NATIONAL COSH WEBINAR
WORKER EXPOSURE TO FLAVORING CHEMICALS

OCTOBER 13, 2016
Occupational Lung Disease overview and Brief History of Flavoring – Related Lung Disease
Hippocrates
(460-377 BCE – Lead mining industry)

Pliny the Elder
(Occupations and associated disorders -
zinc, sulfur and mercury poisoning)

Bernardino Ramazzini
(1700 “Father of industrial medicine”)
"What is your occupation?"

Bernardino Ramazzini (1700)
“It is much better to prevent than to cure, and so much easier to foresee future harm and avoid it rather than have to get rid of it after having fallen prey”

Bernardino Ramazzini (1700)
Early Deadly Occupational Disease

Chimney Sweeper’s Act of 1788
• Chimney Sweep’s Carcinoma

English Factory Acts of 1883
• 1\textsuperscript{st} Effective legislation for industrial safety

PHOSSY JAW – London “Match Girls” Strike 1888
• Banned use of white phosphorus
Deadly Occupational Diseases

1920's RADIUM JAW “Radium Girls”
1930's Silicosis “Hawk's Nest”
Metal and Nonmetallic Mines Safety Act of 1966
1970 OSHA - Asbestos Related Diseases
1990s BYSSINOSIS - Brown lung disease - textile mills
Although the incidence of classic occupational disease have declined, many have not been eradicated.

New Diseases Continue to Appear
- As a result of advances in technology
- Changes in work or working conditions
- Use of chemicals in new industries
• The respiratory tract is often the site of injury from occupational exposures.
• Widespread use of toxic materials in the environment owes a major threat to both the airways and lung parenchyma.
• The respiratory tract has a limited number of ways to respond to injury.
Flavorings are substances that alter or enhance the taste of food. They are composed of various natural and man made chemicals and may consist of a single chemical, but more often they are complex mixtures.
Workers in the Flavorings production industry may be exposed to these substances in the form of solids, liquids, or vapors.
Although the thousands of flavoring ingredients are in use, little is known about most of these in terms of worker health effects, and few have occupational exposure guidelines such as recommend exposure limits (REL), permissible exposure limits (PEL) or threshold limit values (TLV).
Why Are Food Flavorings a Problem For Food Industry Workers

- Some chemicals in food flavorings can cause permanent lung damage when inhaled.
- This danger initially became public when a local occupational physician identified a rare lung disease in a cluster of workers exposed to a chemical known as diacetyl.
Diacetyl and 2,3-pentanedione are volatile organic compounds known as alpha-diketones. These chemicals can be manufactured to make different flavorings that are sometimes added to food products (e.g., microwave popcorn, bakery mixes, flavored coffee) (Day et al. 2011; Kanwal et al. 2006; Bailey et al. 2015).
The Flavoring Chemicals Known to Cause Lung Disease

All Similar in Chemical Structure to Diacetyl (2,3 Butanedione)

2,3 PENTANEDIONE (ACETYL PROPIONYL)

\[ \text{H}_3\text{C} \text{C} = \text{C} = \text{O} \text{CH}_3 \]

2,3 HEXANEDIONE

\[ \text{H}_3\text{C} \text{C or } \text{H}_2\text{C} \text{C} - \text{C} = \text{O} \text{CH}_3 \]

2,3 HEPTANEDIONE

\[ \text{H}_3\text{C} \text{C or } \text{H}_2\text{C} \text{C or } \text{H}_2\text{C} \text{C} - \text{C} = \text{O} \text{CH}_3 \]
Symptoms

Symptoms may include:

• Shortness of breath
• Chronic coughing
• Wheezing
• Extreme fatigue
• Trouble with strenuous tasks
• Fever, muscle aches, night sweats, and weight loss
• Frequent or persistent eye, nose, throat or skin irritation
Flavorings-Related Lung Disease

- Emphysema
- Asthma
- Bronchiolitis Obliterans
- Hypersensitivity Pneumonitis
- Granulomatous Disease
- Interstitial Lung Disease
Bronchiolitis obliterans (BO) is a fibrotic lung disease characterized by narrowing and obliteration of the small airways.[1] BO is most often recognized to occur in the setting of lung or bone marrow transplantation, but has also been described in the setting of occupational exposure to reactive volatile chemicals.[2] Once BO occurs patients develop irreversible airflow obstruction that can progress to respiratory failure, depending on the clinical context.

Source: Severe Airway Epithelial Injury, Aberrant Repair and Bronchiolitis Obliterans Develops after Diacetyl Instillation in Rats – Palmer - 2011
Why Should we be Concerned?

Exposure Can Cause Permanent Debilitating Lung Disease and Death
Victims of Flavoring Exposure

1st Death
Janice Meenach-Irick
Givaudan/Tastemaker
Cincinnati, OH

2nd Death
Add name
Gilster Mary Lee in
Perryville, MO

3rd Death
Linda Redman
Jasper Popcorn Co.
Jasper, MO
Victims 1- Janice Meenach-Irick

- Worked in the liquids mixing area of the plant and was exposed to diacetyl.
- Tastemaker did not provide any respiratory protection and the mixing vats were uncovered.
- She left the company in 1987 on disability leave and died in 1992 at the age of 30.
Victim 2

• In 2003 a 52 year old woman who had worked as a popcorn packager at the Gilster Mary Lee popcorn-packaging plant in Perryville, Missouri, from 1996 until 2003 died of respiratory failure.

• A non-smoker, she suffered from a variety of breathing problems, including wheezing, clinical diagnosis included chronic bronchitis, bronchiolitis and bronchiectasis.

• Doctors suspected her symptoms were work-related.

• Clinical diagnosis was pulmonary arterial hypertensive changes, chronic bronchitis, and bronchiolitis with bronchiectasis.
Victim 3 - Linda Redman

- Worked at Jasper Popcorn Co. Jasper Missouri in 1995 for 18 months began experiencing shortness of breath and cough in 1996.
- A Lifelong non smoker.
- In 2000 she visited Mayo Clinic where physicians diagnosed BO and linked her exposure to chemicals at the popcorn plant.
- Last year's of her life she was confined to a wheel chair with oxygen, suffered from anxiety and depression and was permanently and totally disabled.
Industry Knowledge of the Dangers

1976  Rabbit studies - Research Institute for the Flavorings and Extract Manufacturer’s Association (FEMA) conducted diacetyl dermal toxicity test on rabbits.

1984  Two workers from International Bakers Service Plant, South Bend, Indiana develop Bronchiolitis Obliterans (BO)

1985  Flavor and Fragrance Ingredient Data Sheets – diacetyl harmful and capable of producing systematic toxicity

1992  Givaudan/Tastemaker, Cincinnati, Ohio; employees with bronchiolitis obliterans


1993  BASF - Diacetyl inhalation Rat Studies – dying animals had “dragging respiration, and gasping respiratory sounds”

2000  NIOSH HHE – Glister-Mary Lee microwave popcorn packing facility – flavoring vapors causing lung disease
Preventing Lung Disease in Workers Who Use or Make Flavorings

WARNING!
Breathing certain flavoring chemicals in the workplace may lead to severe lung disease.

Flavorings are complex mixtures of natural and manmade ingredients that are added to many food products in the production process. Depending on the flavoring and the process, workers may be exposed to hazardous flavorings or flavoring ingredients should take the following steps to protect their health:

- Participate in breathing tests provided by your employer.
- Promptly report any persistent shortness of breath or cough, or any problems with

Companies that use or make flavorings...
2003 Agrilink – Ridgway, Illinois
2004 American Pop Corn Company – Sioux City, Iowa
2004 Conagra Snack Food – Marion, Ohio
2006 Gilster Mary Lee – Jasper, Missouri
2007 Carmi Flavor – Commerce, California
2007 Yatsko’s Popcorn - Montana
HHE Reports - Flavoring Epidemic

- **2008** Gold Coast – Commerce, California
- **2009** Chr. Hansen – New Berlin, Wisconsin
- **2009** General Mills – Los Angeles, California
- **2009** Aramark – New York, New York
- **2011** Indiana Flavoring Plant
- **2013** Kentucky Plant
- **2016** Snack Foods Facility in Pennsylvania

2003 Worker at Gilster-Mary Lee dies of lung disease. She was exposed to diacetyl at Gilster-Mary Lee from 1998 to 2003.
Emerging Issues Regarding Flavoring Exposures

Pressure Mounts Against the Flavoring Industry

Diacetyl Substitutes

New And Novel Industries

Scott Hall
MOTLEY RICE LLC
Pressure Mounts Against the Flavoring Industry

Lawsuits

2004
- Lawsuits begin against the flavoring industry
- First lawsuit results in $20 million verdict

2005
$70 Million in Verdicts and Settlements with Many More Cases Filed
“Because a growing body of scientific evidence links inhalation of diacetyl to bronchiolitis obliterans and other forms of respiratory impairment, the FDA can no longer allow the GRAS designation for this food additive.”

— David Michaels, Ph.D., MPH
Pressure Mounts Against the Flavoring Industry

Food and Flavors Worker Unions

Unions representing flavor and food workers (UFCW and IBT) petition Department of Labor for an emergency temporary standard for all employees exposed to diacetyl

"An ETS is needed because workers will continue to be under grave danger of life-threatening illness . . . ."
Pressure Mounts Against the Flavoring Industry

Food and Flavoring Worker Unions

40 Occupational Health Physicians and Scientists Support the Call for Immediate Action to Prevent Lung Disease Among Diacetyl-Exposed Workers

“[T]here is compelling epidemiologic and toxicological evidence linking exposure to diacetyl to severe respiratory impairment and disease . . . It is now time for OSHA to use the scientific evidence to protect American workers from debilitating lung disease.”

2006 - Letter to: Secretary of Labor from Presidents of UFCW and Teamsters
Pressure Mounts Against the Flavoring Industry

Food and Flavoring Worker Unions

2007 - Letter to: Secretary of Labor from Presidents of UFCW and Teamsters

Unions Renew Call for Emergency Temporary Standard After OSHA Fails to Respond

“Over a year ago, we petitioned the Occupational Safety and Health Administration (OSHA) to issue an emergency standard to protect workers from diacetyl and other dangerous flavoring chemicals. OSHA has failed to respond to this urgent request.”
In 2007, FEMA establishes a voluntary program to help flavor manufacturers reduce diacetyl exposure.
Pressure Mounts Against the Flavoring Industry

Congressional Hearing

“

“To direct the Occupational Safety and Health Administration to issue a standard regulating worker exposure to diacetyl”

- Passed in the House of Representative on September 26, 2007.
- Opposed by Bush Administration and Senate Republicans
- Never passed in the Senate

2007 - Congressional Hearing – “Popcorn Workers Lung Disease Prevention Act”
Industry Response

2005-2007 Flavoring Industry Begins to Discontinue Sale of Diacetyl

2004 Polaram

2005 Citrus and Allied Essences Ltd

2005 IFF

2007 FEMA

2007-2008 ConAgra Foods

2007 Weaver

2007 Great American Popcorn Co.
Industry Response

“No Added Diacetyl”
Industry hired litigation experts from ChemRisk present poster at 2007 Society of Toxicology Meeting questioning whether diacetyl causes lung disease

“While it is possible that elevated exposures to artificial butter may have been related to the incidence of respiratory disorders in some popcorn workers, the data collected to date do not appear to be sufficiently robust to draw any firm general conclusions.”
Industry Response

Flavoring Manufacturers Turn to Diacetyl Substitutes

All Similar in Chemical Structure to Diacetyl
(2,3 Butanedione)

2,3 PENTANEDIONE (ACETYL PROPIONYL)

2,3 HEXANEDIONE

2,3 HEPTANEDIONE
Workers who breathe diacetyl on the job have become disabled or have died from severe lung disease. Some diacetyl substitutes may also cause harm.

Diacetyl substitutes that have not been proven to be safe include diacetyl trimer, 2,3 hexanedione, 2,3 heptanedione, and 2,3 pentanedione.

2010 – OSHA Worker Alert
A Rodent Model Of Toxin Induced Bronchiolitis Obliterans


Duke University Medical Center, Durham, NC, United States of America.
REEHS, Research Triangle Park, NC, United States of America.
Aillon, Inc., Fawsarik, Tramble Park, NC, United States of America.

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Background: Recent epidemiological studies have linked bronchiolitis obliterans (BO), a condition of progressive airway obstruction and intraluminal fibrosis, with inhalation exposure to volatile solvents present in artificial flavoring. We hypothesized that intratracheal administration of 2,3-pentanedione (PD) in rats would induce lesions similar to those observed in humans.

Methods: Male Sprague-Dawley rats were treated with a single dose of PD (140 mg/kg) or water by IT on day 0, then sacrificed at day 7. Rats were treated with a single dose of PD (140 mg/kg) or water by IT on day 0, and then sacrificed at day 7. PD-treated rats developed intraluminal polyoid and escaroid fibrotic lesions characteristic of BO in humans.

Results: By day 7, PD-treated rats developed intraluminal polyoid and escaroid fibrotic lesions characteristic of BO in humans.

The fact that PD administration induced histopathological lesions characteristic of BO in rats is a significant finding. It suggests that PD is a potential model for the study of BO.

“...Intra-tracheal administration of 2,3 pentanedione in rats produces histopathological lesions characteristic of BO.”

2010 - A Rodent Model Of Toxin Induced Bronchiolitis Obliterans - F.L. Kelly
“We conclude that 2,3 pentanediolone is a respiratory hazard . . . .”
"The histopathological and biological changes observed in rats raise concerns that PD inhalation may cause BO in exposed humans."

"... based upon the results of this study, the use of PD as a substitute for diacetyl should be reconsidered."
Diacetyl Substitutes
Latency of Cases

1981 General Mills Invents Patents Microwave Popcorn Bag

1985 Diacetyl First Used In Butter Flavored Microwave Popcorn

1996 First Cases Flavoring Related Lung Disease “Confidentially Reported” By Flavoring Industry to Their Trade Association, FEMA

2000 First Cases Lung Disease Recognized In Microwave Popcorn Workers (Public)

2005 - 2007 Diacetyl Substitutes Appear

2016 & BEYOND First Cases of Lung Disease Caused by Exposure to Diacetyl Substitutes?
New and Novel Industries Using Diacetyl and Diacetyl Substitutes

“Popcorn Lung”

“For many years, it was assumed diacetyl related lung disease was limited to the microwave popcorn and flavoring industries.”

We now know that these chemicals affect many more products and industries.
Known Products and Industries

- Flavored Popcorn (both microwaved and bagged)
- Coated snacks such as cheese-flavored chips
- Crackers and butter pretzels
- Refrigerated dough products
- Baked goods such as bread, rolls, crackers & biscuits
- Butter flavorings and starter distillates
- Fruit flavorings
- Dry mixes
- Coffee and flavored coffee creamers
- Substitutes
- Dairy products
- Other food items with flavorings as an ingredient
- Pet foods
- Candies
- Cooking oils (butter flavored)
- Vegetable shortening, margarines and other butter
Unexplored Frontiers

• Preventing the “spread” of flavoring related lung disease to other industries and workers.

• Recognition of pyrolysis products that include diacetyl or diacetyl substitutes (e-cigarettes).

• Prediction of unrecognized hazards through toxicologic study (finding analogous chemical structures).

• Expanding the diagnostic criteria for flavoring related lung disease to include lung function abnormalities beyond fixed obstruction.
“Day in the life”
Nick Moncel