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**Review**

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# Cutaneous Adnexal Cysts Revisited: What We Know and What We Think We Know

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**Keywords**

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**Abstract**

Cutaneous cysts have been classified by dermatopathologists in many different ways. Here, we propose a novel classification of cutaneous adnexal cysts according to their origin in the folliculosebaceous unit and the sweat glands. By examining the lining of the cystic structure, its origin can be easily identified. Epidermal cysts have an epithelial wall containing a granular layer with lamellar keratinization, indicating an infundibular origin. Tricholemmal cysts have an undulating epithelial wall with no granular layer and a compact keratinization, showing an isthmic origin. In steatocystoma, dermoid cyst, and folliculosebaceous hamartoma, the epithelial lining shows a crenulated appearance which is seen in the sebaceous duct. Hidrocystoma shows the characteristic cuboidal epithelial lining of sweat glands with decapitation secretion in its apocrine forms. The hair matrix cyst wall is composed of basaloid cells maturing to squamoid cells, as seen in the normal hair matrix and shadow cells in the lumen. Metabolizing acquired dioxin-induced skin hamartoma (MADISH) is a cystic lesion with lamellar keratinization, and no sebaceous glands. The classification proposed here aims to simplify the complexity of cutaneous adnexal cysts, and to facilitate a better understanding of the origin of cystic lesions of the skin.

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**Table 1.** Classification of cutaneous cysts according to Weedon [1]

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Appendageal cysts

- Epidermal (infundibular) cyst
- HPV-related epidermal cysts
- Proliferating epidermal cyst
- Tricholemmal (sebaceous, isthmus-catagen) cyst
- Proliferating and malignant tricholemmal cyst
- Onycholemmal cyst
- Malignant onycholemmal cyst
- Hybrid cyst
- Hair matrix cyst
- Cystic panfolliculoma
- Pigmented follicular cyst
- Cutaneous keratocyst
- Vellus hair cyst
- Steatocytoma multiplex
- Milium
- Comedo/comedonal cyst
- Eccrine hidrocystoma
- Apocrine hidrocystoma

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This classification is taken from chapter 16: “Cysts, Sinuses and Pits” [1].

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**Table 2.** Classification of cutaneous cysts according to McKee [2]

**Table 2.** Classification of cutaneous cysts according to McKee [2]

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Follicular

- Epidermoid cyst
- Proliferating epidermoid cyst
- Hybrid cyst
- Verrucous cyst
- Epidermoid cyst of the sole
- Comedonal cyst
- Milia
- Trichilemmal cyst
- Vellus hair cysts
- Dermoid cysts
- Cutaneous mature cystic teratoma

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Glandular

- Bronchogenic cysts
- Thyroglossal duct cyst
- Brachial cyst
- Cervical thymic cyst
- Cutaneous ciliated cyst
- Median raphe cyst

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This classification is taken from chapter 30: “Cutaneous Cysts” [2].

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### Historical Classification

Cutaneous cysts have been classified differently by various authors in major dermatopathology textbooks (Tables 1–4). Weedon [1] classifies them as appendageal, developmental, miscellaneous, or lymphatic (Table 1). The classification by McKee [2] includes follicular and glandular cysts (Table 2). Rapini [3] did not make a subclassification of cutaneous cysts

**Table 3.** Classification of skin cysts according to Rapini [3]

Epidermoid cyst
Pilar cyst
Dermoid cyst
Vellus hair cyst
Steatocystoma
Cervical thymic cyst
Cutaneous ciliated cyst
Thyroglossal duct cyst
Branchial cleft cyst
Bronchogenic cyst
Hidrocystoma
Median raphe cyst of the penis
Auricular pseudocyst

This classification is taken from chapter 19: “Cysts” [3].

(Table 3). Barnhill [4] is the only author cited here who classifies cutaneous cysts according to the types of cells in their wall lining (Table 4).

We propose a novel classification of cutaneous adnexal cysts according to their origin in the folliculosebaceous unit and sweat glands (Table 5; Fig. 1). This classification is in accordance with the cytokeratin expression profile of these cysts (Table 6).

## Discussion

Cutaneous cysts have been classified by many prominent dermatopathologists in different ways as explained above. Here, we have proposed a novel classification of cutaneous adnexal cysts according to their origin in the folliculosebaceous unit and sweat glands. By examining the lining of the cystic structure, its origin can be easily identified. Epidermal cysts have an epithelial wall containing a granular layer, and the keratinization through the lumen is lamellar, indicating an infundibular origin (Fig. 2a, b). Tricholemmal cysts have an undulating epithelial wall with no granular layer and a compact keratinization, showing an isthmic origin (Fig. 2c, d). In steatocystoma, dermoid cyst, and folliculosebaceous hamartoma, the epithelial lining shows a crenulated appearance which is seen in the sebaceous duct (Fig. 2e, f, k–n). Hidrocystoma shows the characteristic cuboidal epithelial lining of sweat glands with decapitation secretion in its apocrine form (Fig. 2g, h). The hair matrix cyst wall is composed of basaloid cells maturing to squamoid cells, as seen in the normal hair matrix and shadow cells in the lumen (Fig. 2i, j). Metabolizing acquired dioxin-induced skin hamartoma (MADISH) is a cystic lesion with no sebaceous glands, and shows lamellar keratinization [5, 6] (Fig. 2o, p).

The cytokeratin expression pattern is also consistent with the origin of the cyst. For example, the sebaceous-duct keratin, CK17, is expressed in steatocystoma, dermoid cyst, and folliculosebaceous hamartoma. Epidermal cysts express CK10 as do tricholemmal cysts, which also express CK17. Eccrine and apocrine hidrocystomas show broader expression of cytokeratins (CK1, CK5, CK7, CK8, CK10, CK14, CK18, and CK19). CK16 is only expressed by folliculosebaceous hamartoma [7–9]. In MADISH, as in folliculosebaceous hamartoma, CK15 is expressed (Table 6). The hair matrix cyst, often diagnosed as a part of a follicular hybrid cyst (e.g., epidermal and/or tricholemmal cyst) does not express any cytokeratins [10]; however, the wall of the cyst shows a strong positivity for  $\beta$ -catenin [11].

**Table 4.** Classification of cutaneous cysts according to Barnhill [4]

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*Epithelial-lined cysts*

Stratified squamous

- Epidermoid (infundibular) cyst
- Pilar (tricholemmal) cyst
- Vellus hair cyst
- Milia
- Follicular hybrid cyst
- Pigmented follicular cyst

Stratified squamous with components in cyst wall

- Steatocystoma (simplex and multiplex)
- Dermoid cyst
- Thymic cyst

Cuboidal

- Eccrine hidrocystoma
- Apocrine hidrocystoma

Mixed squamous and nonsquamous ciliated

- Bronchogenic cyst
- Brachial cleft cyst
- Thyroglossal duct cyst
- Cutaneous ciliated cyst
- Ciliated cyst of vulva
- Omphalomesenteric cyst

Pseudostratified columnar

- Median raphe cyst

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*Cysts not lined by an epithelium*

- Digital mucous cyst
- Mucocele
- Metaplastic synovial cyst
- Pilonidal cyst
- Pseudocyst of auricle

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*New entities*

- Proliferating epithelial cyst

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This classification is taken from chapter 25: “Cutaneous Cysts and Related Lesions (Table 25-1: Classification of cutaneous cysts)” [4].

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**Table 5.** Our proposed novel classification of cutaneous adnexal cysts

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Cysts with infundibular epithelial wall

- Epidermal (infundibular) cyst
- Comedon
- Milia
- Vellus hair cyst

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Cysts with isthmic epithelial wall

- Tricholemmal cyst

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Cysts with sebaceous duct epithelial wall

- Steatocystoma
- Cutaneous keratocyst

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Cysts with glandular epithelial wall

- Eccrine/apocrine hidrocystoma

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Cysts with hair matrix epithelial wall

- Hair matrix (pilomatrical) cyst

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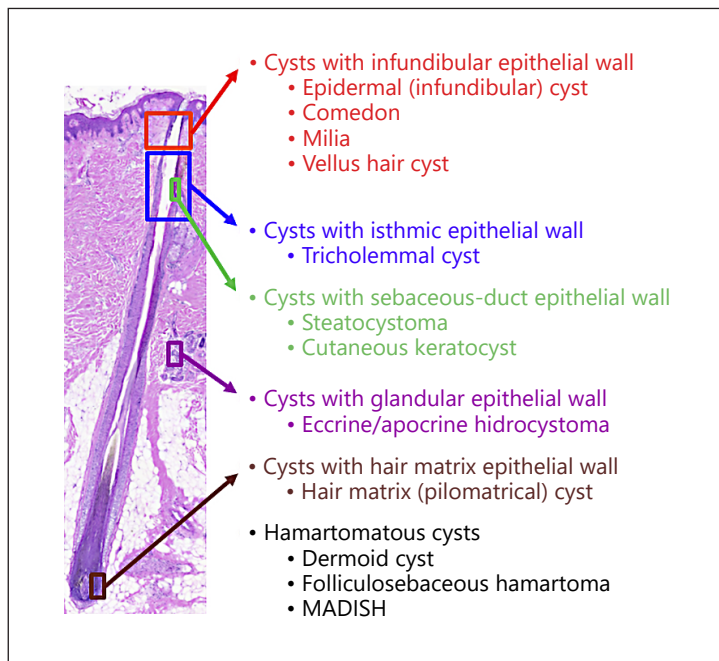
Hamartomatous cysts

- Dermoid cyst
- Folliculosebaceous hamartoma
- MADISH (metabolizing acquired dioxin-induced skin hamartoma)

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**Table 6.** Cytokeratin expression of different cutaneous adnexal cysts (see Table 5)

	CK1	CK5	CK7	CK8	CK10	CK14	CK15	CK16	CK17	CK18	CK19
Epidermal cyst					+						
Vellus hair cyst	+				+				+		
Tricholemmal cyst					+				+		
Steatocystoma					+				+		
Hidrocystoma eccrine	+	+			+	+					
Hidrocystoma apocrine			+	+						+	+
Dermoid cyst	+				+	+			+		
Folliculosebaceous hamartoma	+				+		+	+	+		
MADISH							+				

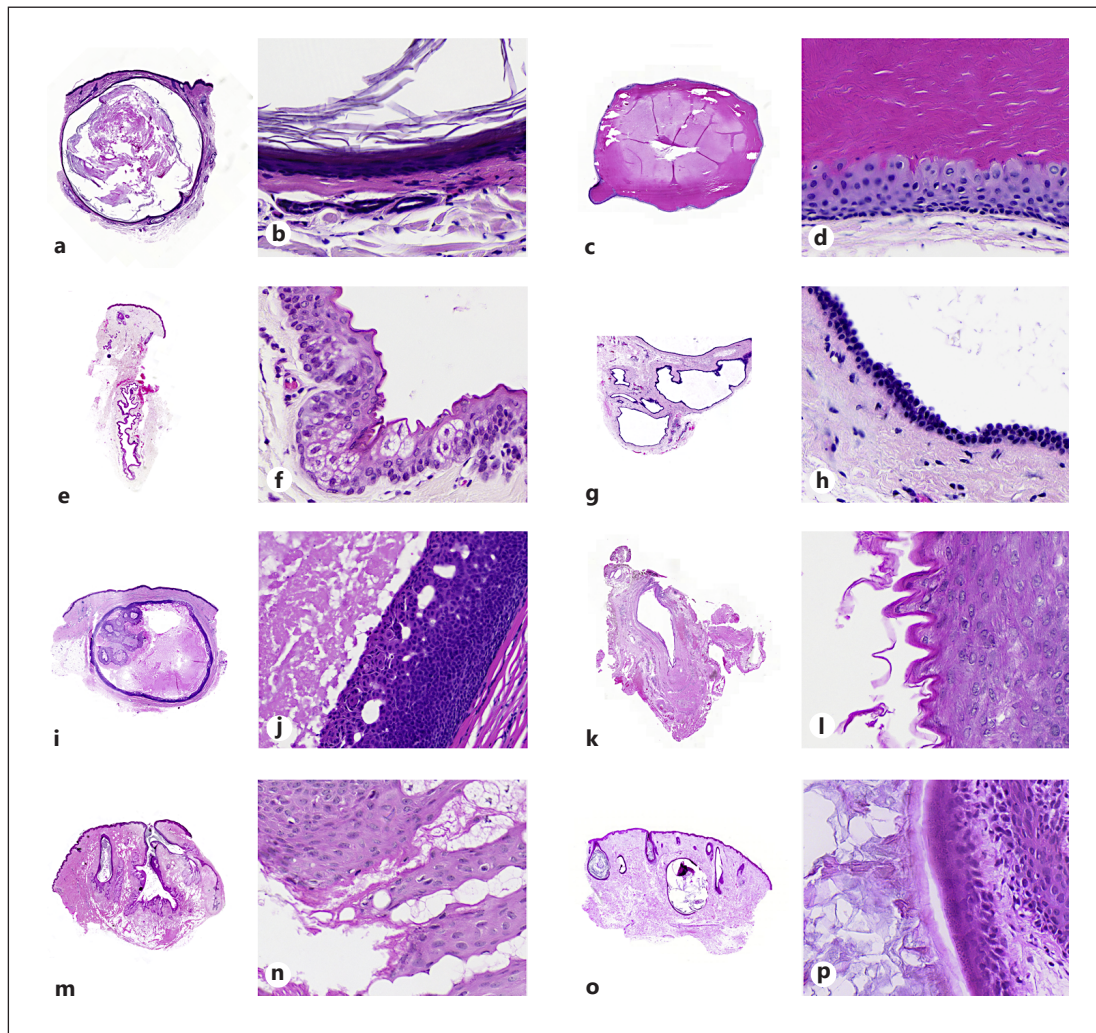


**Fig. 1.** Proposed novel classification of cutaneous adnexal cysts according to their origin in the folliculosebaceous unit and sweat glands.

The follicular stem cell marker Lrig1 is expressed at the isthmic region of the human folliculosebaceous unit [12], and the activation of  $\beta$ -catenin in Lrig1-positive stem cells gives rise to cystic proliferations that are reminiscent of MADISH in mice [13].

Trichoblastic infundibular cyst, cystic trichoblastoma, cystic panfolliculoma, dermoid cyst with basaloid proliferations, folliculosebaceous cystic hamartoma, and BCC occurring in infundibular cysts have also been classified differentially [14]. Recently, cutaneous keratocyst and steatocystoma, unified as sebaceous-duct cyst, have been proposed to be a hamartoma resembling the sebaceous duct [15, 16].

The classification proposed here aims to simplify the complexity of cutaneous adnexal cysts and facilitate a better understanding of the origin of the cystic lesions of the skin.



**Fig. 2.** Epidermal cyst (a), tricholemmal cyst (c), steatocystoma (e), hidrocystoma (g), hair matrix cyst (i), dermoid cyst (k), folliculosebaceous hamartoma (m), and MADISH (o).  $\times 1$ . Close-up of sections shows the epithelial lining with a granular layer and lamellar keratinization (b, p), undulation and tricholemmal keratinization with no granular layer (d), crenulation with sebaceous-duct-type keratinization (f, l, n), cuboidal cells with apocrine-type secretion (h), and basaloid cells with maturation to squamoid cells (j).  $\times 40$ .

### Disclosure Statement

The authors have no conflict of interest to declare.

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