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ThinPrep® Pap Test™

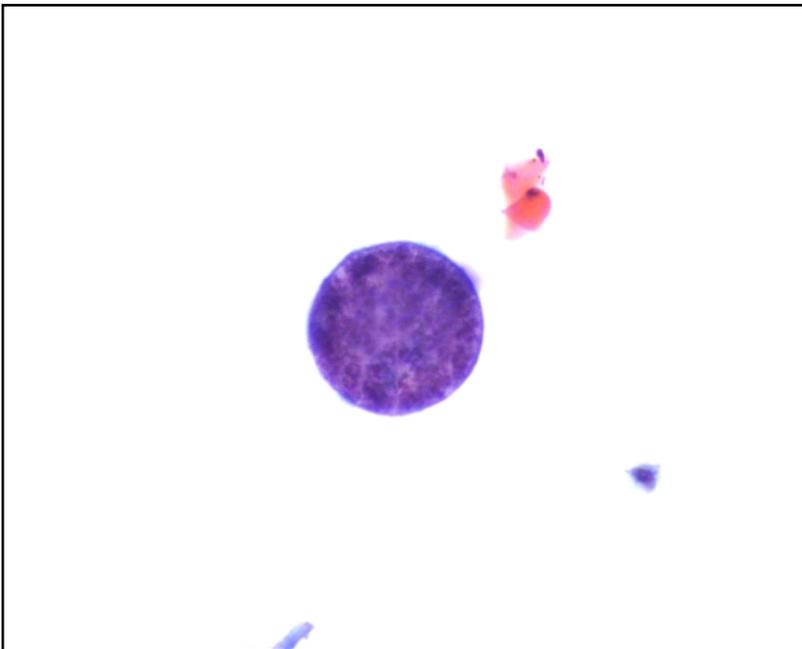
History: 30 Year Old Female

LMP: Pregnant - 1st trimester

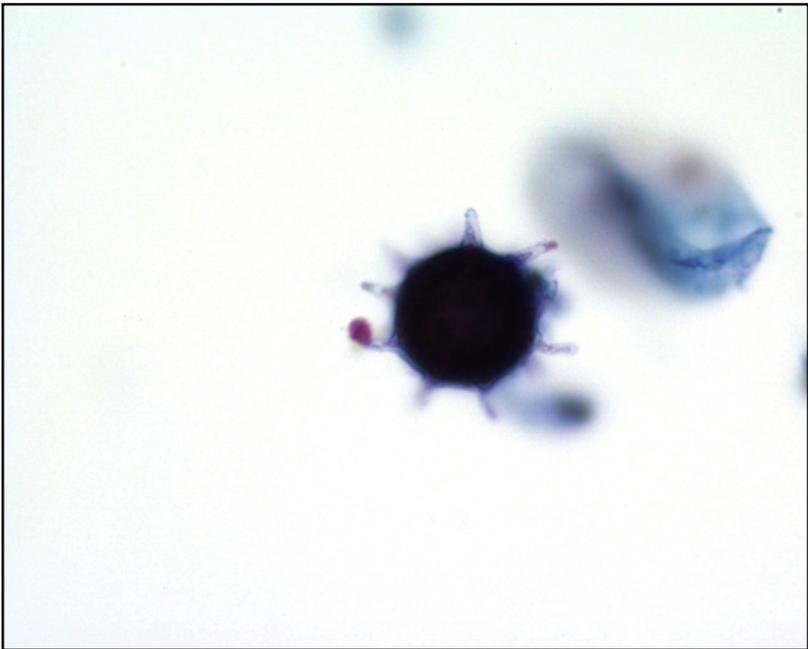
Specimen type: Cervical/Vaginal

Case provided by Kim Absher MD. and Ms. Helen Banks CT, (ASCP), University of Kentucky Chandler Medical Center, Lexington, Kentucky, with the discussion by Julie A. Ribes, M.D., Ph.D., Director of Clinical Microbiology at the University of Kentucky Medical Center.

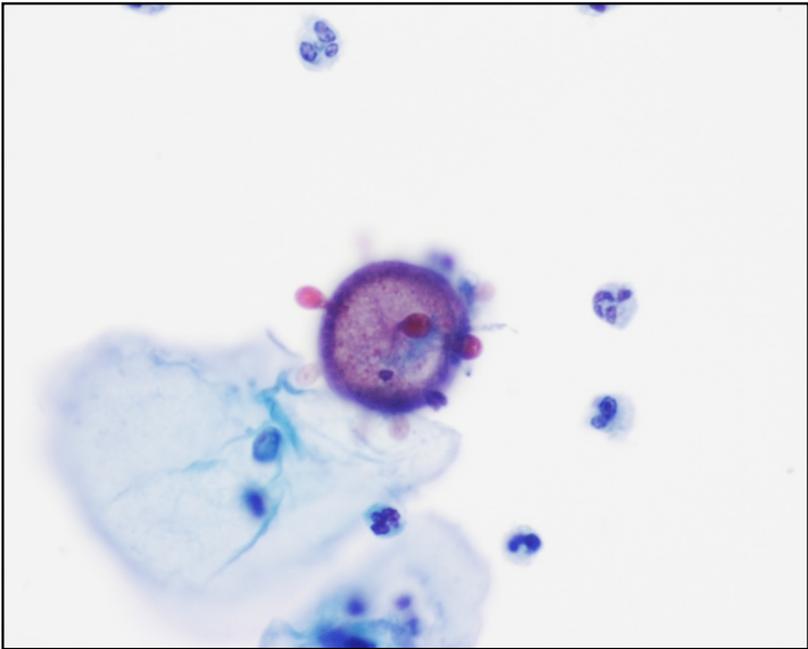
*The images, analysis and diagnosis for this case study were provided to Cytec by independent physicians. All conclusions and opinions are those of University of Kentucky Chandler Medical Center and not Cytec Corporation



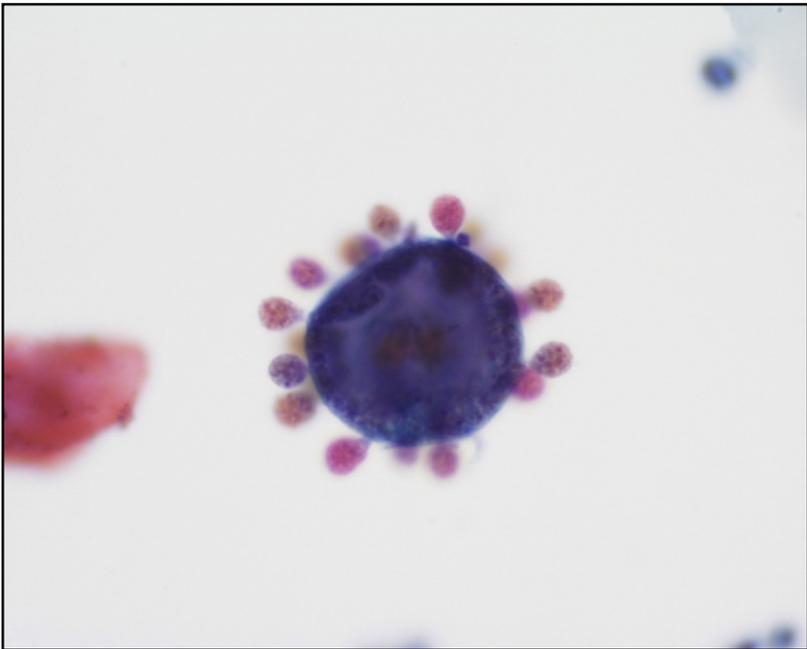
Slide 1 - 60x



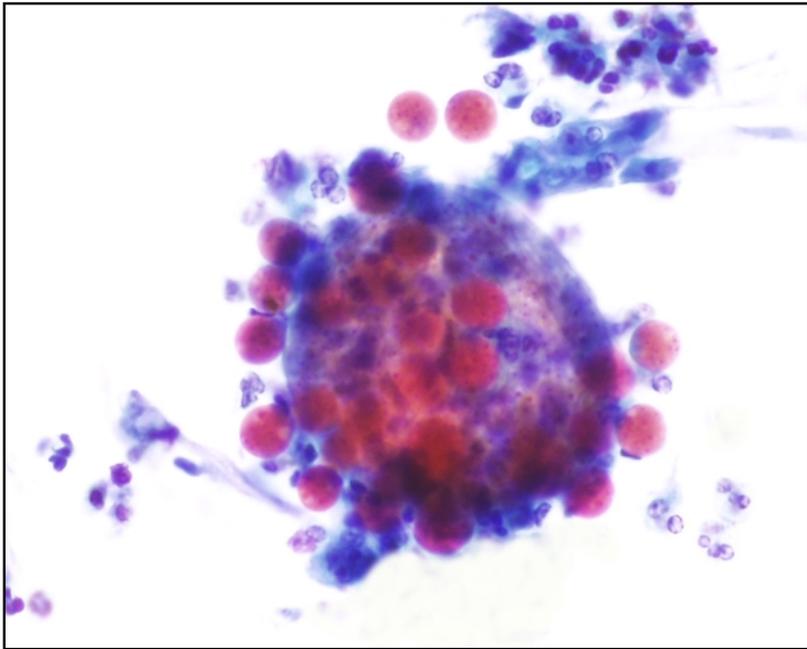
Slide 2 - 60x



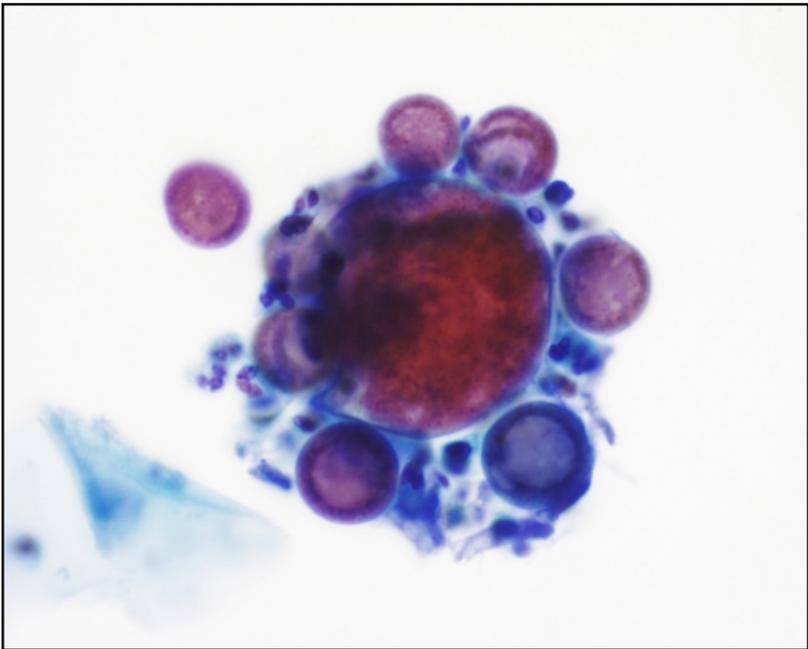
Slide 3 - 60x



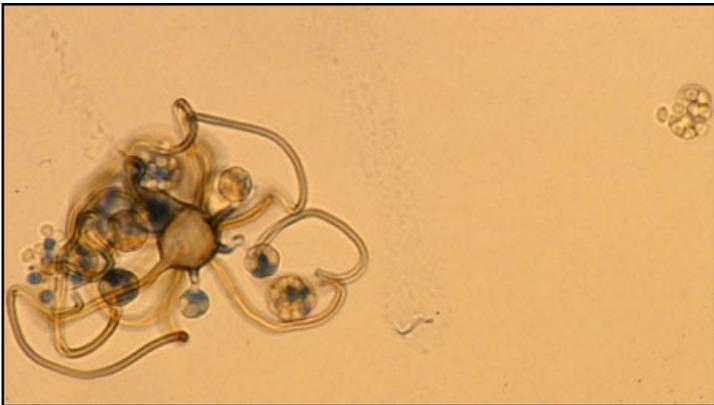
Slide 4 - 60x



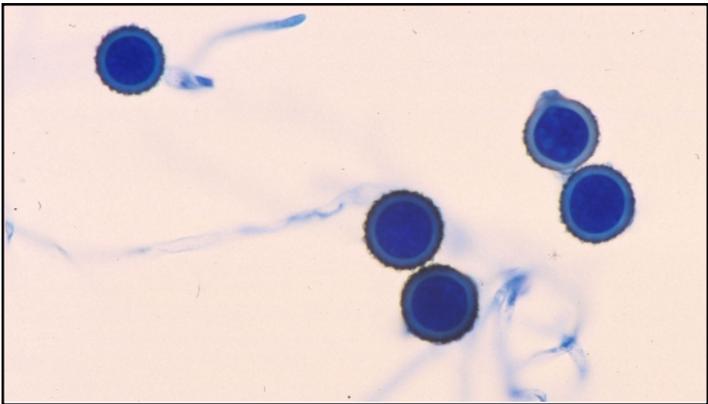
Slide 5 - 60x



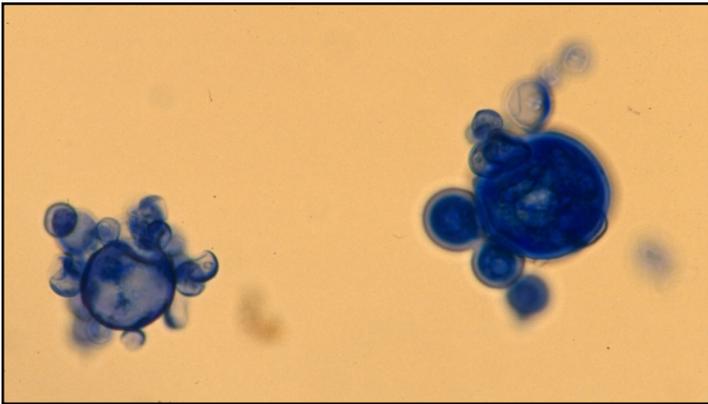
Slide 6 - 60x



Slide 7 - 60x



Slide 8 - 40x



Slide 9 - 40x

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Slide Description:

Slide 1: A spherical large yeast cell (blastoconidium) with thick walls.

Slide 2: Small buds are erupting from the surface of the large parent cell in a “mariner’s wheel” pattern.

Slide 3: The blastoconidia start to take on a bulbous appearance as they continue to grow.

Slide 4: The maturing blastoconidia bud from the parent cell in a corona formation.

Slide 5: The blastoconidia mature and cover the surface of the parent yeast cell.

Slide 6: The buds take on the appearance of the parent cell and start to separate bringing us back to picture 1. The parent cell has also matured in size compared to the squamous intermediate cell.

Slide 7: Culture morphology of the organism when grown at room temperature (filamentous fungal growth). Multicelled sporangiospores are produced asexually at the end of recurving stalks (sterigmata) surrounding a swollen vesicle. No hyphal elements are present in this particular preparation.

Slide 8: Sexual reproduction occurs within a single isolate by the formation of zygospores.

Slide 9: Culture of the organism when grown at 37°C (yeast phase growth). A large central yeast is surrounded by multiple smaller blastoconidia, similar to what was seen in this patient’s specimen.

Cytologic Diagnosis: Satisfactory but limited by sparse to no endocervical cells. Fungal organisms most consistent with *Cokeromyces recurvatus* or similar species present.

Immunostain: GMS stain is positive for numerous silver-staining fungal organisms.

Zygomycosis is a broad term referring to any infection caused by a member of the phylum Zygomycota, class Zygomycetes. The class is further divided into two orders: Mucorales and Entomophthorales. At last count, 665 species of Zygomycetes have been described, however, infection in humans and animals are rare. Approximately 24 species are pathogenic to humans, with the majority of human and animal pathogens falling into one of the six families within the order Mucorales.

Cokeromyces recurvatus poitras falls under the order of Mucorales and is usually found in soil or in rodent and lizard dung. It is a very uncommon isolate from human specimens. Human infections with the Zygomycetes generally occur in the setting of immune compromise. The typical patient with invasive zygomycosis is a diabetic or is a patient with immune compromise due to malignancy, chemotherapy or bone marrow or solid organ transplantation. Invasive rhinocerebral, pulmonary, and cutaneous/subcutaneous disease represent the vast majority of cases. The Zygomycetes tend to be angioinvasive so hematogenous dissemination from the primary site of infection often occurs. Only rarely are the Zygomycetes implicated in noninvasive diseases, such as colonization. In marked contrast to most of the other Zygomycetes, however, *C. recurvatus* has never been shown to produce invasive disease in humans. Instead, *C. recurvatus* appears to be exclusively a colonizer. Six cases of human *C. recurvatus* infection/colonization have been described in the literature. This organism has been isolated from vaginal, cervical, gastrointestinal, and urinary sediment specimens. *C. recurvatus* has been demonstrated in diagnostic specimens only in its yeast form with the notable absence of tissue invasion seen in these cases. These observations suggest this organism’s role as a colonizer rather than an opportunist or an invasive Zygomycete.

Another unique feature of *C. recurvatus* is its dimorphic growth characteristic. Although most of the Zygomycetes grow as filamentous molds in soil, in culture, and in tissue, *C. recurvatus* is one of the few Zygomycetes that has temperature-

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dependent yeast and filamentous mold growth phases. In the human host and in laboratory growth conditions at 37°C, *C. recurvatus* grows in a yeast form, producing a large central parent yeast cell surrounded by smaller budding yeasts in a “mariner’s wheel” pattern (see slides 1-6 and slide 9). In the environment and in culture at temperatures at or below room temperature, however, this organisms grows as a filamentous mold. In this filamentous form, *C. recurvatus* reproduces both sexually and asexually. From the typical wide, ribbon-like vegetative mycelium of the zygomycetes, sporangiohores are produced that terminate in swollen vesicles. Sterigmata grow out from the vesicle and recurve, ending in multicelled sporangiospores (Slide 7). This represents the asexual reproductive phase of the filamentous growth. In addition, sexual reproduction occurs when neighboring mycelial elements combine their genetic materials to form a diploid zygospore (slide 8).

References:

- 1) Kemna, ME et al. *Cokeromyces recurvatus*, a Mucoraceous Zygomycete Rarely Isolated in Clinical Laboratories. *Journal of Clinical Microbiology*. 1994;32:843-845.
- 2) McGough, DA et al. *Cokeromyces recurvatus* poitras, a distinctive zygomycete and potential pathogen: criteria for identification. *Clinical Microbiology Newsletter*. 1990;12:113-117.
- 3) Rippon, JW, and CT Dolan. Colonization of the vagina by fungi of the genus *Mucor*. *Clinical Microbiology Newsletter*. 1979;1:4-5.
- 4) Ribes, JA et al. Zygomycetes in human disease. *Clinical Microbiology Reviews*. 2000;13:236-301