UMC St Radboud

Nijmegen University Centre for Infectious Diseases

The revised EORTC/MSG definitions - DEF II

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- Why revise?
- The process
- Definitions I I

- **Why revise?**
- **The process**
- **Definitions I I**

EORTC-IFICG & NIAID-MSG

Defining Opportunistic Invasive Fungal Infections in Immunocompromised Patients with Cancer and Hematopoietic Stem Cell Transplants: An International Consensus

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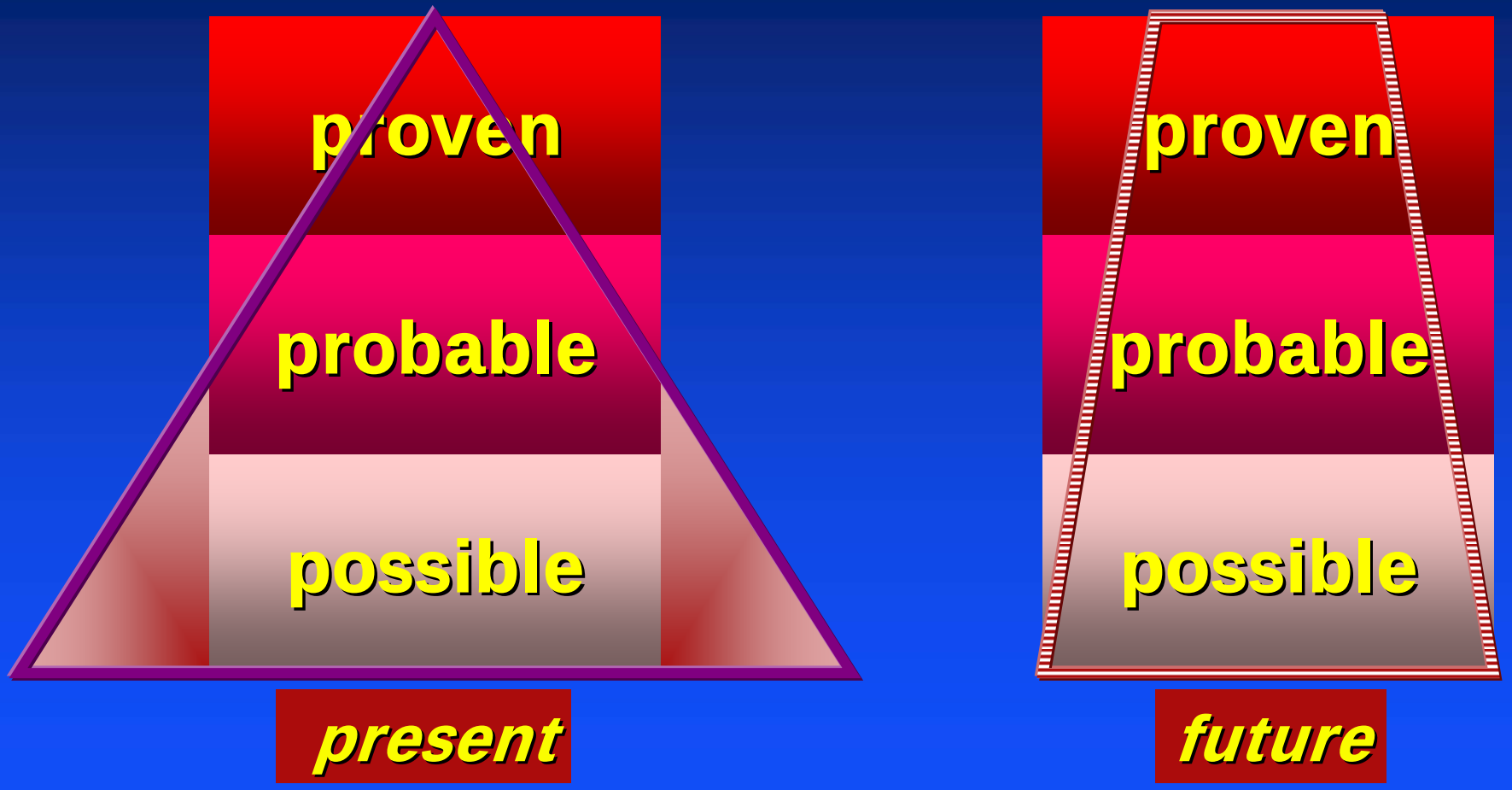
[1]European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group, Brussels; and [2]National Institute of Allergy and Infectious Diseases Mycoses Study Group, National Institutes of Health, Bethesda, Maryland

Clinical Infectious Diseases 2002;34:7–14

GOAL OF ADAPTING DEFINITIONS



Problems with Definitions I

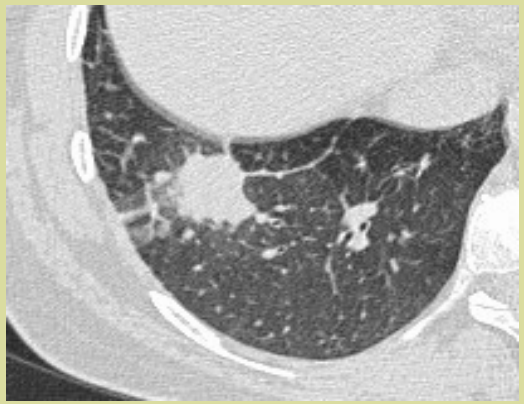
EORTC/MSG definitions - aspergillosis

Host factor

HSCT

+

Clinical features



Halo sign on CT scan

+

Mycology

antigenaemia

Probable

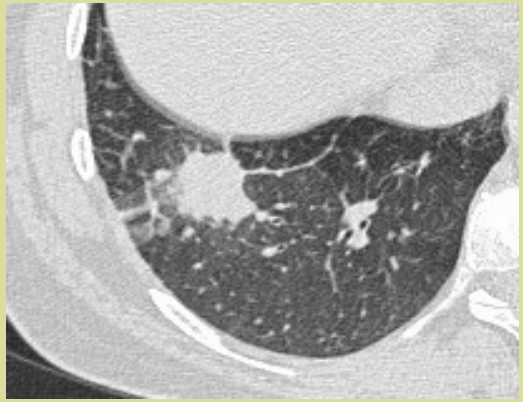
EORTC/MSG definitions - aspergillosis

Host factor

HSCT

+

Clinical features



Halo sign on CT scan

+

Mycology

none

possible

Question

Host factor

neutropenic

+

Clinical features

Halo sign on pulmonary CT

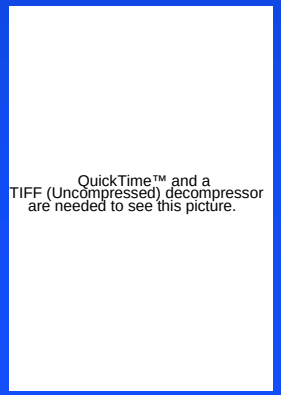
+

Mycology

Blood & BAL: Galactomannan negative

Blood: PCR positive

Diagnosis?



Question

1. **The patient has a possible invasive aspergillosis.**
2. **The patient has a probable invasive aspergillosis.**
3. **The patient has a proven invasive aspergillosis.**
4. **The patient has a possible invasive fungal infection.**

Answer

Host factor → neutropenic

\+

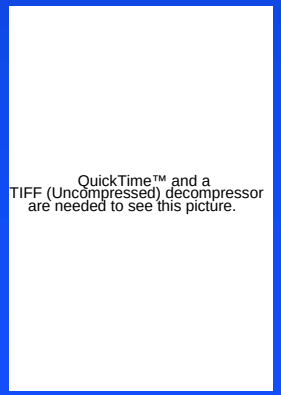
Clinical features → Halo sign on pulmonary CT

\+

Mycology → *Blood & BAL: Galactomannan negative*

~~*Blood: PCR positive*~~

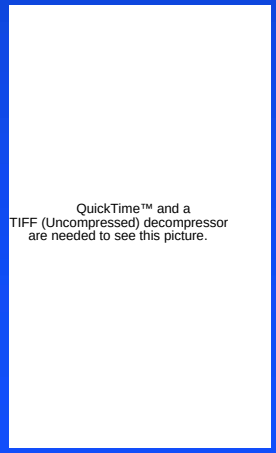
possible invasive fungal infection



- Why revise?
- The process
- Definitions I I

ICAAC 43 Chicago 2003 - working parties

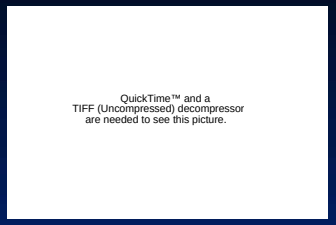
Group	Task
Candidiasis	to propose new criteria for candidaemia
Aspergillosis and infections due to other moulds	to examine imaging and galactomannan, and BAL samples
Cryptococcosis	to review the criteria
Endemic mycoses	to review the criteria



ICAAC 43 Chicago 2004 - working parties

Group	Task
Candidiasis	-
Aspergillosis and infections due to other moulds	-
Cryptococcosis	-
Endemic mycoses	completed

QuickTime™ and a
TIFF (Uncompressed) decompressor
are needed to see this picture.



The best laid schemes o' Mice an' Men,

Gang aft agley,

An' lea'e us nought but grief an' pain,

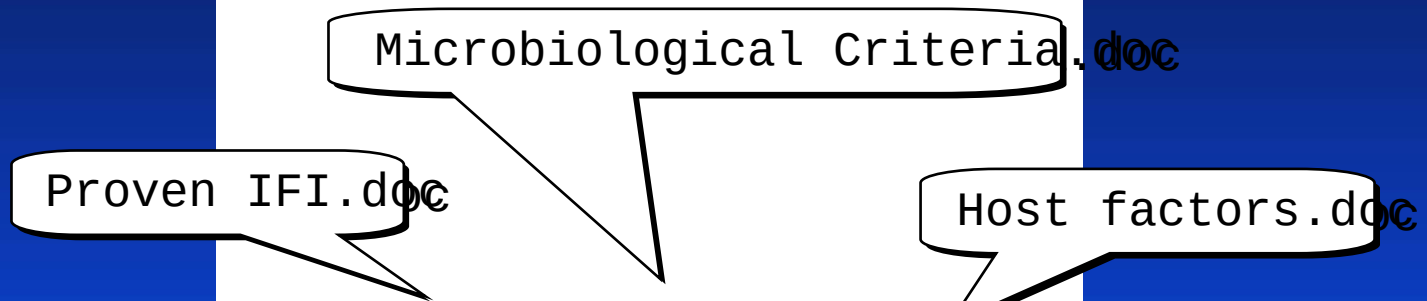
For promis'd joy!

(The best laid schemes of Mice and Men
oft go awry,
And leave us nothing but grief and pain,
For promised joy!)

Robert Burns (1759 - 1796) To a Mouse

Head to head

Plan B



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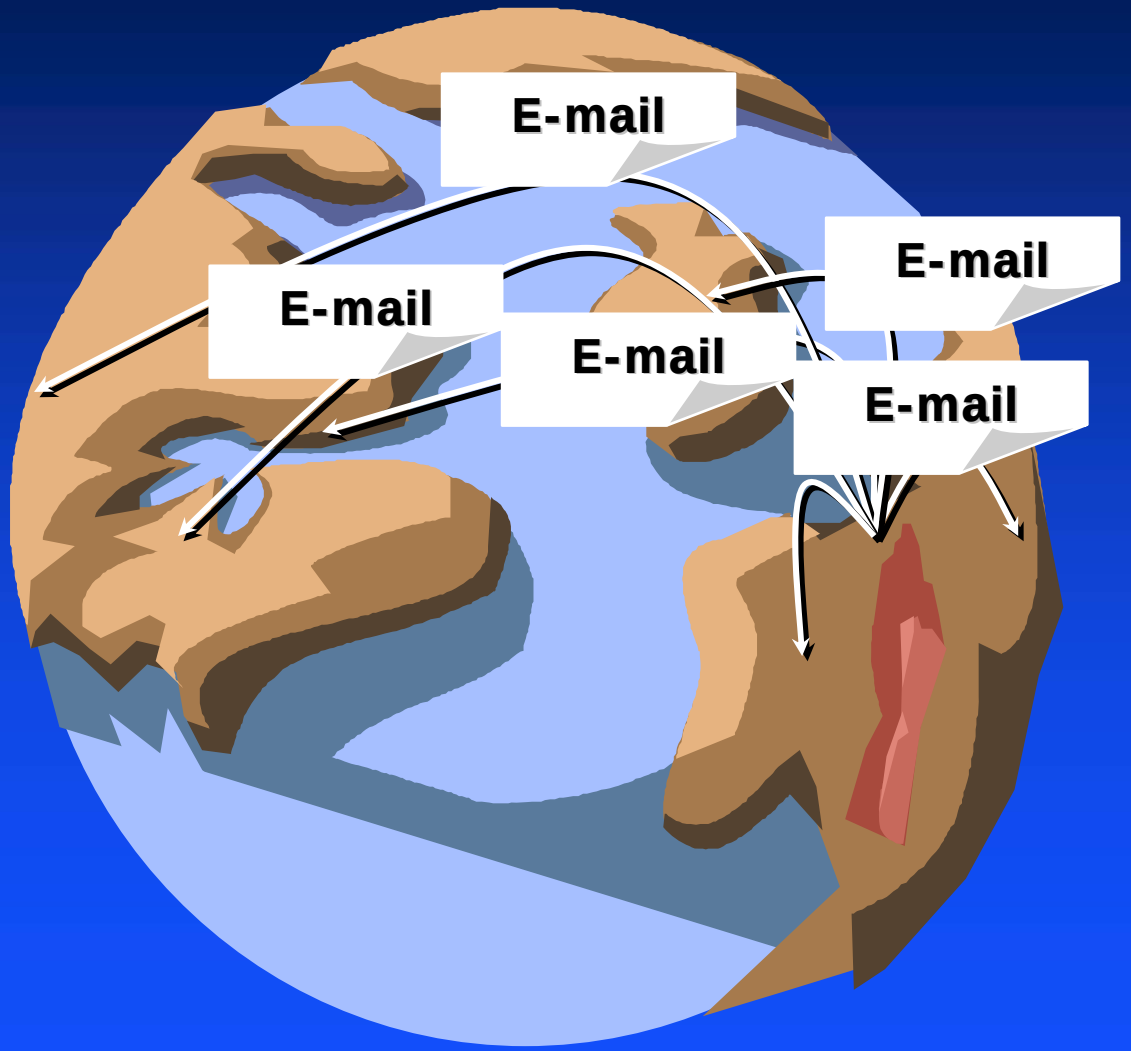
Round 1



Round 2

QuickTime™ and a
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Definitions II process


QuickTime™ and a
TIFF (Uncompressed) decompressor
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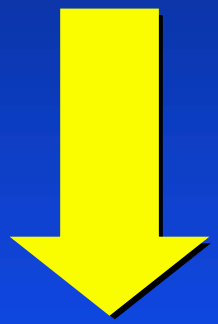
- Why revise?
- The process
- Definitions I I

First change

Whats's in a name?

Invasive Fungal Infection

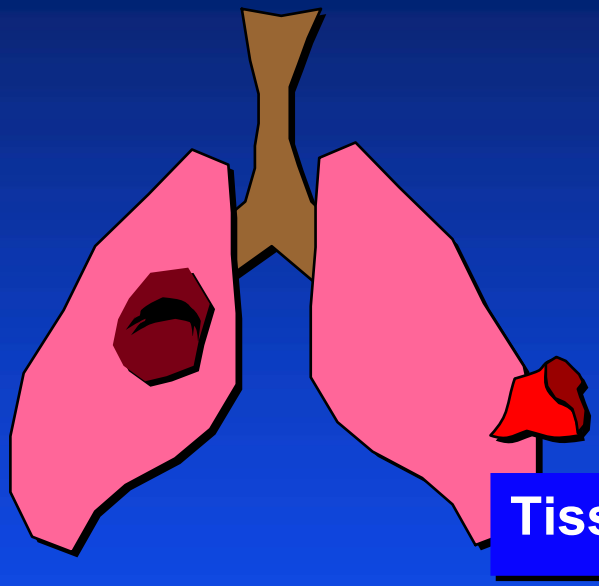


Invasive Fungal Disease

No change

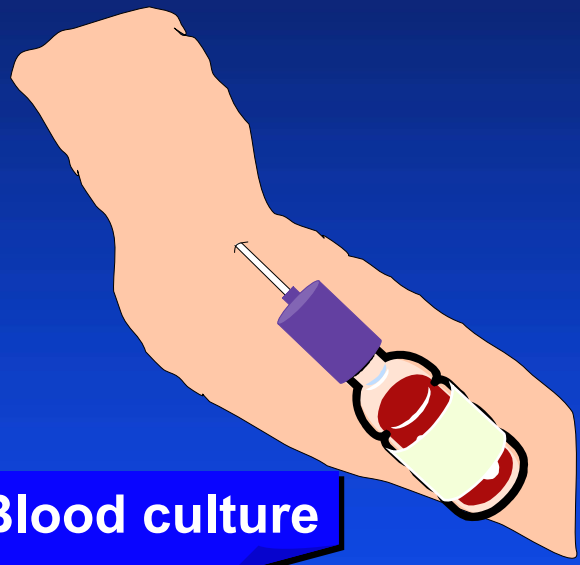
Proven invasive fungal infective disease

histology



Tissue

Mycology



Blood culture

culture

ICAAC 43 Chicago 2003

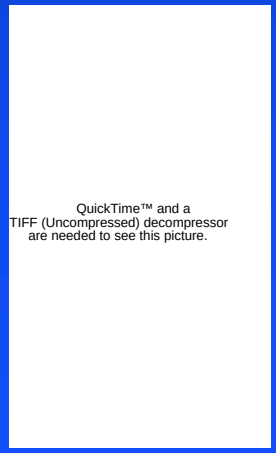
definitions for proven IFI

e.g.

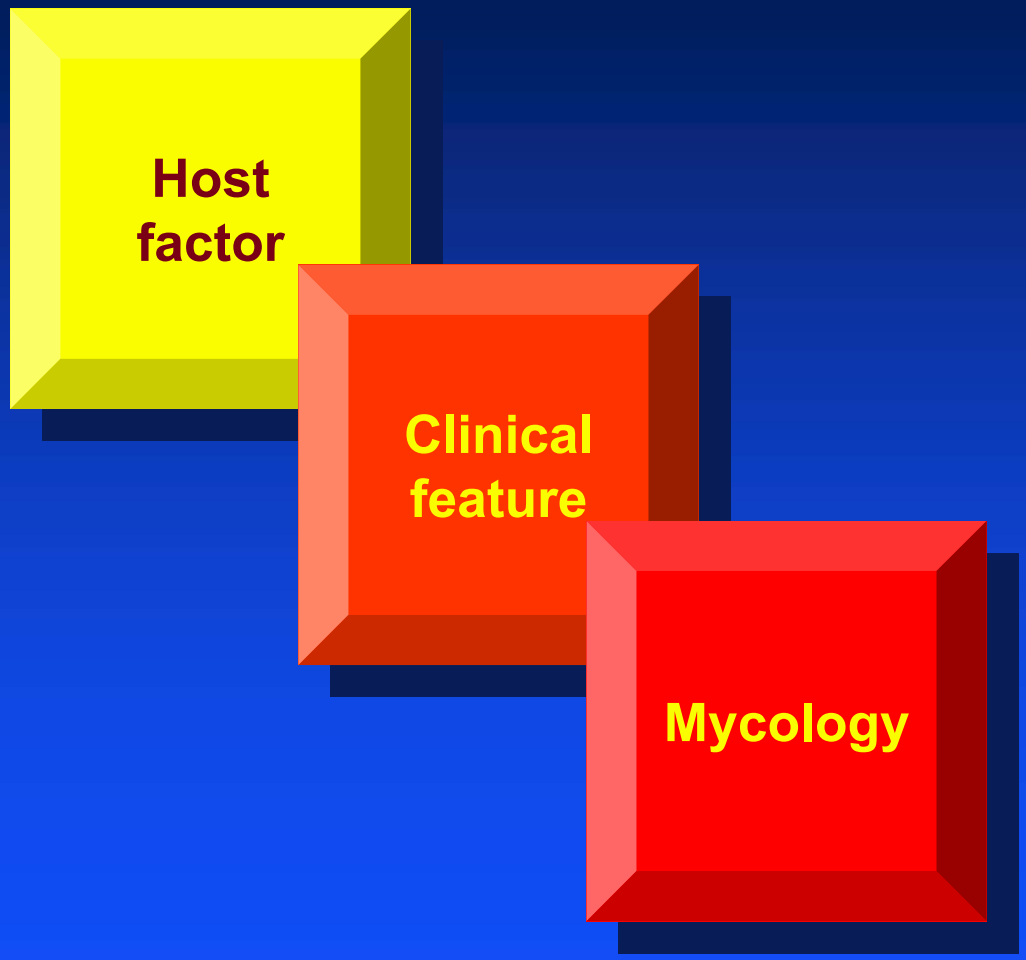
1. **mould detected histologically**
2. **not recovered by culture**
3. **galactomannan antigen is detected**

proven mycosis

probably aspergillosis

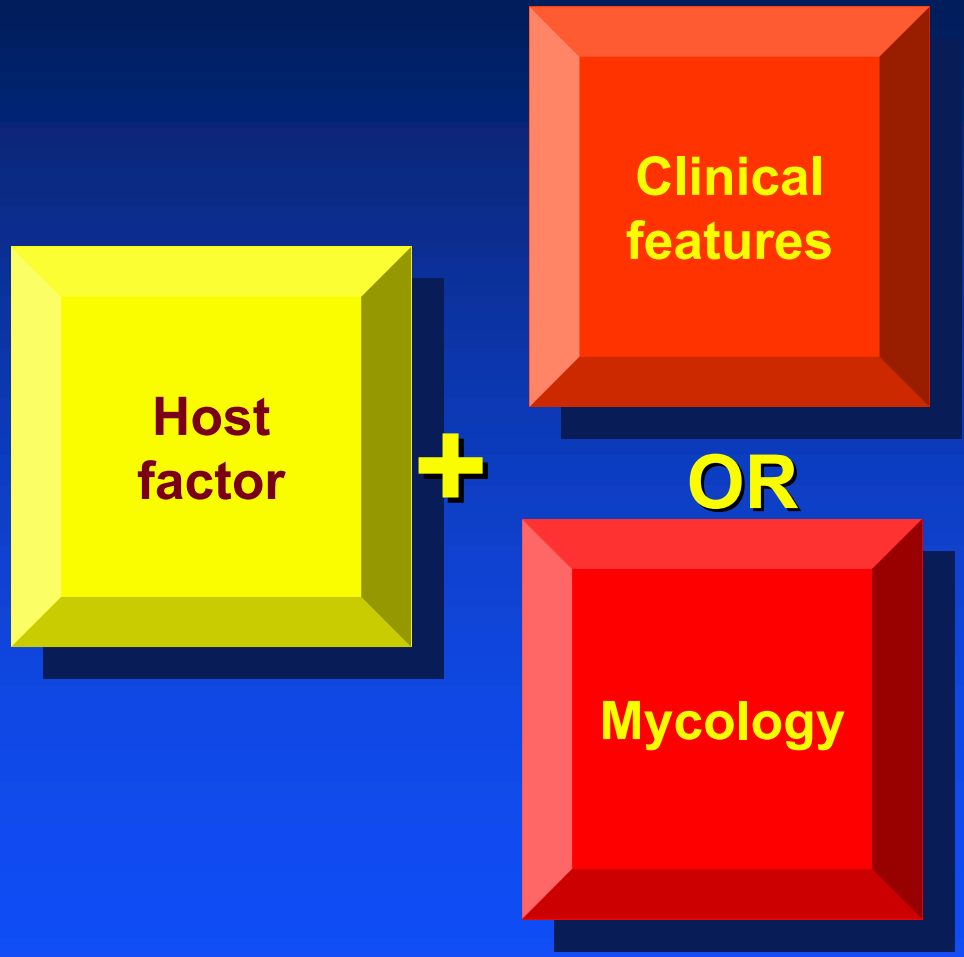


Defining probable invasive fungal disease



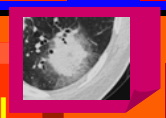
Second change

Definitions I - Possible invasive fungal disease



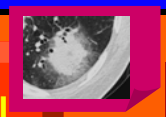
Invasive fungal disease - Definitions I

Host factors	+	Clinical features	+	Mycology (tissue)	=	**Proven**
Host factors	+	Clinical features	+	Mycology	=	**Probable**
Host factors	+	Clinical features		Negative or Not done	=	**Possible**
Host factors	+	Clinical features		Negative or Not done	=	**Possible**
Host factors	+	none		Mycology	=	**Possible**
Host factors		none		Negative or Not done	=	**Not classified**



Invasive fungal disease - Definitions II

Host factors	+	Clinical features	+	Mycology (tissue)	=	**Proven**
Host factors	+	Clinical features	+	Mycology	=	**Probable**
Host factors	+	Clinical features		Negative or Not done	=	**Possible**
Host factors	+	Clinical features		Negative or Not done	=	**Possible**
Host factors	+	none		Mycology	=	**Not classified**
Host factors		none		Negative or Not done	=	**Not classified**



Invasive fungal disease - Definitions II

Host factors	+	Clinical features	+	Mycology (tissue)	=	**Proven**
Host factors	+	Clinical features	+	Mycology	=	**Probable**
Host factors	+	Clinical features		Negative or Not done	=	**Possible**
Host factors	+	Clinical features		Negative or Not done	=	**Not classified**
Host factors	+	none		Mycology	=	**Not classified**
Host factors		none		Negative or Not done	=	**Not classified**

Definitions II - Possible invasive fungal disease

Host factor + Clinical features

Characteristic of invasive fungal disease
BUT
no mycological evidence

Third change

Definitions I - Host factors

neutropenia

> 3 weeks corticosteroids

<36°C or > 38°C and
- prior mycosis
- AIDS
- Immunosuppressive drugs
- > 10 days neutropenia

> 4 days unexplained fever despite broad spectrum antibiotics

Graft versus Host Disease

Host factor

Definitions II - Host factors

neutropenia

> 3 weeks corticosteroids

<36°C or > 38°C and
- prior mycosis
- AIDS
- Immunosuppressive drugs
- > 10 days neutropenia

> 4 days unexplained fever despite broad spectrum antibiotics

Graft versus Host Disease

Host factor

neutropenia

> 3 weeks corticosteroids

Allogeneic HSCT recipient

Treatment with other recognized T-cell immune suppressants

Inherited severe immunodeficiency

Fourth change

Definitions I - Clinical features

MAJOR

≥ 1

Clinical feature

Lower respiratory tract infection

Halo sign
Air-crescent sign
cavity

Sinonasal infection

Radiological evidence

CNS infection

Radiological evidence

Chronic disseminated candidiasis

Bull's eye lesions in liver or spleen

Disseminated fungal infection

Unexplained papular or nodular skin lesions
Chorioretinitis
endophthalmitis

Definitions I - Clinical features

MINOR

≥ 2

Lower respiratory tract infection

Cough, chest pain, haemoptysis, dyspnoea
Physical finding of pleural rub
Any new infiltrate not fulfilling major criterion

CNS infection

CSF
- No pathogens
- no malignant cells
- abnormal biochemistry
- abnormal cell count

Focal neurological
- seizures
- hemiparesis
- cranial nerve palsy

Mental changes
Meningeal irritation

Clinical feature

Sinonasal infection

Nasal discharge. stuffiness
Nose ulceration. eschar or epistaxis
Periorbital swelling
Maxillary tenderness
Black necrotic lesions or perforation of the hard-palate

Definitions II - Clinical features

Lower respiratory tract infection

Chronic disseminated candidiasis

Sinonasal infection

Clinical feature

CNS infection

No more major and no more minor
All in the same key now

Definitions II - Clinical features

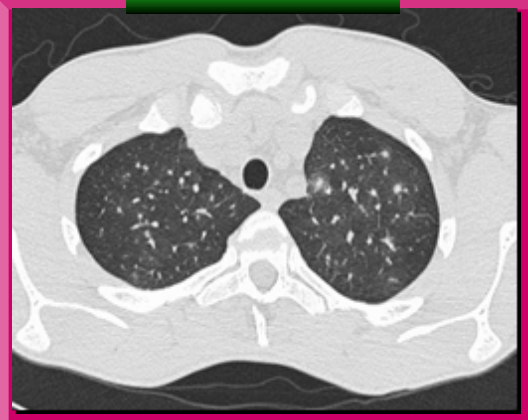
Lower respiratory tract infection

A) the presence of one of the following "specific" imaging signs on CT:-

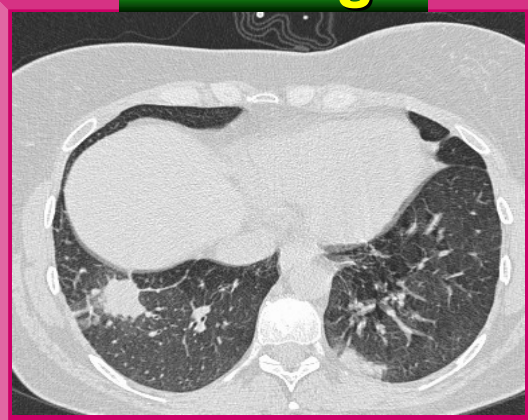
- **Well defined nodule(s) with a halo sign**
- **Well defined nodule(s) without a halo sign**
- **Wedge-shaped infiltrate**
- **Air crescent sign**
- **Cavity**

Specific pulmonary infiltrates on CT scan

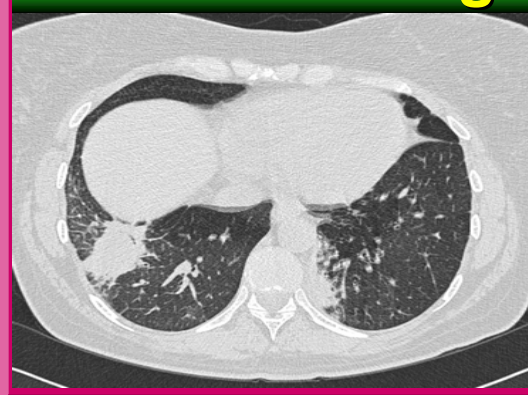
nodules



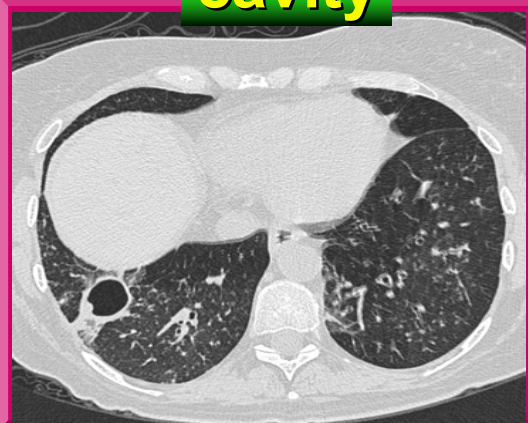
halo sign



air crescent sign



cavity



Definitions II - Clinical features

Lower respiratory tract infection

B) the presence of a new non-specific focal infiltrate

PLUS at least one of the following:-

- **Pleural rub**
- **Pleural pain**
- **Hemoptysis**

Definitions II - Clinical features

sinonasal infection

Imaging showing sinusitis

PLUS

at least one of the following:-

- **Acute localized pain (including pain radiating to eye)**
- **Nasal ulcer, black eschar**
- **Extension from the paranasal sinus across bony barriers, including into the orbit**

Definitions II - Clinical features

CNS infection

at least one of the following:-

- **Focal lesions on imaging**
- **Meningeal enhancement on MRI or CT**

Definitions II - Clinical features

Chronic disseminated candidiasis

Small, peripheral, target like abscesses (new nodular filling defects, bull's-eye lesions) in liver and/or spleen

Fifth change

Definitions I - Mycology

Culture of mould from tissue. aspirate BAL or sputum

antigen in blood, BAL. CSF

mould seen in sinus aspirate

Fungi seen in tissue or sterile body fluids

Definitions II - Mycology

Culture of mould from tissue. aspirate BAL or sputum

antigen in blood, BAL. CSF

Mycology

mould seen in sinus aspirate

Beta-D-glucan in BAL. CSF or blood

Fungi seen in tissue or sterile body fluids

PCR to detect nucleic acid

Not until a PCR system is developed that has been externally validated for blood, tissue, or BAL fluid

EORTC/MSG
Definitions for invasive fungal disease

Thanks
To the consensus group
To the organizers
And to you the audience