The Case of the Cryptic Clustered Cryptococci

(Outbreak of Cryptococcus neoformans var. gattii on Vancouver Island , British Columbia)

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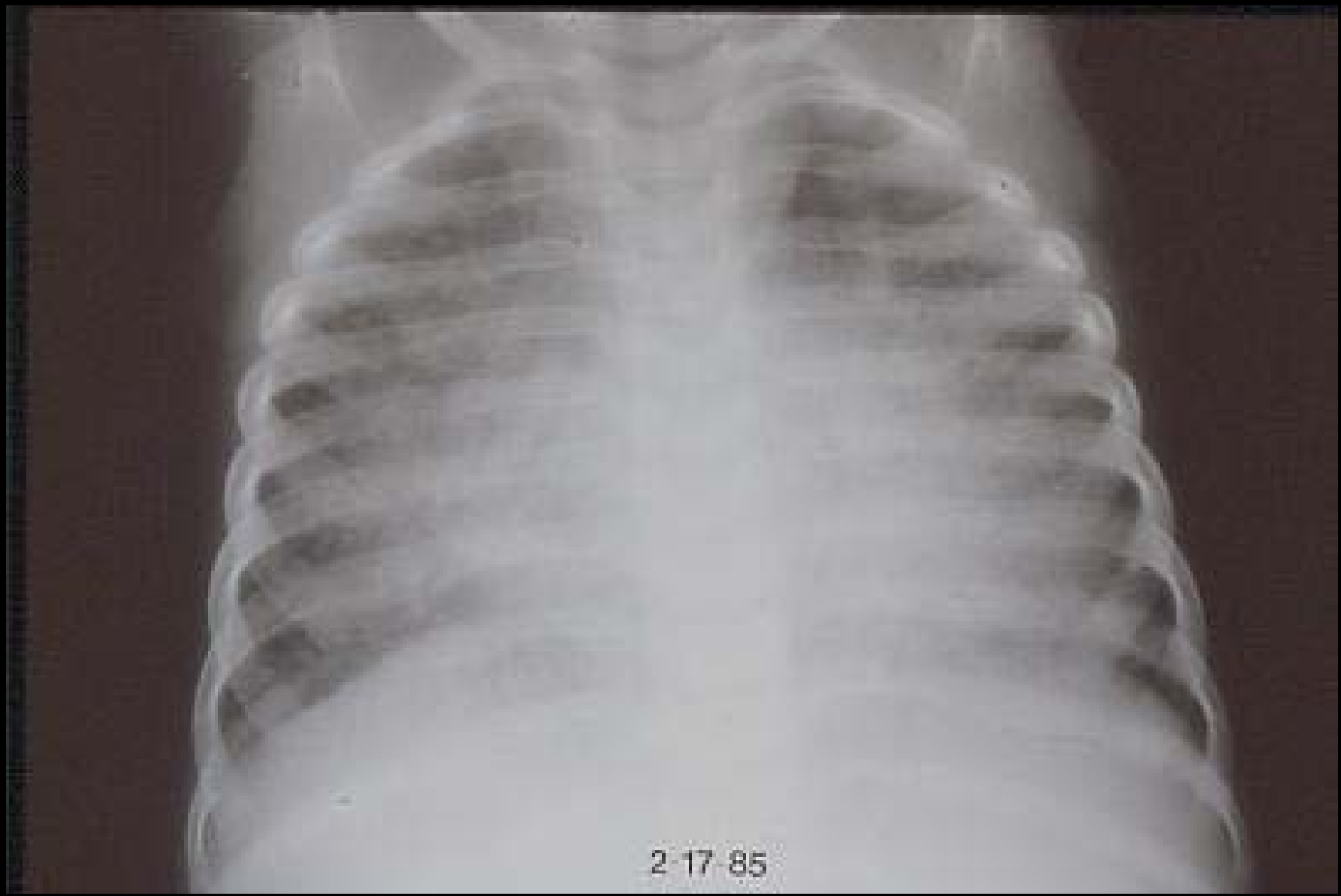
Cryptococcus

- Encapsulated yeast-like fungus
- World-wide distribution
- 37 species
- *C neoformans* is the only species that is pathogenic

C neoformans var. *neoformans*

- 90% of recognised C neoformans disease
- Usually seen as opportunistic pathogen in patients with AIDS
- Most common cause of fungal meningitis
- Pigeon or other avian dung reservoir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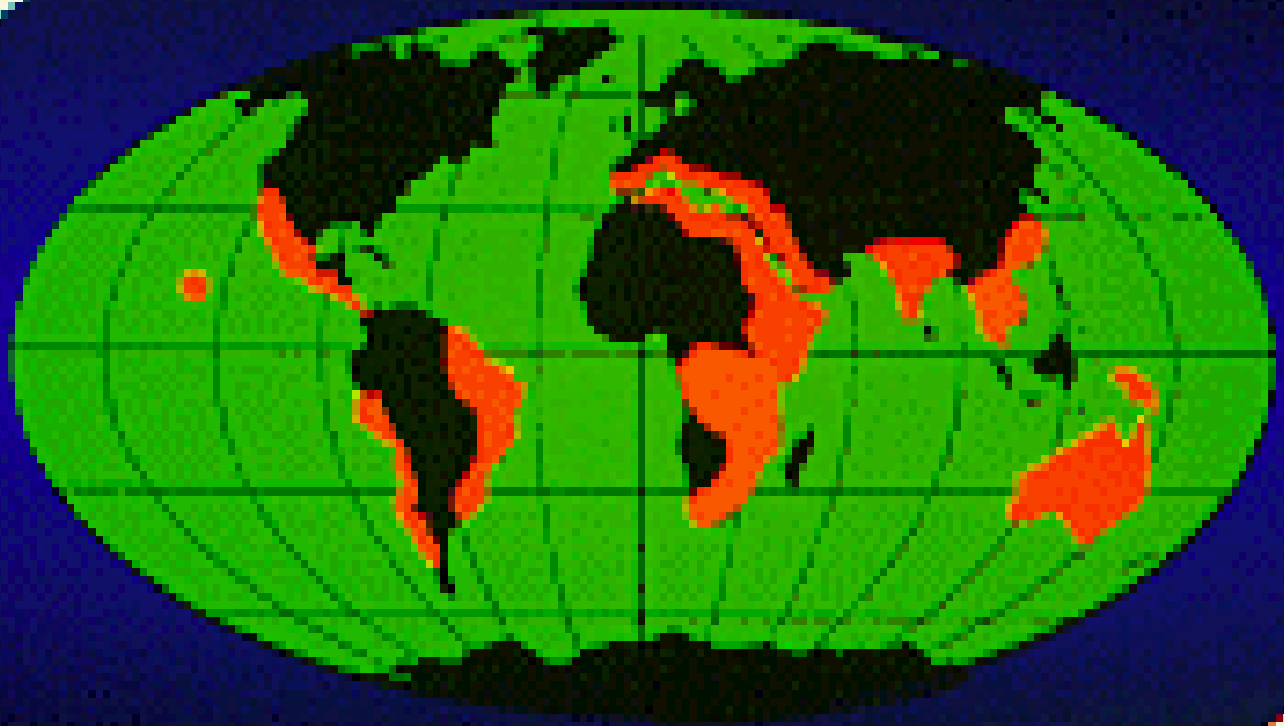
C neoformans var. *gattii* (CNVG)

- Less common pathogen
- Immunocompetent hosts
- Large mass lesions in lung &/or brain
- Geographically restricted
- Specific ecological association with *Eucalyptus camaldulensis*

Worldwide Distribution of Host *Eucalypts* for *Cryptococcus neoformans* var. *gattii*.



WCH Mycology

Vancouver Island Background Information

- Mean Temp: 2.3^{0}C Jan, 17.6^{0}C Aug
- Precip: 857-3295mm/yr
- Population: 703,052
- Median age: 40.2yrs (37.2yrs for BC)
- Over 65 yo: 16.3% (12.8% for BC)
- Aboriginal population: 39,010 (5.5%)

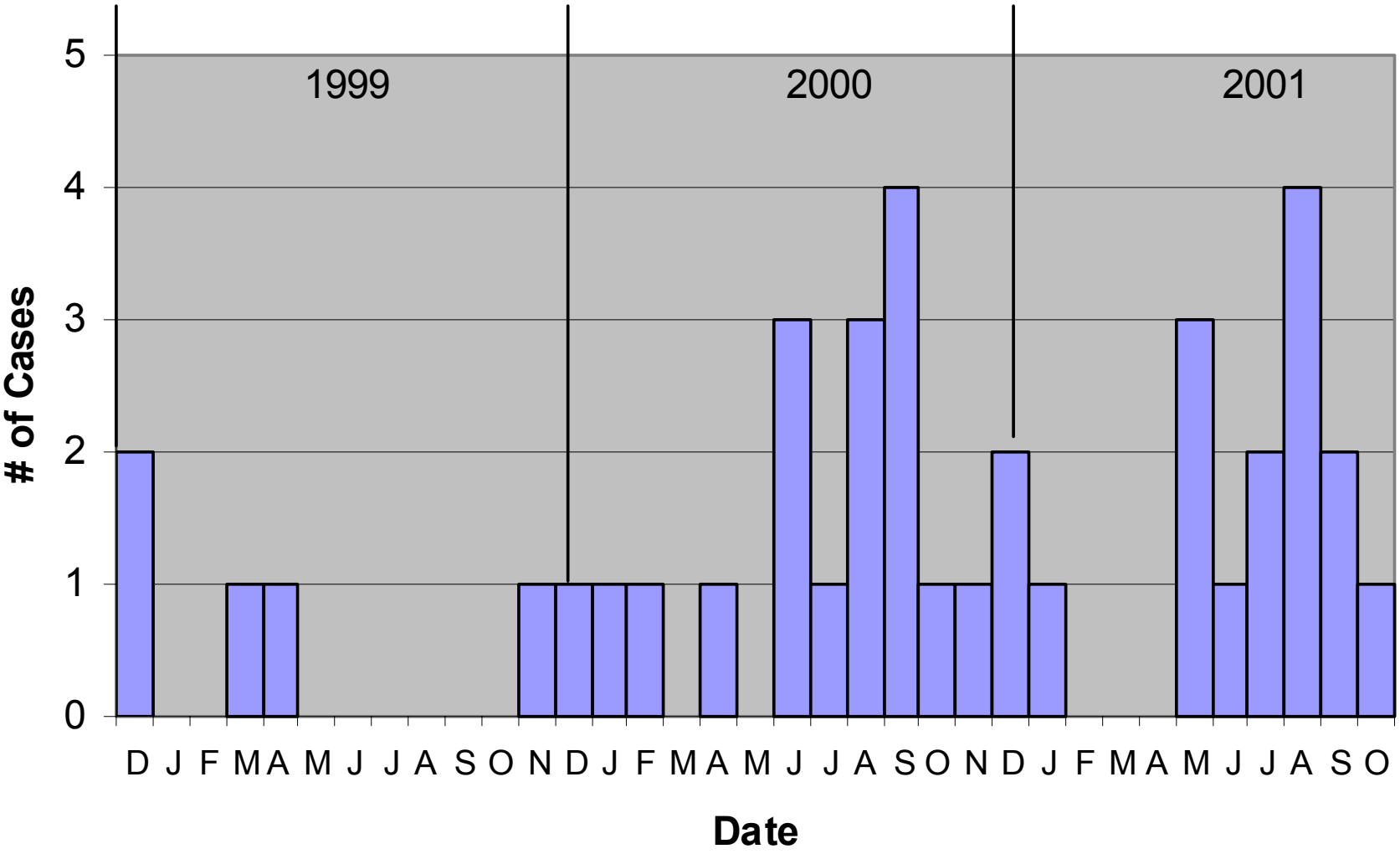
Vancouver Island Cluster

- January 1, 1999 - March 1, 2002:
  41 confirmed cases of Cryptococcal Disease
- Mainly immunocompetent adults
- Over the same period, vets reported
  ↑ cryptococcal cases in domestic pets
- Initial testing suggested isolates to be CNVG

CNVG on Vancouver Island

- Incidence pre-1999: ??
- Incidence since 1999:
  - 1999 = 8.5 per million
  - 2000 = 26 per million
  - 2001 = 24 per million
- (Incidence in Aust: ~1/million/year)

No. of Cases of Cryptococcus by date of initial presentation



Investigation

- Chart Reviews
- Case Interviews
- Case Control Study
- Veterinary Study
- Molecular typing
- Serology
- Environmental Studies

Patient Characteristics

- Mean age 61 years (range 19-88)
- 61% male
- 64% immunocompetent
- 36 cases involved lungs (88%)
- Meningitis in 10 (24%)
- 6 deaths - 2 attributable

Preliminary findings

- Possible exposures
  - Wooded area (70%)
  - Gardening (64%)
  - Fertilizer/compost (60%)
- Unlikely exposures
  - Animal exposures - farms, pets, birds
  - Outdoor leisure activities
  - No ubiquitous exposure to eucalyptus, fig, almond trees

Preliminary findings

- Possible predisposer
  - Smoking (68%)
  - Immunocomp (36%)
  - Steroids (25%)
  - Smoking or Immunocomp (89%)

Distribution of Human and Animal Cryptococcal Cases in Southwestern British Columbia, 1999-2002*

Environmental Sampling

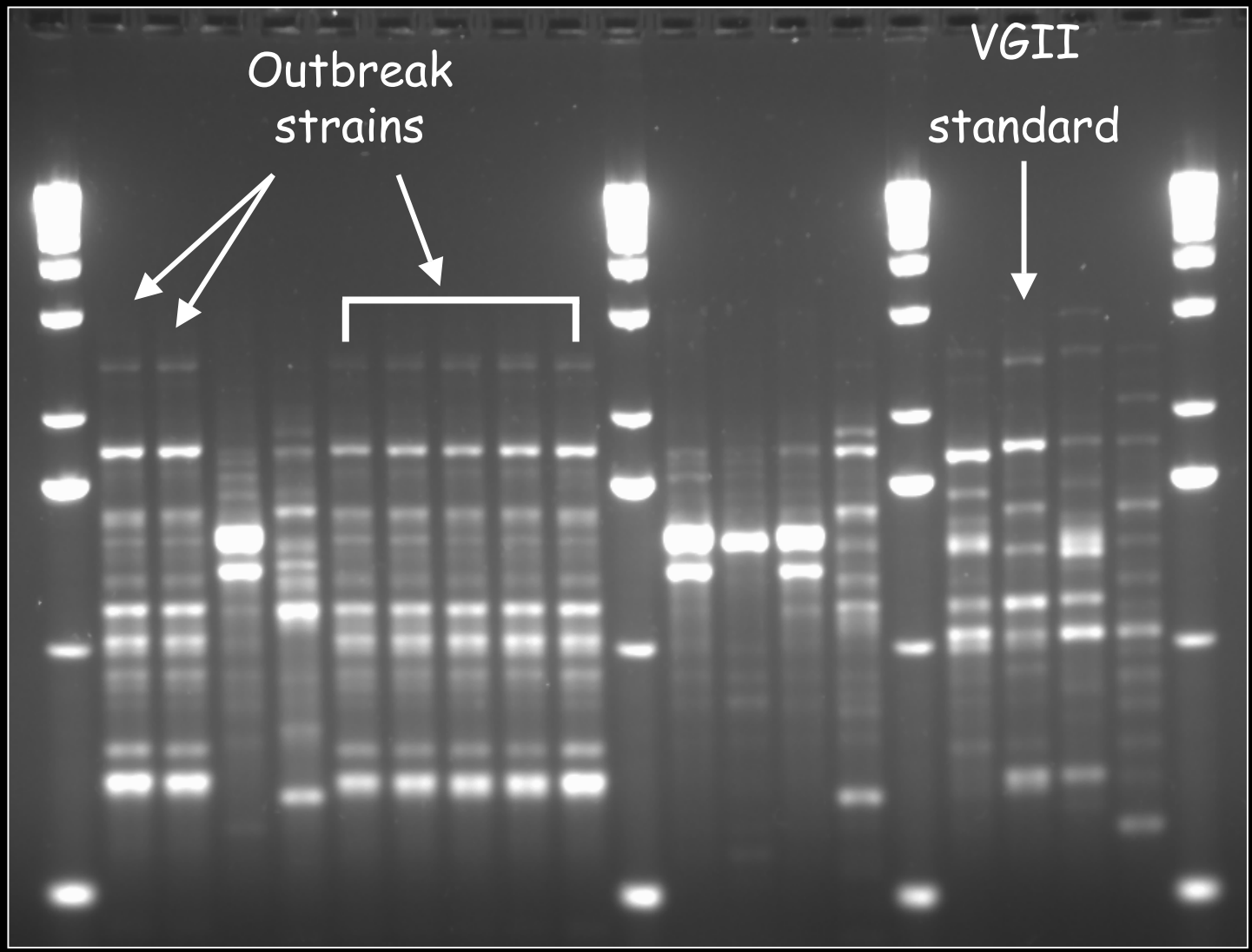
- Samples taken from tree holes, rotting wood in "hot spots"
- Garry Oak and Arbutus
- GPS readings
- Bird seed agar
- No cryptococci to date

Laboratory Typing

- 21 *C neoformans* isolates from humans typed
  - 15 CNVG
  - 1 CNVN
  - 5 not able to be typed
- 4 animal isolates typed – all CNVG

Other typing

- Molecular typing
  - PCR fingerprinting
  - AFLP
- Immunohistochemistry
- Type-specific serology
  - Immunoblotting of sera against CNVG protein extracts
  - IgG reactive to CNVG protein detected


Outbreak
strains
VGII
standard

Conclusions

- CNVG usu seen in tropical/subtropical climate
- Incidence of CNVG in endemic areas like Australia is approx 1/million/year
- Estimated incidence on Vancouver Island since 1999 - 24/million/year
- Concurrent outbreak amongst animals
- This outbreak may in fact represent the emergence of a new disease

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