

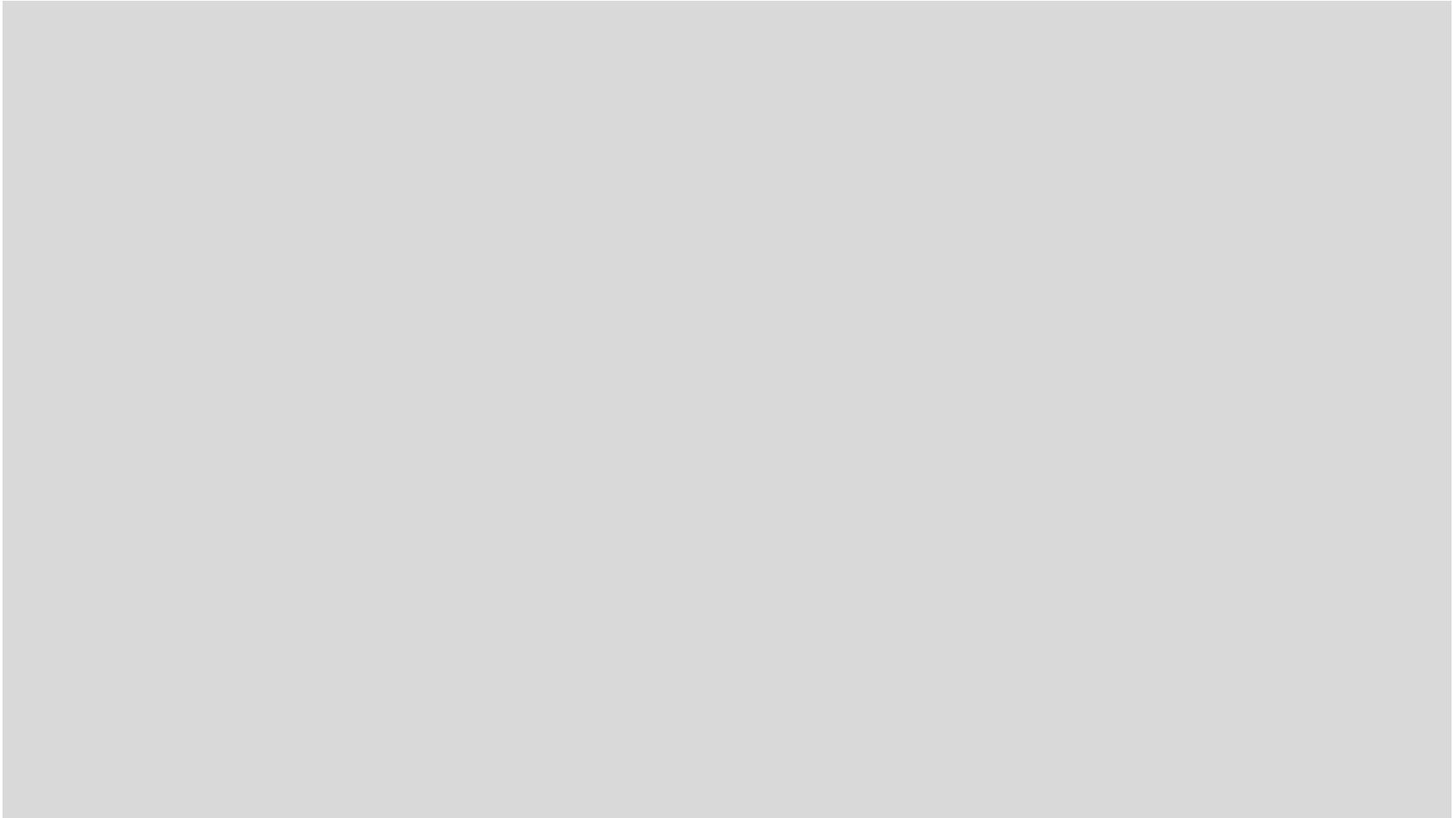
Nosokomiale invasive Aspergillosen (IA)

6. Kölner Hygienetag

28.10.2015

Prof. Dr. Frauke Mattner

**Abgabe von infektiösen Partikeln direkt in die Luft
Schimmelpilzsporen (hier *Aspergillus fumigatus*)**



Wachstum von Aspergillen: Vorkommen in der Umwelt

Hyphen (1) enden in Vesikeln (2) mit Phialiden (3), die dann Konidien (= Sporen, 4) ausbilden, die sich schließlich ablösen

1

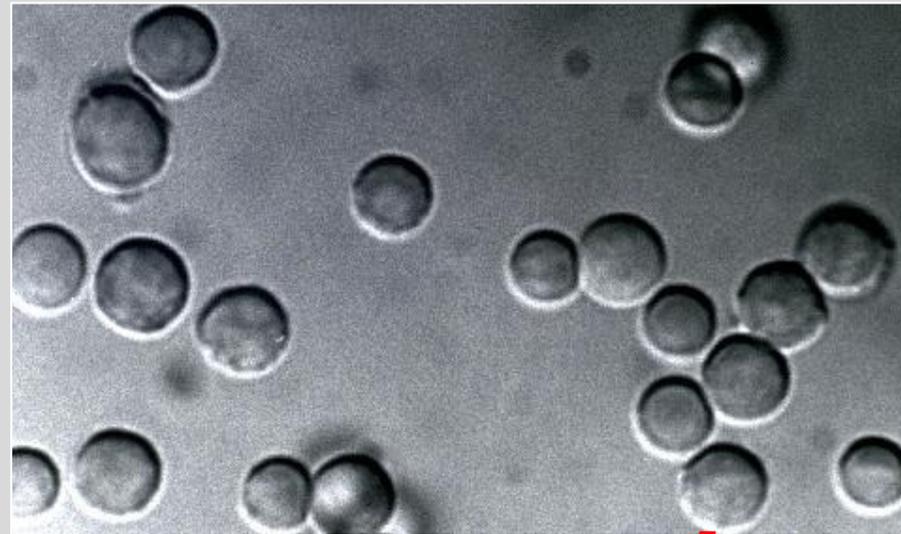
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3

4

Übertragung von Aspergillen: aerogene Transmission

Sporengroße:
2 bis 4 μm



5 μm

- Sporen können bis in die Alveolen inhaliert werden (7 pro Tag!!)
- Elimination des Erregers bei immunkompetenten Menschen in der Regel problemlos
- andere: Risiko einer invasiven Aspergillose (IA)

Wann sind Schimmelpilzsporen „unterwegs“?
Im Sommer und Herbst!!

CAVE Fensterlüftung Sommer und Herbstzeit

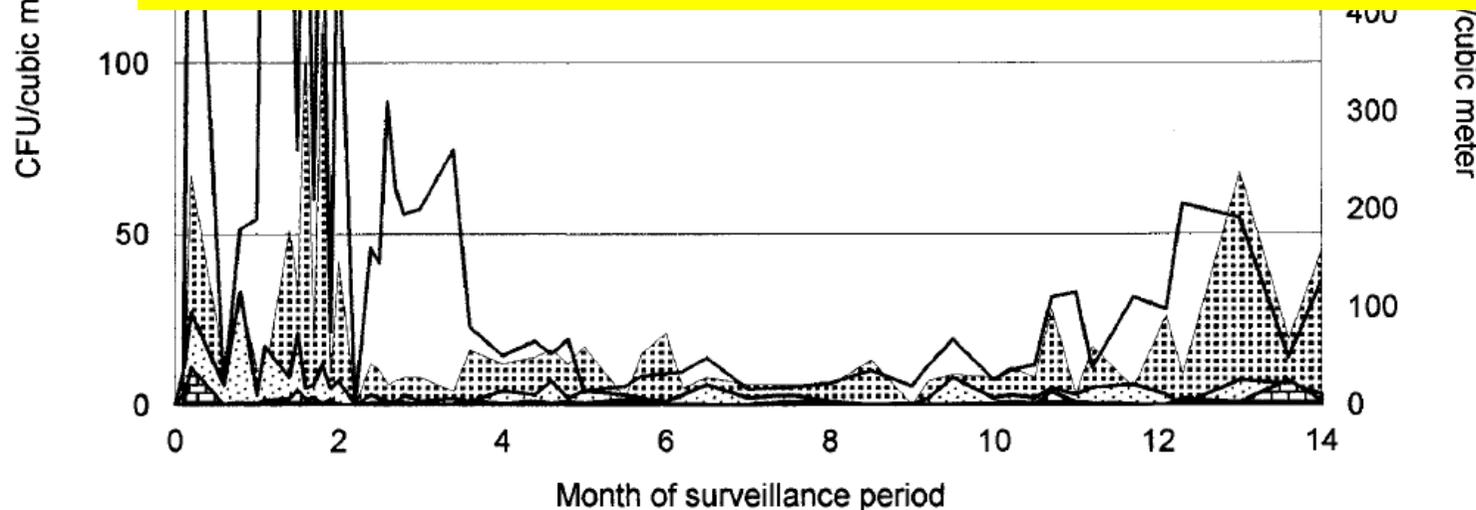
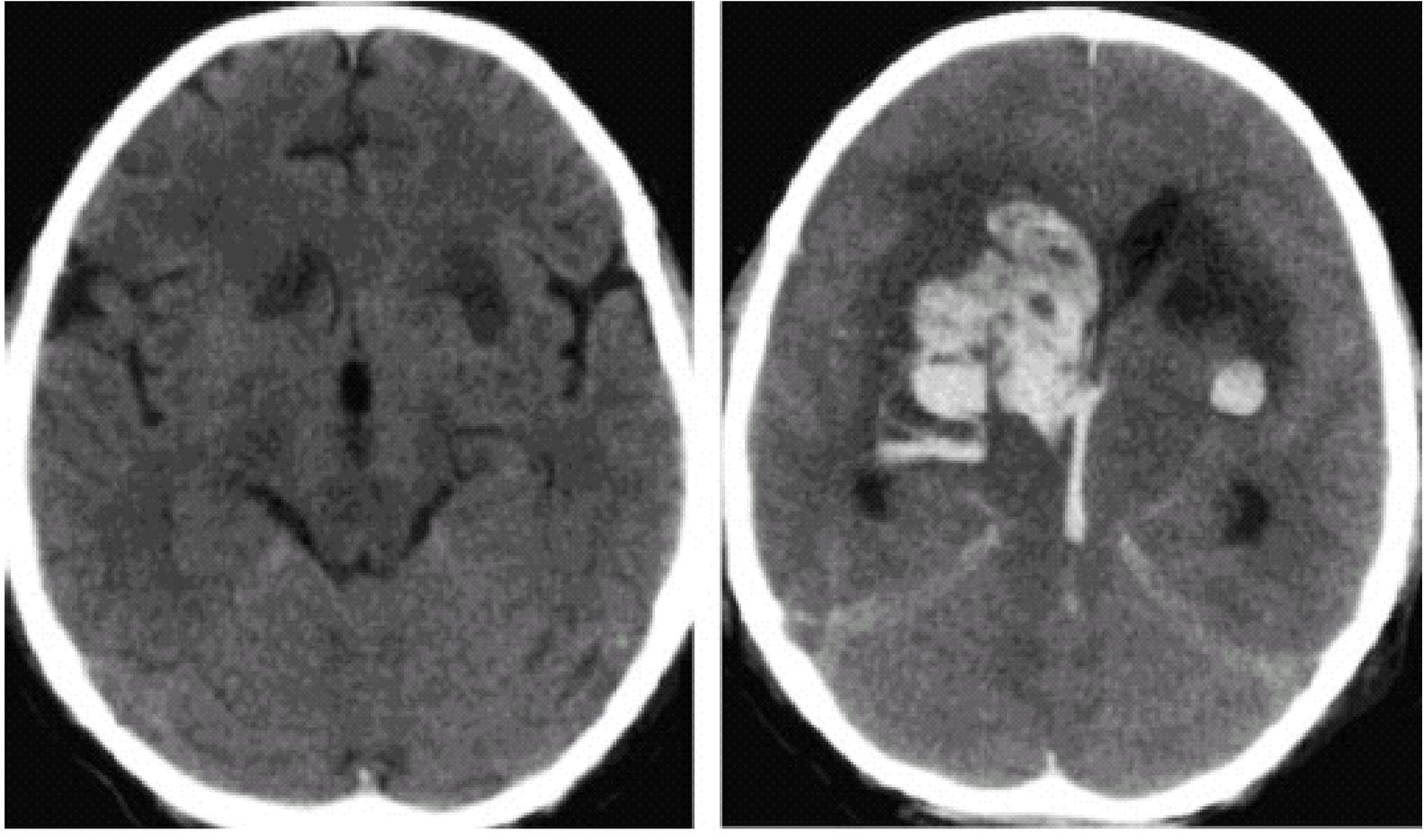


FIG. 1. Results of a 14-month surveillance period of the conidia of nonpathogenic fungi present in air samples from within the hospital outside the department of hematology, air samples within the hematology ward, and air samples in HEPA-filtered rooms. The numbers of conidia outside are depicted in the line (enumeration on the y_2 axis). The surveillance began in July 1994 (0 on the x axis) and ended in September 1995 (14 on the x axis).

- **Prospektive 1-Jahres Studie auf einer hämatologischen Station in Straßburg**
- **21 Umgebungsisolate und 26 klinische Isolate typisiert.**
- **34 unterschiedliche Genotypen festgestellt**
- **2 Patienten hatten mindestens zwei verschiedene Stämme**
- **2 Patienten hatte identische Stämme mit denen, die bei Umgebungsuntersuchungen nachgewiesen wurden**



alle.

Vaskulitisch medierte Infarzierungen im Basalganglienbereich, im Verlauf intrazerebrale Massenblutung, Einklemmung und Hirntod

Mortalität und Patientenrisikogruppen

REVIEW

Nosocomial aspergillosis in outbreak settings

R-P. Vonberg*, P. Gastmeier

53 Ausbrüche zwischen 1970 und 2004 publiziert
insgesamt 458 Patienten analysiert

■ Mattner F, nosokomiale invasive Aspergillose

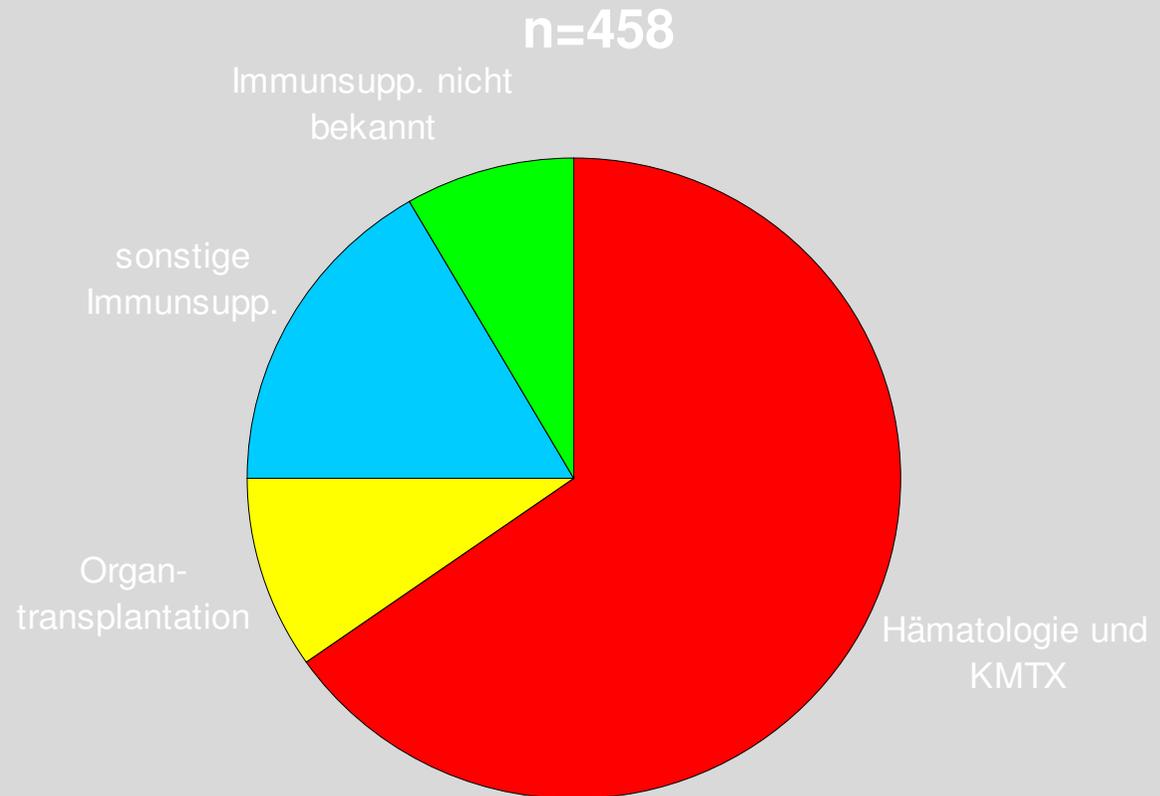
Mortalität

Hämatologie, Onkologie und KMTX	57,6 %	n = 299
Patienten nach Organtransplantationen	55,9 %	n = 44
sonstige Immunsuppression	52,3 %	n = 77
ohne bekannte Immunsuppression	39,4 %	n = 38
gesamt	55,0 %	n = 458

■ Mattner F, nosokomiale invasive Aspergillose

nosokomiale Aspergillose: Risikogruppen

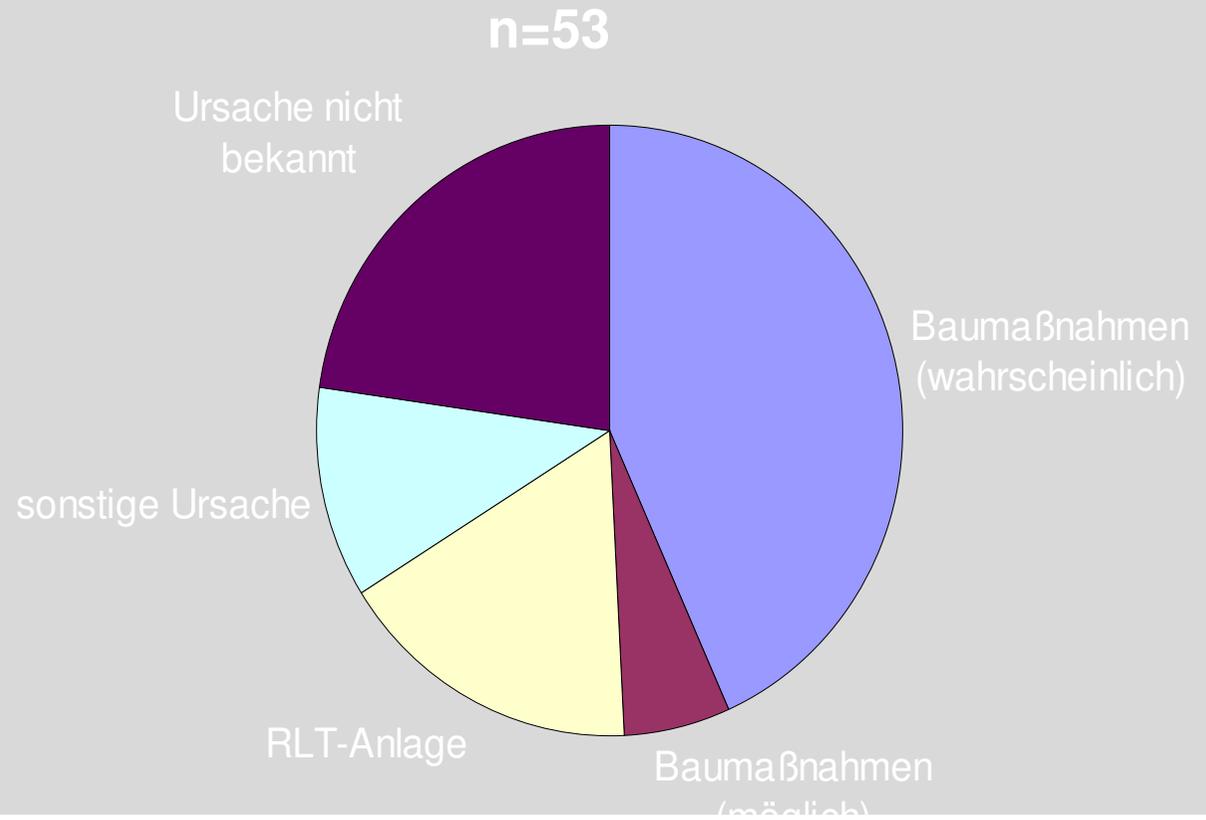
Hämatologie
KMTx
SOT
Intensivpatienten



■ Mattner F, nosokomiale invasive Aspergillose

Aspergillose: nosokomiale Ausbrüche „Ursachen“

Baumaßnahmen
RLT-Anlagen
„Sonstige“
unbekannt



■ Mattner F, nosokomiale invasive Aspergillose

**Beispiel INTERVENTION:
Successful control of an outbreak of invasive aspergillosis
in a regional haematology unit during hospital
construction works**

CAVE Bautätigkeit

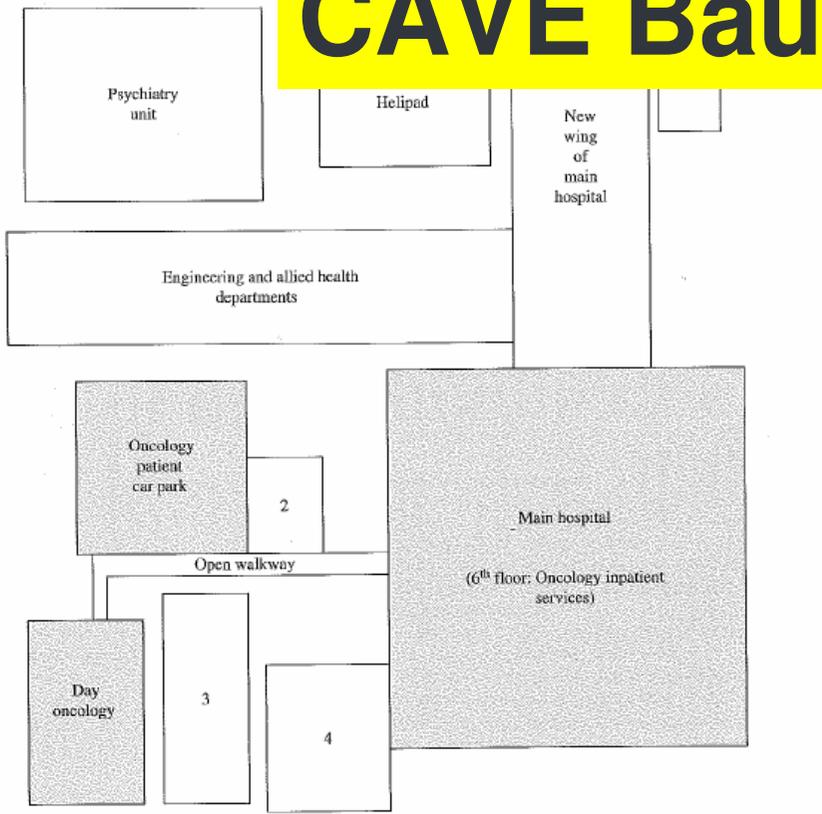


Figure 1 Schematic outline of hospital layout. (1) Endoscopy suite; (2) finance department; (3) library; (4) staff lounge.

-Klinik mit 40 Leukämie-

- Bautätigkeiten um die onkologische Tagesklinik herum bevor die Tagesklinik ins Haupthaus umziehen konnte
- Nach Auftreten von 5 Fällen Umzug ins Haupthaus und „Abschottung“
- Vorikonazol-Prophylaxe
- Ein autopsiebestätigter Todesfall

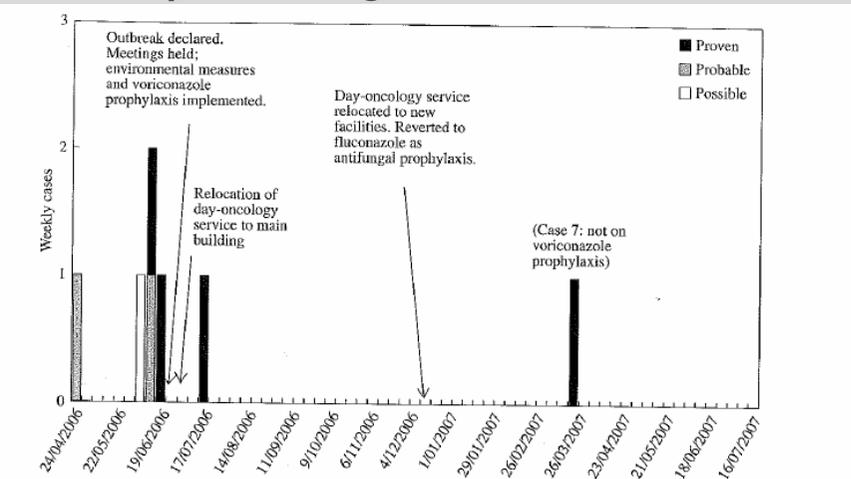


Figure 2 Timeline of invasive aspergillosis outbreak.

■ Mattner F, nosokomiale invasive Aspergillose

- Zwischen Aspergillus cutanen
- ein Fall der rd, UK;
- Positiv unter
- Nach Wasserreservoir von Inkubatoren typische Identität,
- Transmissionsweg: Töpfchen? Kontakt?
- Aufbereitung von Inkubatoren!!!

Ausbruch von invasiver Aspergillose (IA) (*A. fumigatus*) auf einer Intensivstation (Madrid, Spanien)

- Herzchirurgische Intensivstation 2006-2008
- Monatliche kulturelle Luftkeimmessungen mit Differenzierung und Quantifizierung von Schimmelpilzen, Isolate wurden aserviert.
- Auftreten von 7 proven und probable IA Fällen
- 5 lung infection, 1 medaistinitis, 1 lung infection plus mediastinitis), Motalität 85%
- 3 Pat. Herz-Transplantation, 2 Pat. Kortikosteroid-Therapie, 2 Pat. Diab. Mellitus
- Während Ausbruchphase 175, 50,25,20,160, 400 KBE/m³ Luft, davor und danach *A. fumigatus* nur vereinzelt (Median 0 KBE/m³); in 3 Patienten Isolate mit Patientenisolaten identisch
- Keine neuen Fälle nach adäquater Filtrierung (HEPA) der Luft der RLT Anlage der Intensivstation
- Conclusion: Überprüfung der Luftqualitäten auf Intensivstationen

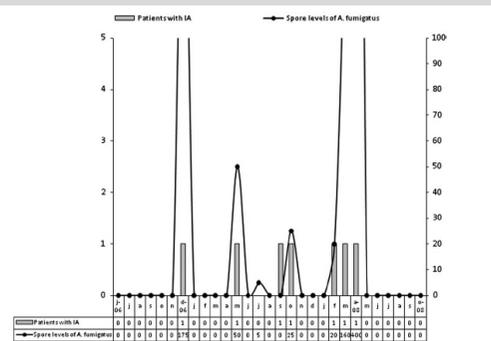


Figure 1. Spore levels of *Aspergillus fumigatus* in the major heart surgery intensive care unit and their relationship with the occurrence of invasive aspergillosis (IA).

TABLE 3. Diagnoses of the 10 patients, clinical samples with isolation of *Aspergillus fumigatus*, and number of different genotypes found^a

Patient	Diagnosis	No. of days of admission to unit	Clinical samples			
			Source	No.	No. of different genotypes	Genotype matching environmental genotype
1	Proven surgical wound IA ^b	31	Surgical wound (n = 8), bone biopsy specimen	9	2	Yes
2	Probable pulmonary IA	33	Bronchial aspirate (n = 4), protected brush catheter	5	1	No
3	Pulmonary colonization	10	Bronchial aspirate	3	4	No
4	Pulmonary colonization	18	Bronchial aspirate	1	2	No
5	Probable pulmonary IA	12	Bronchial aspirate	4	3	Yes
6	Pulmonary colonization	34	Bronchial aspirate	1	1	No
7	Probable pulmonary IA	79	Bronchial aspirate	3	2	Yes
8	Probable pulmonary IA	5	Sputum (n = 3), bronchial aspirate, protected brush catheter	5	3	No
9	Proven surgical wound IA	83	Surgical wound	3	3	No
10	Surgical wound colonization	50	Surgical wound	1	1	No

^a The presence of matches between environmental and clinical genotypes is also shown. Patients with proven/probable invasive aspergillosis are highlighted with shading.

^b IA, invasive aspergillosis.

Ausbruch von invasiver Aspergillose (IA) (*A. fumigatus*)
auf einer Intensivstation (Madrid, Spanien)

**CAVE ungewartete RLT-
Anlagen**



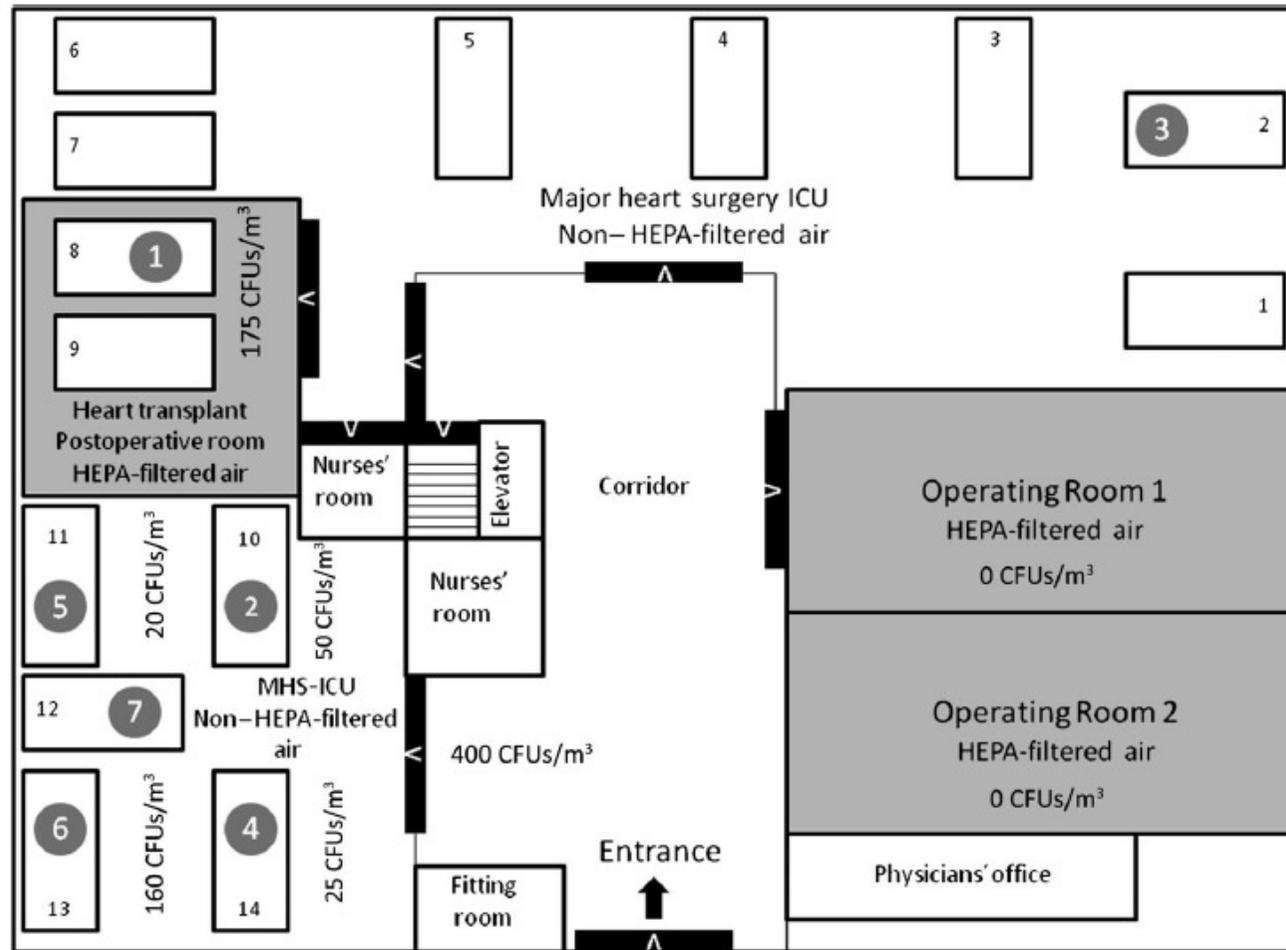
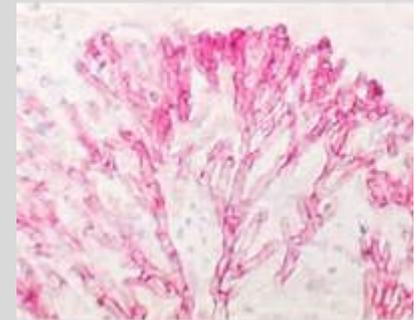


Figure 2. Map of the major heart surgery intensive care unit (MHS-ICU) showing the bed of the seven patients with invasive aspergillosis (circles) and *Aspergillus conidia* load. CFU, colony-forming unit; HEPA, high-efficiency particulate air.

Diagnose invasive Aspergillose

- **Schwierig!! dran denken!!**
- **Aspergillom: durch Immunreaktion abgekapselter Prozess, der KEINE invasive Aspergillose darstellt (z.B. Nasennebenhöhlenaspergillom, Aspergillom der Lunge, cerebrales Aspergillom????)**
- **Pulmonal: antibiotikaresistente Pneumonie**
- **Aspergillussepsis (im Blut kaum nachweisbar)**
- **ungehindertes Wachstum durch Gewebestrukturen**
- **mikrobiologische Kultur in der BAL/Bronchialsekret (Wiederholermaßen oder auch einmalig bei immunsupprimiertem Patienten)**
- **β -D-Glucan oder Gallaktomanan aus dem Blut oder Bronchialsekret/BAL**
- **Radiologische Befunde (Herde mit Halo, interstitielle Bilder)**
- **Biopsie/OP Materialien (Histologie in Pathologie)**



Purpose der Definitionen EORTC-Definitionen

During the past several decades, there has been a steady increase in the frequency of opportunistic invasive fungal infections (IFIs) in immunocompromised patients. However, there is substantial controversy concerning optimal diagnostic criteria for these IFIs. Therefore, members of the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group formed a consensus committee to develop standard definitions for IFIs for clinical research. On the basis of a review of literature and an international consensus, a set of research-oriented definitions for the IFIs most often seen and studied in immunocompromised patients with cancer is proposed. Three levels of probability are proposed: “proven,” “probable,” and “possible.” The definitions are intended for use in the context of clinical and/or epidemiological research, not for clinical decision making.

Definitions of Invasive Fungal Infections • CID 2002:34 (1 January)

Conclusions. These revised definitions of invasive fungal disease are intended to advance clinical and epidemiological research and may serve as a useful model for defining other infections in high-risk patients.

Definitions of Invasive Fungal Disease • CID 2008:46 (15 June)

Table 2. Criteria for probable invasive fungal disease except for endemic mycoses.

Host factors^a

Recent history of neutropenia ($<0.5 \times 10^9$ neutrophils/L [<500 neutrophils/mm³] for >10 days) temporally related to the onset of fungal disease

Receipt of an allogeneic stem cell transplant

Prolonged use of corticosteroids (excluding among patients with allergic bronchopulmonary aspergillosis) at a mean minimum dose of 0.3 mg/kg/day of prednisone equivalent for >3 weeks

Treatment with other recognized T cell immunosuppressants, such as cyclosporine, TNF- α blockers, specific monoclonal antibodies (such as alemtuzumab), or nucleoside analogues during the past 90 days

Inherited severe immunodeficiency (such as chronic granulomatous disease or severe combined immunodeficiency)

Clinical criteria^b

Lower respiratory tract fungal disease^c

The presence of 1 of the following 3 signs on CT:

Dense, well-circumscribed lesions(s) with or without a halo sign

Air-crescent sign

Cavity

Tracheobronchitis

Tracheobronchial ulceration, nodule, pseudomembrane, plaque, or eschar seen on bronchoscopic analysis

Sinonasal infection

Imaging showing sinusitis plus at least 1 of the following 3 signs:

Acute localized pain (including pain radiating to the eye)

Nasal ulcer with black eschar

Extension from the paranasal sinus across bony barriers, including into the orbit

CNS infection

1 of the following 2 signs:

Focal lesions on imaging

Meningeal enhancement on MRI or CT

Disseminated candidiasis^d

At least 1 of the following 2 entities after an episode of candidemia within the previous 2 weeks:

Small, target-like abscesses (bull's-eye lesions) in liver or spleen

Progressive retinal exudates on ophthalmologic examination

antibodies (such as alemtuzumab), or nucleoside analogues during the past 90 days

Inherited severe immunodeficiency (such as chronic granulomatous disease or severe combined immunodeficiency)

Clinical criteria^b

Lower respiratory tract fungal disease^c

The presence of 1 of the following 3 signs on CT:

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Sinonasal infection

Imaging showing sinusitis plus at least 1 of the following 3 signs:

Acute

Nasal

Exter

CNS infec

1 of the

Focal

Meni

Disseminated candidiasis

At least 1 of the following 2 entities after an episode of candidemia within the previous 2 weeks:

Small, target-like abscesses (bull's-eye lesions) in liver or spleen

Progressive retinal exudates on ophthalmologic examination

Mycological criteria

Direct test (cytology, direct microscopy, or culture)

Mold in sputum, bronchoalveolar lavage fluid, bronchial brush, or sinus aspirate samples, indicated by 1 of the following:

Presence of fungal elements indicating a mold

Recovery by culture of a mold (e.g., *Aspergillus*, *Fusarium*, *Zygomycetes*, or *Scedosporium* species)

Indirect tests (detection of antigen or cell-wall constituents)^e

Aspergillosis

Galactomannan antigen detected in plasma, serum, bronchoalveolar lavage fluid, or CSF

Invasive fungal disease other than cryptococcosis and zygomycoses

β -D-glucan detected in serum

EORTC Definitionen werden

Nicht-hämatologischen Patienten

nicht gerecht

ISHLT CONSENSUS STATEMENTS

A 2010 working formulation for the standardization of definitions of infections in cardiothoracic transplant recipients

Shahid Husain, MD, MS,^a Martha L. Mooney, MD, MS, FACP,^b Lara Danziger-Isakov, MD, MPH,^c Frauke Mattner, MD, PhD,^d Nina Singh, MD,^e Robin Avery, MD, FIDSA,^c Michael Ison, MD, MS,^f Atul Humar, MD, MSc,^g Robert F. Padera, MD, PhD,^h Leo P. Lawler, MD, FRCR,ⁱ Andy Fisher, PhD, FRCP,^j Richard J. Drew, MD,ⁱ Kate F. Gould, MBBS, MRCP, FRCP,^k Amparo Sole, MD, PhD,^l Sean Studer, MD, MSc,^m Patricia Munoz, MD,ⁿ Lianne G. Singer, MD, FRCPC,^a and Margaret Hannan, MD, FRCP, FRCPath,ⁱ for the ISHLT Infectious Diseases Council Working Group on Definitions

The Journal of Heart and Lung Transplantation, Vol 30, No 4, April 2011

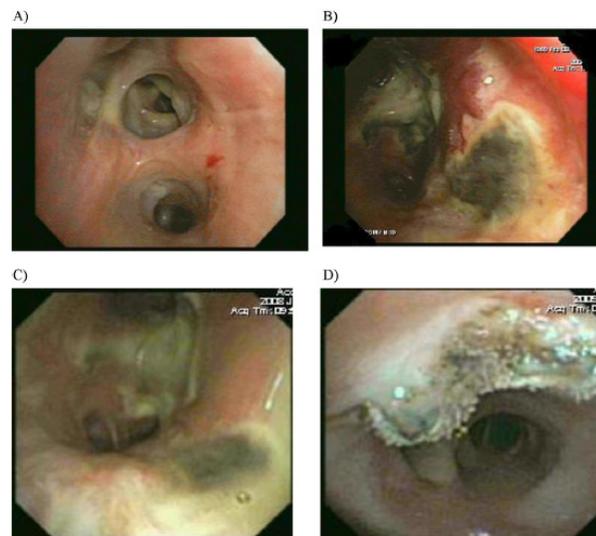


Figure 1 Presentations of tracheobronchitis (TrB) and bronchial anastomotic infection (BAI) in lung transplant recipients. (A) Normal bronchoscopy. (B) Bacterial tracheobronchitis. (C) Fungal tracheobronchitis. (D) Bronchial anastomotic infection.

Table 4c Fungal Bronchial Anastomotic Infection in Lung Transplant Recipients

Syndrome ^a	Signs/symptoms	Radiology	Laboratory
<p>Bronchial anastomotic infection</p> <p>Proven: Histology (biopsy showing histologic evidence of invasion by fungal hyphae or pseudohyphae) or positive culture from the sterile tissue <i>ALONE</i>; <i>OR</i> with sign/symptoms + radiology + laboratory</p> <p>Probable: Sign/symptoms + radiology + laboratory + negative histology</p>	<p>At least one of the following:</p> <ul style="list-style-type: none"> ● New onset of purulent sputum <i>OR</i> change in character <i>OR</i> quantity of sputum <i>OR</i> respiratory secretions suctioned ● New-onset or worsening cough, dyspnea, tachypnea, or bronchial breath sounds <p><i>AND</i> endobronchial lesions restricted to the site of anastomosis without clinical or histologic involvement of other parts of bronchial tree or lung parenchyma (Figure 1b)</p>	<p>Chest radiograph without:</p> <ul style="list-style-type: none"> ● New or progressive and persistent infiltrate ● Consolidation ● Cavitation ● Nodules <p><i>OR</i> CT scan without:</p> <ul style="list-style-type: none"> ● New or progressive and persistent infiltrate ● Consolidation ● Cavitation ● Nodules 	<p>Single positive culture for mold in BAL <i>OR</i> single positive PCR for mold in BAL <i>OR</i> positive galactomannan in the BAL <i>OR</i> at least TWO positive sputum cultures/PCRs of fungal organisms (excluding <i>Candida</i> species)</p>

^aIn the absence of biopsy categorize as probable: In the presence of histologic findings of both acute rejection and fungal invasion it should be classified as acute rejection with proven fungal infection.

Fast alle IA Fälle immunsupprimiert!!!

Seven-year surveillance of nosocomial invasive aspergillosis in a French University Hospital

Cécile Garnaud ^{a,*}, Marie-Pierre Brenier-Pinchart ^{a,b},
Anne Thiebaut-Bertrand ^c, Rebecca Hamidfar ^d, Jean-Louis Quesada ^e,
Annick Bosseray ^f, Bernadette Lebeau ^a, Marie-Reine Mallaret ^{g,b},
Danièle Maubon ^{a,b}, Christel Saint-Raymond ^h, Claudine Pinel ^{a,b},
Virginie Hincky ⁱ, Dominique Plantaz ^{b,j}, Muriel Cornet ^{a,b}, Hervé Pelloux ^{a,b}

Table 1 Characteristics of the 70 patients with a proven or a probable invasive aspergillosis.

	Total (n)	IA type		Age Median [IQR]	Gender Men/ women (n/n)	Origin			First-line treatment			Mortality		
		Proven (n)	Probable (n)			Nosocomial n (%)	Community- acquired n (%)	Undetermined n (%)	Monotherapy n (%)	Bitherapy n (%)	No treatment n (%)	3-month n/n	1-year n/n	
Host factors ^{a,b}														
Neutropenia	40	2	38	55 [46.5–62.2]	28/12	14 (35.0)	11 (27.5)	15 (37.5)	23 (57.5)	11 (27.5)	1 (2.5)	18/37	25/34	
Allogeneic HSCT	11	1	10	55 [30–58]	7/4	3 (27.3)	5 (45.4)	3 (27.3)	5 (45.4)	5 (45.4)	0 (0)	7/10	9/10	
Use of corticosteroids	32	3	29	59 [54.2–62.2]	25/7	9 (28.1)	15 (46.9)	8 (25)	16 (50)	11 (34.4)	2 (6.2)	17/31	22/29	
Immunosuppressants	20	1	19	58 [41.8–61]	13/7	7 (35)	7 (35)	6 (30)	11 (55)	8 (40)	0 (0)	9/19	11/19	
Inherited immune disorder	2	1	1	36 [32–40]	1/1	0 (0)	2 (100)	0 (0)	0 (0)	1 (50)	1 (50)	1/2	2/2	
All patients	70	5	65	58 [47.5–63]	50/20	21 (30)	27 (38.6)	22 (31.4)	39 (55.7)	21 (30)	4 (5.7)	34/66	45/62	

IA: Invasive Aspergillosis, HSCT: Haematopoietic Stem Cell Transplant, IQR: interquartile range.

^a According to Ref.²⁷

^b Patients may have more than one host factors.

**Warum traten keine IA in anderen
Klinikumsbereichen auf???**

RESEARCH ARTICLE

Open Access

Five-years surveillance of invasive aspergillosis in a university hospital

Karolin Graf^{1*}, Somayeh Mohammad Khani^{1†}, Ella Ott^{1†}, Frauke Mattner^{1,2†}, Petra Gastmeier^{1,3†}, Dorith Sohr^{3†}, Stefan Ziesing^{1†} and Iris F Chaberny^{1†}

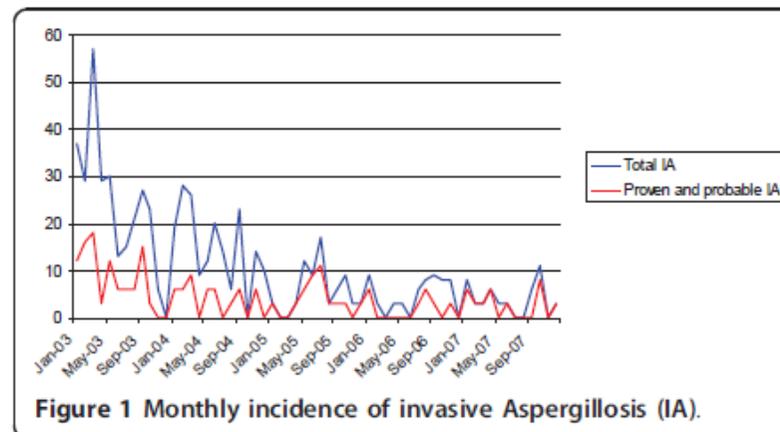
Table 1 Cases found through indicators and IA cases resulting (with each method)

	all cases	cases with one indicator		cases with two indicators			cases with three indicators
		M*	PA*	M, PH*	M, PA*	PH, PA*	M, PH, PA*
no IA	490	231	6	253	-	-	-
proven IA	56	3	6	17	13	2	15
probable IA	25	6	-	17	-	1	1
possible IA	133	45	-	88	-	-	-

* M = Microbiological indicator, PA = Pathological indicator, PH = Pharmacological indicator

Table 2 Incidence densities of IA

Year	# of cases (proven and probable)	# of patient days	incidence density (per 100,000 patient days)	95% CI	p-value (vs. 2003)
2003	32	391.445	24	5.59; 11.54	-
2004	16	407.007	15	2.25; 6.38	0.008
2005	15	407.644	6	2.06; 6.07	0.427
2006	7	415.980	5	0.68; 3.47	0.044
2007	11	431.954	4	1.27; 4.56	0.804



36 von 81 Patienten (=44%) waren nicht transplantiert und hatten keine immunsuppressive Therapie!!

Table 3 Underlying diseases for all confirmed cases of invasive aspergillosis

underlying diseases	proven + probable n = 81	possible n = 133	total (%) n = 214
hematological diseases	17 (38%)	55 (41%)	72 (34%)
organ transplantation	39 (49%)	55 (41%)	94 (44%)
single lung transplantation	1	2	3
double lung transplantation	13	23	36
liver transplantation	9	12	21
heart transplantation	4	2	6
heart-lung transplantation	3	3	6
renal transplantation	4	0	4
stem cell transplantation	4	13	17
pancreas transplantation	1	0	1
liver diseases	12	14	26
lung diseases	15	31	4
kidney diseases	4	4	8
heart diseases	4	1	5
heart and lung diseases	3	5	10
pancreas diseases	1	0	1
malignancy (solid tumor)	10 (22%)	6 (5%)	15 (7%)
human immunodeficiency virus	0	0	0
immunosuppressive treatment	73 (85%)	117 (88%)	190 (89%)

Graf et al. *BMC Infectious Diseases* 2011, **11**:163
<http://www.biomedcentral.com/1471-2334/11/163>

 Mattner F, nosokomiale invasive Aspergillose

Table 4 Underlying diseases for proven and probable cases of invasive aspergillosis (IA) without transplantation or primary immunosuppression

underlying diseases/therapy	proven + probable IA n = 81	total (all proven and probable cases) (%)
tumor diseases	10	12.3%
colorectal cancer (colectomy, rectal resection)	4	4.9%
gastric cancer (gastrectomy)	2	2.5%
cholangiocarcinoma (tumor resection)	1	1.2%
hepatocellular carcinoma	2	2.5%
renal carcinoma (nephrectomy)	1	1.2%
other diseases	26	32.5%
gastroenterologic diseases	10	12.3%
necrotizing enterocolitis	1	1.2%
necrotizing pancreatitis	2	2.5%
chronical hepatitis B infection	3	3.7%
liver cirrhosis	3	3.7%
citrullinaemia	1	1.2%
prematurity	1	1.2%
heart diseases	4	4.9%
congenital heart disease	1	1.2%
dilatative cardiomyopathy	2	2.5%
endocarditis	1	1.2%
vascular diseases	1	1.2%
type B dissection (stent implantation)	1	1.2%
renal diseases	4	6.2%
renal insufficiency	4	4.9%
other diseases	5	6.2%
multiple trauma	3	3.7%
sinusitis maxillaris	2	2.5%

Wer sucht, der findet...

13% aller IA sind lediglich in der Autopsie nachgewiesen worden

- **Geschlossene Räume (Fenster, Türen)**
- **Erhöhte Luftwechselzahl (> 15 pro h)**
- **Dreistufig gefilterte Luft (0,3 µm)**
- **Positiver Druck (10 % mehr Zuluft als Abluft)**
- **Gerichteter Luftstrom**



- **Personaltraining**
- **Surveillance der Fälle**
- **Zimmer mit Luftfiltration und gerichtetem Luftstrom**
- **Vermeidung von stauberzeugenden Tätigkeiten**
- **Besonderer Schutz bei Betreten von Bereichen ohne Luftfiltration (FFP2 Maske bei starker Immunsuppression)**

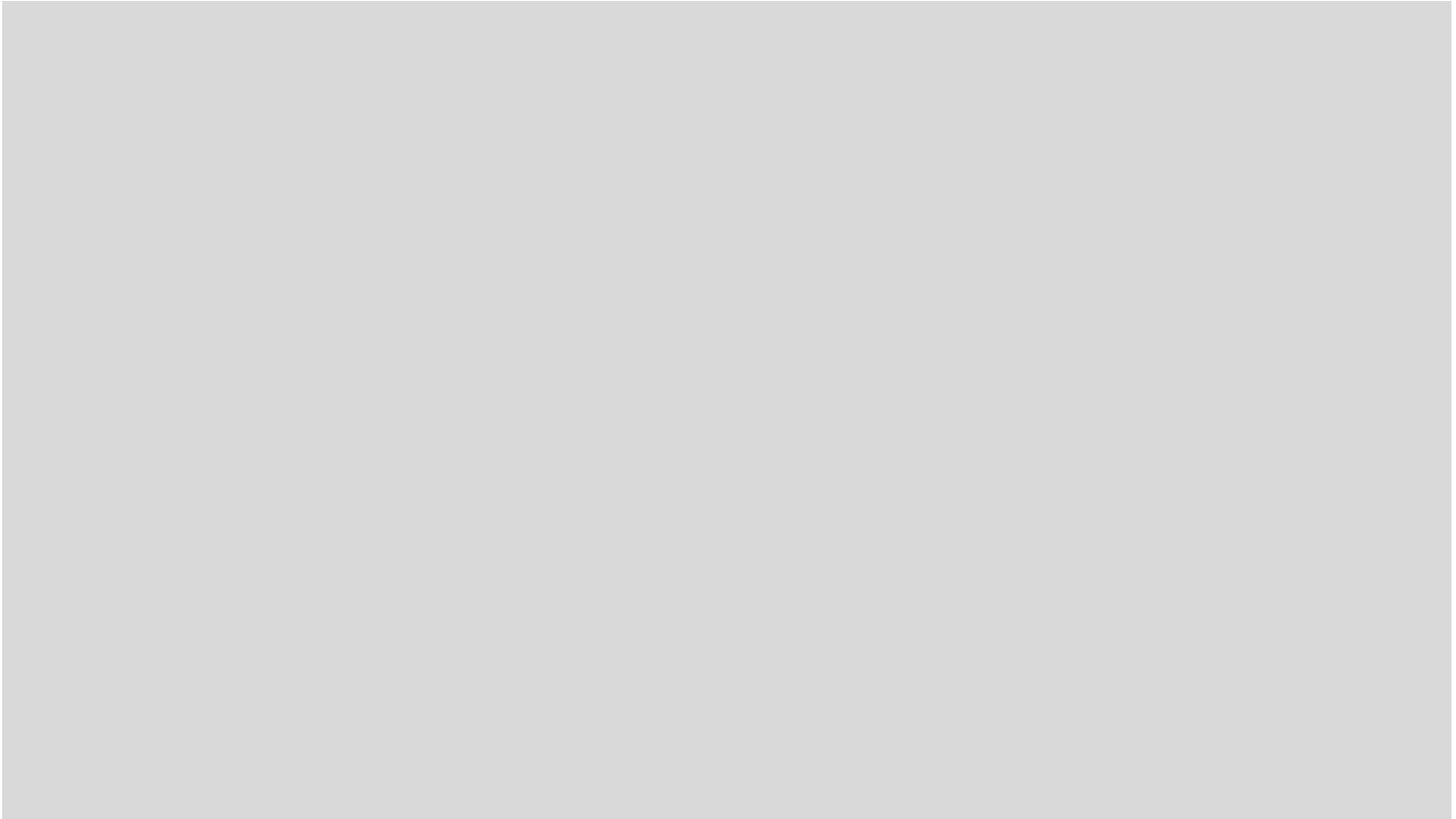


• Protective environment

- Zimmer mit Unterdruck
- Versiegelte desinfizierbare Flächen
- Staubfreiheit (Reinigung/Desinfektion feucht durchzuführen)
- Keine Pflanzen, keine Blumen
- Keine Kartonagen, keine Papiertücher
- Keine rohen Lebensmittel, keine Gewürze
- Keine unabgeschotteten Baustellen
- Tragen einer FFP 2 Maske bei Transporten durch das Haus
- Mitarbeiter tragen Kleidung ohne Schimmelpilzsporen (CAVE Raucher im Sommer-Herbst)
- Fenster geschlossen! Keine Fenster-Türen in den benachbarten Räumen nach außen öffnen

ZUSAMMENFASSUNG

- **Nosokomiale IA kommen recht häufig vor und nur zu ca. 55% bei Immunsupprimierten/Transplantierten**
- **Bei Immunsupprimierten kommt die IA sehr häufig vor**
- **Nosokomiale Ausbrüche können auf Fensterlüftungen, unabgeschottete Baustellen, unzureichende RLT-Anlagen oder auch kontaminierte Wasserreservoirie zurückführbar sein.**
- **Spezifische Präventionsmaßnahmen:
PROTECTIVE ENVIRONMENT**
- **„WEIT VORHER“ DARAN DENKEN.....NICHT ERST BEI DER DIAGNOSEFINDUNG EINES PATIENTEN**



Surveillance nosokomialer IA an einem Universitätsklinikum in Frankreich

- Prospektive Surveillance von 2003 bis 2009 durchgeführt
- Verwendung von EORTC/MSG Kriterien
- 5 proven und 65 probalbe IA festegestellt
- 74% der Patienten hatten maligne Erkrankungen
- 49 Fälle waren bestanden bereits bei Aufnahme, 21 waren nosokomiale Fälle
- Alle 21 nosokomialen Fälle traten auch in Räumen ohne RLT-Anlage oder ohne Luftdekontamination bzw. in der Nähe von Bauarbeiten.
- Die 3-Monats Überlebensrate war in beiden Gruppen 50%.