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ACC Workwise
Auckland

So What Makes You Think You have Been Poisoned? - Concurrent Workshop Repeated

Saturday, 17 August 2013

Start 11:00am

Duration: 55mins

Colosseum

Start 12:05pm

Duration: 55mins

Colosseum



South GP CME 2013

General Practice Conference & Medical Exhibition

15-18 August | Edgar Centre | Dunedin



So you think you have been poisoned?

John Monigatti & Michael Beasley
GP CME Meeting 2013

Was the current illness caused by exposure to toxins at work, perhaps many years ago?



The Straightforward

- Work exposure to agent known to cause that disease
- Disease not known to be caused by any agent
- No disease
- No exposure



The Obsessed

- Nearly always have a grievance
- Often a bit mad
- May put great pressure on GP
- Claim not plausible
- Never go away

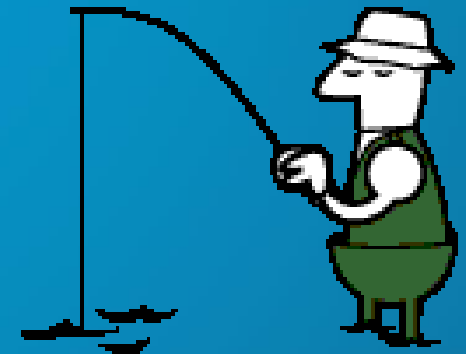


The Bereaved

- Usually unresolved grief
- Often have a grievance
- May have medical sympathiser
- May desist if feels listened to

The Speculative

- Condition known to be caused by some agents
- Agent known to cause some diseases – but not this one
- May have medical support
- May persist



The Challenging

- Some research evidence for an association
- Plausible mechanism exists
- Medically aware
- Often have medical contacts
- Rarely admit defeat



The Toxicology Panel

- Established in 1998 originally for PCP & phenoxyherbicide claims
- Five specialists (one from ACC)
- Meets quarterly (up to 6 new cases)
- Determines cover by consensus



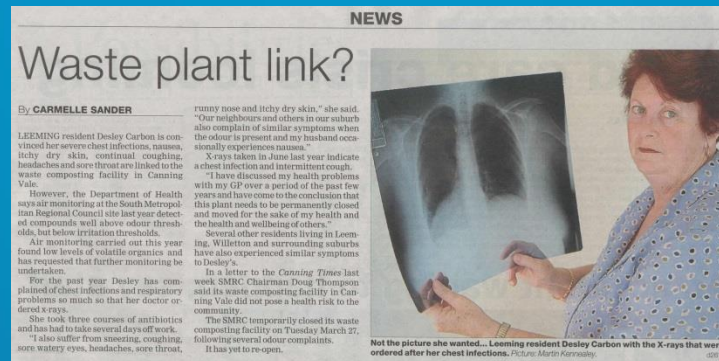
Why have one?

- Transfers responsibility from Branch medical advisor
- Pooled expertise
- Perceived to be independent
- Deters the hired guns
- Individuals less likely to be targeted



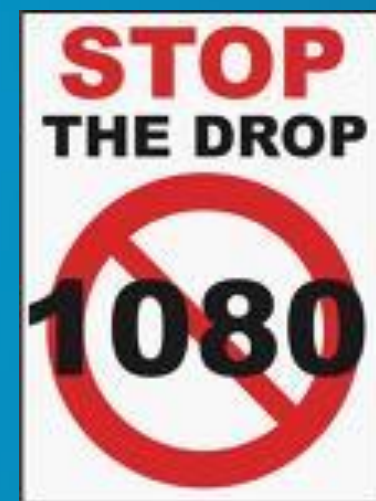
Which cases?

- The challenging
- The speculative (if has medical support)
- The bereaved (if has medical support)
- Those who hassle, complain, go to the media



What is implicated?

- PCP & dioxin
- Pesticides (inc. 1080, Roundup, BTK)
- Solvents, paints, fuels
- Heavy metals
- Any pungent substance
(e.g. onions, chlorine)
- Anything to which people feel they have been
exposed involuntarily



What do people claim for?

- Symptoms – anything you can think of!
- Cancer
 - Leukaemia
 - Lymphoma
 - Lung, bladder, prostate
- Brain injury, neuropathy
- MCS, CFS, CPS, SBS, GWS, ...

Problems

- Exposure usually historical
- Reliance on memory
- No workplace to assess
- Usually no exposure data
- Multiple confounding factors
- No comparison group



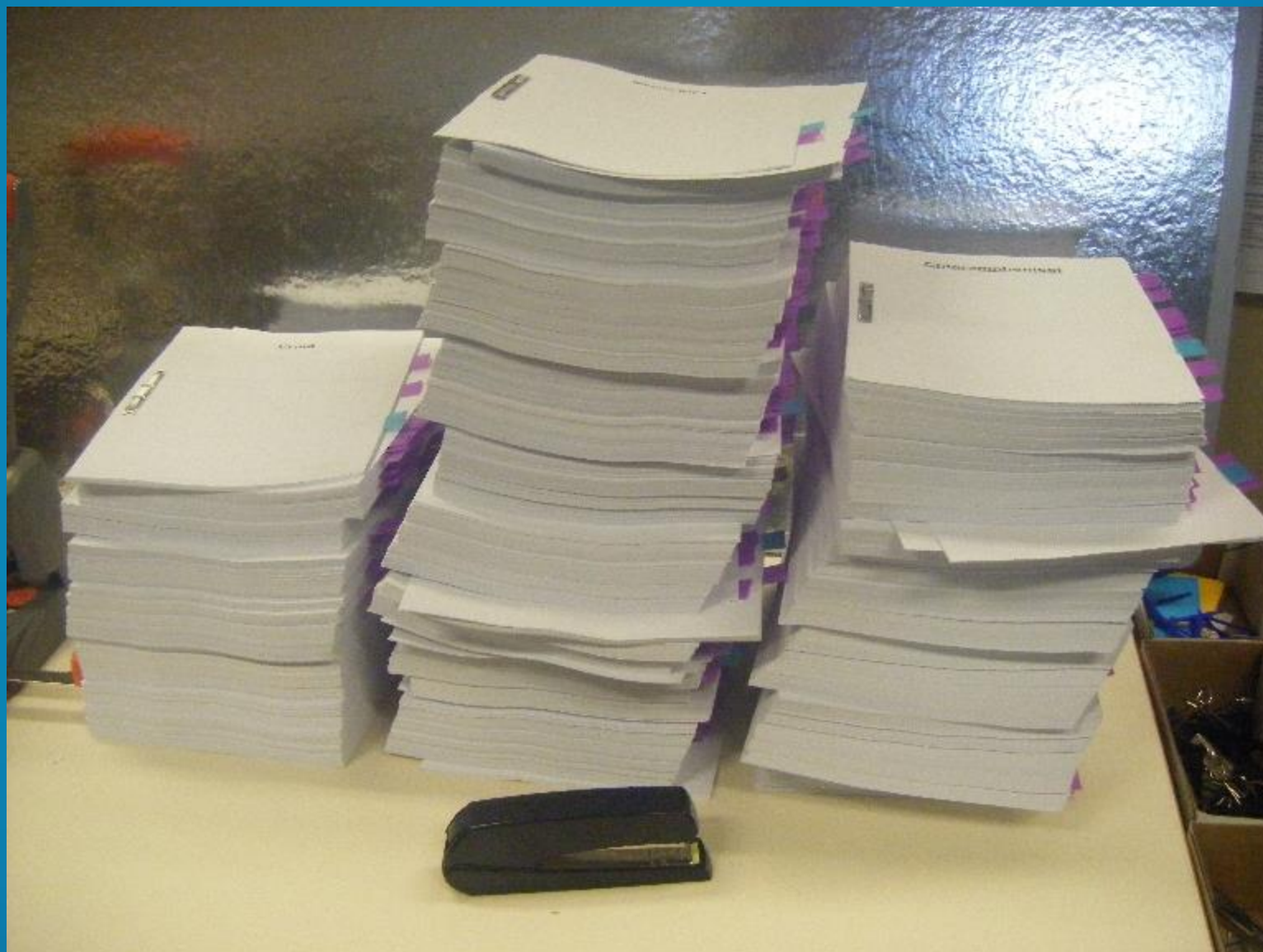
Key questions

- Known effect of the agent?
- Significant exposure? (e.g. indirect measures)
- Increased risk in this occupational group?
- Appropriate timeframe?
- Plausible biological mechanism?
- Background incidence?
- Disease known to be caused by any “toxin”?
- Personal risk factors?
- **IS THERE A BETTER EXPLANATION?**



1) CLL from community spray exposure?

- Male 54, ex-photographer & teacher
- Diagnosed with chronic lymphocytic leukaemia, anxiety, depression, neck pain, hypogonadism & low testosterone in 2002. Now polysymptomatic
- Off work with stress in 2003, never resumed
- Claimed poisoning from aerial exposure in 2002 to Painted Apple Moth spray (Foray 48B); containing "BtK" (Bacillus Thuringiensis Berliner var. kurstaki)



Toxicology

- Undisclosed constituents in formulation
- Information that it contains **chloramphenicol**, added to BtK nutrient broth to suitably modify BtK
- Haematotoxic; primarily aplastic anaemia (AA), though “leukaemia” is also reported.
- But leukaemia is very rare & mostly preceded by AA
- Also, in many AA cases, large doses had been taken repeatedly over many years

Approach

- Known effect of agent? Yes, but leukaemia extremely rare
- Significant exposure? Likely to be extremely low
- Risk known to be increased in occupational group? N/A
- Appropriate timeframe? No (~ 1 yr v 5-10 yrs)
- Plausible biological mechanism? Yes, via blood dyscrasia
- Disease known to be caused by any toxin? Yes – CLL by IR, benzene?, other solvents?
- Background incidence? Yes
- Personal risk factors? No
- **IS THERE A BETTER EXPLANATION?** Probably

Outcome

- Not a plausible cause of his CLL or other medical complaints
- Significant personal & psychological factors are likely to be influencing & modulating the presentation
- Cover withheld

2) Pyrethroids causing hepatic failure in a pest exterminator?

- Male 59, fly/spider pest controller 2005-2010, no occupational chemical exposure beforehand
- Diagnosed with **hepatic cirrhosis** 2010. Already known to have bladder cancer and Type II diabetes
- Lifelong non-smoker & non-drinker
- Claimed liver disease caused by exposure to insecticide sprays containing **pyrethroids**

Toxicology

- Lab studies: hepatic adenomas in rats at high doses
- Humans thought less susceptible to this particular effect of pyrethroids (don't induce human hepatocyte proliferation)
- Hepatotoxicity very seldom reported in human case reports (eg mild AST incr' after ingestion incl' solvents)
- Pyrethroids at relatively low levels in the concentrated (let alone diluted) formulations
- No reporting of classical paresthesia sensations at the time suggests a relatively modest exposure in this case

Toxicology

- What about the **solvents?** – largely a mix of petroleum hydrocarbons; not totally devoid of hepatotoxicity but rare to cause cirrhosis
- Teetotaller, no IV drugs, -ve hepatitis serology, no evidence of haemachromatosis, Wilson's disease
- However, history of diabetes
- Risk factors for nonalcoholic fatty liver disease (NAFLD) include obesity, hypertriglyceridemia & diabetes. A small percentage develop nonalcoholic steatohepatitis (NASH), of whom possibly 10% develop cirrhosis

Approach

- Known effect of agent? **No**
- Significant exposure? **Possibly**
- Increased risk in this occupational group? **No**
- Appropriate timeframe? **Possibly too short**
- Plausible biological mechanism? **No**
- Disease known to be caused by any toxin? **Yes—few solvents**
- Background incidence? **Yes**
- Personal risk factors? **Yes – diabetes**
- **IS THERE A BETTER EXPLANATION?** **Yes – idiopathic**

Outcome

- No risk factors except diabetes, but one-third of cases idiopathic
- Pyrethroids not known to be significantly hepatotoxic to humans
- No irritant symptoms to suggest moderate to high exposures
- Cover withheld

3) Peripheral neuropathy from isocyanates?

- Male aged 70, entire working career as sign writer
- 10-yr history of altered sensation in feet
- NCS showed longstanding symmetrical distal polyneuropathy. Cognitive function normal
- Claimed poisoning from workplace chemicals citing poor exposure controls
- Products included di-isocyanates in paints

Toxicology

- Di-isocyanates are irritants & well known causes of allergic asthma, and occasionally hypersensitivity pneumonitis and allergic contact dermatitis (ACD)
- Used in 2-pot paints, pre-polymers, plastics, surface coatings, polyurethane foam ...
- Neuropathy from dimethylaminopropionitrile (DMAPN), a catalyst used in polyurethane production in 1970's, but this since discontinued

Toxicology

- Growing list of chemicals incl' solvents linked to peripheral neuropathy, but seldom cause this as an isolated finding
- Eg. N-hexane: Symptoms in exposed patients typically included one or more of anorexia, weight loss, nausea, vomiting preceding or accompanying symptoms of P.N.
- With di-isocyanates, would also expect some neuropsychological or neurocognitive effects
- Eg. 3 workers acutely exposed to TDI (1987):
- Neuropsychological Sx (headache, fatigue, irritability, depression, decreased concentration, memory) much more prominent than peripheral nerve effects (only subclinical reduced impulse amplitude & conduction velocity noted)

Approach

- Known effect of Agent? No, historical only. cf known effects of irritant Sx, asthma, CNS neurotoxicity
- Significant exposure? Yes, poor workplace controls
- Risk known to be increased in relevant occupational group? No
- Appropriate timeframe? Yes
- Plausible biological mechanism? Yes, solvents potentially neurotoxic
- Disease known to be caused by any toxin? Yes, n-hexane, CS2 ..
- Background incidence? Yes
- Personal risk factors? No
- **IS THERE A BETTER EXPLANATION?** Very likely

Outcome

- No risk factors but many cases idiopathic
- Isocyanates not known to be peripheral neurotoxins
- No exposure to other recognised causes of toxic peripheral neuropathy
- Despite poor controls, no additional symptoms or evidence of brain injury to suggest toxicity from either isocyanates or solvents
- Cover withheld

4) Benzene-induced AML in a diesel mechanic?

- Male 40, 15 years as diesel mechanic including some welding
- Diagnosed with acute myeloid leukaemia (AML)
- 20-year smoking history
- Claimed causation by exposure to solvents (as degreasers) & fuels
- Some likely or possibly contained benzene

Toxicology

- Benzene is a confirmed cause of aplastic anemia (AA) and acute myeloid leukemia (AML)
- IARC Classification: Group 1
- AML attributed to a genotoxic metabolite
- Individual variability in metabolism (~ 13 fold)
- Relatively extensive occupational data enabling estimates of risk as a function of cumulative dose (average concentration x time; ppm x yrs)

Approach

- Known effect? **Yes; aplastic anaemia, myeloid leukaemia**
- Significant exposure? **Nil benzene in diesel, but in petrol, ? in some other solvents**
- Increased risk in occupational group? **Possibly**
- Appropriate timeframe? **Yes – 5 to 15-year latency**
- Plausible biological mechanism? **Yes, via blood dyscrasia**
- Disease known to be caused by any toxin? **Yes**
- Background incidence? **Yes**
- Personal risk factors? **Yes – smoker**
- **IS THERE A BETTER EXPLANATION?** **Possibly smoking?**

General causation

Can agent X cause effect Y?

Specific causation

Has X caused Y in this case?

e.g. if a study finds $RR > 2$, then $AR > 50\%$
under exposure conditions of that study

Outcome

- Benzene known to be causative (RR 2.0 to 2.9)
 - Plausible, but low exposure, synergy with smoking?
 - “Schedule 2” poison with respect to AML and AA in the Act
 - “Accepted” condition, and no sound evidence to contrary in this case. ie Could not prove a specific alternative cause, nor disprove occupational exposure to benzene
 - Cover awarded
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END

