



Suzana Otasevic

# Maternal genital *Candida* colonization: The major risk for neonates infection. Is it a valid dogma?

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**Generally accepted theory is that colonization by *Candida* spp. in neonates has emerged due to vertical transmission from the mother**

**Molecular evidence is that *Candida* vaginal infection**

- ✓ **is associated with congenital candidosis,**
- ✓ **has the great impact on outcomes of pregnancy with a history of cerclage,**
- ✓ **and can be the large problem in attempts of *in vitro* fertilization**



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## TRANSMISSION

### VERTICAL

- Maternal fungal colonization
- Vaginal delivery



### HORIZONTAL

- Patients to patients transmission
- Contaminated infusates
- Health care worker colonization

**Horizontal** acquisition of *Candida* was proved and it is considered as probably the most common mode of transmission for *C. parapsilosis* strain.

*Waggoner-Fountain et al. Clin Infect Dis. 1996*

*Pfaller & Diekema Clin Microbiol Rev 2007*

*Bendel, Semin Perinatol 2007).*



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Neonatal care has been improved significantly



Invasive fungal infections (IFI) represent a leading cause of sepsis in VLBW and ELBW infants and result in high rates of morbidity and mortality.

- Prevalence of late-onset sepsis ranges from 2.6 to 16.7% in very low birth weight (VLBW  $\leq$  1.500 g) preterm infants
- 5.5% to 20% in extremely low birth weight (ELBW  $\leq$  1.000 g) ones.
- *Candida*-attributable mortality in preterm infants can reach up to even 43%

*Leibovitz, Pediatric Neonatol 2012*

*Lovero et al., Ann Ig, 2016*



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***Most fungal infections in preterm neonates are due to Candida species;***

***Dominant species are *C. albicans* and *C. parapsilosis* which caused approximately 80-90% of infants infections.***

****C. glabrata* infection dramatically has been increased***

***Importance of this strain and recovered representative as *C. krusei* is in fact that they harbor resistance to the antimycotics and may represent therapeutic challenges in IFI.***

In Serbia:

*C. albicans* (77.8%) was common isolates in newborns

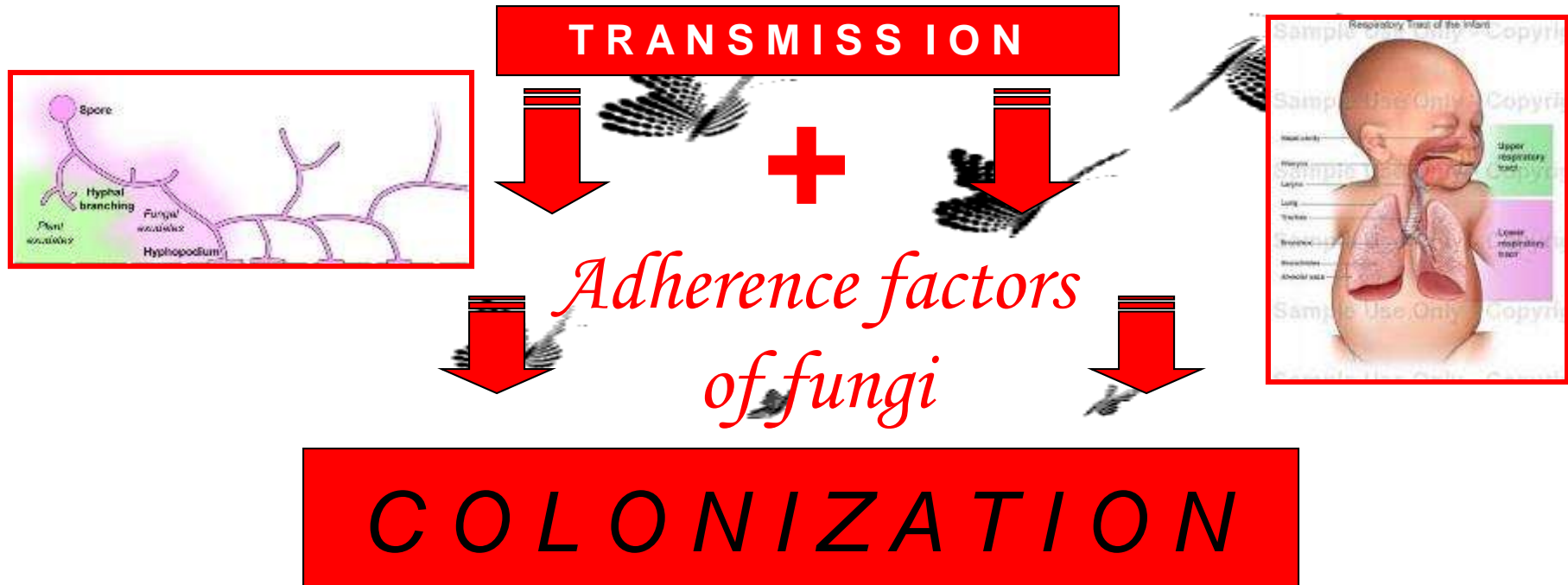
*C. parapsilosis*, *C. tropicalis* and *C. lipolytica* were the non-*albicans* species isolated from blood of infants

*Leibovitz, Pediatric Neonatol 2012*

*Arsić-Arsenijević, Mycoses 2017*



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The first link in the pathogenesis chain of fungal infections in neonates is adherence followed by colonization and dissemination. Adherence factors of fungi, number of microorganism and multiple site colonization are the mostly important virulence property and risk factors which could influence infection

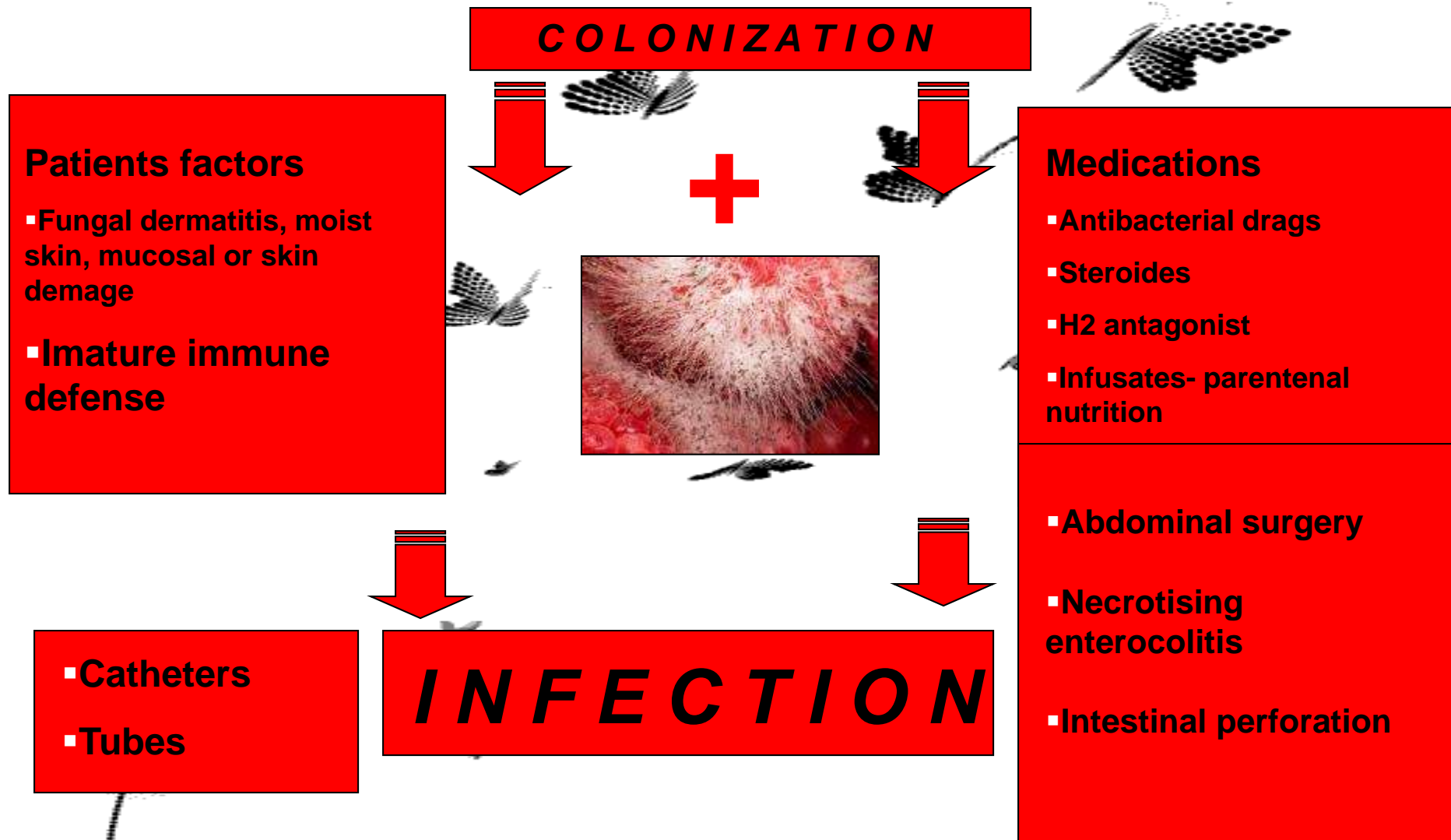
*Bendel, Semin Perinatol 2007*

*Leibovitz, Pediatric Neonatol 2012*



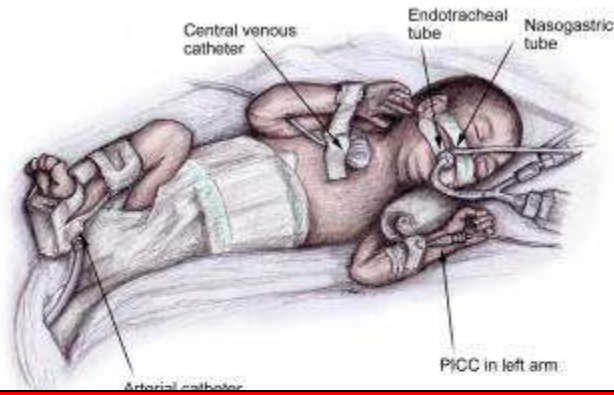


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- Coinfection
- Injures
- delay diagnosis
- late catheter removal
- inadequate antifungal dosing

### **End-Organ Dissemination**

- endocarditis
- abscess-kidneys, liver, brain, skin
- endophthalmitis, bone and joints

*Survival of neonates with low birth weight  
is a miracle of modern medicine*

*John E. Bennett, Clin Infect Dis, 2017*





- ✓ Therapies for systemic fungal diseases are not universally successful
- ✓ Morbidity remains high
- ✓ The management is fraught with numerous complications

**Preventive measures are of the greatest importance**

- So far, the efforts are focused on preventing invasive fungal disease which includes chemoprophylaxis with aim to decrease index of colonization,
- establishing the preemptive diagnostics procedure
- following by preemptive appropriate therapy.

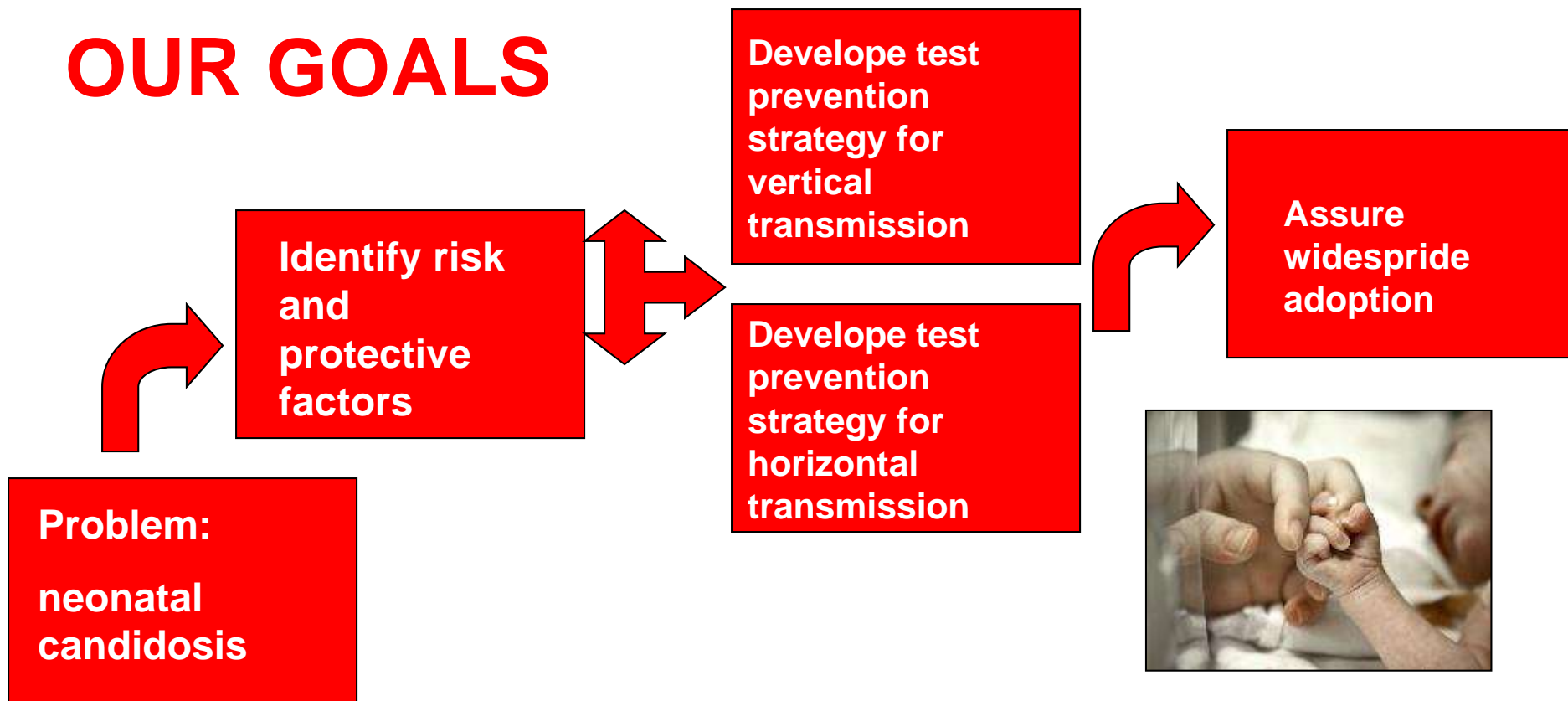
*Benjamin et al. Pediatrics. 2006*



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New challenge: to introduce the preventive procedures with the goal to interrupt the process of agent transmission

## OUR GOALS





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**Identify risk  
and  
protective  
factors**

Despite, some reports where proved **percent** of neonatal colonization is similar after per vias cesarean section **like** after per vias naturalis delivery and detected **14% positive infants from negative mothers**

### *Vertical transmission*



■ **For vertical transmission the wellknown risk factors are maternal genital *Candida* colonization/infection and vaginal delivery.** To develop test prevention strategy for vertical transmission requires:

**the control and treatment of genital candidosis of child-bearing woman**

*Zisova et al. Folia Medica 2016*

*Leibovitz, Pediatric Neonatol 2012*



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**Identify risk  
and protective  
factors**

- Genital candidosis is the most common infection
- 40% of women with vaginal complains have diagnosed GC.
- Up to  $\frac{3}{4}$  of all women have at least 1 lifetime episode
- 55% of women two, or more times have this experience
- 20% of asymptomatic colonization had isolates of *Candida*
- The prevalence of vaginal colonization in pregnant women is the higher up to 30-40%.
- Using molecular typing techniques, vertical transmission of *C. albicans* was documented in 33% of a group of premature infants.

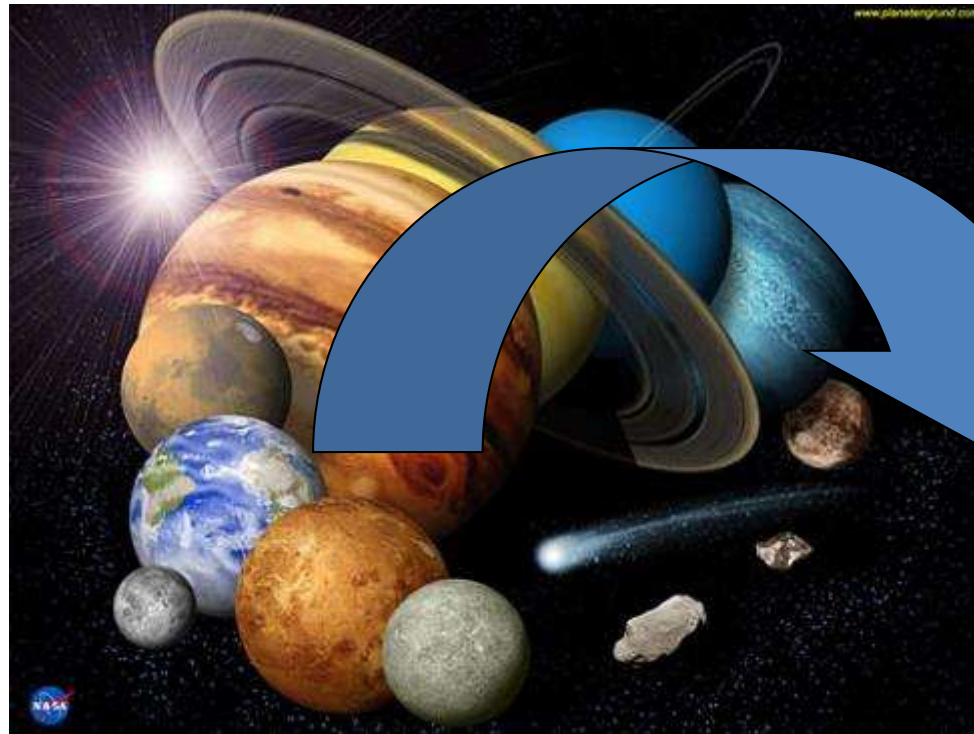
***Moreover: molecular studies proved that  
vulvovaginal Candida-colonization is  
present in 64% of women***

Cauchie et al, [Res Microbiol.](#) 2017

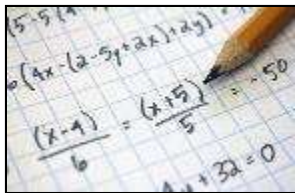


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**Identify risk  
and protective  
factors**



***Endemic  
planet***



***If we evaluate these facts the prevalence of this  
infection on a global level is 1-2%.***





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**Identify risk  
and protective  
factors**

**PROBLEM**

- ✓ 22% prevalence of GC,
- ✓ 8% had RGC
- ✓ Approximately 15% of asymptomatic colonization
- ✓ 23% of expectant mothers

	%
<i>C. albicans</i>	77
<i>C. glabrata</i>	11,5
<i>C. krusei</i>	5,3
<i>C. tropicalis</i>	1,8
<i>Saccharomyces cerevesiae</i>	1,8

*S. Otašević et al. ECCMID 2017, Med Pregl 2009; .  
Biotechnology & Biotechnological Equipment 2008; Eur J  
Pediatric 2012; 7th TIFI 2003; Facta Universitatis 2002;  
Acta Fac Med Naiss 2002,2008*







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Isolated species of genus <i>Candida</i>								ITZ			FCZ						
								The percentage of strains sensitivity									
								MIC≤ 0,125 µg/ml S		MIC=0.25 µg/ml DD		MIC≤ 8 µg/ml S		MIC=16 µg/ml DD		MIC≥64 µg/ml R	
<i>C. albicans</i>								32,8%		<b>67,2%</b>		28,9%		<b>71,1%</b>		0%	
<i>Non Candida</i>								75%		25%		75%		25%			
<i>C. parapsilosis</i> <i>C. guilliermondii</i> <i>C. kefyr</i>								100%		0%		100%		0%		0%	
<i>C. tropicalis</i>								25%		75%		0%		100%		0%	
<i>C. krusei</i>								45,5%		<b>54,5%</b>		0%		0%		<b>100%</b>	
<i>C. glabrata</i>								19,2%		<b>80,8%</b>		3,8%		<b>96,2%</b>		0%	



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**Identify risk  
and protective  
factors**

***Dr Yeast &***

***Mr Hyfa***

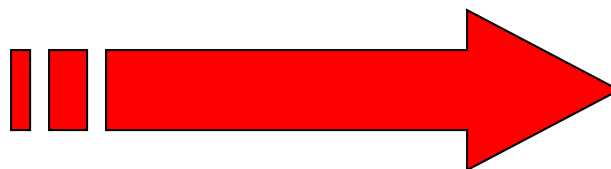
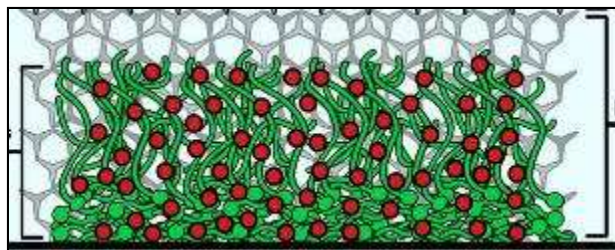
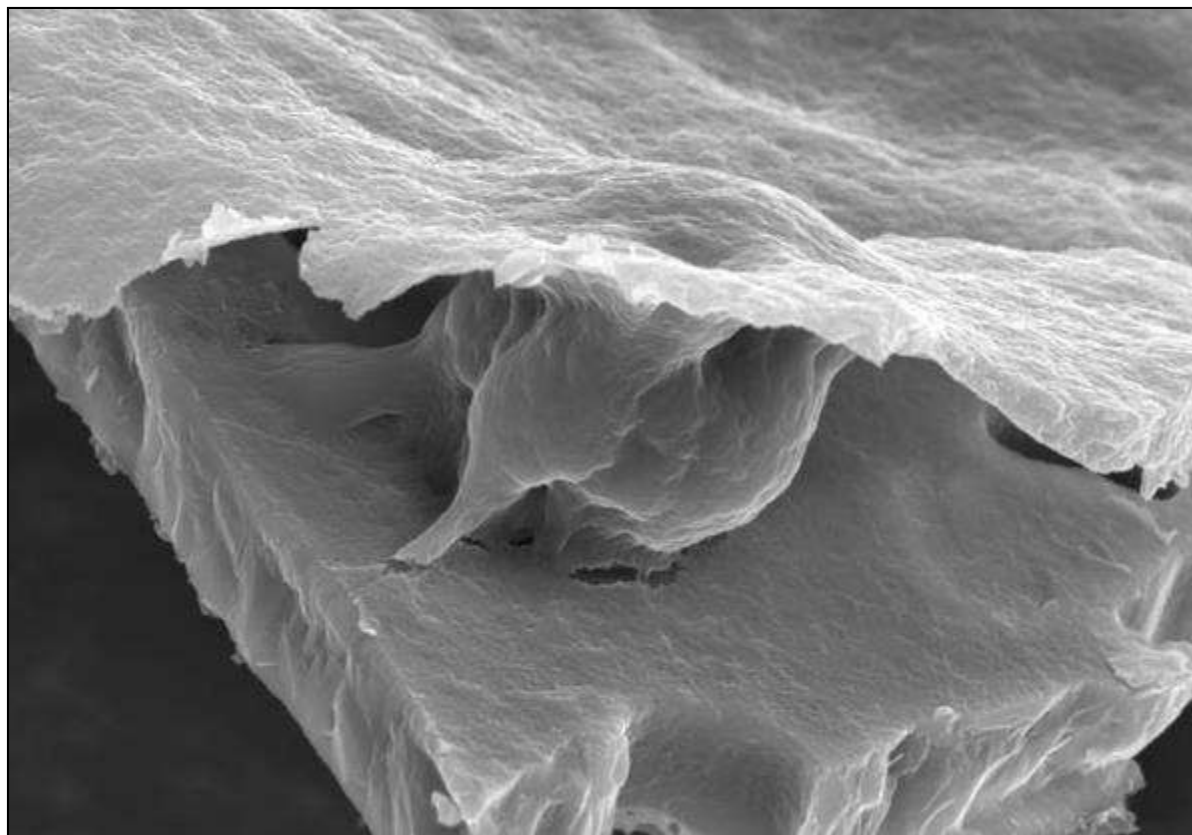
- *Phenotypic variations have been proven in the sense of*
  - > *adherence*
  - > *germination*
  - > *resistance*
  - > *production of virulence factors with unchanged DNA*





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**Identify risk  
and protective  
factors**



*biofilm*



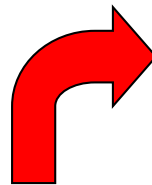
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## **Horizontal** acquisition of *Candida* infection

Transmission of *Candida* species to premature neonates can be due horizontal

### **HORIZONTAL**

- Patients to patients transmission
- through medical procedures



**Identify risk  
and protective  
factors**





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**Identify risk  
and protective  
factors**



- It occurs in the NICU
- It is probably the most common mode of transmission for *C. parapsilosis*.
- In a multicenter study: *Candida* spp. were isolated from the hands of 29% of health workers where ***Candida parapsilosis* was isolated from 19%** and *C. albicans* from 5%
- Medical equipments and procedures are often responsible for infections—such as **contaminated** instruments, needles, or dressings, or contaminated gloves that are not changed between patients

*Leibovitz, Pediatric Neonatol 2012*





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*Moreover*

*Laboratory investigation of moulds and yeasts  
contamination of mobile phones  
Otašević et al. TIMM 2017*





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**Develop test  
prevention  
strategy for  
vertical  
transmission**



## **Tiny Tots with Big Problems**

### **Control of pregnant women:**

- ✓ Personalisation of each case
- ✓ Consideration of RVVC
- ✓ Obligatory mycological analyses with antimycogram test
- ✓ During control examination we have to exclude intestinal overgrowth and possibility of sexual transmission
- ✓ Laboratory control and therapy in the last trimester or month

***Further research will give us some solution for solving the problem  
-the vaccine  
-possibility of alternative treatment with some natural compounds***



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**Develop test  
prevention  
strategy for  
horizontal  
transmission**



# **Tiny Tots with Big Problems**

Integrated measures in NICU

routine measures for prevention of nosocomial infections:

- desinfection,
- sterilization,
- isolation of patient
- fluconazole or? chemoprophylaxis

*Chen et al. A J Infect control 2015*



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**Develop test  
prevention  
strategy for  
horizontal  
transmission**

# **Tiny Tots with Big Problems**

**WITH**

Management of hand hygiene with running water and sanitizer instead of only using of waterless hand sanitizer.





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Develop test  
prevention  
strategy for  
horizontal  
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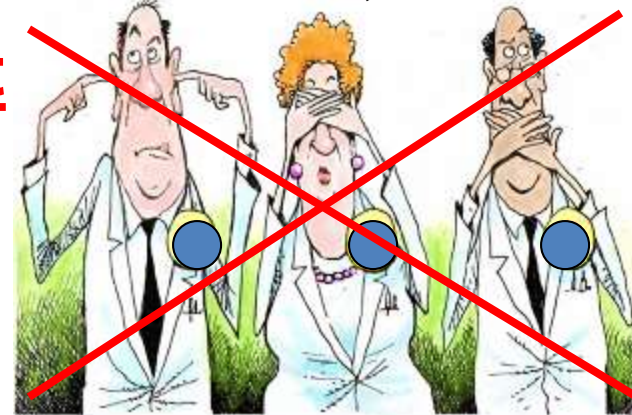
## Tiny Tots with Big Problems



Everybody must be  
supervisor to  
anybody

No one should be blind, deaf or silent

Everybody must  
be:educated  
and  
involved





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**Assure  
widespread  
adoption**

## **Tiny Tots with Big Problems**

***Establishing of official national  
approach and monitoring with real  
support from authorities for this  
infection***



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***Thank you***