SMART DIAGNOS

Rapid detection of Sepsis

Intraabdominal candidosis – Myth or Fact?

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Roma, 20.-22.10.2016

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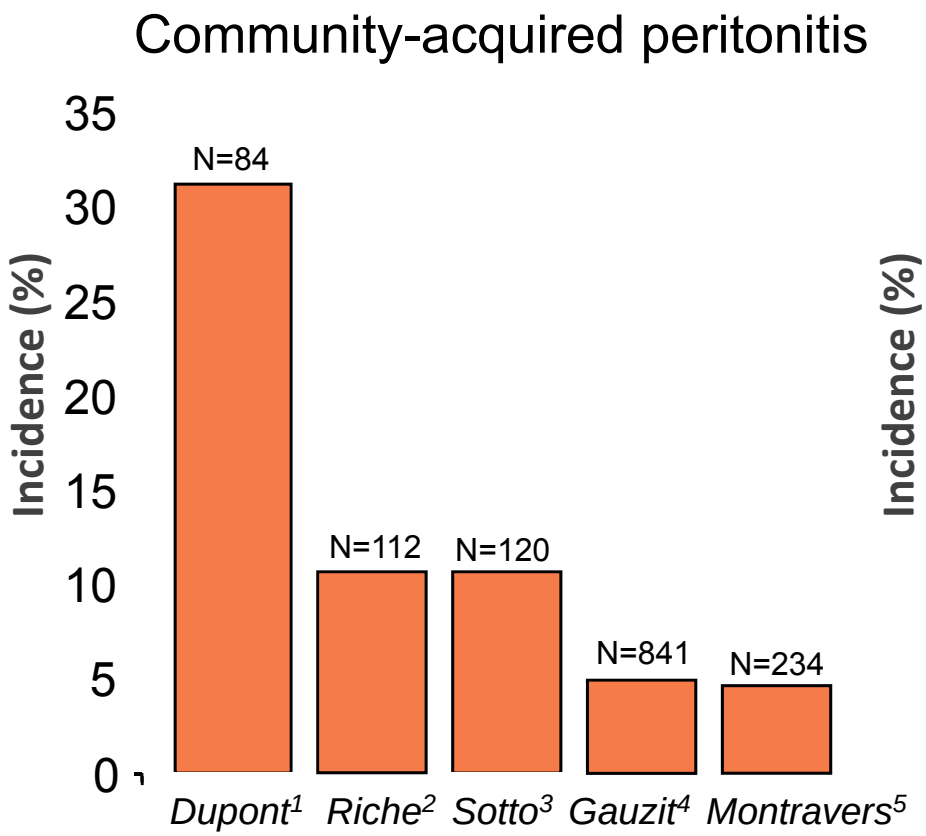
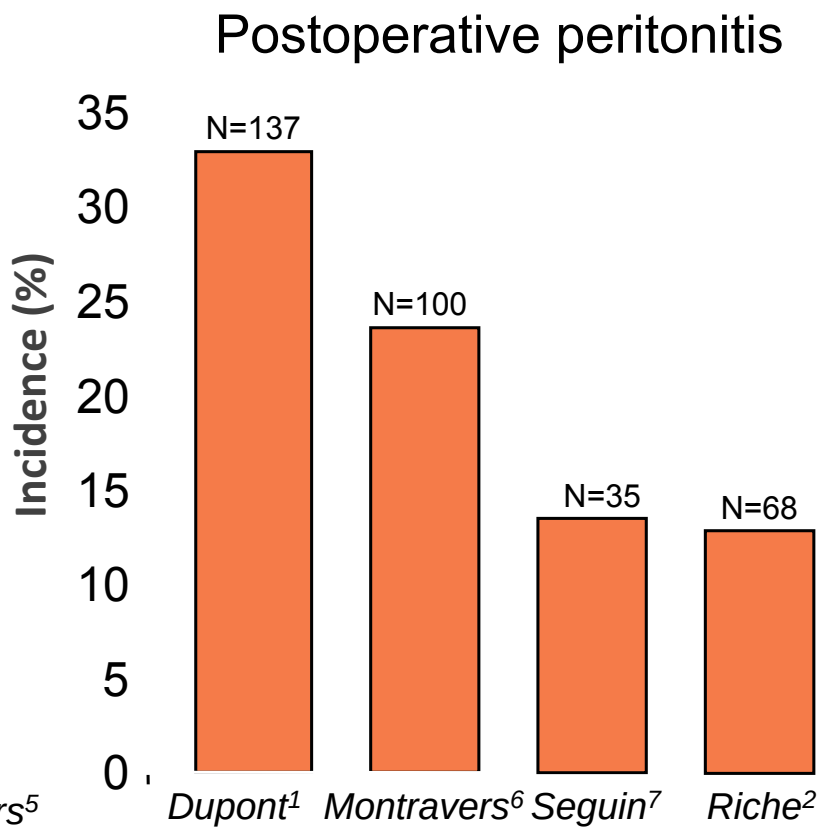
Incidence of *Candida* peritonitis





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2. Riche F. Crit Care 2009;13:R99;
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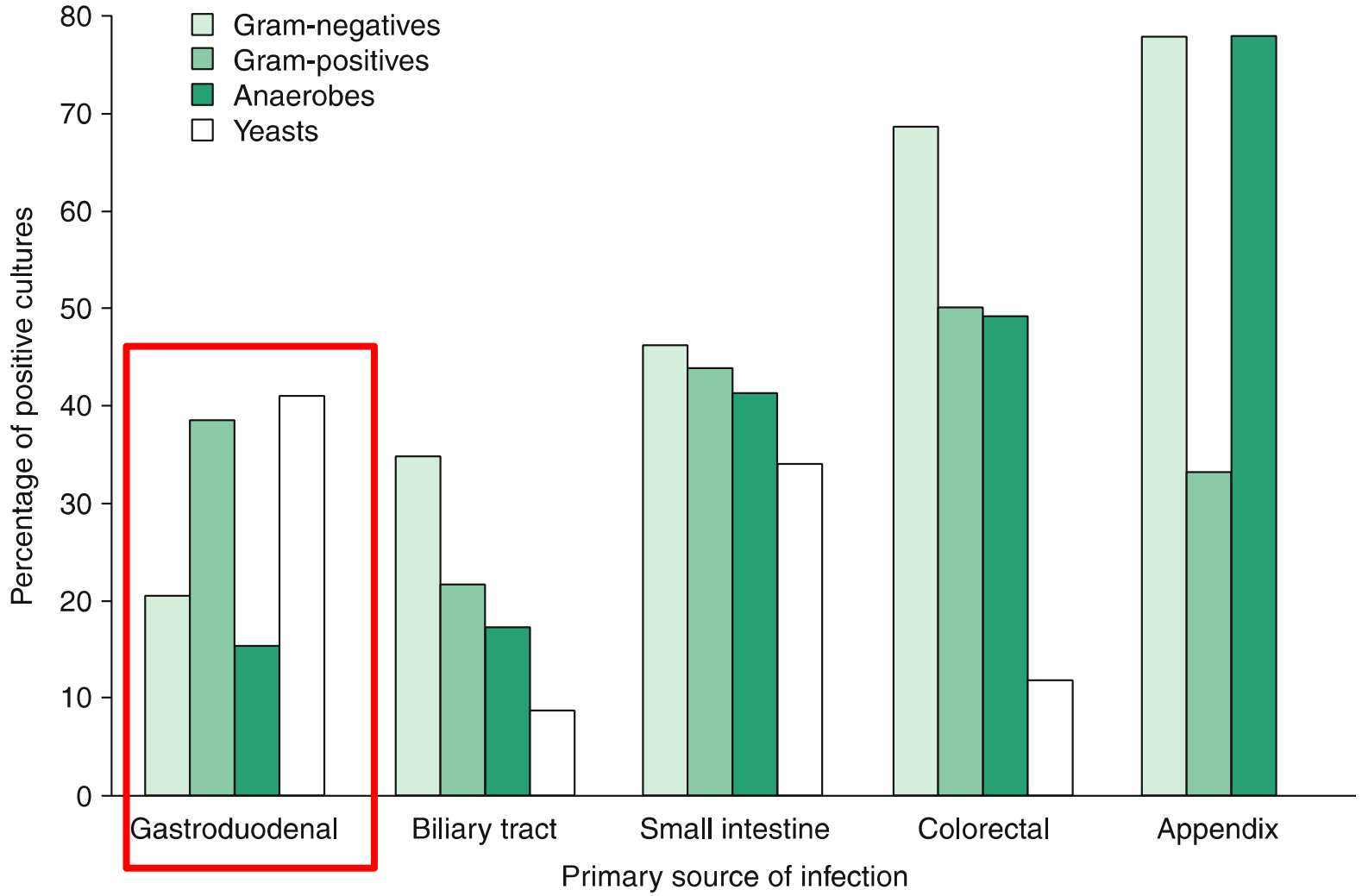
4. Gauzit R, et al. Surg Infect 2009;10:119–27;
5. Montravers P, et al. J Antimicrob Chemother 2009;63:785–94;
6. Montravers P. Clin Infect Dis 1996;23:486−94;
7. Seguin P. Clin Microbiol Infect 2006;12:980−5

Culture results in SP and TP: % positive findings with relation to primary source of infection



deRuiterJ,WeelJ,ManusamaE,etal.Theepidemiologyof intra-abdominal flora in critically ill patients with second- ary and tertiary abdominal sepsis. Infection 2009; 37: 522-7

SMART DIAGNOS

Rapid detection of Sepsis

Man 1942

- 8/2015 – GIT bleeding for gastric ca
- 4.11. gastrectomy; anastomotic leak
- 12.11. oesophageal stent
- 19.11. worsening again
- 20.11. stent dislocation, revision
- 22.11. lungs auscultation, susp. mediastinitis?????? – therapy MER, VAN -> shock
- 23.11. transfer to ICU; CRRT
- 24.11. exitus lethalis

PIP/TAZ

Autopsy findings:

- **Thrombosis of vena cava sup., thrombosis of v. femoralis dx**, persistent foramen ovale, st. p. gastrectomy, left liver lobe necrosis**, spleen infarctions, septic spleen activation, pleural exudate, peritoneal exudate, heart ventricules hypertrophy and dilation, lung oedema,** oesopfageal stent

Microbiological findings:

- Thrombus – *C.albicans* +++
- Spleen tissue - *C.albicans*

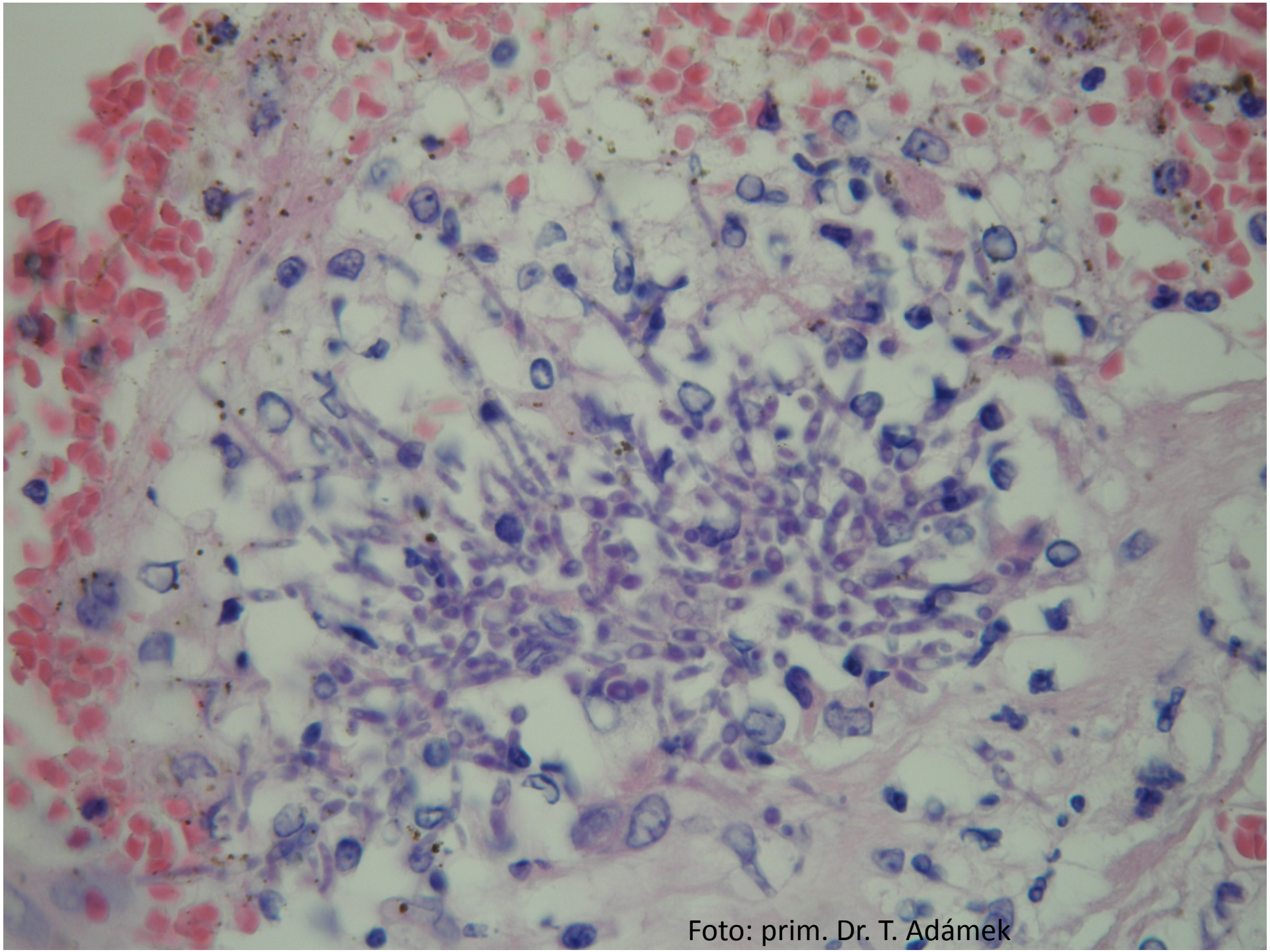


Foto: prim. Dr. T. Adámek

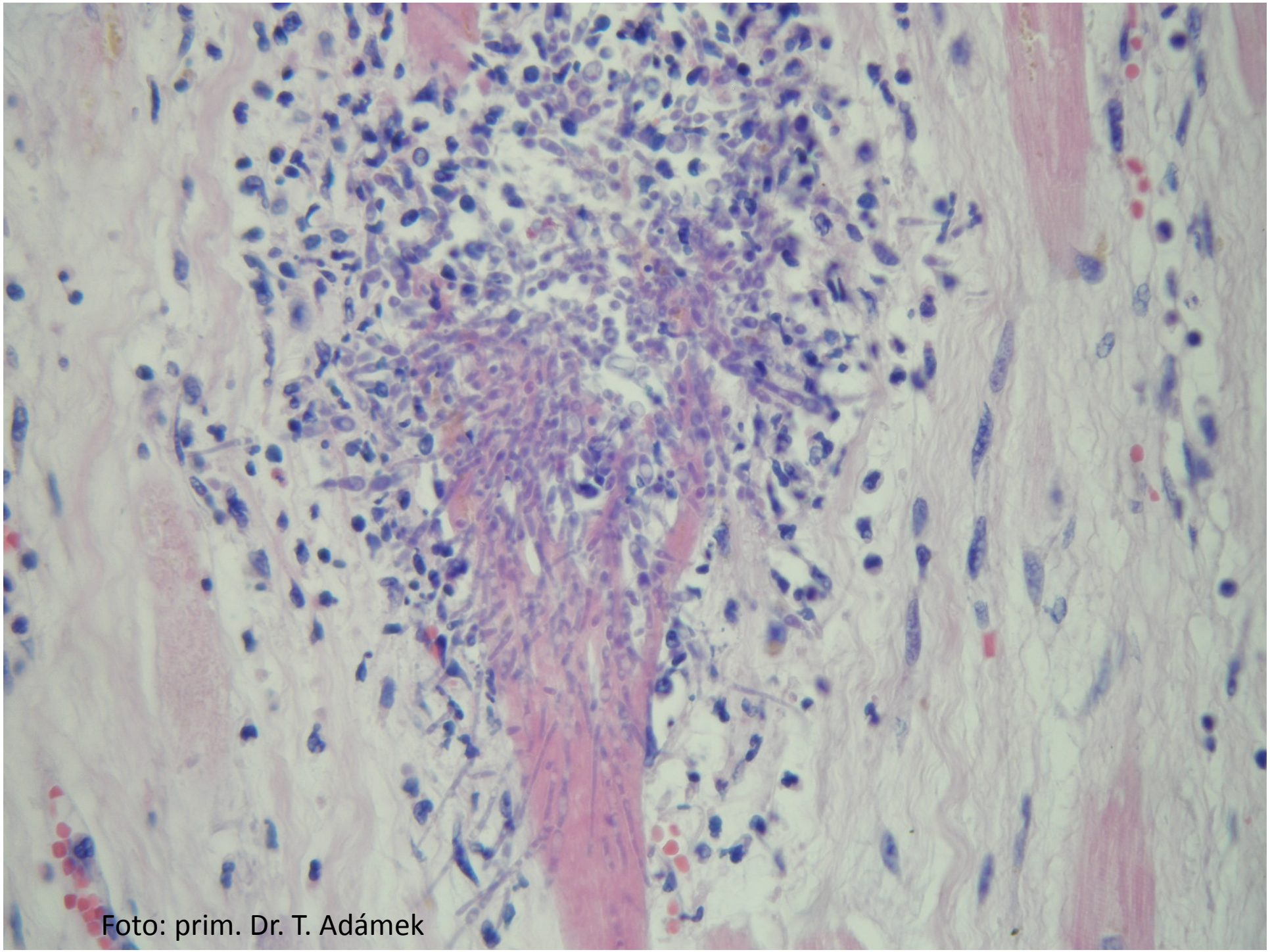


Foto: prim. Dr. T. Adámek

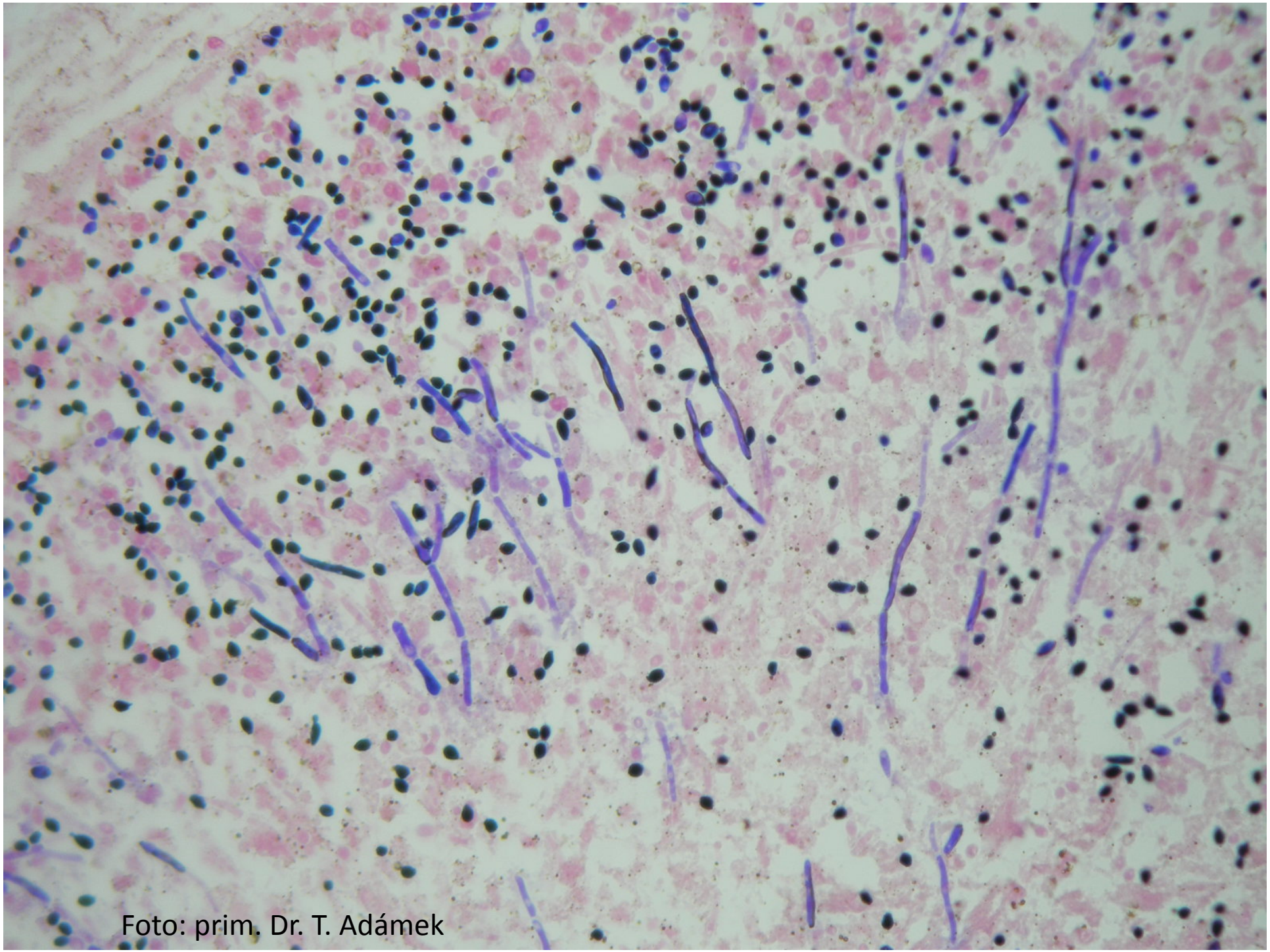
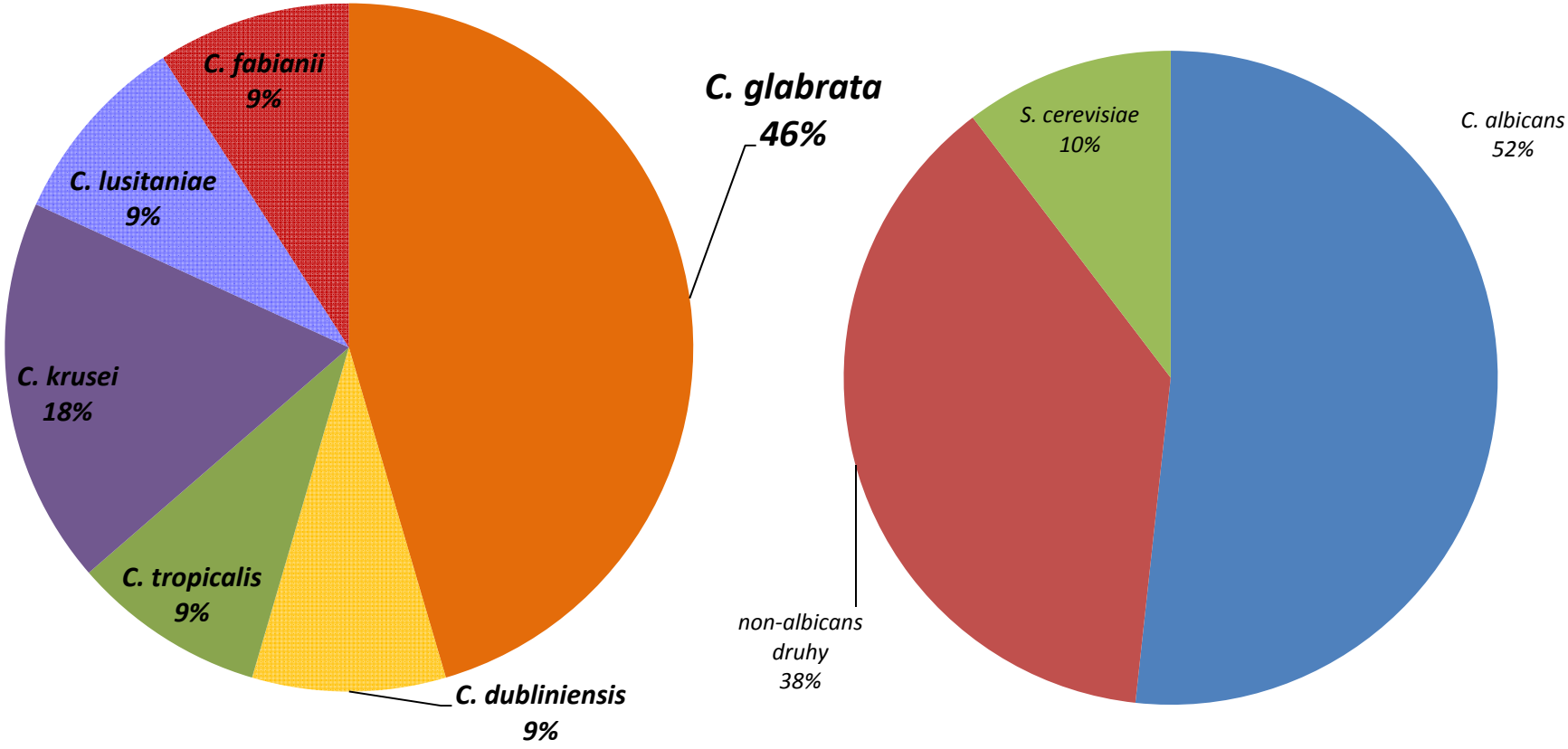
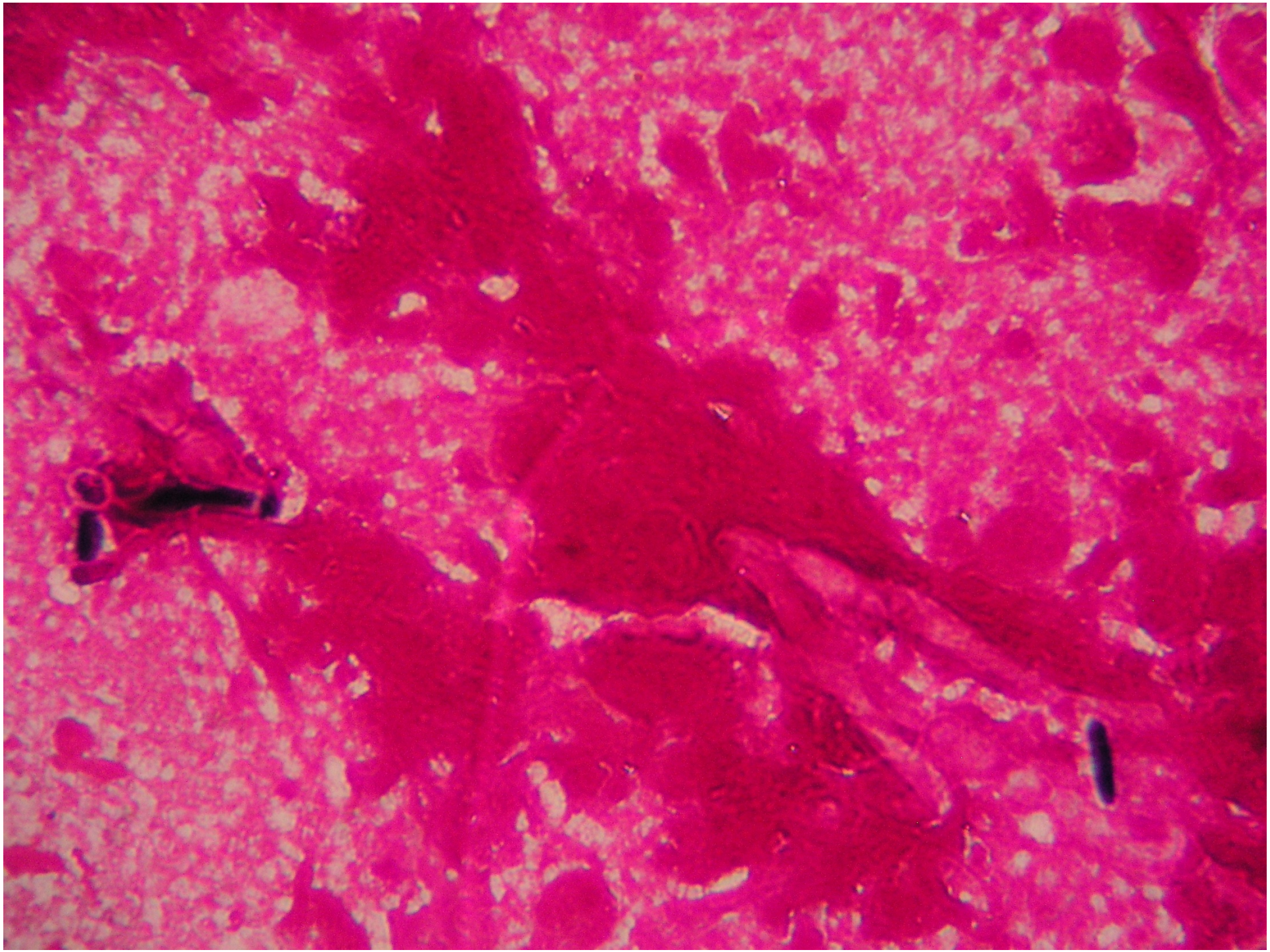


Foto: prim. Dr. T. Adámek

1. Surgical department – 6 m, 123 patients

- Yeasts in 28 patients (9 % of all findings). 13 patients with rupture of upper GIT. The most frequent isolates: *Candida albicans*, *C. glabrata* a *S. cerevisiae*.





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Preventing invasive candida infections. Where could

Pathophysiological characteristics of invasive candidiasis according to immune status

Pathophysiological characteristics	Immunocompromised patients	Critically ill patients
Immunity		
Neutrophils	Decreased	Increased
Macrophages	Decreased	Increased
T-cells	Decreased	Normal
Ulcerations of mucosal surfaces		
Oropharyngeal	++ to +++	0 to +
Upper digestive tract	++ to +++	0 to +
Lower digestive tract	++ to +++	0 to +
Typhlitis	++ to +++	0
Digestive surgery	0	+ + to +++
Antibiotic exposure	++ to +++	+ to ++
Organ failure	+ to ++	++ to +++
Candida colonization	++ to +++	++ to +++
Invasive candidiasis		
Candidaemia	++ to +++	0 to +
Non-candidaemic systemic candidiasis	0 to +	++ to +++

Intensive Care Med (2013) 39:2226–2230
DOI 10.1007/s00134-013-3134-2

EDITORIAL

Philippe Montravers
Herve Dupont
Philippe Eggimann

Intra-abdominal candidiasis: the guidelines—forgotten non-candidemic invasive candidiasis

Table 1 Limitations of current clinical/biological tools in the diagnosis and treatment of intra-abdominal candidiasis

Current clinical/biological tools	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Usefulness to guide empirical antifungal treatment
Clinical risk factors					
Colonization index	Medium high	Medium	++	+++	++ if dynamics is followed
Candida scores	Medium	Medium high	++	+++	++
Predictive rules (+colonization)	Medium	Medium (high)	++	++ (+)	++ (+ if ongoing studies positives)
Biomarkers					
C-reactive protein	Low	Low	+	++	Not useful
Procalcitonin	Low	Medium	+	+++	++ if added to *Candida* score
Mannan/anti-mannan antibodies	Very high	High	++	+++	+++ if dynamics is followed
Beta-D-glucans	Very high	Very high	+++	+++	+++ in high risk patients
Secondary peritonitis					
+*Candida* and nosocomial infection	High	Very high	++	++	++ (but overtreatment)
+*Candida* + upper digestive tract perforation	High	Very high	++	++	++ (but overtreatment)
+Septic shock	High	Very high	++	++	++ (but overtreatment)
Tertiary peritonitis					
Anastomotic leakage	Very high	Very high	+++	+	+++ (>35 % risk of candidiasis)
Repetitive surgery	Very high	Very high	+++	+	+++ (>50 % risk of candidiasis)

?????

Pathophysiological role of *Candida* spp isolated from the peritoneum	–Synergisms and antagonisms with bacteria (*Pseudomonas* spp, *Enterococci*, *Staphylococci*…) –Mechanisms of adhesion/invasion of the epithelial intestinal cell –Role of biofilms –Role of host defense mechanisms (innate immunity)
Distinction between colonization and infection	–Enhanced predictivity of described tools in high risk groups: –Exclusion of low risk patients by negative predictive value of colonization index, of clinical scores and of predictive rules –Positive predictive value of biomarkers in these patients –Role of fungi isolated from mixed cultures –Time course of colonization and infection
Prophylaxis and preemptive antifungal treatment	–When, how, to whom, what drug –What dose, for how long time
Therapeutic challenges	–Comparison of antifungal agents (fungicidal versus fungistatic) –Effects of combinations of antifungals In different but homogenous clinical settings: –Severe or mild to moderate fungal infection –Community-acquired versus nosocomial/health-care associated infections –Prolonged or persistent fungal peritonitis –Clinical and biological makers of clinical and microbiological response –Optimal duration of treatment –Feasibility and advantages of de-escalation

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Intra-abdominal candidiasis: the guidelines—forgotten non-candidemic invasive candidiasis

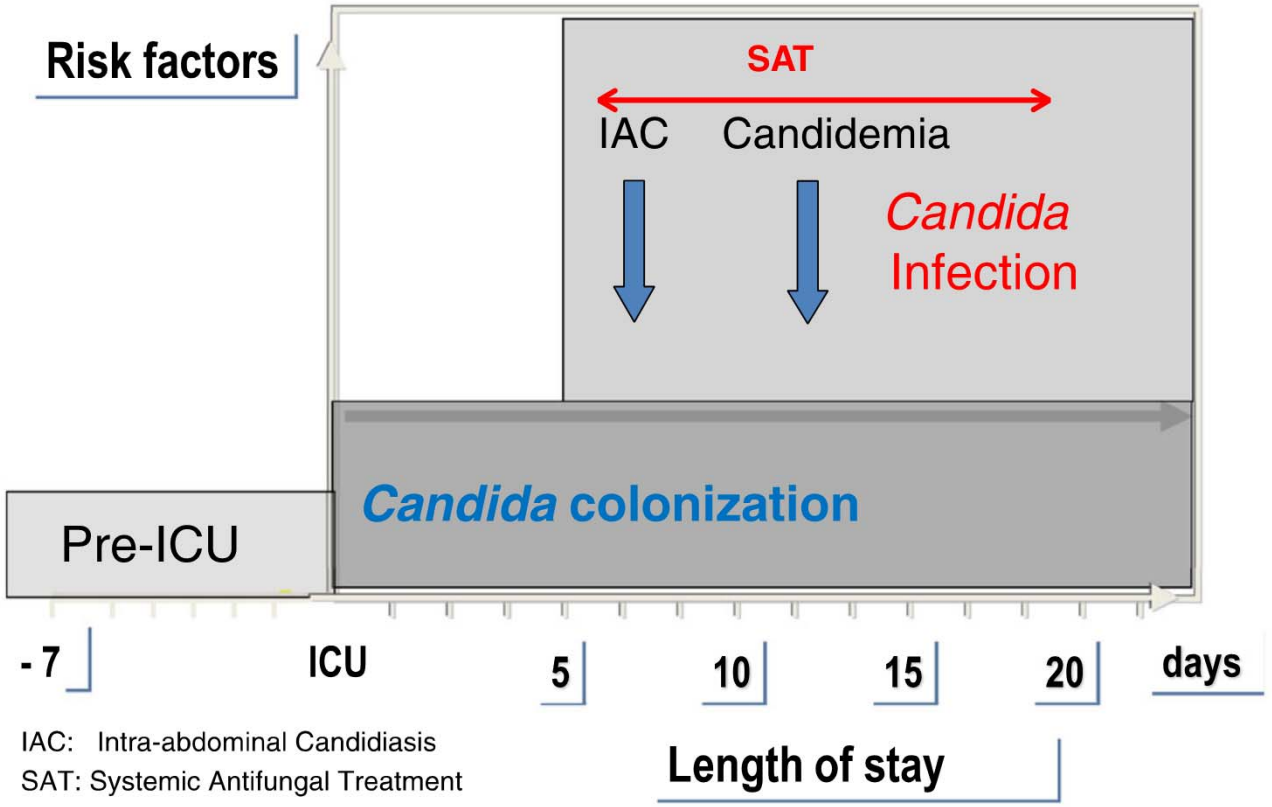


Fig. 1 Invasive candidiasis in ICU. Natural history

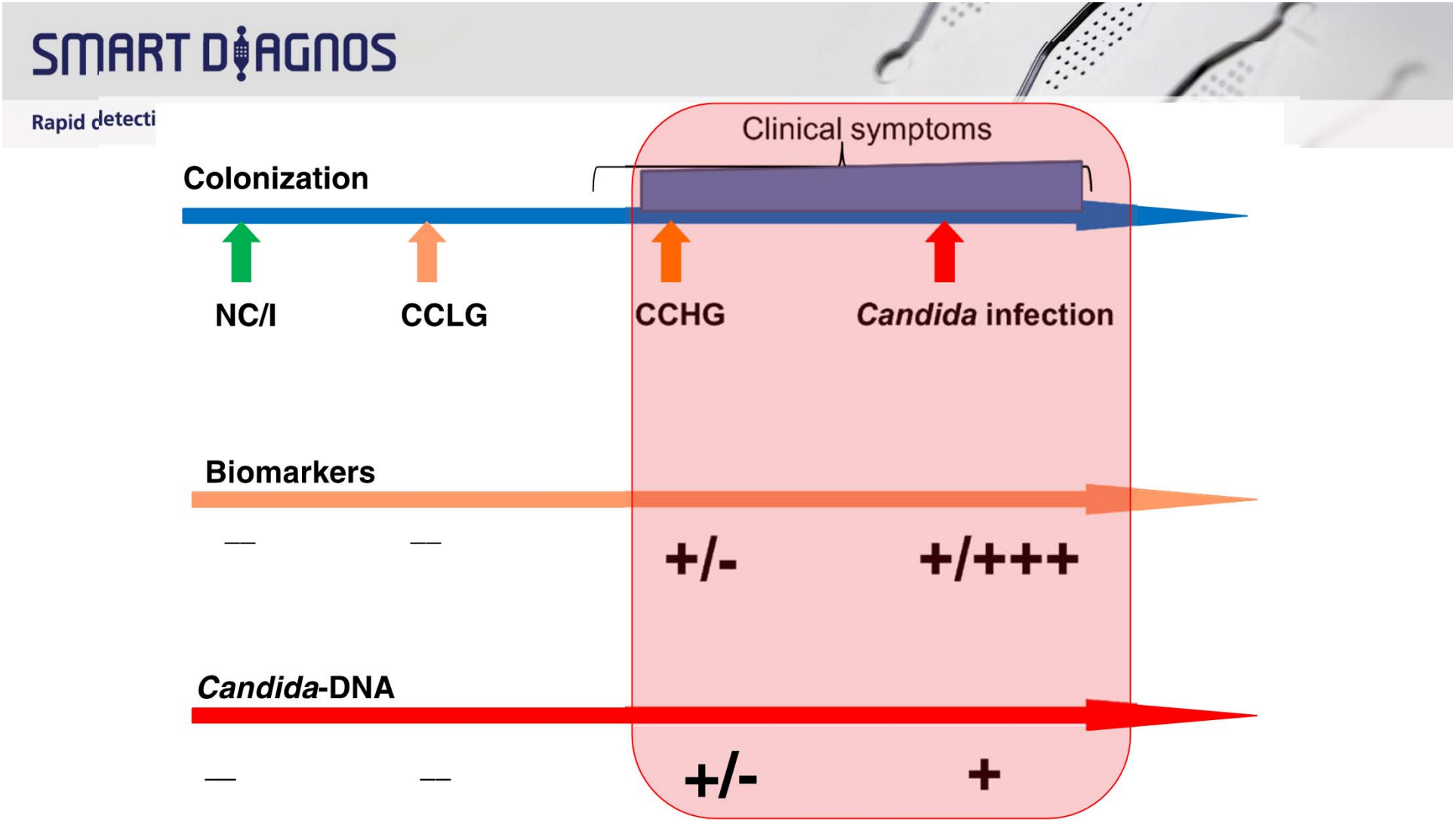
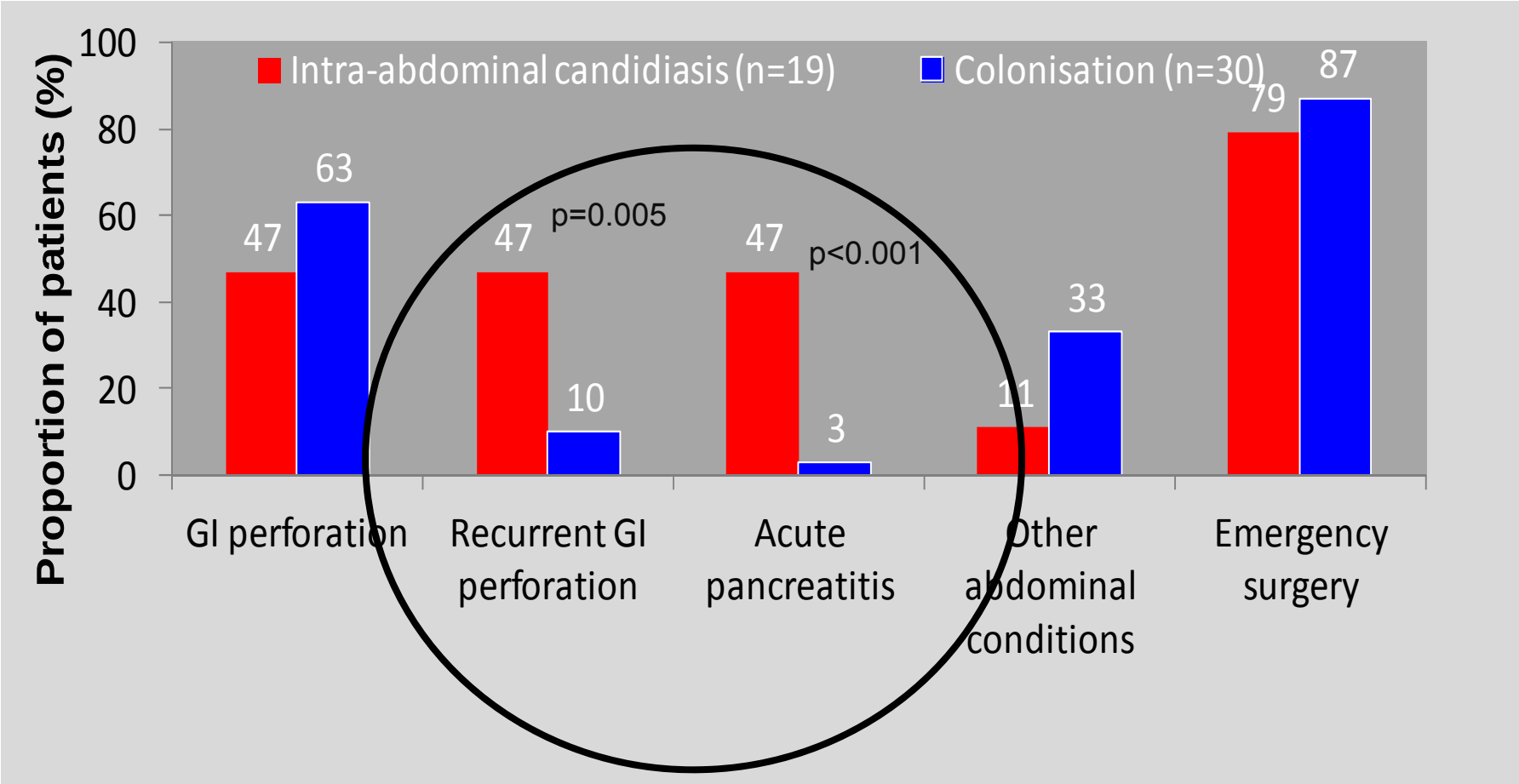


Fig. 2 Interrelation between microbiology, clinical, biomarkers, and *Candida* DNA. *NC/I* no colonized/infected, *CCLG Candida* colonization low grade, *CCHG Candida* colonization high grade

Recurrent GI perforation is associated with IAC

49 sur.pts with positive culture of yeast in peritoneal fluid



*Calandra T et al. Clin Infect Dis 2004;**39**:S185–92*

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Rapid detection of Sepsis

Intensive Care Med (2015) 41:1682–1684
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EDITORIAL

CrossMark

Philippe Montravers
Olivier Leroy
Christian Eckmann

Intra-abdominal candidiasis: it's still a long way to get unquestionable data

- AmarCand 1 Study – IAC in 34 % ICU patients with proven IC
- IAC the second most frequent candidosis on ICU
- IAC - >10 % of all peritonitis
- Mortality 25 – 60 %

Intensive Care Med (2013) 39:2092–2106
DOI 10.1007/s00134-013-3109-3

ORIGINAL

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A research agenda on the management of intra-abdominal candidiasis: results from a consensus of multinational experts

Table 2 Risk factors for intra-abdominal *Candida* infection

Risk factor	Notes	References
1. Specific		
Recurrent abdominal surgery	Laparoscopies included	[33]
GI tract perforations	Recurrent perforations and/or perforations untreated within 24 h[a]	[17]
Gastrointestinal anastomosis leakage	More severe if the leakage is in the upper GI tract[b]	[2, 3, 17, 31]
Multifocal colonization by *Candida* spp.		
2. Additional nonspecific		
Acute renal failure, central venous catheter placement, total parenteral nutrition, ICU stay, severity of sepsis, diabetes and immunosuppression, prolonged broad-spectrum antibacterial therapy		[20, 31]

[a] Surgical control of upper gastrointestinal perforations is more problematic [65]

[b] Gastroduodenal surgery, in particular that involving the esophagus

Principal recommendations on managegent of IAC

Diagnosis	Direct microscopy examination for yeast detection from purulent and necrotic intra-abdominal specimens obtained during surgery or by percutaneous aspiration is recommended in all patients with nonappendicular abdominal infections including secondary and tertiary peritonitis	AII
	Samples obtained from drainage tubes are not valuable except for study of colonization	DIII
	Blood cultures should be taken through peripheral vein punctures upon diagnosis or suspicion of intra-abdominal infections and tertiary peritonitis, and specific media for fungi are recommended, if available	AII
	Antifungal susceptibility test should be performed on yeast isolates from blood, sterile sites, and other appropriate specimens. MICs should be reported to the clinicians, specifying the reference method used (CLSI versus EUCAST)	BIII
Culture interpretation	Systemic antifungal treatment should be considered when adequate intra-abdominal specimens (obtained surgically or within 24 h from external drainage) are positive for *Candida*, irrespective of the fungal concentration and the associated bacterial growth	AII
	Positive cultures from drains should not be treated, especially if the drains are in place for more than 24 h	DIII
Nonculture test	When available, mannan and antimannan tests and BDG should be performed in patients with secondary or tertiary peritonitis and at least one specific risk factor for IAC	BII

Therapy of IAC

Prophylaxis	Patients with recent abdominal surgery and recurrent gastrointestinal perforation or anastomotic leakage should receive treatment with fluconazole	BII
	An echinocandin should be considered if there is a high likelihood of azole resistance	CII
Empirical therapy	Empirical antifungal treatment may be considered in patients with a diagnosis of intra-abdominal infection and at least one specific risk factor for *Candida* infection (Table 2)	CIII
	In patients with intra-abdominal infection with or without specific risk factor for *Candida* infection, empirical antifungal treatment should be administered if a positive mannan/antimannan or BDG or PCR test result is present	BII
	Fungicidal antifungal agents (i.e., echinocandins or lipid formulation of amphotericin B) should be prescribed for the empirical therapy of all critically ill patients or patients with previous exposure to azoles	AII
	Azoles can be adopted for the empirical therapy of non-critically ill patients without previous exposure to azoles unless they are known to be colonized with a *Candida* strain with reduced susceptibility to azoles	BII
Targeted therapy	Fungicidal agents such as echinocandins or lipid formulations of amphotericin B should be used for targeted therapy of all critically ill patients or patients with previous exposure to azoles	BII
	For the subgroup of patients infected with *C. parapsilosis*, lipid formulations of amphotericin B or fluconazole should be preferred	BII
	Azoles (fluconazole) can be used for targeted therapy of non-critically ill patients without previous exposure to azoles unless there is evidence of multisite colonization with a *Candida* strain characterized by reduced susceptibility to azoles	BII

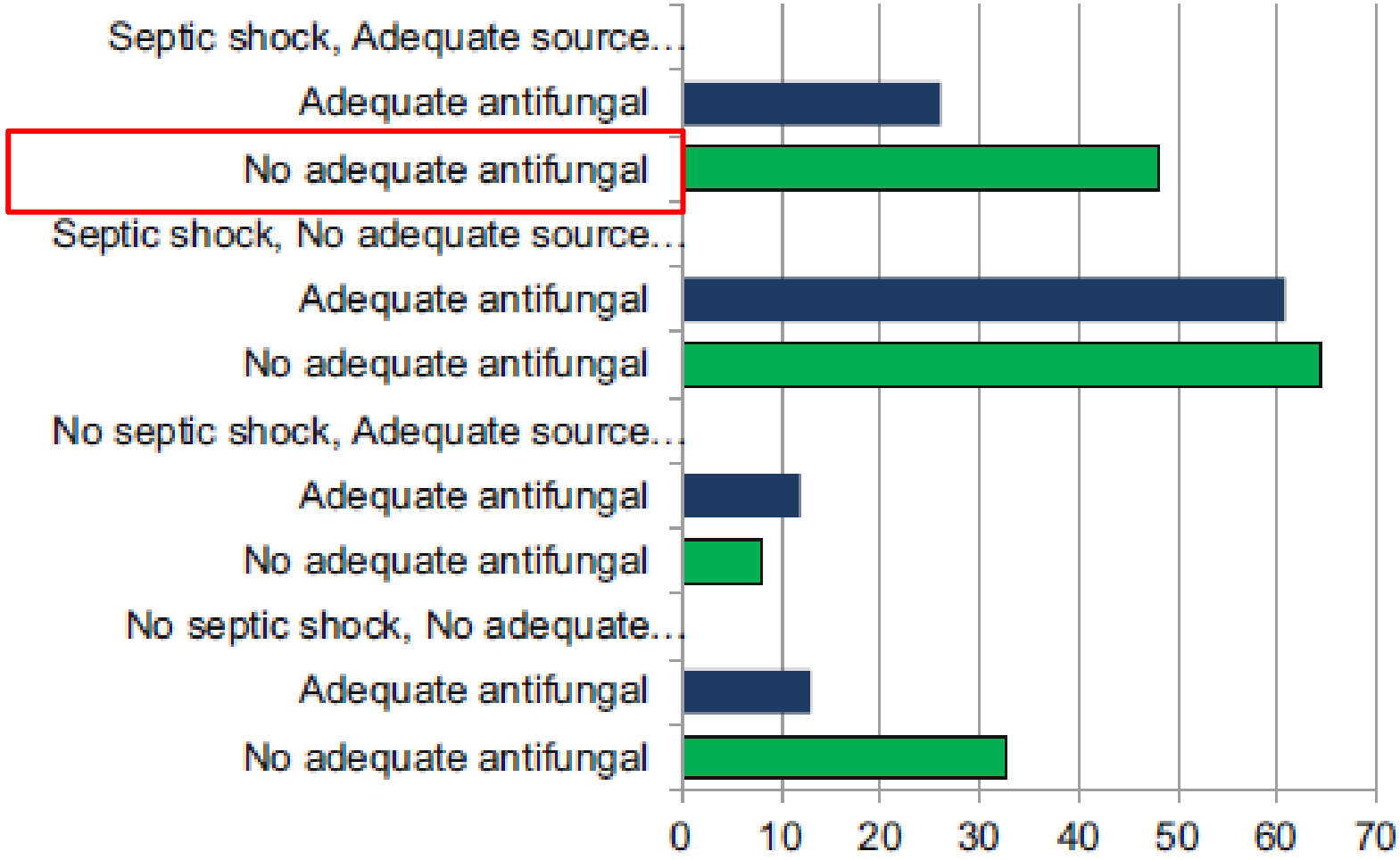

Fig. 1 Thirty-day hospital mortality in patients with or without septic shock and adequate antifungal therapy and/or source control

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Rapid detection of Sepsis
Clinical Infectious Diseases
IDSA GUIDELINE
IDSA Infectious Diseases Society of America
hivma hiv medicine association
OXFORD

Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America

Peter G. Pappas,[1] Carol A. Kauffman,[2] David R. Andes,[3] Cornelius J. Clancy,[4] Kieren A. Marr,[5] Luis Ostrosky-Zeichner,[6] Annette C. Reboli,[7] Mindy G. Schuster, Jose A. Vazquez,[9] Thomas J. Walsh,[10] Theoklis E. Zaoutis,[11] and Jack D. Sobel[12]

VIII. What Is the Treatment for Intra-abdominal Candidiasis?

Recommendations

54. Empiric antifungal therapy should be considered for patients with clinical evidence of intra-abdominal infection and significant risk factors for candidiasis, including recent abdominal surgery, anastomotic leaks, or necrotizing pancreatitis *(strong recommendation; moderate-quality evidence)*.

55. Treatment of intra-abdominal candidiasis should include source control with appropriate drainage and/or debridement *(strong recommendation; moderate-quality evidence)*.

IAC

- Candida peritonitis is life-threatening complication of surgical patients
- With poor prognosis
- Patients with IA catastrophe are at high risk of IAC

- Colonisation vs infection??????

León C, Ostrosky-Zeichner L, Schuster M. What's new in the clinical and diagnostic management of invasive candidiasis in critically ill patients. Intensive Care Med 2014; 40:808-19
Montravers P, Dupont H, Gauzit R, Veber B, Auboyer C, Blin P, et al. *Candida as a risk factor for mortality in peritonitis. Crit Care Med 2006; 34:646-52.*
Montravers P, Dupont H, Eggimann P. Intra-abdominal candidiasis: the guidelines-forgotten non-candidemic invasive candidiasis. Intensive Care Med 2013; 39:2226-30.
Zaragoza R, Ferrer R, Maseda E, Llinares P, Rodríguez A; EPICO PROJECT GROUP. EPICO 2.0 PROJECT: Development of educational therapeutic recommendations using the DELPHI technique on invasive candidiasis in critically ill adult patients in special situations. Rev Esp Quimioter 2014; 27:196-212.

Candida score

- **>7 d at ICU**
- Surgery (1 pt)
- Multifocal Candida colonization (1 pt)
- Parenteral nutrition (1 pt)
- Severe sepsis (2 pt)

- Cut off ≥3 = at high risk for IC
- Sensitivity 81 %, specificity 74 %

Vincent JL. When to start antifungals in abdominal infections: Let us be INTENSE. 34th International Symposium on Intensive Care and Emergency Medicine, Brussels, Belgium, 2014. Oral presentation.
Montravers P, Mira JP, Gangneux JP, Leroy O, Lortholary O. AmarCand Study Group. A multicentre study of antifungal strat- egies and outcome of Candida spp. peritonitis in intensive-care units. Clin Microbiol Infect 2011;17:1061e1067.

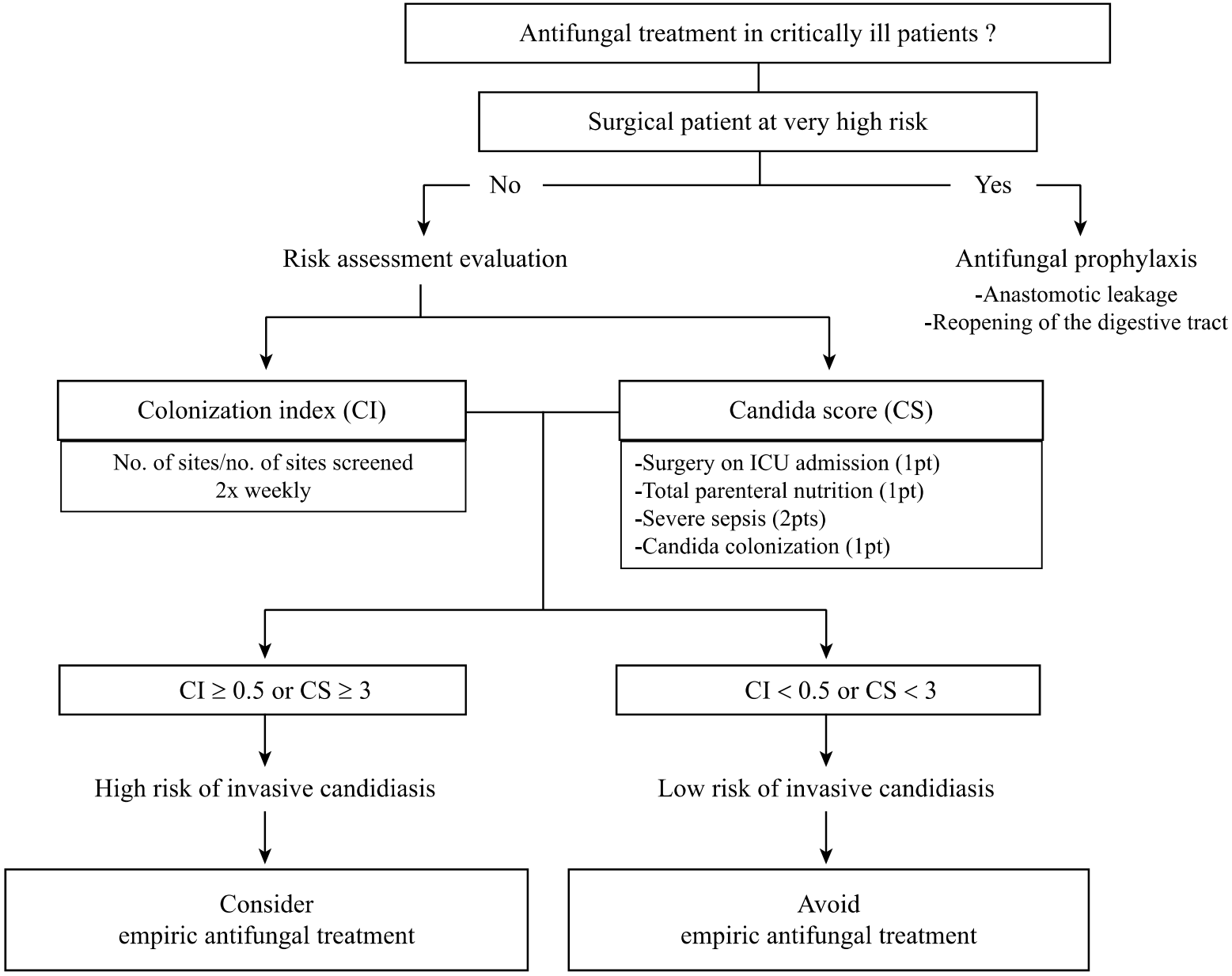
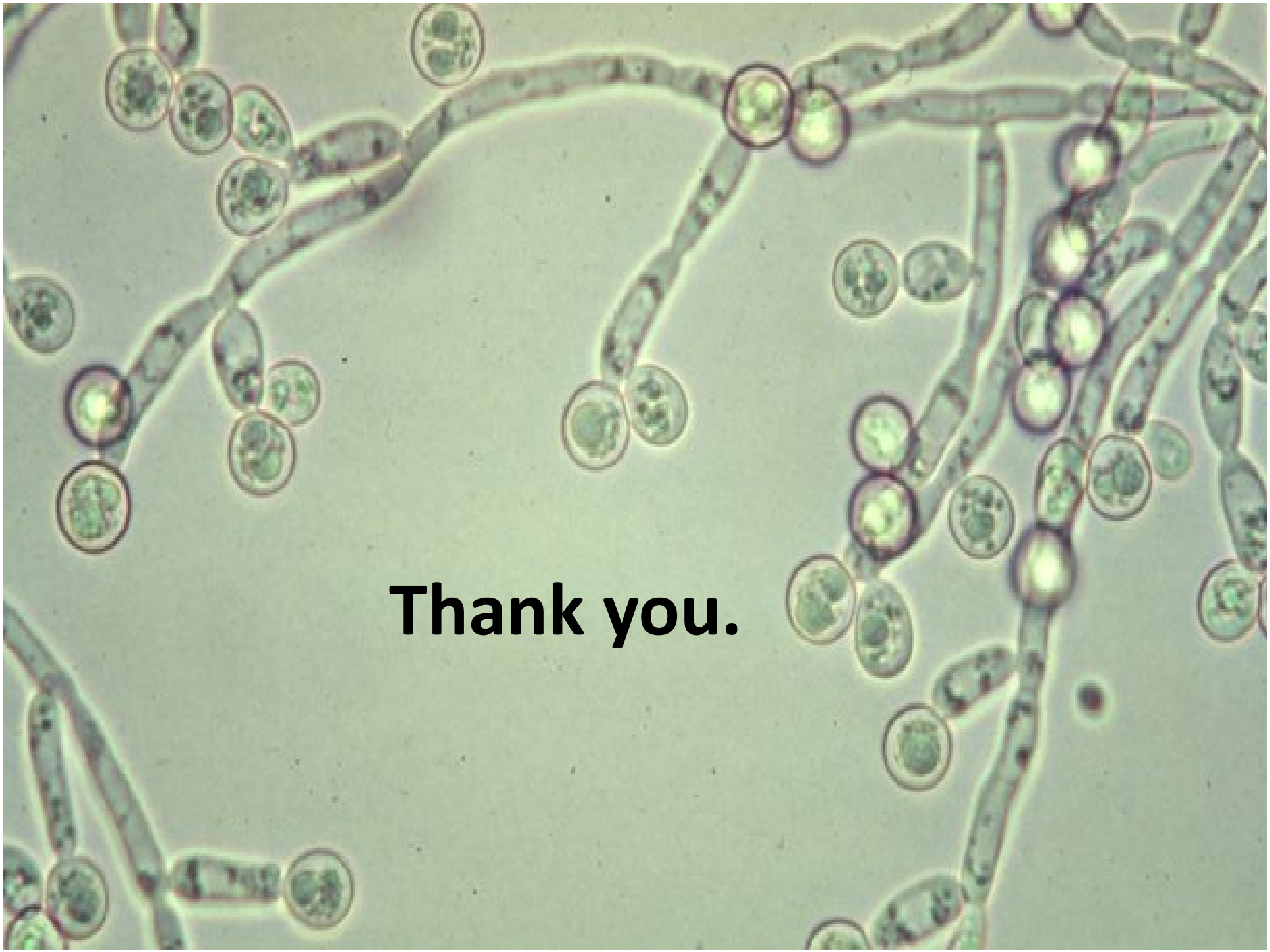


Figure 1. Risk assessment strategies for antifungal treatment.

Conclusion

- Endogenous source, no exogenous
- 7 – 10 days interval between exposition to risk factors and development of IAC
- **Enough time for evaluation of risk factors and consideration of AF prophylaxis/empirical therapy**


Thank you.