Microbes & Metal Working Fluids:
Current Understanding of Potential Health Risks in Exposed Workers

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8th Lubgrax Meeting
São Paulo, Brazil • August 16-17, 2017
LAST YEAR, GAVE PRESENTATION ON:

Microbes & Metal Working Fluids:
Cause, Effect and Strategies for Control
PRESENTATION TOUCHED BRIEFLY ON POTENTIAL HEALTH EFFECTS IN EXPOSED WORKERS ASSOCIATED WITH MICROBIAL CONTAMINATION

RECEIVED QUESTIONS FROM A NUMBER OF PEOPLE ABOUT THESE
SESSION OBJECTIVES & OUTLINE

Objective of today’s presentation is to review current understanding of potential health risks in detail.
SESSION OBJECTIVES & OUTLINE

- **WE’LL LOOK FIRST AT “WHAT WE DO KNOW”**
  - AVAILABLE INFORMATION IN PEER-REVIEWED PUBLISHED PAPERS
  - USE ‘WEIGHT OF EVIDENCE” APPROACH WHERE APPROPRIATE
- **WE’LL ALSO LOOK AT SOME OF THE KNOWLEDGE GAPS THAT HAVE BEEN IDENTIFIED**
PUBLISHED PAPERS GOING BACK AT LEAST TO THE 1940’S DOCUMENT THE ISOLATION OF BOTH FRANK (PRIMARY) PATHOGENS AS WELL AS OPPORTUNISTIC PATHOGENS FROM IN-USE MWF’S.
DIRECT INFECTION RISK

FRANK PATHOGENS¹ ISOLATED INCLUDE:

- *Salmonella typhi* (cause of typhoid fever)
- *Staphylococcus aureus* (boils, wound infections)
- *Klebsiella pneumoniae* (bacterial pneumonia)
- *Streptococcus pyogenes* (wound & systemic infections)

¹ The Isolation of Pathogenic Bacteria from Used Emulsion Oils, Tant, C.O.; Bennett, E.O, Appl Microbiol. 1956 Nov; 6(6): 388-391
DIRECT INFECTION RISK

OPPORTUNISTIC PATHOGENS ISOLATED INCLUDE:

- *Pseudomonas spp.* Including *P. aeruginosa*
- *Proteus spp.*
- *Citrobacter spp.*
- *Enterobacter spp.*

All of these have been shown to able to cause infections in hospital settings / immuno-compromised individuals
DIRECT INFECTION RISK

IN THE US, WHERE MUCH OF THE RESEARCH HAS BEEN DONE, THERE ARE ESTIMATES THAT >1 MILLION WORKERS ARE EXPOSED TO METALWORKING FLUIDS.
DIRECT INFECTION RISK

NO PUBLISHED REPORTS OF WORKERS EVER HAVING CONTRACTED INFECTIONS WITH ANY OF THESE ORGANISMS!
DIRECT INFECTION RISK

BIOLOGICAL PLAUSIBILITY vs. REAL WORLD FACTS

CANNOT SAY THAT THERE’S ZERO RISK, BUT CLEARLY IN PRACTICAL TERMS, THE RISK MUST BE SMALL.
DIRECT INFECTION RISK

AWARE OF ONLY ONE *SUGGESTED* EXCEPTION:

1981 OUTBREAK OF PONTIAC FEVER AT AN AUTO PLANT IN CANADA<sup>2</sup>

► CAUSED BY *Legionella feeleii*

INVESTIGATED BY US CDC AMONGST OTHERS. AUTHORS CONCLUDED THAT A MWF SYSTEM WAS LIKELY THE SOURCE OF THE OUTBREAK

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DIRECT INFECTION RISK

THERE HAVE BEEN OTHER REPORTED CASES OF LEGIONNAIRES DISEASE IN AUTO PLANTS:

- INVESTIGATIONS HAVE FAILED TO ISOLATE Legionella FROM MWF’S IN USE IN THESE PLANTS
- LIKELY SOURCE IS COOLING TOWERS
DIRECT INFECTION RISK

UNRESOLVED QUESTION IS:

IS THERE A POTENTIAL RISK ASSOCIATED WITH GROWTH OF *Legionella* spp. IN MWF’S?
DIRECT INFECTION RISK

2012 STUDY BY UK GOVERNMENT’S HEALTH AND SAFETY LABORATORY:

“SURVIVAL OF *Legionella pneumophila* IN METALWORKING FLUIDS”

DIRECT INFECTION RISK

“SURVIVAL OF *Legionella pneumophila* IN METALWORKING FLUIDS”

TWO DIFFERENT APPROACHES TO TESTING:

- INOCULATED *L. pneumophila* INTO DILUTED MWF’s.
- *qPCR* TESTING TO LOOK FOR *Legionella* DNA IN USED MWF SAMPLES AND COMPARED TO LEVELS IN POTABLE WATER
“SURVIVAL OF Legionella pneumophila IN METALWORKING FLUIDS”

KEY FINDINGS:

- *L. pneumophila* DID NOT GROW IN 3 FLUIDS
- >99.99% KILL WITHIN 4 HOURS

- TESTS OF 70 SAMPLES OF IN-USE MWF’s SHOWED SIMILAR LEVELS OF *Legionella* DNA TO 25 DIFFERENT POTABLE WATER SAMPLES
  - SAMPLES WERE OF 18 DIFFERENT PRODUCTS AND TAKEN FROM 35 PLANTS
DIRECT INFECTION RISK

“SURVIVAL OF *Legionella pneumophila* IN METALWORKING FLUIDS”

KEY CONCLUSION:

“…RISK OF *Legionella* INFECTION FROM FREE-FLOWING MWF IS CONSIDERED TO BE EXTREMELY LOW…”

NOTE: DID NOT LOOK AT POTENTIAL RISKS ASSOCIATED WITH BIOFILM.
DERMATITIS IS THE MOST COMMON HEALTH RELATED ISSUE IN WORKERS EXPOSED TO MWF’S:

- ASSOCIATED WITH ALL TYPES OF FLUIDS
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DO MICROBES PLAY A ROLE IN DERMATITIS?
Irritant or allergic contact dermatitis is reported to occur from exposure to soluble, semisynthetic, and synthetic MWFs. Dermatitis can be caused by:

- **Bacteria** and their by-products.
- Chemicals added to control bacteria (biocides).
- Chemicals added to control rust and corrosion.
- Contact with metal contaminants such as nickel, cobalt and chromium, which are known sensitising agents.

https://www.ccohs.ca/oshanswers/chemicals/metalworking_fluids.html
DERMATITIS

DESPITE THAT STATEMENT, NO PUBLISHED EVIDENCE THAT BACTERIA THEMSELVES CAUSE DERMATITIS

MICROBIAL DEGRADATION PRODUCTS CAN DEFINITELY PLAY A ROLE:

- RANCID FATTY ACIDS AS ONE EXAMPLE
- FLUID CAPACITY TO CAUSE DERMATITIS CAN INCREASE DURING USE
- MOLD PROTEINS
- POSSIBLE ROLE OF BACTERIAL ENDOTOXINS
BACTERIAL ENDOTOXINS

WHAT ARE ENDOTOXINS?

- PART OF THE OUTER MEMBRANE OF THE CELL WALL OF GRAM NEGATIVE BACTERIA
-ALTHOUGH FOCUS TENDS TO BE ON THE LIPOPOLYSACCHARIDE (LPS) PORTION, ALSO INCLUDE LIPOPROTEIN COMPLEXES.
WHAT ARE ENDOTOXINS?

- ALSO KNOWN AS PYROGENS (FEVER CAUSING)
INHALATION EFFECTS OF ENDOTOXINS

- PRODUCE AN INFLAMMATORY RESPONSE IN THE LUNGS
  - ACUTE EFFECTS
  - CHRONIC EFFECTS
INHALATION EFFECTS OF ENDOTOXINS

- REFERENCED AS A POTENTIAL CONCERN IN MWF’s BY R.S. HOLDOM (1976)
  - NOTED THAT ALTHOUGH ENDOTOXIN RESEARCH EXISTED, NO STUDIES INVOLVING MWF’s.
  - “EXPERIMENTAL WORK IN THIS AREA IS LONG OVERDUE”

INHALATION EFFECTS OF ENDOTOXINS

- MOST MWF ENDOTOXIN RESEARCH FROM LATE 1980’s TO LATE 1990’s ALTHOUGH ADDITIONAL PUBLISHED PAPERS SINCE.
- THOROUGH REVIEW OF PUBLISHED PAPERS WAS CONDUCTED BY THE UK HEALTH AND SAFETY LABORATORY IN 2015 – AVAILABLE ON-LINE

BACTERIAL ENDOTOXINS

INHALATION EFFECTS OF ENDOTOXINS

ACUTE EFFECTS

- FEVER
- RESPIRATORY AND FLU-LIKE SYMPTOMS, INCLUDING COUGH, BREATHLESSNESS, CHEST TIGHTENING, SHIVERING, JOINT ACHES
- ACUTE REDUCTION IN LUNG FUNCTION INCLUDING FEV1 (FORCED EXPIRATORY VOLUME)
INHALATION EFFECTS OF ENDOTOXINS

CHRONIC EFFECTS

- RESPIRATORY SYMPTOMS, INCLUDING CHRONIC PRODUCTIVE COUGH DUE TO BRONCHITIS.

NEUTRALIZATION OF ENDOTOXINS

- PUBLISHED WORK DEMONSTRATING THAT ALEDHYDE-BASE BIOCIDES INCLUDING TRIAZINE, OXAZOLIDINE AND GLUTARALDEHYDE CAN NEUTRALIZE ENDOTOXIN\(^4,5\)


BACTERIAL ENDOTOXINS

NEUTRALIZATION OF ENDOTOXINS

- 2003 FINLAND STUDY\textsuperscript{6}
- NOT A ‘STRONG’ STUDY, BUT EVALUATED EFFECTS OF TRIAZINE USE & MACHINE ENCLOSURE ON WORKERS EXPOSURE TO BACTERIA, ENDOTOXINS AND FORMALDEHYDE

\textsuperscript{6} Control of workers’ exposure to airborne endotoxins and formaldehyde during the use of Metalworking Fluids, M.Linnainmaa, H. Kirviranta, J. Laitinen,& S. Laitinen, AIHA J. 64, 496-500 (2003)
KEY FINDINGS OF 2003 FINLAND STUDY

- **ENDOTOXIN AND BACTERIA LEVELS INCREASED RAPIDLY WHEN TRIAZINE LEVEL FELL BELOW 500 ppm.**
- **MACHINE ENCLOSURE & LOCAL EXHAUST VENTILATION SUBSTANTIALLY REDUCED EXPOSURE TO MWF CONTAMINANTS.**
- **AIRBORNE FORMALDEHYDE LEVELS AVERAGED 15% OF THE OEL.**

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6 Control of workers' exposure to airborne endotoxins and formaldehyde during the use of Metalworking Fluids, M.Linnainmaa, H. Kirviranta, J. Laitinen, & S. Laitinen, AIHA J. 64, 496-500 (2003)
RESPIRATORY EFFECTS

- WELL ESTABLISHED KNOWN RANGE OF RESPIRATORY EFFECTS OF EXPOSURE TO MWF MIST
- INCLUDE AIRWAY IRRITATION, LUNG FUNCTION IMPAIRMENT, ALSO BRONCHITIS AND ASTHMA
FIRST DOCUMENTED CASE OF HYPERSENSITIVITY PNEUMONITIS INVOLVING WORKERS EXPOSED TO MWF’s IN US REPORTED IN 1992.

NOW NUMEROUS REPORTED CASES FROM BOTH EUROPE AND NORTH AMERICA.
WHAT IS HYPERSENSITIVITY PNEUMONITIS?

- INFLAMMATION OF THE ALVEOLI CAUSED BY HYPERSENSITIVITY (OVER-REACTION OF THE IMMUNE SYSTEM) TO AN INHALED ANTIGEN
- OFTEN REFERRED TO SIMPLY AS ‘HP’
HYPERSENSITIVITY PNEUMONITIS (EUROPE – EXTRINSIC ALLERGIC ALVEOLITIS)

MANY OTHER NAMES FOR HP, INCLUDING:

<table>
<thead>
<tr>
<th>NAME</th>
<th>CAUSE</th>
</tr>
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<tbody>
<tr>
<td>CHEESE-WASHERS LUNG</td>
<td>Penicillium spp.</td>
</tr>
<tr>
<td>FARMERS LUNG DISEASE</td>
<td>MOLDS /ACTINOMYCETES</td>
</tr>
<tr>
<td>BIRD FANCIERS DISEASE</td>
<td>AVIAN PROTEINS</td>
</tr>
<tr>
<td>MUSHROOM WORKERS LUNG</td>
<td>ACTINOMYCETES</td>
</tr>
<tr>
<td>TOBACCO WORKERS LUNG</td>
<td>Aspergillus spp.</td>
</tr>
<tr>
<td>HOT TUB LUNG</td>
<td>Mycobacterium avium complex</td>
</tr>
<tr>
<td>WINE-GROWERS LUNG</td>
<td>Botrytis cinerea</td>
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</tbody>
</table>
HYPERSENSITIVITY PNEUMONITIS

- CAN INCLUDE ACUTE, SUB-ACUTE AND CHRONIC ILLNESS
- SYMPTOMS CAN INCLUDE FEVER, COUGH, WORSENING BREATHLESSNESS, WEIGHT LOSS
- PROGRESSIVE FIBROTIC CHANGES TO RESULTING IN REDUCED LUNG VOLUME
- SYMPTOMS OF EMPHYSEMA
- CHRONIC CAN INCLUDE ‘HONEYCOMBING’ OF ALVEOLI
DIAGNOSIS IS BASED ON BOTH SYMPTOMS AND CLINICAL TESTS, INCLUDING:

- X-RAY AND/OR CT SCANS
- LUNG FUNCTION TESTS
- BLOOD WORK

ALSO POSSIBLY A LUNG BIOPSY
HYPERSENSITIVITY PNEUMONITIS

- If diagnosed early, removal from exposure to the causative antigen can lead to full recovery.
- If undiagnosed, can lead to permanent lung damage, potentially fatal.
SOME OF THE EARLIEST PUBLISHED PAPERS SUGGESTED MYCOBACTERIA AS THE CAUSE OF HP IN MWF OPERATORS.

ALSO SUGGESTION THAT USE OF TRIAZINE MIGHT BE A CONTRIBUTING FACTOR IN MYCOBACTERIA GROWTH IN MWF’s (PUBLISHED WORK SINCE HAS REFUTED THIS).
HYPERSENSITIVITY PNEUMONITIS

- **NEED TO BE CAREFUL WHEN REVIEWING PUBLISHED PAPERS** – SOME OF THE EARLY STUDIES HAVE BEEN SHOWN TO BE SERIOUSLY FLAWED.
  - MYCOBACTERIA ARE RELATIVELY SLOW-GROWING VS. THE COMMON GRAM NEGATIVE BACTERIA
  - NEED TO USE SELECTIVE CULTURE TECHNIQUES
HYPERSENSITIVITY PNEUMONITIS

ANIMAL STUDIES DO SHOW THAT
*Mycobacterium immunogenenum* ISOLATED
FROM MWF’s CAN CAUSE HP IN MICE

*Mycobacterium immunogenenum* causes Hypersensitivity
Pneumonitis-Like Pathology in Mice

- Heat-killed and lysed *M. immunogenenum* produced HP-like
  pathologic changes in Mice
- Results indistinguishable from exposure to MWF containing *M.
  immunogenenum*
- Using different strains of mice, also demonstrated that genetic
  factors may contribute to susceptibility to HP.
- Conclusions: Study provides indirect evidence for
  *Mycobacterium immunogenenum* as A cause of HP in MWF
  outbreaks.
HYPERSENSITIVITY PNEUMONITIS

ANIMAL STUDIES DO SHOW …

8 Metalworking Fluid with Mycobacteria and Endotoxin Induces Hypersensitivity Pneumonitis in Mice
P. S. Thorne et al.

KEY FINDING: mice exposed to *M. immunogenenum* in MWF develop lesions consistent with HP, and that these are worsened by the addition of small amounts of endotoxin.

CONCLUSIONS:
“.. Control of mycobacteria and endotoxin contamination of in-use MWF is likely of importance for the prevention of HP among machinists.”
SUMMARY AND CONCLUSIONS

- ANIMAL STUDIES DO DEMONSTRATE THE POTENTIAL OF MYCOBACTERIA TO CAUSE HP
- SINCE MYCOBACTERIA DO NOT APPEAR TO BE INVOLVED IN ALL MWF OUTBREAKS OF HP, OTHER FACTORS MUST BE INVOLVED IN AT LEAST SOME HP CASES.
SUMMARY AND CONCLUSIONS

- MWF’s SUPPORT THE GROWTH OF OTHER BACTERIA AND FUNGI THAT ARE KNOWN ANTIGENS, AND THAT HAVE BEEN INVOLVED IN CASES OF HP IN NON-MWF SETTINGS.
- ANIMAL STUDIES SHOW THAT COFACTORs SUCH AS ENDOTOXINS MAY PLAY A ROLE.
- ROLE OF GENETICS – CLEAR THAT INDIVIDUAL SUSCEPTIBILITY TO HP VARIES.
KNOWLEDGE GAPS

METALWORKING FLUID MICROBES: WHAT WE NEED TO KNOW TO SUCCESSFULLY UNDERSTAND CAUSE-AND-EFFECT RELATIONSHIPS


- EXCELLENT REVIEW PAPER. ALTHOUGH ALMOST 10 YEARS HAVE PASSED, MUCH OF THIS IS STILL VALID.
- LITTLE NEW KNOWLEDGE PUBLISHED SINCE.
ENDOTOXINS

THE ONLY JURISDICTION THAT CURRENTLY HAS AN ESTABLISHED RECOMMENDED OCCUPATIONAL EXPOSURE LIMIT (ROEL) IS THE NETHERLANDS:

- 90 ENDOTOXIN UNITS PER CUBIC METER (EU / M³)
KNOWLEDGE GAPS

▶ ENDOTOXINS

▶ THERE’S INSUFFICIENT DATA TO DETERMINE WHETHER THE ROEL IS IN FACT PROTECTIVE FOR ALL WORKERS

▶ RELATIONSHIP BETWEEN ENDOTOXIN LEVELS IN SUMPS VS FLUID MIST NOT CLEAR.

▶ NEED MORE STUDIES
KNOWLEDGE GAPS

- HYPERSENSITIVITY PNEUMONITIS
- STILL DON’T HAVE A CLEAR UNDERSTANDING OF ALL THE FACTORS INVOLVED.
- IN MANY OF THE EARLY OUTBREAKS, IT WAS CLEAR THAT THERE WAS A GENERAL LOSS OF MICROBIAL CONTROL IN FLUID SYSTEMS.
- MAY NOT BE TRUE FOR MORE RECENT CASES\(^9\)

\(^9\)PERSONAL COMMUNICATION, DR. GARETH EDWARDS, UK HSL
HYPERSENSITIVITY PNEUMONITIS

NOW KNOW THAT MYCOBACTERIA ARE BIOFILM ‘PIONEERS’.

SO CONTROL OF BIOFILM MAY BE VERY IMPORTANT.

VERY LITTLE REPORTED WORK ON BIOFILMS IN MWF SYSTEMS, MOST STUDIES ARE ON THE PLANKTTONIC POPULATION.
KNOWLEDGE GAPS

- MYCOTOXINS

- MANY OF THE FUNGAL SPECIES IDENTIFIED IN CONTAMINATED MWF’S ARE KNOWN TO PRODUCE MYCOTOXINS.

- AS PASSMAN POINTED OUT IN HIS PAPER,
  - NO INDICATIONS IN THE LITERATURE THAT MYCOTOXINS HAVE BEEN A CAUSE OF RESPIRATORY ISSUES IN MWF OPERATORS.
  - “NOT CLEAR WHETHER THIS REFLECTS AN ABSENCE OF EFFECT, OR AN ABSENCE OF DATA.”
WHAT’S THE MESSAGE?

- STILL A LOT THAT WE DON’T KNOW
- VERY CLEAR THAT MWF OPERATOR EXPOSURE TO BACTERIA AND/OR FUNGI AND THE BY PRODUCTS OF THEIR GROWTH PLAYS A ROLE IN POTENTIAL HEALTH ISSUES.
WHAT’S THE MESSAGE?

SO CONTROL OF MICROBES CONTINUES TO BE IMPORTANT, BOTH FOR:

▶ MAINTAINING FLUID QUALITY AND PERFORMANCE

▶ BUT PERHAPS MORE IMPORTANTLY, TO MINIMIZE POTENTIAL HEALTH EFFECTS IN EXPOSED WORKERS.
Thank You

QUESTIONS?

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