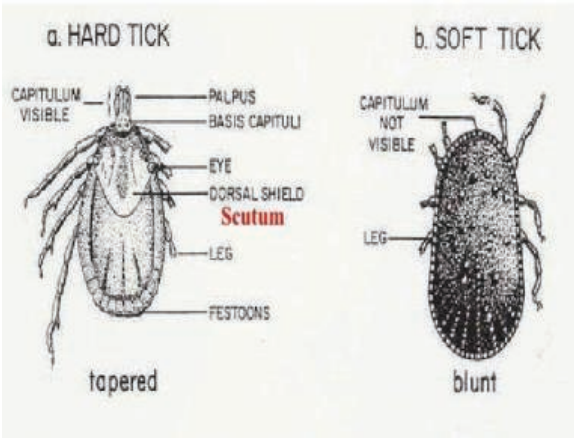

Figure. 6.21: Generalized dorsl view of female Hard and soft tick

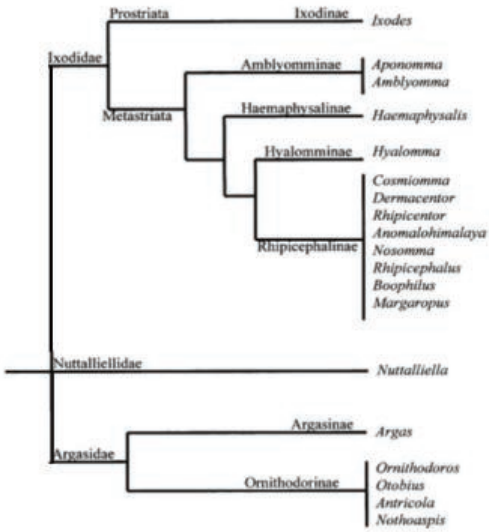

Figure. 6.22: Hoogstraal classification for ticks (Hoogstraal, 1985) [23]

Table. 6.3: The differences between hard and soft tick

Characteristics	Ixodidae (hard tick)	Argasidae (soft tick)
1. **Capitulum**	Terminal end can be seen in dorsal view.	Ventral or subterminal end can not be seen in dorsal view.
Papli	Rigid, not leg-like and of various form	Leg-like with subequal segments.
Basis capituli	Females have many small pits called **porose areas** on their basis capituli	No porose areas on basis capituli.
2. **Body**		
Scutum	Present. It covers the entire back in males but only a small portion in front in females.	Absent
Festoons	Generally present	Absent
Eyes (when present)	Dorsal on the sides of the scutum	Lateral on supra-coxal folds
3. **Legs**		
Coxae	Usually armed with spurs	Unarmed
Tarsi	Generally armed with 1 or 2 ventral spurs	Without ventral spurs.
Pulvilli	Always present	Absent or rudimentary.
4. **Life cycle**	Only one nymphal instar	Two to eight nymphal instars.
5. **Sexual dimorphism**	Marked	Slight
Examples	*Dermacentor andersoni, Haemophysalis spinigera, Ixodes, Scabularis* etc.	*Ornithodorus mouba, Otobius megnini, Argas persicus* etc.

The ticks undergo several metamorphoses during their life cycle from egg to larva to nymph to adult form. This cycle lasts a few months to several years, depending on climate and temperature. Ticks can survive for long periods without feeding. Some tropical species are rather resistant to desiccation at each stage in their life cycle. Larvae and nymphs are usually small and difficult to detect. There are two types of life cycles. In some species of tick, the larva, nymph and adult remain on the same, individual host, not dropping to the ground between stages. In others, the different stages feed on 2 or 3 different individuals. The host can be identified by the origin of the blood in the tick's stomach, e.g. by PCR analysis. Ticks with a host change are usually better vectors for pathogenic organisms. According to the number of hosts they require to fulfill their lifecycle, ticks are classified into the following three categories:

- The one-host ticks: All the three instars engorge (take their blood meals) on the same host. The two ecdyses also take place on the same animal: e.g. Boophilus spp.
- The two-host ticks: The larva engorges and moults on the host. The nymph after feeding drops onto the ground where it moults and the imago then seeks a new host: e.g. some Rhipicephalus spp.
- The three-host ticks: These need a different host for every instar, which drops off the host after engorging and then moults on the ground: e.g. some Ixodes (e.g. I. ricinus) and Rhipicephalus (e.g. R. appendiculatus) spp.

The ticks cease sucking blood, after completing their feeding. It drop-off their mouth-parts and fall away the hosts. This phenomenon is not random but controlled and timed to occur during the day and/or night [24]. Balashov, (1972) [25], mentioned that the timing of drop-off has dual ecological implications; an engorged tick tends to drop in areas where conditions are favourable for its development, and where it is likely to encounter a new host subsequently. Studies on the survival periods showed that longevity is negatively correlated with temperature and positively with the relative humidity [26].

Biological behaviour of H. dromedarii regarding the feeding periods and drop-off rhythms of engorged females and nymphs together with engorgement weights of females were recorded by ELGhali & Hassan, (2010) [27]. The survival periods of newly hatched larvae and newly moulted adults, which were released in nylon mesh bags at the base of a tree, were seasonally monitored. H. dromedarii react entirely as two-host ticks under field conditions. This study explained that the larval–nymphal feeding periods ranged between 16 and 27 days according to the season, whereas females fed for 6–9 days. The peak drop-off rhythms of nymphs and females occurred between 18:00 and 20:00 h. Engorgement weights of females at dropping ranged between 0.84 g on day 6 and 0.60 g on day 9 of attachment. Survival duration of the flat adults showed that 18.4%, 5.3% and 4.8% of ticks released in January, April and July, respectively, survived for 1 month. A very few number of ticks survived for extra periods of 3 months, 2 months and 1 month in January, April and July, respectively. They concluded that increased air temperature and lower humidity led to decreased survival duration. Larvae released in February, May, June and August died within 1 week, although they survived under laboratory conditions (35 ◦C and 49–90% Relative Humidity (RH) for 49–60 days.

c. Geographical distribution of ticks found on Camelids

OWC can be infected by a large number of tick species. However, there are only a few tick species (adults) that are camel host-specific. Hard ticks specially *H. dromedarii* is widely distributed throughout North Africa, the northern regions of West, Central, and East Africa; Asia Minor, the Middle East, and Central and South Asia [28]. Three camel soft tick species are recorded: the most important is *Ornithodoros savignyi,* followed by *O. Lahorensis* and *O. tholozani.* Studies on ticks infesting camel worldwide are meager. Most of studies on the tick population dynamic are carried out on sheep and cattle. In the rapidly changing environments of the world, as a result of exploitation by increasing numbers of humans and domestic animals, the patterns of tick–host–pathogen interrelationships are frequently modified by changes in population densities of one or each of three elements in the epidemiological processes of an infectious agent [29].

Several epidemiological studies on the occurrence of ticks in camels have been reported. For example, Hoogstraal, (1981) published a comprehensive article regarding tick distribution, prevalence, biology and epidemiological significance in camels in the Middle East, Saudi Arabia and North African regions. Details report about ticks found on camels in Ethiopia, Yemen Arab Republic and Kenya have been published by Pegram *et al.,* (1981, 1982) [31, 32], Dolan *et al.,* (1983) [33] and Pegram and Higgins, (1992) [34].

In Borana, tick seasonal burden and species dynamics showed that the average udder tick counts were 2.8, 3.6 and 4.3 with higher burden during the minor wet season. Pooled seasonally collected ticks belonged to the three genera, namely *Rhipicephalus* (83.2%), *Amblyoma* (13.6%) and *Hyaloma* (1.2%). The species identified include *R. pulchalus* (77.5%), *R. eversi* (18), *Amblyoma gemma* (13.4%), *Amblyoma vargatum*, *Amblyoma lipedum* and *Hyaloma dromedari*. Amblyomas - long mouthed ticks – are more important in inflicting udder damage and is a risk factor for mastitis in camels [17]. Selected camel herds of Borana lowland, southern Ethiopia were used as samples in a cross-sectional study. The percentage of various species ticks infestation were 97.7 and 25.9% from a total of 560 camels examined. The tick species identified and their relative abundance were as follows: *Rhipicephalus pulchellus* (69.6%), *Amblyomma*

gemma (12.4), *Hyalomma dromedarii* (10.8%), *Boophilus decoloratus* (4.2%), *Amblyomma variegatum* (2.6%) and *Amblyomma lepidum* (0.4%). The overall half-body region observed mean tick burden was 48.4 ticks/camel [17].

A survey study of ticks of the one humped camel was conducted in Borno State, Nigeria [35]. They found that out of the 1054 ticks collected from 96 camels *Hyalomma dromedarii* had 928 (88.1%); *Boophilus decoloratus* 114 (10.8%); *Amblyomma variegatum* 9 (2.9%), while *Rhipicephalus evertsi* had 3 (0.3%) prevalence rates ($p<0.05$). Tick species had the highest preference for the perineum 82 (85.4%) with a tick burden of 354 and least preferred the abdominal flanks with 3(3.1%) with tick burden of 13, the scrotum 3(3%) with a tick burden of 13 and the hump 3(3.1%) with a tick burden of 5($p<0.05$).

In Tunisia, first study was monitored the camel tick population dynamics on 30 camels (*Camelus dromedarius*) over one year in Kairouan region, Central Tunisia [36]. They found that ticks belonged to 2 genera and 5 species: *Hyalomma impeltatum* (53%) and *Hyalomma dromedarii* (45%) were the dominant species followed by *Hyalomma excavatum* (1%), *Hyalomma marginatum* (0.5%), and *Rhipicephalus turanicus* (0.5%) ($p < 0.001$). Mean infestation prevalence was 90.6%; all the animals were infested by at least one tick from May to September. The highest mean prevalence was observed in *H. impeltatum* (60%), the lowest was reported in *R. turanicus* (0.03%) ($p < 0.05$). Mean overall intensity of infestation was 4.4 ticks/animal. The highest mean intensity was observed in *H. impeltatum* (2.7 ticks/animal). Overall mean abundance of ticks was 4.4 ticks/animal. Different abiotic factors, namely monthly mean minimum and monthly mean maximum temperatures and the number of sunny days were positively correlated with overall monthly tick burdens which were in turn negatively correlated with the monthly mean relative humidity.

In Mauritania, has been observed that the camel tick Hyalomma dromedarii, appears to be the main vector of Theileria annulata in cattle which resulted from mixing of herds of camels and cattle [37].

In Kenya, Dolan *et al.,* (1983) [33] collected *H. dromedarii*, *H. m.rufipes* and *Rhipicephalus pulchellus* from camels. Moreover, in Kenya and Southern Ethiopia tick infestation of the one-humped camel is widespread [38,39,40,41] .

M. Dioli *et al.,* (2001) [15] reported ixodid ticks that infested three herds of one humped camels (*Camelus dromedarius*) in two separate areas of Kenya and one area of Southern Ethiopia. Species composition, attachment sites, sex ratio and seasonal incidence were described. The species observed were
Rhipicephalus appendiculatus, *R. evertsi evertsi*, *R. praetextatusa*, *R. pulchellus*, *R. pravus*, *Hyalomma dromedarii*, *H. marginatum rufipes*, *H. truncatum*, *Amblyomma gemma*, *A. lepidum* and *A. variegatum*.

In the North, North East, East and Sahara-Sahel regions of Africa, *H. dromedarii* is the most prominent camel tick. It has a two host or occasionally uses three hosts [11]. Camels are the principal host of the *H. dromedarii* adults with some records also showing that cattle and goats are also susceptible. The immature stages can parasitize rodents, leporids, hedgehogs and birds [41].

Ayele and Mohammed, (2013) [16] reported the prevalence of tick infestation in camels in and around Dire Dawa, Eastern Ethiopia. *Rhipicephalus, Hyalomma, Ambylomma* and *Boophilus* were the four identified genera of ticks. The most abundant tick species was *Rhipicephalus pulchellus* (46.78%), followed by *Hyalomma dromedarii* (26.85%), *Ambylomma gemma* (11.35%), *Hyalomma trancatum* (7.19%), *Hyalomma marginatum rufippes* (3.95%), *Ambylomma variegatum* (2.59%) and *Boophilus decoloratus* (1.24%).

In Burkina Faso, *H. dromedaries* and *H. marginatum rufipes* are the most identified ticks to infest camels. However, few studies have reported *H. truncatum* [44].
In India / Haryana, *H. dromedarii* is found to be the most common followed by *H. anatolicum*. Other genera of hard ticks found on camels are *Amblyomma, Rhipicephalus* and *Dermacentor*. In addition, *Boophilus microplus*, the cattle tick has been reported attacking dromedaries [45]. *Hyalomma dromedarii, H. anatolicum, H. Marginatum isaaci, Rhipicephalus spp., Ornithodoros spp.* are also reported as the commonly camel ticks in India [46].
In Australia, the cattle tick *Boophilus microplus* has been reported attacking dromedaries. In Iran, several studies have been reported the tick prevalence. In Yazd Province, (central Iran), the distribution of ticks, infested the domestic ruminants were reported [47]. They found the occurrence of seven species of hard ticks. The population frequencies of the species of genus *Hyalomma* were higher than the others. *Hylaomma Dromedarii* was the most frequent species. The host preference of main hard ticks was camel, sheep, cow, and goat, respectively. Sex ratio of ticks were 57% male and remaining female. The hard Ticks Infestation in Qeshm Island/ Iran in one-Humped Camels (*Camelus dromedaries*), were also reported. A total number of 912 adult ticks (472 males and 440 females) were collected and identified. Hyalomma dromedarii was the predominant tick specie and accounted for 61.9% of the adult ticks. Other hard ticks were *H. anatolicum excavatum* (22 %), *H. asiaticum asiaticum* (14.2 %), *H. marginatum* (1.9 %), *H. impeltatum* (0.4 %) and *Ripicephalus bursa* (0.4 %) [48].
The diversity and intensity of ticks in camels (*Camelus dromedarius*) and their seasonal population dynamics, reported in Kerman, southeast of Iran also. They found 217 infested camels out of a total of 426 tick specimens in southeast of Iran during activating seasons of ticks (April 2009 to March 2010). The species collected from camel were *Hyalomma dromedarii* (84.7%), *Hyalomma marginatum* (8.7%), *Hyalomma anatolicum excavatum* (5.4%), and *Hyalomma anatolicum anatolicum* (1.2%). The highest seasonal activities occurred in summer. The ratio of male ticks was more than female ticks. *H. dromedarii* was the predominant tick species and accounted for 84.7% of the ticks.
Tick species infesting camels in in eleven towns and cities in the three provinces of Northeast Iran (Khorasan Razavi, Northern Khorasan, and Southern Khorasan) were also identified [49]. Tick infestation was observed in 171 (85.5%) camels. *Hyalomma dromedarii* was found to be the predominant tick species (90.7%). Other tick species were found in low numbers and were as follows: *Hyalomma anatolicum* (6%), and *Hyalomma marginatum* (2.9%), *Hyalomma asiaticum* (0.4%).
Distribution of ticks (Acari: Ixodidae) infesting camels in mountainous areas of Golestan province, Iran were also reported [50]. They reported ticks in 4 male and 9 female. These ticks belong to *R. sanguineus* in 1.6 and 2.0 % in male and female respectively, *H. marginatom* 0.4 % in both male and female and *H. anatolicum* 0.8% in female and 0% in male. However, the total percentage was 2% and 3.1% in male and female respectively.
In Pakistan, Javaid Ali Gadahi, (2013) [51] reported the prevalence of ticks' infestation in the camel population of Thar Desert of Sindh. Only *Hyalomma dromedarii* species of tick was found and the overall incidence of the tick infestation was recorded as 83% (83/100).
In Libya, thirteen species of ixodid ticks and two species of argasid ticks were collected during a three-year survey from 58 farms. These included *Boophilus annulatus, B. microplus, B. decoloratus*, and seven species of *Hyalomma, Rhipicephalus sanguineus, Rh. evertsi, Rh. bursa, Argas persicus* and *Ornithodoros foleyi*. Of 20,391

animals examined by random sampling, 2020 (9.6%) had ticks; particularly common were *H. dromedarii* on camels [52].

In Saudi Arabia, camels (*Camelus dromedarius*) are considered as the most heavily tick-infested domestic animals. In addition, it acts as a source of infection to other livestock. It causes severe economic loss and the risk of fatal human tick-borne viral disease [53] . A total of 1 045 adult *H. dromedarii* and 174 *H. a. excavatum* together with 110 ticks that included *H. a. anatolicum, H. impeltatum, Hyalomma schulzei, Hyalomma truncatum, Hyalomma marginatum rufipes* and *Hyalomma marginatum turanicum*, as well as, 143 *Hyalomma spp*. nymphs were collected from 10 camels [54].

In Egypt, camels were found to be primarily infested by *Hyalomma dromedarii* (95 %) together with *Hyalomma marginatum* subspecies, *Hyalomma anatolicum excavatum* and *Hyalomma* species nymphs [55]. In the same area and on the same animal species Diab *et al.,* (2001) [56] found that *H. dromedarii*, *Hyalomma impeltatum*, *H. a. excavatum* and *H. a. anatolicum* represented 96 % of the tick population with a higher infestation in March to November and a mean monthly total of 22–78 ticks per animal. About 62 % of adult ticks were collected from the tail, anus, brisket and udder, and 91 % of nymphs were found infesting humps, neck, ears and sides.

In the Sudan, Karrar *et al.,* (1963) [57] reported that *H. dromedarii* was the main tick species of camels together with *Amblyomma lepidum*, *H. impeltatum*, *Rhipicephalus sanguineus sanguineus*, *Rhipicephalus simus*, *H. a. excavatum*, *H. truncatum* and *H. m. rufipes*. Elghali& Hassan, (2009) [58] identified the ticks (*Acari: Ixodidae*) infesting camels (*Camelus dromedarius*) in Northern Sudan. They found that *Hyalomma dromedarii* was the predominant (89 %) tick species infesting the camels. Other tick species found in very low numbers were *Hyalomma impeltatum* (7.7 %), *Hyalomma anatolicum anatolicum* (3.3 %), *Hyalomma truncatum* (0.29 %), *Hyalomma marginatum rufipes* (0.25 %), *Rhipicephalus praetextatus* (0.30 %) and *Rhipicephalus sanguineus* group (0.09 %). Nymphs of the genus *Hyalomma* were collected in significant numbers. Adult ticks significantly preferred to attach to the lower parts of the camel's body for feeding while the nymphs preferred the back of the animal. Female camels harboured more ticks than males, while higher infestations were recorded on camels with a grey coat colour compared to those with a brown coat colour. Ticks were found on camels throughout the year and increased in numbers during March to October with a peak in September. Tick species infesting camels, was also identified in the El Butana area mid-eastern Sudan [59]. Eleven species of ixodid ticks were reported in this area. These ticks found to belong to four genera namely: *Hylomma, amblyomma, Boophilus and Rhipicephalus*. Tick species were found throughout the year, with varied infestation rates. *Hyalomma dromedarii* appeared to constitute 69.64% followed by *H. rufipes, H.impeltatum, H. anatolicum, H. truncatum, Amblyomma lepidum* and *Rhipicephalus sanguineus*. However, *Boophilus decoloratus, H. detritum* and *R.e.evertsi*, were much less encountered [59].

In Yemen, Arab Republic, the most abundant livestock ticks were Hyalomma spp., particularly on camels, but with a very low burden [60].

In Jordan, *Hyalomma dromederii* and *Hyalomma anatolicum* are reported .These ticks may be present on any part of the camel's body, but the predilection site was a perennial, inguinal and axial region, between the toes and around the ears, eyes and lips [61, 62].

In Iraq, the distribution of Ixodes ticks were isolated from *Camelus dromedaries* in Al-Qadysia city [63]. *Hyalomma Spp. and Boophilus Spp*, were isolated from 182 (83%) out of 218 examined camels. *H. marginatum turanicum, H. anatolicum excavatum* were also reported in Basra [64, 65]. Moreover, heavey infestation of different tick species were

also identified between *Camelus dromedaries* in Al Muthhanna province / Samawah desert (Figure. 6.23). Al Salihi *et al.,* (2017) mentioned that heavey tick infestation are more important in imposing udder damage and is a risk factor for mastitis in camels (Figure. 6.24).

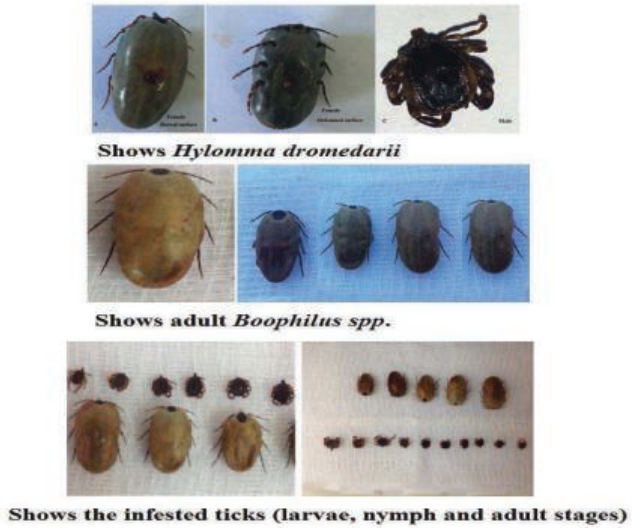

Figure. 6.23: Identified tick in Bediat Al Samawah/ Al Muthanna province/ Iraq.

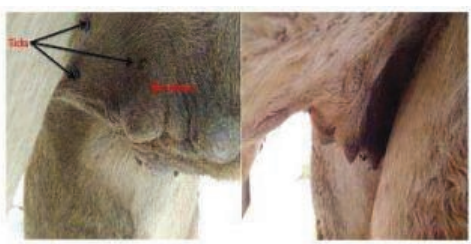

Figure. 6.24: Shows the severe udder lesions due to ticks infestation

In NWC, there are few reports that list particular species of hard ticks. However, *Dermacentor sp*. and *Ixodes holocyclus* are found to cause tick toxicosis in a llama [68, 69]. Hard ticks are also reported to be a problem, particularly on llamas in the western USA, during treks [70]. Amblyomma parvitarsum Neumann was found parasitizing vicunas in Peru [71]. Among the soft ticks (*Argasidae*), one species mentioned causing disease in llamas is the spinose ear tick (*Otobius megnini*), which may infest other hosts, including humans. The soft ticks may cause problems in llamas and alpacas in certain localities in the western USA [14].

Table. 6.4: Represent the ticks identified from camel in different geographical area.

Species	Localization		Reference
A. 20 species in imported camels and only 12 species in indigenous camel. B. Three species of the genus Amblyomma were recorded(A. gemma, A. lepidum, A.variegatum) C. 10 species of genus Hyalomma (H. anatolicum anatolicum, H. anatolicum excavatum, H. dromedarii, H. erythraeum, H. impeltatum, H. impressum, H. marginatum rufipes, H.erythraeum, H. impeltatum, H. impressum, H. marginatum rufipes, H. marginatum turanicum, H. schulzei, H. turanicum. D. 7 species of the genus Rhipicephalus (R. evertsi, R.gulhoni, R. pulchellus, R.sanguineus, R. simus, R.camicasi, R.turanicus).	Saudi Arabia		Hoogstraal, H. and Kaiser, M. N .. Ticks (Ixodidae) of Arabia with special reference to the Yemen. Fieldiana . Zoology 39: 297-322(1959). Hoogstraal, H. wassef, H.Y. and Buttiker, W. Ticks (Acarina) of Saudi Arabia . Fam. Argasidae, Ixodidae. Fauna of Saudi Arabia 3: 25-110(1981). A.A.Banaja and A.M. Ghandour . (1994) . A review of parasites of camels (Camelus dromedarius) in Saudia Arabia. JKAU Sci., Vol.6 pp.75-86.
Hyalomma anatolicum excavatum, Hyalomma schulzei and Hyalomma marginatum turanicum	Saudi Arabia		Al-Asgah, N.A., H.S.Hussein, M.S. Al-Khalifa and F.M. Diab. 1985. Hyalomma schulzei (The large Camel Tick): Distribution in Saudi Arabia. J. Med. Entomol., 22: 230-231.
Hyalomma species, H. dromedarii, H. rufipes, H. impeltatum and H. truncatum.	Sokoto, Nigeria		M.D. Lawal, I.O. Ameh and A. Ahmed, 2007. Some Ectoparasites of Camelus dromedarius in Sokoto, Nigeria. Journal of Entomology, 4: 143-148.
Hyalomma dromedarii and Hyalomma anatolicum.	Jordan		21. F.K. Al-Ani, L. A. Sharrif, O.F. Al-Rawashdeh K. M. Al- Qudah and Y. Al-Hami.(1998). Camel Diseases in Jordan. Proceedings of the Third Annual Meeting for Animal Production Under Arid Conditions, Vol. 2: 77-92. © 1998 United Arab Emirates University.
Hyalomma dromedarii, H. anatolicum, H. marginatum isaaci, Rhipicephalus spp., Ornithodoros spp. etc. Heavy infestions lead to decrease in draught capacity, milk production in lactating dams and growth rate in young animals. Chrysomyia spp. and Wohlfahrtia magnifica are the most important myiasis producing flies affecting camel and cause vaginal and preputial myiasis. Cephalopina titillator fly was found to cause nasal myiasis in camel.	India		Parsani, H.R., Veer Singh and Momin,R.R. 2008. Common Parasitic Diseases of Camel. Veterinary World, Vol.1(10): 317-318.
Hyaloma dromedarii and H. marginatum rufipes	Burkina Faso		M.L. Dia. (2006). Parasites of the camel in Burkina Faso. Trop Anim Health Prod (2006) 38: 17–21. DOI 10.1007/s11250-006-4303-x.
Ornithodoros savignyi	Egypt		Helmy, N. (2000). Seasonal abundance of Ornithodoros (O.) savignyi and prevalence of infection with Borrelia spirochetes in Egypt. Journal of the Egyptian Society of Parasitology, Vol. 30, No. 2, (August 2000), pp. 607-619, ISSN 0253-5890.
Hyalomma dromedarii	sub-Saharan Algeria	Rickettsia africae, the agent responsible for African tick-bite fever	Tahar Kernif, Amel Djerbouh, Oleg Mediannikov, Boulanoa Ayach, Jean-Marc Rolain, Didier Raoult, Philippe Parola, Idir Bitam, (2012). Rickettsia africae in Hyalomma dromedarii ticks from sub-Saharan Algeria. Ticks and Tick-borne Diseases 3 (2012) 376– 378.
Rhipicephalus pulchellus (69.6%), Amblyomma gemma (12.4), Hyalomma dromedarii (10.8%), Boophilus decoloratus (4.2%), Amblyomma variegatum (2.6%) and Amblyomma lepidum (0.4%).	southern Ethiopia	pose a potential health hazard	Megersa, B.D., Bekele, J, Adane, B, Sheferaw, D. 2012. Ticks and mange mites infesting camels of Boran pastoral areas and the associated risk factors Southern Ethiopia.. J. Vet. Medicine Anim. Health, 4(5) 71-77
eastern Ethiopia include Rhipicephalus pulchellus, Amblyomma gemma, Hyalomma dromedarii, (Dinka et al., 2010; Zeleke and Bekele, 2004).	eastern Ethiopia		Dinka A, Eyerusalem B, Yacob HT (2010). A study on major ectoparasites of camel in and around Dire-Dawa, Eastern Ethiopia. Revue Méd. Vét. 161(11):498-501. Zeleke M, Bekele T (2004). Species of Tick on camels and their seasonal population dynamics in Eastern Ethiopia. Trop. Anim. Health Prod. 36:225-231.
H. marginatum turanicum, H. anatolicum excavatum. Hyalomma Spp and Boophilus Spp,	Basra/ Iraq Al-Qadysia / Iraq	isolated from 182 (83%) out of 218 examined camels.	**AHH. Awad and M. A. Abdul – Hussein.(2006).** New Record of Two Species of Hard Ticks from Some Domestic Animals in Basrah - Iraq J.Basrah Researches (Sciences) Vol.32. Part.1. 1-6 (2006). M. H. Hussein and M. A. A. AL- Fatlawi (2009) Study the epidemiology of ticks infected Camelus dromedaries in Al- Qadysia city
Hyalomma dromedarii was found to be the predominant tick species (90.7%). Other tick species were found in low numbers and were as follows: Hyalomma anatolicum (6%), and Hyalomma marginatum (2.9%), Hyalomma asiaticum (0.4%).	Northeast of Iran		Iman Janpoor, Gholamreza Mohammadi, Sadegh Chinikar, Gholamreza Razmi, Ehsan Mostafavi and Tahmineh Jalali. (2013). Ixodid tick and the influence of age and sex of camel on tick infestation rates in one humped camel (Camelus dromedarius) population in the Northeast of Iran. International Journal of Veterinary Science: 1(2):89-95. September, 2013.
Eleven species of ixodid ticks belonging to four genera namely: Hyalomma, Amblyomma, Boophilus and Rhipicephalus. Most of the tick species were found throughout the year, with varied infestation rates. Hyalomma dromedarii constituted 69.64% followed by H. rufipes, H. impeltatum, H. anatolicum, H. truncatum, Amblyomma lepidum, and Rhipicephalus sanguineus, while Boophilus decoloratus, H. detritum and R. e. evertsi, were much less encountered	Sudan		Maha A. El Tigani. and Mohammed, A. S. (2010). Ticks (Acari: Ixodidae) Infesting Camels in El Butana Area Mid-Central Sudan. Sudan J. Vet. Res. 25: 51-54.
Hyalomma dromedarii	northern Sudan		Elghali, A. and Hassan S. M. (2009). Onderstepoort J. Vet. Res., 76: 177-185.
Sudan are Hyalomma dromedarii, H. anatolicum, Amblyomma lepidum, A. variegatum and Ornithodoros savignyi	Sudan		A.M. SHOMMEIN and A.M. OSMAN (1987). Diseases of camels in the Sudan. Rev. sci. tech. Off. int. Epiz., 1987, 6 (2), 481-486.
Amblyomma, Hyalomma, Rhipicephalus	Somalia		Omar Sh. Abdurahman and Set Bornstein. (1991).Diseases of camels in Somalia and prospects for better health. Nomadic peoples, Number 29, pp104-112, 1991.
The species collected from camel were Hyalomma dromedarii (84.7%), Hyalomma marginatum (8.7%), Hyalomma anatolicum excavatum (5.4%), and Hyalomma anatolicum anatolicum (1.2%).	Iran		Saeid Reza Nourollahi Fard & Saeid Fathi & Ehsan Norouzi Asl & Hojat Asgary Nazhad & Soleim Salehzadeh Kazeroni (2012). Hard ticks on one-humped camel (Camelus dromedarius) and their seasonal population dynamics in southeast, Iran. Trop Anim Health Prod (2012) 44:197–200.
Hyalomma dromedarii was the predominant tick specie and accounted for 61.9% of the adult ticks. Other hard ticks were H. anatolicum excavatum (22 %), H. asiaticum asiaticum (14.2 %), H. marginatum (1.9 %), H. impeltatum (0.4 %) and Rhipicephalus bursa (0.4 %).	Iran		Saeed Nazifi, Amin Tamadon, Mohammad-Amin Behzadi, Shahram Haddadi, Ali-Reza Raayat-Jahromi (2011). One-Humped Camels (Camelus dromedarius) Hard Ticks Infestation in Qeshm Island, Iran Veterinary Research Forum . Vol: 2, No: 2, June, , 135 – 138.
7 species including Hyalomma dromedarii (55.02%), Hy. marginatum (13.20%), Hy. anatolicum (9.78%), Hy. detritum (4.98%), Hy. asiaticum (3.94%), Rhipicephalus sanguineus (11.84%), and Dermacentor marginatus (0.34%).	Iran		Salim abadi, Y., Telmadarraiy, Z., Vatandoost, H., Chinikar, S., Oshaghi, M.A., Moradi, M., Mirabzadeh Ardakan, E., Hekmat, S. and Nasiri, A., 2010. Hard Ticks on Domestic Ruminants and their Seasonal Population Dynamics in Yazd Province, Iran. Iranian Journal Arthropod-Borne Disease, 4, 66–71
Rhipicephalus appendiculatus, R. evertsi evertsi, R. praetextatus, R. pulchellus, R. pravus, Hyalomma dromedarii, H. marginatum rufipes, H. truncatum, Amblyomma gemma, A. lepidum and A. variegatum.	Kenya and Southern Ethiopia		M. Dioli, S. Jean-Baptiste, M. Fox (2001). Ticks (Acari: Ixodidae) of the One-Humped Camel (Camelus dromedarius) in Kenya and Southern Ethiopia: Species Composition, Attachment Sites, Sex Ratio and Seasonal Incidence Revue Elev. Méd. vét. Pays trop., 54 (2) : 115-122
Thirteen species of ixodid ticks and two species of argasid ticks . These included Boophilus annulatus, B. microplus, B. decoloratus, seven species of Hyalomma, Rhipicephalus sanguineus, Rh. evertsi, Rh. bursa, Argas persicus and Ornithodoros foleyi.	Libya	Of 20,391 animals examined by random sampling, 2020 (9.4%) had ticks; particularly common were H. dromedarii on camels.	42. Al Wser O. R. (2004). Epidemiological study on camel ticks infestation in Libya and vaccine trials using Boophilus derived vaccine against Hyalomma dromedarii ticks. M.Sc. Thesis. Institute Agronomique et vétérinaire Hassan II, Morocco.

d. Economic importance

The earliest studies on the camel (*Camelus dromedarius*) mentioned that ticks play a less important role than with some other domestic livestock as vectors of major diseases but can cause severe debility, where heavy infestation occurs. However, recent studies approved that ticks are undoubtedly the most important economically ectoparasites of livestock on global scale [73, 74]. They are responsible for a great variety of livestock health problem. Apart from transmitting diseases, they also reduce milk, meat production and increase susceptibility to other diseases [7, 8]. Ticks cause widespread distress, morbidity and seriously affect the economic conditions of camel-rearing country. The injuries and diseases related to ticks are more prevalent and severe than what is commonly perceived [49]. Because of the direct and indirect effect on their host, ticks are considered to be not only a significant threat to successful livestock production, but also a seriously interfere with economy of the countries [73]. In addition to feeding on animal blood, ticks considered as the most important vectors for infectious diseases worldwide causing tick paralysis, and the interest in tick-borne diseases has increased in recent years [76]. *H. dromedarii* is a vector of bacteria [77], rickettsia [78], and viruses [79]. Additionally, ticks are responsible for direct damage to livestock through their feeding habits. The damage manifested as hide damage, damage to udders, teats and scrotum, so that opening door for opportunistic micro-organisms and fly larvae, myiasis due to infestation of damaged sites by maggots and secondary microbial infections. In fact it may also lead to skin rejection at tannery factories [80, 81]. In Algeria, the role of *H. dromedarii* in the epidemiology of *Rickettsia africae* has been approved. The spotted fever group (SFG) rickettsioses are an important group of emerging, worldwide occurring tick-borne human infections [82]. The same genotype of *R. africae* was also identified in Egypt [83]. *Rickettsia africae*, the agent of African tick bite fever (ATBF), had been detected in *H. dromedarii* collected from camels (*C. dromedarius*). They concluded that *H. dromedarii* act as a potential vector of *R. africae* and play important role in the transmission of the ATBF in North Africa. Camel ticks are also reported as vectors of viruses infecting humans. The *Hyalomma anatolicum* is an important vector of *Crimean-Congo hemorrhagic fever* (CCHF) virus, which was reported in the former USSR, Pakistan and Nigeria [84]. This virus has also been isolated from the ticks commonly found on camels, *H. dromedarii* and *H. impeltaturn* (Table 57). The group of Zoonosis associated with camel infesting ticks are presented in (Table. 6. 5) [34].

e. Susceptibility

Significant differences are observed in tick burden between females and males ($p<0.01$). Comparison of older and younger animals showed no significant difference in the number of ticks ($p>0.05$) [49]. No Significant differences were observed between tick burden carried by males and females or different eco-types of camels ($P\geq0.05$). Significant differences ($P\leq0.01$), however, it was observed between ticks collected in different months and from the different age groups of camel [59]. Elghali& Hassan, (2009) [58] also reported that female camels harboured more ticks than males. While higher infestations were recorded on camels with a grey coat colour compared to those with a brown coat colour. Ticks were found on camels throughout the year and increased in numbers during March to October with a peak in September.

Table. 6. 5: A group of Zoonosis diseases associated with camel infesting ticks [34]

Vector	Agents of diseases	References
Hyalomma dromedarii	Rickettsia africae, the agent responsible for African tick-bite fever	Tahar Kernif, Amel Djerbouh, Oleg Mediannikov, Bouhous Ayach, Jean-Marc Rolain, Didier Raoult, Philippe Parola, Idir Bitam, (2012). Rickettsia africae in Hyalomma dromedarii ticks from sub-Saharan Algeria. Ticks and Tick-borne Diseases 3 (2012) 376– 378.
Rhipicephalus pulchellus (69.6%), Amblyomma gemma (12.4), Hyalomma dromedarii (10.8%), Boophilus decoloratus (4.2%), Amblyomma variegatum (2.6%) and Amblyomma lepidum (0.4%).	pose a potential health hazard	Megersa, B.D., Bekele, J, Adane, B, Sheferaw, D. 2012. Ticks and mange mites infesting camels of Boran pastoral areas and the associated risk factors Southern Ethiopia., J. Vet. Medicine Anim. Health, 4(5) 71-77
Hyalomma dromedarii	Rickettsia africae, the agent responsible for African tick-bite fever.	Tahar Kernif et al 2012
Hyalomma dromedari on camels	Tick paralysis caused by the secretion of toxin with saliva	Amira A. Abd el-rahman mosabah, and Tosson A. Morsy. (2012). Tick paralysis: first zoonosis record in egypt. Journal of the Egyptian Society of Parasitology, Vol. 42, No. 1, April 2012
H. anatolicum	Thogoto virus H. excavatum Rickettsia prowazeki H. dromedarii Dhori virus Khadam virus CCHF virus Q-fever (Coxiella burnetii)	(Pegram and Higgins, 1992
H. impeltatum	Wanowrie virus CCHF virus	(Pegram and Higgins, 1992
H. marginatum H. scupense H. truncatum R. pulchellus R. praetextatus	CCHF virus ? virus (Paralysis) CCHF virus ? virus (Paralysis) Rickettsia prowazeki Thogoto virus	(Pegram and Higgins, 1992

Ayele and Mohammed , (2013) [16] showed that infestation rate of ticks were 148 (90.2%) in males and 213 (96.8%) females camels. The infestation rate was varied significantly ($p<0.05$) between sex groups as well as between origin of the animals. However, there was no statistical significant difference observed ($p>0.05$) in prevalence of tick infestation between the age groups and among the body condition of the animals. Megersa *et al.,* (2012) reported that the total tick burden was significantly higher in camels 1-3 years of age with poor health condition. They found that the total half-body regions mean tick burden was significantly higher in young males (1 to 3 years of age) with poor body conditions, large herd size (greater than 40 camels) and in wet season. They mentioned that mixing camels with sheep and goats, and cattle significantly affect the mean half-body tick burden of camels. Biu and konto, (2012) [35] also found that tick infestation was highest on camels aged between 3 and 8 years with 52 (54.2%) and least be 8(8.3%) between 15 and 19 years, while female camels were more infested 63(65.6%) than the male with 33 (34.4%) ($p<0.05$).
Moreover, Hussein and AL- Fatlawi, (2009) [63] found that the 75.3% of she camel were infected and only 24.7% was male. The most infested camels were 5-10 years old. And the ticks were isolated from different site on the body. Meanwhile, Javaid *et al.,* (2013) [51] findings revealed highest prevalence of tick infestation in young camels less than 7 years age group (85.29%) as compared to age group 7 years and above (81.81%).

f. Pathogenesis and pathology

The animals become more prone to tick infestation when they are kept in poor husbandry practices. The summer considers as the tick highest seasonal activities and the fluctuations in their numbers throughout the year depend on the variations in temperature, relative humidity and live cycle duration. However, tick species may be found throughout the year. Tick adopts off-host on-host life cycle strategy and called gorging-fasting organisms [87]. Ticks as a group, can survive without food or water for long time outside their host rather than any other arthropod. Tick owns their adaptive capacity which are dealing with the conservation of energy and water, to the extent that, life might be extended for months or even years [88, 89, 90]. The ticks on camels are mostly attached in the perineal, inguinal, and axillary regions, around the eyes, lips, in/on the ears, the nostrils and in the nose, between the toes and on the mammary glands. The gorging interval is characterized by rapid metabolism and development accompanied by the elimination of excess ions and water back into the host. Such intimate association might result in the exchange of body fluids between the tick and its host, which might facilitate the infection of the former with microorganisms, or in the transmission of disease agents to the latter. Ticks able to transmit a greater variety of infectious agents than any other group of blood-sucking arthropods. Saliva of the ticks, able to maintain the lesion through the secretion of anti-edema components [91], when their mouthparts secured in place by an attachment cement serving a gasket [92]. The immatures and adult female soft body integument grows unfolds and stretches to held their high-volume fluid diet [93]. The males, feed less than female, but they generally mate with females on the host. Later on, the females acts to complete their engorgement and, together with engorged immatures, leave the host for subsequent development to be completed off that host [94]. The numbers of ticks play important role in the pathogenesis of tick effects. It may be high, thereby interfering with the well-being of the host, causing irritation and direct injury to the skin. Wounds may become secondarily infected, leading to pyoderma. *Streptococcus agalactiae*is isolated from wounds caused by *Hyalomma sp.* in a herd of dromedaries. The effected skin is rough and thickened and reveal scar tissue with. Sores are often seen at dermato-mucosal borders on the nose, lips and vulva. Tick bites may predispose to myiasis. However, It is not known if ticks able to introduce secondary bacterial infections to the mammary glands. It is suggested that heavy tick loads contribute to reduced growth rates and calf mortality [95]. Sizable numbers of ticks may lead to anaemia.

g. Clinical signs

Tick infestations in animals are much more severe than in humans. Hundreds or even thousands of ticks can be found on the animals. Ticks are obviously multiplies the effect on the host, either by direct injuries or disease transmission.

A. Direct effects

In general the direct injuries to animals can be very serious. Camels can be attacked by many different ticks. It cause widespread distress and morbidity. Ticks usually attach to the legs, head, the underbelly, axilla, foot, udder, perineal area and tail (Figure. 6.25). Moreover, *Hyalomma dromedarii*, attaches predominantly itself in the

nostrils of the camel, lips and vulva. In this cases, sores are often seen at dermato-mucosal borders on the nose, lips and vulva.

Figure. 6.25: Shows the direct effects of heavy tick infestation in camel (Bediat Al Samawah / Al Muthanna province/ Iraq 2018 , Phato captured by Dr. Karima Al salihi).

The direct effects of tick infestation in camel, is depended on the size numbers of ticks. It may be severe to mild anaemia, damage to: udders teats and scrotum,hide (the rejection of skin at tannery factories happened with sever ticks infestation), appetite loss with consequent reduced growth rate, productivity, which contribute to a general loss of condition. The most frequent of these direct forms of damage include:

1. Biting stress and lost production. The prolonged feeding of ticks, tissue destruction and inflammation is caused by the tick mouth parts at the wound, followed by acquired immune reactions in the skin (dermal hypersensitivities types 1 and 4) to the foreign proteins in tick saliva.
2. Physical damage; at the feeding site of hard ticks granuloma and wound healing produce a scar that remains for years after the tick has detached.
3. Loss of blood, which in massive infestations can cause acute anaemia.
4. paralyses caused by salivary toxins, such as the holocyclotoxin from the Australian tick Ixodes holocyclus, a tick species that can paralyze and kill a young animal with only one female bite.
5. Toxicoses, such as the Sweating sickness caused by the African *Hyalomma truncatum*; in ruminants this disease elicits eczematous skin lesions, hyperexcretion of exudates and more than 75% mortality in young animals.
6. Immunosuppression, which renders animals more susceptible to pathogen transmission.

Tick's mouthparts lesions are small but it is a portal to secondary bacterial infections and attract flies; some causing myiasis due to infestation of damaged sites by maggots. In India, *Chrysomyia spp*. and Wohlfahrtia magnifica are the most important myiasis producing flies affecting camel and cause vaginal and preputial myiasis. Cephalopina titilator fly was found to cause nasal myiasis in camel [62]. The attachment sites of ticks commonly show dried blood with scabs (inflammatory reaction) and frequently these sites, following infestations by *Amblyomma lepidum*, develop into large ulcerations (sores). Infested camels are often irritated and exhibit pruritus. Apparently, some ticks also cause paralysis in camels as well as in other livestock 43 species of 10 different genera have been incriminated in causing toxic reactions according to Fowler, (2010) [72], and 60 species according to Hoogstraal, (1985) [23] , Jabbar *et al.,* (2007), Hart, (1990) [97]; Nelson et al., (1977) [98] ; Schwartz *et al.,* (1983) [99].

B. Indirect effect as vectors of Disease Pathogens (Tick born diseases)

Ticks are the major vectors of pathogens in animals and humans. Injuries and diseases related to ticks are more prevalent and severe than what is commonly perceived. Ticks considered as the most important vectors for infectious diseases worldwide.
Crimean–Congo hemorrhagic fever (CCHF) virus was isolated from ticks species collected from camels in Turkmen SSSR (Hoogstraal, 1979) [84]. In Saudi Arabia, Kadam (KAD) virus was isolated from a pool of male H. dromedarii taken near a dead camel in Wadi Thamamah in Riyadh Province [100]. Other viruses that have been isolated from *H. dromedarii* include Dera Ghazi Khan virus and Dhori virus [42]. There is also evidence that *Amblyomma lepidum* or *A. gemma* may transmit *Cowdria ruminantium* (Heartwater) to cattle [57] and that *H. dromedarii* is the vector of Q fever and camel Theileria camelensis [42]. Anaplasmosis is also non contagious tick born disease. Its natural infection with Anaplasma marginale was reported in 52 camels in Iraq withpercentage of parasitemia (5-11%) [101]. *H. dromedarii* has been found to act as a potential vector for Rickettsia africae in North Africa [82, 83]. The Rickettsia africae, the agent of African tick bite fever (ATBF), had been detected in H. dromedarii collected from camels (*C. dromedarius*).

h. Tick paralysis

The saliva of some ticks is neurotoxic and "tick paralysis" can occur. Tick paralysis occurs in OWC as well as NWC. It is a syndrome that appears to be rare; it has only been reported in Sudan and is apparently caused by Hyalomma spp. adults and/or Rhipicephalus spp. adults or nymphs [102]. It is known that there are more than 60 tick species which are capable of causing paralysis [23] In OWC, the larva of *H. dromedarii* has the ability to cause of paralysis. It is reported to cause high mortality (above 24%) in calves in the Sudan. Epidemics of suspected tick paralysis incriminating both Hyalomma spp. and Rhicephalus spp. have also been reported in
Sudan [102]. The poisons from some ticks affect the nervous system and muscles and the animal cannot move (paralysis) which can lead to death. The camel suddenly shows signs of paralysis and its body temperature will drop [103].

i. Diagnosis

Ticks are easily seen on their predilection places, often relatively deeply imbedded in the skin. Ticks should be identified to species. All visible attached adult ticks can be collected carefully and gently remove exerting a horizontal pull to the body surface by rotating the tick not to damage the host by the tick's mouth parts and then the ticks are preserved properly in plastic container containing 70% ethanol. The body region that used for ticks collections are: ear, under tail, sternum, nose, scrotum/ udder, ventral and dorsal surface of the body of the animals (Figure. 6, 26).
The ticks are label with date, place, sex, age and site of the body and then transport to the laboratory. The ticks from each animal are placed onto Petri dishes and examined under stereomicroscope to identify the species using tick identification keys described by Onkello-Onen et al. and Walker et al. Briefly, the main identification features of the ticks are color, size, and shape of mouthparts, scutum, anal groove, festoon, punctuation and legs.
Detection of infective pathogens (viral, parasitic, and bacterial) in ticks is also important parameter in epidemiological studies. There are different techniques used for detecting infections in ticks. The conventional staining method have been for long time ago, however, the more specific PCR technique is widely used nowadays

worldwide. This technique which uses specific oligonucleotide primers and Tag DNA polymerase to synthesise a large number of copies from a single DNA template has very rapidly become a standard laboratory technique, and is more sensitive than nucleic acid hybridisation. For example, PCR has been shown to be a valuable tool for the detection of *Cowdria ruminantium* in *Amblyomma spp*.. In general, one can differentiate between closely related pathogens within ticks, which is not possible using conventional staining techniques.

Figure. 6.26: Shows the hand collecting of ticks from heavy infestated camel (Bediat Al Samawah / Al Muthanna province/ Iraq 2018, Phato captured by Dr. Karima Al salihi).

j. Treatment and control of tick infestations

Eradication of ticks is generally not doable, except on small lands, where successful combats have sometimes been carry out. Three methods are now available to control ticks in camels:

A. Treating with acaricidal agents

Individual animals can be effectively treated by the application of any one of a number of acaricides applied either as a spray or by dipping. The choice of acaricide depends largely on three factors:

1. The prolongation period for the existence of the compound on the skin and hair coat.
2. The probability of residues toxic to man emerging in the milk or meat.
3. Whether or not the ticks in the area have developed resistance to the particular acaricide.

The same criteria apply in chemical control as in treatment except that cost becomes a limiting factor when large numbers of animals require frequent treatments. In camelids, routine preventive tick control is not practiced, because camel breeding always be in the desert, with continuous movement far away, making it difficult to reach them. However, some breeders requesting for treatment and prevention for their camels. Control of significant numbers of ticks attacking camels is recommended. A suitable acaricides (synthetic chemical pesticides specific for ticks) can be apply to the infected sites (chlorinated hydrocarbons, organophosphates, carbamates, synthetic pyrethroids or the macrocyclic lactones). The sterilizing effect of pour-on flumethrin on the camel tick, *Hyalomma dromedarii* (Acari: *Ixodidae*) are worked successfully in its controlling. By a direct contact method, ticks were exposed in vitro to 87 /µg active ingredient for 1, 5, 10, 30 or 72 min. Generally, the study is revealed a correlation

between the action of flumethrin and the exposure time. The longer exposure to the compound resulted in more inhibition of tick fertility/ The 5 or 10 minutes exposure of flumethrin in females were the significant sterilizing activity. However, after 30 rain exposure the action was highly pronounced; out of ten females, only one laid eggs and these did not hatch. Usually, the drug (1 to 2mL/10kg) is poured from the shoulder along the middle of the back over the hump to the tail.

A field trial on pyrethroid flumethrin (Bayticol) has demonstrated that flumethrin is safe and effective when used to control ticks on dromedaries, and the pour-on method for insecticide application is fast and easy and is suitable for use by camel owners in the desert. The heavily infested herd was treated with 2 ml 10 kg -t body weight per animal whereas the lightly infested herd was treated with 1 ml 10kg- 1 body weight per animal. The drug is poured from the shoulder along the middle of the back over the hump to the tail. However, no side-effects of treatment were observed (. Ivermectin as acaricidal has been used to treat and control the ticks (Acari: *Ixodidae*) infesting the Arabian camel (*Camelus dromedarius*) in the Sinai, Egypt. It appeared as efficient acaricidal in camel. Macrocyclic lactone products based on ivermectin, moxidectin, eprinomectin, and doramectin have been reported to have variable to good effects. Subcutaneous injections of 10mg/50 kg ivermectin are also effective in controlling both larvae and nymphs of the spinose ear tick. The ear canals may be cleaned manually and solutions of insecticides or acaricides instilled. By spraying or dousing, Lindane (Gamatox) are approved as the best acaricide to treat and control the camel ticks in Sudan [104]. It is beyond the expectations to make specific recommendations on methods of application and the most efficient acaricides to use because these vary widely between species of ticks. However, at any possible time, treatment should be given systematically in a program based on the life cycle (unfed larvae, diapausing nymphs, unfed adults and laying females) and epidemiology of the tick (Figure.6.27). A number of treatments may be used early in the tick season to prevent the increase in tick numbers. The use of acaricides in tick control has been comprehensively reviewed by the Food and Agriculture Organization of t h e United Nations (Food and Agriculture Organisation of the United Nations (FAO) (1984).

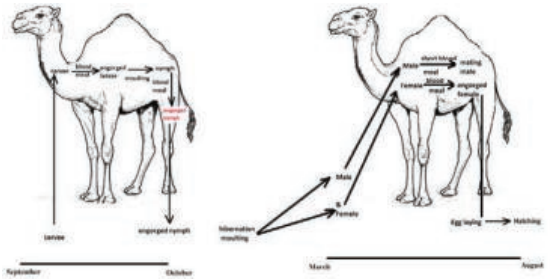

Figure.6.27: Treatment of ticks systematically in a program based on the life cycle (unfed larvae, diapausing nymphs, unfed adults and laying females) and epidemiology of the tick.

B. Vaccination

Tissues and saliva of the ticks are able to stimulate immune defenses of the hosts. It is approved that the host stimulated immune system can disrupt blood meal acquisition,

impair physiological responses and/ or kill the arthropod. The acquired resistance to ixodid ticks has been recognised as a possible biological control method [105]. It was approved that the guinea pigs immunized with whole larval extract of Dermacentor variabilis were resistant to the challenge of the larvae. Such resistance, acquired after repeated infestations by ticks, is immunologically mediated [106]. Acquired immunity is expressed by a reduction in the number of ticks which attach to the host, reduced engorgement weights, and reduced egg and larval production resulting in significantly reduced tick populations [107]. Unchanged Y-immunoglobulins in the blood of the host can cross the intestinal wall into the haemolymph of ticks. This observation is at the origin of the idea of inducing artificial resistance against ticks through the use of ' concealed ' antigens, which do not normally contact the host [108]. The development of an anti - tick vaccine against Hyalomma dromedarii is a major new approach in the control of ticks and encourage numerous researcher nowadays. Manuel Rodríguez-Vallea *et al.,* (2012) [109] , were conducted a vaccination trials using a *Rhipicephalus* (*Boophilus*) *(R.) microplus* recombinant Bm86- based vaccine against immature and adult ticks of *Hyalomma dromedarii* and *Amblyomma cajennense* in camels and cattle respectively. The results of this field trial confirmed the efficacy of the vaccination with *R. microplus* recombinant Bm86 for the control of *H. dromedarii* infestations in cattle and camels. They suggested that the immunization of cattle and camels with the Bm86 vaccine represents an effective alternative for controlling H. dromedarii tick infestations. The vaccinated cattle, showed 89% reduction in the number of H. dromedarii nymphs engorging on, and a further 32% reduction in the weight of the surviving adult ticks. While in vaccinated camels, a reduction was 27% and 31% of tick engorgement and egg mass weight respectively. The egg hatching was reduced by 39%. El Hakim, *et al.,* (2011) [110] were isolated three major immunogenic glycoproteins (GLPs) from the adult and larval *H. dromedarii*. GLPs were characterized and used as a protective vaccine against experimental infestation challenges of adult H. dromedarii ticks using a rabbit model. The results of this study showed reduction in the tick's reproductive index and significantly reduced in the egg hatchability in the immunized animals. The study showed that immunization with the purified GLPs provides protection against *H. dromedarii* infestation.

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6.4 Miscellaneous insects found on Camelids

There are several orders among the class insectea that have particular veterinary interest. These are:

- Anoplurida (sucking lice)
- The Mallophagida (biting lice)
- The Siphonapterida (fleas)
- The Dipterida (flies)

1. Lice infestation

Lice infestations are very common throughout the world. The louse species are host-specific and divided into biting and sucking lice. There are two orders of lice which are reported in camelids: the sucking lice, Anoplurida, and the biting lice, Mallophagida. However, the Mallophagida have not yet been reported on OWC. In South American camelids, Lice are the most common causes of parasitic skin disease in camelids. It identify easily by their characteristic shape and leading to pruritus with matted wool and alopecia in heavy infestations. There are 2 main types: Microthoracius sp (Sucking lice) affecting the head, neck and withers; Bovicola breviceps (Biting lice) affecting the base of the tail and along the neck and trunk [1, 2, 3].

The transmission of lice is either by direct close contact of the host or indirectly by grooming equipment, blanket, and saddles, scratching posts or dust bath areas.

Sucking lice

All life cycle stages are found on the host (Figure.6.28). Microthoracius cameli is the only blood-sucking lice , which is reported to occur both on Bactrians and dromedaries in Asia as well as in Africa [4]. Both sexes are obligate blood feeders, taking small meals from capillaries in the upper skin. Females lay 2-6 eggs per day which are attached to individual hair shafts. Eggs complete embryonation and hatch within 8-11 days of deposition. Lice have three nymphal stages, which bear a morphological similarity to the sexually mature adult stage. Each nymphal stage will take 2-4 days to complete. Lice show a seasonal periodicity and the Louse development rate, at all stages, is highly temperature dependent and requires a narrow temperature range. The optimal development takes place between 33°C and 37°C. The louse population become very low in the summer, when conditions are hot. Temperatures above 41°Cand 46°C are lethal for eggs and adults. In late winter, lice populations is reaching a maximum levels because of cooler fall temperatures.

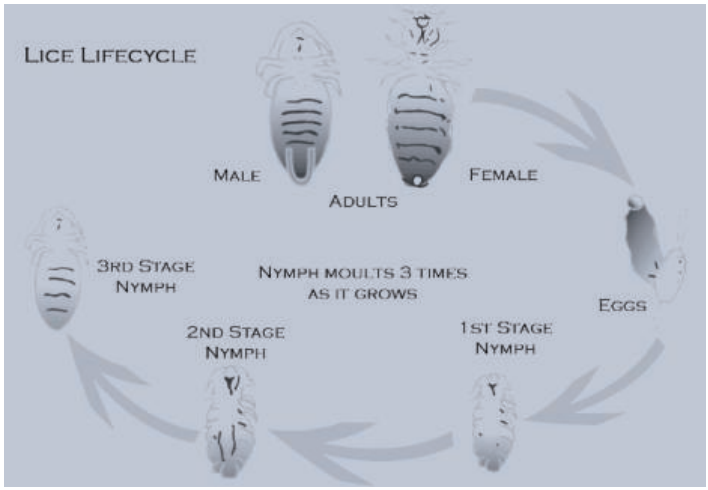

Figure. 6.28: Life cycle of lice in animals

Clinical Symptoms and Lesions

Sucking lice infestation is characterized by licking, scratching and rubbing. In young animals, the heavy infestations lead to develop anaemia. The lice are usually aggregated around the head, neck and withers. Secondary bacterial infections may follow the intense itching. The coat becomes rough and may result in damaged hides. Camels of the temperate regions which have long winter hair are always suffering from lice infestation. In NWC, may be infested with *M. praelongiceps*, *M. mazzai* and *M. minor* . The sucking lice are usually aggregated around the head, neck and withers of the alpaca and llama and show same clinical signs of camel lice. The sucking lice are

smaller than the biting lice (two-thirds their size) and often hidden in the fiber and may be quite difficult to see with the naked eye.

Biting lice (Chewing Lice)

The common llama biting louse (Figure. 6.29), is *Damalinia breviceps* [2]. The Llama wool infested with biting lice lacks brightness and the hide is ragged. Lice Heavy infestation may result in tangled wool and alopecia. The host experiences itching, resulting in self-trauma. The tail, the back along the vertebral column and the sides of the neck and body are the inclination sites of this louse. Lice feed on dead skin cells, hair, and oil secretions which they abrade from the surface using their chewing mouthparts. All stages of the life cycle are found on the host and lead to some abrasion of the upper skin layers. Females deposit <1 egg per day. Embryonation is completed in 7-10 days producing nymphs which molt three times before reaching sexual maturity. As with the sucking lice development is highly regulated by temperature with a narrow range for optimal development and survival. Chewing lice can survive off the host for up to 2 weeks.

Figure.6.29: The common biting louse of camelids, the arrow showing the mouth parts.

Treatment and Prevention

The most treatment is the chemical treatment that include the following coumpunds:

1. Coumaphos 0.05% on skin and wet the coat thoroughly, Dosage Forms: wetable powder, 50%.
2. Methoxychlor, Dusting powder 50% directly onto skin
3. Ivermectin, Inj. 0.2 mg/kg S.C 0.2 mg/kg, Subcutaneous
4. Iverrnectin 0.5 mg/kg Pour on.

2. Flea infestation (Siphonapterida)

In camelids, fleas haven't been reported as a vectors of infectious pathogens, albeit they are transmitted typhus-like rickettsia, Yersinia pestis, and act as an intermediate host for filarids and cestodes. Fleas have reported to infest camelids in cooler countries and Bactrian camels in zoos [5] and llamas [2]. Further, several other species may attack camelids, as is the case of CtenocephaIides felis felis [6].

Treatment and Control

Similar lice chemical treatment such as Organophosphates, macrocyclic lactones and synthetic pyrethroids are used for treatment flea's infestation in camelids. Pour-on and injectable treatments control lice on camelids. Good husbandry practices, especially in the zoo will reduce infestations. Spray used on camels, all camels should be treated.

3. Infestation with Flies

Introduction

The infestation of living human tissue and vertebrate animals by the larvae of flies in the order Diptera (true flies; ie, those whose adults have two wings) is called Myiasis. These larvae feed for varying time periods on the host's dead or living tissue, body substances, or ingested food [7]. Originally, the term myiasis was supposed by Hope in 1840 and dervides from the Greek myia (***μVĨα***), meaning a fly [8]. Myiasis may be categorized parasitologically or clinically. The parasitologic categories of the Myiasis-causing flies are classified into three: obligatory, facultative, and accidental (Table.6.6) [9,10].

Table 6.6: Classification of myiases according to the parasitic relationship of the Diptera with the host.

Group	Subgroup	Remarks
Specific/obligatory		Parasite dependent on host for part of its life cycle
Semi-specific/facultative	Primary	Normally free-living but may initiate myiasis
	Secondary	Normally free-living and unable to initiate myiasis but may be involved once animal is infested by other species
	Tertiary	Normally free-living, but may be involved in myiasis when host is near death
Accidental/pseudomyiasis		Normally free-living larvae that may be accidentally ingested and cause pathological reactions

Obligatory parasites require living tissue for larval development. Facultative parasites usually develop on carrion or vegetable matter, but may occasionally develop on living tissue. Some facultative myiasis-causing flies have adapted so well to a parasitic existence that they essentially become obligatory parasites. In such cases, the distinction blurs between the two categories [11]. In an accidental parasitism, the eggs or larvae are accidentally ingested and are not killed in the intestine [12,13].
The clinically categories, are more useful classification scheme and it is based on the area of the body infested. The cutaneous, enteric, ophthalmic, nasopharyngeal, auricular, oral, and Urogenital [14] are common classification.
The Cutaneous form is the most common type of myiasis, and can be divided into furuncular, migratory, and wound myiasis [15, 16].

Causative agents and distribution

In camels, the larvae of six fly species known to cause myiasis in camels. The five of these belong to the blowflies (*Calliphoridae*) and one to the Oestridae [7, 17, 18]. Obligate parasites such as *Chrysomya bezziana* (Figure.6.30. A&B) has been reported in Iraq [19]. In Nairobi, Myiasis was not encountered in live animals but five camel carcasses examined at Isiolo abattoir were found to harbour the third-stage larvae of the camel nasal bot fly, *Cephalopina titillator*, although the animals appeared in good health during antemortem inspection. Moreover, facultative parasites such as *Lucilia cuprina* may also cause myiasis. The Lucilia fly (*Calliphoridae*) is widespread throughout the world. The larvae feed on necrotic tissue. The larvae may cause myiasis (wounds) of the dromedaries. The wounds are found on the neck, shoulder, flanks and on other parts of the body. The fly deposits the eggs on the wounds. The larvae can cause a considerable stress on the infested dromedaries, rubbing and biting the wounds [20].

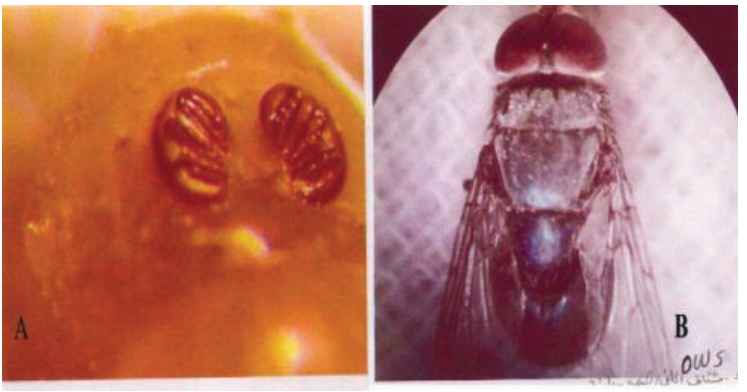

Figure. 6.30. A&B: A. The posterior spiracle of larvae of Chrysomy bezziana, B.The adult fly of Chrysomya bezziana. (Mushtaq AM Al-helfi, Khawla B Al-jassim, Zainab M. Salem. (2012). A case report of cutaneous myiasis by chrysomya bezziana (ows) in camel at Basra province. Bas.J.Vet.Res.Vol.11, No.2.pp 108-112) [19].

Wounds in camel become also infested by larvae of Wohlfahrtia magnifica and W. nubae [21]. In southwest Iran, myiasis by an obligatory parasite the maggots of Wohlfahrtia magnifica has been reported in the genital in camel herds [22]. *Musca domestica* can also cause myiasis. Myiasis may be cutaneous (e.g. caused by *Lucilia spp.*), nasal (e.g. caused by *Oestrus*), or somatic (e.g. caused by *Hypodermu spp*.).
Camel-flies, Hippobosca camelina were found in all camel herds except those treated with Ectopor. Hippobosca camelina (Hippoboscidae, Louse flies) is continuously causing nuisance to the dromedary and it may transmit T.evansi of camel trypanosomiasis [20]. Tabanids (Horse flies) (*Tabanidae*) are biting flies and the most important vector of *T. evansi* of camel trypanosomiasis. They can also transmit anthrax and other bacterial infections. Tabanids are large and robust flies with strong wings which attack furiously on dromedaries' abdomen and ventral regions causing irritations and stress. They also feed on the blood of dromedaries which leads to emaciation and loss of productivity. Other flies were very common and numerous around the manyattas where they attacked all livestock species. Camels suffering or recovering from pox were particularly vulnerable and were severely disturbed by these

flies [23]. Stomoxys (*Muscidae, Muscid flies*) is a vector of *T. evansi* of camel trypanosomiasis. It is also a vector for several bacterial and viral infections. The fly feeds on dromedaries causing irritations and stress as well as milk reduction. The febrile disease (Kulule) is reported by the herders as transmitted by biting flies and the disease needs to be elucidated [20]. In addition, Mosquitoes (*Suborder Nematocerina*) cause severe irritations and nuisance to the dromedaries. Aedes species (*Culicidae – Mosquitoes*) are vectors of *D. evansi* of camel filariasis.

Myiasis caused by *Sarcophagidae* (Flesh Flies)

(*Surcophugu dux, Wohlfahrtiu nuba*, *Wohlfahrtiu magnifica*)
The most important fly that causing myiasis in camels is *WohZjiuhrtiu magnifica* (Figure.6.31 A&B). It is an obligate parasite that occurs in the Mediterranean basin [25, 26], southern Russia, Turkey, Iran, the Far East [25], Spain [27], and Mongolia [28, 29]. The female fly deposits larvae near any skin wound, mucous membrane or tick bite as well as in the nasal and aural cavities.

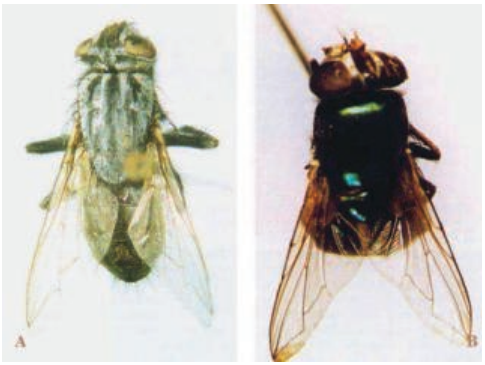

Figure.6.31. A&B: A. Wohlfahrtia **spp.** fly (flesh fly) from vaginal myiasis of a Bactrian camel from Mongolia (courtesy of Prof. Dr. R. Ribbeck, Germany) , B. Lucilia cuprina (Ulrich Wernery, Oskar Ruger Kaaden. (2002). Infectious Diseases in Camelids. Blackwell Publishing Limited edition, Hardcover in English - 2 edition) [24].

The fly seems to prefer camels, although other domestic animals and humans are infested [18]. There have been several reports of the larvae of *W. mugnifcu* causing severe vaginal myiasis in the Bactrian camels in Mongolia [29, 30, 31, 32]. A case of preputial myiasis was also reported in a camel. Mucous membranes of the female genital organs, the eyes and the nose may be attacked without pre-existing wounds [18]. The prevalence of Wohlfahrtian myiasis in thirteen Mongolian Bactrian camel herds ranged between 6.5 to 19% [30]. Valentin *et al.,* (1997) [29] found an infestation rate of 8 to 15% among female camels in Mongolia, and Hadani *et al.,* (1989) [32] reported a prevalence of 10% in dromedary camels in the Sinai. The clinical signs characterized by Ulceration and blood-oozing lesions, sometimes the size of a tennis ball, may be seen on the vagina and vulval labia. Numerous larvae may be seen in the inflamed wounds, deeply embedded in the sensitive dermis. Valentin et al., (1997) [29] counted an average of 105 larvae per affected Bactrian in Mongolia. The vulval region is usually swollen and the hind legs encrusted with blood. Affected animals often show nervous behavior, tripping with their hind legs and bending their backs [29]. These camels often are in bad

condition. Some may even be emaciated, with a history of chronically recurring genital myiasis [29]. All three instars may be found concurrently in the wounds suggesting that superinfestations, acute as well as chronic stages, occur simultaneously with various stages of cicatrization. The genital area may become fibrotic and deformed. *Wohlfahrtia nuba* causes myiasis in humans and animals particularly in camels in Sudan [17], Ethiopia and "eastwards to Karachi" (Soulsby, 1982). The larva was reported to be the only facultative parasite in wounds of camels and humans in Sudan 17. The larvae of Sarcophaga dux have been found in skin lesions of camels, cows and bullocks in India [33].

Myiasis caused by Calliphoridae / (Blowflies) *Luciliu cuprinu*

The larvae of *L. cuprinu*, is the most important blowflies belong to the genus *Luciliu*. It is the main cause of blowfly strike in sheep in Australia and South Africa. Camels raised together with sheep are susceptible to the larvae of *L. cuprinu* and the infection have long been reported to infest camels [17]. *L. cuprinu* is greenish to bronze and is therefore also called the green-bottle fly. The green-bottle fly is widely distributed around the world, found not only in Australia but also in the Middle East, India and Africa [17]. The female fly lays clusters of light yellow eggs in carcasses, infected wounds and soiled and matted fur around infected sores and discharges. Attracted by the smell, it even lays eggs onto rotting vegetation. A green-bottle female may lay about 1,000 eggs altogether during her lifespan. Depending on the temperature, it takes between 8 hours to 3 days for the first stage larvae to hatch. The larvae feed on epidermal cells, lymph and necrotic tissue. The preferential sites for a fly strike are folds of skin, e.g. in the perineal area where urine and feces attract the ovipositing fly. The larvae may cause considerable stress to the infested camel, which may be seen rubbing and biting the infested parts. Infested wounds may be 10 to 15 cm in diameter [17].

Myiasis caused by *Chysornyu bezziunu*

The fly of the “old world screwworm”*Chrysornyu bezziunu*, occurs in Africa and in Southern Asia and wherever camels are found. It is an obligate parasite. The fly is bluish-green with four black stripes on the prescutum. Its face is orange-yellow. It may lay eggs on the skin of both humans and domestic animals, including camels [4]. The fly deposits clusters of 150 to 500 eggs at the edge of a wound of a living host. Even small wounds, such as tick bites and injection sites, as well as any discharge from natural orifices will attract the female fly. Wounds resulting from accidents, castration, branding, and scalding by dips may also attract the fly. The “new world screwworm” (*Cochliomyiu horninivorax*) infested 17 out of 500 dromedaries near Tripoli, Libya [34]. The infestation was most severe on the legs and umbilical cord, from which second and third instars were collected. Since this finding, the new world screwworm has been eradicated from Libya. The maggots penetrate and often liquefy the tissue considerably extending the lesions (Figure. 6.32. A&B), which may develop a foul odor and ooze a foul-smelling liquid. Severe infections are common and many cause death. Cattle and camels are often attacked around the ears and under the tail, causing perineal myiasis [17].

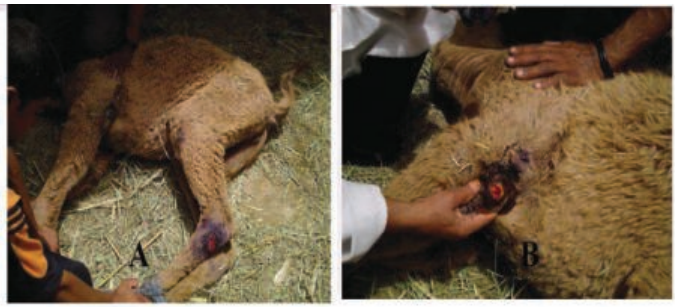

Figure. 6.32. A&B: The site of *Chrysomya bezziana* fly, infection in different sites in camel ((Mushtaq AM Al-helfi, Khawla B Al-jassim, Zainab M. Salem. (2012). A case report of cutaneous myiasis by *chrysomya bezziana* (ows) in camel at Basra province. Bas.J.Vet.Res.Vol.11, No.2.pp 108-112) [19].

Insecticides are used to kill the larvae. Once they are destroyed the wound should be cleaned and dressed, and any necrotic tissue should be removed. However, care should be taken to use as little insecticide as possible to avoid further irritation of the lesions. Hydrogen peroxide, ether or chloroform may cause hidden larvae to crawl out from crevices and cavities. Ivermectin may also be used.

Muscidae Infestation (House and Stable Flies)

OWC and NWC are annoyed by the same fly species that irritate other domestic livestock. The Muscidae family includes many biting and non-biting flies. The most important genera are *Musca* (house fly), *Stomoxys* (stable fly), *Hydrotaea* (sheep-head fly), *Haematobia* (horn fly) and *Fannia* (the lesser house fly). Many of these are responsible for livestock "fly-worry" and are vectors of significant bacterial, helminth and protozoal pathogens causing disease. *Musca auturnnalis,* the face fly, a very common fly in some temperate and subtropical areas, causes fly-worry to cattle and horses on pasture. It is the intermediate host of several pathogenic parasites, e.g. *Thelazia* spp. and *Paraflaria bovicola,* and may transmit *Moraxella bovis,* causing "pink eye" or infectious bovine keratoconjunctivitis in bovines. *Stomoxys calcitrans* is a vector of *T. evansi* and several other pathogens causing severe diseases such as anthrax, brucellosis, leptospirosis and vesicular stomatitis. It was shown in India that the fly preferred to feed on camels rather than horses [17]. Pestered camels may have significant milk reduction.

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