National Institute of Occupational Health

Mould and farming revisited

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ICOH 2012 March 18-23, Cancun, Mexico

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Health effects from farm dust probably related to fungal exposures in have been known for a long time

In **1555** bishop Olaus Magnus writes in "*Historia de gentibus septentrionalibus*":

When separating the grain from the chaff, care must be taken to choose the time when there is suitable wind that will sweep away the dust, so that it will not damage the vital organs of threshers. This is so fine that it will almost unnoticeably penetrate into the mouth and accumulate in the throat. If this is not quickly dealt with by drinking fresh ale, the thresher may never again or only for a short period eat what he has threshed.

Rask-Andersen A 1988: PhD thesis Uppsala University, Sweden

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Health effects from farm dust probably related to fungal exposures in have been known for a long time

In **1700** Bernardino Ramazzini writes in the 1st edition of *De morbis artificum:*

" the result is a dry and obstinate cough; the eyes are much inflamed and watery; and almost all who make a living by sifting or measuring grain are short of breath and catechetic and rarely reach old age …"

He stated also that the most dangerous dust came from stored grain which could ferment and become heated when stored damp

Rask-Andersen A 1988: PhD thesis Uppsala University, Sweden
http://www.ausl-cesena.emr.it/Azienda/Sanit%C3%A0Pubblica/PrevenzioneeSicurezzadegliAmbientidiLavoro/MedicinadelLavoro/tabid/261/Default.aspx

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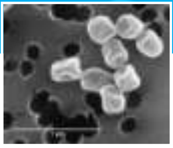
20th century research



Campbell (1932) *Brit Med J* 2:1143-1144

First description of 5 cases of farmers lung in farmers handling mouldy hay after an extremely wet hay-making season including severe breathlessness, weightloss , X-ray changes and fibrosis
The classical example of allergic alveolitis/hypersensitivity pneumonitis

Gregory and Lacey (1963) *J Gen Microbiol* 30:75-80

demonstrate that spores blown from mouldy hay are dominated by actinomycetes (spore forming bacteria)

Pepys et al (1963) *Lancet* Sept 21; 2(7308): 607-611

challenge 5 farmer's lung patients with extracts of *Saccharopolyspora rectivirgula** which induced typical symptoms of farmer's lung

*Synonyms: *Thermopolyspora polyspora, Micropolyspora faeni, Faeni rectivirgula*

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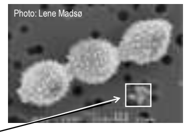
20th century research

Since than a number of fungal and actinomycete species have been identified as causes of hypersensitivity pneumonitis by brochial provovation with the extracts of the suspected organism

Fungi

- *Aspergillus clavatus, A. fumigatus, A. glaucus*
- *Geotrichum candidum*
- *Lentinus edodes*
- *Penicillium glabrum*
- *Pleurotus ostreatus*
- *Scopulariopsis brevicaulis*
- *Trichosporon cutaneum*
- *Serpula lacrymans*
- *Ustilago esculenta*



Actinomycetes

- *Saccharomonospora viridis*
- *Saccharopolyspora rectivirgula*

Occupations

- farmers
- mushroom workers
- malt workers
- greenhouse workers
- cork workers
- logger
- tobacco worker

Eduard W (2009). *Crit RevToxicol* 39:799-864 (review)

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20th century research

Several fungal and one actinomycete species have also been identified as causes of asthma by brochial provovation in farmers, tomato growers and hospital workers:

Fungi

- *Alternaria alternata*
- *Penicillium sp.*
- *Verticillium albo-atrum*
- *Sporobolomyces salmicolor*

Actinomycete *Saccharopolyspora rectivirgula*

Eduard W (2009). *Crit RevToxicol* 39:799-864

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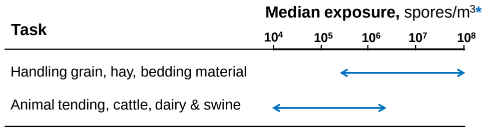
20-21th century research

However, more recent epidemiological studies of farmers did not include fungi in the exposure assessment:

Population	Outcomes	Measured agents	Reference
207 swine farmers	lung function	dust, endotoxins, ammonia	Donham *et al* 1995
42 swine farmers	lung function	dust, endotoxins, ammonia	Kirychuk *et al* 1998
171 swine farmers	lung function	dust, endotoxins, ammonia	Vogelzang *et al* 1998
47 poultry farmers	lung function	dust, endotoxins	Thelin *et al* 1984
257 poultry farmers	lung function	dust, endotoxins, ammonia	Donham *et al* 2000
111 poultry farmers	chronic phlegm	dust, endotoxins	Kirychuk *et al* 2006

☞ The effects of fungal exposure on the respiratory system of farmers can therefore not be deducted from these studies

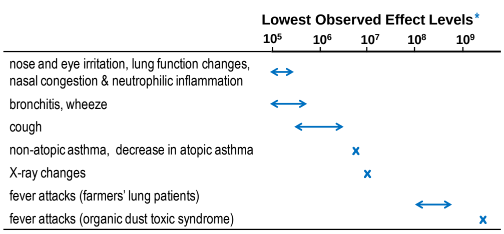
Exposure levels of fungi in agriculture (by personal sampling)



*spore count ≈10 x culture count

Eduard (1997) *Ann Agric Environ Med* 4:179-186. Review

Review of the toxicological and epidemiological studies on health effects of fungal spores at the workplace



Occupations: farmers, waste handlers, school staff, sawmill, cork and day-care workers

*for spores from non-pathogenic and not mycotoxin-producing fungi

Eduard W (2007). www.medicine.gu.se/avdelningar/samhallsmedicin_folkhalsa/amm/aoh/2006_21/

Eduard W (2009). *Crit RevToxicol* 39:799-864

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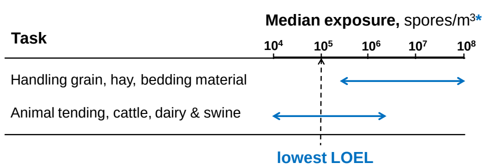


*spore count ≈10 x culture count

Eduard (1997) *Ann Agric Environ Med* 4:179-186. Review

The Norwegian farmer study

Population

89-8482 farmers (crops, swine, dairy, cattle, sheep and poultry)

Exposure by task-based personal sampling of

total dust	ammonia	bacteria	endotoxins
organic dust	hydrogen sulphide	actinomycetes spores	
inorganic dust	nitrogen dioxide	fungal spores	β(1→3)-glucans
quartz			*Asp&Pen* antigens
		storage mites (in fine dust)	

☞ **Exposure response associations with fungal spore exposure**

acute work-related eye irritation, nasal irritation and cough - strongest for fungal spores
non-atopic asthma, atopic asthma *(decreased)*, - strongest for fungal spores
chronic bronchitis (many agents were highly correlated)

Eduard *et al* 2001 *Occup Environ Med* 58:113
Eduard *et al* 2004 *Thorax* 59:381
Eduard *et al* 2009 *Chest* 136:716

In conclusion

Fungal spore exposure can be expected to represent a risk for farmers' respiratory health beyond farmers' lung

Challenges: β(1→3)-glucans?

Glucans are constituents of the fungal cell wall but also present in some bacteria and plants

- animal challenge studies show both allergic and non allergic inflammation, minor effects in humans ("low" dose)
- small epidemiological studies in municiple waste workers have shown associations inflammation but no associations have been found in farmers yet
- NB: β(1→3)-glucans are not specific to fungi

Reviews :Sigsgaard 2005 *Toxicol Appl Pharmacol* 207:S310
Douwes 2005 *Indoor Air* 15:160
Rylander 2010 *Ann Agric Environ Med* 17:9

Challenges: Mycotoxins

- very potent toxins produced by species from the genera *Fusarium, Aspergillus* and *Penicillium* e.g. aflatoxins, ochratoxin, trichothecenes, zearalenone
- mycotoxins have carcinogenic, genotoxic, teratogenic and immuno-suppressive properties (most is known about oral exposure)
- contaminants of grain and grain dust
- sensitivity of analytical methods too low for personal measurements (yet)
- mycotoxin producing *Fusarium* species have been quantified by real-time PCR in personal samples of farmers handling grain
- lip cancer, and hormone dependent cancer and reproductive outcomes have been ascribed to mycotoxin exposure among grain farmers

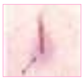
Need for more sensitive analytical method for mycotoxins
exposure data (personal sampling)
effects on farmers health

Review: Halstensen et al 2008 *Stewart Postharvest Review* 6:6, 9pp

Challenges: Hyphal fragments

- were shown to occur airborne in outdoor air in the 1950ies (Pady & Kramer *Mycologia* 1960; 52:681)

- animal studies show that hyphae induce allergic inflammation while spores induce non-allergic inflammation
- occur indoors (Green et al *Med Mycol* 2006; 44:S245)



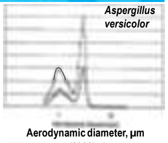
- grain farmers are exposed during grain handling at ≈10% of the concentration of fungal spores but hyphae may contain many cells (Halstensen et al *Ann Occup Hyg* 2007; 51:581)

Need for improved analytical method for hyphal fragments
exposure data (personal sampling)
effects on respiratory health

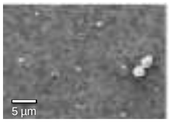
Green et al, in Fundamentals of Mold Growth in Indoor Environments and Strategies for Healthy Living, ed. Adnan & Samson, Wageningen Academic Publishers, Amsterdam, 2011,pp. 211–245.

Challenges: sub-micronic fungal fragments

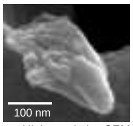
Several studies have demonstrated that numurous particles that are smaller than spores can be blown from fungal cultures using single particle counters, but little morphological data support their origin

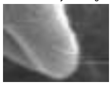


Kildesø J et al (2000). *Proceedings of Healthy Buildings 2000;1:313*



Górny RL et al (2002). *Appl Environ Microbiol 2002;68:3522*





High-resolution SEM demonstrated that some of the sub-micronic particles were of fungal origin
Photo: Anani Afanou

Need for analytical method for submicronic fungal fragments
exposure data
toxicity

Conclusions

Fungal spore exposure represent a health risk to farmers beyond farmers' lung

The role of other fungal agents should be subject for further study

mycotoxins	in farmers
hyphal fragments	in farmers
glucans	in organic dust exposed populations
sub-micronic fungal fragments	occupational exposure