# Perforating Dermatoses – Review Article

***Dr. Mohd El Sayed, PhD, Egypt***
***Dr. Adel Al Abdul Razzaq, MD, Germany***
***Dr. Salim Alotaibi, MD, Kuwait***

***Abstract:***

*The perforating dermatosis is characterized by the cardinal histologic feature of epidermal perforation or "transepithial elimination" (TEE). The extrusion of altered dermal substances through epidermal channels without disruption of the surrounding structures is their hallmark. Kyrle's disease, perforating folliculitis, reactive perforating collagenosis (RPC) and elastosis perforans serpiginosa (EPS) are essentially primary perforating disorders.*

***Key words:***

*Perforating dermatoses, reactive perforating, collagenosis, inherited, acquired, kyrle's disease.*

## Introduction:

The perforating disease constitutes a group of disorders characterized by the trans-epidermal elimination of some components of the dermis. Because the pathogenesis seems to involve activity on the part of the epidermis rather than active perforation of the epidermis by the material being extruded, some authors have preferred to call these diseases examples of "transepidermal elimination" rather than "perforating diseases"[1].

A variety of substances found in the upper dermis apparently stimulate the epidermis to become hyperplastic, eventually surrounding the material to be eliminated. Once these substances are contained within the epidermis, it is natural that they would be transepidermally eliminated to the surface by normal keratinocytes maturation. Although this explanation may be valid in some cases, this view may be too simplistic to explain all examples of transepidermal elimination. Besides the classic four perforating diseases (EPS, RPC, perforating folliculitis and Kyrle's disease), some authors have expanded the concepts transepidermal elimination to include a wide variety of unrelated disorders, such as perforating foreign material (calcium, silica, wood, splinter, etc), infectious agents (chromomycosis, botryomycosis, spirochetes, etc), granulomas (granuloma annulare, necrobiosis lipoidica, sarcoidosis etc), neoplastic cell (malignant melanoma, paget's disease, mycosis fungoides, etc) or other degenerated endogenous substances (chondrodermatitis nodularis helices, hematomas, etc)[2].

**Correspondence:**
*Dr. Adel Al Abdul Razzaq, MD, Germany*
*Senior Registrar*
*Department of Dermatology, Al Adan Hospital*
*MOH – State of Kuwait*
*P.O. Box: 3088, Safat - Code No. 13031, Kuwait*
*Tel. No. 00965-3940600, Ext. 5156-5652 - Fax No. 00965-3941707*

## 1- Reactive Perforating Collagenosis (RPC)

### A- Inherited RPC

**Clinical Picture:**

RPC is found most frequently on trauma prone areas; the dorsal aspects of the hands, forearm, elbows and knees[3]. Lesions are triggered by abrasions, scratches and insect bites[3]. Linear lesions are common because of koebnerization and can be induced experimentally by needle scratches [4]. Surgical excision and deep Cutaneous injuries do not induce RPC papules [5]. Such papules sometimes develop on the face from acne comedones[4].

RPC begins as a pinhead-sized,skin colored papules, approximately 7-10 day after minor trauma. Gradually the lesions develop a central umbilication with keratotic plug and enlarge up to a size of 4-6mm. Approximately one month later, the papules start to regress, healing with an atrophic scar or temporary pigmentary change. The entire cycle takes 6-8 weeks [3]. The appearance of new lesions and the regression of old ones may continue for many years [6]. Some patients have fewer lesions during the summer months [4].

Pruritus is not prominent in the inherited form of RPC[7]. (Fig.1).

**Pathology of Inherited RPC**

In early nonumbilicated lesion (small papules) stained with H & E, the earliest change in RPC is a bluish discoloration of collagen in papillary dermis. A fully mature lesion (umbilicated papule) shows a cup-shaped epidermal invagination that is filled with parakeratotic keratin, necrobiotic connective tissue, degenerated inflammatory cells. The epidermis is acanthotic in the lateral walls and atrophic in the base. Perpendicularly oriented but otherwise normal collagen bundles penetrate the floor of the

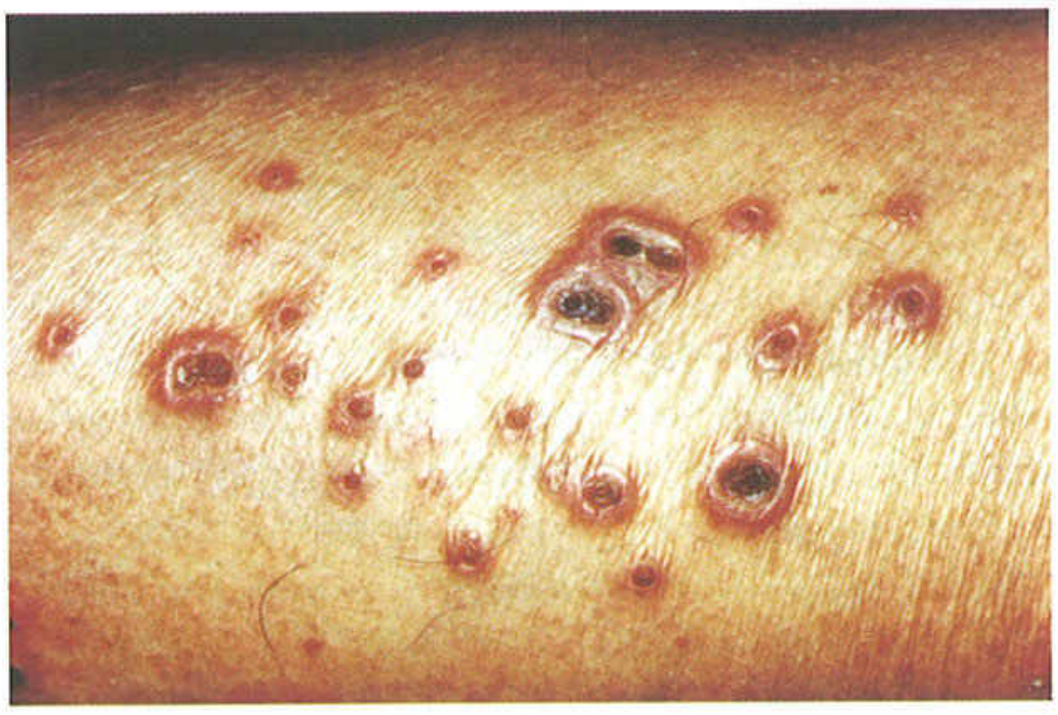

*Fig.1 : Inherited RPC: skin colored hyperkeratotic papules with Keratotic scars and hyperpigmentation.*

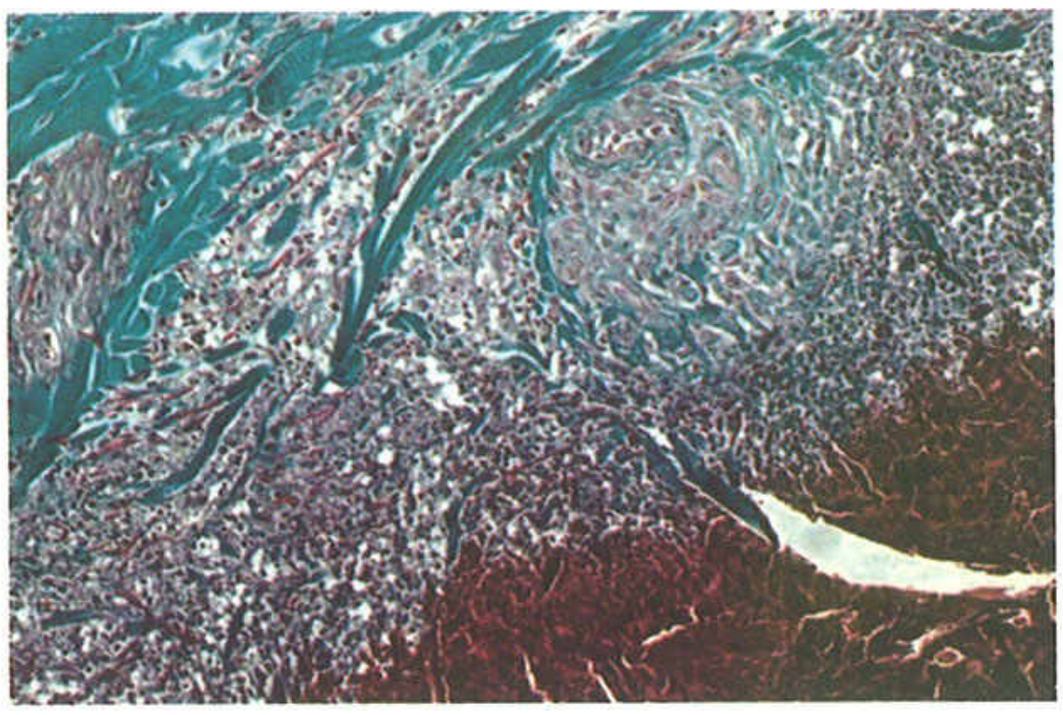

*Fig.2 : Masson-trichrome stain: Vertically oriented perforating bundles of collagen (blue) are present interposed between the keratinocytes of the attenuated bases of the invagination.*

invagination into the central plug. No elastic fibres are present within the crater. The lesion is not connected to hair follicle. Once the supply of degenerated collagen is exhausted the epidermis begins to regenerate, and to close the perforation [3]. (Fig.2).

**Pathogenesis of Inherited RPC.**

Mehregan et al [3] originally reported the cases of inherited form of RPC and postulated that a response to superficial trauma leads to the necrobiosis of collagen fibres in the dermal papillae, followed by sequences of epithelial reaction and transepidermal elimination of the necrobiotic connective tissue. Linear development of the eruption along the scratch marks (Koebner phenomenon) is seen in almost all patients with RPC. A significant finding was the absence of such lesions following deep incision wounds while needle scratch succeeded in producing the skin lesion.[4,5] These finding suggest that the primary defect is in the pars papillaris of the dermis where a posttraumatic necrobiotic change sets off an RPC lesion.

**Treatment of lesion of inherited RPC**

Avoidance of cutaneous trauma is essential. One woman achieved remission with a course of psoralen and long wave ultraviolet A radiation and no lesion could be induced experimentally in that case.[8] Another had marked clinical improvement after treatment with topical tretinoin. [9] Other treatments, which may help include oral isotretinoin, methotrexate, emollient creams and topical steroids under occlusion. [10]

## B- Acquired (Adult) – RPC (ARPC)

**Clinical Picture:**

The skin lesions appear in form of hyperkeratotic papules, hyperpigmented, whitish to skin colored, ranging in size from 2 to 10mm in diameter often with hyperkeratotic plug in patients with renal failure and coalescence of the papules into plaques may occur. Lesions occur mainly on the extremities, especially the legs, but may also be found on the trunk or face [1]. [Fig.3].

The majority of patients with an acquired perforating dermatosis of adult onset has renal failure, diabetes or both, with the renal disease most often developing secondary to diabetic nephropathy. Occasional patients with acquired adult RPC have been described and they primarily had pruritus that was associated with liver disease [11] or underlying malignant neoplasm [12]. Acquired perforating dermatosis often occurs following

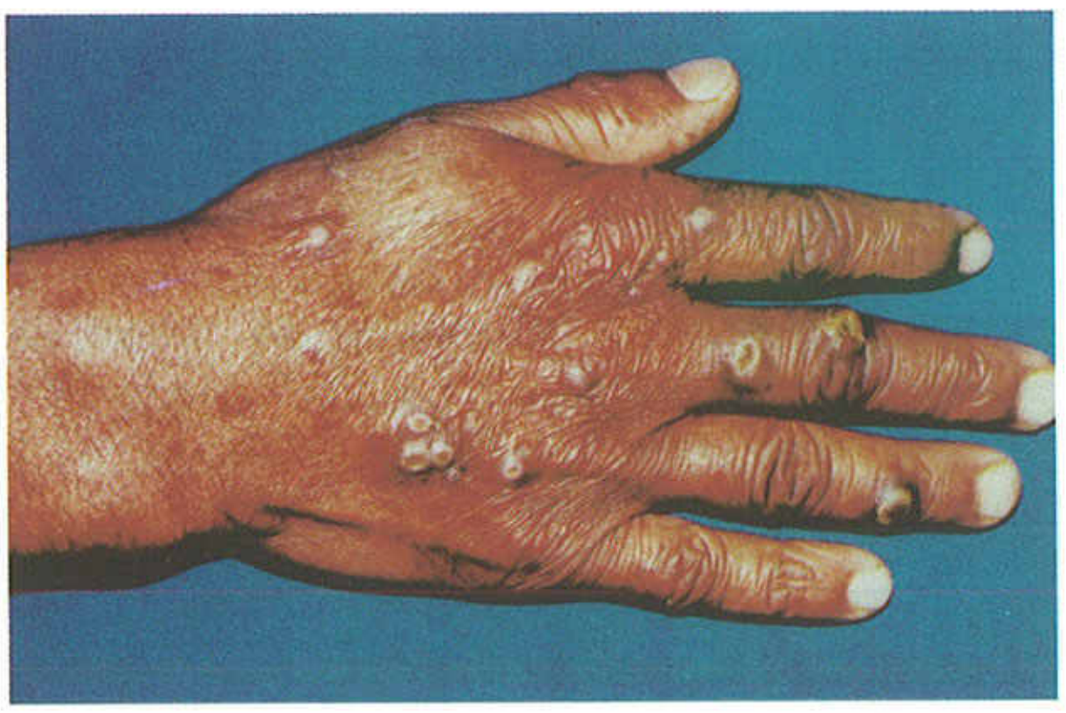

*Fig.3 : Hyperkeratotic papules with keratotic plug.*

hemodialysis, although the onset of lesion may occur before dialysis. It has been estimated that it occurs in 5% to 10% of all patients undergoing hemodialysis [1].

Some investigators described clinically the acquired reactive perforating collagenosis without formation of papules and nodules through their course and divided the course of lesion to pass in three stages. The lesion in the early stage was polygonal and slightly depressed, excoriated scratch with red halo, 1-2mm in size, and showed a linear arrangement. The lesions in the developing stage were red or brown crusts with a red halo. The lesions in mature stage had a keratotic verrucous surface with erythema.[13]

Some investigators reported a case of ARPC clinically and pathologically in site previously affected by herpes zoster (4 weeks before) in an adult female patients, who had neither diabetes mellitus nor chronic renal failure but she was suffering from adult onset Still's disease for 8 years and her ARPC may be associated with that disease. [14]

Some investigators reported a case clinically and pathologically as ARPC developed on Rt. Sole during bed-ridden state in male adult patient suffering from diabetes mellitus and chronic renal failure and Rt. Sole cannot be rubbed by the patient, so they diagnosed the lesion as "perforating disorder of renal disease" rather than acquired RPC. [15]

Some authors proposed the following criteria for the adult (acquired) form of RPC:

1- Histopatological findings of elimination of necrotic basophilic collagen bundles into a cup-shaped epidermal depression.
2- Clinical lesions of umbilicated papules or nodules with central, adherent keratotic plugs and
3- Onset of the lesions is after age 18 years. [16]

**Pathology of Acquired RPC with Papules and Nodules**

The characteristic features include a dome shaped lesion with a central crater that extended from the epidermis to the reticular dermis and contained parakeratotic horny material, neutrophils, basophilic granular debris and degenerated collagen in vertical strands. Masson trichrome staining showed transepidermal elimination of the collagen. Van Gieson staining for elastic fibres was negative in the epidermis and in the crater. The surrounding dermis contained numerous vessels, many of which had a thickened and PAS –positive wall and a mixed infiltrate of mononuclear cells and neutrophils with occasional eosinophils [17].

**Pathology of Acquired RPC without formation of papules and nodules**

In the lesions of the early stage, an ulcer due to excoriation is filled with eosinophilic necrotic material, which contains many pyknotic nuclei of inflammatory cells and degenerated collagen bundles. The collagen bundles in the necrotic materials are in continuity with those in the dermis. The epidermis surrounding the ulcer shows the regeneration towards the center of the ulcer. The thin collagen bundles arranged perpendicular to the surface of the ulcer were seen among the regenerated epidermal cells.

In the lesions of developing stage, the necrotic material contained nuclear debris and pyknotic nuclei of inflammatory cells and was present on the epidermis. The perpendicular collagen bundles perforated through the epidermis. The collagen bundles were stained red by eosin. There was no or a thin horny layer between the necrotic materials and the epidermis.

In the lesions of the mature stage, the keratotic plugs on the cup-shaped epidermis consisted of two layers. The upper half of the plug contained the basophilic debris and the collagen bundles, and the lower half of he plug was formed by a thick horny layer. Many collagen bundles were present in the vertically oriented narrow tunnels within the horny layer and epidermis. The eliminating collagen bundles were in continuity with the bundles in the reticular dermis. At the dermoepidermal junction, mononuclear cells with oval nuclei were seen on eliminating-collagen bundles. Elastic fibres did not perforate through the epidermis. [13]

**Pathogenesis of Adult (Acquired) RPC with formation of Papules and Nodules**

Poliak et al was the first author who reported adult cases of RPC associated with severe diabetes mellitus and thought that trauma such as scratching probably played a large part in the development of their patient's lesions.[7] Other authors suggested that diabetic vasculopathy accompanied by trauma from scratching might be the underlying factor in this eruption and that the trauma from scratching produces dermal necrosis because of poor blood supply due to the diabetic vasculopathy. Then, the necrotic dermal material is extruded through the epidermis. [18] Other authors reported two patients with Hodgkin's disease also with RPC. In both patients pruritus was severe. They suggested that perforating collagenosis was simply a consequence of intense scratching. [12]

**Pathogenesis of Adult (Acquired) RPC without formation of Papules and Nodules**

The eruption occurred in the excoriated lesions of the patients with uncontrolled diabetes mellitus. In excoriated wounds, the necrotic mass on the bottom of the ulcer contained the collagen bundles, which were continuous with the collagen in the reticular layer. In the developing stage, the epidermis regenerated between the necrotic mass and the reticular dermis, and the collagen bundles in the reticular dermis were continuous with those in the necrotic mass through the epithelial tunnels. The collagen in epidermal channels did not degenerate ultra structurally. (13)

From these finding, the mechanism of the formation of the eruption in ARPC might be as follows:

1- In the developing stage, the regeneration of epidermis progress between the necrotic mass and the reticular dermis, and among the collagen bundles. As a result of this regeneration process the collagen bundles remain in the channels of the epidermis.
2- And then the regenerated epidermis makes a thick horny layer. As a result, the necrotic masses are lifted up and the collagen bundles are pulled up from the dermis through the epidermal channels. In this stage, the keratotic plugs are formed. If this hypothesis is true it is not necessary that the collagen fibres in the epidermis show degeneration. (13)
3- In the mature stage of ARPC, the fibroblasts are present on the collagen bundles at the mouth of epidermal channels and the collagen fibres are found in their cytoplasm. It is known that fibroblasts phagocytose the collagen fibres and degrade them in their cytoplasm. So it is supposed that the fibroblast on the collagen bundles might degrade and cut the collagen bundles in their cytoplasm at the mouth of the epidermal channels, and sometimes later the elimination of the collagen bundles come to an end. (13)

**Treatment of Acquired (Adult) RPC**

The same as treatment of inherited RPC.

**2- <u>Kyrle's Disease (Hyperkeratosis Follicularis et Parafollicularis in Cutem Penetrans (KD)</u>**

Definition: KD is characterized by the development of large papules with central Keratotic plugs, often in a widespread distribution, Histologically, a Keratin plug mixed with necrotic debris is found in an epidermal invagination and may show contact with the underlying dermis. (19)

**KD occurs in two forms:**

1- One in children and adolescent and is genetically determined disorder (20)
2- Other occurs in older age people with diabetes and or renal failure (21) And also occurs in hepatic abnormalities and congestive heart failure (22)

**Incidence:**

There is no sexual predilection and no racial predilection had been noted (20).

**Clinical Picture:**

1- Chronic, scattered, generalized papular and nodular eruptions with hyperkeratotic cone shaped plugs.
2- Lesions may or may not involve follicles.
3- Lesions may or may not coalesce and linear lesions related to possible Koebnerization have been described
4- No involvement of the mucous membranes and the palmar and plantar surface (Fig.4).

**Pathology:**

The Pathological criteria needed for diagnosis of KD have been reassessed by Constantine and Carter, 1968(21) (Fig.5). They suggest that the following features should be present for diagnosis of KD:

1- Keratotic plug that fills an epidermal invagination, follicular or extrafollicular
2- Para Keratosis present in parts of the plugs
3- Basophilic cellular debris that does not stain elastic tissue but stains what is within the plug.
4- Abnormal Keratinization of dyskeratotic cells of epithelial cells that extend to the basal cell zone
5- An inflammatory component that is typically granulomatous.
6- In most instances it is important to perform elastic tissue stains and even trichrome stains to exclude perforating elastic fibres as in elastosis perforans serpiginosa (EPS) or collagen fibres as in reactive perforating collagenosis (RPC).

**Pathogenesis of KD: -**

1- In the genetically determined disorder, the primary event is claimed to be disturbance of epidermal Keratinization characterized by the formation of dyskeratotic foci and acceleration of the process of Keratinization. This leads to the formation of Keratotic plugs with areas of parakeratosis. Because the rapid rate of differentiation and Keratinization exceeds the rate of cell proliferation, the parakeratotic col-

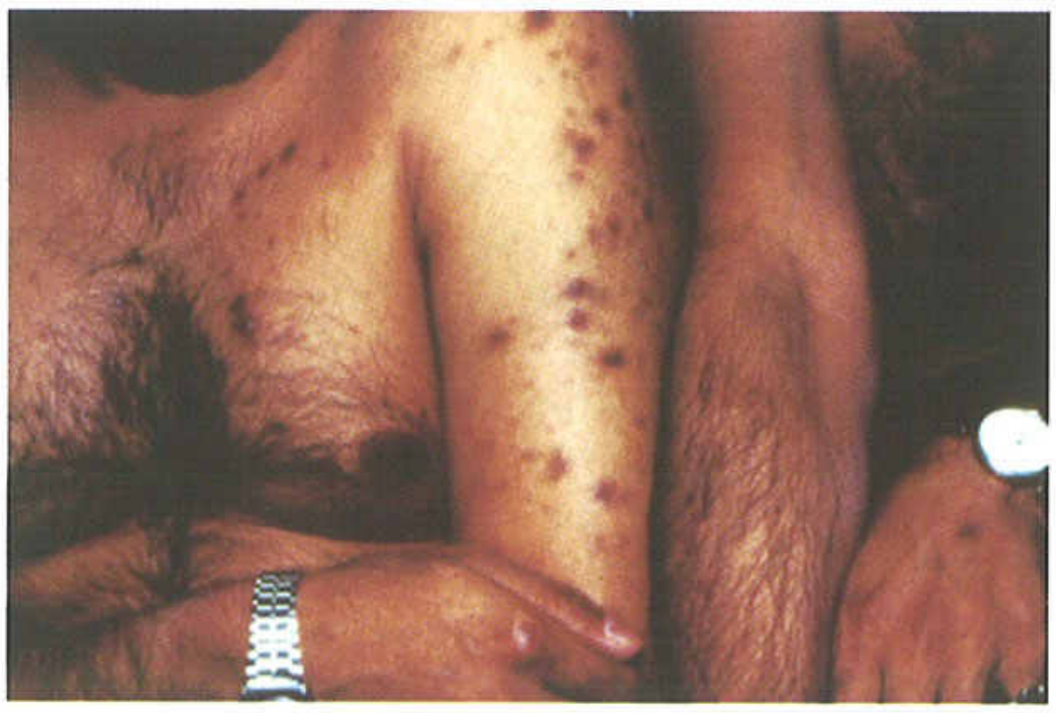

*Fig.4 : Kyrle's disease, genetically determined disorder, two brothers,show hyperkeratotic papules and hyperpigmentation.*

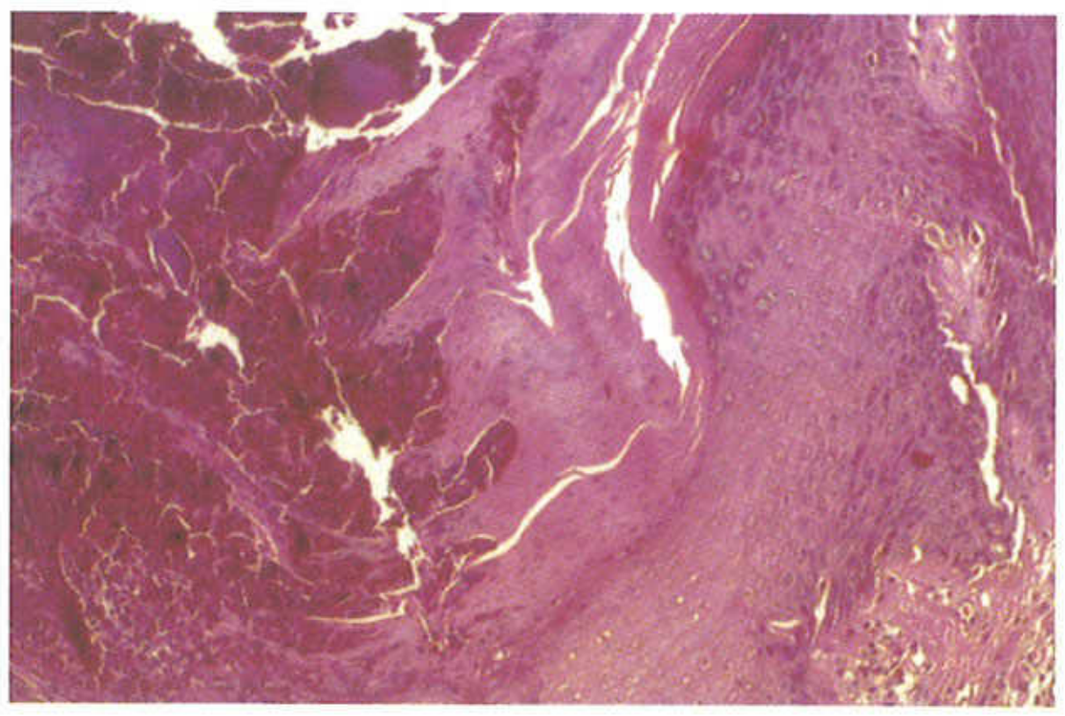

*Fig.5 : There is a heavy keratotic, partly para-eratotic plug lying in the invagination of the epidermis,*

- *On the right side of the invagination a parakeratotic column arises from the epidermal cells*
- *On the left side dyskeratotic cells are seen.*
- *Dermis show inflammatory cells.*

umn gradually extends deeper into the abnormal epidermis, leading in most cases to perforation of the parakeratotic column into the dermis. Perforation is not the cause of Kyrle's disease, as was originally thought but rather represents the consequence or final event of the abnormally speed-up keratinization. This rapid production of abnormal Keratin forms a plug, which acts as a foreign body, penetrating the epidermis and inciting a granulomatous inflammatory reaction. [23]

2- In the acquired disorder seen with diabetes mellitus and or renal failure several hypothesis have been proposed, including diabetes linked microangiopathy, microtrauma due to chronic pruritus, rubbing and dysregulation of vitamin A or vitamin D metabolism.[21]

**Differential Diagnosis of KD:**

Perforating folliculitis, elastosis perforans serpiginosa, reactive perforating collagenosis and Flegel's disease. Perforating folliculitis is often confused with Kyrl's disease but is a condition that is confined to hair follicles. The perforation is at infundibular portion of the invagination and pseudoepithelization commonly occurs at this site [24]. In elastosis perforans serpiginosa there is a marked increase of elastic tissue that is not a feature in KD. RPC exhibits degeneration of collagen as a primary change [19].

The differential diagnosis also includes Flegel's disease (Hyperkeratosis Lenticularis Perstans). Histologically, Flegel's disease shows massive orthokeratosis and inconspicuous foci of parakeratosis. No basophilic debris is present in the keratin layer. Beneath the keratin layer the epidermis is attenuated with thinning or absence of the granular layer. At the basal layer of the epidermis there may be vacuolar degeneration. At the periphery of the lesion there is acanthosis of the epidermis. In the papillary and upper reticular dermis there is edema with dilation of the capillaries and a band like lymphocytic and histolytic inflammatory cell infiltrate closer to the dermoepidermal junction [25]

**Treatment of KD**:-

There is no effective therapy. Topical Tretinoin may be helpful but does not inhibit the development of new lesions in other sites [22].

**3- Perforating Folliculitis (PF)**

**Definition:-**

In PF, Keratotic, follicular papules appear especially over extensor surfaces of the extremities. Microscopically, the lesions are characterized by perforation of the infundubular portion of the hair follicle [19].

**Incidence: -**

Most patients have been in their second through fourth decades, with ages ranging from 6 to 72 years. PF occurs in both male and female patients [19].

**Clinical Picture:-**

The lesions consist of erythematous, follicular papules,

with a small central Keratotic plug or with central hair. They are usually 2 to 8 mm in diameter but may become even larger. The papules are located on the hairy portion of the extremities and on the buttocks. Although lesions are prominent in areas subjected to low – grade frictional forces, obvious Koebnerization with superficial trauma has only occasionally been observed. The eruption may be widely scattered. The lesions may last for a period of months to years, with periods of remission and relapses [19]. Diseases associations of PF have included psoriasis, Juvenile acanthosis nigricans [26], hypertension and atherosclerotic cardiovascular disorders [27], diabetes mellitus and chronic renal failure [28], and HIV infected man [29].

**Pathology of PF:**

PF is characterized by a dilated follicular infundibulum filled with necrotic debris, ortho and parakeratotic keratin and degenerated inflammatory cells. The infundibular portion of the follicle may show one or more perforations, and a curled-up hair may be visible, but it is not invariable (Patterson, 1984) [19].

**Pathogenesis of PF:**

The precise etiology of PF is unknown. [26] Curled – up hair is noted in most cases, so that mechanical disruption of follicular epithelium by hair is thought to play a role. Such hairs are not always found, however, even after careful sectioning [27]. Perhaps hairs become entrapped in the necrotic debris within the perforation and are eventually eliminated, or are lost during biopsy processing, thus they may be absent from mature lesions[29]. It was suggested that formaldehyde in clothing might be an inciting agent [30] and was suggested also that perforation of follicular epithelium and not transepidermal elimination is the primary event in PF [31].

Because of the close clinical and histologic resemblance of PF to KD, and since KD has been attributed to an abnormality of keratinization [20]. The same mechanism could also be operative in PF. The location of PF on extensor surfaces of the extremities implies that low-grade friction may play a role. Perhaps chronic friction incites abnormal keratinization within the follicular infundibulum, eventually leading to epithelial perforation and exposure of dermis to follicular contents. At times, an entrapped hair may hasten the process. The resulting inflammatory and necrotic material is then eliminated through the perforating canal by means of transepidermal elimination. The possibility of an as yet undetected connective tissue alteration as an initiating factor cannot be entirely ruled out.

**Differential Diagnosis of PF: -**

Clinically these lesions may resemble folliculitis of diverse origins, including bacterial and fungal folliculitis and acne vulgaris. Cultural studies and distribution patterns should help to rule out these possibilities. Keratosis pilaris has a close clinical resemblance to PF of both lesion type and location. It seems likely that if multiple biopsies were to be taken from examples of keratosis pilaris, an occasional perforating follicle would be found. PF should perhaps could be considered a phenomenon rather than a specific disease, although the perforating process may dominate the clinical picture [19].

Histologically, all of the major perforating disorders must be considered. EPS shows increased numbers of thickened elastic fibres within the dermis and in the perforation. PF lesions may contain elastic fibres, but they are not enlarged or increased in number. RPC in its classic form does not involve follicles, shows basophilic alteration of papillary connective tissue as an early finding, and no elastic fibres in the perforation. Keratosis pilaris shows a conical, orthokeratotic plug in a widened follicular infundibulum without perforation. Acne and bacterial and fungal folliculitis often show pronounced inflammation accompanying follicular rupture, rather than a narrow infundibular perforating channel [19].

**Treatment o PF :**

The same as KD.

**4- <u>Elastosis Perforans Serpiginosa (EPS)</u>**

**Definition:**

EPS is a disorder in which course, thickened elastic fibres from the papillary dermis are extruded through narrow epidermal channels to produce umbilicated papules on the skin. These papules are characteristically grouped to form arcuate or serpiginous patterns [19].

**Incidence:**

It begins most often in young persons, particularly in the second decade. Both sexes are involved, with a male: female ratio of 4:1 [32].

**<u>Clinical Picture</u>:**

The primary lesion is a flesh-colored or red papule with a central plug that when removed results in bleeding. Classically, papules form arcuate or ser-

piginous patterns. However, not all patients present with these patterns. Papules may be grouped or may exist as discrete lesions [32]. Koebnerization has been observed [33]. EPS has a predilection for the base of the neck, upper portion of the trunk, the face and the extremities. A remarkable symmetry of lesions has been noted; and some suggested the possibility of a genetic defect or an embryopathy [34]. Lesions persist for 6 months to 5 years and undergo spontaneous resolution, however, new lesions may continue to form [35], and the disorder may be quite extensive and persistent [36]. EPS is associated with many diseases as, Down's syndrome, Marfan's syndrome [37], some types of Ehlers – Danlos syndrome [32], Osteogenesis imperfecta[38], Acrogyria [39], Rothmund Thomson syndrome [40] and pseudoxanthoma elasticum [41]. EPS was also reported in association with pathologic bone (Hitch & Lund, 1959) [35], progressive systemic sclerosis [42], Morphea [43], and congenital heart anomalies. [44]

**Pathology of EPS:**

The earliest findings in EPS consists of overlap of fine papillary dermal elastic fibres with the lower border of basal cell [32]. In a fully developed lesion, thick, coarse elastic fibres fill the papillary dermis and enter the epidermis, which in response often becomes hyperplastic and engulfs the abnormal fibres; which are then extruded through the skin, along with basophilic debris and inflammatory cells, by Transepidermal elimination (TEE). Fibres may be discharged through the epidermis of follicular epithelium, acrosyringia might also be involved, but often the narrow channels of elimination in their course through the epidermis simply mimic sweat ducts. The dermal elastic fibres, stain normally, as normal reticular fibres [35]. As fibres enter the perforating canal, they lose normal staining, possibly as a result of enzymatic action emanating from degenerating inflammatory cells[45]. As EPS resolves, the epidermis is repaired and a dermal scar, usually devoid of elastic fibres remains – overlying these scar may be multiple. Multiple widened papillae filled with amorphous elastic material may be overlying these dermal scars. [32]

**Pathogenesis of EPS:**

The precise defect in EPS is unknown, but there is evidence of morphologically and biochemically altered elastic tissue from normal [19].

The abnormal material in EPS is elastin, but in a form altered morphologically and biochemically from normal. There are similarities between this material and the altered elastic of experimental animals subjected to lathyrogens or copper deficiency. The occurrence of EPS in penicillamine treatment of Wilson's disease is further evidence that interference with normal cross – linking may be related to the development of EPS. To rely on the explanation of the entire case of EPS soly upon the role of circulating lathyrogens or copper deficiency is controversial because:

1- Penicillamine, even in high doses, does not regularly produce EPS.
2- As pointed out by Kersch[46] that patients with Menke's kinky hair syndrome have typical changes of copper deficiency in vessel elastica but show no EPS.
3- The elastic changes of EPS are restricted to the cutaneous lesions, although there may be other connective tissue abnormalities resulting from an associated connective tissue disorder – an autopsy study has shown absence of changes in vessels and other organs [4].
4- Morphologically, the elastic fibres in EPS associated with penicillamine differ somewhat from those of idiopathic EPS.
5- It appears likely that there is a delicate interplay of factors, genetic and environmental, leading to EPS. Copper and penicillamine may be two of several factors, the deficiency or excess of which alone or in combination, may result in the formation of an abnormal elastin.
6- EPS may simply be the final common pathway for more than one abnormality of elastic fibres [19].
7- Some investigators found that elastin is a potent inducer of migration and terminal differentiation of cultured keratinocyte, and this is mediated by the 67 Kda elastin receptor. In the lesional skins of patients with EPS, the 67 Kda elastin receptor was specifically expressed in the epidermis immediately surrounding the elastic materials that were being eliminated. The elastin receptor may be involved in the interaction between Keratinocytes and elastin in EPS [47].

**Differential Diagnosis of EPS:**

The picture of papules with central scale, arranged in arcuate or serpiginous patterns in a typical distribution, is highly suggestive of the diagnosis. Other clinical considerations include granuloma annulare, tinea corporis, sarcoidosis and porokeratosis of Mibelli. Histologically these diagnoses can be readily ruled out, but other perforating disorders must then be considered. Confirmatory procedures include elastic tissue stains of microscopic sections will demonstrate the presence of abnormal elastic fibres [19].

**Treatment of EPS: -**

Variable success has been achieved with the use of electrodessication and curettage, liquid nitrogen [48], Subcutaneous hydrocortisone, and carbon dioxide snow application [35].

## 5- Acquired Perforating Dermatosis (APD)

**Definition: -**

Acquired perforating dermatosis is a skin disorder occurring in patients with diabetes mellitus and or renal failure requiring hemodialysis [1].

**Incidence:**

It has been estimated that it occurs in 5% to 10% of all patients undergoing hemodialysis. [1]

**Clinical Picture:**

The skin lesions reported in patients with renal disease or diabetes are hyperkeratotic papules and or nodules often with hyperkeratotic plug. Koebner's phenomenon may occur, and severe pruritus and chronic rubbing may bring about coalescence of the lesions into plaques. Lesions may or may not be centered on follicles. Lesions occur mainly on the extremities, especially the legs, but may also be found on the trunk or face [1].

**Pathology of APD:**

The Pathology seen in acquired perforating dermatosis [49], may be similar to RPC [18], KD[50], PF[28], EPS[51], perforating pseudoxanthoma elasticum [52] and some skin biopsy specimens demonstrated combined transepidermal elimination of both collagen and elastic fibres. This finding is not characteristically seen in any of the four perforating dermatosis described before [1].

**Pathogenesis of APD: -**

Despite numerous studies, the exact etiopathogenesis of APD remains unclear. Several hypothesis have been proposed and included diabetes-linked microangiopathy[18], microtrauma due to chronic pruritus and rubbing [7], acquired abnormality of collagen and / or elastic fibres [2] and dysregulation of vitamin A [53] or vitamin D metabolism [54].

**Treatment of APD: -**

The treatment for this disorder is often frustrating. The most widely recommended therapies include topical keratolytics such as salicylic acid, topical tretinoin, phototherapy or liquid nitrogen cryotherapy [1].

**Summary:**

This article reviews the diseases that may show epidermal perforation as a histologic feature. Many of these represent examples of transepithelial elimination (TEE), a mechanism by which the skin rids itself of abnormal substances. After a review of disorders in which perforation is an occasional finding, four diseases have been considered essential perforating disorders are discussed and these four diseases are:

- Elastosis Perforans Serpiginosa (EPS)
- Reactive Perforating Collagenosis (RPC)
- Perforating Folliculitis (PF)
- Kyrle's Disease (KD)

A review of the literature, including recent reports of perforating diseases associated with diabetes mellitus and or chronic renal failure, suggests that there may be considerable clinical and histologic overlap among PF, KD and the adult form of "perforating collagenosis".

**References: -**


1- *Rapini RP, Herbert AA, Drucker CR. Acquired perforating dermatosis. Evidence for combined transepidermal elimination of both collagen and elastic fibres. Arch Dermatol. 1989, 125:1074.*

2- *Woo Ty, Rasmussen JE. Disorder of transepidermal elimination. Int. J Dermatol. 1985, 24:267-279.*

3- *Mehregan AH, Schwartz OD, Livingod CS. RPC. Arch Dermatol. 1967, 96:277-282.*

4- *Bovenmyer DA. RPC. Epidermal production of the lesion. Arch Dermatol. 1970, 102:313-317.*

5- *Kanan MW. Familial reactive perforating collagenosis and intolerance to cold. Br J Dermatol. 1974, 91:405-414.*

6- *Nair BKH, Sarajini PA, Bschear AM, et al: RPC. Br J Dermatol. 1974, 91:399-403.*

7- *Poliak SC, Lebwohl MG, Parris A, Prioleau PG: RPC associated with diabetes mellitus. N Engl J Med, 1982, 306:81-84.*

8- *Serrano G, Aliaga A, Lorente M, et al: RPC response to PUVA. Int. J Dermatol. 1988, 27:118-119.*

9- *Cullen S: Successful treatment of RPC with tretinoin Cutis, 1979, 23:187.*

10- Patternson JW.: Progress in the perforating disorder. Arch Dermatol. 1989, 125:1121-1123.

11- Kahana M, Trau H, Dolev E, Schewach-Millet M, Gilon E.: Perforating folliculitis in association with primary sclerosing cholangitis. Am J Dermatopathol. 1985, 7:271-276.

12- Pedragosa RP, Knobel HJ, Hugnuet P, Oristrell J, Valdes M, Bosch JA.: Reactive perforating collagenosis in Hodykin's disease. Am J Dermatopathol, 1987, 9:41-44.

13- Yanagihara M, Fugita T, Shirasaki A, Shiguro K, Kawahara K, Ueda K.: The pathogenesis of the transepithelial elimination of the collagen bundles in acquired RPC. J Cutan Pathol. 1996, 23:398-403.

14- Nakanishi G, Tsunenrrsu R, Okagio: RPC occurring in a zosteriform distribution. Br J of Dermatology. 1999, 141:367-368.

15- Yanag K, Lee HK, Choi JH, Sung KJ, KoH JK: Perforating disorder on the sole of the foot. Br J Dermatol. 1999, 140:176.

16- Faver JR, Daovd MS, Daniel WP: Acquired RPC. J Am Acad Dermatol. 1994, 30: 575.

17- Kawakami T and Saito R.: Acquired RPC associated with diabetes mellitus: eight cases that meet Favers's criteria. Br. J of Dermatology. 199, 140:521-524.

18- Cochran RJ, Tucker SB, Wilkin JK: Reactive perforating collagenosis of diabetes mellitus and renal failure. Cutis. 1983, 31:55.

19- Patterson JW: The perforating disorders. J Am Acad Dermatol. 1984. 10:561.

20- Carter VH & Constantine VS: Kyrl's disease. 1-Clinical findings in five cases and review of literature. Arch Dermatol. 1968, 97:624-632.

21- Constantine VS & Carter VH: Kyrl's disease II- Histopathologic findings in five cases and review of the literature. Arch Dermatol. 1968; 97:633.

22- Moschella SL & Hurley HJ. Disorder of collagen, elastic and ground substance. 1993, 3: 1299-1300.

23- Elder D, Elenitsos R, Jaworsky C, Johnson B. Lever's Histopathology of the skin. Degenerative diseases and perforating disorders. 1977, 1:343.

24- White CR, Hisket N, Pokamy D: Perforating folliculitis of haemodialysis. Am J Dermatopathology. 1982, 4: 109-114.

25- Cunnigham SR, Mathews R, Burrows D.: Kyrl's disease. J A Acad Dermatol, 1987. 16:117-123.

26- Mehregan AH, Coskey RJ.: Perforating folliculitis. Arch Dermatol. 1968. 97:394.

27- Paterson JW, Craff JW, Eubanks SW.: Perforating folliculitis and psoriasis. J Am Acad Dermatol, 1982. 7:369-376.

28- Hurwitz RM.: The evolution of perforating folliculitis in patient with chronic renal failure. Am J Dermatopathol, 1985; 4:231-9.

29- Rubio FA, Herranz P, Robayna G, Pena JM, Contreras F, Casado M.: Perforating folliculitis. Report of a case in an HIV infected man. J Am Dermatol. 1999; 40:300-2.

30- Mehregan AH. Perforating Dermatoses: A clinicopathologic review. Int. J Dermatol. 1977; 16:19-27.

31- Burkhart CG.: Perforating folliculitis: A reappraisal of its pathogenesis. Int J Dermatol. 1981; 20:597-99.

32- Mehregan AH: EPS. Arch Dermatol. 1968; 97381-393.

33- Haber H: Miescher's elastoma. Br J Dermatol. 1959; 71:85-96.

34- Macanlay WL: Symmetry in elastosis perforans serpiginosa. Arch dermatol, 1963; 88: 215-217

35- Hitch JM & Lund HZ: EPS. Arch Dermatol, 1959; 79:407-421

36- Tschen E & Head E: Elastosis perforans serpiginosa and other complications. Arch Dermatol, 198; 116:1348.

37- Rasmussen JE: Disseminated elastosis perforans serpiginosa in four mongoloids. Br J Dermatol, 1972; 86:9-13.

38- Carey TD: EPS. Arch Dermatol, 1977; 113:1444-1445.

39- Tafelkmyer J & Mees R: Acrogyria and elastosis perforans serpiginosa. Dermatologica, 1978; 156:309-312.

40- Whyte HJ & Winkelmann RJ: Elastosis Perforans: The association of congenital anomalies, salient facts in the histology, studies of enzyme digestion and a report of necropsy in a case. J Invest Dermatol, 1960; 35:113-122.

41- Reed RJ, Clark WH, Mihm MC: The Cutaneous elastoses. Hum pathol, 1973; 4:187-199.

42- Pai SH & Zak FG: Concurrence of pseudoxanthoma elasticum, elastosis perforans serpiginosa and systemic sclerosis. Dermatologica, 1970; 140:54-59.

43- Barr RJ, Siegel JM, Graham JHL: Elastosis perforans serpiginosa associated with morphea. An example of "perforating morphea". J Am Acad Dermatol, 1980; 3:19-22.

44- Klein AW & Newcomer VD: EPS: Report of a family. Cutis; 1975; 16:259-261.

45- Mehregan AH: Transepidermal elimination. Curr pobl Dermatol, 1970; 3:124-147.

46- Kirsch N & Hukill PB: Elastosis perforans serpiginosa induced by penicillamine: Electron microscopic observation. Arch Dermatol, 1977; 113:630-635.

47- Fujimoto N, Tajima S, Ishibashi A: Elastin peptides induce migration and terminal differentiation of cultured Keratinocytes Via 67 Kda Elastin receptor in vitro: 67 Kda Elastin receptor is expressed in the Keratinocytes eliminating elastic materials in elastosis perforans serpiginosa. J Invest Dermatol, 200; 115:633-639.

48- Rosenblum GA: Liquid nitrogen cryotherapy in a case of elastosis perforans serpiginosa. J Am Acad Dermatol, 1983; 8:718-721.

49- Haftek M, Evarard S, Kanitakis J, Delawant E, Schmitt D.: Acquired perforating Dermatosis of diabetes mellitus and renal failure. Further ultrastructural clues to its pathogenesis. J Cutan Pathol 1993; 20:350-355.

50- Igarashi A, Ishibashiy, Otsuka F.: Kyrle disease associated with sarcoidosis and renal failure. Int. J Dermatol 1991; 30:211.

51- Schamroth JM, Kellen P, Grieve TP.: EPS in a patient with renal disease. Arch Dermatol, 1986; 122:82.

52- Nickoloff BF, Noodlenam FR, Abel EA.: Perforating pseudoxanthoma elasticum associated with chronic renal failure and hemodialysis. Arch Dermatol, 1985; 121:1321.

53- Hurwitz RM, Melton ME, Creech FT, Weiss F, Handt A.: PF in association with hemodialysis. Am J Dermatopahtol, 1982; 4:101.

54- Brand A, Brody N.: Keratotic papules in chronic renal disease. Cutis, 1981; 28:637.