Cryptococcosis

*Cryptococcosis is a Class C reportable disease in Louisiana as an AIDS defining illness and should be reported within five business days*

**Epidemiology**

Cryptococcosis is a fungal infection caused by encapsulated yeast of the genus *Cryptococcus*. Most cases are caused by *Cryptococcus neoformans*.

The yeast is most commonly found in the debris around pigeon roosts, decaying wood and soil contaminated with pigeon or chicken droppings. *C. neoformans* grows to high concentrations in pigeon feces, with the birds not being infected. Transmission results from the inhalation of aerosolized organisms. *Cryptococcus* infection most commonly leads to cryptococcal meningitis, the most serious form of the disease. Infection may also lead to pulmonary manifestations, which include coughing and chest pains.

Because the organism is ubiquitous, it is presumed that exposure to *C. neoformans* is common. Skin test surveys of healthy subjects provide some support for this assumption. Nevertheless, natural resistance to infection must be high because new cases were relatively rare before the advent of acquired immunodeficiency syndrome (AIDS). Unlike other aerosol-borne mycoses, cases of cryptococcosis rarely occur in clusters.

Patients with immunologic defects in T-cell–mediated host defense mechanisms appear to be at increased risk for progressive cryptococcosis. Among AIDS patients in the United States, cryptococcosis is the defining illness in 5% of patients. The incidence of cryptococcosis is also increased in patients with lymphoreticular malignancies (especially Hodgkin's disease), as well as sarcoidosis (even in the absence of corticosteroid therapy).

*Primary infection* is acquired by inhalation of aerosolized fungal elements and often is inapparent or mild. *Pulmonary disease* is characterized by cough, hemoptysis, chest pain and constitutional symptoms. Chest radiographs may reveal a solitary nodule or focal or diffuse infiltrates.

**Invasive Disease**

Hematogenous dissemination to the central nervous system, bones and joints, skin and mucous membranes can occur, but dissemination is rare in individuals without defects in cell-mediated immunity (eg, transplantation, malignant neoplasm, collagen-vascular disease, long-term corticosteroid administration, or sarcoidosis). Usually, several sites are infected, but manifestations of involvement of one site predominate. Cryptococcal meningitis is the most common and serious form of cryptococcal disease. Cryptococcal fungemia, without apparent organ involvement, occurs in patients with human immunodeficiency virus (HIV) infection but is uncommon in children.
Incidence

Since 1980, there have been 946 reported cases of cryptococcosis in Louisiana; however, incidence rates began to increase significantly in the mid-90’s, coinciding with the rise in AIDS cases (Figure 1).

**Figure 1:** Rates of cryptococcosis per 100,000 population – Louisiana, 1980-2015

Age, Gender & Race Distribution

Prior to 1993, males and females experienced similar trends for acquiring cryptococcosis. Post-1993, males have shown to have higher rates of acquiring cryptococcosis than women. For both genders, incidence rates have been on the rise (Figure 2).

**Figure 2:** Rates of cryptococcosis per 100,000 population by gender – Louisiana, 1987-2015
As with trends of cryptococcosis when examining gender, incidence rates for race between Whites and African-Americans were similar until 1993. However, post-1993 the disparity in incidence rates of cryptococcosis between Whites and African-Americans increased dramatically. This is likely due to co-infection with HIV/AIDS, a disease which nationally has affected African-Americans the greatest (Figure 3).

**Figure 3:** Rates of cryptococcosis per 100,000 population by race – Louisiana, 1987-2015

Cryptococcosis varies greatly among different age groups and by gender; with males aged 35 to 44 years and females aged 25 to 34 years most at risk. Cases are less frequently observed in younger persons (under 19 years), and moderately observed in the elderly (Figure 4). These patterns are likely due to increased immunosuppression due to HIV/AIDS in middle-aged groups (particularly among males), and other conditions in the elderly.

**Figure 4:** Rates of cryptococcosis per 100,000 population by gender and age group – Louisiana, 1988-2015
An Unusual Cluster of Cases Among Immuno-competent Individuals

In Louisiana in 2003, three cases of cryptococcal meningitis were reported in immunologically competent hospital employees within a period of six months. Common factors identified among the three employees included hospital employment and parking on the third floor of the hospital’s garage. None reported to have a history of risk factors for high-level exposure to pigeon droppings.

Large numbers of pigeons had inhabited different areas surrounding the hospital. Pigeons were roosting near the parking garage and air duct with a “large pile of pigeon droppings” having been reported near the fifth floor of the parking garage. Pigeons also roosted on the mechanical pipes and hospital roofs. The final measure taken to address the pigeon problem was to hire a company to extinguish the pigeon population (poisoning).

No definite source was identified for this cluster of three cases. No further cases were identified from that location.

Hospitalization Surveillance

Hospitalization surveillance is based on the Louisiana Inpatient Hospital Discharge Data (LaHIDD). In 1997, the Louisiana legislature mandated the reporting of hospital discharge data. LaHIDD serves as the state registry containing hospital discharge data submitted to the Louisiana Department of Health (LDH). The Office of Public Health (OPH) is responsible for making the data available to OPH sections as needed. The data is available with a delay of two years. The Infectious Disease Epidemiology Section uses these data sets for the surveillance of infectious diseases in hospitals. LaHIDD data sets contain demographic information (names, gender, age, date of birth, address, admit diagnosis, discharge diagnoses (main plus eight more diagnoses), procedures (main plus five), charges, length of stay and hospital name. The diagnoses and procedures are coded with ICD-9 codes. The data are based on the years 1999 to 2014.

Records of patients with cryptococcosis were extracted using the following ICD9 code whether in the main diagnosis or in the eight additional secondary diagnoses:

<table>
<thead>
<tr>
<th>CODE</th>
<th>DISEASE</th>
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<tbody>
<tr>
<td>1175</td>
<td>CRYPTOCOCCOSIS</td>
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Hospitalization Numbers, Rates and Trends

For the entire period from 1999 to 2014, approximately 1,900 hospitalized patients were diagnosed with cryptococcosis; more than twice number of cases which were reported between 1980 and 1999. The rate of patients diagnosed with cryptococcosis in Louisiana remained relatively stable, ranging between 2.4 and 4.6 cases per 100,000 population per year (Figure 5).
Cryptococcosis rates among hospitalized patients have been higher among males versus females. Rates for both genders have been highest among persons older than 20 years of age, yet the rates are significantly the greatest in males aged 35 to 44 years. This hospitalization data shows consistent trends with reportable data (Figure 6).

Figure 5: Hospitalized patients diagnosed with cryptococcosis, Louisiana 1999-2014

Rates of cryptococcosis among African-American patients have been much higher than the rates for White patients in the 20 to 54 year-old age group. The largest disparity is observed in 35 to 44 year olds, where the rate of cryptococcosis for African-American patients is six times greater than the rate for White patients (Figure 7).

Figure 6: Hospitalized patients diagnosed with cryptococcosis, by age and gender Louisiana, 1999-2014
Of all the patients who were diagnosed with cryptococcosis and were hospitalized in Louisiana from 1999 to 2014, 73% were co-infected with HIV. The proportion of co-infected patients was greatest in the age range of 20 to 44 year-olds, which is the highest-risk age group for HIV nationally (Figure 8).

Figure 7: Hospitalized patients diagnosed with cryptococcosis, by age and race
Louisiana, 1999-2014

Figure 8: Hospitalized patients diagnosed with cryptococcosis and HIV, by age group
Louisiana 1999-2014
Only 18% of cryptococcosis-associated hospitalizations had cryptococcosis as the primary diagnosis; the majority (60%) was due to HIV. Other primary diagnoses included pneumonia unspecified (1%), congestive heart failure (0.6%), and various other conditions.

**Mortality**

Between 1999 and 2014 there were 215 deaths among hospitalized patients diagnosed with cryptococcosis (Figure 9).

**Figure 9:** Fatalities among hospitalized patients associated with cryptococcosis, by age Louisiana, 1999-2014