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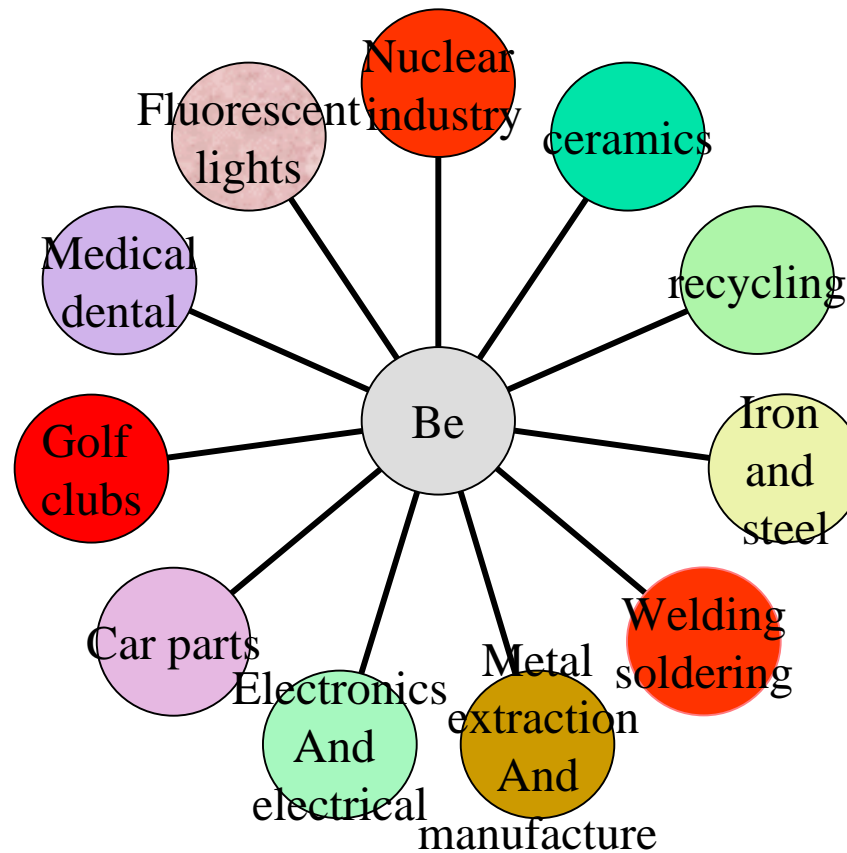
“Making sense and ‘non-sense’ of international research on beryllium toxicity”

The history of using, neglecting and ‘skewing’ research?

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Beryllium usage in UK industry and workplaces

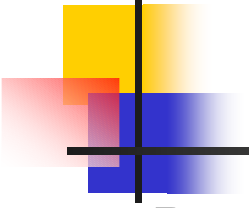




Key questions

- What research on beryllium toxicity was wanted and by whom?
- What research was needed?
- What research was available?
- How was the research used?
- Why, where and when?
- How were data gaps interpreted?

The barriers that existed and do exist to effect control of beryllium hazards and risk?

- 
-
- Dominance of market or national political interests (Defence, arms sales, shareholder interests over worker health and safety?)
 - Dominance of industry in obtaining, doing, framing, controlling, reporting, validating research?
 - Powerlessness of government researchers?
 - Government resistance to research findings
 - Long latency of disease and misdiagnosis and 'opportunities' for non-diagnosis, non recording and non reporting of beryllium-related diseases

Dates of knowledge about beryllium adverse health effects

1799

Beryllium was first identified by French chemist LN Vanquelin

1886

P Siem explores beryllium toxicity in animals (Dorpat Dissertation cited by Hardy 1961)

1900s

First reports of adverse health effects among those mining beryllium

1930s

First reports of adverse health effects among those manufacturing or processing beryllium products

1933 Weber and Engelhardt in Germany**

1935 Fabroni in Italy**

1936 Gelman in Russia**

1938

First cases of contact dermatitis reported in workers exposed to dust and fumes

1938

ILO Encyclopaedia reported 1936 Russian clinical beryllium fluoride poisoning cases including skin pulmonary problems (Hamilton and Hardy 1949)**

1940

Berkovitz and Israel on Russian workers poisoned by beryllium

1943

Dermatitis as well as respiratory illnesses were reported in USA beryllium workers but ascribed to fluorine compounds and NO_x (Shilen 1943)

1948

First UK reported fatality in physicist** who worked on the development of fluorescent lamps (Hunter 1959)

1951

Eisenbud proposed that CBD was immunologically mediated (Lang 1994)

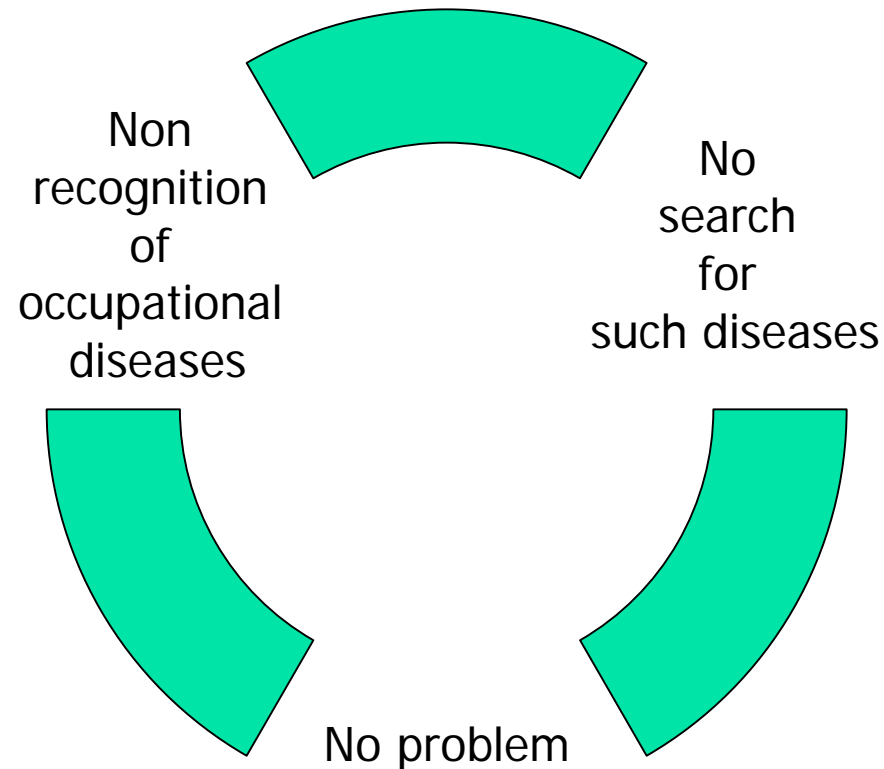


Beryllium monitors

- HMFIs (Ministry of Labour) 1940s-60s
- Government funded research institutes
- Ministry of Supply (Atomic Energy)
1940s
- JSCs for non-ferrous metals 1960s
- HSE and HSEIs post-1974

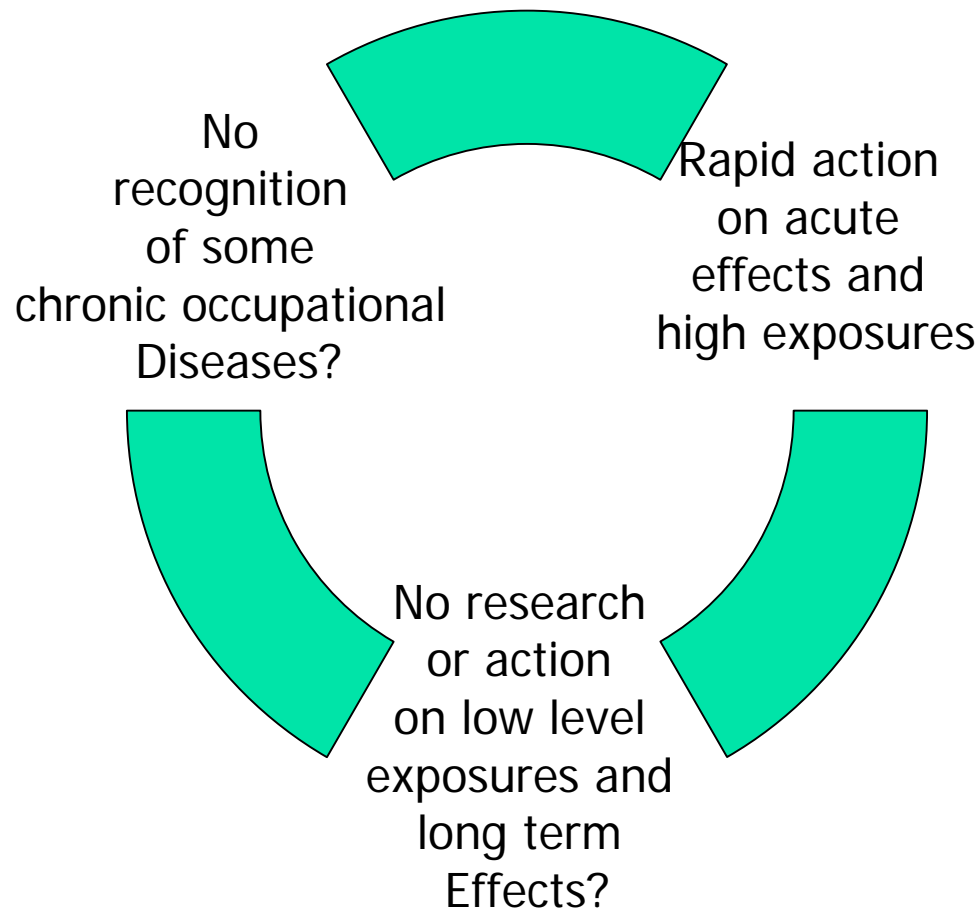
The problem?

Karen Messing's 'vicious circle' in occupational health



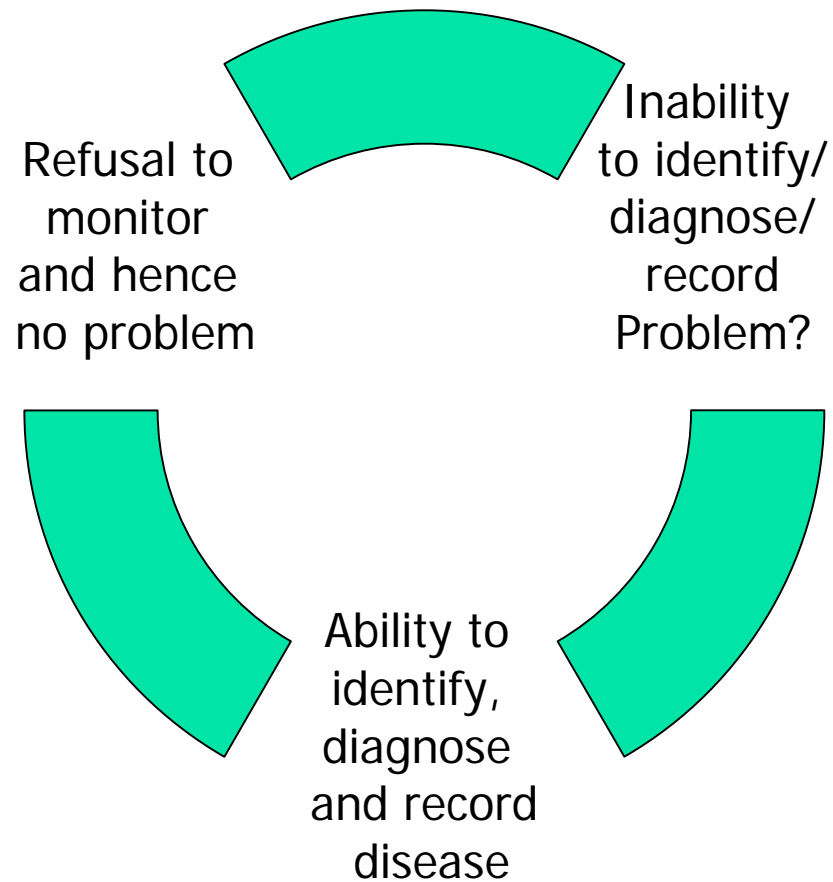
The problem?

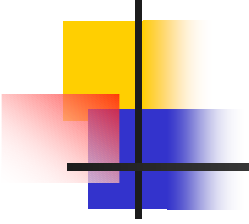
An adapted 'vicious circle' in occupational health



The problem?

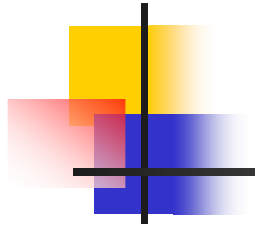
A more complex vicious circle



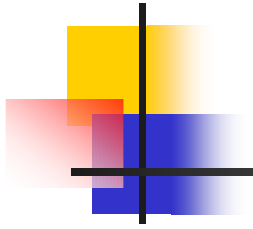


'Delay until death or employees
depart the workplace: '
occupational disease
management strategies?

- governmental?
- legal?
- corporate?
- labour?



-
- 5-10% of workers in developing countries have access to occupational health services
 - 20-50% of workers in industrialized countries have access to occupational health services (WHO 2004)



1940s



1940s

- “ Although the adverse responses to beryllium compounds had been recognized in Germany and the Soviet Union in the 1930s and early 1940s, the relevant reports in the medical literature of these countries were not widely distributed. From a practical point of view then, beryllium disease, or more accurately beryllium diseases, became recognized in the early 1940s...”
- (Lloyd Tepper. Industry occupational physician in Rossman et al 1991: 3)



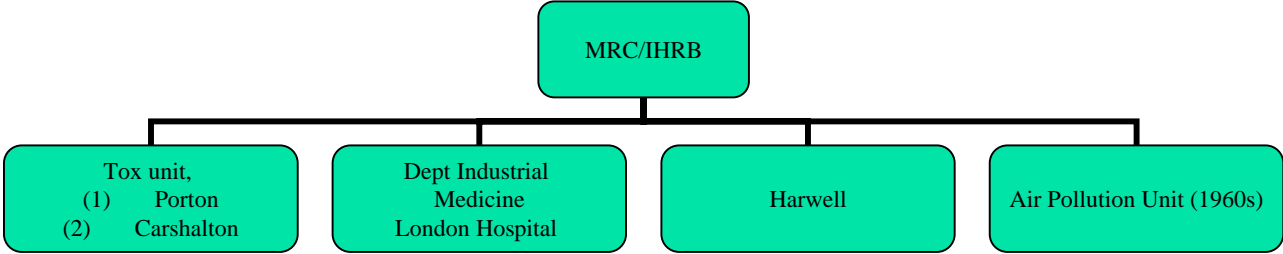
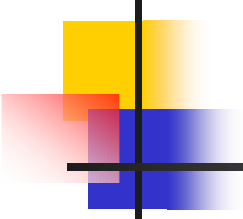
UK research view in 1940s (1)

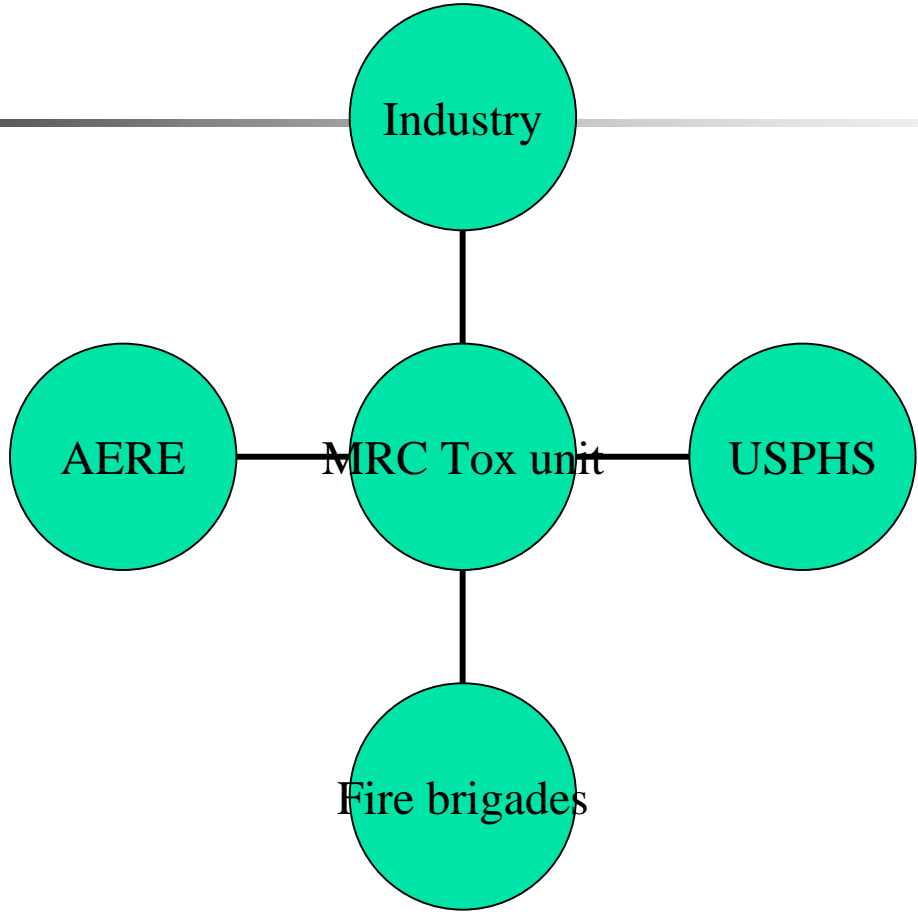
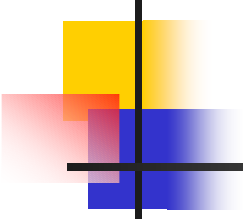
- Occupational physicians recognized that the new materials used in industrial development often became indispensable 'but their properties may remain for a long time insufficiently understood' (Hunter 1994:A2).
- Hunter already knew in 1942 about the problems associated with beryllium in cutting copper-beryllium alloys in aircraft construction and that the manufacture of beryllium steel produced beryllium oxide and beryllium fluoride dust linked to molten salt electrolytic baths. He was also well aware too that 'the dusts of all these compounds are known to be toxic to animals' (Hunter 1944: 6).
- Other researchers working with Hunter, such as John Agate at the MRC Industrial Medicine Department in the London Hospital, following diagnosis of beryllium poisoning cases in 1948 went much further. Agate believed: "Where possible, substitution of other compounds in place of those of beryllium is clearly the best preventive measure. In processes where this element must still be used, vigorous suppression of all dust and fumes, and regular medical supervision of workers are necessary" (Agate 1948:533).



UK research view in 1940s (2)

- Barnes at MRC Toxicology Unit based in Carshalton and Porton accepted USPHS line that beryllium itself was not toxic and told UK industry so - explaining illnesses on the basis of exposure to other substances (1947)
- UK beryllium industry company pointed out that they did not share his view and thought Be itself was toxic





Strategies of 1940s in USA for dealing with occupational exposures to beryllium

- "The errors in judgement that were made are, in retrospect, surprising. The story of beryllium poisoning illustrates well the fact that in this country (USA) we tend to believe that though a trade does cause a disease elsewhere, it will not do so here."
- 1933.1934, 1936 papers on Russian, German and Italian research are cited by Hardy
[Hardy 1965 NEJM Nov 25: 1191-2]



USA perspective

- Alice Hamilton , writing in 1948, viewed the beryllium story at that time as a success for toxicology and occupational medicine. “To anyone, who like me, can look back to the early days of industrial medicine, this story of beryllium poisoning is an amazing thing. Here in the space of some six or eight years, a form of industrial poisoning that was highly dubious, involving only a small number of cases, not included under compensation laws except in full-coverage states, observed by a small number of physicians , was promptly made the subject of thorough study will full publicity... When I look back on the days when we were urged not to mention such a thing as TNT poisoning lest we drive all workers out of the plants, I can hardly believe it is the same country” (Hamilton 1948:428).



HMFI and other reports on GB beryllium poisoning

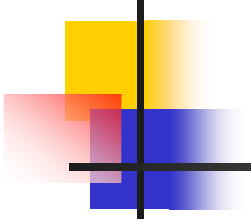
1930s - 1960 only one acute case (1949) and 6 chronic cases recorded (Browning in Schilling 1960:79)

* yet Browning's source cited 54 chronic cases including 10 non-work cases linked to living nearby, washing clothes and fishing in area

1974 – 2 cases of beryllium poisoning recorded

- - 12 samples of beryllium analysed
- - beryllium not recognised as a carcinogen

(HMFI 1975)



1950s



The Lancet view 1951

- “Beryllium seems to be the Admiral Crichton of metals
- It is nearly as light as magnesium and is more elastic than steel
- It is strong and hard and it resists heat and corrosion
- Under nuclear bombardment it is a most efficient source of neutrons”
- “to charge such an admirable metal with having poisonous properties is about as distasteful as accusing a trusted butler of stealing the family plate”
- The story of beryllium is ‘fascinating and contradictory’
- “Few people are completely sure that beryllium is the sole cause of illnesses ascribed to it”

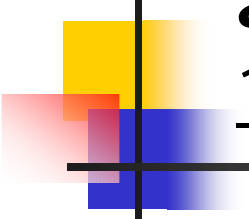


UK Industry activity 1950s

- AEA needed beryllium
- ICI plant was developed to produce beryllium. Prior to its opening, ICI did test on background beryllium levels near the planned plant and found that Be levels were ten times higher than US permitted levels ($0.01\mu\text{g}/\text{m}^3$) even before plant opened
- MRC Radiobiology unit view was that US community standard had been produced 'perhaps in panic' (MRC papers 1959)

Two species and two site carcinogenicity assessment for beryllium

1950s



<u>Date</u>	<u>Species</u>	<u>Site</u>	<u>Author</u>	<u>Place</u>
■ 1946	Rabbits	Bone	Gardner	USA
■ 1950	Rabbits	Bone	Barnes **	UK
■ 1953	Rats	Lung cancer	Vorwald	USA



MRC view from Hunter (1950)

- Hunter in Q&A session at an MRC Conference on Scientific Evidence and Occupational health noted, to an industrial Medical Officer (Dr Bourne from AC Cossor Ltd) that just because the MO had never come across a beryllium poisoning case in 8 years work in a plant where it had been used for 15 years, didn't mean that workers who'd left the plant hadn't possibly developed the disease.
 - (* Cossor Ltd must have used beryllium from 1935 onwards
 - * Hunter later worked as a consultant on occupational medicine for beryllium companies in UK)



1950s UK medical view

- By 1953 public health physicians as well as occupational physicians were aware that the prescribed industrial disease schedule: “as we obtain more extensive knowledge of the different hazards of work: for instance poisoning by beryllium and its compounds [was] added in 1949” (Leff 1953:139)



1955 UK cases of beryllium disease

- Physicians in the UK were diagnosing berylliosis in industrial locations where exposures were limited to trimming beryllium –copper alloys with no other dust exposures (Sneddon 1955: 1448).

Strategies of 1950s for dealing with some occupational exposures to beryllium: the philosophy



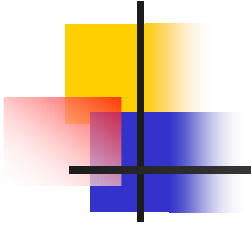
- “Substitution is to be preferred to other methods where the process in question is highly dangerous or materials are particularly toxic. In these cases it offers the only commercially practicable solution to the problems. Even where expensive research is necessary, it may still be a cheaper method in the long run”
- [Harvey and Murray 1958:147]

Harriet Hardy in ILO Encyclopaedia for 1971 advocated a less rigorous exposure approach

Strategies of 1950s for dealing with some occupation exposure to beryllium - the practice



- UK found non-beryllium based phosphors that would replace those of beryllium in fluorescent lights
- “beryllium is so highly toxic that there is reason to suppose the precautions necessary to make safe its use might have been financially crippling”
- [Harvey and Murray 1958:147]



1960s



USES OF BERYLLIUM 1962

[Hunter 3rd ed]

- Alloys of copper, nickel and aluminium
- Deoxidiser in steel making where dust was given off from electrolytic baths
- Rods to work graphite pile in atomic energy industry
- Transparent foil in industrial X-ray tube windows
- Powdered phosphors in fluorescent strip and electrical sign lamps and tubes
- Crystals in radios
- Electrical porcelain

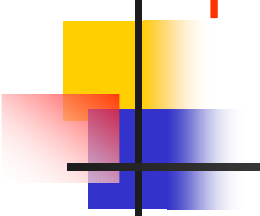
UK strategies of early 1960s for dealing with occupational exposure to beryllium – Browne (1)

■ The metal had become common between 1941 and 1961 especially in copper and steel alloys

- “ Where beryllium is breathed in as a powder, dust or fume, it has a most damaging effect on the lungs”
- “some people are so susceptible that it has been known for more cases to occur in the population outside a factory where beryllium is worked than inside among workpeople themselves”
- “All beryllium work should be segregated in a special department, the staff of which should be carefully chosen for their sense of responsibility, care , cleanliness and intelligence”

[RC Browne 1961: 109-110]

UK strategies of early 1960s for dealing with occupational exposure to beryllium – Browne (2)

- 
- ‘No touch techniques” should be developed and automatic filling, emptying and conveyance should be planned. ‘Automatic processes are less dusty, more easily ventilated and are less prone to human hygienic error
 - Exhaust extraction ventilation should always apply and air from systems should always be filtered before exhausted externally
 - Outside one beryllium plant 10 cases of illness were recorded within three quarters of a mile when it was estimated that the atmospheric concentration of the metal was as low as $0.1\mu\text{g}/\text{m}^3$
 - Maintenance workers dealing with beryllium plant should have positive pressure respiratory protective equipment
 - Occupational hygiene and stack records should be carefully collected and kept and linked to medical monitoring with lung function tests and X-rays. X-rays have limited value

[RC Browne 1961: 111]

UK strategies of early 1960s for dealing with occupational exposure to beryllium

- “Since the poisonous nature of beryllium and its compounds has been known only since 1933(sic), there is much room still for education of those who handle it”
 - Need to use safer substitutes in strip lights
 - Alternative to beryllium copper existed
 - “ In all industries where beryllium and its compounds are used, strict measures for dust suppression must be enforced”
 - Engineering controls and associated PPE and laundry techniques were linked to dust control strategies
- [Hunter 1961]



UK medical expertise and its role with industry?

- 1963. A worker pursuing a case for CBD lost his case in court
- Hunter (MRC Dept Research Industrial Medicine. London Hospital) and Kazantis (MRC Air Pollution Unit, Barts) were both called to give evidence for the beryllium company (MRC 1963)

UK technical view

- British Chemist, DA Everest, in 1964 noted in the lab context that if 'the safety rules are carefully followed the risk [from beryllium] is infinitesimal'; 'usually laboratories handling beryllium have been designed under expert guidance and the personnel are subject to regular medical examination' (Everest 1964:133).
- This may reflect the earlier problems where a beryllium researcher had died and the possibility of applying such controls in a foundry or engineering works at the time must have been rather different.
- Everest was, however, very conversant with the scientific literature and knew Gelman in Russia in 1936 recommended beryllium be machined only in well ventilated rooms with gloves and other protective clothing provided and washing accommodation available.
- Everest knew of only two UK beryllium fatalities and both occurred before 1949 but he also knew of US reports that there were 47 'well established' neighbourhood cases (Everest 1964).
- Everest promulgated the USA worker selection criteria that Tepper and others produced for beryllium workers. Namely that personnel should be selected on the basis of 'medical history, a physical examination and a chest X-ray. It is usual to reject those with greater than average chance of developing beryllium disease through their suffering from chronic respiratory diseases or from skin diseases which might make them susceptible to beryllium dermatitis". Also those with asthma, heart disease, TB and abnormal chest X-rays should also be rejected (Everest 1964:138)

UK 1960s cases

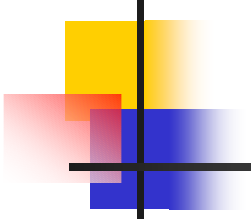


- In 1964, medical researchers in Wales had identified 2 industrial ceramics workers out of a workforce of 130 with CBD and a third case in a smelter and followed them for 10 years (Axford, Cotes and Gilson 1976:492)



UK industry activity 1960s

- Semiconductor industry expressed concern about HMFI enforcement variations on beryllium control
- Industry (VASCA) argued for a code of practice
- Working group between VASCA and Ministry of Labour (including HMFIs) was set up to produce CoP
- Industry did not want workers involved as the code would be 'entirely technical' and pressed for less rigorous wording: didn't like 'shall' (Min Lab 1968)



1970s

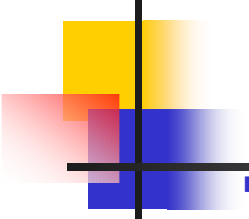


UK view in 1970s

- Evidence indicates that the UK simply accepted the ACGIH TLVs almost without question and the beryllium standard was never questioned.
- One British chemist in 1964 felt able to observe that the existing standard had 'no sound scientific basis and is probably highly conservative' (Everest 1964:138).

It is difficult to resolve this statement's contradictions

UK position

- 
- The use of beryllium in UK industry increased and medical researchers recognised that UK occupations at risk included not only metal workers and ceramic manufactures but also those in the electronics industry – TV manufacture, transistors and heat sinks - and those working in scrap metal disposal. Women especially pregnant women were categorised as at special risk and because the fatality rate for all workers with CBD was around 35%, beryllium poisoning was clearly a major threat (Jones Williams 1977:93). By 1973 the pathologist Jones Williams and colleagues had found, through in vitro testing, that 7 of 50 healthy beryllium workers were sensitised to beryllium (Jones Williams 1977:95)
 - Two apparently acute case of beryllium disease were reported in the UK. The diagnosis was prefaced by a qualifying remark that each worker could already have had CBD as each had worked for several years with the metal. Each case followed a high exposure – one of a worker smelting beryllium in a factory where a batch had apparently been wrongly labelled: the other in a factory where there had been a breakdown in a furnace extraction process (Rees 1979:192-3). Both these incidents show how dangerous the beryllium worker's life was and only relatively small failures of plant and systems could lead to acute disease cases.

Medical surveillance and tests for beryllium exposure . NIOSH 1977

Pre-employment tests should include:-

- chest X-rays
- baseline pulmonary function tests (FVC and FEV₁)
- **body weight measurements**

■ Health checks of workers should include:-

- Spirometry (FVC and FEV₁)
- Medical history questionnaire on respiratory symptoms
- Chest X-ray
- General health, liver and kidney function, possible skin effects also to be evaluated

[Occupational Diseases: A Guide to their recognition
NIOSH 1977]



1980s



The UK Beryllium register

- Between 1945 and 1985, recorded 49 cases of CBD and 21 of these had died from respiratory failure (Delic 1992:44 citing Jones Williams 1985). Between 1985 and 1988, nine new CBD cases were reported (Delic 1992:44; Jones Williams 1988)

Medical surveillance and tests for beryllium exposure . EU 1983

Pre-employment tests advised:-

- chest X-rays
- baseline pulmonary function tests (FVC and FEV₁)
- **liver and kidney function**

Health checks of workers yearly :-

- chest X-rays
- baseline pulmonary function tests (FVC and FEV₁)
- **liver and kidney function**
- **bodyweight surveillance**

Other

- beryllium is a known carcinogen in 3 animal species and literature shows greater predisposition to lung cancer in workers with a Be-induced disease

[Roi R et al, Occupational Health Guidelines for chemical risk. ISPRA. EC 1983:30-31]



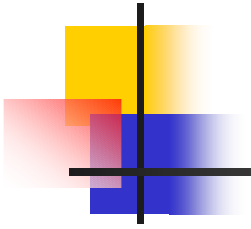
1980s UK case

- AWRE Beryllium plant at Cardiff reported no cases of CBD between 1961 and 1997 using traditional medical monitoring with chest X-rays and lung function tests.
- In the 1980s they reported 1 case of CBD in a 'unique' case, as AWRE described it, based on a systematic reaction to BeO through blood lymphocyte testing. **The Cardiff medical staff then viewed the latter test as unreliable and stopped testing**

(Brush Wellman Health and Safety Update
March 2002)

UK medical view

- Occupational health researchers looking at UK beryllium epidemiology studies observed that: “little information is available (however) on the dose-response relationship so it is not at present known if the standard is adequate or should be revised” (Cotes et al 1983:13). The researchers did feel able to conclude that “Thus the present TLV as related to geometric mean concentrations obtained by static environmental sampling **does not protect fully against berylliosis**” and they felt able to conclude that:-
 - “**The present threshold limit was proposed at a time when there was no direct evidence on which to base it: in addition the techniques for control of the environmental concentrations were relatively unsophisticated and lower concentrations difficult to achieve. Now there is both evidence and the means to achieve lower concentrations of environmental beryllium oxide so there is a strong case for the threshold being reviewed**” (Cotes et al 1983:20)
 - They further recognised that lab test indicated there could be triggers for CBD including pregnancy, withdrawal from exposure and patch testing. This information had been available in published studies in 1946 and 1957 yet does not appear to have been fully acted upon in UK occupational health practice by the mid 1980s.



1990s



UK prescribed industrial disease poisoning cases by beryllium

1980 -2001

18 cases

1986 1987 1988 1989 1990 1991 1992

2 4 3 - 2 1 -

1993 1994 1995 1996 1997 1998 1999

1 - - - - -

2000 2001

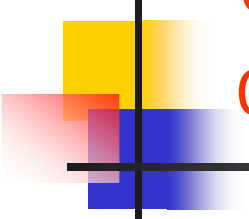
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(DWP and HSE Statistics 2003)



UK Beryllium Registry

- 1995 – 59 cases on registry including 5 acute and 7 with skin lesions.
- Accepted that 'it is virtually certain that an unknown number have not been included and may remain undiagnosed' (Jones Williams 1995:582)
- Unlike USA, no estimates existed or exist of numbers of UK workers exposed to beryllium



UK HSE commissioned response to the carcinogenicity of beryllium 1992

- review placed significant emphasis on a critique of early USA beryllium cancer studies that were viewed as often 'poorly conducted and recorded and reported mainly in non-peer reviewed literature'
- The critique, produced on behalf of the beryllium industry in 1987 was unpublished and hence is nowhere to be found in any literature, reviewed or otherwise
- the irony escaped the HSE reviewer

(Delic 1992:25)



1990s. UK chest physician views of beryllium carcinogenicity

- A number of authors (five in all) have claimed a marked increase of lung cancer in beryllium process workers but the data are considered suspect and largely to be discounted" (**US Public Health Service 1988**. quoted in UK by W Jones Williams in Parkes 1994 revised print 1995)
- **1993 IARC had assessed beryllium as a human carcinogen**



UK estimated workforce exposure to beryllium in 1990s

- 250 workers continuously exposed
- 1000 workers occasionally exposed to 'very low concentrations of beryllium or beryllium oxide' (HSE statement 2003)

Back to the beginning of the vicious circle?

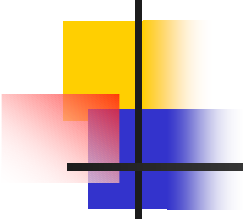
Don't look or don't have the resources to look, don't inspect or monitor, don't find or record, no problem.....sense or nonsense?



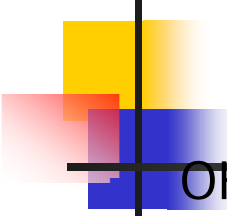
The beryllium story 'ozonoffed'(1): the 'non sense' analysis based on data

- Beryllium is a wonderful metal: no problem (early 1930s through to 2005)
- Beryllium is a wonderful metal and it is not necessary for manufacturers to look at European and Russian research showing otherwise (1946). Anyway there's only animal evidence from Europe that beryllium is toxic.
- OK. Beryllium is a wonderful metal that we can/must use but some materials linked to it may cause problems. Beryllium workers may get acute poisoning but that's only due to fluorides and sulphates
- OK. Beryllium workers can get poisoned but that's only because of specific production methods - if the oxide is produced at low temperatures, hence has smaller particle size and is more chemically reactive and so toxic (1950). So USA stopped making the low fired beryllium oxide and problem was solved?

(2)

- 
-
- The wrong type of beryllium is a problem and there are safe types
 - OK. Beryllium can be used safely if workers take the right precautions; but when they don't, it their fault they get acute beryllium poisoning
 - 1949 Beryllium poisoning added to UK NI industrial disease list. Very fast and viewed as complete solution thereafter
 - OK, Beryllium can cause chronic poisoning but only at high doses. Careful workers won't be exposed to high doses
 - OK, beryllium is a human health hazard but we set a TLV for it that has big safety margins (TLV calculated in 1940s on back of an envelope in taxi?)
 - OK. Beryllium can't poison communities because the levels they are exposed to will be too low.
 - OK. Some communities may be poisoned by beryllium but that's because it comes from beryllium workers' clothes and not from the factory stack**.

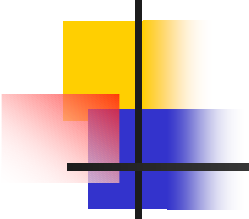
(3)



OK. There is evidence that beryllium dust may reach communities and poison them by means other than workers clothes but the levels are so low, there'll be no adverse health effects

- There is no evidence that beryllium is a carcinogen.
- OK. There is evidence that beryllium is a carcinogen but that's only in animals
- OK. There is evidence that beryllium could be/is a human carcinogen but epi studies aren't conclusive
- OK beryllium may be a human carcinogen but it's a low potency one (ACGIH. Industry ref 2001 on debate in OSHA 1975)
- OK In UK we operate such good industrial hygiene practices that we never have had a case of CBD.

(4)

- 
- **OK. There has been a case of sensitisation but that doesn't mean CBD will develop. The tests were no good and so any results indicating human 'sensitisation' to beryllium here are wrong and we'll now stop this form of testing that showed a problem and so there's no problem**
 - **OK, if CBD does develop, it will be very mild and workers don't need to worry**
 - **OK we don't have the data bases that have tracked workers for long periods of time and we don't have the clinical knowledge to diagnose all CBD cases but exposures are usually so low there won't be a problem and there won't be many cases even if they are reported**
 - **OK. Workers may get chronic beryllium poisoning at low doses but that because they are the wrong sort of workers. They are genetically flawed and we can screen out these susceptible workers whose immune systems are deficient**
 - **OK beryllium may cause problems at levels below the TLV but that's because the particles are the wrong shape (2001)**
 - **OK, there may be some OH problems but at this stage it would be 'premature' to lower the 'TLV' for beryllium (1949- 2005)**