Cryptococcal Antigen Testing in an Integrated Medical System: Eastern Wisconsin

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BACKGROUND

- Cryptococcosis (crypto) is a serious environmentally-acquired endemic fungal infection causing meningitis, pneumonia and disseminated disease in usually immunocompromised hosts.

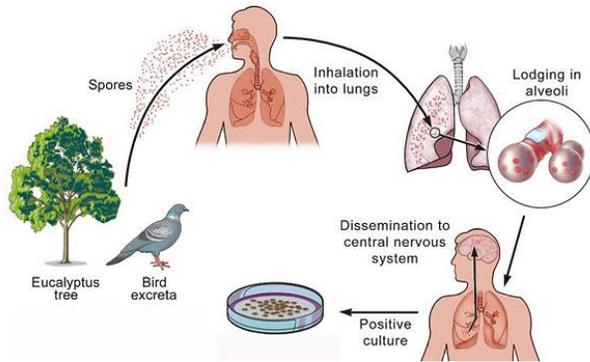- Proper diagnosis is important to avoid increased morbidity and mortality.

FIGURE 1. Life Cycle of *Cryptococcus neoformans*
C. neoformans and *C. gattii* are two major human pathogenic species of *Crytococcus*. Note that *C. gattii*, has not been isolated from avian guanos and it is significantly less frequent globally (<20%) than *C. neoformans* (80%). Moreover, cryptococcal antigen detection tests do not differentiate between the two.

INTRODUCTION

- Environmental associations of the pathogenic *Cryptococcus* species include certain trees, soils, bird guano and sites such as parks.

- Little is known regarding the frequency or distribution of cryptococcosis in Wisconsin.

- Cryptococcal antigen detection tests (CrAg), more than 90% sensitive and specific, are frequently used to screen patients with likely disease.

OBJECTIVE

We aimed to explore the geodemographic and clinical features of Eastern Wisconsin patients tested with CrAg.

METHODS

Design
- Retrospective review of 1465 CrAg tests from January, 2013 through April, 2017 for geodemographic characteristics and clinical features.

  - If patient was ever positive, they were always considered positive; and the demographics, clinical feature were also used from the first identified positive test.

  - If patient was always negative, we took information from the first test done during the time period.

- Descriptive statistics were compared with chi-square or t-tests; binary logistic regression was used for multivariable analysis.

Participants
- Every patient having CrAg performed within time period.

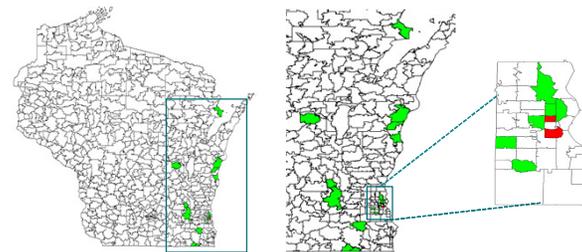**Setting**
- Large Eastern Wisconsin medical system.

FIGURE 2. Map of Positive Crypto Cases in Eastern Wisconsin
Overall, 17 separate Zip codes had 1 positive case (green shaded), 2 City of Milwaukee Zip codes had 3 each (red shaded), the closest 2 living 193 meters apart.

RESULTS

- A total of 1465 CrAg (741 on serum, 723 on CSF, 1 other) were performed on 1211 unique patients (50.2% female, 73.9% White, mean age 53.7 +/-16.5) during this time.

- Overall:
  - CrAg was positive in 23/1211 patients (1.9%)
  - 4 cases had pneumonia only
  - 21/23 were immunocompromised (6 transplant patients, 5 HIV, 4 malignancy, 3 steroid use, 2 diabetes, 1 combined deficiency)
  - Positive patients were more likely to be male (82.6%) non-Hispanic White (12/23 [3.8% of those tested] vs 11/23 [1.2% of those tested])
    - These associations (both p<0.03), but not age, were significant independent predictors in multivariable models.

- Positive patients were more likely in Milwaukee Zip codes (9.1% of those tested vs. 1.1% rest of the state, likely due to increase in immunocompromised patients); no other case clustering or close proximity to waterways was observed (41% were <162m from green space, similar to historical controls).

Characteristics	Total (N=1210*)	Positive CrAg (N=23)	Negative CrAg (N=1187*)
Male	603 (49.8%)	19 (3.2%)	584 (96.8%)
Female	607 (50.1%)	4 (0.7%)	603 (99.3%)
White	894 (73.9%)	12 (1.3%)	882 (98.7%)
All Non –White	316 (26.1%)	11 (3.5%)	305 (96.5%)

TABLE 1. Demographic features of CrAg Positive subjects versus CrAg Negative subjects
*One patient missing demographic information.

CONCLUSION

Among ill CrAg-tested patients, male gender and non-White race/ethnicity, not natural environmental features, predicted positive tests.

REFERENCES

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- Kwon-chung KJ, Fraser JA, Doering TL, et al. Cryptococcus neoformans and Cryptococcus gattii, the etiologic agents of cryptococcosis. Cold Spring Harb Perspect Med. 2014;4(7):a019760.