# Respiratory cytology case study

Clinical and cytopathological correlation

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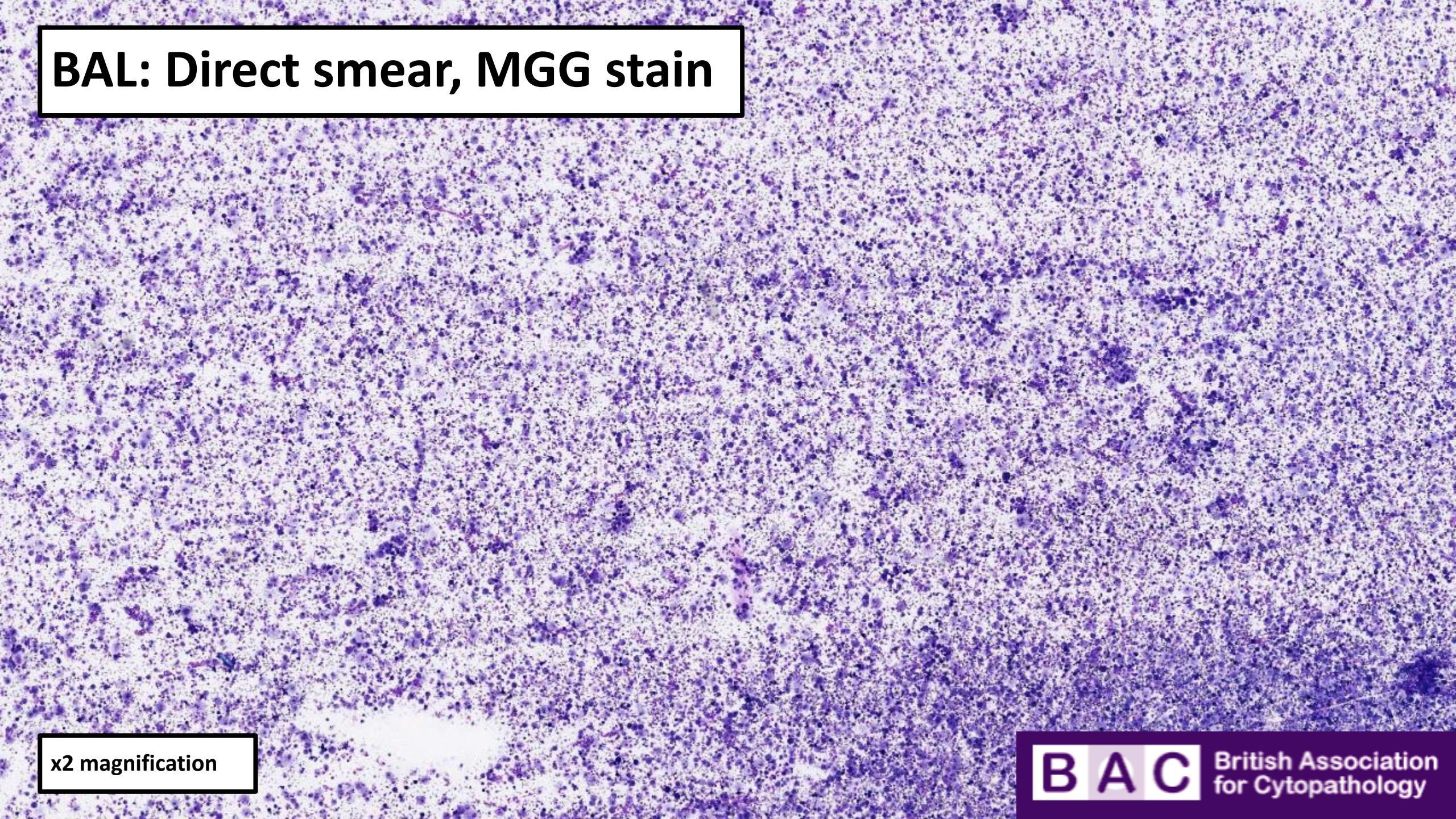
# Case study

- 59F.
- PMH: Renal transplantation in the last 6 months, CMV, EBV, BK virus positive.
- Persistent non-productive cough and recurrent RML infection with no improvement with antibiotics and no underlying clear cause.
- Patient underwent many investigations including bronchoalveolar lavage (BAL) for cytology.

# BAL: Direct smear, MGG stain



x2 magnification

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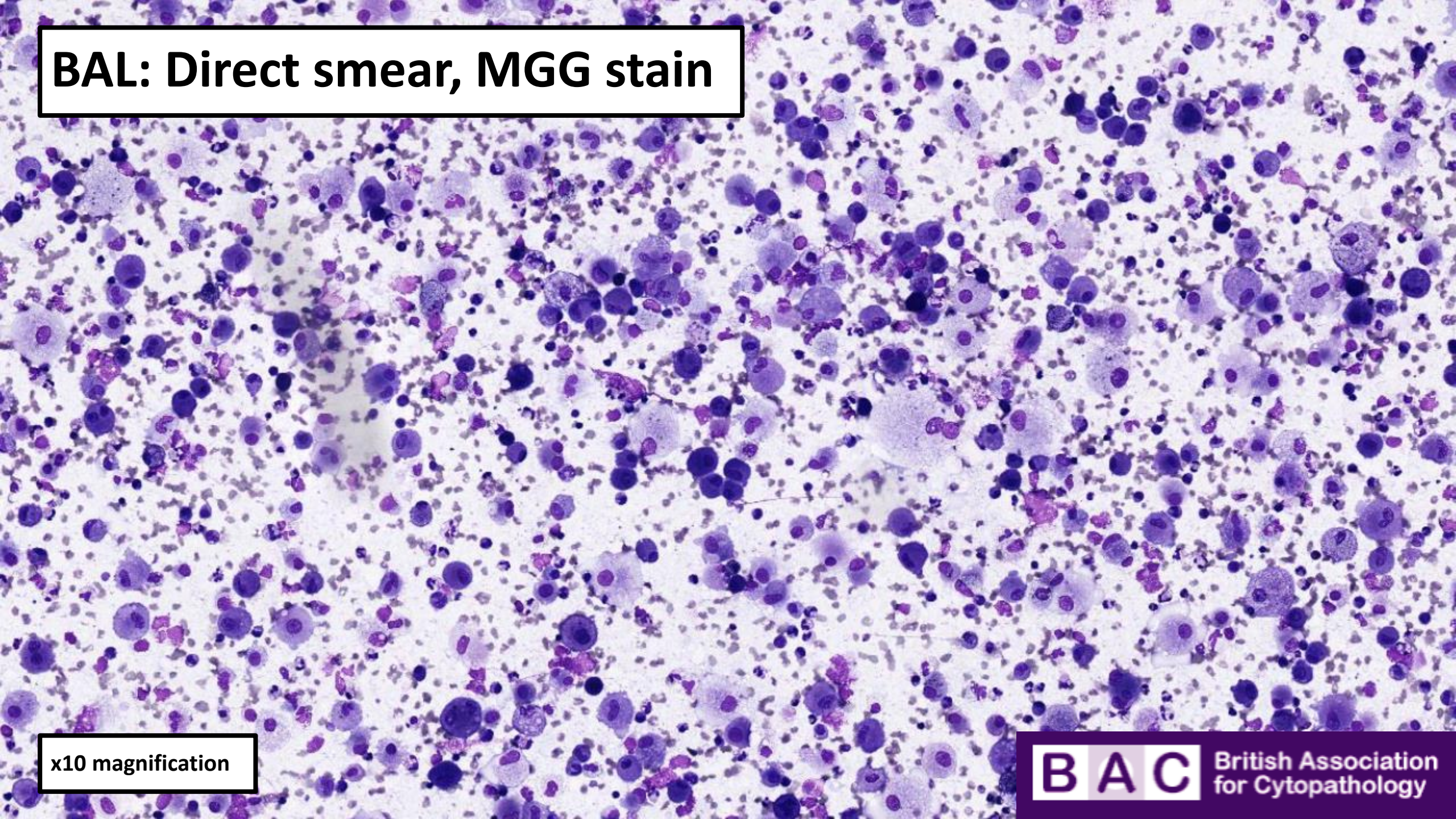
# BAL: Direct smear, MGG stain



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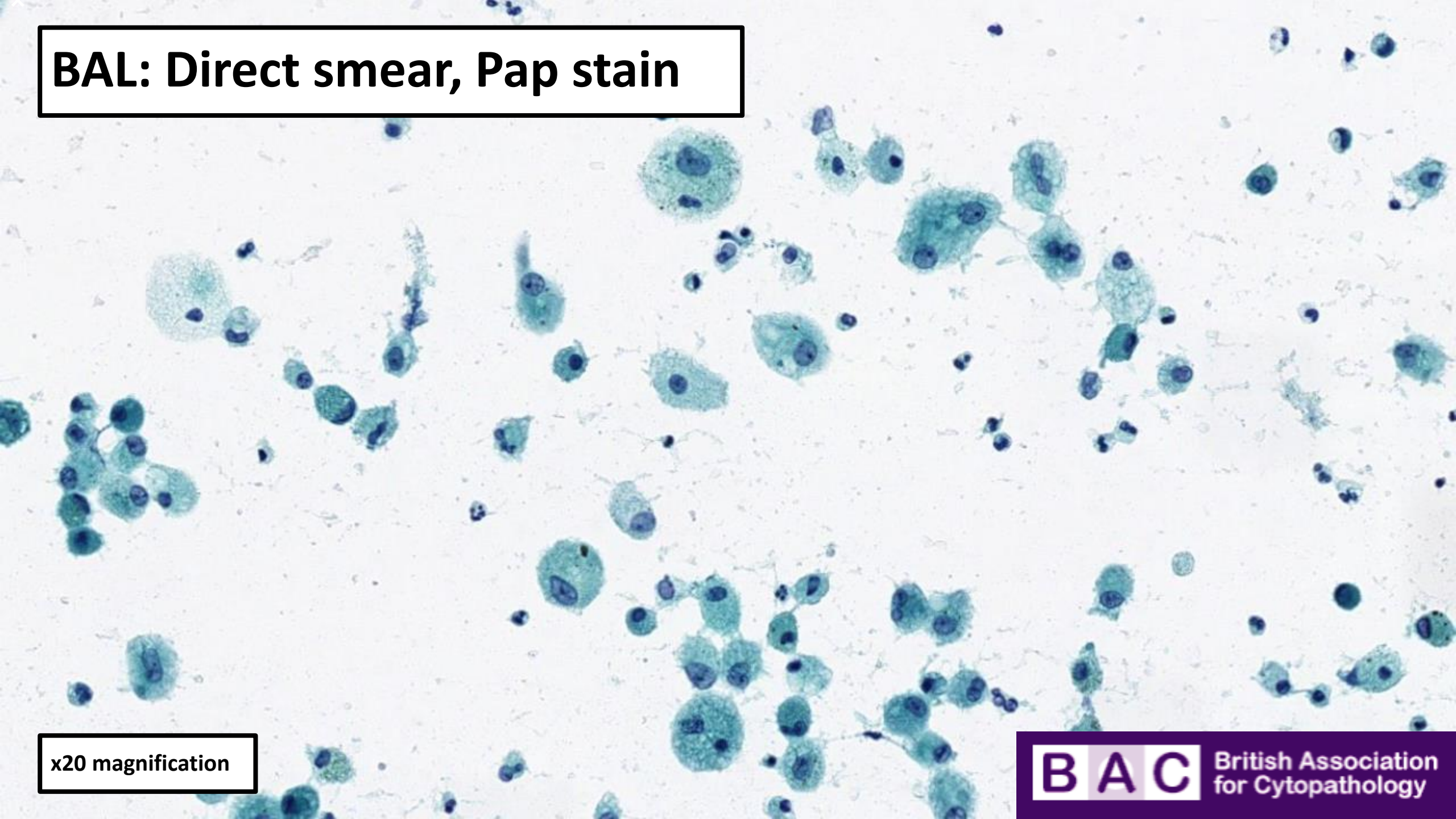
# BAL: Direct smear, Pap stain



x20 magnification

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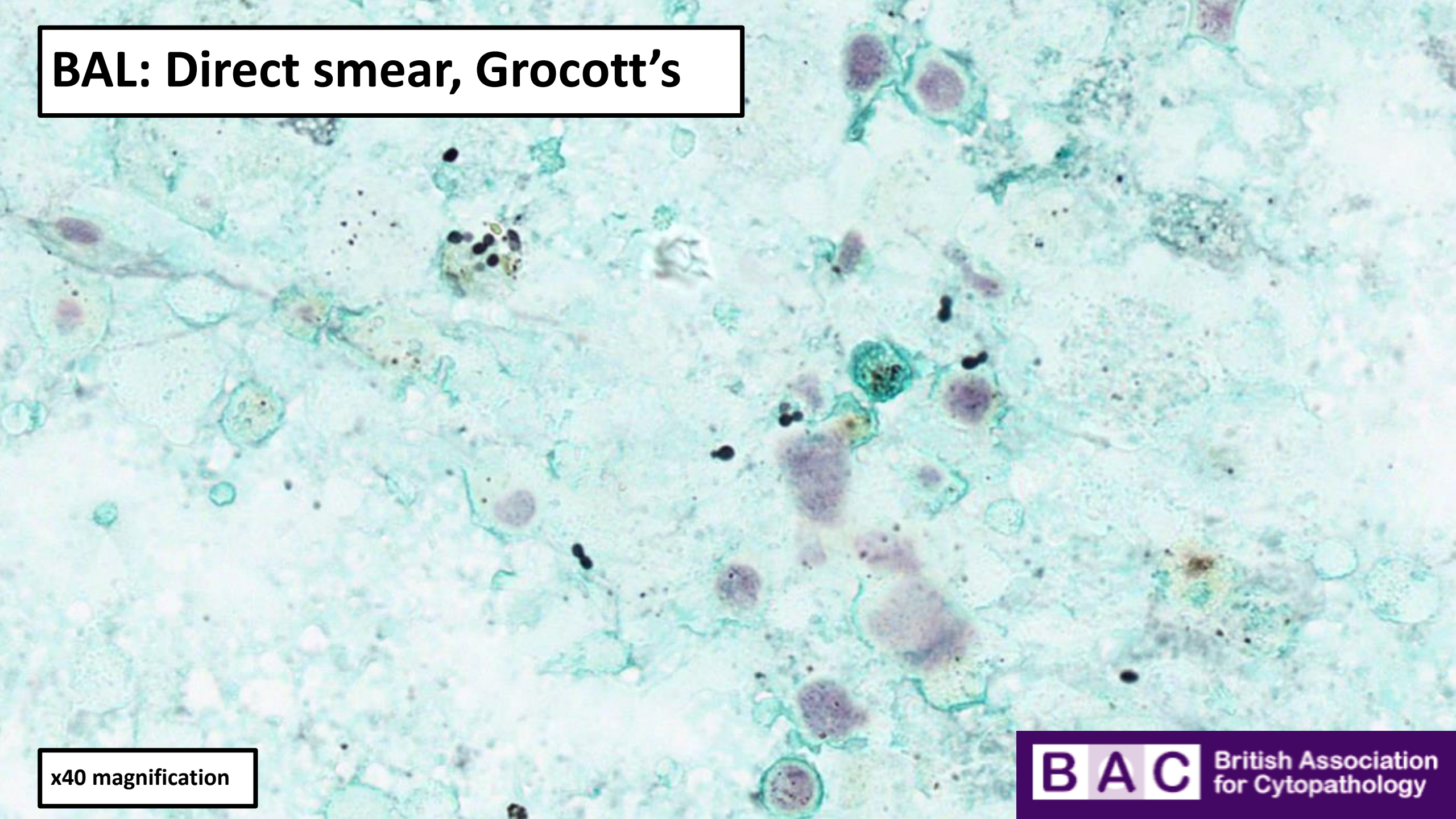
# Cytological findings of BAL

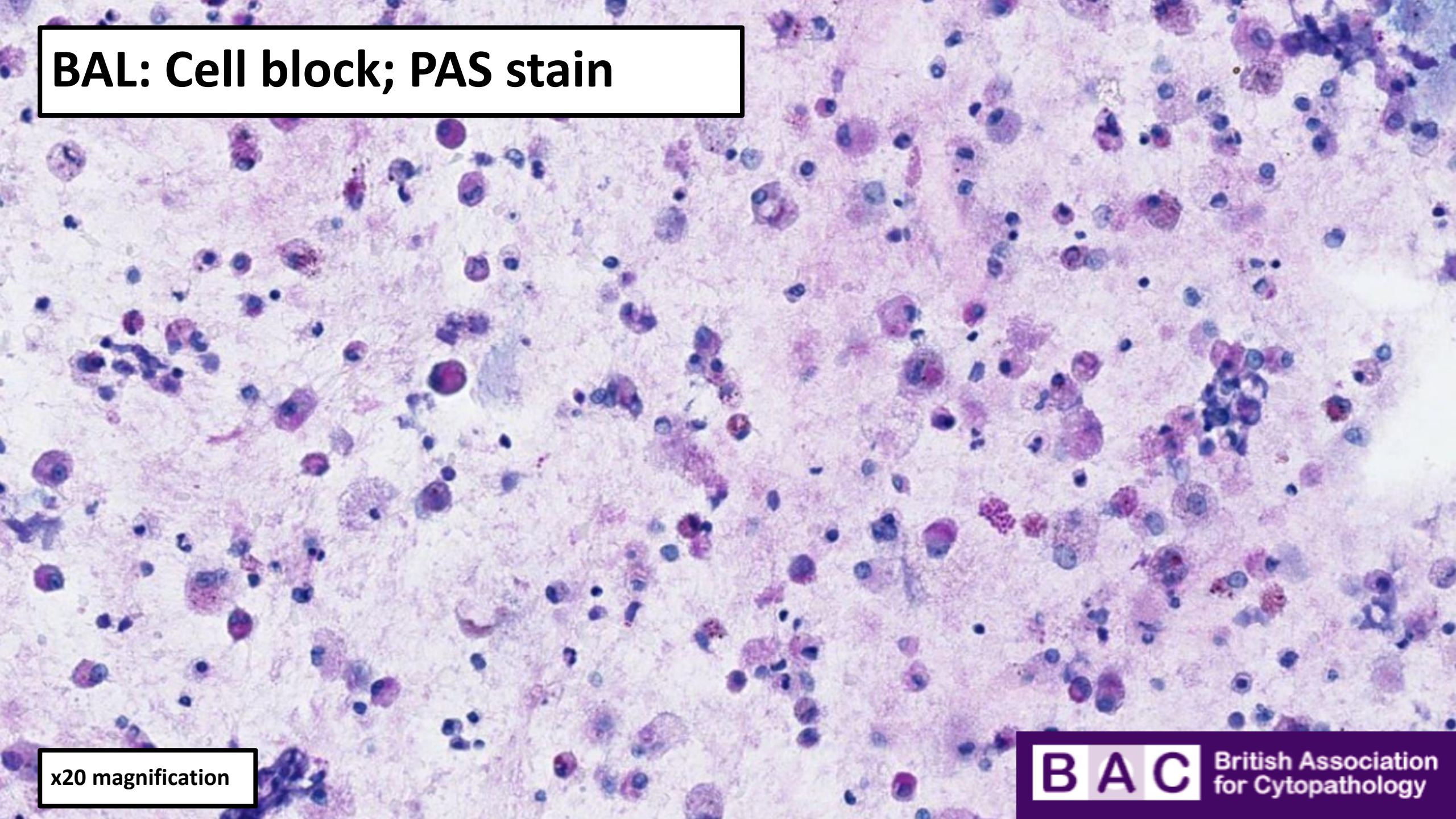
- Cellular sample with predominantly macrophages and some neutrophils.
- Some of the macrophages, the cytoplasm appear to have the impression of ovoid or rounded holes.
- Special stains were performed including Grocott's and PAS stains.

# BAL: Direct smear, Grocott's



x40 magnification

# BAL: Cell block; PAS stain



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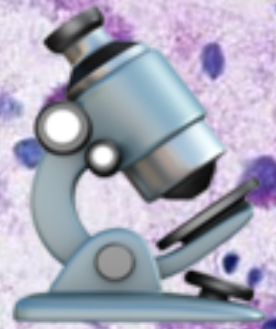
# Diagnosis?



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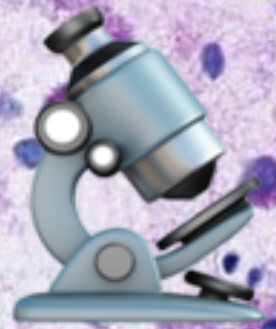
# *Histoplasmosis capsulatum*



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# Management

- Findings were discussed with the Microbiology team, unexpected diagnosis and subsequently, the patient started on treatment and improved clinically.
- Microbiology performed further tests for urine antigen and serology (sent to the US!), as well as PCR undertaken on BAL sample to a specialist reference lab - results took a few weeks until confirmed positive.
- This chronic pulmonary infection was thought to be reactivation from previous exposure many years ago, the patient is originally from West Africa.
- After starting treatment, the patient states, it is the best she has felt in ages.

# Discussion: *Histoplasmosis* [1, 2]

- Endemic in North and Central America, and Africa.
- *Histoplasmosis capsulatum* is a dimorphic saprophytic fungus which resides in soil as a mould, usually containing bird and/or bats droppings.
- The microconidia (non-pathogenic form) can be inhaled into the respiratory tract and due to the changes in the environment e.g., temperature, they make a dimorphic transition into yeast (pathogenic form).
- The yeast have adapted ways to evade the immune system and therefore are able to survive intracellularly within macrophages after phagocytosis.

# Discussion: Infection and risk factors [1, 2]

- Majority of infection is asymptomatic, restricted to the lung and self-limiting, particularly in the immunocompetent patient.
- Symptomatic disease mostly affects the respiratory tract and can manifest as acute pulmonary infection, disseminated disease and least commonly chronic pulmonary infection. It is able to reactivate.
- Immunocompromised patients with HIV/AIDS, solid organ transplant, haematological malignancy, high-dose corticosteroid have a 10 – 15 increased risk of dissemination and is fatal.

# Discussion [1-2]

The gold standard diagnosis is culture of specimens:

- Antigen and serology testing are the most sensitive methods but can take time and requires sending to specialist laboratories many of which more common in endemic countries such as the US.

- Similarly, other fungal cultures can take 2 - 3 weeks or more, thereby, cytology provides rapid diagnosis and presence of yeast is considered diagnostic

# Discussion [1-3]

- Sensitivity is related to burden of infection; it is increased in BAL fluid in immunocompromised patients and chronic infection, and reduced in acute and subacute infection.

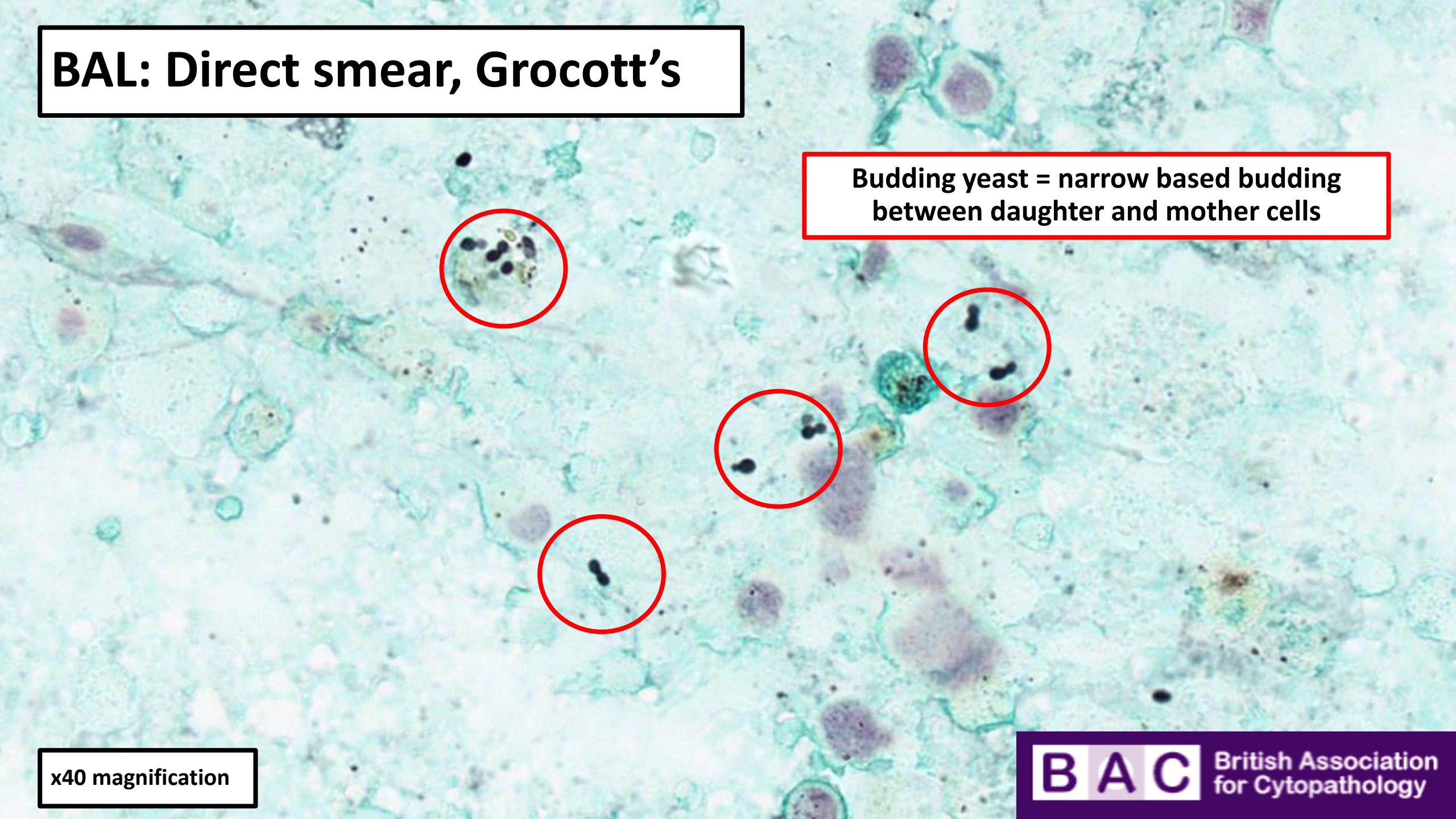
- Therefore, in acute pulmonary histoplasmosis, BAL cytology combined with antigen testing, sensitivity increases to 97% (BAL alone the sensitivity is 48%) is helpful.

- Discussion with the microbiology team is essential for further patient management.

# Cytological features: Pulmonary Histoplasmosis [5-6]

- Ovoid budding yeasts measuring 2 – 5 microns, can be visible on Romanowsky stains but best seen with Grocott-Gormori's Methenamine Silver and PAS stains.
- Predominantly present intracellularly in macrophages but can be extracellular.
- Can have a 'pseudocapsule' or artefactual clearing around the yeast which are negative on staining with mucin stains.
- BALs show predominantly macrophages but can show an increase of neutrophils (2 - 30% cellularity), then lymphocytes (up to 18% of cellularity). Plasma cells and eosinophils are usually present occasionally.
- An increased number and clustering of yeast have been found most likely to occur in patients with HIV compared to the immunocompetent, as well as being inversely proportional to CD4 counts.

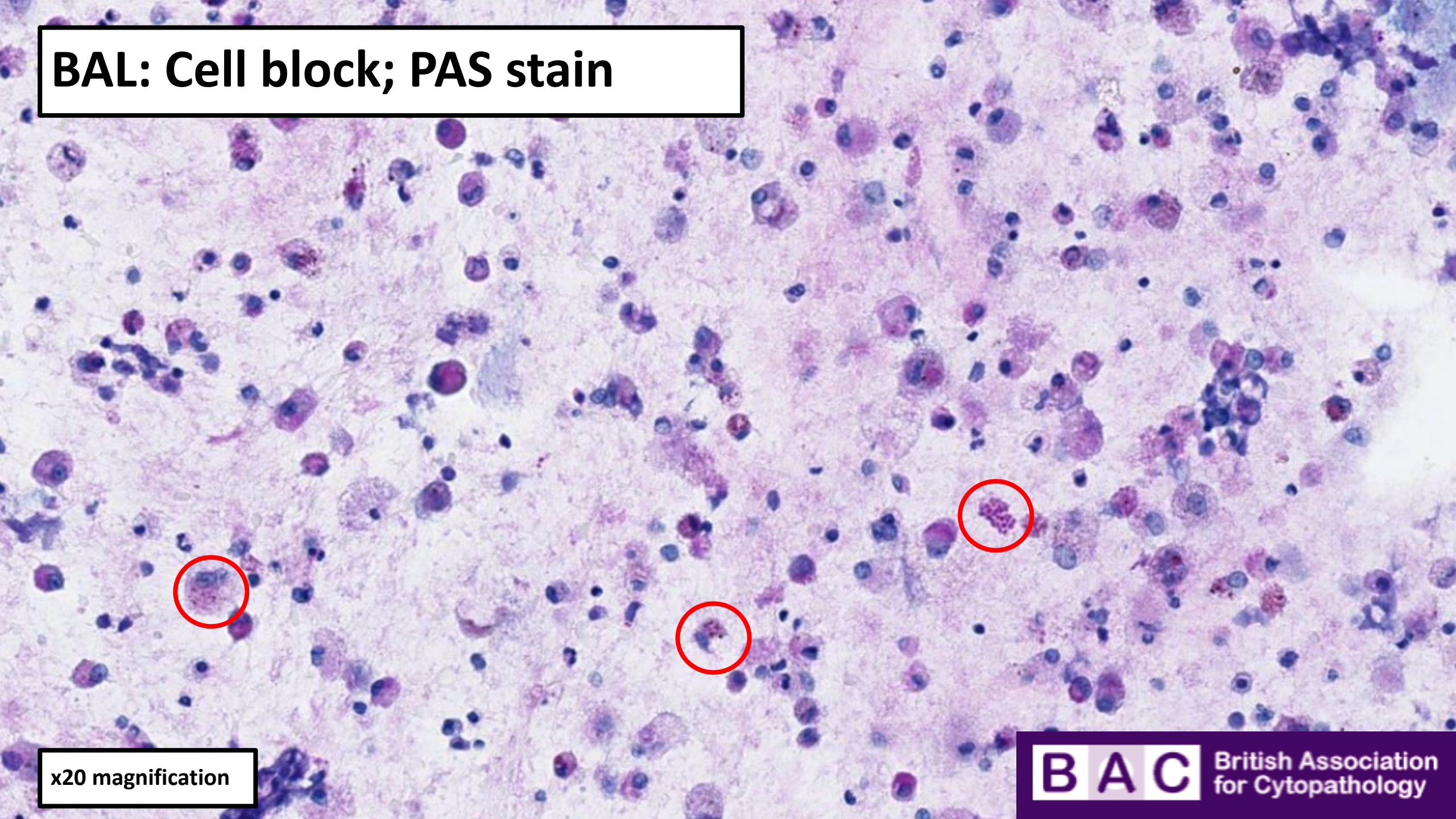
# BAL: Direct smear, Grocott's



Budding yeast = narrow based budding between daughter and mother cells

x40 magnification

# BAL: Cell block; PAS stain



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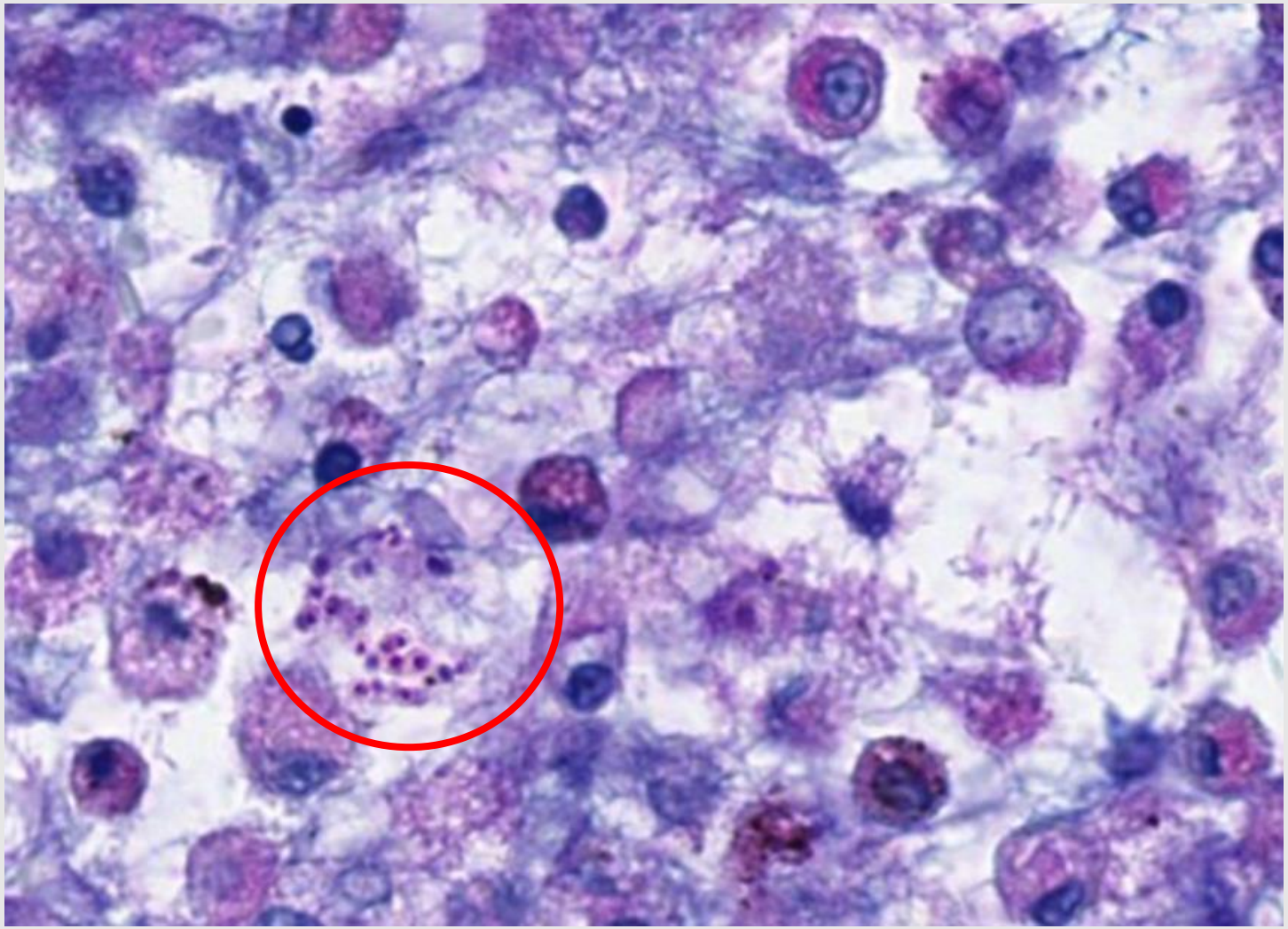
# PAS stain on cell block



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# Cytological features: Pulmonary Histoplasmosis [5-6]

- Always look for other organisms as co-infection in the immunosuppressed can occur i.e. Mycobacteria

- Differential diagnosis of other organisms:
  - Cryptococcus: 5 – 10 microns, teardrop-shaped bud and mucopolysaccharide capsule (mucicarmine positive)
  - Blastomycosis: 7 – 20 microns
  - Coccidiodes: 20 – 100 microns

# Conclusion: Pulmonary Histoplasmosis

- Can be a difficult and overlooked, especially as it is rare in the UK, therefore, time should be taken to look for any organisms in BALs especially in the immunocompromised.

- Discussion and collaboration with the microbiology team is essential; detection of yeast on cytology is rapid in comparison to gold standard culture methods which can take weeks.

- Always assess for co-infection with other organisms such as Mycobacterial infection.

# References


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