COVID-19 und Pilzinfektionen Diagnostik

Giftiger Live-Stream
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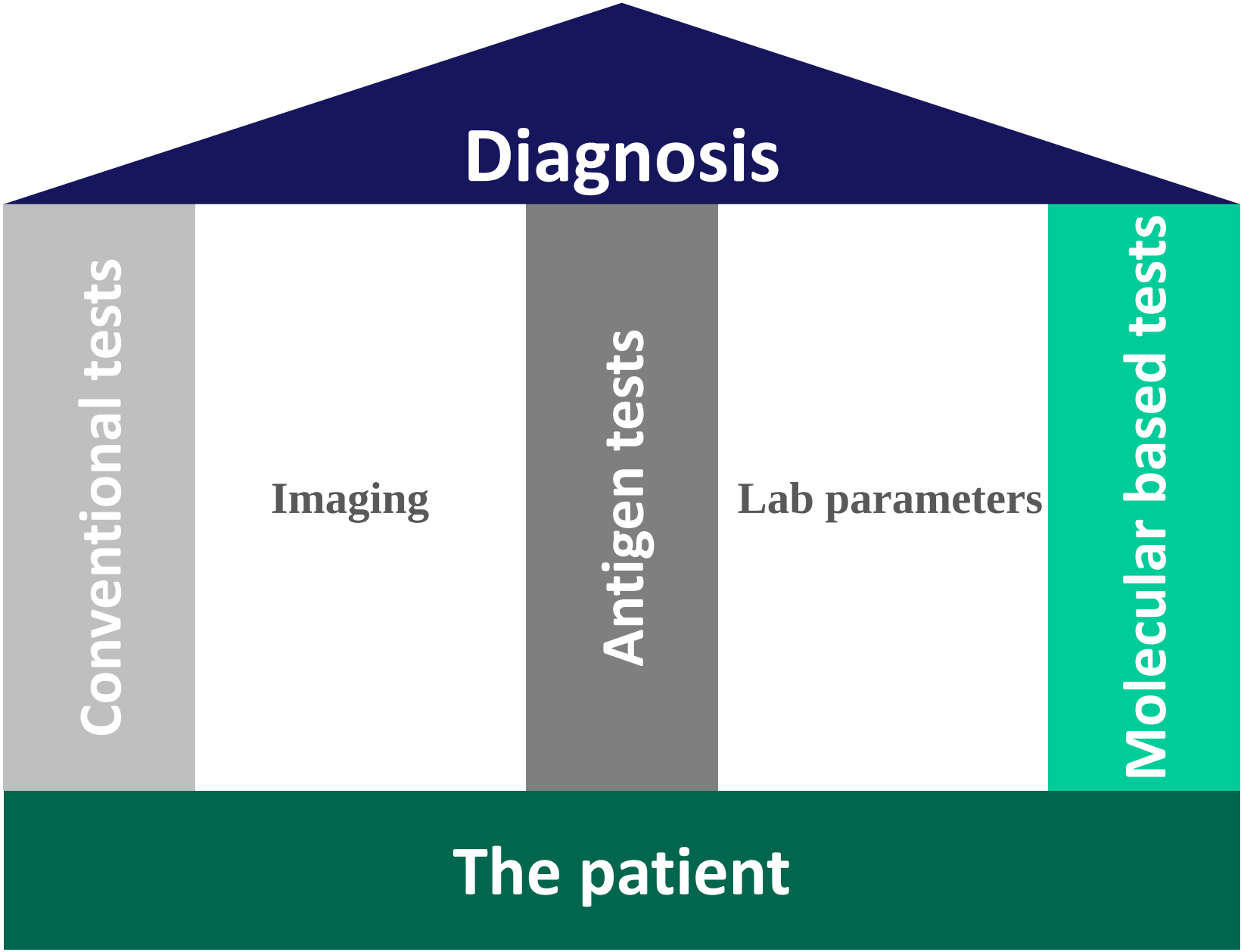
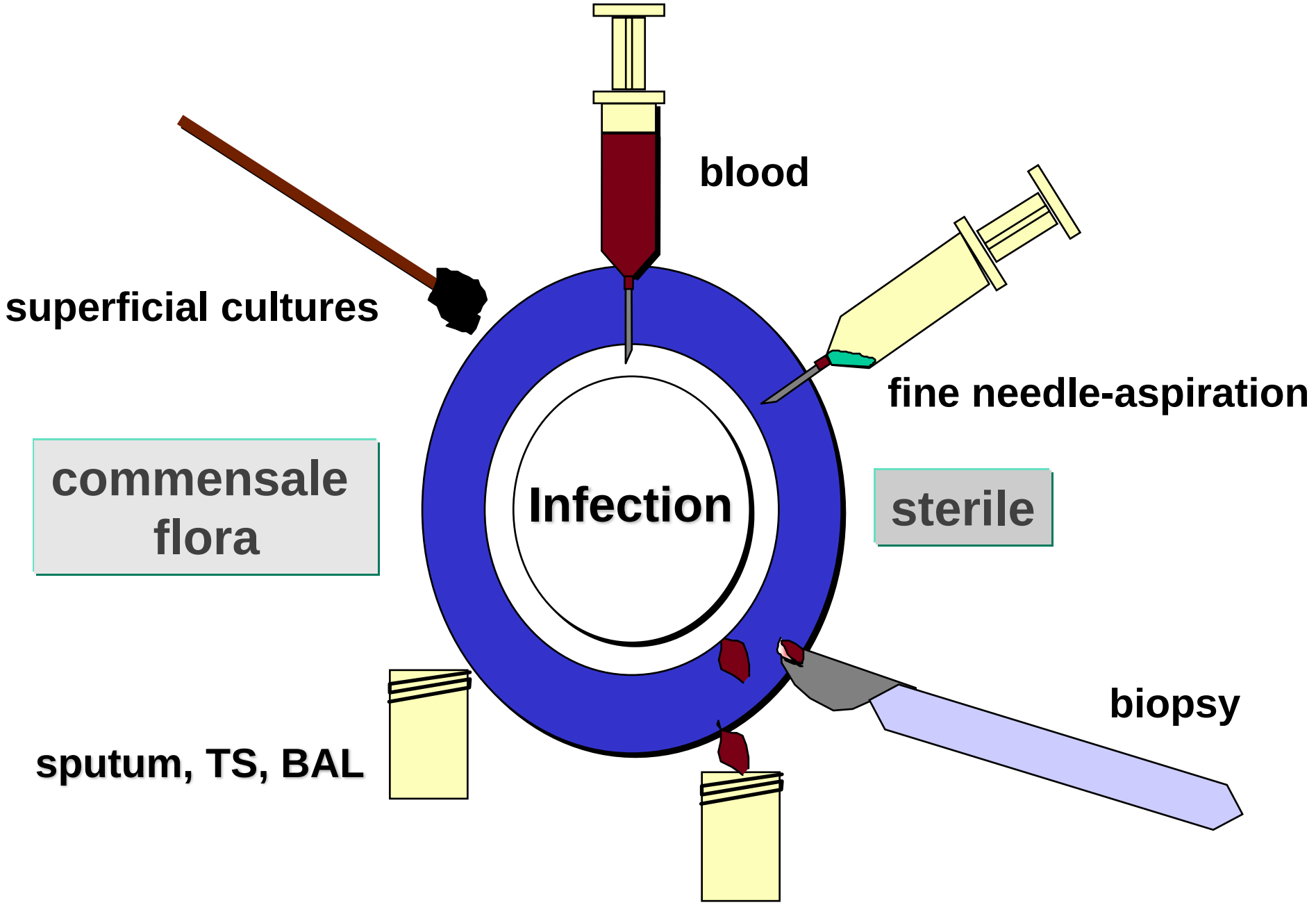
CAPA

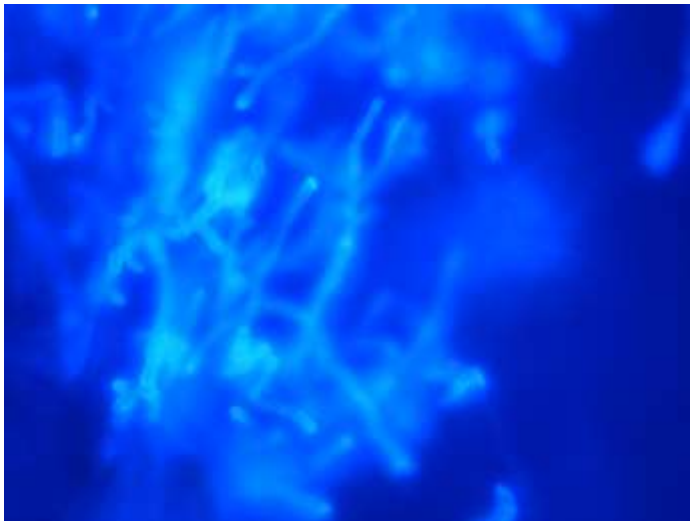
Covid-associated pulmonary aspergillosis



The human specimen



- Microscopy is a must have for primarily sterile specimens



- Culture

➢ **Differentaition betweeen colonisation and infection!**

- Microscopy is a must have for primarily sterile specimens

- Culture is a must have

- Antigen tests:

GM EIA

IMMY

Lateral Flow Device
- ✓ CE-marked
- ✓ Extracellular mannoprotein
- ✓ JF5 monoclonal antibody
- ✓ Serum
- ✓ BAL

Lateral Flow Assay
- ✓ CE-marked
- ✓ Galactomannan
- ✓ With reader
- ✓ Serum
- ✓ BAL

- Imaging

- Interventions

Pros and Cons of diagnostic procedures in COVID-19

Diagnostic procedure	Pros	Cons	Comments related to CAPA
Lung biopsy	Provides proof of IPA	Risk of sampling error Scarcely used due to high risk of complications	CT-guided post-mortem biopsies have been used as alternative to autopsy
Bronchoscopy with BAL	Allows visualization of lesions (plaques) BAL well validated for the diagnosis of IPA/IAPA Validated specimen for Aspergillus Ag (EIA and LFA), and PCR Targeted sampling possible	Aerosol generation and contamination of surfaces	Use is restricted because of risk of nosocomial transmission and SARS-CoV-2 infection of HCWs
Non-bronchoscopic lavage	Obtains material from lower respiratory tract Technique validated for VAP diagnosis Closed system sampling	Not fully validated for IPA diagnosis Not fully validated for *Aspergillus* Ag and PCR detection Non-targeted sampling	Has been suggested as alternative for BAL to diagnose CAPA Limited number of validation studies
Tracheal aspirate	Easy to obtain in intubated patients	Less representative for lower respiratory tract Not validated for biomarker detection	Often positive in critically-ill COVID-19, but may represent upper airway colonization

Ag, antigen; BAL, bronchoalveolar lavage; CT, computed tomography; EIA, enzyme immunoassay; HCW, health care worker, IAPA, influenza-associated pulmonary aspergillosis; IPA, invasive pulmonary aspergillosis; LFA, lateral flow assay; PCR, polymerase chain reaction; VAP, ventilator associated pneumonia

Koehler et al, submitted

Pros and Cons of diagnostic procedures in COVID-19

Diagnostic procedure	Pros	Cons	Comments related to CAPA
Sputum	Easy to obtain in most patients	Less representative for lower respiratory tract Not validated for biomarker detection	Often positive in critically-ill COVID-19, but may represent upper airway colonization
Serum	Highly indicative for IPA (GM, LFA and PCR) Validated specimen for GM, LFA BDG and PCR Easy to obtain	Variable performance in non-neutropenic patients BDG not pathogen specific for Aspergillus	Commonly negative in CAPA, including proven cases

BAL, bronchoalveolar lavage; BDG, beta-D-glucan; GM, galactomannan; LFA, lateral flow assay; PCR, polymerase chain reaction;

Koehler et al, submitted

SARS-CoV-2: ICU and acute respiratory distress syndrome

COVID- associated pulmonary aspergillosis (CAPA)

Proposed CAPA case definition	Host	Bronchoscopy	Mycology findings
Tracheobronchitis or other pulmonary form (proven) Adapted from EORTC/MSGERC, AspICU, IAPA expert case definition	COVID-19 positive patient needing intensive care + temporal relationship	Tracheobronchial ulcerations **OR** Nodules **OR** Pseudomembranes **OR** Plaques **OR** Eschar	Histopathologic or direct microscopic detection of fungal hyphae showing invasive growth with associated tissue damage **Or** *Aspergillus* recovered by culture or microscopy/histology or PCR obtained by a sterile aspiration or biopsy from a pulmonary site showing an infectious disease
Tracheobronchitis (probable)	COVID-19 positive patient needing intensive care + temporal relationship		And at least one of the following: Serum GM index >0.5 or Serum LFA index >0.5* **OR** BAL GM index ≥1.0 or BAL LFA index ≥1.0* **OR** Positive BAL culture or PCR**

BAL, bronchoalveolar lavate; CT, computed tomography; EIA, enzyme immunoassay; GM, galactomannan; LFA, lateral flow assay; PCR, polymerase chain reaction;

* visual reader must be used, to be used as primary result, while confirmatory GM testing must be sought
** in case of COPD/chronic respiratory disease patients the PCR/culture results should be confirmed by GM testing to rule out colonization/chronic aspergillosis.

Koehler et al, submitted

SARS-CoV-2: ICU and acute respiratory distress syndrome

Proposed CAPA case definition	Clinical factors	Imaging	Mycology findings
Pulmonary forms (probable)	Refractory fever **OR** Pleural rub **OR** Chest pain **OR** Haemoptysis	Pulmonary infiltrate, preferably documented by chest CT **OR** cavitating infiltrate (not attributed to another cause)	And at least one of the following: Serum GM index >0.5 or Serum LFA index >0.5* **OR** BAL GM index ≥1.0 or BAL LFA index ≥1.0* **OR** Positive BAL/NBL culture** **OR** Multiple (≥2) positive *Aspergillus* PCR in plasma, serum, or whole blood** **OR** A single positive *Aspergillus* PCR in BAL fluid (<36 cycles)** **OR** A single positive *Aspergillus* PCR in plasma, serum, or whole blood and a single positive in BAL fluid (any Ct permitted)**
Pulmonary forms (possible)⁺	Refractory fever **OR** Pleural rub **OR** Chest pain **OR** Haemoptysis	Pulmonary infiltrate, preferably documented by chest CT **OR** cavitating infiltrate (not attributed to another cause)	And at least one of the following: Single NBL GM-index >4.5 **OR** ≥2x NBL GM-index >1.2 **OR** NBL GM-index >1.2 plus another NBL mycology test positive (NBL PCR, LFA)

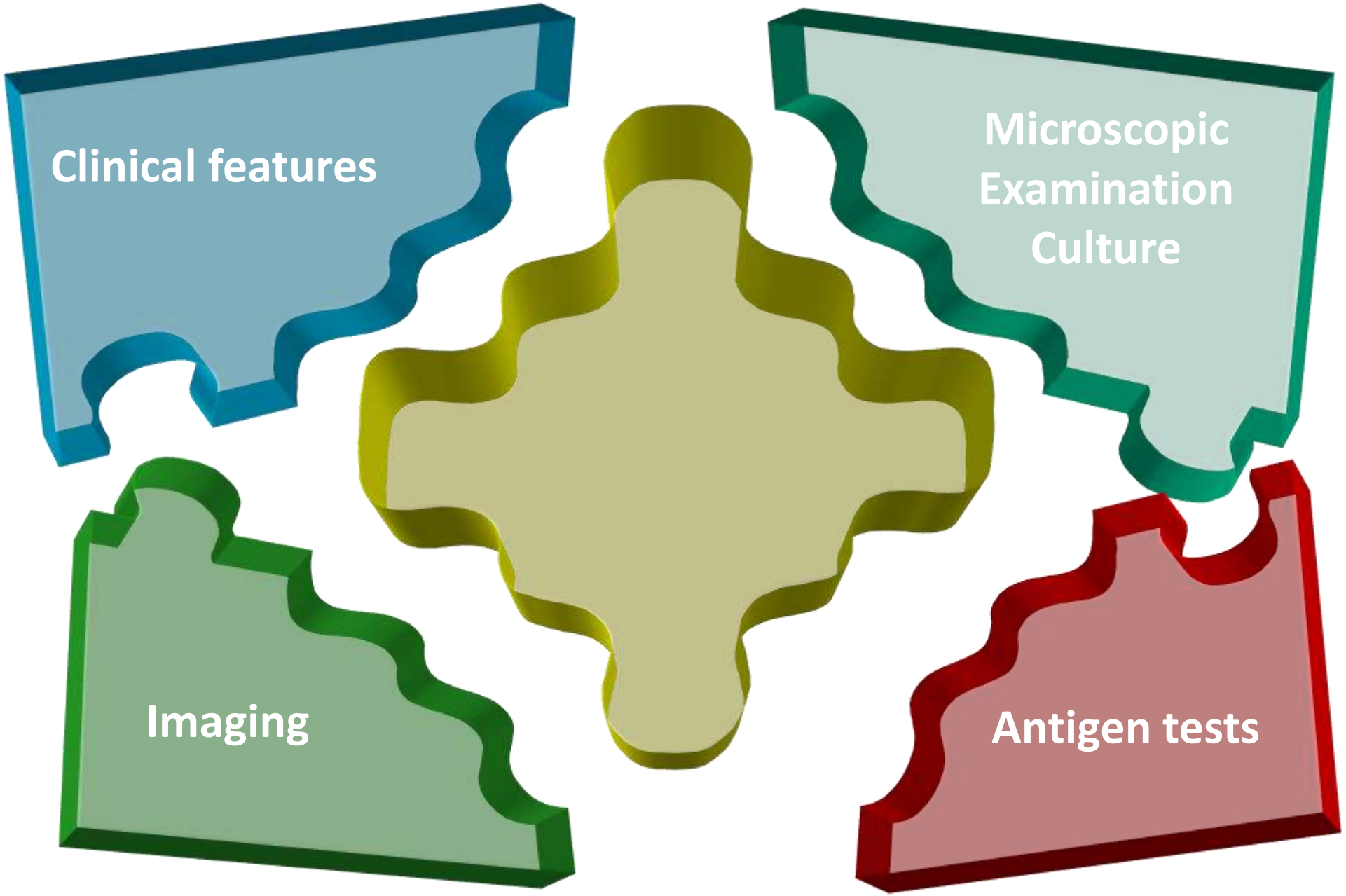
BAL, bronchoalveolar lavate; CT, computed tomography; EIA, enzyme immunoassay; GM, galactomannan; LFA, lateral flow assay; PCR, polymerase chain reaction; NBL, non-bronchoscopic lavage (considered a blind application of 10-20 ml saline recovered by aspiration via the closed suction system in an intubated patient)

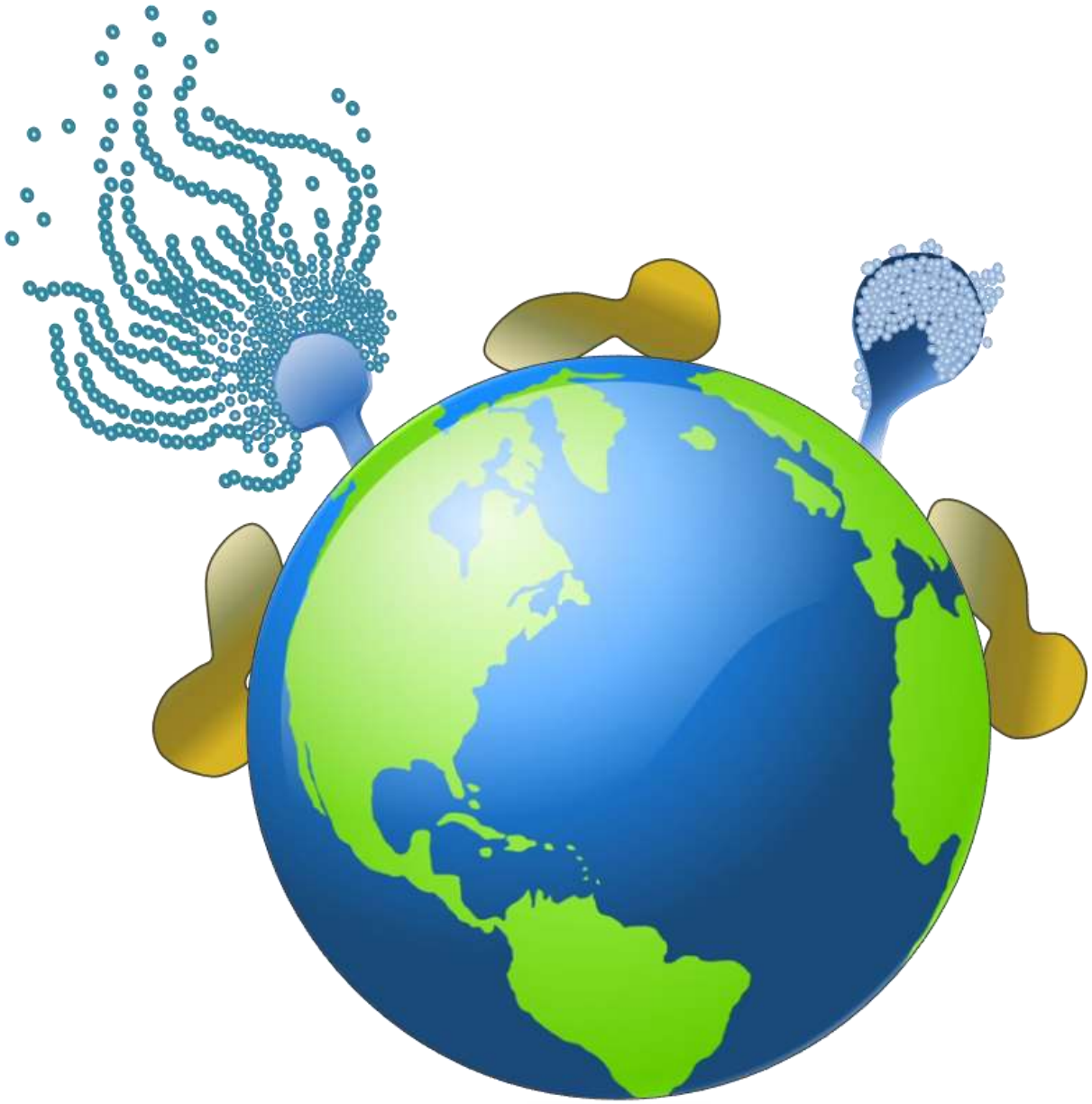
* visual reader must be used, to be used as primary result, while confirmatory GM testing must be sought
** in case of COPD/chronic respiratory disease patients the PCR/culture results should be confirmed by GM testing to rule out colonization/chronic aspergillosis

BAL and NBL are currently not considered equal for diagnosing CAPA

Koehler et al, submitted

„Puzzle diagnosis“





Thank you for your attention!