

# Compendium

## Cutaneous Viral Dermatoses in Dogs and Cats

**Masahiko Nagata, DVM, PhD, Dip. Asian College of Veterinary Dermatology**

Animal Specialist Center Dermatology Service  
Chofu, Tokyo, Japan

**Wayne Rosenkrantz, DVM, DACVD**

Animal Dermatology Clinic  
Tustin, California

**Abstract:** Cutaneous viral dermatoses are often underdiagnosed in dogs and cats because they are rare, and because it is difficult to identify an exact causative agent. Even so, practitioners in primary care may encounter some characteristic clinical features. This article reviews commonly encountered dermatoses, particularly papillomavirus-associated dermatoses in dogs and cats. It also provides a brief overview of several other dermatoses associated with feline herpesvirus, feline calicivirus, FeLV, and feline poxvirus.

**V**iral skin disorders are considered rare in dogs and cats, and many that have been reported are associated with the natural habitat or living circumstances of the animal involved. Cutaneous viral dermatoses are often underdiagnosed in dogs and cats because it is difficult to identify an exact causative agent. However, most of the recognized viral dermatoses have a characteristic clinical appearance unlike that of common diseases seen in everyday practice. Diagnosis of these disorders is essentially based on clinical features with or without histopathology. Immunohistochemistry and/or polymerase chain reaction (PCR) can be useful for identifying the infection. The cutaneous viral dermatoses most commonly encountered by clinicians in primary care are papillomavirus-associated dermatoses. A detailed discussion of these diseases, as well as a brief overview of several other disorders associated with feline herpesvirus, feline calicivirus (FCV), FeLV, and feline poxvirus, is presented in this article. Previous reports of cutaneous viral dermatoses in dogs and cats are summarized in **TABLE 1** and **TABLE 2**.

### Papillomavirus-associated Dermatoses

The papillomaviruses (PVs) are grouped with the polyomaviruses to make up the papovaviruses. PVs are small, naked viruses containing double-stranded circular DNA; they lack a lipid envelope, which may account for their relative resistance to physical and chemical destruction. PVs are difficult to eliminate with disinfectants, and PV infections appear to be limited to the epidermis and epithelium.

Almost 150 different strains of human PVs have been identified, and at least nine genetically distinct canine and three feline PVs have been sequenced to date.<sup>1-3</sup> Clinical manifestations of PV infection

depend on the type of virus, the phylogeny and immune competency of the host, and the anatomic site affected. Differences in clinical and histopathologic features and in the viral strains involved (identified by transmission studies, immunohistochemistry, in situ hybridization methods, and PCR) indicate that there are several distinct PV-associated skin disorders in dogs and cats.

### Canine Oral Papilloma

Canine oral papilloma is a self-limited infectious disease that is normally confined to the mucosal tissue of the oral cavity or lips



**Figure 1.** Clinical features of canine oral papilloma in a young dog. Note the whitish, cauliflower-like hyperkeratotic papillomatosis in the oral mucosa.

**Table 1. Cutaneous Viral Dermatoses in Dogs**

Disease	Virus(es)	Clinical Features
Canine oral papilloma	CfPV-1	Whitish, cauliflower-like hyperkeratotic papillomatosis in the oral mucosa in young dogs as well as on the skin in immunosuppressed dogs; generally spontaneous regressing
Cutaneous exophytic papilloma	CfPV -2, CfPV-7	Isolated sessile or pedunculated papilloma on the skin; generally spontaneous regressing
Cutaneous inverted papilloma	CfPV-1, CfPV-2, CfPV-6	Single or multiple rounded papule(s) to nodule(s) with or without a central pore; lesions often found on the ventral abdomen. Most commonly seen in young dogs; generally nonregressing
Canine pigmented plaques	CfPV-3, CfPV-4, CfPV-5, CfPV-8	Pigmented plaques on the ventral neck, ventral trunk, abdomen, and extremities, mainly in young pugs and miniature schnauzers; generally nonregressing
Canine pigmented papules	CPV	Multiple black, rounded papules on the ventral abdomen; generally spontaneous regressing
Canine digital papillomatosis	CPV	Multiple papillomas, strictly limited to the junction of the footpad and adjacent skin on multiple digits on all four feet
Pad inverted papilloma	CPV suspected, but not identified	Grayish papule on the pad
Nail bed inverted squamous papilloma	CPV suspected, but not identified	Single swollen digit, usually with a thickened, abnormally soft nail that may be broken or absent
Nail bed epithelial inclusion cyst	CPV suspected, but not identified	Subungual cyst formation
Canine genital papillomatosis	CPV suspected, but not identified	Whitish, cauliflower-like hyperkeratotic papillomatosis on the tip of the penis or vaginal mucosa
Bowenoid in situ carcinoma	CfPV-3, CfPV-7	Crusting pigmented plaques
Invasive SCC	CfPV-1, CfPV-2, CfPV-3	Proliferative and ulcerative tumor
Hard pad disease	Canine distemper virus	Mild to severe nasal and digital and nasal hyperkeratosis in young, unvaccinated dogs
Pseudorabies	Canine alphaherpesvirus	Intense pruritus, typically of the head and ears, with ptialism and death typically within 48 h of the onset of clinical signs. The main reservoir is the pig.

CfPV = Canis familiaris papillomavirus, CPV = canine papillomavirus

in young dogs, but it occasionally produces papillomas on the conjunctiva and external nares.<sup>4</sup> The lesions begin as white, flat, smooth, shiny papules and plaques, and progress over 4 to 8 weeks to whitish gray, pedunculated, or cauliflower-like hyperkeratotic masses (FIGURE 1). Light microscopy reveals papillomatous proliferations of thick squamous epithelium in which some cells are swollen with vesicular cytoplasm. Canine oral PV-induced generalized papillomas may occasionally be the presenting sign in immunosuppressed dogs or those receiving cyclosporine.<sup>5,6</sup> The lesions regress spontaneously over another 4 to 8 weeks in most cases, although in some cases they may be persistent. Malignant transformation into carcinoma has been reported in rare situations.<sup>7</sup>

### Cutaneous Exophytic Papilloma

Cutaneous exophytic papilloma develops in dogs of any age, but it is more common in younger and elderly dogs. Single or multiple skin lesions may be present, mainly found on the head, eyelids,

and feet. They present as white, pink, or pigmented papillated masses that may be sessile or pedunculated. Lesions are typically <1 cm in diameter with a fimbriated surface. Microscopically, cutaneous exophytic papilloma consists of marked epithelial proliferations on numerous thin fibrovascular stalks. These lesions may persist for 6 to 12 months; many, but not all, regress spontaneously over a period of weeks to months.

### Cutaneous Inverted Papilloma

Cutaneous inverted papillomas present as a single mass or as multiple small masses. They are unpigmented, raised, firm, and covered by skin with a central pore opening to the surface.<sup>8</sup> The disorder is usually seen in dogs younger than 3 years, although older dogs may also be affected. Masses are most commonly found on the ventral abdomen and groin but may appear on the distal extremities, including the digits and footpads (FIGURE 2). Lesions are <2 cm and are supported by thin fibrovascular stalks.

Table 2. Cutaneous Viral Dermatoses in Cats		
Disease	Virus(es)	Clinical Features
Feline oral papilloma	FdPV-2	Multiple, oval, raised, flat-topped masses in the oral cavity, especially the ventral tongue
Feline exophytic papilloma	FdPV	Small, pedunculated, hyperkeratotic papilloma
Feline viral plaques	FdPV-1, FdPV-2	Multiple hyperkeratotic plaques anywhere on the body
Bowenoid in situ carcinoma	FdPV-2	Progressive crusted or erosive pigmented plaques on the haired pigmented skin
Invasive SCC	FdPV-2	Proliferative ulcerative lesions
Feline sarcoid (fibropapilloma)	Feline sarcoid-associated papillomavirus (FeSarPV)	Single or multiple firm nodules on the face, tail, and paws in younger cats from rural areas
Feline herpesvirus-associated dermatitis	Feline herpesvirus-1	Ulcerative and necrotizing facial dermatitis
Feline calicivirus-associated virulent systemic disease	Feline calicivirus	Severe edema and ulceration of the face and limbs along with varying degrees of pyrexia, anorexia, and jaundice
FelLV-associated giant cell dermatitis	FelLV	Pruritic and alopecic exfoliative dermatitis with a diffuse distribution, but typically involving the face
Cutaneous horn	FelLV, feline papillomavirus	Multiple protruding growths of keratin on the footpads
FIV-associated dermatitis	FIV	Chronic or recurrent infection and increased risk for developing tumors Nonpruritic, generalized, papulocrustous eruption with alopecia and scaling, which is most severe on the head and limbs
Feline sarcoma virus-associated dermatosis	Feline sarcoma virus	Multicentric fibrosarcomas in young cats and liposarcomas in kittens, possibly along with uveal melanomas
Feline cowpox virus-associated dermatosis	Feline cowpox virus	Initially ulcerating macules, then papules, plaques, and nodules on the head, neck, and forelimb
Feline infectious peritonitis-associated dermatosis	Feline coronavirus	Granulomatous nodule and ulcer caused by vasculitis around the head and neck in conjunction with systemic signs

FdPV = *Felis domesticus* papillomavirus



**Figure 2.** Clinical features of cutaneous inverted papilloma. Note the multiple rounded papules with central pores on the footpads.

Light microscopy reveals an inverted flask-like structure below the level of the normal epidermis. Cutaneous inverted papillomas

do not usually undergo spontaneous regression, although a spontaneously regressed case has been reported.<sup>9</sup>

**Canine Pigmented Plaques**

Canine pigmented plaques are mainly found in pugs and miniature schnauzers during young adulthood.<sup>10</sup> They may be an inherited autosomal dominant trait, and immunocompromised individuals are also suspected to have an increased incidence of this papillomatous lesion.<sup>11</sup> Lesions are multiple, scaly, deeply pigmented macules, plaques, and sometimes papules, commonly located on the ventral neck, ventral trunk, abdomen, and extremities (**FIGURE 3**). Histopathologically, they are characterized by demarcated, irregularly serriform acanthosis with marked hyperkeratosis and hyperpigmentation. Canine pigmented plaques develop progressively over time and generally do not regress, which is very different from other canine papillomavirus-associated dermatoses.<sup>10</sup> The potential for transformation to squamous cell carcinoma (SCC) has also been reported.<sup>10</sup> The presumed familial nature of canine



**Figure 3.** Clinical features of canine pigmented plaques. Note the multiple pigmented papules and plaques on the ventral abdomen.

pigmented plaques suggests that they may be equivalent to epidermodysplasia verruciformis (EV) in humans. EV is considered to be genetically determined and is caused by an unusual susceptibility to EV-specific human PV infections.

### Canine Pigmented Papules

Canine pigmented papules were reported in a boxer undergoing long-term corticosteroid therapy.<sup>12</sup> Multiple black, rounded papules up to 2 mm in diameter were present on the ventral skin. A single lesion was also reported at the concave aspect of the pinna of a Rhodesian ridgeback.<sup>13</sup> Histologically, the lesions consisted of well-demarcated, cup-shaped foci of epidermal endophytic hyperplasia with marked parakeratosis and no papillary proliferations. These lesions do not recur after surgical removal and may regress spontaneously after the cessation of corticosteroid therapy.

### Feline Viral Plaques

Feline viral plaques (verruca plana, feline cutaneous papilloma) typically appear as multiple, scaly plaques of variable size that are sometimes hyperpigmented (**FIGURE 4A** and **FIGURE 4B**); they can develop anywhere on the body but are predominantly found on the trunk.<sup>14-16</sup> Three of the first four cases described<sup>14-16</sup> were in Persians, but most infected cats are common domestic breeds. All are middle-aged or older. Although immunosuppression may predispose an animal to this disorder, feline viral plaques have also been reported in cats without any immunocompromised status.<sup>15,17</sup>

Histopathology shows well-demarcated foci of acanthosis with an undulating configuration and laminated hyperkeratosis. The viral plaques also affect the follicular infundibula, which are plugged with cornified debris. Keratinocytes within the plaques often undergo PV cytopathic changes, such as nuclear shrinkage, koilocytosis, and increased quantities of blue-grey foamy cytoplasm.<sup>14,16</sup> The histologic appearance of plaques containing

prominent PV cytopathic changes is similar to that of viral plaques seen in people with EV.<sup>16,17</sup> PV antigen was detected in a high proportion of feline viral plaques by immunohistochemical analysis.<sup>18</sup> In addition, PV DNA was amplified from a feline viral plaque by PCR. This  $\lambda$ -PV was closely related to canine oral PV and was designated FdPV-1.<sup>19-21</sup> FdPV-2 is constantly present within the plaques and is the likely etiologic agent.<sup>22</sup> The incidence of carcinogenesis is unknown but is probably fairly high, given the frequency of feline bowenoid in situ carcinoma. The DNA of FdPV-2 is frequently present within feline bowenoid in situ carcinoma.<sup>22</sup>

### Feline Sarcoid

The term “sarcoid” refers to PV-induced fibroblastic proliferations, which have been documented in horses.<sup>23,24</sup> Feline sarcoid, previously called *feline cutaneous fibropapilloma* or *papillomavirus-associated cutaneous fibrosarcoma*, is induced by the feline sarcoid-associated PV (FeSarPV).<sup>25,26</sup> Feline sarcoid develops in free-roaming young cats in rural areas, and half of the reported cases were known to have been exposed to cattle because of the cross-species infection.<sup>26,27</sup> The lesions are slow-growing solitary or multiple firm nodules that may measure up to 2 cm in diameter. The exophytic masses may be pedunculated and are often ulcerated. They are most commonly located on the head, neck, tail, and digits. One of the authors (W. R.) has seen a case with gingival and nasal involvement (**FIGURE 5A** and **FIGURE 5B**). Histopathologically, the lesions show a dense proliferation of fibroblastic cells with epidermal hyperplasia in a rete-peg configuration.

Although PV antigens were not detected in any of the reported cases by immunohistochemical analyses, PV DNA was confirmed in



**Figure 4.** Clinical features of feline viral plaques. Note (A) scaly, pigmented plaques on the haired skin of the nose bridge; and (B) scaly, crusted, pigmented plaques on the haired skin.



**Figure 5.** Clinical features of feline sarcoid. Note multiple firm nodules on the (A) nose and (B) gingiva.

individual mesenchymal cells or cell nests by in situ hybridization.<sup>25-28</sup> Short sections of FeSarPV L1 gene showed 72% similarity to bovine PV (BPV)-1 and ovine PV 2 and 71% similarity to BPV-2.<sup>26</sup>

### **Bowenoid in situ Carcinoma**

Bowen disease was first reported by Bowen in 1912 as a precancerous dermatosis, and the adjective *bowenoid* is often used to connote the distinctive epithelial features of the lesions. Bowenoid in situ carcinoma (multicentric squamous cell carcinoma in situ, Bowen disease) is characterized by heavily scaled, crusted, and pigmented papules and plaques with some erosion (**FIGURE 6**).<sup>29</sup> Lesions can present in any location but mostly appear on the face, shoulders, and limbs.<sup>30</sup> They are multicentric and discrete, and the affected area may or may not be exposed to the sun. The lesions are distinctive, but differentiation from actinic keratosis may be required if they are limited to sun-exposed areas.

The lesions are mostly seen in cats older than 10 years, and 22% of reported feline cases were positive for either FIV or FeLV.<sup>30-32</sup>



**Figure 6.** Clinical features of feline bowenoid in situ carcinoma. Note ulcerative crusted plaques on the haired skin of the mandible.

The lesions show moderate to severe, irregular, epidermal and follicular hyperplasia with hyperkeratosis. There is full-thickness dysplasia manifested by marked loss of nuclear polarity and disruption of normal epithelial stratification. Groups of cells often have dorsoventrally elongated nuclei that are tilted in one direction. Koilocytosis and clusters of large round keratohyalin granules may also be detected.

Immunohistochemical staining resulted in positive nuclear staining of cells within the granular cell layer in 28 out of 63 cases reported by Clark.<sup>33</sup> Primers designed to amplify FdPV-2 detected PV DNA within 20 of 20 bowenoid in situ carcinomas.<sup>34</sup> Sequencing of six amplicons in that study revealed that five bowenoid in situ carcinomas contained FdPV-2, whereas the other carcinoma contained a PV that had previously been amplified from a swab of human skin.<sup>35</sup> It is possible that the virus is transmitted from humans to cats or vice versa.<sup>35</sup>

The lesion may become locally invasive as SCC. Invasive SCCs are strongly associated with sun exposure and are most common in lightly pigmented, poorly haired areas, such as the eyelids, nose, and pinnae.<sup>36</sup> Although high rates of feline SCC are reported in cats infected with FIV,<sup>37</sup> most cats that develop cutaneous invasive SCCs are not immunosuppressed.

### **Treatment of Papilloma-associated Dermatoses**

The search for an effective treatment for PV-associated skin diseases has been frustrated by the nature of PV immunity. Fortunately, routine treatment for many of these lesions is not crucial. Most PV infections regress spontaneously after the development of a cell-mediated immune response, and elderly animals have developed solid immunity as a result of previous exposure to the virus.<sup>38</sup> The disappearance suggests a cause such as stress, and it should be kept in mind that glucocorticoids can trigger and exaggerate the virus expression. Because PV-associated diseases are generally caused by exposure and/or increasing susceptibility to specific

viral agents, topical and oral glucocorticoids are generally contraindicated.<sup>39</sup> Lack of regression of the papillomas, functional interference, cosmetic embarrassment, or risk of malignancy may indicate more vigorous therapy.

Surgery and other therapies such as cryotherapy and laser therapy have been used, but they may need to be repeated. Previously, etretinate, a synthetic retinoid, was used and was found helpful in cases of extensive and hyperkeratotic warts in dogs. For example, extensive and hyperkeratotic canine pigmented plaque lesions were treated daily with oral etretinate 1 mg/kg q24h.<sup>10</sup> However, etretinate was discontinued because it had a narrow therapeutic index as well as a long elimination half-life, making dosing difficult in people. It has been replaced by its active metabolite, acitretin, which has a shorter half-life, making it safer and easier to dose. It has been used to treat some human warts, but no reports are available for its value in dogs.<sup>40</sup>

Azithromycin has been shown to sometimes be effective in the treatment of oral and cutaneous papillomatosis in dogs and cats at an oral dose of 10 mg/kg once daily for 10 days.<sup>41</sup> The exact mechanism of how azithromycin functions as an antiviral agent is not known, but one potential mechanism proposed in a study with human bronchial epithelial cells is that it increases the production of interferon-stimulated genes.<sup>42</sup>

The immune response modifier 5% imiquimod (Aldara, 3M Health Care Limited) has also been reported to be effective when applied topically three times a week. Twelve cats with a histologic diagnosis of bowenoid in situ carcinoma were treated with 5% imiquimod cream in one study.<sup>43</sup> Initially, all of the cats responded to 5% imiquimod therapy, but most cats (75%) developed new lesions that also responded to the application of the 5% imiquimod cream in all of the cats that were re-treated. Five cats (41%) experienced adverse effects suspected to be associated with the use of the 5% imiquimod cream, including local erythema (25%), increased liver enzyme levels and neutropenia (8%), and partial anorexia and vomiting (8%).

Interferon (IFN) is produced in the body and exerts a biologic action to protect cells from viral infection. There are three main classes of human IFNs: IFN- $\alpha$ , IFN- $\beta$ , and IFN- $\gamma$ . IFN- $\alpha$  elicits broad activities that inhibit virus replication. An intracellular mechanism by which IFN- $\alpha$ -2a inhibits human papillomavirus (HPV)-transformed cell proliferation, and presumably HPV-induced papillomas, operates through the suppression of viral oncoprotein expression and cytostatic arrest of cycling at the G1 stage of mitosis. In dogs, 1.5 million units (MU) to 2 MU/m<sup>2</sup> of IFN- $\alpha$ -2a (Roferon-A, Hoffman-LaRoche) given subcutaneously three times a week has been reported to be effective for the treatment of severe cases of oral and/or cutaneous viral papillomatosis.<sup>38</sup> In addition, IFN- $\alpha$ -2a therapy (1000 units given orally once daily on a 21-day-on, 7-day-off schedule) has been reported as an adjunct therapy for canine pigmented plaques.<sup>11</sup> The effectiveness of IFN- $\alpha$ -2b (Intron A, Schering-Plough) administered orally at 30 units/mL has been reported anecdotally, but the recommended dose and frequency vary widely.<sup>38</sup> In some instances, combining IFN- $\alpha$  with other treatments could increase the likelihood of effective treatment.

The efficacy of IFN- $\gamma$  therapy has also been evaluated in several studies in humans, but it remains controversial. There are no reports on the use of IFN- $\gamma$  in dogs, but one report indicated that IFN- $\omega$  could be useful as an alternative agent for reducing the size of the papillomas.<sup>44</sup> In one study, a 4½-month-old dog with papillomatosis on the mucocutaneous junctions was treated with 2 MU of the intralesional injection of a recombinant type 1  $\omega$  IFN of feline origin (rFeIFN- $\omega$ ; Virbagen Omega, Virbac; Intercat, Toray), which is closely related to the human  $\alpha$  and  $\beta$  IFNs. The lesions regressed in size and number without any adverse effects and were removed surgically. Furthermore, rFeIFN- $\omega$  1 MU/kg given subcutaneously three times a week for a month has been helpful in the treatment of canine pigmented plaques.<sup>38</sup>

In humans, common side effects of IFN treatment are influenza-like symptoms, such as fever, chills, nausea, fatigue, myalgia, and loss of appetite. These effects usually tend to be less severe over time and are generally tolerable. No properly controlled studies of IFN therapy for canine papillomatosis have been conducted so far, nor have there been any studies of the safety of such therapy. The benefit-to-expense ratio should be discussed carefully with owners before proceeding with this treatment option.

## Feline Herpesvirus-associated Dermatoses

Feline herpesvirus-1 (FHV-1; felid herpesvirus 1 [FeHV-1]) is a member of the *Varicellovirus* genus of the herpesvirus subfamily Alphaherpesvirinae, which is closely related to canine herpesvirus-1. Similar to other herpesviruses, FeHV-1 contains double-stranded DNA and has a glycoprotein-lipid envelope. It is therefore relatively fragile in the external environment and is highly susceptible to the effects of common disinfectants. It can only survive for up to 18 hours in a damp environment (less in dry conditions) and is relatively unstable as an aerosol.

After airborne infection, the virus multiplies in the upper respiratory mucosa and tonsils and remains latent in the trigeminal ganglion. Viral reactivation may be spontaneous but is most likely after a stress such as moving, entering a multicat household, boarding, pregnancy, surgery, or receiving glucocorticoids.<sup>45,46</sup>

FeHV-1 infection generally causes acute upper respiratory disease (feline rhinotracheitis) as well as conjunctivitis and stomatitis. Although the main target tissue is the respiratory epithelium, the epidermis and hair follicle epithelium are also affected. FeHV-1-associated dermatitis (ulcerative facial and nasal dermatitis and

### Key Points

- Cutaneous viral dermatoses are rare in dogs and cats. It may be difficult to identify an exact causative agent.
- Most of the recognized viral dermatoses have a characteristic clinical appearance dissimilar to that of common diseases seen in everyday practice.
- The diseases are generally caused by exposure and/or increasing susceptibility to specific viral agents, so topical and oral glucocorticoids are generally contraindicated.



**Figure 7.** Clinical features of FeHV-1 associated dermatitis. Note the ulcerative and necrotizing dermatitis on the nose and on the perinasal skin.

stomatitis syndrome, ulcerative and necrotizing facial dermatitis) has been described in a series of cats, and the role of FeHV-1 has been demonstrated.<sup>47,48</sup> Cats of all ages and both sexes can be similarly affected, with or without a history of respiratory disease. Typical lesions consist of vesicles, crusts, and ulcers on the nasal planum or haired skin of the face such as the bridge of the nose, perinasal skin, and periocular skin (**FIGURE 7**). Skin lesions can also appear anywhere on the body, and ulcerative dermatitis with lesions located on the flanks has also been reported in the absence of facial lesions.<sup>49</sup>

Microscopically, the lesions are vesicular, ulcerative, and necrotizing. The epidermis appears hyperplastic with necrotic zones. Mixed inflammation, often with numerous eosinophils, is noted in the dermis. Some adnexa, including epitrichial sweat glands, are destroyed. Free hair in the dermis is associated with many eosinophils, so the lesions may be misinterpreted on histopathology as allergic dermatitis or eosinophilic granuloma complex, in particular attributed to a mosquito bite. Intranuclear inclusion bodies are present in the surface and adnexal epithelium in variable numbers and are often close to necrotic tissues. The inclusion bodies are amphophilic or glassy, fill the nucleus, and are associated with margined chromatin and cytoplasmic swelling. Immunohistochemical analysis or PCR is the most commonly used technique for obtaining evidence of infection.<sup>50,51</sup> However, a positive PCR result may be an incidental finding caused by a cat's previous exposure to the virus or sample contamination.<sup>52</sup> There is also evidence that many PCR assays detect vaccine virus, but immunohistochemical analysis at the lesion does not.<sup>51</sup> FeHV can also be an underlying trigger of erythema multiforme in cats without any of the ulcerative, erosive lesions described here.<sup>45</sup>

A number of antiviral agents, including famciclovir, ganciclovir, and cidofovir, have shown efficacy against FeHV-1 in vitro.<sup>53</sup> Oral famciclovir (Famvir, Novartis) can be effective at 62.5 to 90 mg/kg once or twice daily or 125 mg/cat three times daily.<sup>54,55</sup> In vitro studies have also shown that FeHV-1 is susceptible to feline IFN or recombinant human IFN- $\alpha$ , and that the effect of acyclovir

and recombinant human IFN- $\alpha$  is synergistic.<sup>56</sup> Doses of IFN- $\alpha$  vary widely from 1 MU/m<sup>2</sup> subcutaneously three times a week to 0.01 to 1 MU/kg once daily for up to 3 weeks.<sup>57</sup> The most commonly used dosage for dermatologic conditions is 30 units/day.<sup>45</sup> rFeIFN- $\omega$  (1.5 MU/kg perilesionally and subcutaneously) is used to treat FeHV-1-associated disorders, but no controlled trials have yet been undertaken.<sup>58</sup>

The effect of L-lysine on FeHV-1 replication has been explored both in vitro and in experimental cat studies.<sup>59,60</sup> L-lysine inhibits virus replication by blocking the availability of the amino acid arginine. There is evidence that dietary lysine supplementation is not effective in groups of cats and that oral bolus administration (200 to 500 mg q12–24 h) may be essential.<sup>61</sup> Its effectiveness in clinical cases remains highly controversial.

Bovine lactoferrin has shown some in vitro activity, most likely by preventing attachment and penetration of FeHV-1 into susceptible cells, but its in vivo efficacy has not yet been evaluated.<sup>62</sup> Topical rFeIFN- $\omega$  and imiquimod (2 to 3 consecutive days a week) have also been proposed, and clinical responses have been seen, but imiquimod can cause irritation.<sup>45,46</sup> Topical antiviral eyedrops, including cidofovir, trifluridine, and idoxuridine, may also be used for ulcerative keratitis.<sup>57</sup> In practice, good nursing care is always essential, and, when indicated, broad-spectrum antibiotics are recommended to prevent secondary infection. Topical and oral glucocorticoids and cyclosporine are contraindicated.

### Feline Calicivirus-associated Dermatoses

FCV is a small, unenveloped, single-stranded RNA virus belonging to the family Caliciviridae, which includes important human pathogens such as noroviruses, the most common causes of infectious gastroenteritis in humans. There are many different strains of FCV, which spreads by direct contact with an infected cat that sheds the virus on a regular basis.<sup>63</sup>

The most common clinical signs are vesiculoulcerative stomatitis and conjunctivitis, and some strains induce lameness caused by arthropathy.<sup>64</sup> Pustular dermatitis was also reported on the abdomens of two cats after routine ovarioectomy.<sup>65</sup> The histopathologic diagnosis was panepidermal pustulosis and necrotizing dermatitis. Positive immunohistochemical staining consistent with the FCV antigen was detected in epithelial cells within the pustular lesions. More worryingly, highly virulent strains of FCV have emerged and are associated with outbreaks of disease with high mortality and a new range of clinical features (FCV-associated virulent systemic disease [VSD]).<sup>66</sup>

Cats affected by FCV-associated VSD show subcutaneous edema of the face and limbs and variable levels of ulceration of the skin, particularly on the pinnae, footpads, and nares, along with varying degrees of pyrexia, anorexia, and jaundice. Up to 50% of cats die or are euthanized in extremis. Viral isolation, reverse-transcriptase PCR assays, and fluorescent antibody testing may be used to identify viral antigens in swabs from the oropharynx or conjunctiva, blood samples, skin scrapings, or lung tissue.<sup>67</sup> Positive PCR results should be interpreted with caution as they may be a consequence of low-level shedding by persistently infected carriers.

The prognosis is usually good for non-VSD acute infection if the cat receives general supportive and nursing care and regular cleaning of discharges. Mucolytic drugs (e.g., bromhexine) or nebulization with saline may offer relief.<sup>67</sup> rFeIFN- $\omega$  is registered for control of FCV disease in Japan and Australia. Three injections of rFeIFN- $\omega$  (5 MU/kg IV every other day) can reduce the duration and severity of fever and oral ulceration associated with FCV.

In one study, daily oromucosal treatment with 0.1 MU of rFeIFN- $\omega$  was associated with a significant improvement of clinical lesions (caudal stomatitis and alveolar/buccal mucositis) and a decrease in pain.<sup>68</sup> Chronic infection may be difficult to treat because the oral disease is progressive and the prognosis is guarded for the virulent form, but a virus-specific antiviral phosphorodiamidate morpholino oligomer (PMO) resulted in an excellent response among kittens during outbreaks of severe viral disease.<sup>69</sup> The PMO was first administered on day 1 of disease onset (0.7 to 5.0 mg/kg SC q24h) and continued for up to 7 days. A total of 47 of 59 cats receiving PMO survived, but only three of 31 survived without PMO treatment. Antiviral treatment reduced viral shedding and hastened clinical recovery as measured by weight gain and clinical condition.

FCV can persist in the environment for about 1 month and is resistant to many common disinfectants.<sup>67</sup> Recently, neutral solutions of an electrochemically activated anolyte in which the active chemical ingredient is hypochlorous acid<sup>70</sup> and of copper iodide nanoparticles have proven to be powerful disinfectants against FCV.<sup>71</sup>

### Feline Leukemia Virus-associated Dermatoses

FeLV is an immunosuppressive, oncogenic retrovirus. It can induce skin tumors, such as lymphoma and fibrosarcoma, but most commonly affects the skin by its cytosuppressive action. Clinical signs may include chronic or recurrent infections, including pyoderma, dermatophytosis, demodicosis, and *Malassezia* dermatitis, as well as poor wound healing, seborrhea, and generalized pruritus. In addition, pruritic crust, scale, and alopecia caused by giant cell dermatoses, especially on the muzzle, lips, perioral area and head, have been reported, and severely affected cases may show erythema and focal erosions.<sup>72,73</sup>

An affected cat can have lesions on the pinnae that have progressed to nasal and perioral sites as well as to the ventral neck, mammary region, and toes. Histopathologically, irregular acanthosis is accompanied by numerous, massive, multinucleated giant cells throughout the epidermis and hair follicles. Single or multicentric cutaneous horn(s) in the centers of the digital, central, or metacarpal/metatarsal pads, and sometimes on the face (e.g., nasal planum and eyelids), as well as severe necrosis caused by vasculitis on the pinnae and tail, are rarely seen.<sup>74</sup>

Immunohistochemical staining may be used to confirm the presence of a gp70-positive FeLV antigen within the lesions. FeLV genomic material can be confirmed in affected skin by PCR. As FeLV antigens and genomic material were found in a serologically negative cat, focal skin FeLV replication may develop.<sup>73</sup> Over time, affected cats often show signs of internal disease. To date, no treatment has proven effective in eliminating FeLV.



**Figure 8.** Clinical features of feline cowpox virus-associated dermatosis. Note erythematous plaques and papules on the mandible. Photo courtesy of Dr. Brett Wildermult.

### Feline Poxvirus-associated Dermatitis

Poxvirus infections in cats are most commonly caused by the cowpox virus, a member of the *Orthopoxvirus* genus. These infections have been reported in many animals and are endemic to Europe and Western Asia.<sup>75</sup> Rodents are the natural hosts, so the virus is found in rural hunting cats. It is most common during summer and autumn, coinciding with the most active and breeding seasons of the rodents, but it can be transmitted between cats.<sup>76</sup>

The initial skin lesion is a bite wound, commonly on the head, neck, or forelimb. Widespread, randomly distributed, pruritic, erythematous macules, papules, and nodules may develop (**FIGURE 8**). Some cases show ulceration in the oral cavity and on the tongue, along with systemic signs such as fever, anorexia, depression, and diarrhea during the viremic period 1 to 3 weeks after infection. The varying clinical features might be related to the genetic diversity of the feline cowpox virus.<sup>77</sup>

Histopathology reveals hydropic degeneration of the keratinocytes and the presence of intracytoplasmic eosinophilic inclusion bodies.<sup>78</sup> Virus isolation or PCR analysis are preferred for a conclusive diagnosis. There is no specific therapy, so symptomatic treatment should be tailored to the severity of clinical signs. The prognosis is good. Skin lesions heal slowly over 3 to 8 weeks. The virus can be transmitted to dogs as well as cats and has zoonotic potential.<sup>79</sup> All infected cats should be isolated and handled carefully until the lesions heal.

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