Treatment of Canine Papillomatosis

Chainarong Phumratanaprapin, DVM., M.Sc.
Faculty of Veterinary Medicine, Mahanakorn University of Technology
http://www.lab-retriever.net/board/dog-warts-should-t7305198.html?
Treatment of Canine Papillomatosis

- **Spontaneous Regression**
- **Surgical Excision**
  - Cryosurgery: with liquid nitrogen
  - Electrodessication and curettage
- **Immunotherapy**
  - Autogenous formalin inactivate vaccine
  - Immunoenhancers
- **Miscellaneous treatment**
  - 40% salicylic acid
  - 30-50% lactic acid
  - Antibiotic
Treatment of Canine Papillomatosis

- **Canine mucous membrane papillomatosis**
  - Presence on oral mucous membrane from lips to esophagus and on conjunctival mucous membrane: young dog
    - (Canine Oral Papilloma)

- **Canine Cutaneous Papillomatosis**
  - Presence on intracutaneous epithelium: old dog
Treatment of Canine Papillomatosis

Spontaneous Regression in case canine oral papillomas

- Warts usually regress spontaneously in several months. (1-6 months)
- The immune response to papillomaviruses associated with the spontaneous regression of warts and is mediated by both cellular and humoral immune responses.
How we fight the intruders

Pathogen attacks
Security breached

Sentinel cells sending SOS

Inflammation

Phagocytic cell entering the site

Killing and clearing of invaders

Pathogen clearance & Tissue repair

Immediate action

Effector cells entering the site

Activation of adaptive immunity in the lymphoid tissues

APC migration (APC leave the crime scene)

Back up plan
Host response to viral infection

Production of IFN-α, IFN-β, TNF-α and IL-12

NK-cell mediated killing of infected cells

T-cell mediated killing of infected cells

Virus titer

Sannipa S., 2006
From *Immunology: The Immune Response in Infectious and Inflammatory Disease* by DeFranco, Locksley and Robertson

- Virus
- CD8 T cells
- CD4 T cells
- Neutralizing antibody
- Neutralizing antibody in chronic infections

Spontaneously Regressing Oral Papillomas Induce Systemic Antibodies That Neutralize Canine Oral Papillomavirus

Shin-je Ghim,* Joseph Newsome,* Judith Bell,† John P. Sundberg,‡ Richard Schlegel,* and A. Bennett Jenson*

*Department of Pathology, Georgetown University School of Medicine, 3900 Reservoir Road, Washington, DC, 20007; †Marshall Farms, North Rose, New York; and ‡The Jackson Laboratory, Bar Harbor, Maine

Received October 1, 1999
TABLE 1

Passive Immunization of Groups of Beagle Dogs That Received Purified Normal IgG (Group 1) or Hyperimmune Total Immunoglobulin (Group 2) or IgG Fractionated and Purified by Protein A (Group 3)

<table>
<thead>
<tr>
<th>Group</th>
<th>Antibody (mg/kg wt)</th>
<th>Donor of sera</th>
<th>Dog with warts/dog challenged</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>Purified IgG (28 mg/kg)</td>
<td>Naive</td>
<td>4/4</td>
</tr>
<tr>
<td>Group 2</td>
<td>Total Ig (150 mg/kg)</td>
<td>Regressor</td>
<td>0/4</td>
</tr>
<tr>
<td>Group 3</td>
<td>Purified IgG (20 mg/kg)</td>
<td>Regressor</td>
<td>0/4</td>
</tr>
</tbody>
</table>
Regression of Canine Oral Papillomas Is Associated with Infiltration of CD4+ and CD8+ Lymphocytes

Philip K. Nicholls,*† Peter F. Moore,† Davina M. Anderson,* Richard A. Moore,* Nigel R. Parry,‡ Gerald W. Gough,† and Margaret A. Stanley*

*Department of Pathology, University of Cambridge, Tennis Court Road, Cambridge, CB2 1QP, United Kingdom; †Department of Pathology, Microbiology and Immunology, School of Veterinary Medicine, University of California, Davis, California 95616; and ‡GlexoWellcome Medicines Research Centre, Stevenage, Herts, SG1 2NY, United Kingdom

Received September 20, 2000; returned to author for revision October 27, 2000; accepted December 6, 2000

Canine oral papillomavirus (COPV) infection is used in vaccine development against mucosal papillomaviruses. The predictable, spontaneous regression of the papillomas makes this an attractive system for analysis of cellular immunity. Immunohistochemical analysis of the timing and phenotype of immune cell infiltration revealed a marked influx of leukocytes during wart regression, including abundant CD4+ and CD8+ cells, with CD4+ cells being most numerous. Comparison of these findings, and those of immunohistochemistry using TCRαβ, TCRγδ, CD1a-, CD1c-, CD11a-, CD11b-, CD11c-, CD18-, CD21-, and CD40L-specific monoclonal antibodies, with previously published work in the human, ox, and rabbit models revealed important differences between these systems. Unlike bovine papillomavirus lesions, those of COPV do not have a significant gamma/delta T-cell infiltrate. Furthermore, COPV lesions had numerous CD4+ cells, unlike cottontail rabbit papillomavirus lesions. The lymphocyte infiltrate in the dog resembled that in human papillomavirus lesions, indicating that COPV is an appropriate model for human papillomavirus immunity.

Key Words: HPV; COPV; immunity; animal models; immunohistochemistry.
FIG. 1. Wart progression and regression after experimental infection. Infections in both animals showed a similar growth pattern. The maximum wart diameter was measured each week. Warts were visible 5 weeks after infection and grew rapidly to reach their greatest diameter at 8 weeks. Regression was rapid, with the lesions disappearing by 10 weeks postinfection. Infections in both animals showed a similar growth pattern.
Surgical Excision
Surgical Excision

- Surgical removal is recommended if the wart are sufficiently, however because surgery in early growing stage of warts may lead to recurrence and stimulation of growth, the warts should be removed when near the maximum size or when regressing. (from The Merck Veterinary Manual)
  - The other technique:
    - Cryosurgery is the preferred treatment, two freeze-thaw cycles are used.
Immunotherapy

- Autogenous formalin-inactivated wart vaccines
  - Autogenous warts vaccine are considered of questionable valve in treatment
  - Favorite in Cow (farm management)
  - Principle method:
    - Using 10-20% warts suspension in normal saline and inactivate virus by 40% formalin
    - Repeat dose are recommended.
Effects of oral administration Beta Glucan on cytokines

Cytokines | Producing Cell | Target Cell | Function
--- | --- | --- | ---
IL-2 | Th1 cells | Activated T & B cells, NK cells | Growth, proliferation, activation
IFN-γ | Th1 cells, Tc cells, NK cells | various | Viral replication
TNF-α | Macrophages, mast cells, NK cells | Tumor cells | Cell death

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Control</th>
<th>WGP Beta Glucan</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-2</td>
<td>9.7 +/- 0.5 pg/ml</td>
<td>23.4 +/- 2.1 pg/ml*</td>
</tr>
<tr>
<td>IFN-γ</td>
<td>107.8 +/- 8.4 pg/ml</td>
<td>475.8 +/- 42.3 pg/ml*</td>
</tr>
<tr>
<td>TNF-α</td>
<td>487.8 +/- 58.2 pg/ml</td>
<td>1083.5 +/- 44.6 pg/ml*</td>
</tr>
</tbody>
</table>
Autogenous formalin-inactivated wart vaccines

การใช้วัคซีนหูกระสาโรคหูในปากสุนัข

* ปราณี ศินดีวิช แพทย์บ.• M.S.

บทย่อ

รายงานการทดลองใช้วัคซีนที่ทำจากเนื้อเยื่อของตัวเอง (autogenous tissue vaccine) และชนิดที่ไม่ได้ทำจากเนื้อเยื่อของตัวเอง (non-autogenous tissue vaccine) เพื่อรักษาโรคหูในปากสุนัข 10 ตัว ผลจากการทดลองปรากฏว่าถ้าใช้วัคซีนชนิดที่ทำจากเนื้อเยื่อของตัวเองจะได้ผลในการรักษา 100% แต่ถ้าใช้วัคซีนชนิดที่ไม่ได้ทำจากเนื้อเยื่อของตัวเองจะได้ผลในการรักษาเพียง 85% เท่านั้น
Autogenous formalin-inactivated wart vaccines

<table>
<thead>
<tr>
<th>สุนัข</th>
<th>ข้าวต้นธากที่ 1.</th>
<th>ข้าวต้นธากที่ 2.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 2 3 4</td>
<td>1 2 3 4 5</td>
</tr>
<tr>
<td>1</td>
<td>0.3 0.4 -  -</td>
<td>1 0.5 0.5 0.5  -</td>
</tr>
<tr>
<td>2</td>
<td>0.5 0.4 0.2 0</td>
<td>2 1.5 - - -</td>
</tr>
<tr>
<td>3</td>
<td>0.5 0.5 0  0</td>
<td>3 0.6 0.8 1.2  -</td>
</tr>
<tr>
<td>4</td>
<td>1.5 0.5 0  0</td>
<td>4 0.6 0.6 0.5 0.2</td>
</tr>
<tr>
<td>5</td>
<td>1.5 1.0 0  0</td>
<td>5 0.5 0.6 0.2 0</td>
</tr>
</tbody>
</table>

- = ไม่มีการรักษา

0 = สัดทรายจากโรค
At week 1
At week 1
At week 2
At week 3
At week 4
ขอบขอบคุณ

- นายแบบบีเกิ้ลสุดหล่อ
- คณะสัตวแพทยศาสตร์ มหาวิทยาลัยเทคโนโลยีมหานคร
- สุนัขทาโร ที่เป็นแรงบันดาลใจเสมอมา
- ลูกสัตว์ที่เป็นแรงบันดาลใจเสมอมา
Thank you for your attention