

Syndromes associated with children exposure to mycotoxins and health risk assessment to multiple mycotoxins in infant foods

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National Institute of Health Doutor Ricardo Jorge, IP

ASPOMM meeting
"LOCAL MYCOLOGY MEETING", 10 october 2015, Lisbon



OUTLINE

1. Children health and mycotoxins
2. Routes of exposure
3. Syndromes associated with children exposure to mycotoxins:
ingestion and inhalation
4. Health risk assessment to multiple mycotoxins in infant foods -
MYCOMIX project (PTDC/DTP-FTO/0417/2012)
5. Critical role of health professionals

1. Children health and mycotoxins

Children are more vulnerable than adults to health risks because:

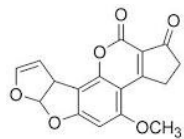
- Children are constantly growing. They breathe more air, consume more food, and drink more water than adults do, in proportion to their weight.
- Children's central nervous, immune, reproductive, and digestive systems are still developing. At certain early stages of development, exposure to environmental toxicants (as mycotoxins) can lead to irreversible damage.



(<http://www.who.int/ceh/en/>)



Aspergillus fungus



Aflatoxin B1

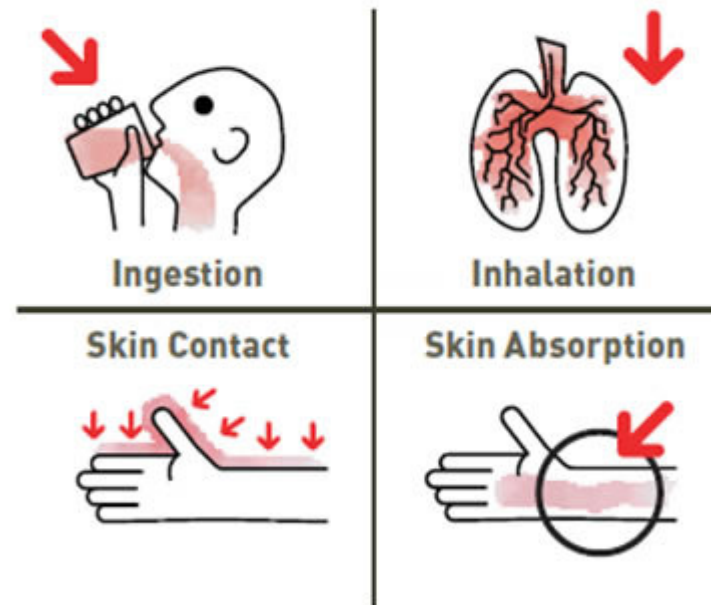
Mycotoxins are secondary metabolites of fungi that cause toxic and carcinogenic outcomes in humans and children are a population group particularly vulnerable to the biological effects of these compounds.

Table 1. Selected mycotoxin-producing fungi of relevance to children’s health

Fungus	Mycotoxins	Associated health effects
<i>Aspergillus flavus</i>	Aflatoxins	Vomiting, hepatitis
<i>Aspergillus parasiticus</i>		Liver cancer
<i>Fusarium verticillioides</i>	Fumonisin	Vomiting
<i>Fusarium proliferatum</i>		Neural tube defects
<i>Aspergillus ochraceus</i>		Esophageal cancer
Trichothecenes, Nonmacrocylic		
<i>Fusarium culmorum</i>	Deoxynivalenol	Vomiting
<i>Fusarium graminearum</i>		
<i>Fusarium cerealis</i>		
<i>Fusarium sporotrichiodes</i>	T-2 toxin	Alimentary toxic aleukia Vomiting, hemorrhage
Trichothecenes, Macrocylic		
<i>Stachybotrys chartarum</i>	Satratoxins	Protein synthesis inhibition
<i>Trichoderma viridi</i>		Hemorrhage
<i>Trichothecium roseum</i>		
<i>Aspergillus ochraceus</i>	Ochratoxins	Balkan nephropathy
<i>Aspergillus niger</i>		Renal cancer
<i>Aspergillus alliaceus</i>		
<i>Penicillium verrucosum</i>		
<i>Penicillium expansum</i>	Patulin	Vomiting, cancer (suspect)
<i>Fusarium graminearum</i>	Zearalenone	Estrogenic effects, cervical cancer (suspect)
<i>Claviceps purpurea</i>	Ergot alkaloids	Ergotism

(Etel, Curr Probl Pediatr Adolesc Health Care, 2006)

2. Routes of exposure



1. Eating food or drink containing mycotoxins
2. Breathing moldy air in damp indoor areas
3. Dermal absorption

3. Syndromes associated with children exposure to mycotoxins

1. Eating food or drink containing mycotoxins – major foods.

Toxic and biological effects of mycotoxins in foods	Mycotoxins	Major foods
Hepatotoxicity Carcinogenicity	Aflatoxins	maize, groundnuts, figs, tree nuts, milk, milk products, meat
Nefrotoxicity	Ochratoxins	maize, cereals, coffee beans, wine
Vomiting, gastrointestinal disturbs	Deoxynivalenol	cereals and derivatives
Oestrogenecity Infertility	Zearalenone	maize, barley, wheat
Esophageal cancer	Fumonisin	maize
Edema, hemorrhage, possibly cancer	Patulin	apple and pear juice pear, damaged apples & pears
Neurotoxicity	Ergot alkaloids	rye

(Alvito et al, 2014)

1. Eating food or drink containing mycotoxins – clinical presentation

Acute toxicity
(high dose exposures)

Table 3. Clinical features of vomiting illness from exposure to mycotoxins

Toxin	Latent period	Clinical features	Foods associated
Vomitoxin	3-15 min	Vomiting Nausea Headache Abdominal cramps Prompt resolution No sequelae	Food made from wheat and corn (eg, burritos) 1997,98 – USA, 1700 school children
T-2	5 min-1 h	Nausea Vomiting Diarrhea (bloody) Abdominal pain Dizziness "Burning" in mouth Symptoms improve in 3-9 days	Food made with wheat, rice, millet, or corn 1942, 48 – Alimentar Toxic Aleukia, Russia (bone marrow failure) , 100 000 died
Aflatoxins	~8 h	Vomiting Diarrhea Abdominal pain Dizziness Seizures Fever Hepatic toxicity can occur in weeks	Peanuts, maize, soybeans, cassava 2004 – Kenya, 317 people ill and 125 died
Fumonisin	N/A	Nausea Vomiting	Food made from corn (1990 - neural tube defects, USA)
Patulin	N/A	Nausea Vomiting	Apple juice, other nonfermented apple products

Inespecific clinical features

(Etzel, Curr Probl Pediatr Adolesc Health Care, 2006)

➔ Exposure to mycotoxins must be considered in differential diagnosis



Questions to consider in the clinical history if INGESTION of mycotoxins is suspected:

- Have other persons who ate the same food become ill?
- Did the symptoms begin within minutes to 3 hours of eating?
- Did any pets or animals eat the same food and become sick?
- Was diarrhea absent or a minor part of the illness?

Chronic toxicity
(low dose exposures)

IARC classification for carcinogenicity

IARC group	Definition	Mycotoxins
1	carcinogenic to humans	Aflatoxins (AFB1, AFB2, AFG1, AFG2)
2B	possibly carcinogenic to humans	AFM1, FB1, FB2, OTA
3	not classifiable as to its carcinogenicity to humans	DON, PAT, ZEA, T-2, NIV

(Lerda, 2011; Mycotoxins factsheets JCR)

AFTs – hepatocellular carcinoma (hepatitis B infection)

FB – esophageal cancer

OTA – renal cancer (testicular cancer?)

2. Breathing moldy air in damp indoor areas – clinical presentation

INFANT ACUTE PULMONARY HEMORRHAGE



Emerging data show an association with indoor exposure to moldy home environments (tricothecene mycotoxins).

Mycotoxins on surface of spores may lead to capillary fragility.

Massive pulmonary hemorrhage associated with mycotoxins - 1994 (10 child, USA, New Zealand)

Living in moldy indoor environment could also be associated with :

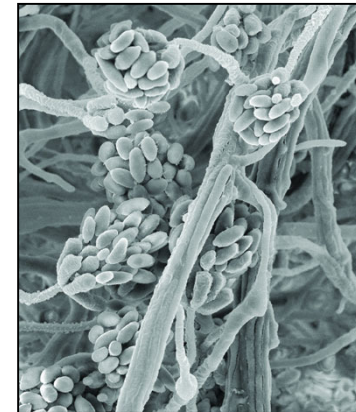
Recurrent apnea and /or “pneumonia”

- Recurrent apnea
- Cyanosis
- Cough
- “Pneumonia”



Sick Building Syndrome:

- Fatigue
- Headache
- Difficulty in concentrating





Questions to consider in the clinical history if INHALATION of fungi and mycotoxins is suspected:

- Has the house or apartment been flooded?
- Is there any water-damaged wood or cardboard in the house?
- Has there been a roof or plumbing leak?
- Have occupants seen any mold?
- Have occupants noticed a musty smell?

Mycotoxins associated health effects could be increased by:

Climate change

- Extreme precipitation, storms and floods
- Drought
- Increased temperatures



(WHO, Climate change and Health, 2011)

Mycotoxins mixtures



The natural co-occurrence of mycotoxins is an increasing concern due to the hazard of exposure of combined mycotoxins to humans and particularly to children, which could be expected to exert greater toxicity and carcinogenicity than exposure to single mycotoxins.

(Speijers & Speijers, Toxicology Letters, 2004)

INSA CONTRIBUTION...

Are children exposed to mycotoxins through diet?

TASK 1 - MULTIMYC. ANALYSIS

Interactive effects in toxicity of mixtures of mycotoxins?

**TASK 2 – CYTO & GENOTOXICITY
TASK 3 - BIOAVAILABILITY**

CHILDREN ARE EXPOSED TO MYCOTOXIN MIXTURES THROUGH THEIR DIET AND THIS CONSTITUTES A HEALTH THREAT

Could this exposure be a health threat to children?

TASK 4 – RISK ASSESSMENT TO MULTIPLE MYCOTOXINS IN INFANT FOODS

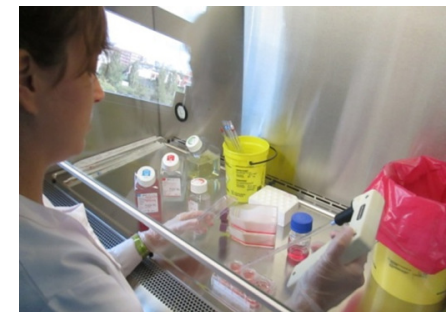


MYCOMIX

PTDC/DTP-FTO/0417/2012

4. Health risk assessment to multiple mycotoxins in infant foods MYCOMIX project

- 92% of the analyzed breakfast cereals revealed the presence of two to six mycotoxins, simultaneously, in the same sample (Tox Letters, 238, 2015).
- Interactive toxic effects between binary mixtures of AFM₁ & OTA, FB₁ & OTA, and PAT & OTA indicate that these effects should be taken into account for the hazard assessment of mycotoxins (World Mycotoxin Journal, 2013; Tox Letters, 238, 2015).
- Cumulative risk assessment suggests an urgent need to establish legal limits for multiple mycotoxins in breakfast cereals (submitted, 2015).



5. CRITICAL ROLE OF HEALTH PROFESSIONALS

Do research and publish results

Detect sentinel cases

Inspire community-based interventions

Take history of childhood exposures

Diagnose and treat

Educate

Patients and families

Colleagues and students

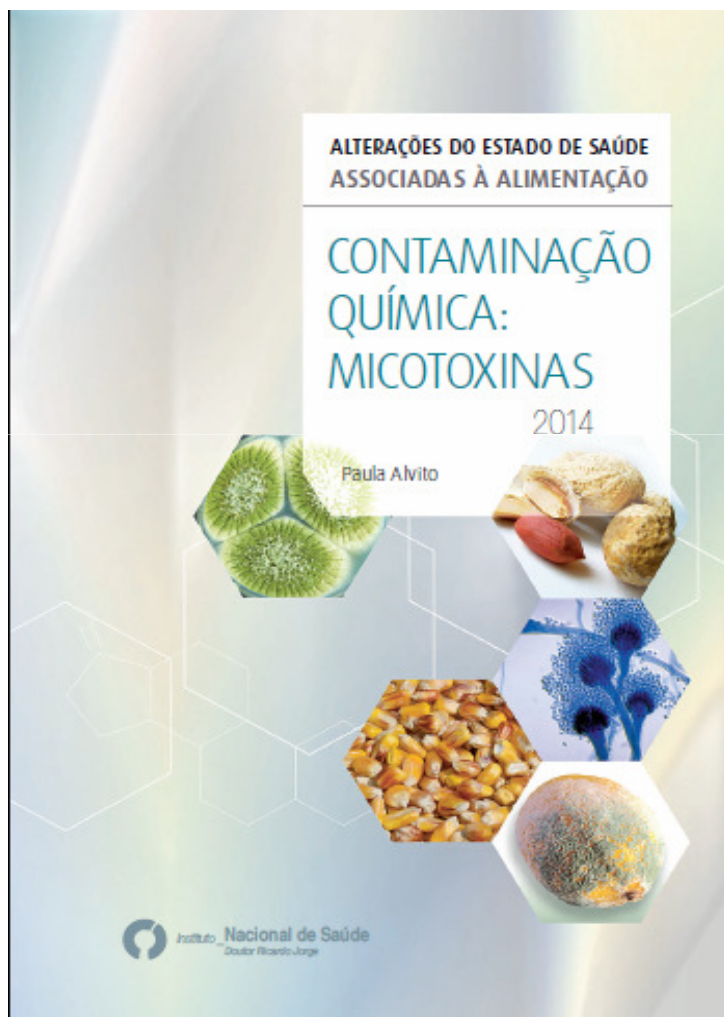
Advocate

Provide good role model

TOGETHER,
WE CAN DO BETTER!



For more informations, consult INSA publications available at: **www.insa.pt**



Avaliação do estado nutricional, dos hábitos alimentares e da probabilidade de exposição a micotoxinas na alimentação infantil: contributo do estudo-piloto efetuado na USF Cidadela, Cascais

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reprodutivo e digestivo ainda em desenvolvimento. Uma alimentação pouco segura pode provocar danos irreversíveis na saúde pelo que é importante avaliar a probabilidade de exposição deste grupo populacional aos contaminantes alimentares.

Em Portugal, são escassos os estudos desenvolvidos no domínio dos hábitos alimentares e estado nutricional das crianças até aos 3 anos, e não existem, até ao momento, dados sobre a probabilidade

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Applicability of In Vitro Methods to Study Patulin Bioaccessibility and Its Effects on Intestinal Membrane Integrity

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