



Canine Papillomatosis



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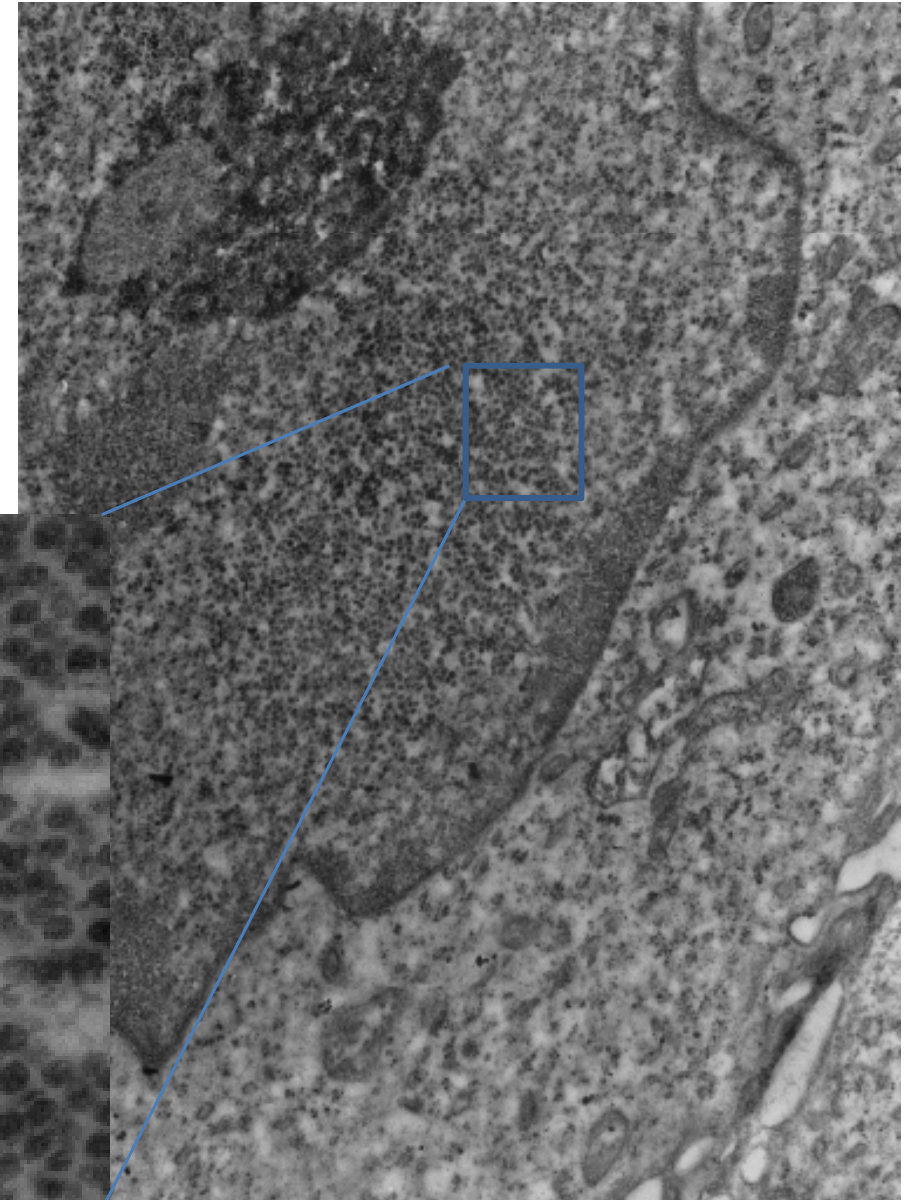
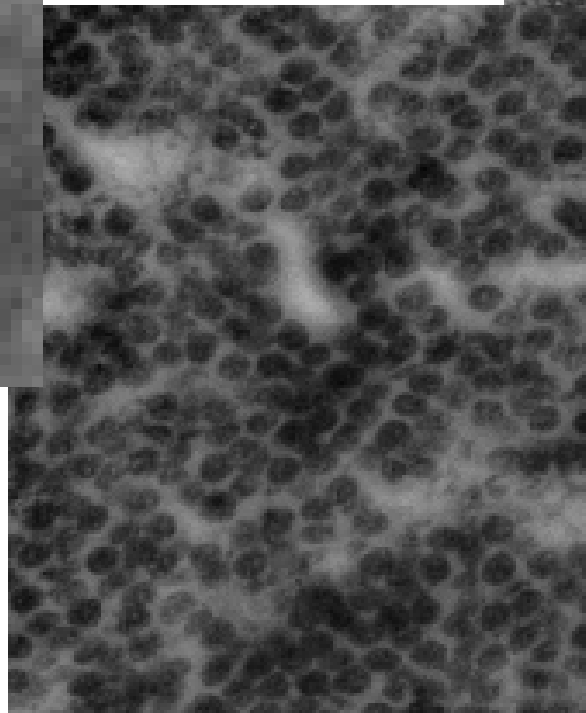
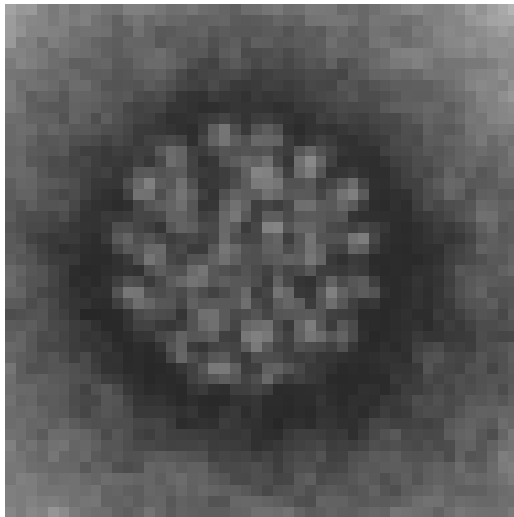
Introduction

- **Definition:** *A benign, exophytic, neoplastic proliferation of the squamous epithelium caused by infection with papillomavirus*
- **Synonyms:** ***Warts*** or ***verruca vulgaris***
- **First reported:** *1898 by M'Fadyean and Hobday*



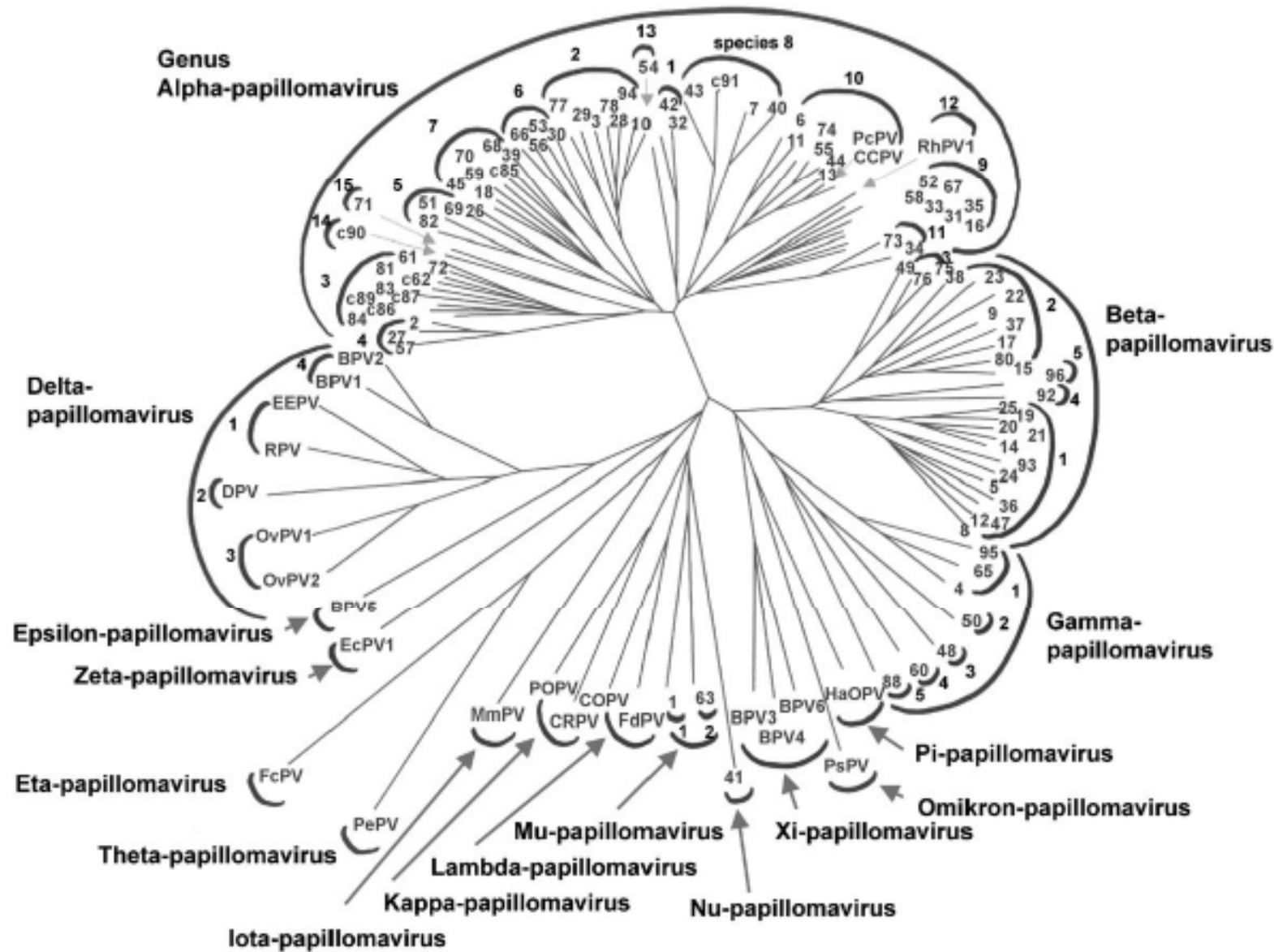
Etiology

- a papillomavirus: double stranded DNA virus
- 45-48 nm





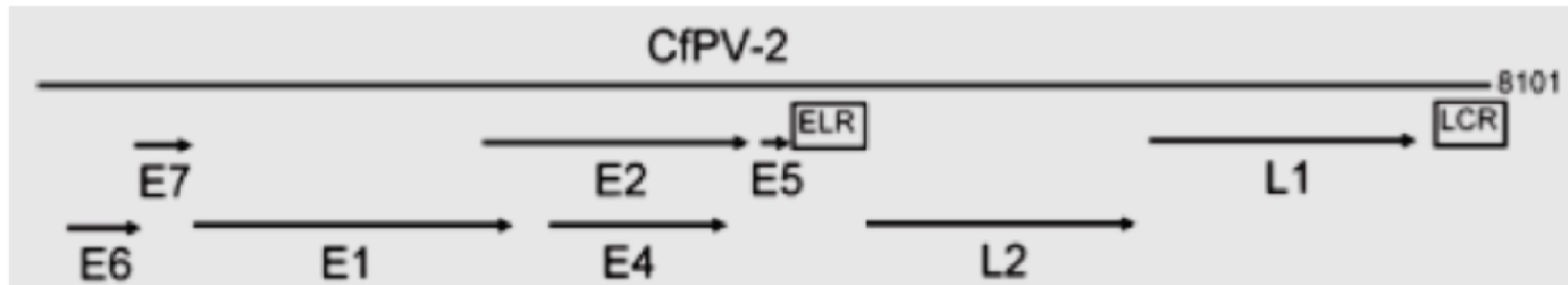
Phylogenetic analysis of the L1 sequences of CfPV-2



After EM de Villere *et al.* (2004); H. Yuan *et al.* (2007)



Linear representation of ORFs of COPV and CfPV-2 genome





Characteristics of papillomavirus infections in mammals

(Theilen, 1983; Jubb, Kennedy and Palmer, 1993)

Virus	Carrier	Location	Histology
Human papillomaviruses	Human	Different	Papilloma
Equine papillomaviruses	Horse	Skin (lip)	Papilloma
Canine papillomaviruses	Dog	Oral mucosa and skin	Papilloma
Rabbit papillomaviruses (Shope)	Rabbit	Skin	Papilloma
Rabbit oral papillomaviruses	Rabbit	Oral mucosa	Papilloma
Mastomys natalensis papillomaviruses	Rodents	Skin	Papilloma
Chaffinch papillomaviruses	Birds	Skin	Papilloma
Bovine papillomaviruses			
type 1	Cattle	Skin	Fibropapilloma
type 2	Cattle	Skin	Fibropapilloma
type 3	Cattle	Skin	Papilloma
type 4	Cattle	Digestive tract	Papilloma
type 5	Cattle	Udder	Papilloma
type 6	Cattle	Skin	Papilloma
Sheep papillomaviruses	Sheep	Skin	Fibropapilloma
European elk papillomavirus	Elk	Skin	Fibropapilloma
Deer fibromavirus	Deer	Skin	Fibroma ⁶



Etiology

- two different papillomaviruses in dogs
- species and tissue specific

1.Canine Oral Papilloma Virus (COPV):
responsible for the oral papilloma

2.Canine Papilloma Virus (CPV):
responsible for the cutaneous and inverted papilloma



Etiology (in Human)

- Warts are caused by a virus called [human papilloma virus](#) or [HPV](#).
- There are approximately 130 strains of human papilloma viruses. [\[2\]\[3\]](#)
- Types 1, 2, and 3 cause most of the common warts. [\[3\]](#)

Type 1 is associated with deep plantar (sole of the foot) and palmar (palm of the hand) warts.

Type 2 causes common warts, filiform warts, plantar warts, and mosaic plantar warts.

Type 3 causes plane warts, commonly known as flat warts.

Anogenital warts are caused by types 6, 11, 16, 18, 30, 31, 33, 34, 35, 39, 40 and others.

HPV **types 6 and 11** cause about 90% of [genital warts](#) cases.

HPV **types 16 and 18** currently cause about 70% of [cervical cancer](#) cases, [\[4\]\[5\]](#) and also cause some [vulvar](#), [vaginal](#), [\[6\]](#) [penile](#) and [anal cancers](#). [\[7\]](#)



Prevalence

- The 7th rank, found 6.2 % among skin neoplasm of dogs in eastern area of Bangkok (n = 210) *

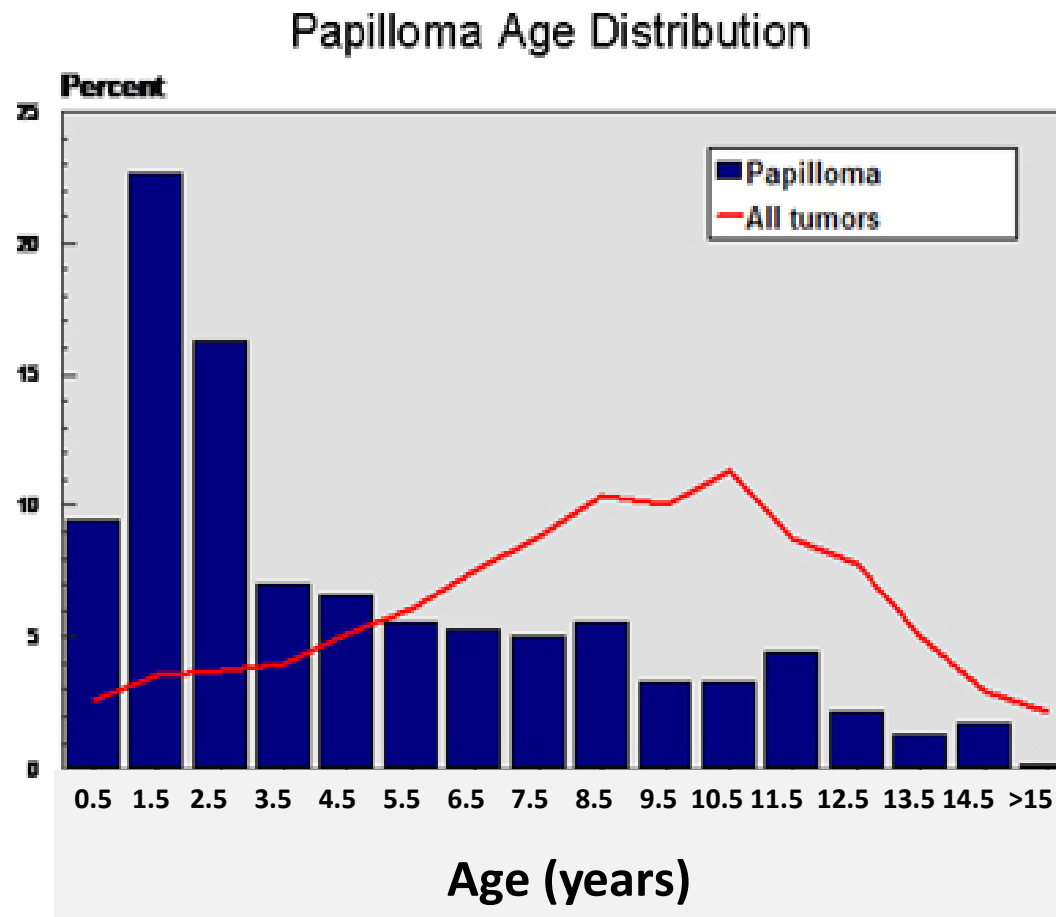
Type of epithelial and skin gland tumors	Percentage (%)
1.Transmissible venereal tumor (TVT)	13.3
2.Squamous cell carcinoma (SCC)	11.4
3.Mastocytoma (Mast cell tumor)	11.0
4.Sebaceous gland adenoma/epithelioma	7.1
5.Benign mixed mammary tumor	7.1
6.Mammary carcinoma	7.1
7.Papilloma (squamous/fibrous)	6.2

* Mamom (2009): on process of publishing data



Epidemiology

- Most common in dogs less than 3 years of age.



Source: <http://www.oncolink.org/types/article.cfm?c=22&s=69&ss=807&id=9513&p=1>



Epidemiology

- No sex predilection

Sex	N	Percent
Female	101	21% (21%)
Female Spayed	150	32% (33%)
Male	108	23% (25%)
Male Castrated	111	24% (21%)
(Normal Population %)		



Epidemiology

- Some breeds **increased** risk

Breeds at Increased Risk	N	Probability	OR	95% Confidence Interval	
Whippet	5	<0.0001	12.1	5.0	29.4
Rhodesian Ridgeback	8	<0.0001	6.7	3.3	13.6
Weimeraner	10	0.0001	4.5	2.40	8.4 5
Mastiff	5	0.0062	4.4	1.83	10.76
Greyhound	8	0.0008	4.2	2.09	8.51
American Pit Bull Terrier	11	0.0001	4.2	2.30	7.6 4
Great Dane	13	<0.0001	4.1	2.33	7.0 5
Jack Russel Terrier	9	0.0006	4.0	2.09	7.8 4
Beagle	16	0.0507	1.7	1.01	2.74
Labrador Retriever	51	0.0331	1.4	1.04	1.87

Source: <http://www.oncolink.org/types/article.cfm?c=22&s=69&ss=807&id=9513&p=1>



Epidemiology

- Some breeds **decreased** risk

Breeds at Decreased Risk	N	Probability	OR	95% Confidence Interval	
Mixed Breed	75	<0.0001	0.6	0.47	0.78
Cocker Spaniel	8	0.0022	0.4	0.19	0.75
Miniature Poodle	3	0.0046	0.2	0.08	0.78
Shetland Sheepdog	1	0.0021	0.1	0.02	0.78

Source: <http://www.oncolink.org/types/article.cfm?c=22&s=69&ss=807&id=9513&p=1>



Epidemiology

- Common location in dogs.

Site	Percent
Head	52.1%
Forelimb	12.5%
Hindlimb	11.2%
Multiple Sites	10.6%
Abdomen	2.9%
Thorax	1.6%
Neck	1.3%
Perianal Region	0.8%
Tail	0.5%
Back	0.3%



Clinical Presentation

There are 3 different presentations of canine papillomatosis.

1.Oral Papillomatosis

- with multiple papillomas found in the oral cavity

2.Cutaneous Papilloma

- solitary or multiple lesions found on the skin surface.

3.Inverted Papilloma

- a benign endophytic (growing inward) proliferation of the epidermis.



Clinical Presentation

- A narrow based mass projecting upward and outward from a thickened epidermis.
- Cut section often consist of multiple finger-like projections covered by keratinous material
- Normal adjacent skin
- Secondary bacterial infections may be found.



Clinical Presentation

Vary with form of disease

- Oral Form: halitosis, ptyalism, oral bleeding, and reluctance to eat

Lesions: vary from smooth, white mucosal elevations to cauliflower-like warts on the lip margins, oral mucosa, tongue, palate, pharynx, and epiglottis. Tumors (50-100) may be present at time of first diagnosis.



Clinical Presentation

- Ocular Form: wart lesions on conjunctiva, cornea, and eyelid margins
- Cutaneous Form: papilloma site distribution is variable.

Lesions have been noted on the lower extremities, foot pads, and subungually.



Pathogenesis

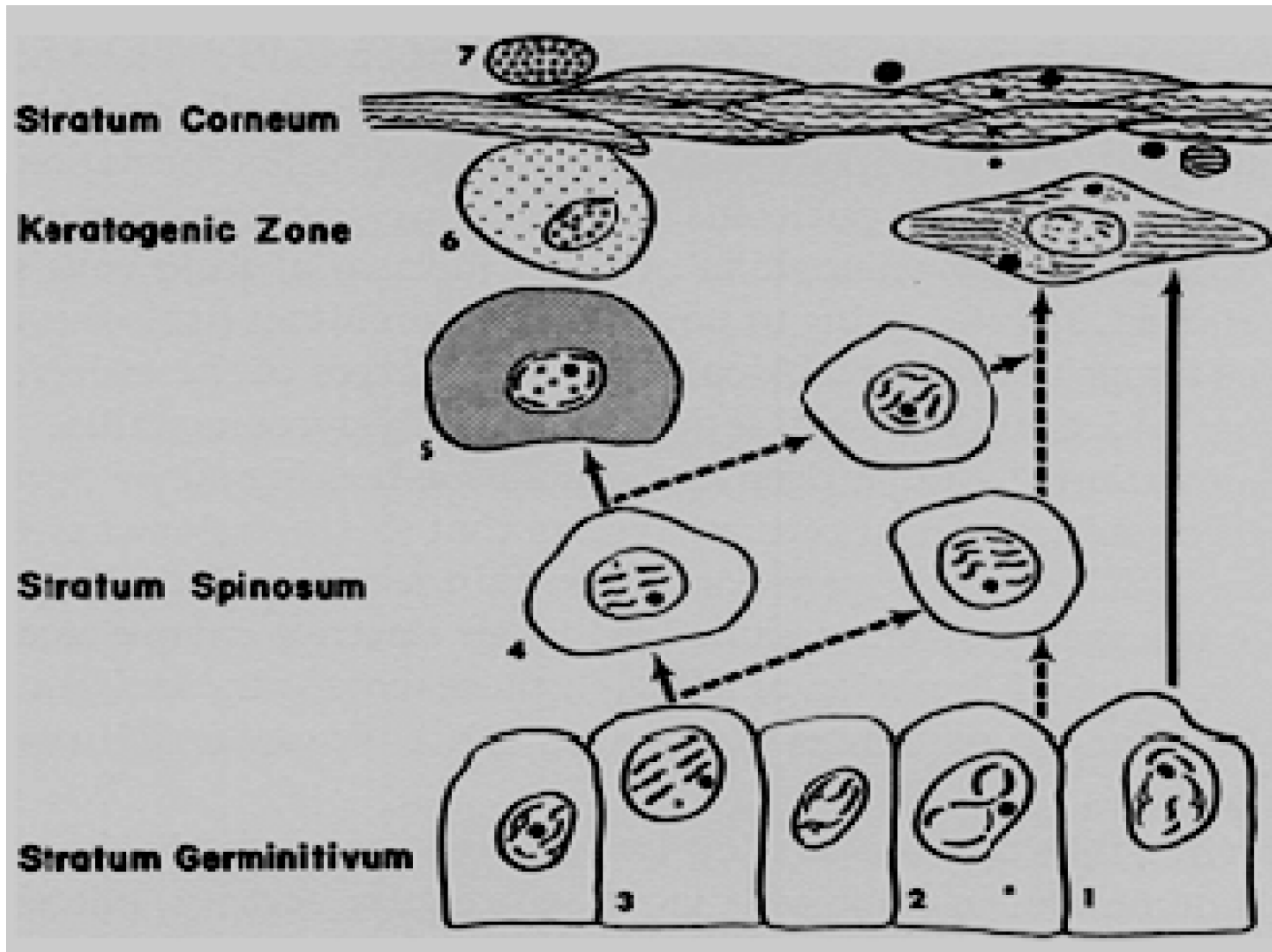
- Papillomavirus enter epidermis and induce proliferation of epidermal cells result to cutaneous lesion.
- Naturally developing lesions was divided into three phases:
 1. a growing phase
 2. a developing phase
 3. a regressing phase.



Pathogenesis

1. The growing phase: characterized by
 - basal cell hyperplasia
 - Acanthosis
 - hyper- and parakeratosis
 - a few intranuclear inclusion bodies.
2. The developing phase: characterized by
 - marked acanthosis with cell swelling
 - marked hyper- and parakeratosis with presence of many intranuclear inclusion bodies in swollen or degenerating cells in stratum spinosum and granulosum.
3. The regressing phase: characterized by
 - mild epidermal hyperplasia around dermal core
 - moderate fibroplasias and collagen deposition
 - lymphocytic cells infiltration at epidermal-dermal interface.

Pathogenesis



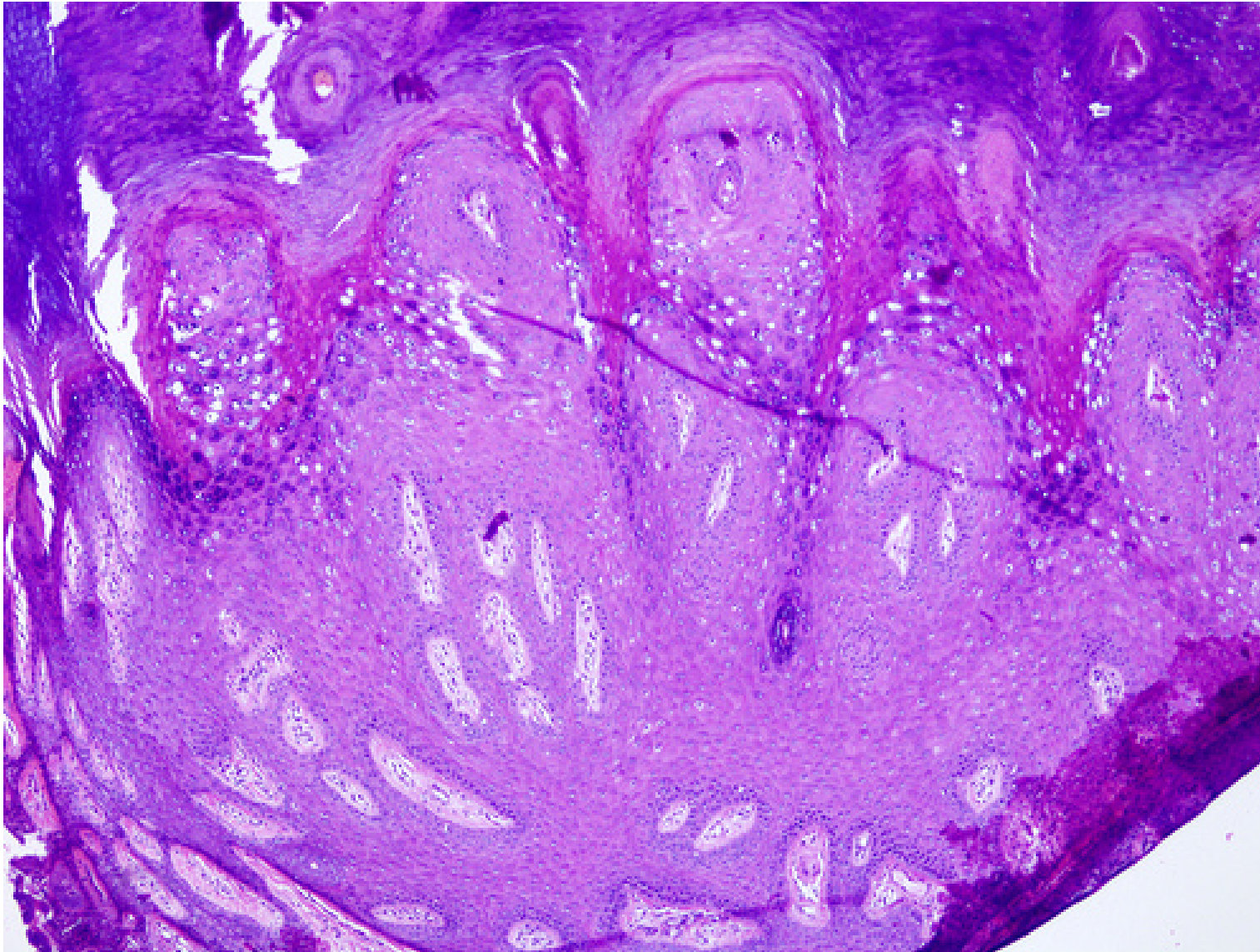


Pathology

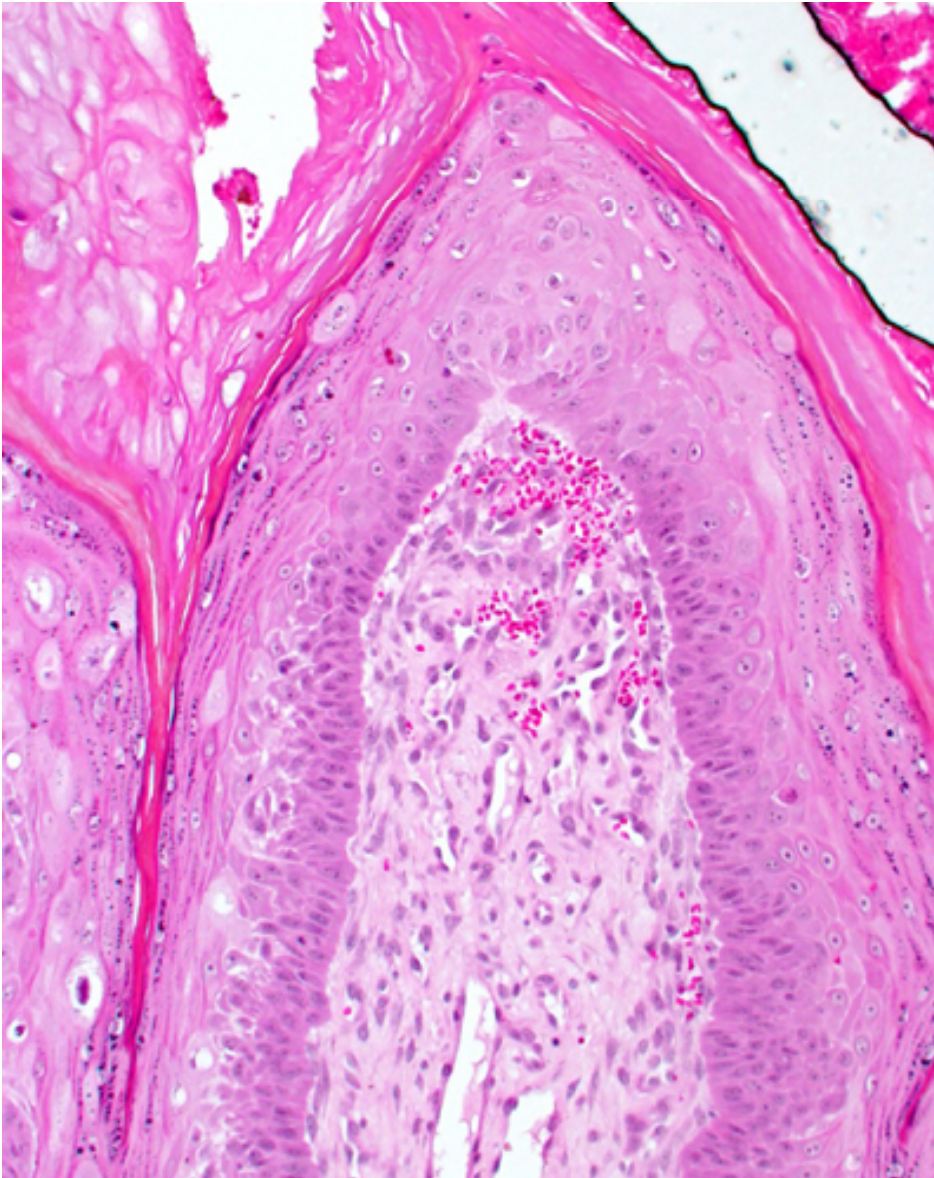
Cytology

- intranuclear eosinophilic inclusion bodies may be seen in some cells from the granular cell layer.
- lymphocytes, plasma cells, and neutrophils may be seen, which is indicative of secondary inflammatory changes.

Pathology



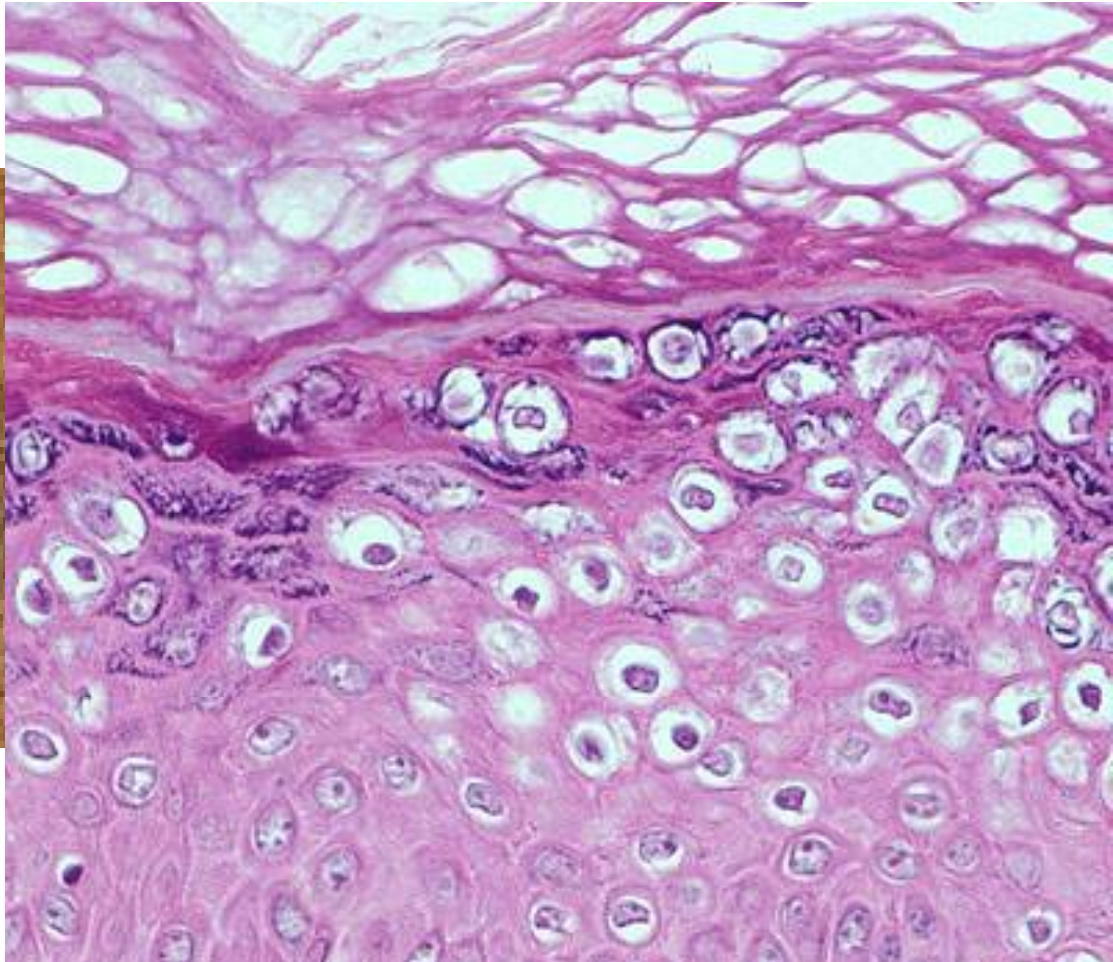
Pathology



Papilloma- Papilliferous Subtype

- elongated rete at the periphery of the papilloma which are slanted towards the center
- supported by a thin core of dermal fibrous connective tissue
- epidermal hyperplasia, thickened stratum corneum, may be orthokeratotic or parakeratotic
- granular cell layer absent or very prominent with enlarged keratohyaline granules in the cytoplasm
- in some cells the normal cell eosinophilic (red) cytoplasm of the cells of the spinous layer is replaced by a grey-blue finely granular material (viral cytopathic effect)
- occasional intranuclear pale basophilic inclusions (virus)
- lymphoplasmacytic and neutrophilic infiltration of the dermis.

Pathology



Pathology



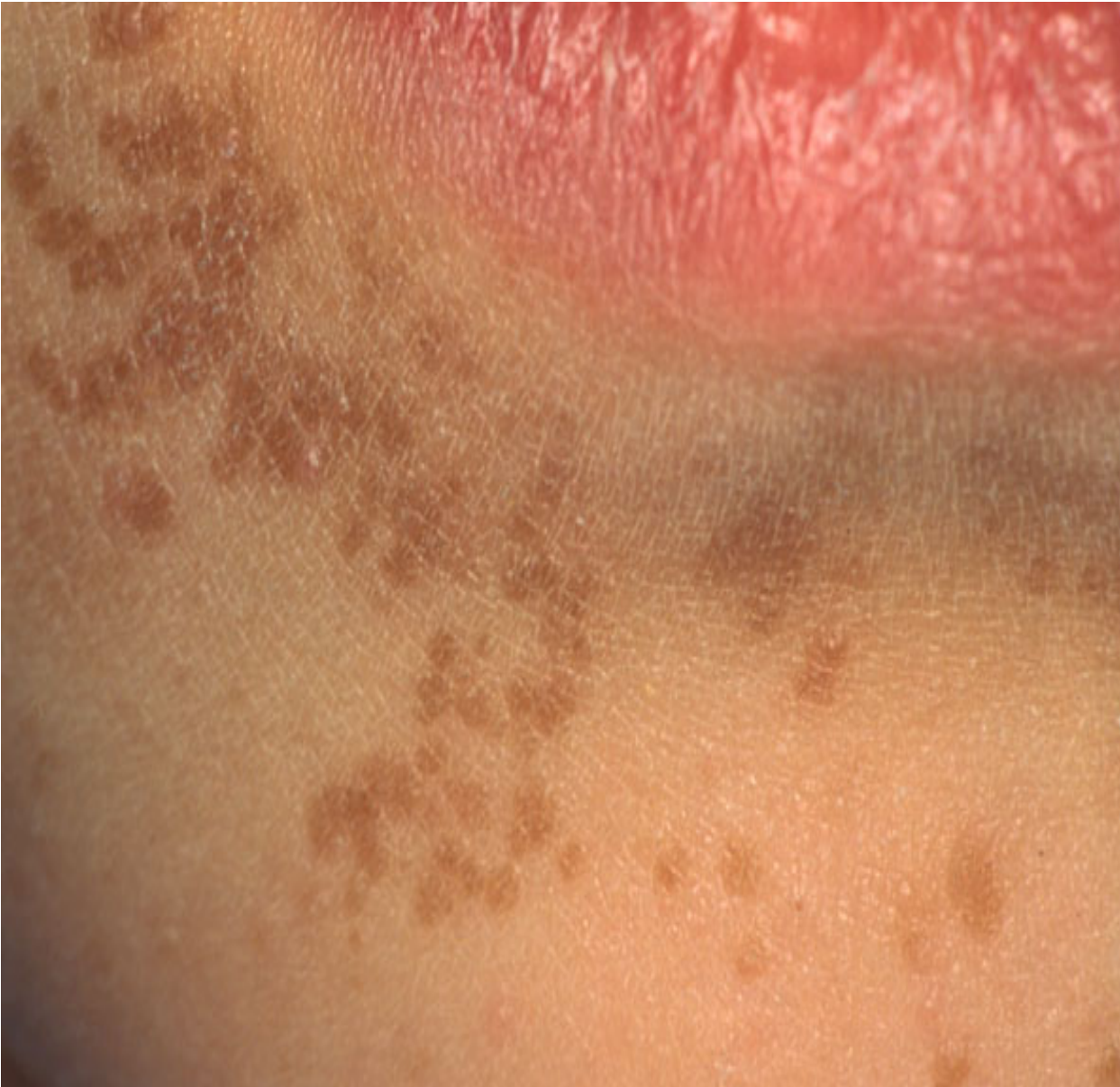
Pathology



Immunostaining for human papillomavirus antigen. Positivity is seen in the koilocytic nuclei and vacuolated cornified layer component.



Pathology



Verruca plana is often encountered on the face of the young, and HPV, types 3 or 10 is the causative agent.



Diagnosis

DIFFERENTIAL DIAGNOSIS

- Transmissible venereal tumor ([TVT](#))
- Squamous cell carcinoma
- Fibromatous [epulis](#)

CBC/BIOCHEMISTRY/URINALYSIS

Usually within normal limits unless dogs have become malnourished as a result of prolonged [dysphagia](#)

OTHER LABORATORY TESTS N/A

IMAGING N/A

OTHER DIAGNOSTIC PROCEDURES

- Rarely needed



Research and Case reports



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Virology 359 (2007) 28–36

VIROLOGY

www.elsevier.com/locate/yviro

An epidermotropic canine papillomavirus with malignant potential contains an E5 gene and establishes a unique genus

Hang Yuan ^a, Shinje Ghim ^b, Joe Newsome ^c, Tania Apolinario ^a, Vanessa Olcese ^a, Mary Martin ^a, Hajo Delius ^d, Peter Felsburg ^e, Bennett Jenson ^b, Richard Schlegel ^{a,*}

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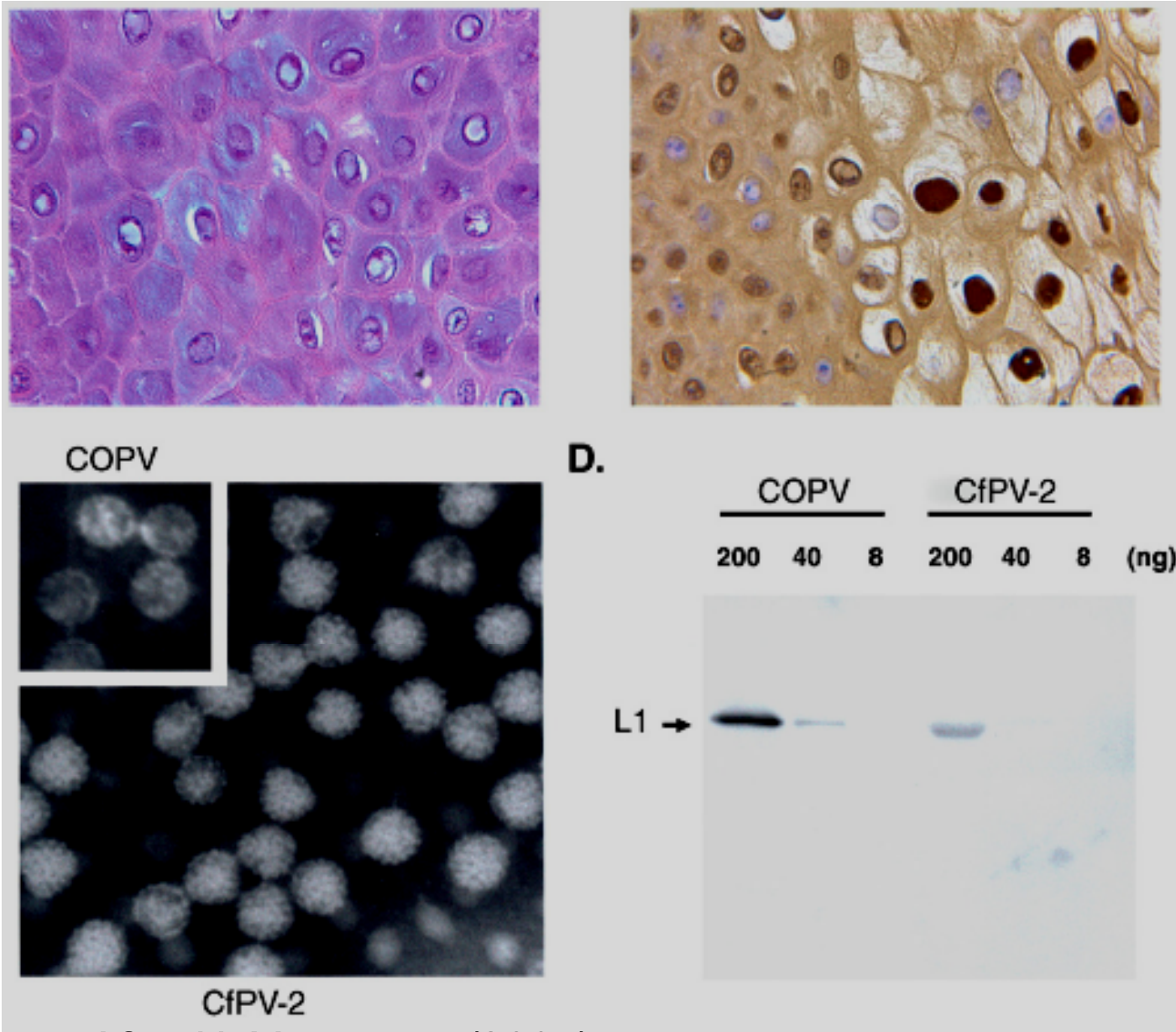
^d Division for the Characterization of Tumourviruses, Deutsches Krebsforschungszentrum, Heidelberg, Germany

^e Department of Clinical Studies, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA, USA

Received 25 April 2006; returned to author for revision 1 June 2006; accepted 11 August 2006

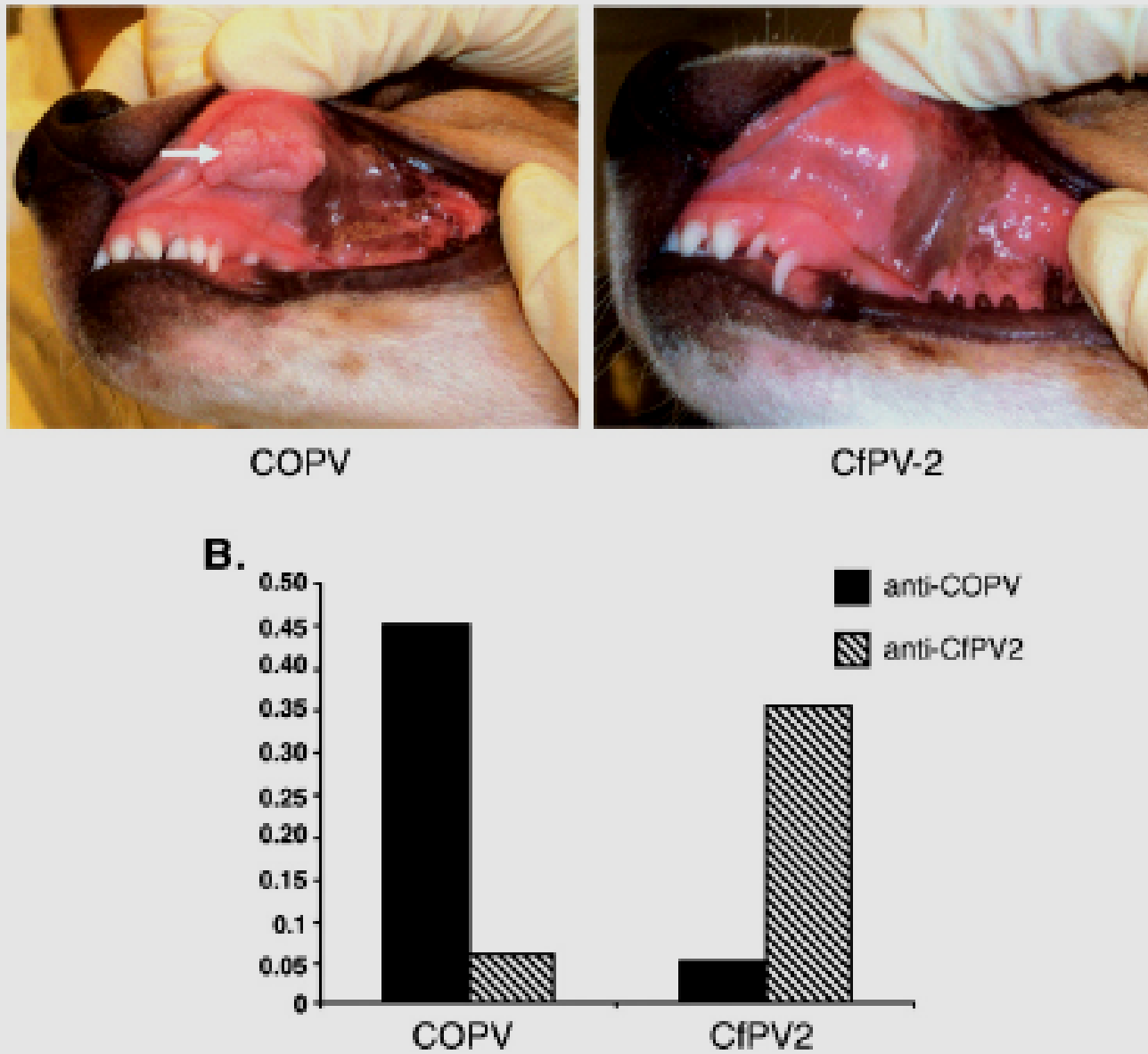
Available online 10 October 2006

Research and Case reports



After H. Yuan et al.(2007)

Research and Case reports



After H. Yuan et al.(2007)



Research and Case reports

J Vet Diagn Invest 13:346–348 (2001)

Digital papillomatosis in a confined Beagle

Brad M. DeBey, Mary Bagladi-Swanson, Sanjay Kapil, Frederick W. Oehme

Abstract. Papillomavirus-induced papillomas were diagnosed on multiple digits of all 4 feet of a young Beagle. No other cutaneous or oral involvement was identified. Papillomavirus antigen was confirmed by immunoperoxidase localization within keratinocyte nuclei. In addition to the typical basophilic intranuclear inclusions associated with papillomavirus infections, keratinocytes within the papillomas contained large, eosinophilic cytoplasmic inclusions that previously have been described in a Boxer with cutaneous lesions associated with a papillomavirus infection. The papillomas in this Beagle regressed completely within 2 months of the initial diagnosis.

Research and Case reports



After

Debbey et.al. (2001)





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Virology 324 (2004) 17–27

VIROLOGY

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Minireview

Classification of papillomaviruses

Ethel-Michele de Villiers,^a Claude Fauquet,^b Thomas R. Broker,^c
Hans-Ulrich Bernard,^{d,*} and Harald zur Hausen^a

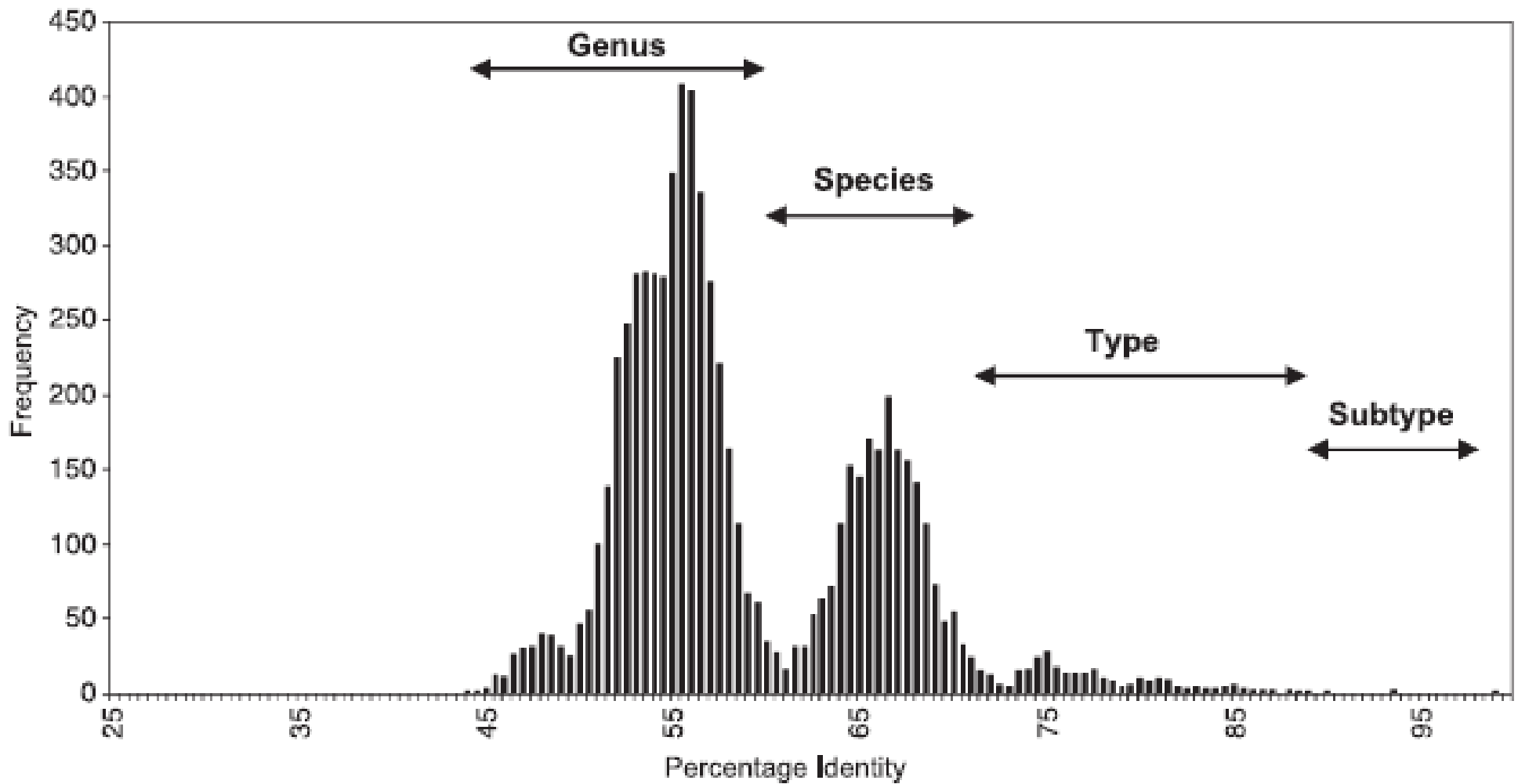
^a*Reference Center for Papillomaviruses, Division for the Characterization of Tumorviruses, Deutsches Krebsforschungszentrum, 69120 Heidelberg, Germany*

^b*ILTAB, Danforth Plant Science Center, St. Louis, MO 63132, USA*

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Received 2 February 2004; returned to author for revision 9 March 2004; accepted 24 March 2004





Canine cutaneous papilloma. Study of seven cases

Authors: Kaldrymidou, E.; Papaioannou, N.; Poutahidis, T.h.; van Garderen, E.; Karayanopoulou, M.

Source: [Journal of the Hellenic Veterinary Medical Society](#), Volume 52, Number 2, April - June 2001 , pp. 126-134(9)

Publisher: [Hellenic Veterinary Medical Society](#)

Abstract:

Seven cases of canine papilloma were studied histopathologically using light and electron microscopy. Papillomavirus was detected immunohistochemically and by the polymerase chain reaction (PCR) method.

- The classical squamous papilloma was found in four dogs (#1,2,3,4)
- the inverted papilloma in one dog (#5)
- the fibropapilloma in two dogs (#6,7).
- Virus particles were detected electromicroscopically in two cases (#1,2)
- Immunohistochemistry, revealed the presence of the papillomavirus antigen in three cases (#1,2,3).
- The PCR method resulted in positive for COPV in two cases (#1,2).

These results support the view that except for the canine oral papillomavirus, there might be other types of papillomavirus that induce papilloma in dogs.



- Papillomas caused by COPV are typically multiple and occur in young dogs.
- Noninfectious papillomas are solitary and occur typically in older patients.
- Dogs only: Papillomaviruses are usually species specific.
- Affected animals are typically younger than 2 years of age with oral papillomas, 6 months to 4 years with ocular papillomas, and the age range for cutaneous papillomas caused by virus is uncertain.
- Owners may report difficulty eating or apparent discomfort.



<u>Variants of Canine Papillomavirus:</u>	<u>Associated Syndromes:</u>
• Canine Oral Papillomavirus (COPV)	• Oral papillomatosis
• Canine Papillomavirus (variants)	• Canine exophytic cutaneous papillomatosis
	• Cutaneous inverted papilloma
	• Pigmented epidermal plaques
	• Squamous cell carcinoma



Clinical Behavior

- Many papillomas regress spontaneously (weeks to months) due to cell mediated immunity and humoral immunity
- Failure to regress: may indicate immunodeficiency or an immunocompromised animal (receiving corticosteroid therapy).
- Some papilloma virus infections have been known to progress into carcinomas, primarily squamous cell carcinomas.



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6. Yager, J.A. & Wilcock, B.P. (1994). *Color atlas and text of surgical pathology of the dog and cat*. Ontario, Canada: Mosby Year Book



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***Thank you
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your attention !***