

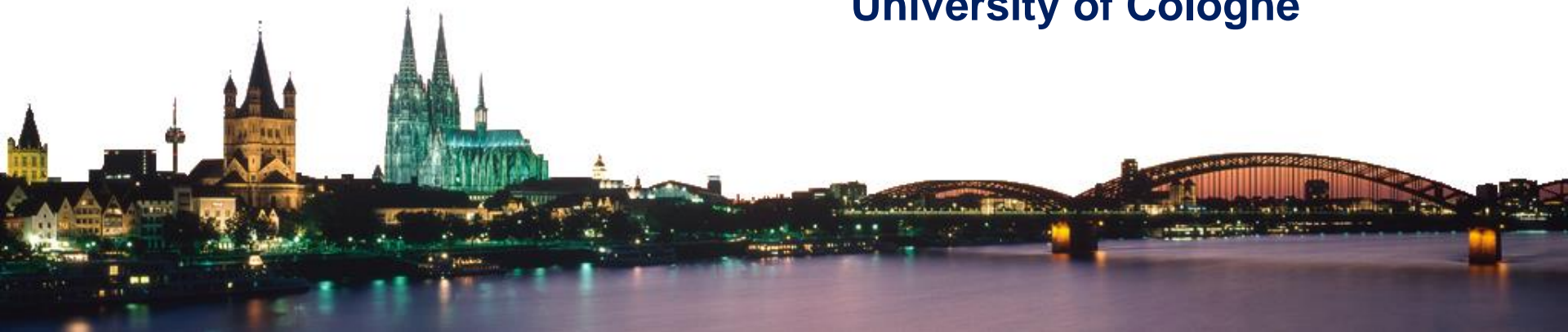


**UNIKLINIK
KÖLN**

Fungal Infections of Bone and Joint

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**Chair, Translational Research Institute
Chair, Centre for Clinical Trials
Deputy Head, Infectious Diseases
University of Cologne**





- European Commission
 - FP7, IMI-JU 6 (COMBACTE), 8 (APC), 9 (CARE)
- European Organisation for Research and Treatment of Cancer (EORTC)
- European Society for Clinical Microbiology and Infectious Diseases (ESCMID)
- European Confederation of Medical Mycology (ECMM)
- German Federal Ministry of Research and Education
 - BMBF 01KN1106, 01KN0706, 01GH1001E, 01EZ0931, 01EK1422
- German Center for Infection Research (DZIF)
- German Research Foundation (DFG)
- German José Carreras Leukaemia Foundation (DJCLS)
- SME & Industry Research Grants, Trial Design, or Presenting for
 - 3M, Actelion, Astellas, Basilea, Bayer, Celgene, Cubist, Da Volterra, F2G, Genentech, Genzyme, Gilead, GSK, Menarini, Merck Serono, MSD, Miltenyi, NanoMR, Novartis, Optimer, Parexel, Pfizer, Quintiles, Roche, Sanofi Pasteur, Summit/Vifor, Viropharma

Candida Infection of the Bone



EFISG

ESCMID FUNGAL INFECTION
STUDY GROUP

European Society of Clinical Microbiology and Infectious Diseases

Population	Intention	Intervention	SoR	QoE	Reference
Osteomyelitis / spondylodiscitis	Cure	Surgical debridement*	C	III	Hendricks CID 2001 Miller CID 2001
	Cure	Fluconazole 400 mg 6-12 months	A	II _u	Hennequin CID 1996 Sugar DMID 1990 Miller CID 2001
	Cure	Liposomal Ampho B / ABLC 2-6 wks followed by Fluconazole 400 mg, total 6-12 months	A	II _u	Hennequin CID 1996 Miller CID 2001
	Cure	Echinocandin 2-6 wks followed by Fluconazole 400 mg total 6-12 months	B	III	Cornely JAC 2007 Legout Scand JID 2006
	Cure	Voriconazole 2x3 mg/kg ≥6 weeks	B	III	Schilling Med Mycol 2008

*Indications for surgery are instability, or e.g. large abscess.

Candida Infection of the Joint



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STUDY GROUP

European Society of Clinical Microbiology and Infectious Diseases

Population	Intention	Intervention	SoR	QoE	Reference
Arthritis	Cure	Fluconazole 400, ≥6 wks	A	II _u	Pérez-Gómez Sem Arth Rheum 1998 Hansen Scand JID 1995
	Cure	Liposomal Ampho B / ABLC 2 wks, followed by Fluconazole 400, total ≥6 wks	A	II _u	Hansen Scand JID 1995
	Cure	Echinocandin ≈2 weeks followed by Fluconazole 400, total ≥6 wks	B	III	Cornely JAC 2007 Sim Hon Kon Med J 2005
	Cure	Voriconazole 2x3 mg/kg ≥6 wks	B	III	Sili CID 2007
Prosthetic joint infection	Cure	Prosthesis removal	A	III	Tunkel AJM 1993
Prosthetic joint infection with prosthesis retention	Chronic suppression	Fluconazole life long	A	III	Merrer J Infect 2001 Kelesdis Scand JID 2010 Levine Clin Orthop Relat Res 1986

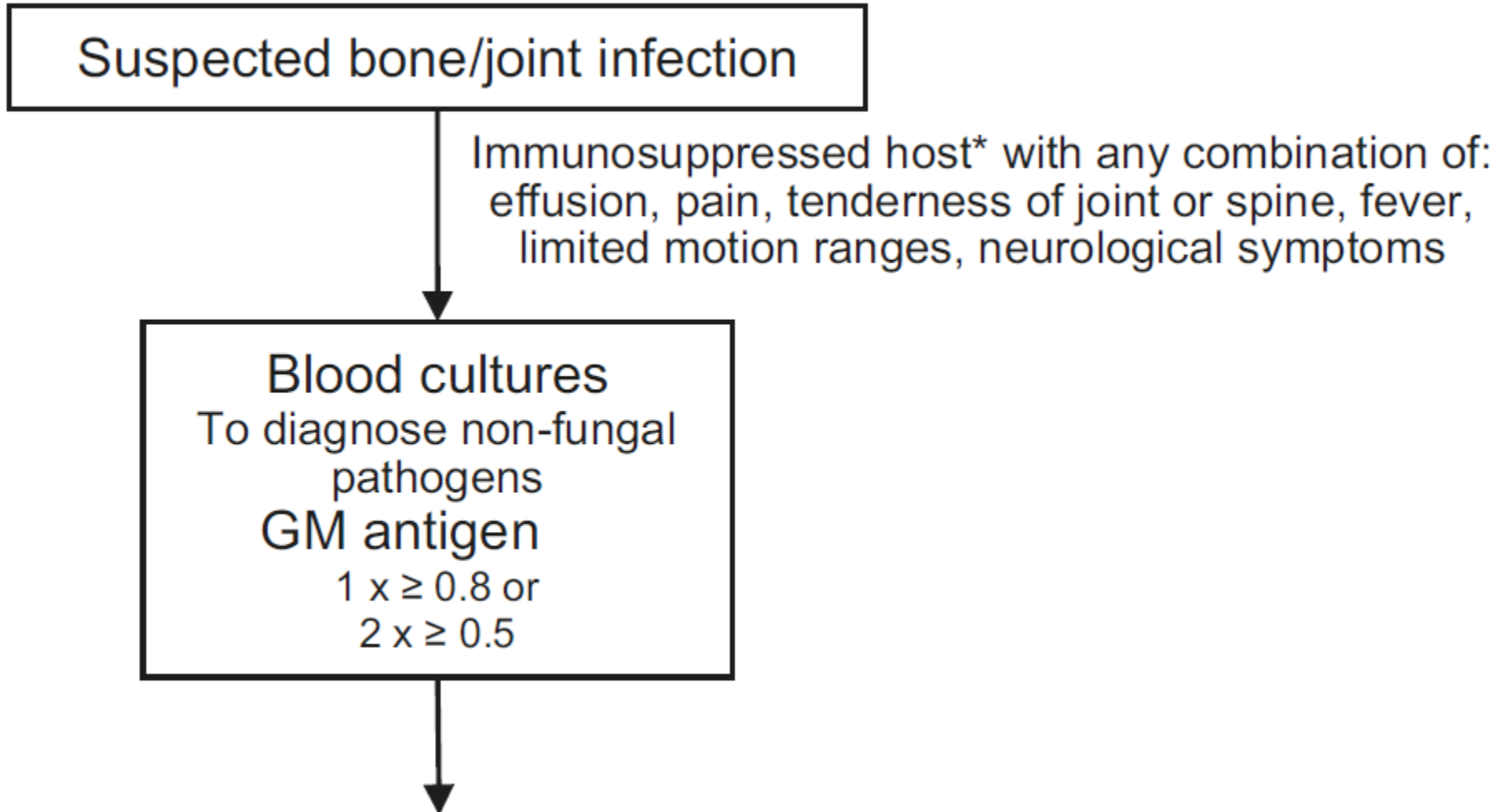


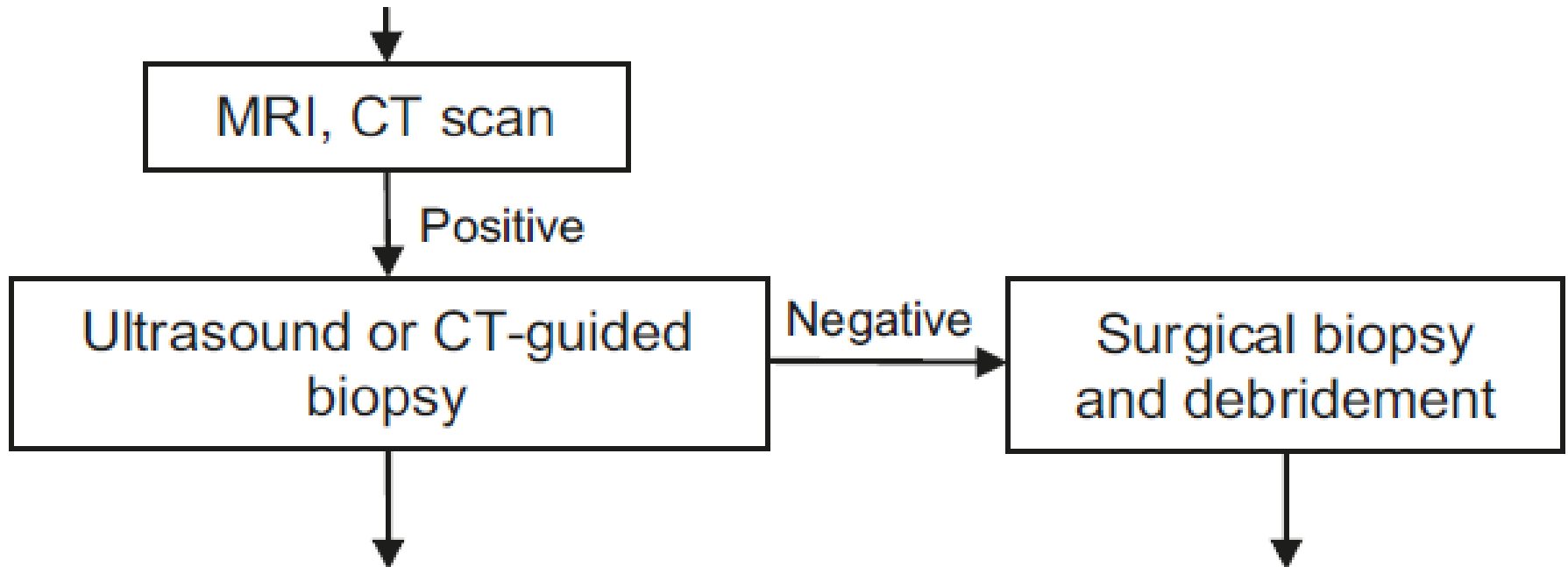
Aspergillosis of bones and joints – a review from 2002 until today

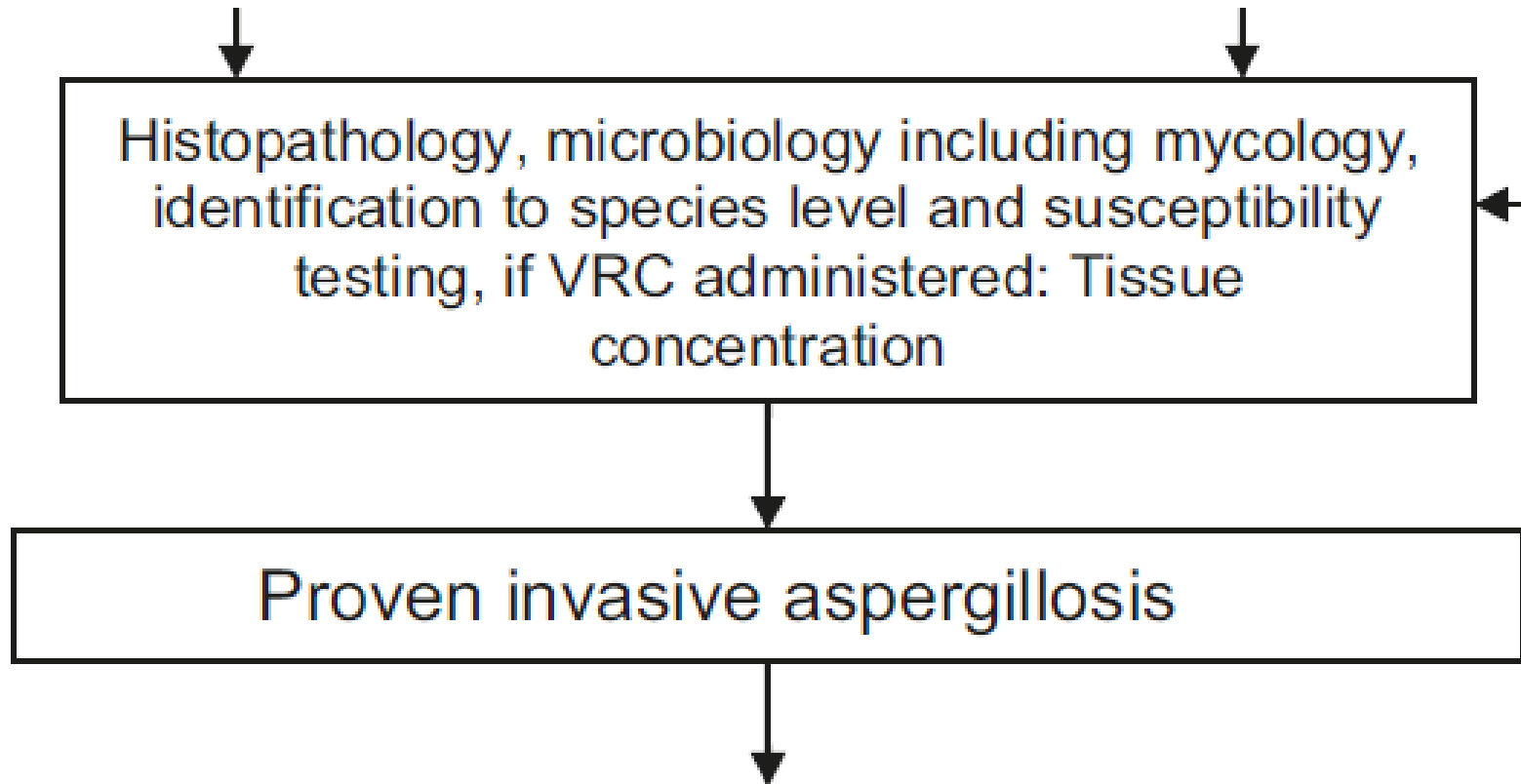
Philipp Koehler, Daniela Tacke and Oliver A. Cornely

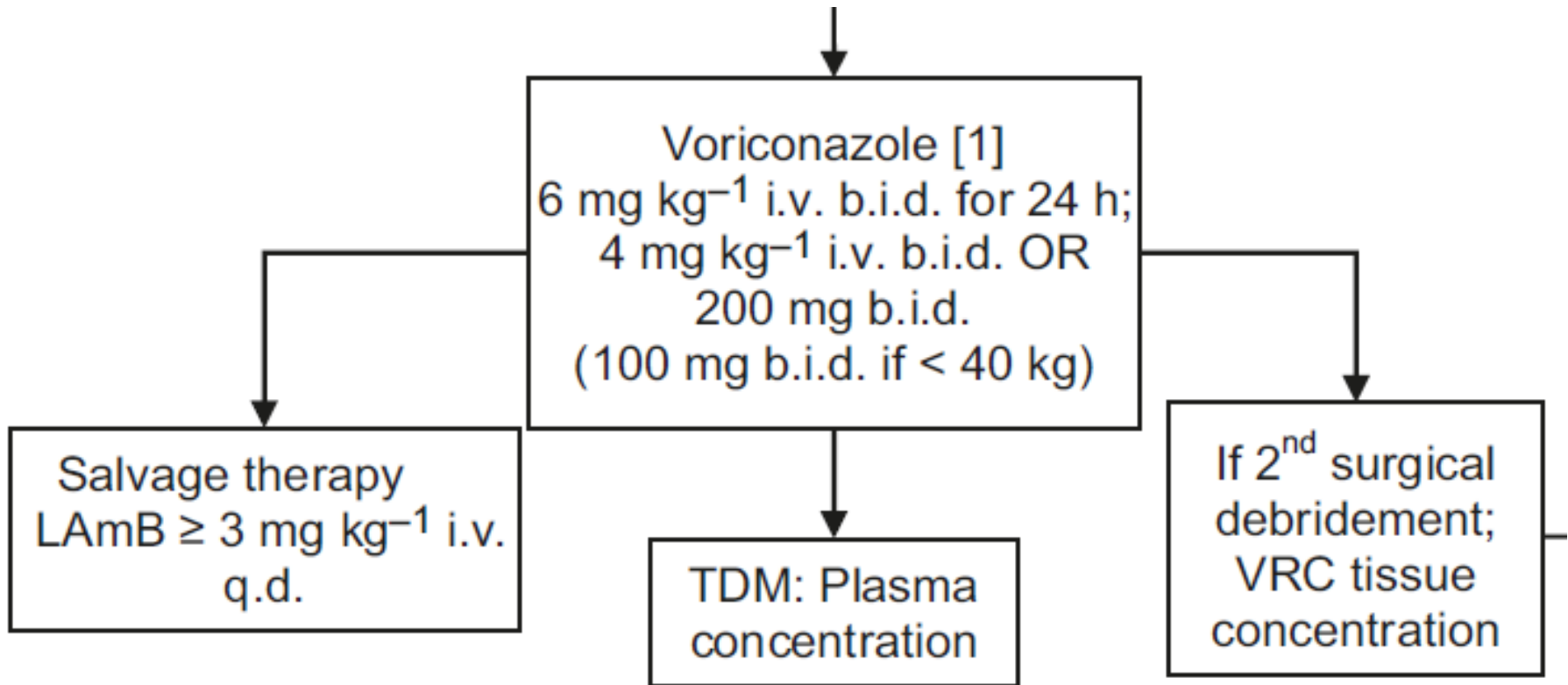
1st Department of Internal Medicine, University Hospital of Cologne, Zentrum für Klinische Studien (BMBF 01KN1106), CECAD – Cologne Excellence Cluster on Cellular Stress Responses in Aging–Associated Diseases, Cologne, Germany

- Literature review
- N=47
 - 40 osteomyelitis
 - 5 arthritis
 - 2 osteomyelitis & joint











REVIEW ARTICLE

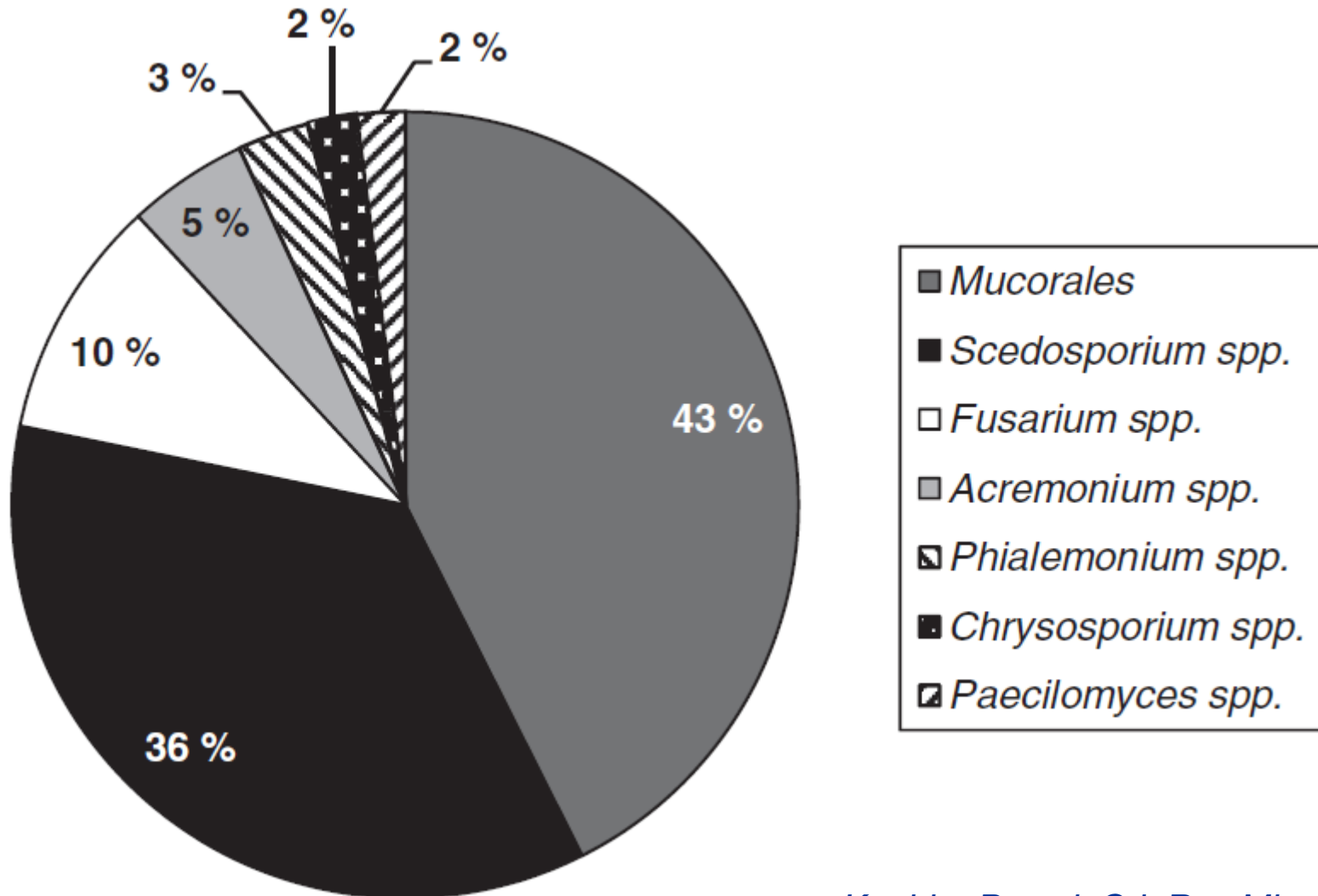
Bone and joint infections by *Mucorales*, *Scedosporium*, *Fusarium* and even rarer fungi

Philipp Koehler^{1,2,3}, Daniela Tacke^{1,2}, and Oliver A. Cornely^{1,2,3,4,5}

• N=61



Incidence rates of published non-Aspergillus moulds causing bone and joint infection





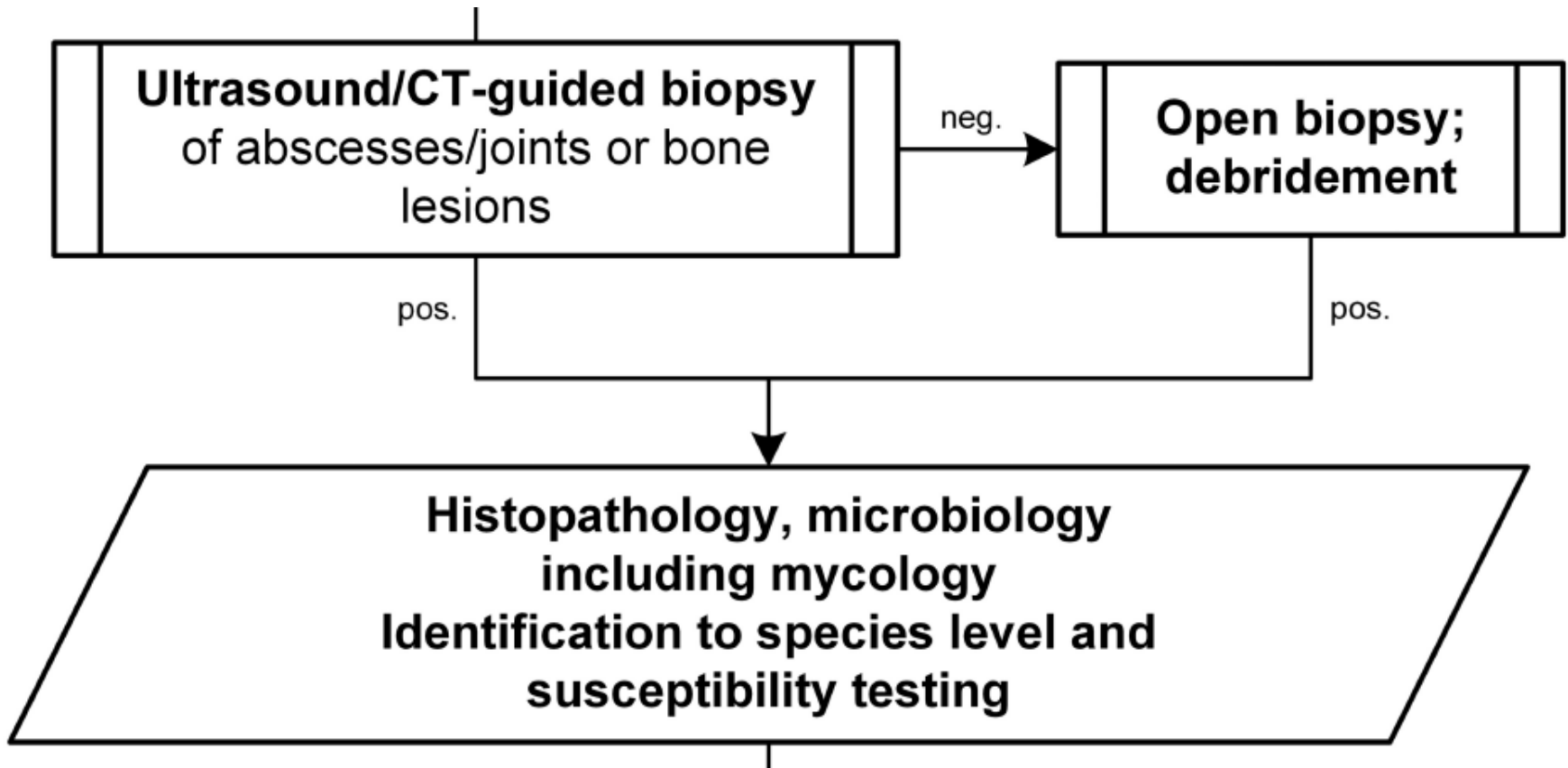
Suspected bone/joint infection

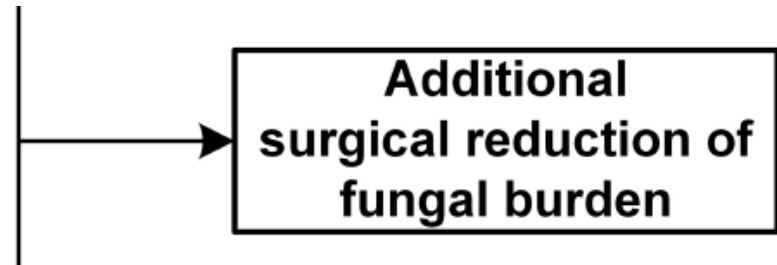
Clinical presentation, effusion of joints, pain, tenderness in spinal region, fever, limited motion ranges, neurological deficits

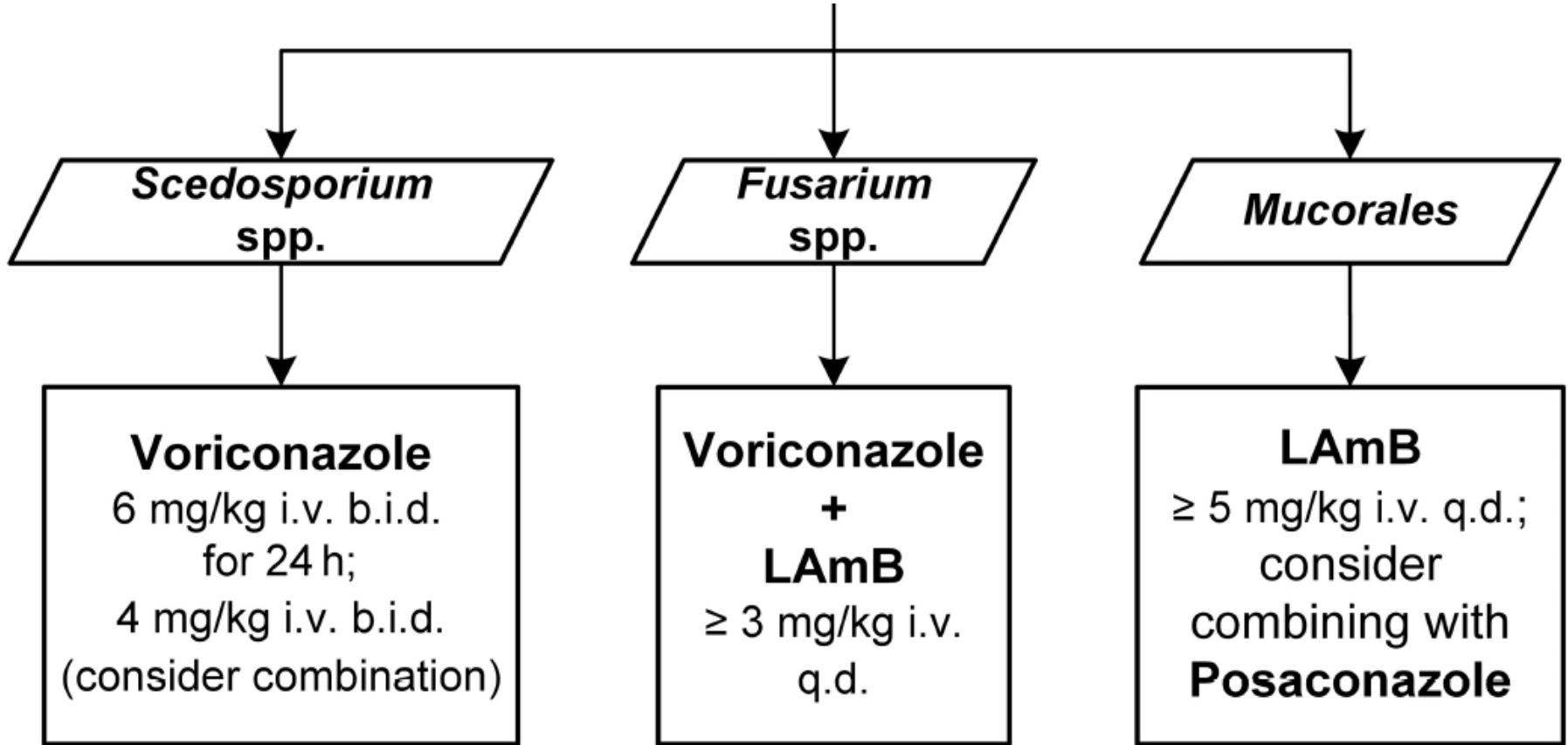
Blood cultures
to proof fungemia or
non-fungal causes

MRI, CT scan

pos.









Dose adjustment according to susceptibility testing
Therapeutic drug monitoring (TDM)



- Fungal bone and joint diseases
 - appear to be very rare
 - usually need combined modality treatment
- Recommendations are based on transferred evidence
- Should be entered into registries, such as those of the European Confederation of Medical Mycology (ECMM), or in similar national registries

Chair:
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Clinicalsurveys.net:
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Documentation:
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Culture Banking:
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Fungi scope

Global Emerging Fungal Infection Registry

Initiated in 2003

ISHAM and ECMM Working Group
www.fungiscope.net

Molecular Biology:
S. De Hoog
V. Rickerts

Histopathology:
B. Markiefka

Thoracic Surgery
K. Hekmat

Pharmacokinetics:
F. Farowski



- 81 y/o lady
- 22 years ago knee endoprosthesis
- Day 1 Loosening, removal, tissue biopsies
 - *Candida glabrata* (3/3 pos.)



MIKROSKOPIE:

Grampräparat

Keine Bakterien nachgewiesen.

Erythrozyten

Massenhaft

Leukozyten

Vereinzelt

KULTUR:

Nachweis von

1) Vereinzelt *Candida glabrata*

ANTIBIOGRAMM:

Amphotericin B MHK

1
0.380

Handelsname (z.B.)
(mg/l)

Amphotericin B

S

Ampho-Moronal, Amphotericin B

Fluconazol MHK

8.000

(mg/l)

Fluconazol

DS*

Diflucan, Fungata

Voriconazol MHK

0.180

(mg/l)

Voriconazol

S

VFand

Caspofungin MHK

0.094

(mg/l)

Caspofungin

S

Cancidas

Keine Bakterien nachgewiesen.

Vorläufige Befundmittlung erfolgte.

* Dosisabhängig Sensibel



- Day 3 Voriconazole 6/4 mg/kg
- Day 14 Haematoma, revision, biopsy
 - *Candida glabrata*
- Day 180 Biopsy
 - Staph. epidermidis
 - fungal culture and PCR neg.
- Day 210 Biopsy
 - Staph. caprae, Staph. epidermidis, Corynebacterium sp.
- Multiple revisions until Day 420,
unremarkable after 18 months of F/U