Occupational diseases-old and new. How can they be traced?

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"Il sistema Malprof e le reti di rilevazione delle malattie professionali"
Objectives of presentation

• Introducing concepts of ‘new’ occupational diseases and new ‘causes’ of occupational disease.

• Outlining the MODERNET network

• Introducing subsequent speakers with special reference to:
  • Tracing new occupational diseases or causes of disease
    (*Dr Vincent Bonneterre)
  • Tracking trends in known occupational disease and evaluating interventions
    (*Dr Roseanne McNamee)
  • Stimulating a dialogue with all concerned (especially the audience) regarding what we hope and expect from MODERNET
    (*Professor Claudio Colosio)
Why this interest? – 1 (the Physician)

For ‘old’ / ‘known’ diseases

• To recognise situations of high risk e.g. jobs, exposures
• To understand ‘trends’ in incidence
• To evaluate interventions

For ‘new’ diseases or ‘new’ causal agents

• To be aware of new causes of disease i.e. new ‘agents’ when these are presented by a patient whose symptoms and other aspects suggest occupational ill health of recognised pathology

• To be aware of new diseases i.e. new pathological processes when the presenting symptoms appear work related but the pathological process has not been previously known as occupational
Why this interest? – 2 (the Hygienist)

• To assess risk, and especially the quantitative relationship with exposure

• To take or recommend appropriate preventive steps

• To understand which interventions work best

• To be able to predict new hazards, perhaps even risks
Why this interest – 3 (the Statistician)

- To achieve an evidence based consensus on appropriate methods of data collection, handling and analysis
- To understand the strengths as well as the difficulties and limitations of the methods, and to work to improve these methods
- To have comparable results (as far as possible) across different countries or other contexts
‘New’ disease example

• It had already been well known that dibromochloropropane (DBCP) a nematocide pesticide (widely used from 1952-1977) causes male infertility through a decline in production of spermatozoa (after damage to Sertoli and/or Leydig cells):

$$\text{CH}_2\text{Br-CHBr-CH}_2\text{Cl}$$

• Later (Kim et al 1996, etc) it was shown that 2-bromopropane (maybe also 1-bromopropane) can cause ovarian failure (and even pancytopenia):

$$\text{CH}_3\text{-CHBr-CH}_3$$

• Is there an analogy between the two?
‘New’ disease example

- Popcorn workers’ lung:

Bronchiolitis obliterans in microwave popcorn workers using the artificial butter flavouring 2,3-butanedione (‘diacetyl’):

$$\text{CH}_3\text{-CO-CO-CH}_3$$

Note that similar pathology also reported with an analogous alpha-diketone i.e. 2,3-pentanedione (a flavouring substitute for diacetyl):

$$\text{CH}_3\text{-CO-CO-CH}_2\text{-CH}_3$$
‘New’ disease example

- Textile sprayers’ lung:

Various polyamines (poly-cationic) causing a complex interstitial / bronchiolitic / organising pneumonia in Spain and Algeria (Ardystil syndrome)

Acramin FWR i.e.

Bis-(3-aminopropyl)methylamine

\[
\text{H}_2\text{N}-\left(\text{CH}_2\right)_3-\text{N}-\left(\text{CH}_2\right)_3-\text{NH}_2
\]

\[
\text{CH}_3
\]

+ Hexamethylenediisocyanate

\[
\text{O}=\text{C}=\text{N}-\left(\text{CH}_2\right)_6-\text{N}=\text{C}=\text{O}
\]
The ‘old’ … asbestos (and mineral pneumoconiosis):

...and the ‘new’ … nanoparticles including nanotubules:

The evidence* suggests that the hazard is governed by the same ‘rules’ as for the ‘old’ hazards:

• agents very resistant to biological dissolution
• longer fibres than 5 microns
• aspect ratio (similar to asbestos)

* Donaldson et al 2012
But…

This is not just about:
• rare diseases
• investigated by academics
• in other parts of the world
• in highly specialised workplaces

It is also about:
• common everyday workplaces which we all know (offices, hospitals)
• where agents are used for common and important tasks (such as cleaning or disinfecting)
• new products, substitutes and working practices appearing all the time
‘New’ causes of a recognised disease
(example: occupational asthma)

• As reported in 2011 in the UK to SWORD (Surveillance of work-related and occupational respiratory disease)

• which is a component scheme of THOR (The Health and Occupation Research Network)

• and which in turn is a component of MODERNET (Monitoring trends in Occupational Diseases and tracing new and Emerging Risks in a Network)

• Hydroxychloroquine (process operator)
• Denatonium (nurse)
Health care, disinfecting, cleaning and other common occupational contexts …
Substitution of a recognised hazard

Glutaraldehyde
Substitutes … How ‘safe’ are they?

O:CH-CH₂-CH₂-CH₂-HC:O

(Glutaraldehyde; pentan-di-al)

O:CH-CH₂-CH₂-HC:O

(Succinyl dialdehyde; butan-di-al)

O:CH-HC:O

(Dialdehyde; ethan-di-al)

O:CH-<C₆H₄>-HC:O

(Ortho-phtalaldehyde; ‘OPA’)
Phthalic anhydride (above) – a well recognised asthmagen – but simple reduction $\Rightarrow$ ortho-phtalaldehyde (OPA)
(Structure activity relationships predicted OPA as an asthma hazard and now it too has been reported as an asthmagen)
The same concerns can apply to a range of other contexts ...

Examples:

• Quaternary ammonium compounds in cleaning
• Alcohol gels and other agents in hand rubs
• Biological agents in current ‘industrial’ food processing
• Other new technologies (e.g. ‘nano’)
• Non-ionising radiation from modern technology
• etc etc

How can we collectively address such issues for the common good?
Monitoring trends in Occupational Diseases and tracing new and Emerging Risks in a Network MODERNET

- FRANCE (RNV3P)
- ITALY
- NETHERLANDS
- UK (THOR)
- Total of 16 EU countries
- 2 non-EU countries
Ingredients for a successful recipe include...

Quality (Workgroup1) Stefano Mattioli

• Definitions and/or guidelines for diagnosing occupational disease
  • (not just lists)
  • Evidence based (or at least consensus based)
  • Consistent and generally applicable

• Reporter base
  • Motivated and competent
  • Representative
Ingredients … continued …

• **Numerator data collection**
  - Comprehensive (‘disease’, exposure…), and feasible
  - (any limitations recognised and understood)

• **Denominator**
  - Properly matching the numerator
  - Basic demographics (age, gender, geography …)
  - Industry and job (occupation)
  - (by exposure would be ideal but difficult)
A challenge: Calculating risk to inform decisions.

Denominator (Population at risk) + Other information e.g. exposure

Numerator (Surveillance Reports)
Basic cooking technique …

- *Trends (Workgroup2) Roseanne McNamee*

- **Calculation of incidence**
  - From the numerator, denominator and time
  - But also proceed to determine trends in incidence
  - …Prospects of comparing incidence and trends in incidence
  - …Evaluation of interventions
Cases of *occupational asthma* attributed to *latex* exposure reported to SWORD (1991-2007)
Ingredients and methods… continued ...

• New hazards / emerging risks (Workgroup3) Vincent Bonneterre

• Comprehensive data collection (‘disease’, occupation, exposure)
• Means of identifying possible links and signals
• Validation of the above

A special example of a complementary technique to help predict new asthma hazards now follows ….
**Not-asthmagens vs Asthmagens**

- **Ethylamine** \( \text{CH}_3\text{CH}_2\text{NH}_2 \)
- **Ethylenediamine** \( \text{H}_2\text{NCH}_2\text{CH}_2\text{NH}_2 \)
- **Piperazine**
- **Piperidine**
- **Aniline** \( \text{NH}_2 \)
- **P-Phenylenediamine** \( \text{H}_2\text{N} \)
- **Isonicotinic acid hydrazide** \( \text{CONH-NH}_2 \)
- **Hydralazine**
Asthma ‘Hazard Index’ determined by QSAR (Quantitative Structure Activity Relationship)
SWORD 2011   Reports of occupational asthma (sensitisation) due to novel LMW agents & corroboration by QSAR

Hydroxychloroquine*  

CAS 118-42-3

\[
\text{Hazard Index} = 1
\]


Denatonium  (CAS No. for Denatonium benzoate 86398-53-0)

Cation structure:

\[
\text{Hazard Index} = 0.92
\]
Summary learning points for chemical structure & asthma

The following suggest an a possible asthma hazard:

• For low molecular weight organic chemicals:
  • Presence of >1 ‘reactive group’, especially if
  • Nucleophilic eg amines or
  • Electrophilic eg aldehydes, anhydrides or
    unsaturated (perhaps ? biotransformation needed)

• For large molecular weight organic chemicals e.g. enzymes and
  other proteins
  • IgE epitopes (? Role of critical core amino acid residues)

• For inorganics
  • Certain transition metals either when cations or [perhaps especially] if in anions bound to organic moieties
  • Gases which when hydrated generate H+ and/or oxygen radicals
Summary learning points for ‘function’ / ‘application’ in respect of asthma hazard of Low Molecular Weight organics

• If it is a gas or an easily volatile vapour or respirable (fine light dust) and

• It is intended to denature proteins (e.g. disinfectants, antimicrobials etc) or

• It has ‘superglue’ properties, or is a ’reactive dye’ or it paints through a chemical reaction (not just drying)

• Or it is used as a chemical hardener, or can readily polymerise or form a resin

=> Then watch out – it may well be asthmagenic!
Sharing the recipe ...

Dissemination (Workgroup 4) Claudio Colosio

• The output of MODERNET is intended to be of benefit to a variety of stakeholders in the EU (such as yourselves) and beyond

• MODERNET will be strengthened by your input

• Therefore the importance of continuous dialogue (i.e. two way communication) is recognised
Cosa speriamo, o ci aspettiamo, da MODERNET?

“Linee guida cliniche per le diagnosi di …”

“Dati statistici sui trend delle malattie professionali”

“Informazioni sulle attività lavorative a più alto rischio”

“Agenti di rischio non noti in precedenza”

“Metodi adeguati a prevedere rischi sconosciuti”

“Confrontare I rischi presenti sul mio luogo di lavoro con quelli presenti in altri ambiti lavorativi…”

“… ??? … ??? …”
Come pensiamo, o speriamo, che MODERNET o i progetti successivi possano portare a ciò?

“Un sito web ampio ed esaustivo”

“una “e-Newsletter” così concepita …”

“Flusso “top-down” di informazioni a organismi nazionali”

“Pubblicazioni così concepite……”

“Conferenze e riunioni …”

“Altri mezzi…”

“... ??? ... ??? ...”
Commenti, domande e suggerimenti a...

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