SPATIAL AND TEMPORAL CLUSTERING AND RISK FACTORS FOR CALCIUM OXALATE COMPARED TO STRUVITE UROLITHS IN DOGS

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OUTLINE

- PATHOPHYSIOLOGY & EPIDEMIOLOGY
- STUDY # 1: SPATIAL AND TEMPORAL CLUSTER ANALYSES
- STUDY # 2: RISK FACTOR ANALYSIS
- DISCUSSION
PATHOPHYSIOLOGY
& EPIDEMIOLOGY
OF CANINE
UROLITHIASIS
Burden of illness

- Proportional morbidity - 0.05 - 1.2 %
- 95% occur in the lower urinary tract
- Calcium oxalate & magnesium ammonium phosphate (struvite) - 92% of submissions
- Require surgery, other assisted voiding, or medical (struvite-only) therapy
Development of uroliths

- **supersaturated solution**
  - spontaneous crystal formation

- **saturated solution**
  - crystal aggregation
  - inhibitors and promoters

- **under saturated solution**
  - some crystals will dissolve
    - (struvite)

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urine

ionic concentration
gradient
Contrasting struvite and CaOx uroliths

- also a function urine pH
  (alkaline urine - struvite; neutral to acidic - CaOx)

- Struvite – bacterial infection

- CaOx – low dietary levels: minerals, protein & moisture
  (Lekcharoensuk et al., 2002)

- Small breeds vs. other pure breeds
### Demographic risk factors

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>CaOx</th>
<th>Struvite</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Mean &gt; 7 years</td>
<td>Mean &lt; 7 years</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td>Males</td>
<td>Females</td>
</tr>
</tbody>
</table>

CaOx – neutering and obesity increased risk

(Lekcharoensuk et al., 2000)
Contextual risk factors

- City vs. farm dogs - CaOx (Lekcharoensuk et al., 2000)
- Affluence and meat consumption (human)
- Water hardness (human)
CVUC

- Canadian Veterinary Urolith Centre
  free service to veterinarians

- 32,000 canine uroliths submitted to the CVUC from across Canada

- Quantitative analysis
Overall study objectives

- Identify contextual variables
- Evaluate complex interactions among individual level demographic and dietary risk factors
STUDY # 1

SPATIAL AND TEMPORAL CLUSTER ANALYSES
Objectives

- Spatial clustering:
  1. environmental (water, diet, clinic)
  2. socioeconomic

- Temporal clustering:
  1. trends in diet
  2. trends in therapy
Methods & Materials
### Data

#### Study # 1

<table>
<thead>
<tr>
<th></th>
<th>Incident Cases</th>
<th>CaOx &amp; Struvite</th>
<th>Geo-coded</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ontario</td>
<td>11,414</td>
<td>92%</td>
<td>93%</td>
<td>9,735</td>
</tr>
</tbody>
</table>

- **Geo-coded cases:**
  1. 52% CaOx
  2. 48% struvite
Geo-coding to latitude and longitude coordinates with Geopinpoint Suite 5.4 v.2006.2 DMTI spatial

- Geocoding was done using owner address information
- Geocoding assessment done with a random sample of 100 locations in ArcGIS 9.2 (ESRI)
- Visual comparison to 2001 forward sortation area (FSA)
- Geographic Coordinate System Datum 1983 projection
Biases resulting from matching addresses to geocoded locations

- **Positional inaccuracies**
  - Addresses are assigned locations unacceptably far from their actual position (Oliver, et al., 2005)
  - 100% of our sample was within or within adjacent FSAs

- **Differential match rate** – non-random unmatched locations
  - Risk factors related to “missingness” are also the same risk factors for the disease (Oliver, et. al., 2005). In this study, population density related factors could be potential confounders
  - High match rate in our study, 93%
Data analysis

- Spatial scan statistic with SaTScan™ v.7.0.3 (Kulldorff and Information services)

- Bernoulli model – calcium oxalate compared to struvite urolith submissions
  1. spatial scan - household location
  2. temporal scan - date received

- Max. scanning window: 50% of population and/or study period
- 999 Monte Carlo simulations
Data analysis (cont.)

- Adjusted analysis using multiple datasets option (8):

1. Age (< 7 yrs : 7 + years)
2. Sex
3. Breed (small breed : non-small breed)
Results
Adjusted spatial analysis

- **Calcium oxalate:**
  - Toronto
  - O/E - 1.06
  - p-value - 0.001

- **Struvite:**
  - Hastings Highlands
  - O/E - 1.33
  - p-value - 0.02
Discussion

- Significant clustering in space

- Spatial and temporal clusters reflect:
  1. Contextual risk factors (biologic/socioeconomic)
  2. Submission bias

- Subsequent statistical modeling will account for diet, clinic, and regional socio-economic factors
STUDY # 2

RISK FACTOR ANALYSIS
Objectives

- Identify animal level risk factors (demographic, dietary)
- Identify community level contextual variables (distance, statistical area classification (SAC), cluster, income)
Statistical methods

- Multi-level modeling in a mixed logistic regression model with STATA v.10
- Owner census subdivision (CSD) as the random intercept (n=302)
- Demographic, dietary, community-level variables (median family income, statistical area classification, distance between owner and clinic locations) and year
- n = 7,297 observations
Dog-level variables

- Age and quadratic
- Sex
- Breed type:
  1. large and medium pure breeds
  2. small pure breeds
  3. mixed breeds
- Body condition (thin/normal vs. obese)
- Neuter status

- Two-way interactions among these variables:
  1. sex*age
  2. body condition*age
  3. sex*neuter status
<table>
<thead>
<tr>
<th>Dietary variables</th>
<th>OR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vet diet =&gt;6months vs. other diet</td>
<td>1.54</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Canned vs. dry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Small breed</td>
<td>0.70</td>
<td>0.03</td>
</tr>
<tr>
<td>2. Mixed breed</td>
<td>0.76</td>
<td>0.44</td>
</tr>
<tr>
<td>3. Large breed*</td>
<td>7.71</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Canned vs. both</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Small breed</td>
<td>0.80</td>
<td>0.21</td>
</tr>
<tr>
<td>2. Mixed breed</td>
<td>0.88</td>
<td>0.74</td>
</tr>
<tr>
<td>3. Large breed*</td>
<td>7.03</td>
<td>0.001</td>
</tr>
<tr>
<td>Community and time level variables</td>
<td>OR</td>
<td>P-value</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>------</td>
<td>---------</td>
</tr>
<tr>
<td>Year 2006 (ref: 1998)</td>
<td>1.59</td>
<td>0.011</td>
</tr>
<tr>
<td>Cluster:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CaOx vs. struvite</td>
<td>2.38</td>
<td>0.004</td>
</tr>
<tr>
<td>CaOx vs. outside</td>
<td>1.38</td>
<td>0.004</td>
</tr>
<tr>
<td>Struvite vs. outside</td>
<td>0.60</td>
<td>0.052</td>
</tr>
<tr>
<td>Statistics Canada 2006 - ArcGIS</td>
<td>1.41</td>
<td>0.020</td>
</tr>
<tr>
<td>CSD Median family income $70,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(ref &lt;$54,000 category)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>* SAC, distance</td>
<td></td>
<td>N/S</td>
</tr>
</tbody>
</table>
Discussion

- Complex interactions among the individual dog level risk factors
Discussion

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- Dietary variables:
  1. Dietary moisture and breed-type
  2. Vet diets require further evaluation
Discussion

- Complex interactions among the individual dog level risk factors

- Dietary variables:
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  2. Vet diets require further evaluation

- Impact of income and cluster
  1. lifestyle
  2. treatment choice
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