


NEUROLOGICAL DISEASE – A REVIEW OF THE CHEMICAL EXPOSURE HEALTH RISKS AND A CRITIQUE OF THE OCCUPATIONAL HYGIENE STUDIES

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▶ Aims of the presentation

1. DESCRIBE NEUROLOGICAL DISEASES (ND)
 2. THE RELATIONSHIP TO CHEMICAL EXPOSURE
 3. A LOOK AT CLUSTER CASES INVOLVING CHEMICALS
 4. LINKS WITH GLUTAMATE BIOCHEMISTRY
 5. CRITICAL REVIEW OF OCCUPATIONAL HYGIENE STUDIES
 6. CONCLUSION
 7. REFERENCES
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► NEUROLOGICAL DISEASE

1. SEVERAL MAIN ND – MOTOR NEURONE DISEASE (AMYOTROPHIC LATERAL SCLEROSIS), PARKINSON'S DISEASE, MULTIPLE SCLEROSIS AND ALZHEIMER'S DISEASE.

2. ND ACCOUNT FOR 4% OF ALL DEATHS (OCCUPATIONAL ?). AFFECT MOTOR NEURONS CAUSING MUSCLE WEAKNESS ETC.

3. DISEASES HIGHER IN MEN THAN IN WOMEN (RELATED TO GENETIC MUTATIONS SOD1 AND 30 OTHERS).

4. MND IS THE MOST COMMON ND WITH DEATH WITHIN 2 TO 5 YEARS. PERSONS LIFETIME RISK OF DEVELOPING MND IS AROUND 1 IN 300.

5. THERE ARE MULTIFACETED CAUSES FOR ND APART FROM CHEMICAL EXPOSURE FOR EXAMPLE HEAD INJURIES.

▶ CHEMICAL EXPOSURES RELATED TO CAUSES OF MND (AND ND)

- LEAD
- FORMALDEHYDE
- METHYL CHLORIDE
- MERCURY
- ALUMINIUM
- SOLVENTS
- PESTICIDES
- CADMIUM
- INORGANIC ARSENIC
- MANGANESE

- NON-CHEMICAL CAUSES INCLUDE EXPOSURE TO ELECTROMAGNETIC RADIATION, HEAD INJURY, PHYSICAL ACTIVITY (FOOTBALL),

▶ CASES OF CLUSTERS OF MND

1. OCCUR SPORADIC OR IN CLUSTERS. CLUSTER IS A GROUPING OF UNCOMMON DISEASE
2. CLUSTER MAY BE BASED ON TIME, SPACE OR TIME/SPACE
3. IN LANCASHIRE AND CUMBRIA HIGH NUMBER OF MND CASES BETWEEN 1989-1993 – LITTLE OCC HYGIENE EXPOSURE OBTAINED FROM 130 PATIENTS. NEED TO STUDY/INVESTIGATE SUCH CLUSTERS AS THEY ARISE
4. ANOTHER CLUSTER - METHYL BROMIDE FUMIGANT ASSOCIATED WITH MND CLUSTER IN NZ – BETWEEN 1995-2005 16 RECORDED CASES IN NELSON/TASMAN AREA
5. EXAMINED THIS CLUSTER IN DETAIL AS METHYL BROMIDE EXPOSURE WAS SEEN AS A MND HIGH RISK FACTOR

▶ METHYL CHLORIDE EXPOSURE – CAUSATIVE MECHANISM?
NEED TO LOOK AT ENVIRONMENTAL ASPECTS

1. IN NELSON/TASMAN DOCK AREA , FOODSTUFFS HANDLED INCLUDING CYCLADS
2. BETA-METHYL-AMINO-ALANINE (BMAA) (– EXPOSURE LINKED TO HIGHER INCIDENCE OF MND) FOUND IN CYCLADS
3. BMAA RELEASED FROM CYCLADS WHEN METHYL CHLORIDE ADDED DURING FUMIGANT TREATMENT
4. POTENTIAL RESPIRATORY, DERMAL AND INGESTION OF BMAA DURING METHYL CHLORIDE USE AS A FUMIGANT
5. BODY BUILD-UP IN DOCK WORKERS
6. HIGH RISK OF NEUROLOGICAL SYMPTOMS IN THOSE WITH GENETIC DEFICIENCY IN GLUTAMATE METABOLISM
7. IN 2014 A FRENCH STUDY LINKED BMAA TOXINS TO MND (DELZOR, COURATIER ET AL BMJ). PRODUCED BY CYANOBACTERIA IN ENVIRON
8. IN STUDIES ON CHEMICAL EXPOSURE AND ND/MND LITTLE DATA GIVEN ON ENVIRONMENTAL HAZARDS


CHEMICAL EXPOSURE AND GLUTAMATE BIOCHEMISTRY

1. If exposure to chemicals is a high risk factor in causing ND/MND then we would expect to find higher than expected cases in those industries handling the chemicals e.g. lead battery dismantling, mercury recycling, foundry work, welding but this is not the case except in a few clusters.
2. In only 1% - 2% of the studies on MND, have monitoring data for exposure assessments of those chemicals related to high ND risks, been included.
3. There is evidence that exposure to chemicals used in the workplace may affect glutamate metabolism in genetically disposed workers.
4. For example, disturbances in lead metabolism have been linked to disturbances in glutamate homeostasis that could significantly reduce motor neurone function.
5. Exposure to formaldehyde has been shown to cause deficiencies in glutamate metabolism. Such chemicals that have been shown to affect glutamate biochemistry should be identified and studied in depth.


CRITIQUE OF OCCUPATIONAL HYGIENE PAPERS (1)

1. Pearce and Kromhout (Neurodegenerative disease: the next occupational disease epidemic. *Occup. Environ Med*; 71: 594-595 2014.) have stated that the occ hyg peer review papers on MND/ND are poor, inadequate and repeat the same data from the same peer review papers. I agree with their conclusions.
2. In most papers there is little occ hygiene qualitative and quantitative data given on which to assess the level of risk.
3. There is also little information on the controls used to mitigate chemical exposure in high risk areas.
4. There also tends to be little mention of the WELs and whether there was compliance with the WELs during the study. What were regarded as high levels of exposure on which to assess the health risks?
5. Furthermore, there was a lack of data on the tasks carried out by the high risk workers, on the numbers of workers exposed and on the time etc as one would expect in a full study.


CRITIQUE OF OCCUPATIONAL HYGIENE PAPERS (2)

1. Prospective cohort studies have not been widely used in assessing the chemical exposure health risks (Blair et al 2015).
 2. Garzillo et al (2016) have investigated the literature on occupational exposure and MND onset and they have found a lot of biases in the studies design including the statistical analyses that do not allow any conclusions.
 3. Baxter et al (2009) have shown that in numerous studies there have been little statistical analysis of the results.
 4. Meta-analysed data have tended to ignore historical and prospective cohort studies.
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CRITIQUE OF OCCUPATIONAL HYGIENE PAPERS (3)

1. There is a need to provide a better means to understand and record the symptoms of ND.
 2. Detailed occupational hygiene studies need to be undertaken so that exposures can be accurately assessed and grouped and the effectiveness of the control measures ascertained i.e. intervention studies by HSE?
 3. There is also a need to evaluate the role of multi-task factors within appropriate chemical and population based studies.
 4. Furthermore, it is necessary to accurately record the potential risk factors and try to standardise the results.
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CONCLUSIONS

1. Undertake more in-depth occupational hygiene studies.
 2. Use the appropriate statistical analyses e.g. cohort studies.
 3. Set up a register of cases of ND (improve diagnosis) and use the data for future studies.
 4. Improve the standardisation of data assessment so that the results of surveys can be better interpreted e.g. improve the training of hygienists so that judgements made of the results are more consistent.
 5. Carry out studies on the biochemistry of glutamate metabolism e.g. to understand how chemical exposure can disturb glutamate metabolism in susceptible workers and lead to damaged neurones as found in ND/MND.
 6. Measures could then be available to screen high risk individuals, develop suitable bio-markers, understand the changes in glutamate malfunction and eventually find a means to treat ND/MND.
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