

Bacterial and fungal infections after HCT



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Oh, I would like to eat such
a Beibe, oh, I would like!

OJ, ZZARŁOBY SIĘ TAKIE
STWORZONKO, OJ, ZZARŁO!



A handwritten signature or mark, possibly the artist's name, located in the bottom right corner of the page. It consists of stylized, overlapping lines.

Solution of the problem of bacterial and fungal infections...

- ◆ Is critical for achieving survival of patients undergoing transplantation of hematopoietic cells.
- ◆ It is because one of the characteristic features of these patients is **transient or chronic depression of immunity.**

What are the enemies?

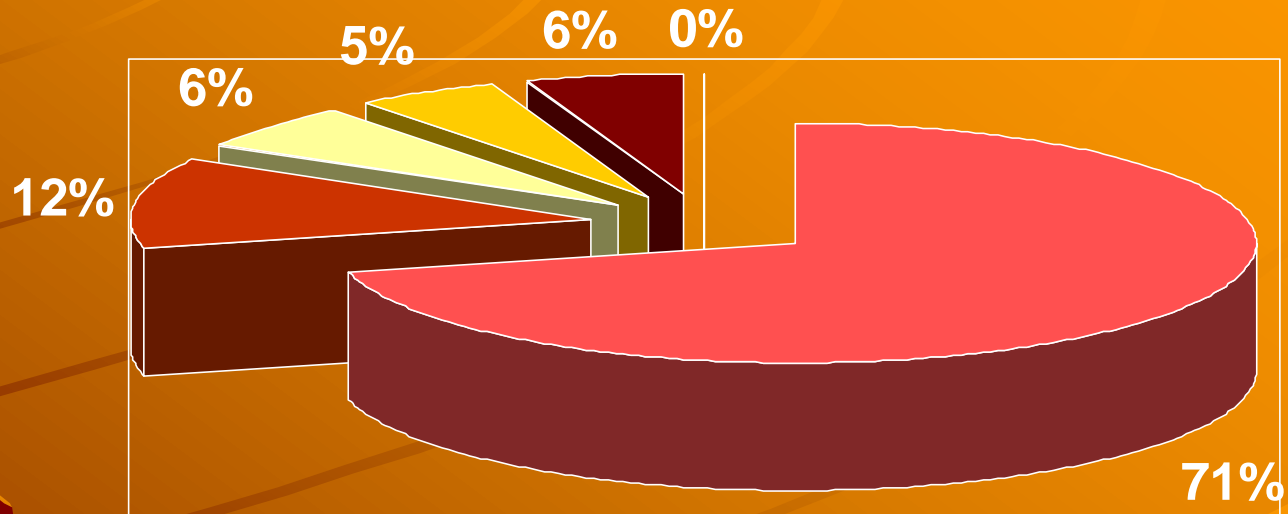
✦ Bacteria


- Gram positive: Staph. Aureus, epidermis, Streptococcus, Corynebacterium sp.
- Gram negative: E. coli, Klebsiella pneumoniae, Pseudomonas, Proteus, Enterobacter

✦ Fungi

- Yeast: Candida albicans, glabrata and other; Cryptococcus
- Filamentous: Aspergillus, Fusarium, Mucor

Positive blood cultures (160) – Department of Hematology, Oncology and Internal Diseases MUW



 Staphylococcus sp.	 E.coli
 P.mirabalis	 E.cloacae
 other	

115 cases of Staphylococcus spp., including :
57 S. epidermidis, 17 S. haemolyticus, 15 S. saprophyticus,
15 S. aureus and 15 S. hominis

Periods of increased susceptibility of BMT patients to infections

- ◆ **Early**: till recovery of hematopoiesis
- ◆ **Intermediate**: till recovery of specific immunity
- ◆ **Late**
 - In patients with chronic graft versus host disease
 - In patients without graft versus host disease

Periods of increased susceptibility of BMT patients to infections

- ◆ **Early**: till 14-45 days after transplantation
- ◆ **Intermediate**: till 6-12 months after transplantation
- ◆ **Late**
 - In patients with chronic graft versus host disease – life long.
 - In patients without graft versus host disease – not different from other people



Early period after transplantation

- ◆ It is a period of **agranulocytosis**
- ◆ And the susceptibility of patients to all types of bacterial and fungal infections is critical
- ◆ Management includes:
 - Prophylaxis
 - Diagnosis
 - Treatment



Later periods after transplantation

◆ **Risk** of bacterial and fungal infection gradually **decreases with time** after transplantation with exception of patients with poor graft function and patients with chronic graft versus host disease.

◆ These latter patients are more susceptible to encapsulated organisms.

Sources of infections in BMT patients

◆ Internal

- Local infections
- Physiological flora

◆ External

- Premises
- Air
- Food
- Visitors



Prophylaxis

- ◆ Has to target all these factors
- ◆ The main principle is:
- ◆ **Personal hygiene** and
- ◆ **Clean environment**: as clean as possible



HCT patients are similar to acute leukemia patients during remission induction treatment but...

- ✦ Actually acute leukemia patients are in worse situation because they have been struck by the disease suddenly not being prepared for the situation.
- ✦ So they may have many local foci of infections and sometimes they have not been educated how to maintain hygiene and limit risk of exposure to bacteria and fungi.

HCT patient requires „cleaning” prior planned procedure

- ◆ All possible local sites of infection should be identified and appropriately treated.
- ◆ Particular attention should be put to teeth and sinuses.
- ◆ Viral and parasitic infections should be eliminated as well, as they may facilitate bacterial or fungal coinfections.

HCT patients require training how to maintain personal hygiene and observe isolation procedures

◆ Personal hygiene

- Shower once a day and preferably after defecation
- Mouth hygiene
- Daily routine if bedridden

◆ Isolation procedures

- Patient has to be able to strictly comply with the regulations in his/her ward
- Check what patient is bringing into his/her room

In early period after transplantation..

- ◆ Extreme attention to the **central line**.
- ◆ Each patient has central line and this offers many advantages particularly drawing blood for analyses and administration of drugs, blood components and nutrition as well as easy access to the patient in the case of emergency
- ◆ However, it introduces the risk of catheter related infections
 - It is going through the skin tunnel and this increases the risk of Staph. epidermis infection
 - It is susceptible to personnel errors
 - Also patient him- or herself may contaminate it more easily.

Building

◆ **For the patient:**

- Single/double room with bathroom
- Washable surfaces
- Electronic communication with outside world (or external corridor with a window)
- Easy access for personnel
- Good ventilation system

◆ **For the personnel**

- Adequate area for all supporting activities
- Also washable surfaces
- Good communication with other emergency services of the hospital

Hospital

- ◆ No construction in the vicinity of transplant unit (danger of *Aspergillus* spore spread)



Hospital room

- ◆ Cleaned and sterilized prior patient entry
- ◆ New sterile bedding
- ◆ No flowers
- ◆ Particular attention to bathroom: fungi (*Aspergillus*) may grow in all places where water may stay little bit longer
- ◆ Sterilize syphons (*Pseudomonas*)

Air

- ◆ Preferably 12-15 exchanges of filtered air per hour
- ◆ However, ventilation and air-conditioning systems have to be periodically tested for contamination
- ◆ Alternatively HEPA filtered systems in the hospital room.
- ◆ Good ventilation and air-conditioning (low humidity)

Also in the US air cleaning using portable HEPA filters (UCLA)



Food

- ◆ Well cooked or sterilized and freshly made
- ◆ No fresh fruits such as strawberries, that have contact with soil
- ◆ Dry fruits are also not allowed
- ◆ No cheese containing fungi
- ◆ Drinks should be sterile or pasteurized
- ◆ Not use tap water and periodically disinfect syphons (*Pseudomonas*)

Visitors

◆ Medical personnel (and all other persons visiting patients) must observe reverse isolation procedures

◆ **Reverse isolation**: isolation protecting patient from infections of other people.

◆ Levels:

- 1. washing hands, sterile mask
- 2. sterile gowns, shoes, cap + 1
- 3. complete change of clothing + 1

Prophylactic drugs

◆ **Antibacterial**

- Cotrimoxazole (also prophylaxis of *Pneumocystis jiroveci*, which is a fungus)
- Ciprofloxacin

◆ **Antifungal**

- Fluconazole
- Posaconazole (in high risk patients)
- Oral mycostatin, oral amphotericin B
- Amphotericin B inhalations

Diagnosis

◆ Surveillance

◆ Fever

◆ Local signs:

– Mucositis

– Pneumonia

– Diarrhea

– Anal ulcer

◆ Septic shock

Diagnosis

- ◆ **Radiology:** filamentous fungi: spiral chest CT, sinuses CT, OUN CT; yeast abdomen CT.
- ◆ **Galactomannan test (*Aspergillus*):** suggested twice a week and more frequently in high risk patients.
- ◆ **Blood cultures: bacteria, *Candida*, *Fusarium***
- ◆ Cultures of stool and urine, body foramens
- ◆ **PCR** – if available

Neutropenic fever

- ◆ Fever (over 38-38.3 degrees C as the only sign of infection in patient with neutropenia (below 500/ μ l)
- ◆ Empiric treatment (targeted against pathogens most frequently occurring in this particular ward)
 - Piperacillin/tazobactam
 - Cefepim +/- aminoglycoside
 - Ceftazidim +/- aminoglycoside

Treatment modification

- ◆ If progression to septic shock
 - Carbapenem + aminoglycoside
 - Fluids
 - Pressing amines
- ◆ If positive blood cultures without septic shock
 - Change according to sensitivity testing
- ◆ If no resolution of fever for 5 days, negative cultures, without significant worsening of the general condition
 - Add antimycotic

Local signs

◆ Mucositis

- Mouth washes
- Opioids
- mycostatin

◆ Catheter-related infection

- Vancomycin
- linezolid

◆ Infectious diarrhea

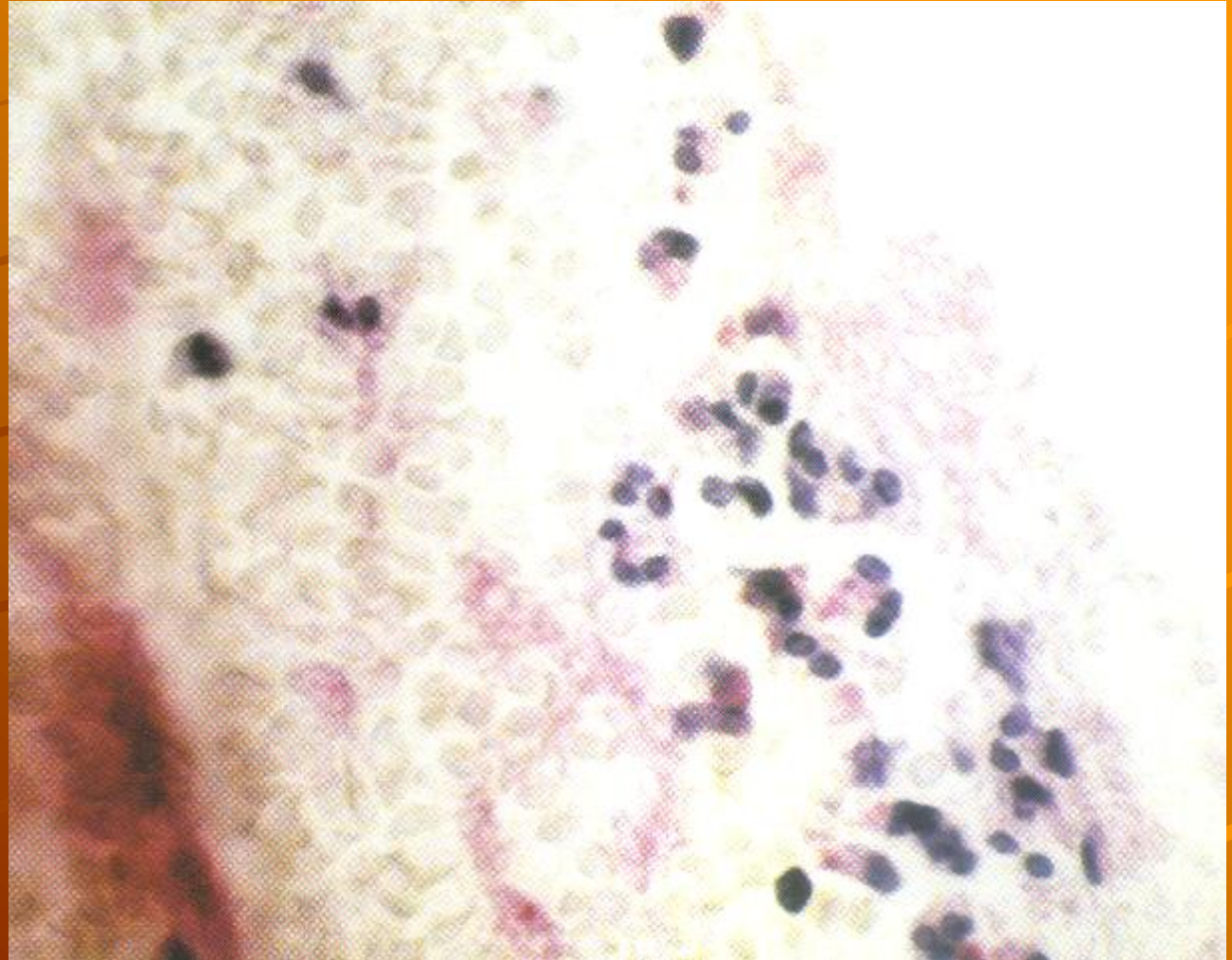
- metronidazole

Invasive Candida infection - definition

- ◆ Candidemia: presence in blood
- ◆ Organ involvement: liver and spleen most frequent: „bulls-eye” abscesses in CT
- ◆ Maculo-papular skin rash with central necrosis
- ◆ Eye ball changes (chorioretinitis) – view of „cotton ball”

Candida sp infection (PAS, 40x)

(Andreoni et al. Medical Mycology Atlas)

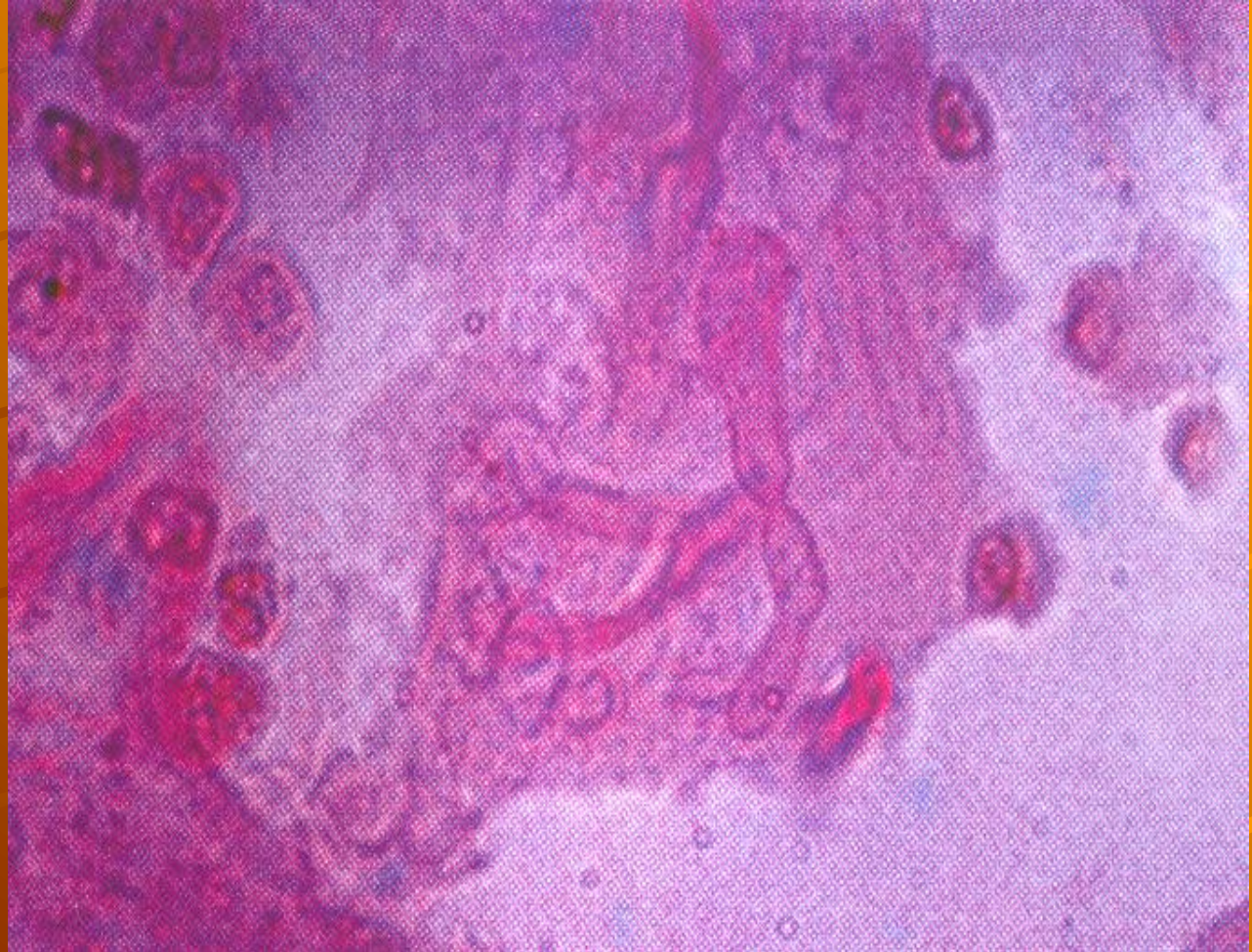


Invasive Aspergillus infection - definition

- ◆ Most frequently pneumonia with characteristic picture in CT „halo“ sign with multiple smaller foci around the main lesion.
- ◆ Confirmation (difficult): galactomannan, culture of BAL material
- ◆ Progression with caverna formation
- ◆ Other localizations: CNS and sinuses.

Aspergillosis (PAS, 100x)

(Andreoni et al. Medical Mycology Atlas)



Fungal infections treatment

◆ Azoles

- voriconazole

◆ Amphotericin B

- Amph B deoxycholate
- Amph B lipid complex
- Amph B liposomal

◆ Echinocandins

- Caspofungin
- Edulafungin
- Micafungin

Economic solution

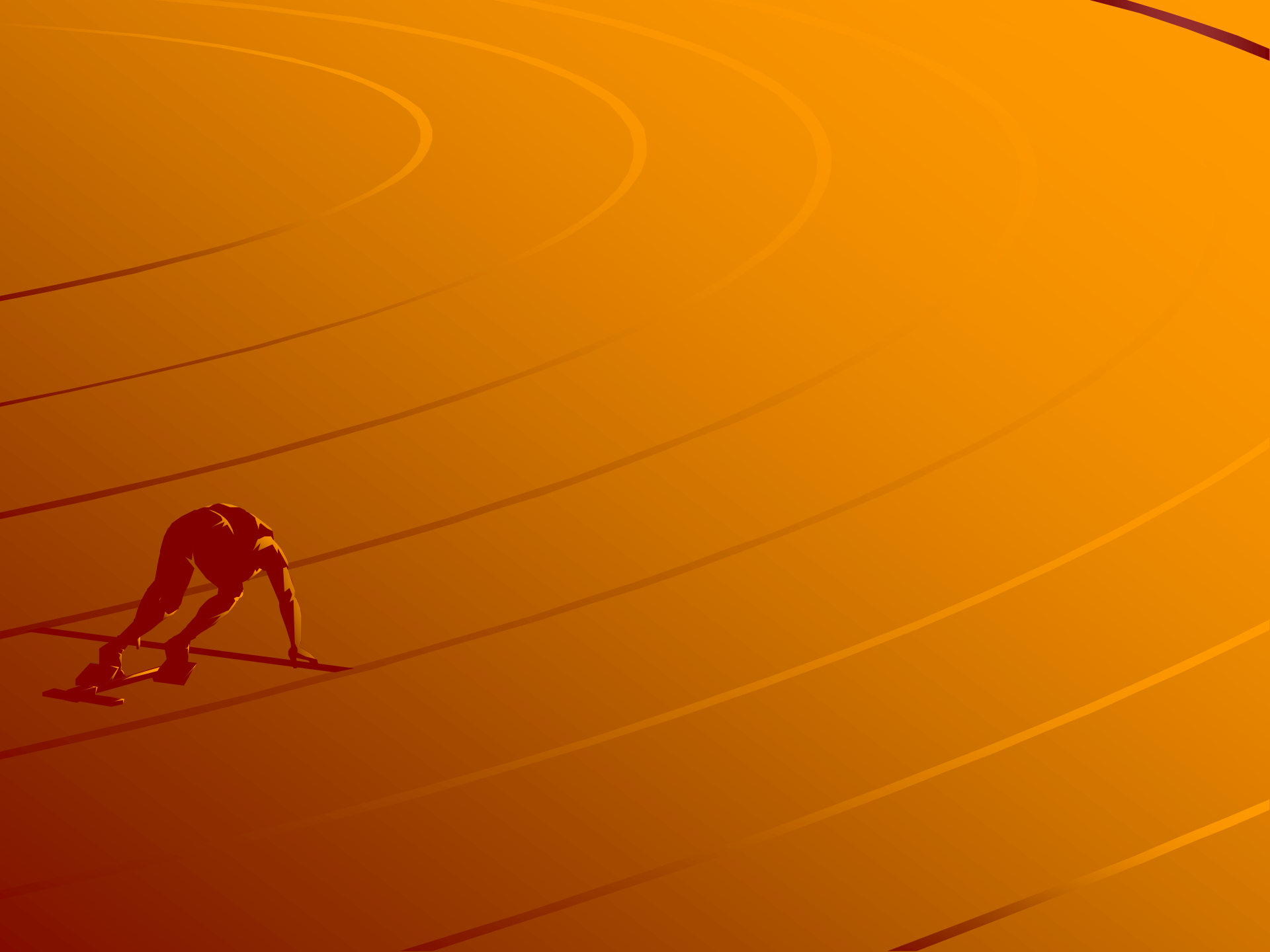
- ◆ Nebulized conventional amphotericin B inhalations
- ◆ Conventional amphotericin B 1-1.5 mg/day after proper hydration for 2 weeks.



Conclusion

◆ **It is better to prevent than to treat**





Cryptococcus i Fusarium

- ✦ W zakażeniu Cryptococcus kAmf B 0,7-1 mg/kg/d + flucytozyna 37,5 mg/kg co 6 godzin
- ✦ W zakażeniu Fusarium worikonazol, jeśli niedostępny kAmf B 1-1,5 mg/kg/d, ale znacznie lepiej liposomalna Amf B 5 mg/kg/d, w razie braku reakcji flucytozyna.