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Managing Health in the Aluminium Industry

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The international aluminium industry has developed rapidly during the last 50 years. It has been vigilant concerning health issues relevant to its production workforce and of health concerns raised from within the community at large.

The Aluminum Association, the International Primary Aluminium Institute and several of the aluminium/aluminum associations, which function in many areas of the world, have with the involvement of their health committees, sponsored research and organised several scientific conferences for in-depth, open discussion. These have brought together research scientists and health professionals from both within and beyond the aluminium industry – together with relevant management personnel. Subsequently, wide dissemination of advances in knowledge has been facilitated by the publication of the proceedings of such meetings. This volume has a similar aim.

In his introduction George Haymaker, Chairman of the IPAI, indicates that the industry’s leadership remains concerned and committed to health. It welcomes scientific appraisal of current approaches to prevention, as well as to workforce health surveillance and management.

The Montreal conference began with an overview of the past 25 years. John Kelly, a leading physician within the aluminium industry, indicated that the health issues relevant to industry arose from two different perspectives:

- The occupational concerns associated with aluminium production, e.g., respiratory problems such as occupational asthma and chronic obstructive disorders; potential risks of lung and bladder cancer due to smoking and exposure to coal tar pitch volatiles; the question as to whether there is any risk to employees from exposure to electromagnetic fields.
- The wider community controversies surrounding aluminium and health, e.g., issues relating to Alzheimer’s disease and neurocognitive dysfunction.
This book includes reviews and analyses of research from within the industry together with presentations from leading figures from many international research and academic institutions.

Gone are the days when the occupational health specialist could regard occupational hazards and occupational diseases in isolation. An approach is required which embraces both health, welfare and management issues. Some of the management strategies that have evolved to meet current challenges are described within this volume.

It may be concluded, from the above, that the target audience for this book extends beyond those immediately concerned with health and safety issues within the aluminium industry.
ADDRESS TO DELEGATES

George T. Haymaker Jr.
Chairman and CEO, Kaiser Aluminum Corporation;
Chairman, International Primary Aluminium Institute

It is a distinct pleasure for me to open this forum of so many distinguished participants from around the world. Let me add my welcome to that of Robert Chase and Barry Meyer, and compliment all the regional and international aluminium industry bodies that have cooperated so well in the organisation and planning of such an important event for our industry. My purpose this morning is threefold:

- First, to emphasise the importance of this work to the worldwide aluminium industry.
- Second, to encourage you to review and re-assess the work that has been done in the past, so that you and we may learn from our successes and our mistakes; Third, to urge you to proactively identify the issues and challenges that we will face as an industry in the future and devise new strategies and initiatives to meet them.

The International Primary Aluminium Institute held its twenty-fifth jubilee in London earlier this year. In anticipation of that meeting the Institute assembled a task group of industry leaders, drawn from around the world, to ask whether our mission and objectives, drafted twenty-five years ago, were still as relevant as they were at the founding, or whether time and events had changed the areas in which we should focus our energies. This group worked very hard and conscientiously over many months, and reported to the Board of Directors and the Annual General Meeting on its findings.

As might be expected, there were some changes to sharpen our focus and update language to better capture the current and future setting for the industry. Most of these changes are not relevant to our purpose here today, but I think three items are worthy of particular note.

First, it was very clear at every stage of this effort that the industry’s leadership remains concerned and committed about health, safety and the environment. The IPAI now has six principle objectives, one of which is “Encouraging and assisting continuous progress in the healthy, safe and environmentally sound production of primary aluminium”.

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Second, we initiated a new proactive planning process to be sure that we have active programmes aimed at achieving all our objectives, and have asked all our committees, including the Health and Safety Committees to bring forward comprehensive programmes to achieve the objectives we have set out. As we have taken our first look forward at the programmes for the next three years and the funding necessary to carry them out, it is no surprise that the largest amounts are projected, at this stage, to be spent on programmes aimed at our health, safety and environment objective.

Third, we recognised the importance of increased co-operation between the regional and national aluminium associations and the IPAI so that we assure efficiency and effectiveness globally as we leverage off each other's efforts in a co-ordinated way. This conference is an excellent example of that co-operation and the importance that the leadership of the companies in the industry around the world attaches to these issues.

Given the importance of the subject, this conference comes none too soon. It has been fifteen years since the last aluminium industry occupational health conference was convened. That conference gathered the best thinking of the day into a set of proceedings the industry has drawn upon ever since.

In that fifteen years our industry has changed dramatically. Part of the good news about this change is that demand for our products has continued to grow - testimony to the remarkable characteristics of aluminium and the ingenuity of our people in its marketing and manufacture. And as the world economy has become more global, we find the industry with new operations around the world at all levels in the production chain, providing more products of better quality at lower cost than ever before, and providing new jobs and economic growth.

In that fifteen years our knowledge about occupational health issues has also increased – but I must be quick to point out, so has the number of occupational health issues - both real and perceived - we must address. The time is ripe to meet and review our progress. Dr. Kelly will shortly provide a perspective I am sure we will all find thought provoking and helpful on health issues in our industry for the past twenty-five years.

But of course the focus of the conference will be on the future. I feel very sure that our industry will change even more dynamically than in the past, as the world’s economy continues to expand, driven by the world-wide adoption of free market systems and the energies of people striving for a better life. We will have new consumers for our products, and we will need new production capacity in new and different places.
What challenges might we anticipate in this changing environment? Some of you may have seen an article in the May edition of The American Industrial Hygiene Association Journal, written by Lawrence Birkner and Ruth McIntyre-Birkner. It was titled: “2020 Vision: The Future of the Occupational and Environmental Hygiene Profession”.

This article paints an arresting picture of the world over the next twenty-three years. Now we all know that forecasting is a risky and difficult business. We can look back at the projections of some past futurists that were wide of the mark. But I think parts of this “Vision” might be useful in stimulating our thinking about the issues that are important to our industry. Let me share a few of its elements with you:

- In 2020, the authors forecast, the United States (and other developed industrial countries) are de-industrialised so that only ten percent of the nation's jobs are in manufacturing - and those that remain are highly automated with fewer, highly skilled workers. A high-tech environment, not forgiving of the undereducated.
- The age of the population in the industrialised world has increased dramatically, with the retirement age in the United States at age 70. Older workers, working longer.
- In 2005 a major health breakthrough occurred with the mapping of all human chromosomes. Through the use of genetic engineering, most genetically related diseases are now on the verge of elimination, rapidly increasing the life span in developed nations.
- The health care profession has downsized dramatically since the major causes of disease and death are on the verge of elimination. Health care costs are coming under control, and health care is focused on prevention and maintenance.
- As robotics has reduced the number of workers needed in most plants by 75%, the number of occupational injuries and illnesses have decreased as well.
- The United States, Europe and Japan design and engineer products for the world, but almost all products are built elsewhere, in manufacturing hubs in East Asia and South America.
- Although fuel efficiencies have kept energy costs low, cheap clean water and food are in short supplies in some parts of the world. Water, natural resource availability, and environmental pollution are some of the most contentious issues facing humanity.
- Competition is so fierce that fractions of cents separate the winners from the losers. Safety and health issues are driven by global (not national) health, safety and environmental issues and economic competition.
• As the earth's population increases to 8 billion, pollution prevention and quality of life will be major issues, with protecting water supplies a key focus.
• Because of these changes, employers will not look on environmental, health, and safety issues as separate and distinct elements of business operations - we already know they are related - but they will be merged together for efficiency and effectiveness.

I will leave it to you to decide which of these elements of this “Vision” fit with your own vision. I will also leave it to you to decide what the implications are for the aluminium industry, its workers, and the communities in which it operates. But regardless of the specifics of our individual visions of the future, a number of challenges for you, as the occupational health leadership of the industry, are quite clear. I believe you must:

• Do your best to anticipate what risks to the safety and health of our employees lie ahead, and through your associations and in your companies to provide pro-active guidance to the leadership of the industry so that it may respond effectively in a timely way.
• Continue to seek out and support the right research efforts and learning opportunities, such as this conference, which will help us and the outside world separate science from science fiction.
• Work with your governmental and public affairs people to present the facts to legislators and media.
• Bring a more holistic approach to health issues - in the workplace, at our customer sites, and in the community. We need to continue to expand our thinking from what happens to employees within the plant fence to what happens outside that fence - not just to our employees but to the surrounding community.
• Continue to maintain a high degree of quality in your company's management of health issues while at the same time managing these issues more cost-effectively. This is not contradictory - just the same kind of good business practice we employ in every other element of our businesses, producing higher quality at lower cost.
• Strive to assure that your company in-house occupational health programmes are of a quality that will allow us, as an industry, to monitor the impact of health issues that are indeed unique to our industry.
• Support the interactive co-operative efforts between the national, regional and worldwide aluminium bodies, so that we avoid redundancy and leverage talents, and make our goals and programmes truly worldwide.
Finally - don't lose sight of why you do the work you do. You and I know that the industry is committed to the safe, healthy and environmentally sound production of aluminium and aluminium products. That commitment is based in the concerns that each of us and the employees and leadership of the industry's companies has for our fellow workers and for the communities where our families and neighbours live. The challenge for all of us is to be farsighted enough to continue to fulfil that commitment in the future.
1. OVERVIEW OF HEALTH ISSUES FOR THE PAST TWENTY-FIVE YEARS IN THE ALUMINIUM INDUSTRY

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SUMMARY

The principle of the process for reducing alumina to aluminium and the transformation of aluminium ingots into end products by rolling, casting and extrusion has not changed significantly over the past hundred years. What has changed are working conditions, which as a result of technical improvements have greatly reduced the physical effort required and worker exposure to air contaminants and physical agents. A potroom worker in the 1960's had a physically demanding job, was highly exposed to air contaminants, heat and noise. He worked eight hours a day, forty-eight hours a week and because of the difficult working conditions he hurried to complete his work in the first four hours. Respiratory protection, hearing conservation and heat stress programmes were rudimentary at best. This overview examines the health issues from two different perspectives - the occupation disorders associated with aluminium production, and the controversies surrounding aluminium and health.

OCCUPATIONAL DISORDERS ASSOCIATED WITH ALUMINIUM PRODUCTION

Because of the poor working conditions in aluminium smelters during the second world war, and for a period thereafter, it is not surprising that occupation related disorders were observed in health studies in the 1970's and 1980's.

RESPIRATORY DISORDERS

Respiratory disorders among primary aluminium workers were reported as early as 1936 by Frostad (1) who observed asthma attacks among Norwegian potroom workers. Gilson (2) in 1987 and Abramson (3) in 1989 reviewed the numerous studies that had been conducted in Europe,
Australia and North America that had identified two primary disorders - acute airway obstruction (an asthma-like condition) and a chronic airway obstruction (a type of chronic bronchitis). These respiratory disorders are attributable to two sources - air pollutants in the workplace and to smoking.

CANCER RISKS

The concern about potential cancer risk in the primary aluminium industry is because of smoking and exposure to coal tar pitch volatiles (CTPV). CTPV and polynuclear aromatic hydrocarbons (PAH) are mainly associated with potroom jobs using the Söderberg process. The strongest association between potroom exposures and cancer was reported for bladder and lung cancer by Gibbs (4) and Armstrong (5). Risk was related to the level and duration of exposure to CTPV and smoking. Suggested and inconsistent rate increases, without clear association with specific exposures or work areas, have been reported for leukaemia, pancreatic, kidney and brain cancer.

INDUSTRY’S RESPONSE

The many epidemiological studies conducted by the industry identified aluminium smelter workers to be at increased risk for respiratory disorders and that Söderberg workers were at increased risk for lung and bladder cancer. The industry responded to these findings by implementing major programmes to reduce worker exposure to total particulate, sulphur dioxide and fluoride - the suspected aetiological agents in respiratory disorders, and to reduce exposure to CTPV - the suspected aetiological agent in occupational cancer.

ELECTRIC MAGNETIC FIELDS

Reports suggesting a link between an increased incidence of leukaemia and brain cancer in children and adults exposed to magnetic fields from residential exposure and nearby power lines have been inconsistent. All of these studies concerned AC current.

In the aluminium industry the high exposure jobs are mainly those in the smelters where potroom workers can be exposed to high DC fields. No definite health study has been conducted on exposure to DC magnetic fields.
EVALUATING THE EFFECT OF SMELTER OPERATIONS ON COMMUNITY HEALTH

It is well known that Söderberg potroom workers are at an increased risk of lung and bladder cancer. In Quebec these risks have been shown to increase with estimated cumulative coal tar pitch volatile (CTPV) exposure, using benzo(a)pyrene (B[a]P) as a surrogate. This raises the question whether populations living in close proximity to a Söderberg smelter, despite the much lower atmospheric exposure, could be at increased risk for bladder or lung cancer.

Gibbs (6) examined the scientific basis for the extrapolation of occupationally derived risk to the population living near a Quebec smelter. Based on presently available information, it was concluded that such an extrapolation is not justified.

Ronneberg (7) using the data from the Norwegian Cancer Registry found that, compared to the national average, no increased incidence of any form of cancer was found in the aluminium plant municipalities. The risk analysis indicated an increase in absolute lifetime risk of 0.02 - 0.05% for cancer of the lung and bladder combined due to exposure to PAH in the ambient air near aluminium smelters. There are great uncertainties attached to these estimates, and the validity of extrapolating such a dose-response relationship from high to very low concentration is questionable.

COMPENSATING OCCUPATIONAL DISORDERS WITH MULTIFACTORIAL CAUSES

This has always been a challenging task. Workers compensation plans have generally been set up to compensate victims of industrial accidents, where it can usually be established with relatively little difficulty whether the accident was caused by work. In the case of compensating occupational illness there is frequently an appreciable incidence of the disorder in persons not exposed occupationally. Lifestyle factors such as smoking habits may be an important contributing factor as well. Armstrong (8,9) has suggested criteria for fairly compensating bladder and lung cancer victims employed in Quebec aluminium smelters.

SMOKING IN THE WORKPLACE

Smoking is a worldwide health problem that is difficult to eliminate. Smoking in the workplace may, in addition, act synergistically with workplace airborne contaminants to increase the risk of incurring
occupation-related disorders. Smoking cessation programmes in the workplace present special challenges.

CONTROVERSIES SURROUNDING ALUMINUM AND HEALTH

Dialysis dementia is the only neurological disorder scientifically linked to aluminium. There is no scientific evidence to support a primary causal role of aluminium in Alzheimer's disease. Furthermore, aluminium does not induce Alzheimer's disease pathology in vivo in any species, including humans.

Aluminium was initially associated with Alzheimer's disease mainly because of three things: 1) injection of aluminium salts directly into the brains of animals produced neurofibrillary tangles thought to resemble those found in Alzheimer's disease. Subsequent research found that the tangles artificially produced in experimental animals were single strands of filaments, while those in the brains of Alzheimer victims were comprised of paired helical filaments which are significantly different: 2) In the mid-1970's Dr Donald McLachlan measured aluminium in human brains of both "normal" and "demented" patients. In Alzheimer's disease victims brains they appeared to have found about twice the amount of aluminium. Other studies attempting to replicate these findings correlating aluminium brain content with Alzheimer's disease yielded conflicting results: 3) Dialysis dementia is a condition observed in patients on dialysis treatment who have severely impaired or absent kidney function. Initially untreated tap water was used in the dialysate solution. This untreated tap water contained variable amounts of aluminium. In addition, massive doses of aluminium compounds were administered to these patients because they were needed to bind the phosphorus that they were unable to excrete. Lack of kidney function allowed aluminium concentration in the blood to build up to a level at which it was able to cross the blood brain barrier and accumulate in the brain. A dialysis dementia syndrome resulted which resembled the symptoms in Alzheimer's disease. Aluminium blood levels are now carefully monitored and controlled in dialysis patients and dialysis dementia is now rarely observed. This is the only neurological disorder scientifically linked to aluminium.

The controversy surrounding the relationship between elevated aluminium concentration in drinking water and increased risk of Alzheimer’s disease in elderly populations has ignited the debate about setting standards for aluminium in drinking water. At present there is inadequate scientific bases for setting a health based standard for aluminium in drinking water.

The Canadian Environmental Protection Act (CEPA) recently included aluminium chloride, aluminium nitrate and aluminium sulphate
on its Priority Substance List, making them possible candidates for review of their toxicity. They were considered toxic if:

- there is an immediate or long term effect on the environment;
- they may constitute a danger to the environment on which human life depends;
- they may constitute a danger in Canada to human life or health.

The World Health Organisation (WHO) commissioned the development of a criteria document for health effects from exposure to environmental aluminium under its International Programme on Chemical Safety (IPCS) in 1995. The international panel of experts concluded that aluminium has not been shown to pose a health risk to healthy non-occupationally exposed populations.

**OCCUPATIONAL EXPOSURE TO ALUMINIUM**

Several studies have reported a relationship between aluminium exposure in workers and health effects attributed to this exposure:

- *Ontario Gold Miners* (10) showed a 4.5 fold risk of impaired scores on tests of cognitive function compared to nickel/copper miners.
- In *Aluminium Welders* (11,12) because of the small particle size of aluminium oxide, welding fume penetrates deeply into the lungs. Welders serum and urinary aluminium were three to nine times higher than those in the general population. However those who regularly used respirators had close to normal levels. In another report neuropsychiatric symptoms were attributed to their aluminium exposure.
- *Flake Powder Workers* (13) after five years of exposure had urinary excretion of aluminium eighty times that of controls, and retirees had retained and stored aluminium for up to eight years after retirement.
- *Aluminium Foundry Workers* (14) after sixteen to eighteen years of exposure to aluminium fume and dust were found to have impaired memory and co-ordination difficulties.
- *The Aluminum Association Study* (15) of 235 aluminium workers and 44 controls in 15 plants found pre-shift post-shift serum aluminium and urinary aluminium/creatinine ratios to be increased in the exposed group and were greater in plants with higher aluminium exposures. The results were consistent with the systemic absorption of aluminium from occupational exposure and suggest the presence of a sensitive uptake process for airway aluminium.
In other studies *Potroom Workers* \(^{(16)}\) \(^{(17)}\) have been reported to incur neurological and cognitive impairment.

**INDUSTRY SPONSORED RESEARCH**

Cookware was the first commercial application for aluminium. Soon after competing cookware salesmen alleged adverse effects from exposure to aluminium. The various allegations have persisted until this day. In 1955 the Aluminum Association asked scientists at the Kettering Laboratory of the University of Cincinnati to review the world literature on aluminium and health. They concluded there was no need for health concern regarding exposure to aluminium. They reached the same conclusion again in 1974 and 1979. These results were published in the scientific literature. These reassuring findings gave the industry a false sense of security, delaying a response to the allegation that aluminium was a cause of Alzheimer’s disease. In 1980 the Kettering team was mandated to continuously review the literature on aluminium and health, which they did until 1988. Since then the literature review has been conducted by the New York State Institute for Basic Research in Developmental Disabilities directed by Dr. Henry Wisniewski. The Aluminum Association has also published many monographs and sponsored international health conferences in 1989, 1992 and 1994. The International Primary Aluminium Institute has published several monographs and sponsored two international conferences in 1977 and 1981.

*Aluminum Association Sponsored Research:*

The Aluminum Association has sponsored several research projects:

- welding aluminium alloys. Reports have been issued and a future study of welding aluminium/beryllium alloys is under consideration.
- for a number of years has funded research at The New York State Institute for Basic Research in Developmental Disabilities for investigation of aluminium and neurological disorders. The Institute also conducts an ongoing review of the scientific literature on aluminium and health and responds to requests for advice on issues concerning aluminium and health.
- supports research on the presence of aluminium in plaques and tangles at The National Institute on Ageing.
International Primary Aluminium Institute and The Aluminum Association Co-sponsored Research

- four sponsored studies on the behaviour of $^{26}$Al in human volunteers at AEA Technology plc. in the United Kingdom.
- funding research at New York University a study on respiratory tract translocation and bioavailability of aluminium.

REFERENCES

2. WHAT DO WE NEED TO MONITOR IN THE WORKPLACE?

Joe Damiano
Alcoa, 1501 Alcoa Building, Pittsburgh, Pennsylvania, 15219, USA

SUMMARY

We can measure the incidence of illnesses but this can be many years after an exposure. Moreover it may be extraordinarily difficult to separate the normal incidence of disease from the occupational incidence of disease. We must realise and express to management that occupational hygiene exposure assessments including exposure monitoring are good leading indicators of our performance in protecting the health of our workers. Within the paper, recommendations are made and standards described regarding the monitoring of health risks in bauxite mining and refining, aluminium smelting, casting, rolling, extrusion by chemical, physical or biological methods.

WHY MONITOR?

My definition of “monitor” is to measure exposures to chemical, physical and biological agents. There are many ways to respond to this question. Rather than simply identify what I feel are the most significant exposures in the aluminium industry, what I plan to do is create some context for what we need to monitor, by first addressing why we need to monitor. Once I’ve established the purpose and strategy for monitoring, I’ll then address some of the more remarkable exposures in the various aluminium industry production processes.

Why do we need to monitor exposures in the workplace? The easy and simple answer is, we monitor to compare measured values for dust, fumes, gases, vapours, noise, and radiation to Occupational Exposure Limits (OELs). Essentially, we are assessing compliance with exposure limits.

Of course, all of us who attended the Montreal meeting, attended because we take a more comprehensive view of occupational health, and in this more comprehensive approach, “monitoring” is an element of exposure assessment, and exposure assessment is an element
of the health protection process. The broad objectives for exposure assessment are:

- To differentiate acceptable from unacceptable exposures in the workplace. This is essentially an occupational risk assessment. We want to expeditiously and effectively control unacceptable exposures to acceptable levels.

- The other major reason is to document our exposure assessment findings, including monitoring data, to help answer future questions regarding past exposures. Exposure histories are needed to respond to future health issues for individuals and work groups. Good exposure assessment data are indispensable to epidemiology.

COMPREHENSIVE APPROACH

I am happy to report that within the occupational hygiene profession, there is a growing international consensus and acceptance of the “comprehensive approach” toward occupational exposure assessment. The comprehensive approach strives to assess the exposures for all workers, on all days to all environmental agents. The comprehensive approach strives to assess the exposures for all workers, not just those workers who are monitored but all workers. We do this by linking each worker to one or more Similar Exposure Groups, and assessing the exposures for the group. The comprehensive approach strives to assess the exposures across all work days, not just those days that were monitored but all days. We do this through a statistically based random sampling strategy. The comprehensive approach strives to account, within reason, for all chemicals, physical and biological agents in the workplace. We want to assess all exposures, not just those exposures having assigned occupational exposure limits, but all exposures. Finally, the comprehensive approach strives to rigorously measure the significant exposures present in the workplace. Various thresholds for exposure monitoring are employed in industry; these thresholds generally vary from 10 to 50% of the OEL. The American Industrial Hygiene Association recommends a 10% of the OEL threshold for exposure monitoring. Generally, at 10% of the OEL there is less than a 5% probability that the upper confidence limit on an arithmetic mean in the presence of a log-normal distribution will exceed the OEL.
PROCESS-RELATED EXPOSURES

At this point I would like to describe some of the significant exposures present in each major segment of the aluminium industry. It should be emphasised that whether or not a specific exposure is significant should be determined by a workplace specific exposure assessment.

BAUXITE MINING

The logical place to start is with bauxite mining. In my experience, the most significant exposure in bauxite mining is noise. Dust exposures may or may not be a concern depending upon weather conditions, material handling equipment and proximity of employees to dusty operations. Bauxite is a mixture of Gibbsite and other minerals, and as with any ore, the bauxite contains various elements and minor impurities. Exposure to crystalline silica could be a concern, but for most bauxite’s, quartz is not present at significant levels. Among the minor elements are the radioactive isotopes of radium, thorium and uranium. In general, the concentrations of these isotopes in most forms of bauxite are insignificant.

BAUXITE REFINING

Similar to mining, noise is generally the most significant health risk in refining. Exposure to bauxite dust can also be a concern, again depending upon weather and operating equipment. The large quantities of concentrated hot caustic used to extract the alumina from bauxite are a serious safety concern but airborne concentrations of caustic mist are seldom present at significant levels. Other significant exposures in bauxite refining include asbestos and mineral fibres used in thermal insulation, and crystalline silica refractories used in calciners. The structural steel and some process equipment are frequently coated with paints containing lead, and exposures to lead occurring in conjunction with maintenance activities can be significant.

Most Bayer plants process very large quantities of bauxite, and we should not overlook the possibility that some of the trace elements in bauxite could concentrate and create identifiable exposures. For example, we have looked at mercury vapour exposures in our refineries, and they are generally insignificant. Similarly, the naturally occurring radioactive materials present in bauxite will concentrate in the Bayer process, and our investigations have shown that these elements partition to the bauxite residue rather than the alumina product.
Alumina is the major feedstock for our aluminium smelters. Aluminas are also manufactured into various chemical products including adsorbents and catalysts. Noise and dust are the significant exposures in these operations.

**ALUMINIUM SMELTING**

The exposures in aluminium smelting include noise, alumina, coal tar pitch, fluorides and sulphur dioxide. Crystalline silica exposures are associated with furnace relining operations.

**CASTING**

Casting operations include conventional ingot casting facilities in an aluminium smelter and specialised foundries. In general, noise exposure is a concern, originating from combustion blowers, compressed air sources and vehicle engines. Furnaces are lined with refractories, and dust exposures to crystalline silica and other contaminants are a concern during relining operations. Mineral fibres are used in molten metal processes. Originally asbestos was common, and its use has largely been eliminated. Initially, refractory ceramic fibres were a substitute, but the health concerns associated with refractory ceramic fibres have driven much of its substitution as well. Today mineral fibres, rock wool and fibreglass are used in molten metal processing.

Depending upon the aluminium alloy, master alloy additives can be a concern (e.g. manganese). There is considerable attention in general industry at this time on controlling beryllium exposures because there is some evidence that the 2 µg m\(^{-3}\) OEL is not adequately protective.

Various inorganic and organic chemicals are used in metal purification. Acute exposure to chlorine is a concern wherever it is used in its gaseous form. Some foundries use hexachloroethane and its molten metal fluxing emissions include hydrogen chloride, hexachlorobenzene and hexachloroethane \(^3\). Hexachlorobenzene is a suspect carcinogen, and its ACGIH TLV is 2 µg m\(^{-3}\) \(^4\).

Finally, aluminium scrap is the metal feedstock for many casting operations, and the impurities in scrap can present occupational hygiene concerns. For example, I am aware of more than 30 documented incidents involving the discovery of radioactivity in aluminium scrap, and four incidents where inappropriately disposed synthetic isotopes were melted in aluminium casting operations. This problem has led many casting operations to install radiation monitors at truck and rail gates.
ROLLING

The significant exposures present in hot and cold rolling operations are noise and metal working fluids. Solvent vapour exposures may be present in metal coating and finishing operations. Inert atmospheres are used to heat treat some products, and if the source of the inert atmosphere is a gas generator, exposure to carbon monoxide can be a serious health hazard. Industrial vehicles are a source of diesel emissions.

EXTRUSION

Noise is the most significant exposure in aluminium extrusion. Some extrusion plants anodise their products. In anodising, there can be significant exposure to acid gases, as well as acid and caustic mists.

FORGING

The most significant exposures in forging are noise and metal working fluids. Also, the metal working fluids are applied to hot metal and die surfaces, and there is exposure to products of combustion.

SPECIFIC EXPOSURES

NOISE

Noise was identified in each process. We must be concerned with assessing and controlling noise exposures. I believe that in an effective occupational hygiene programme that fully half or more of our collective efforts should be placed on assessing and managing noise exposures. Where that is not the case, I suggest that we are under-managing what might be the most significant of all health risks in the aluminium industry.

Now I would like to turn to what I see to be some of the emerging and unanswered issues for exposure monitoring in the aluminium industry:
POTROOM AIR CONTAMINANTS

In a Söderberg potroom, coal tar pitch is probably the most significant occupational exposure. Coal tar pitch aside, I would like to discuss aluminium smelting pot emissions and potroom exposures to dusts, fumes and gases.

A near standard practice in the aluminium industry is to measure potroom worker exposure to dust and gases including particulate fluoride, hydrogen fluoride and sulphur dioxide. The potroom atmosphere is much more complex than is indicated on the basis of three or four analyses (5). However, we do not routinely measure other exposures because either we have determined the exposures to be insignificant, as is the case for carbon monoxide, or we simply do not have an adequate understanding of the toxicity to establish a limit.

Cryolite exists in both a solid phase and vapour phase. The vapour phase is sodium tertafluoroaluminate (Atmolite). Researches in Scandinavia have suggested that tetrafluoroaluminate may play role in potroom asthma. Also, there is one report of an association between the use of potassium aluminium tetrafluoride as a soldering flux and occupational asthma (6). Of course, hydrogen fluoride is the principal gaseous form of fluoride in a potroom.

Bjorn Gylseth and others from the Norwegian Institute of Occupational Health have measured airborne concentrations of fibrous sodium aluminium tetrafluoride ranging in concentrations from 9 to 720 fibres / cc (7). The fibres were generally less than 1 µm in diameter and shorter than 5 µm. It is believed the fibres are formed by rapidly cooling vapours.

In North America, the commonly applied exposure limit for fluoride is 2.5 mg m\(^{-3}\); this limit is based upon the prevention of Fluorosis, not respiratory disease. The Norwegians have established a total fluoride limit of 0.6 mg m\(^{-3}\), and it is based upon the prevention of both chronic and acute respiratory disease.

The sulphur compounds present in a potroom include sulphur dioxide, carbonyl sulphide, carbon disulphide, sodium sulphate and various sulphites. Only sulphur dioxide is present at significant exposure levels. One of our monitoring challenges is creating the ability to accurately measure peak exposures to acid gases including hydrogen fluoride and sulphur dioxide. The short term peak concentrations of acid gases can be as high as 30 ppm.

Fluorocarbons including carbon tetrafluoride are generated by aluminium reduction. These gases are of low toxicity but have been associated with environmental concerns.
Trace amounts of vanadium, chromium, nickel and other metals have been reported, and there has been speculation about what role, if any, the low-level exposures to these metals play in respiratory health.

In aluminium potrooms, the challenge before us is to understand the chemical nature of the potroom atmosphere in terms of risks for respiratory disease, and then to devise exposure limits and sampling methods for meaningfully assessing the exposures.

**Coal Tar Pitch Volatiles**

Assessing exposure to coal tar pitch volatiles has been, and will continue to be a challenge for our industry. Coal tar pitch volatiles are a complex mixture of particulate phase and vapour phase polynuclear aromatic hydrocarbons (PAHs). Some of the PAHs are known carcinogens, and some are known not to be carcinogens while the carcinogenic potential of many PAHs is uncertain. The questions before us are:

- What to measure?
- What is a reasonable airborne exposure limit?
- How do we measure exposures?
- How do we assess dermal exposures?

The principal standard is the ACGIH TLV of 0.2 milligrams of benzene soluble (BSF) particulate per cubic metre. Exposures are averaged over eight hours, and the ACGIH expects that all, or nearly all, day-to-day exposures should be maintained well below the 0.2 mg m$^{-3}$ TLV. Some years ago, Alcan lowered its standard for BSF to 0.1 mg m$^{-3}$. While in Norway, coal tar pitch exposure is assessed as the sum of 18 specific particulate phase PAHs with an OEL of 40 $\mu$g m$^{-3}$.

Exposure to BaP is generally 4 - 8% of the total PAH. Some countries have established exposure limits for benzo(a)pyrene. The standard in the Canadian province of Quebec is 5 $\mu$g BaP m$^{-3}$, while in Russia it is 0.15 $\mu$g BaP m$^{-3}$. A standard of 0.1 mg m$^{-3}$ BSF corresponds with 1 - 2 $\mu$g m$^{-3}$ of BaP.

I believe it would be a worthwhile challenge for our industry to come to some consensus on an occupational exposure limit for coal tar pitch volatiles. There are some important questions. For example, if exposure to particulate phase coal tar pitch exceeds the OEL, should the vapour phase exposure be controlled as well? Also, should exposure limits for coal tar pitch be adjusted in the presence of 12 hour work schedules?

The occupational exposure limit must correlate with health risk, and Alcan’s Arvida case control study showed good correlation between...
BSF values and health risk (9). PAHs can also serve as good OELs since studies by McGill university researches have shown good correlation between various PAHs and coal tar pitch measured as BSF (10).

In selecting an exposure limit, we must also consider how well it can be measured. The benzene soluble fraction is determined gravimetrically, and gravimetric methods exhibit poor sensitivity and high variability. In Alcoa, we made some significant improvements to the BSF method, but from an analytical perspective it remains inferior to determining specific PAHs by high pressure liquid chromatography.

Finally, as I mentioned earlier, we need to address dermal exposures to coal tar pitch. Is it adequate to control dermal exposures to prevent photosensitization, or is more control of dermal exposures needed? More on that later.

**Biomarkers**

 Biological monitoring is the measurement of the chemical or its metabolite in a biological specimen. It is my observation that biological monitoring has largely fallen out of favour. However, I am hopeful as we move toward the challenges ahead in occupational hygiene, we’ll see that biological monitoring will in some instances be the best method of assessing occupational exposures.

All of us who are familiar with the history of the aluminium industry know the role urinary fluoride monitoring played in the prevention of fluorosis. Today, with good control of airborne exposures to fluoride and good personal hygiene, the risk for fluorosis is so low that many of us have reduced or eliminated urine fluoride surveillance. Instead some organisations are now using urinary fluoride as a surrogate for historic exposures to potroom dusts and gases in epidemiologic studies.

There are several major advantages of biological monitoring over air monitoring. Biological monitoring reflects the total exposure for the individual: inhalation, ingestion and dermal absorption. Moreover, biological samples are normally collected on all exposed workers, and this practice largely eliminates the between worker variability, and between day variability associated with air monitoring. Unfortunately there are relatively few good biomarkers. In order to establish a biological exposure index, the pharmacokinetics of the toxin must be understood, including its half-life. Also, the measured values of the chemical or its metabolite in blood or urine must correlate reasonably well with either airborne exposures or the harmful health effect. Finally, there is hesitancy in some organisations to use biological monitoring because this practice is seen as an after the fact use of the employee to assess the safety of the work environment.
Two biomarkers of interest at this time for the aluminium industry are aluminium in urine for assessing exposure to aluminium, and 1-hydroxypyrene for assessing exposure to coal tar pitch volatiles. The German Commission for the investigation of health hazards has established an aluminium biological tolerance value of 200 \( \mu g \ L^{-1} \) in urine sampled at the end of the shift \(^{11}\). I am not aware of the health risk relevance of this standard, but we as an industry should form some opinion, and perhaps a consensus on urinary aluminium monitoring.

The other exciting development in the area of biomarkers is 1-hydroxypyrene, the metabolite of pyrene. Dr. Frans Jongeneelen has written a paper on this subject. I have been following his contributions, and I believe the most significant finding that has surfaced from his research is the suggestion that dermal absorption of coal tar pitch is a significant route of exposure, and as airborne exposures are reduced, dermal exposures may become more significant than airborne exposures. We need to follow this subject closely and as an industry act on the research findings.

**DIESEL EMISSIONS**

Diesel powered vehicles are commonly used in most segments of the aluminium industry. Animal studies have shown a positive association between diesel emission exposures and lung tumours, and at least four epidemiological studies have shown an association between lung cancer and exposure to diesel emissions. IARC has classified diesel emissions as a group 2A carcinogen (probably carcinogenic to humans). The ACGIH has proposed a 0.15 mg m\(^{-3}\) TLV for diesel exhaust \(^{4}\). NIOSH has established an air sampling and analytical method utilising an open-face quartz fibre filter and determination of elemental carbon, the exposure metric, by thermal optical analysis.

**PARTICLE SIZE SELECTIVE OELS**

There has been a very serious and progressive effort among the standard setting organisations to establish more particle size selective occupational exposure limits. The ACGIH, the International Organisation for Standardisation (ISO) and the European Standardisation Committee (CEN) agree upon the underlying criteria \(^{12}\). The ACGIH has adopted a three tier system: The first tier is known as inhalable or inspirable particulates; this replaces total dust. Inhalable particulates are less than 100 \( \mu m \) in diameter. Inhalable particulates deposit through out the respiratory system depending upon their aerodynamic size. The largest particles in the 25 to 100 \( \mu m \) size range deposit in the nasophyranx. Particles in the
10 to 25 \( \mu \text{m} \) range deposit in lung’s airways, while the smallest particles deposit in the alveoli.

The second tier is known as “thoracic” particulates. This fraction is less than 2.5 \( \mu \text{m} \) in diameter, and the particles deposit in the airway and gas exchange regions of the lung.

The third tier is known as “respirable” particulates. These particles are less than 1.0 \( \mu \text{m} \) in diameter and mostly deposit in the gas exchange region of the lungs.

The new system of particle size selective OELs will sooner or later have an enormous impact on measured exposure values and / or exposure limits for specific air contaminants. The ACGIH has established two particle size selective limits for particulates not otherwise classified. The limit for inhalable particulates is 10 mg m\(^{-3}\), and the limit for respirable particulates is 3 mg m\(^{-3}\). Two sampling heads are available for inhalable dust, the IOM Personal Inhalable Sampler, and the UK Atomic Energy Authority’s (now AEA Technology plc) so called “Seven Hole Sampler.”

There are standing respirable dust TLVs for crystalline silica and coal dust. Perhaps most significantly, there is strong interest in reclassifying each of the existing “total dust” TLVs for specific chemical agents to particle size selective TLVs (e.g. inhalable, thoracic, respirable). Inspirable dust sampling has been prescribed for some years now in Australia as a replacement for total dust. Inhalable dust values are always greater than total dust values. Correlation studies in the aluminium industry report inhalable dust values 30% and up to 300% greater than total dust values \(^{(12)}\).

If total dust OELs are being supplanted by inhalable dust OELs, do we compare the measured inhalable dust values to total dust OELs, or do we adjust the total dust OELs to a higher inhalable dust limit? Occupational exposure limits should be based upon a dose-response relationship. If the dose is based upon measured workplace exposure values using a total dust sampling method, the OEL should be adjusted to a proportionally higher value in the presence of an inhalable dust sampling method, or we can choose to simply retain the total dust metric. On the other hand, if the dose is an estimated absorbed dose, perhaps based upon toxicological studies in animals, it may be appropriate to compare the inhalable particulate exposure values to pre-existing exposure limits. I suspect we will be discussing particle size-selective exposure limits for many years to come.

**SILICA**

Furnaces are commonly featured in many, and perhaps most workplaces in the aluminium industry. Furnaces are used in alumina calcination,
anode baking, casting and numerous heat treat processes. The furnaces are constructed and insulated with various refractories. At one time, much of our occupational health focus was on the use of asbestos, and the exposures associated with furnace overhauls. Later, the focus was on the use of refractory ceramic fibres, and other synthetic mineral fibres. Asbestos and mineral fibres remain on our occupational health agendas, while there has been an increased focus in recent years on exposures to the crystalline phases of silica. Many refractories contain significant percentages of both quartz and cristobalite. IARC has recently classified crystalline silica as a group 1A carcinogen.

The ACGIH TLV for respirable quartz is 0.1 mg m\(^{-3}\) and for cristobalite the TLV is 0.05 mg m\(^{-3}\). It is sometimes challenging to accurately measure exposures close to the TLV because of the limited sensitivity of the analytical method. The lower limit of sensitivity for crystalline silica ranges from 10 to 30 µg per sample.

METAL WORKING FLUIDS

Exposure to metal working fluids is of course a very significant exposure in our industry, and in some ways the issues parallel the challenges that I have described regarding coal tar pitch exposure assessments. Exposure to oil mist is associated with respiratory morbidity, and I believe a challenge for our industry is to come to some consensus on adequately protective occupational exposure limit. Similar to coal tar pitch in our smelters, there is exposure to both particulate (i.e. oil mist) and vapour phase metal working fluids in our rolling mills. We can measure exposures to these hydrocarbon vapours, but to assess the exposures we need to identify appropriate occupational exposure limits. Finally, any of us who have been in a rolling mill, and especially the oil house servicing a mill, knows that skin contact is indeed a route of exposure. We simply do not know enough about the dermal absorption characteristics of our lubricants and coolants, and even less about how to assess dermal exposures. This is another challenge for our industry.

OZONE

Ozone exposures associated with aluminium welding can be a significant occupational hygiene issue for three reasons:

- First, ozone exposures can easily exceed occupational exposure limits. The ACGIH has proposed three limits for ozone, with values ranging from 0.05 to 0.1 ppm depending upon the physical workload.
- Second, ozone exposures are difficult to measure. The standard method has been liquid impingers, but the use of impingers in the
workplace is generally impractical. The standard OSHA method in the US involves the use of nitrite impregnated glass fibre filters. Ozone converts the nitrite to nitrate. The method has not been fully validated and there is some question about its accuracy under conditions of low humidity. Finally, some instrument manufacturers now market electrochemical sensors for monitoring ozone exposures, but again adequate validation information on accuracy, precision and interference’s are not available.

- A third reason why ozone is a significant issue is the difficulty in controlling ozone exposures. Unlike welding fumes, ozone is generated by the effect of ultraviolet light on oxygen. Hence ozone is generated at some distances from the welding arc thereby reducing the effectiveness of conventional local exhaust ventilation.

WHY MONITOR? TO MEASURE WORKER HEALTH PROTECTION!

In conclusion, I’d like to return to the question, why monitor? At the 10,000 meter level, I believe we monitor exposures to prevent occupational illnesses and disease. We can measure the incidence of illnesses, but that’s after the fact, and in view of some of the latency periods, this can be many years after the fact. Moreover, it is sometimes extraordinarily difficult to separate the normal incidence of disease from the occupational incidence of disease. There is a lot to be learned through morbidity and mortality studies, but we must also realise and express to management that occupational hygiene exposure assessments including exposure monitoring, are good leading indicators of our performance in protecting the health of our workers.

REFERENCES


This report describes three large studies and one smaller study designed to measure the emissions produced during the welding of aluminium alloys. The studies also demonstrated the effectiveness of a helmet in limiting the exposure of workers to these fumes. It was shown that the concentration of most alloying metals outside the helmet was in excess of TLV values. The element beryllium was found to cause a particular problem, even when its levels in the alloy were very low.

INTRODUCTION

Electric arc welding of aluminium inherently produces chemical and physical emissions to the welding environment. Since aluminium is seldom used as the pure metal, but is far more often alloyed with other metals to improve strength and other physical properties, the interaction of the arc with the metal being welded generates ultraviolet radiation, various metallic fumes, oxides and gases. The exact composition of these emissions will, of course, depend on the alloys being welded.

With oversight provided by the USA’s Aluminum Association’s Health Committee, four laboratory investigations were sponsored to characterise the emissions from arc welding aluminium using the metal inert gas (MIG) and Tungsten Inert Gas (TIG) processes and various combinations of base and filler alloys. Tests were conducted to estimate "worst case" emissions.

MARTIN MARIETTA STUDY

The first study to determine emissions from welding aluminium alloys was conducted for the Aluminum Association at the Martin Marietta Laboratories in Baltimore, Maryland\(^1\). In this study, 10 series of tests were conducted using MIG and TIG welding processes. Five different
base metal/electrode alloy combinations were investigated. Table 1 lists the five different base alloy/electrode combinations used:

- Al-Mg-Si base alloy (6061) MIG and TIG welded with Al-Si filler alloy (4043).
- Al-Mg-Si base alloy (6061) MIG and TIG welded with Al-Mg filler alloy (5356).
- Al-Cu base alloy (2219) MIG welded with Al-Cu filler alloy (2319).
- Al-Mg base alloy (5456) MIG and TIG welded with Al-Mg filler alloy (5356) using two different inert gas mixtures: 100% Ar and a 75% He-25% Ar mixture.
- Commercially pure base alloy (1100) MIG welded with commercially pure filler alloy (1100).

### Table 1

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<thead>
<tr>
<th>TEST</th>
<th>WELDING PROCESS</th>
<th>BASE</th>
<th>ELECTRODE</th>
<th>SHIELDING GAS</th>
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<td></td>
<td>POSITION 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>MIG</td>
<td>6061</td>
<td>4043</td>
<td>Ar*</td>
</tr>
<tr>
<td>2</td>
<td>MIG</td>
<td>6061</td>
<td>5356</td>
<td>Ar</td>
</tr>
<tr>
<td>3</td>
<td>MIG</td>
<td>2219</td>
<td>2319</td>
<td>Ar</td>
</tr>
<tr>
<td></td>
<td>POSITION 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>MIG</td>
<td>5456</td>
<td>5356</td>
<td>Ar</td>
</tr>
<tr>
<td>5</td>
<td>MIG</td>
<td>5456</td>
<td>5356</td>
<td>75:25 He/Ar</td>
</tr>
<tr>
<td>6</td>
<td>MIG</td>
<td>2219</td>
<td>2319</td>
<td>Ar</td>
</tr>
<tr>
<td>7</td>
<td>MIG</td>
<td>1100</td>
<td>1100</td>
<td>Ar</td>
</tr>
<tr>
<td></td>
<td>POSITION 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>AC-TIG</td>
<td>6061</td>
<td>5356</td>
<td>Ar</td>
</tr>
<tr>
<td>9</td>
<td>AC-TIG</td>
<td>6061</td>
<td>4043</td>
<td>Ar</td>
</tr>
<tr>
<td>10</td>
<td>AC-TIG</td>
<td>5456</td>
<td>5356</td>
<td>Ar</td>
</tr>
<tr>
<td>11</td>
<td>AC-TIG</td>
<td>5456</td>
<td>5356</td>
<td>75:25 He/Ar</td>
</tr>
</tbody>
</table>

*100% Argon as shielding gas

Welding was performed at the Martin Marietta Aerospace Advanced Manufacturing Technology Laboratory (AMTL) because of the extensive experience with fabricating and welding aluminium alloys at that site. AMTL was fully equipped for welding and staffed with certified welders, two of whom conducted the tests.

In order to simulate manual welding in a reproducible manner, a mannequin was constructed and fitted with a standard curved-chin helmet modified for sample collection. During the tests, the mannequin and arc remained stationary while the work piece (6" x 36" x 3/8" plate)
moved under the arc at speeds of 12” /min for MIG welding and 5” /min for TIG welding.

**Table 2**
**Martin Marietta Study, May 1983, Emission Spectrograph Analyses of Alloys (%)**

<table>
<thead>
<tr>
<th>ALUMINIUM ALLOY</th>
<th>1100</th>
<th>2219</th>
<th>2319</th>
<th>4043</th>
<th>5356</th>
<th>5456</th>
<th>6061</th>
</tr>
</thead>
<tbody>
<tr>
<td>Al</td>
<td>99.30</td>
<td>93.11</td>
<td>93.07</td>
<td>95.33</td>
<td>94.85</td>
<td>93.9</td>
<td>97.7</td>
</tr>
<tr>
<td>Cu</td>
<td>0.10</td>
<td>6.53</td>
<td>6.38</td>
<td>0.05</td>
<td>0.05</td>
<td>0.07</td>
<td>0.27</td>
</tr>
<tr>
<td>Mn</td>
<td>&lt;0.01</td>
<td>0.24</td>
<td>0.31</td>
<td>0.09</td>
<td>0.66</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Mg</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>0.02</td>
<td>0.01</td>
<td>4.69</td>
<td>5.19</td>
<td>1.09</td>
</tr>
<tr>
<td>Cr</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.09</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>Ti</td>
<td>0.02</td>
<td>0.06</td>
<td>0.13</td>
<td>&lt;0.01</td>
<td>0.07</td>
<td>0.02</td>
<td>0.03</td>
</tr>
<tr>
<td>Be</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.0007</td>
</tr>
<tr>
<td>Si</td>
<td>0.07</td>
<td>0.06</td>
<td>0.09</td>
<td>4.61</td>
<td>0.16</td>
<td>0.08</td>
<td>0.67</td>
</tr>
</tbody>
</table>

Note: Elements considered to be of interest are shaded

**Table 3**
**Martin Marietta Study, May 1983, Geometric Mean Values for Ozone, Nitric Oxide & Nitrogen Dioxide outside the Welding Helmet**

<table>
<thead>
<tr>
<th>TEST</th>
<th>ALLOY SELECTION BASE/ELECTRODE</th>
<th>OZONE* (ppm)</th>
<th>NITRIC OXIDE (ppm)</th>
<th>NITROGEN DIOXIDE (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MIG-POSITION 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>6061/4043</td>
<td>0.52</td>
<td>0.52</td>
<td>0.24</td>
</tr>
<tr>
<td>2</td>
<td>6061/5356</td>
<td>0.47</td>
<td>1.22</td>
<td>0.43</td>
</tr>
<tr>
<td>3</td>
<td>2219/2319</td>
<td>0.50</td>
<td>1.94</td>
<td>1.45</td>
</tr>
<tr>
<td></td>
<td>MIG-POSITION 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>5456/5356</td>
<td>1.54</td>
<td>8.04</td>
<td>3.77</td>
</tr>
<tr>
<td>5</td>
<td>5456/5356</td>
<td>0.31</td>
<td>3.06</td>
<td>0.82</td>
</tr>
<tr>
<td>6</td>
<td>2219/2319</td>
<td>1.97</td>
<td>1.22</td>
<td>1.39</td>
</tr>
<tr>
<td>7</td>
<td>1100/1100</td>
<td>4.70</td>
<td>0.82</td>
<td>2.39</td>
</tr>
<tr>
<td></td>
<td>TIG-POSITION 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>6061/5356</td>
<td>N.A.</td>
<td>16.60</td>
<td>4.05</td>
</tr>
<tr>
<td>9</td>
<td>6061/4043</td>
<td>N.A.</td>
<td>11.75</td>
<td>7.85</td>
</tr>
<tr>
<td>10</td>
<td>5456/5356</td>
<td>0.59</td>
<td>1.60</td>
<td>2.33</td>
</tr>
<tr>
<td>11</td>
<td>5456/5356</td>
<td>1.26</td>
<td>6.28</td>
<td>5.25</td>
</tr>
<tr>
<td></td>
<td>ACGIH-TLV</td>
<td>0.10</td>
<td>25.0</td>
<td>3.0</td>
</tr>
</tbody>
</table>

* Underestimate due to the interference of sampling train
Samples for ozone, nitric oxide, nitrogen dioxide, and metal fumes were collected simultaneously inside and outside the helmet. Each test involved about 100 minutes of arc time, which is the estimated time a welder strikes an arc during an eight-hour work shift. All sampling was conducted under controlled conditions. Analyses were performed by standard National Institute for Occupational Safety and Health (NIOSH) methods for total particulates, metallic elements, ozone, and oxides of nitrogen. Aluminium was determined by neutron activation analysis at the University of Kentucky. All base and electrode alloys were analysed and found to be within specifications prior to testing. In Table 2 elements of interest are highlighted.

<table>
<thead>
<tr>
<th>TEST</th>
<th>ALLOY/SELECTION</th>
<th>TOTAL WELDING FUME</th>
<th>Al OXIDE FUME</th>
<th>ELEMENTS OF PRIMARY INTEREST</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BASE/ELECTRODE</td>
<td>(mg m(^{-3}))</td>
<td>(mg m(^{-3}))</td>
<td></td>
</tr>
<tr>
<td>MIG POSITION 1</td>
<td>1 6061/4043</td>
<td>24.9</td>
<td>23.0</td>
<td>Si</td>
</tr>
<tr>
<td></td>
<td>2 6061/5356</td>
<td>34.3</td>
<td>-----</td>
<td>Si, Mg, Be</td>
</tr>
<tr>
<td></td>
<td>3 2219/2319</td>
<td>71.6</td>
<td>67.3</td>
<td>Cu</td>
</tr>
<tr>
<td>MIG POSITION 2</td>
<td>4 5456/5356</td>
<td>611.5</td>
<td>491.3</td>
<td>Mg, Be</td>
</tr>
<tr>
<td></td>
<td>5 5456/5356*</td>
<td>101.1</td>
<td>94.4</td>
<td>Mg, Be</td>
</tr>
<tr>
<td></td>
<td>6 2219/2319</td>
<td>259.8</td>
<td>253.4</td>
<td>Cu</td>
</tr>
<tr>
<td></td>
<td>7 1100/1100</td>
<td>84.3</td>
<td>81.3</td>
<td>Al</td>
</tr>
<tr>
<td>TIG POSITION 2</td>
<td>8 6061/5356</td>
<td>18.4</td>
<td>3.9</td>
<td>Mg, Be</td>
</tr>
<tr>
<td></td>
<td>9 6061/4043</td>
<td>6.5</td>
<td>1.5</td>
<td>Si, Mg</td>
</tr>
<tr>
<td></td>
<td>10 5456/5456</td>
<td>12.2</td>
<td>1.0</td>
<td>Mg</td>
</tr>
<tr>
<td></td>
<td>11 5456/5356*</td>
<td>12.8</td>
<td>0.9</td>
<td>Mg, Be</td>
</tr>
<tr>
<td>ACGIH-TLV</td>
<td>5.0</td>
<td>5.0</td>
<td></td>
<td>* 75% He &amp; 25% Ar as shielding gas</td>
</tr>
</tbody>
</table>

Two head positions were used in the test program. Emissions were found to vary with head placement relative to the welding plume, with all base alloy/electrode combinations and with the welding process. A complete description of the test procedures and results are contained in the final report to the Association dated May 1983.

Ozone and the oxides of nitrogen are formed in the welding arc by the combination of heat and ultraviolet radiation. (Table 3) The ozone measurements, unfortunately, represented an underestimate of...
actual emissions due to reactions with Tygon tubing used in the sampling train. The magnitude of ozone emissions, however, were as high as 4.7 ppm when welding on the 1100 Series alloys - which is in excess of the American Conference of Industrial Hygiene's Threshold Limit Values (TLVs)\(^{(2)}\) of 0.1 ppm.

It should be noted that the concentrations of airborne contaminants reported in these studies reflect time weighted average concentrations for the period the arc was struck. As a result, this information represents "worst case" conditions and are not reflective of employee exposures. To determine actual exposure requires monitoring of employees under the conditions in the workplace. Results indicate that nitric oxide emissions do not exceed the TLV for either welding process or alloy combination. Nitrogen dioxide emissions were consistently elevated above the TLVs for the TIG welding process, however, only one alloy/electrode combination 5456/5356 was in excess of the TLV for the MIG process.

### Table 5
Martin Marietta Study, May 1983, Geometric Mean Values for Total Welding Fume & Magnesium Oxide Fume outside the Welding Helmet

<table>
<thead>
<tr>
<th>TEST</th>
<th>ALLOY SELECTION BASE/ELECTRODE</th>
<th>TOTAL WELDING FUME (mg m(^{-3}))</th>
<th>MAGNESIUM OXIDE FUME (mg m(^{-3}))</th>
<th>ELEMENTS OF PRIMARY INTEREST</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIG-POSITION 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>6061/4043</td>
<td>24.9</td>
<td>0.1</td>
<td>Si</td>
</tr>
<tr>
<td>2</td>
<td>6061/5356</td>
<td>34.3</td>
<td>2.0</td>
<td>Si, Mg, Be</td>
</tr>
<tr>
<td>3</td>
<td>2219/2319</td>
<td>71.6</td>
<td></td>
<td>Cu</td>
</tr>
<tr>
<td>MIG-POSITION 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>5456/5356</td>
<td>611.5</td>
<td>75.6</td>
<td>Mg, Be</td>
</tr>
<tr>
<td>5</td>
<td>5456/5356</td>
<td>101.1</td>
<td>21.5</td>
<td>Mg, Be</td>
</tr>
<tr>
<td>6</td>
<td>2219/2319</td>
<td>259.8</td>
<td></td>
<td>Cu</td>
</tr>
<tr>
<td>7</td>
<td>1100/1100</td>
<td>84.3</td>
<td></td>
<td>Al</td>
</tr>
<tr>
<td>TIG-POSITION 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>6061/5356</td>
<td>18.4</td>
<td>1.0</td>
<td>Mg, Be</td>
</tr>
<tr>
<td>9</td>
<td>6061/4043</td>
<td>6.5</td>
<td>0.2</td>
<td>Si, Mg</td>
</tr>
<tr>
<td>10</td>
<td>5456/5356</td>
<td>12.2</td>
<td>0.2</td>
<td>Mg</td>
</tr>
<tr>
<td>11</td>
<td>5456/5356</td>
<td>12.8</td>
<td>1.3</td>
<td>Mg, Be</td>
</tr>
<tr>
<td>ACGIH-TLV</td>
<td>5.0</td>
<td>5.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4 shows the total welding fume emissions outside the welding helmet for the different base alloy/electrode combinations as
well as the amount of aluminium oxide fume recovered. Aluminium oxide fume recovery for the MIG process is as high as 97% whereas recovery using the TIG process is only up to 23%, as seen in Test 6 and 9, respectively. Total welding fume emissions appear to be reduced when using a 75% Helium + 25% Argon as the shielding gas. This is less obvious for the TIG process in that all total welding fume emissions are substantially reduced.

Table 5 shows the effects of welding on alloys containing magnesium. The total welding fumes generated in Test 4 are up to 122 times the TLV for the total welding fume. Test 5, which utilises 75% He + 25% Ar as the shielding gas, demonstrates a 5-fold reduction in total welding fume emissions. Data from welding on 2219/2319 - i.e., Test 3 and 6, demonstrate that the welders head position shows high variations between Position 1 and Position 2 and that the TIG welding process is associated with substantially less welding emissions than the MIG process.

Table 6
Martin Marietta Study, May 1983, Geometric Mean Values for Total Welding Fumes and Copper Fume

<table>
<thead>
<tr>
<th>TEST</th>
<th>ALLOY SELECTION BASE/ELECTRODE</th>
<th>TOTAL WELDING FUME (mg m⁻³)</th>
<th>COPPER FUME (mg m⁻³)</th>
<th>ELEMENTS OF PRIMARY INTEREST</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIG-POSITION 1</td>
<td>1 6061/4043</td>
<td>24.9</td>
<td>.03</td>
<td>Si</td>
</tr>
<tr>
<td></td>
<td>2 6061/5356</td>
<td>34.3</td>
<td>.01</td>
<td>Si, Mg, Be</td>
</tr>
<tr>
<td></td>
<td>3 2219/2319</td>
<td>71.6</td>
<td>.80</td>
<td>Cu</td>
</tr>
<tr>
<td>MIG-POSITION 2</td>
<td>4 5456/5356</td>
<td>611.5</td>
<td>N.A.</td>
<td>Mg, Be</td>
</tr>
<tr>
<td></td>
<td>5 5456/5356</td>
<td>101.1</td>
<td>N.A.</td>
<td>Mg, Be</td>
</tr>
<tr>
<td></td>
<td>6 2219/2319</td>
<td>259.8</td>
<td>2.98</td>
<td>Cu</td>
</tr>
<tr>
<td></td>
<td>7 1100/1100</td>
<td>84.3</td>
<td>0.03</td>
<td>Al</td>
</tr>
<tr>
<td>TIG-POSITION 2</td>
<td>8 6061/5356</td>
<td>18.4</td>
<td>N.A.</td>
<td>Mg, Be</td>
</tr>
<tr>
<td></td>
<td>9 6061/4043</td>
<td>6.5</td>
<td>&lt;0.002</td>
<td>Si, Mg</td>
</tr>
<tr>
<td></td>
<td>10 5456/5356</td>
<td>12.2</td>
<td>N.A.</td>
<td>Mg</td>
</tr>
<tr>
<td></td>
<td>11 5456/5356</td>
<td>12.8</td>
<td>N.A.</td>
<td>Mg, Be</td>
</tr>
<tr>
<td>ACGIH-TLV</td>
<td>5.0</td>
<td>0.10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 6 demonstrates the effect of welding on alloys containing copper. In MIG welding, copper fume emissions can exceed the TLV up to 30 times. Again, there is high variability with head position. Controlling total welding fume emissions to below the 5 mg m⁻³ TLV will also control copper fume exposure. Emissions of copper fume from TIG welding are below the TLV for copper fume.
Table 7 shows the effect of welding on aluminium alloys containing beryllium at 0.0007%. Beryllium was not detectable in any alloy combination and was well below the TLV of 2 µg m$^{-3}$.

Table 7  
**Martin Marietta Study, May 1983, Total Welding Fume and Beryllium Fume**

<table>
<thead>
<tr>
<th>TEST</th>
<th>ALLOY SELECTION BASE/ELECTRODE</th>
<th>TOTAL WELDING FUME (mg m$^{-3}$)</th>
<th>Be FUME (µg m$^{-3}$)</th>
<th>ELEMENTS OF PRIMARY INTEREST</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIG-POSITION 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>6061/4043</td>
<td>24.9</td>
<td>---</td>
<td>Si</td>
</tr>
<tr>
<td>2</td>
<td>6061/5356</td>
<td>34.3</td>
<td>&lt;0.5</td>
<td>Si, Mg, Be</td>
</tr>
<tr>
<td>3</td>
<td>2219/2319</td>
<td>71.6</td>
<td>---</td>
<td>Cu</td>
</tr>
<tr>
<td>MIG-POSITION 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>5456/5356</td>
<td>611.5</td>
<td>&lt;0.5</td>
<td>Mg, Be</td>
</tr>
<tr>
<td>5</td>
<td>5456/5356</td>
<td>101.1</td>
<td>&lt;0.5</td>
<td>Mg, Be</td>
</tr>
<tr>
<td>6</td>
<td>2219/2319</td>
<td>259.8</td>
<td>---</td>
<td>Cu</td>
</tr>
<tr>
<td>7</td>
<td>1100/1100</td>
<td>84.3</td>
<td>---</td>
<td>Al</td>
</tr>
<tr>
<td>TIG-POSITION 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>6061/5356</td>
<td>18.4</td>
<td>&lt;0.5</td>
<td>Mg, Be</td>
</tr>
<tr>
<td>9</td>
<td>6061/4043</td>
<td>6.15</td>
<td>---</td>
<td>Si, Mg</td>
</tr>
<tr>
<td>10</td>
<td>5456/5356</td>
<td>12.12</td>
<td>&gt;0.05</td>
<td>Mg</td>
</tr>
<tr>
<td>11</td>
<td>5456/5356</td>
<td>12.8</td>
<td>&lt;0.5</td>
<td>Mg, Be</td>
</tr>
<tr>
<td>ACGIH-TLV</td>
<td></td>
<td>5.0</td>
<td>2.0</td>
<td></td>
</tr>
</tbody>
</table>

Table 8 shows welding fume emissions inside and outside the welding helmet and demonstrates the effect of the welding helmet on reducing airborne emissions. For MIG, welding reductions range from 29% - 99%, whereas the TIG process consistently demonstrated above 90% reduction in potential exposure to emissions.

While the standard welding helmet is not intended to provide protection against welding fumes, it is apparent that some reduction does occur, but it is not predictable and should not be regarded as a control procedure for reducing welding fumes.

**ALCOA 1985 STUDY**

In 1985, a second welding study was undertaken by Alcoa Laboratories (3). The objectives of this study were to (1) determine emissions from welding on other base alloy/electrode combinations using the MIG welding process, (2) determine the effect of increased power (Amps) on welding emissions, (3) measure emissions from alloys...
containing specific elemental additions, e.g., beryllium. Tables 9 and 10 show an emission spectrographic analysis of the base alloy and electrode alloys used with specific elements of interest highlighted.

Table 8
Martin Marietta Study, May 1983, Geometric Mean Values for Total Welding Fume inside and outside the Welding Helmet

<table>
<thead>
<tr>
<th>TEST</th>
<th>ALLOY SELECTION: BASE/ ELECTRODE</th>
<th>TOTAL WELDING FUME (mg m⁻³)</th>
<th>% REDUCTION INSIDE HELMET</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>OUTSIDE</td>
<td>INSIDE</td>
</tr>
<tr>
<td>MIG-POSITION 1</td>
<td></td>
<td>24.90</td>
<td>12.03</td>
</tr>
<tr>
<td>1</td>
<td>6061/4043</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>6061/5356</td>
<td>34.28</td>
<td>14.08</td>
</tr>
<tr>
<td>3</td>
<td>2219/2319</td>
<td>47.69</td>
<td>23.10</td>
</tr>
<tr>
<td>MIG-POSITION 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>5456/5356</td>
<td>611.50</td>
<td>260.67</td>
</tr>
<tr>
<td>5</td>
<td>5456/5356</td>
<td>101.11</td>
<td>0.89</td>
</tr>
<tr>
<td>6</td>
<td>2219/2319</td>
<td>259.82</td>
<td>121.11</td>
</tr>
<tr>
<td>7</td>
<td>1100/1100</td>
<td>84.27</td>
<td>59.14</td>
</tr>
<tr>
<td>TIG-POSITION 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>6061/5356</td>
<td>18.45</td>
<td>0.80</td>
</tr>
<tr>
<td>9</td>
<td>6061/4043</td>
<td>6.52</td>
<td>0.33</td>
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<td>10</td>
<td>5456/5356</td>
<td>12.23</td>
<td>0.09</td>
</tr>
<tr>
<td>11</td>
<td>5456/5356</td>
<td>12.82</td>
<td>&lt;0.04</td>
</tr>
<tr>
<td>ACGIH-TLV</td>
<td></td>
<td>5.0</td>
<td>5.0</td>
</tr>
</tbody>
</table>

Table 11 shows the base alloy/electrode combination:

- Al-Cu base alloy (2219) welded with Al-Si filler alloy (4145).
- Al-Mg base alloy (5456) welded with Al-Mg filler alloy (5556); two thicknesses and two welding currents were employed.
- Al-Si-Mg-Be casting alloy (A357.0) welded with Al-Si filler alloy (4047).
- Al-Si-Mg-Be casting alloy (358.0) welded with Al-Si filler alloy (4047); two plate thicknesses and two welding currents were employed.
- Al-Zn-Mg base alloy (7039) welded with Al-Mg filler alloy (5039).
### Table 9
ALCOA Study, July 1985, Emission Spectrograph of Aluminium Base Metal Alloys

<table>
<thead>
<tr>
<th>BASE ALLOY</th>
<th>Si</th>
<th>Cu</th>
<th>Mn</th>
<th>Mg</th>
<th>Cr</th>
<th>Zn</th>
<th>Be</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/4&quot; A357.0</td>
<td>7.28</td>
<td>0.02</td>
<td>0.00</td>
<td>0.63</td>
<td>0.00</td>
<td>0.00</td>
<td>0.0540</td>
</tr>
<tr>
<td>1/4&quot; 358.0</td>
<td>7.79</td>
<td>0.02</td>
<td>0.0002</td>
<td>0.51</td>
<td>0.00</td>
<td>0.01</td>
<td>0.3300</td>
</tr>
<tr>
<td>1/2&quot; 358.0</td>
<td>7.77</td>
<td>0.02</td>
<td>0.0002</td>
<td>0.51</td>
<td>0.00</td>
<td>0.02</td>
<td>0.2500</td>
</tr>
<tr>
<td>1/4&quot; 2219</td>
<td>0.06</td>
<td>6.60</td>
<td>0.250</td>
<td>0.01</td>
<td>0.00</td>
<td>0.01</td>
<td>0.0000</td>
</tr>
<tr>
<td>1/4&quot; 5456</td>
<td>0.10</td>
<td>0.03</td>
<td>0.740</td>
<td>5.17</td>
<td>0.08</td>
<td>0.02</td>
<td>0.0002</td>
</tr>
<tr>
<td>1/2&quot; 5456</td>
<td>0.10</td>
<td>0.03</td>
<td>0.710</td>
<td>4.81</td>
<td>0.09</td>
<td>0.08</td>
<td>0.0004</td>
</tr>
<tr>
<td>1/4&quot; 7039</td>
<td>0.08</td>
<td>0.07</td>
<td>0.260</td>
<td>2.86</td>
<td>0.18</td>
<td>4.10</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Note: Elements of interest are highlighted

### Table 10
ALCOA Study, July 1985, Emission Spectrograph of Spectrograph Electrode Alloys

<table>
<thead>
<tr>
<th>BASE ALLOY</th>
<th>Si</th>
<th>Cu</th>
<th>Mn</th>
<th>Mg</th>
<th>Cr</th>
<th>Zn</th>
<th>Be</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/4&quot; 4047</td>
<td>12.1</td>
<td>0.00</td>
<td>0.00</td>
<td>0.01</td>
<td>0.00</td>
<td>0.00</td>
<td>0.0000</td>
</tr>
<tr>
<td>3/32&quot; 4047</td>
<td>12.1</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.0000</td>
</tr>
<tr>
<td>1/16&quot; 4145</td>
<td>9.71</td>
<td>3.68</td>
<td>0.01</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.0000</td>
</tr>
<tr>
<td>1/16&quot; 5039</td>
<td>0.06</td>
<td>0.01</td>
<td>0.40</td>
<td>3.60</td>
<td>0.14</td>
<td>2.70</td>
<td>0.0001</td>
</tr>
<tr>
<td>1/16&quot; 5556</td>
<td>0.06</td>
<td>0.01</td>
<td>0.60</td>
<td>5.24</td>
<td>0.07</td>
<td>0.02</td>
<td>0.0001</td>
</tr>
<tr>
<td>3/32&quot; 5556</td>
<td>0.08</td>
<td>0.01</td>
<td>0.70</td>
<td>4.72</td>
<td>0.06</td>
<td>0.02</td>
<td>0.0001</td>
</tr>
</tbody>
</table>
Table 11
ALCOA Study, July 1985, Welding Parameters

<table>
<thead>
<tr>
<th>TEST</th>
<th>ALLOY SELECTION BASE/ELECTRODE</th>
<th>WELDING CURRENT (DC Amps)</th>
<th>ELEMENTS PRIMARY INTEREST</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1/4&quot; 2219 / 1/16&quot; 4145</td>
<td>240</td>
<td>Cu, Si</td>
</tr>
<tr>
<td>B</td>
<td>1/4&quot; 5456 / 1/16&quot; 5556</td>
<td>240</td>
<td>Mg, Mn, Be</td>
</tr>
<tr>
<td>C</td>
<td>1/2&quot; 5456 / 3/32&quot; 5556</td>
<td>360</td>
<td>Mg, Mn, Be</td>
</tr>
<tr>
<td>D</td>
<td>1/4&quot; A357.0 / 1/16&quot; 4047</td>
<td>240</td>
<td>Si, Be</td>
</tr>
<tr>
<td>E</td>
<td>1/4&quot; 358.0 / 1/16&quot; 4047</td>
<td>240</td>
<td>Si, Be</td>
</tr>
<tr>
<td>F</td>
<td>1/2&quot; 358.0 / 3/32&quot; 4047</td>
<td>360</td>
<td>Si, Be</td>
</tr>
<tr>
<td>G</td>
<td>1/4&quot; 7039 / 1/16&quot; 5039</td>
<td>240</td>
<td>Zn, Mg</td>
</tr>
</tbody>
</table>

Table 12
ALCOA Study, July 1985, Geometric Mean Values of Measured Ozone

<table>
<thead>
<tr>
<th>TEST</th>
<th>ALLOY SELECTION BASE/ELECTRODE</th>
<th>OZONE INSIDE (ppm)</th>
<th>OZONE OUTSIDE (ppm)</th>
<th>% REDUCTION WITH HELMET</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1/4&quot; 2219 / 1/16&quot; 4145</td>
<td>5.10</td>
<td>17.60</td>
<td>71.0</td>
</tr>
<tr>
<td>B</td>
<td>1/4&quot; 5456 / 1/16&quot; 5556</td>
<td>0.05</td>
<td>0.20</td>
<td>75.0</td>
</tr>
<tr>
<td>C</td>
<td>1/2&quot; 5456 / 3/32&quot; 5556*</td>
<td>0.55</td>
<td>4.82</td>
<td>88.6</td>
</tr>
<tr>
<td>D</td>
<td>1/4&quot; A357.0 / 1/16&quot; 4047</td>
<td>7.39</td>
<td>20.1</td>
<td>63.2</td>
</tr>
<tr>
<td>E</td>
<td>1/4&quot; 358.0 / 1/16&quot; 4047</td>
<td>3.04</td>
<td>21.1</td>
<td>85.6</td>
</tr>
<tr>
<td>F</td>
<td>1/2&quot; 358.0 / 3/32&quot; 4047*</td>
<td>3.63</td>
<td>20.4</td>
<td>82.2</td>
</tr>
<tr>
<td>G</td>
<td>1/4&quot; 7039 / 1/16&quot; 5039</td>
<td>0.02</td>
<td>0.04</td>
<td>50.0</td>
</tr>
</tbody>
</table>

* High Current

Table 12 shows ozone concentrations associated with welding on this series of aluminium alloys. Ozone concentrations ranged up to 200 times the TLV outside the welding helmet. Ozone concentrations inside the welding helmet were, however, reduced by 50 - 89% depending on the specific alloys welded. As with total welding fume, the welding helmet afforded some reduction of gaseous emissions, which is not predictable.

Table 13 shows the concentration of welding fume and magnesium oxide outside the welding helmet. Alloys containing magnesium oxide have high fuming characteristics, however, if total welding fume is controlled for the TLV then corresponding airborne concentrations of magnesium oxide are controlled to below its TLV.
From this data, it is not clear whether high current affects fuming characteristics. Set B and C show a reduction, whereas Set E and F show the opposite. Table 13 also shows total welding fume and copper emissions outside the welding helmet. Again, copper fume can exceed the TLV, but if total welding fume is controlled to the TLV of 5 mg m\(^{-3}\), copper fume will also be controlled.

Table 14 shows total welding fume and manganese and beryllium and zinc outside the welding helmet. Manganese fume can exceed the TLV of 1 mg m\(^{-3}\) however, if total welding fume is controlled to 5 mg m\(^{-3}\) manganese is also controlled. It can also be seen that where beryllium exists in the base/electrode alloy at a concentration of greater than 0.054%, beryllium emissions exceed the TLV of 2 µg m\(^{-3}\). In this case, controlling welding fume levels to the TLV of 5 mg m\(^{-3}\) will not sufficiently control beryllium emissions. It can be seen that alloys containing zinc oxide also tend to have high fuming characteristics. Zinc oxide emissions can exceed the TLV for zinc oxide of 5 mg m\(^{-3}\). Controlling total welding emissions will control zinc oxide emissions as well.

### Table 13

**ALCOA Study, July 1985, Geometric Mean Values of Total Welding Fume, Magnesium Oxide and Copper Fume outside the Welding Helmet**

<table>
<thead>
<tr>
<th>TEST</th>
<th>ALLOY SELECTION BASE/ ELECTRODE</th>
<th>TOTAL WELDING FUME (mg m(^{-3}))</th>
<th>Cu FUME (mg m(^{-3}))</th>
<th>Mg OXIDE FUME (mg m(^{-3}))</th>
<th>ELEMENT OF PRIMARY INTEREST</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1/4” 2219 / 1/16” 4145</td>
<td>9.1</td>
<td>0.2</td>
<td>&lt;0.1</td>
<td>Cu, Si</td>
</tr>
<tr>
<td>B</td>
<td>1/4” 5456 / 1/16” 5556</td>
<td>641.0</td>
<td>2.32</td>
<td>56.7</td>
<td>Mg, Mn, Be</td>
</tr>
<tr>
<td>C</td>
<td>1/2” 5456 / 3/32” 5556*</td>
<td>265.0</td>
<td>1.09</td>
<td>17.9</td>
<td>Mg, Mn, Be</td>
</tr>
<tr>
<td>D</td>
<td>1/4” A357.0 / 1/16” 4047</td>
<td>17.0</td>
<td>----</td>
<td>0.2</td>
<td>Si, Be</td>
</tr>
<tr>
<td>E</td>
<td>1/4” 358.0 / 1/16” 4047</td>
<td>11.5</td>
<td>----</td>
<td>0.2</td>
<td>Si, Be</td>
</tr>
<tr>
<td>F</td>
<td>1/2” 358.0 / 3/32” 4047*</td>
<td>25.2</td>
<td>----</td>
<td>0.3</td>
<td>Si, Be</td>
</tr>
<tr>
<td>G</td>
<td>1/4” 7039 / 1/16” 5039</td>
<td>516.0</td>
<td>0.1</td>
<td>22.6</td>
<td>Zn, Mg</td>
</tr>
</tbody>
</table>

* High Current
Table 14
ALCOA Study, July 1985, Geometric Mean Values
Total Welding Fume, Beryllium, Manganese and Zinc
Outside Welding Helmet

<table>
<thead>
<tr>
<th>TEST</th>
<th>ALLOY SELECTION BASE/ELECTRODE</th>
<th>TOTAL WELDING FUME (mg m^3)</th>
<th>Mn FUME (mg m^3)</th>
<th>Zn OXIDE FUME (mg m^3)</th>
<th>Be FUME (µg m^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1/4&quot; 2219 / 1/16&quot; 4145</td>
<td>9.1</td>
<td>0.2</td>
<td>----</td>
<td>&lt;0.2</td>
</tr>
<tr>
<td>B</td>
<td>1/4&quot; 5456 / 1/16&quot; 5556</td>
<td>641.0</td>
<td>2.25</td>
<td>0.38</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>C</td>
<td>1/2&quot; 5456 / 3/32&quot; 5556*</td>
<td>265.0</td>
<td>1.05</td>
<td>0.19</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>D</td>
<td>1/4&quot; A357.0 / 1/16&quot; 4047</td>
<td>17.0</td>
<td>----</td>
<td>----</td>
<td>16.0</td>
</tr>
<tr>
<td>E</td>
<td>1/4&quot; 358.0 / 1/16&quot; 4047</td>
<td>11.5</td>
<td>----</td>
<td>----</td>
<td>31.9</td>
</tr>
<tr>
<td>F</td>
<td>1/2&quot; 358.0 / 3/32&quot; 4047*</td>
<td>25.2</td>
<td>----</td>
<td>----</td>
<td>45.8</td>
</tr>
<tr>
<td>G</td>
<td>1/4&quot; 7039 / 1/16&quot; 5039</td>
<td>516.0</td>
<td>1.19</td>
<td>20.3</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td></td>
<td>ACGIH-TLV</td>
<td>5.0</td>
<td>1.0</td>
<td>5.0</td>
<td>2.0</td>
</tr>
</tbody>
</table>

*High Current

Table 15 provides additional data on the effect of wearing a welding helmet. Again, total welding fumes are reduced inside the helmet by 65 - 85 percent.

ALCOA 1991 STUDY

A third study was completed at Alcoa Laboratories in October, 1991 (4), to more fully evaluate beryllium emissions and to consider the emissions from welding on alloys containing lithium and antimony. In addition, similar measurements were made for a third process - i.e., plasma arc cutting. Table 16 lists the emission spectrographic analyses for the base and electrode alloys used for this.

Table 17 lists the total welding fume copper and beryllium fume concentrations for this alloy series. Information is consistent with previous studies. The data indicates that alloys containing beryllium exceed the TLV of 2.0 µg m^3 by almost five-fold. Controlling total welding fume levels to below the TLV will not sufficiently limit beryllium exposure. Similar data for lithium indicted that lithium oxide
emissions would not exceed the American Industrial Hygiene Association (AIHA) Workplace Environmental Exposure Limit (WEEL) (5).

Table 15
ALCOA Study, July 1985, Geometric Mean Values
Total Welding Fume
Inside and outside the Welding Helmet

<table>
<thead>
<tr>
<th>TEST</th>
<th>ALLOY SELECTION BASE/ELECTRODE</th>
<th>TOTAL WELDING FUME</th>
<th>% REDUCTION INSIDE HELMET</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>INSIDE (mg m^{-3})</td>
<td>OUTSIDE (mg m^{-3})</td>
</tr>
<tr>
<td>A</td>
<td>1/4” 2219 / 1/16” 4145</td>
<td>3.2</td>
<td>9.1</td>
</tr>
<tr>
<td>B</td>
<td>1/4” 5456 / 1/16” 5556</td>
<td>5.2</td>
<td>17.0</td>
</tr>
<tr>
<td>C</td>
<td>1/2” 5456 / 3/32” 5556*</td>
<td>3.2</td>
<td>11.5</td>
</tr>
<tr>
<td>D</td>
<td>1/4” A357.0 / 1/16” 4047</td>
<td>8.7</td>
<td>25.2</td>
</tr>
<tr>
<td>E</td>
<td>1/4” 358.0 / 1/16” 4047</td>
<td>94.1</td>
<td>641.0</td>
</tr>
<tr>
<td>F</td>
<td>1/2” 358.0 / 3/32” 4047*</td>
<td>59.4</td>
<td>266.0</td>
</tr>
<tr>
<td>G</td>
<td>1/4” 7039 / 1/16” 5039</td>
<td>81.8</td>
<td>517.0</td>
</tr>
</tbody>
</table>

*High Current

Table 18 summarises the data on beryllium from all four studies. Based on this information, concentrations of beryllium in excess of 0.008% produces emissions in excess of the TLV.

In addition to the above, a fourth study was conducted by Alcoa Laboratories (6) concerning potential chromium emissions. In this study, a special chamber was constructed to collect all emissions from welding, plasma arc cutting and grinding. As hexavalent chromium may be formed during these processes, potential hexavalent chromium emissions were evaluated. The study showed that as long as total welding fume concentrations are controlled to below 5 mg m^{-3}, hexavalent chromium will be controlled to well below 0.5 mg m^{-3}.
### Table 16
ALCOA Study, October 1991, Emission Spectrograph of Aluminium Base Alloy and Electrode Alloy Combinations (weight percent)

<table>
<thead>
<tr>
<th>ALLOY SELECTION</th>
<th>Si</th>
<th>Cu</th>
<th>Mg</th>
<th>Mn</th>
<th>Be</th>
<th>Li</th>
<th>Sb</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BASE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/4&quot; 2090</td>
<td>0.04</td>
<td>2.70</td>
<td>0.01</td>
<td>----</td>
<td>----</td>
<td>1.60</td>
<td>----</td>
</tr>
<tr>
<td>1/2&quot; 2090</td>
<td>0.04</td>
<td>2.70</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>2.10</td>
<td>----</td>
</tr>
<tr>
<td>1/4&quot; A356.0</td>
<td>7.73</td>
<td>----</td>
<td>0.35</td>
<td>----</td>
<td>0.008</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td>1/4&quot; A356.0</td>
<td>7.32</td>
<td>----</td>
<td>0.30</td>
<td>----</td>
<td>0.006</td>
<td>----</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>ELECTRODE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>1/16&quot; 2319</td>
<td>0.07</td>
<td>6.07</td>
<td>----</td>
<td>0.30</td>
<td>----</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td>1/16&quot; 1100</td>
<td>0.03</td>
<td>0.10</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td>5/32&quot; 2319</td>
<td>0.07</td>
<td>6.06</td>
<td>----</td>
<td>0.29</td>
<td>----</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td>1/16&quot; 4043</td>
<td>5.11</td>
<td>0.11</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td>1/16&quot; 4043</td>
<td>5.11</td>
<td>0.11</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td>1/16&quot; 4043</td>
<td>5.11</td>
<td>0.11</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
</tr>
</tbody>
</table>

Note: Elements of interest are highlighted.

### Table 17
ALCOA Study, October 1991, Geometric Mean Values of Total Welding Fume Copper Fume and Beryllium outside the Welding Helmet

<table>
<thead>
<tr>
<th>TEST</th>
<th>ALLOY SELECTION BASE/ ELECTRODE</th>
<th>TOTAL WELDING FUME (mg m(^{-3}))</th>
<th>Cu FUME (mg m(^{-3}))</th>
<th>Be (µg m(^{-3}))</th>
<th>ELEMENT OF PRIMARY INTEREST</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MIG WELDING</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>K</td>
<td>2090/2319</td>
<td>39.3</td>
<td>1.23</td>
<td>----</td>
<td>Cu, Li</td>
</tr>
<tr>
<td>L</td>
<td>2090/1100</td>
<td>26.5</td>
<td>0.05</td>
<td>----</td>
<td>Cu, Li</td>
</tr>
<tr>
<td>M</td>
<td>2090/2319</td>
<td>0.53</td>
<td>----</td>
<td>----</td>
<td>Cu, Li</td>
</tr>
<tr>
<td>N</td>
<td>A356.0/4043</td>
<td>12.7</td>
<td>0.04</td>
<td>9.29</td>
<td>Be, Si</td>
</tr>
<tr>
<td>O</td>
<td>A356.0/4043</td>
<td>4.56</td>
<td>----</td>
<td>&lt;0.99</td>
<td>Be, Si</td>
</tr>
<tr>
<td>P</td>
<td>A356.0/4043</td>
<td>2.50</td>
<td>----</td>
<td>&lt;0.63</td>
<td>Be, Si, Sb</td>
</tr>
<tr>
<td><strong>PLASMA ARC CUTTING</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q</td>
<td>2090</td>
<td>2.91</td>
<td>----</td>
<td>&lt;0.50</td>
<td>Cu, Li</td>
</tr>
<tr>
<td></td>
<td>ACGIH-TLV</td>
<td>5.0</td>
<td>0.1</td>
<td>2.0</td>
<td></td>
</tr>
</tbody>
</table>
CONCLUSIONS

From the studies it may be concluded that:

- Welding emissions vary by welding process, base alloy/electrode, shielding gas and current.
- Specific alloy constituents such as copper, magnesium, manganese, and zinc when welded can produce emissions in excess of their respective TLVs.
- Welding or plasma arc cutting of aluminium alloys can produce ozone concentrations in excess of the TLV of 0.1 ppm.
- Welding on alloys as low as 0.008% Be can produce emissions in excess of the TLV of 2 µg m⁻³.
- The TLVs for total welding fumes, specific metallic constituents and gases may be exceeded during welding. A hazard determination must be made to select the appropriate personal protective equipment.
- The data indicates that welding emissions inside a welding helmet are lower than those outside.
- The position of a welder's head relative to the plume may be a consideration in controlling welding emissions.

Table 18  
Beryllium Emissions Summary

<table>
<thead>
<tr>
<th>ALLOY SELECTION</th>
<th>BERYLLIUM EMISSIONS (µg m⁻³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASE/ELECTRODE</td>
<td></td>
</tr>
<tr>
<td>MIG WELDING</td>
<td></td>
</tr>
<tr>
<td>7039 (0.0001%)*/5039 (0.0001%)</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>1/4” 5456 (0.0002%)/5556 (0.0001%)</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>1/2” 5456 (0.0004%)/5556 (0.0001%)</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>5456 (0.0007%)/5356 (0.000%)</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>6061 (0.0007%)/5356 (0.000%)</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>A356 (0.002%)/4043 (0.00%)</td>
<td>&lt;0.6</td>
</tr>
<tr>
<td>A356 (0.006%)/4043 (0.00%)</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>A356 (0.008%)/4043 (0.00%)</td>
<td>9.3</td>
</tr>
<tr>
<td>A357 (0.054%)/4047 (0.00%)</td>
<td>16.0</td>
</tr>
<tr>
<td>A358 (0.25%)/4047 (0.00%)</td>
<td>45.2</td>
</tr>
<tr>
<td>A358 (0.33%)/4047 (0.00%)</td>
<td>31.9</td>
</tr>
<tr>
<td>TIG WELDING</td>
<td></td>
</tr>
<tr>
<td>6061 (0.0007%)/5356 (0.00%)</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>5456 (0.0007%)/5356 (0.00%)</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>5456 (0.0007%)/5356 (0.00%)</td>
<td>&lt;0.5</td>
</tr>
</tbody>
</table>

Numbers in parentheses indicate percent beryllium
REFERENCES

2. 1997 TLVs and BEIs, The American Conference of Governmental Industrial Hygienists, 1997.
SUMMARY

Heat stress may be a seasonal phenomenon. The wet-bulb globe temperature index has been selected for monitoring heat stress among workers. Three different types of preventive measures are usually applied; engineering controls, administrative controls and personal protection. In primary aluminium smelting micro-environments such as air-conditioned or insulated cabs provide a microclimate to promote cooling or reduce heat gain in such as overhead crane cabs. Worker training is the cornerstone of a prevention programme involving knowledge of heat-related disorders and heat stress hygiene practices. Success requires strong management commitment, joint union - management approval, consistent and repeated training, and communication and worker involvement.

INTRODUCTION

In Canada, heat stress is a seasonal phenomenon. In primary aluminium smelting, radiant heat is the most important contributing factor to occupational heat exposures. This presentation will share Alcan’s experience in managing heat stress disorders through an array of administrative controls.

DEFINITIONS

- Hot environment: A workplace where the WBGT (Wet-bulb globe temperature) index is equal to or greater than 25°C.

The wet-bulb globe temperature index (WBGT) is used worldwide for recording heat stress. It is therefore discussed in more detail here.

The WBGT is calculated by using the following formula:
• In exterior environment with sunlight

\[ \text{WBGT} = 0.7 \, T_{wb} + 0.2 \, T_g + 0.1 \, T_{db} \]

• In interior or exterior environment without sunlight

\[ \text{WBGT} = 0.7 \, T_{wb} + 0.3 \, T_g \]

where:

\[ \text{WBGT}_{1 \rightarrow n} = \text{wet-globe temperature index for specific time periods} \]

\[ T_{wb} = \text{wet-bulb temperature (°C)} \]

\[ T_g = \text{globe temperature (°C)} \]

\[ T_{db} = \text{dry-bulb temperature (°C)} \]

• Continuous exposure: This concept relies on the duration of exposure to hot environmental conditions. It varies according to the applicable regulations or scientific agencies’ recommendations. As an example, in Québec, a continuous exposure is defined as one lasting more than 15 minutes in a hot environment; whereas, according to ACGIH, this has to last several hours. This inconsistency is not unusual for companies conducting business in many countries.

HEAT STRESS MONITORING

Core temperature is impractical for measuring workers’ heat load. The WBGT index was selected for the following reasons: regulatory requirement, simplicity and the existence of some correlation between core temperature and environmental factors. The biggest difficulty with this approach is to accurately evaluate workloads. A continuous exposure to a hot environment requires the use of the hourly time-weighted average, whereas an intermittent exposure calls for the two hourly time weighted average.

Occupational monitoring covers all work shift exposures to hot environments. While performing it within potrooms, we identify: the hour with the highest WBGT and its corresponding workload, as well as the hour with the greatest workload and its corresponding WBGT. These calculations are performed with a custom software. We then take the more stringent approach, and determine the applicable permissible heat exposure using the continuous work curve for un-acclimatised workers. The latter is strictly a management decision, based on the following factors: no re-acclimatisation is carried out after vacations or
sick leaves, some workers are physically unfit and finally, the acclimatisation process requires continuous daily exposure lasting from 60 to 100 minutes.

We determine the gap between measured WBGT and the applicable permissible heat exposure. If it is greater than +1°C, we consider it as an overexposure; whereas, if it is smaller than -1°C, we then consider that we are in compliance. We also adjust the applicable permissible heat exposure as follows:

- **Body weight**: -1°C (worker’s average body weight equals 81 kg)
- **Air velocity (when applicable)**: +2°C
- **Safety garments**: no adjustment

Workload has to be corrected according to body weight. Adjustments for air cooling effect are allowed providing that air temperature is lower than 35°C and air velocity is in the range of 300 fpm to 700 fpm. No adjustment is made for safety garments: these are loose fitting, aerated under the arms as well as in the back, and shirt is worn over pants in summer.

**PREVENTATIVE MEASURES**

Three different types of preventative measures are usually applied; engineering controls, administrative controls and personal protection. In primary aluminium smelting, few engineering controls are applicable. Micro-environments, such as air-conditioned or insulated cabs, provide a microclimate to promote cooling or reduce heat gain.

Examples of these are: overhead crane cabs, the new generation of mobile potroom equipment, cool-rooms and control rooms. Adequate ambient temperature must be maintained within these work sites; which means a WBGT index of 20°C or a dry-bulb temperature of 23 - 24°C.

**ADMINISTRATIVE CONTROLS**

These are defined as risk management through control of exposures. Their implementation requires: management commitment, union support, job modifications, a great deal of training and communication. Union support is usually obtained through joint OH&S (Occupational Health & Safety) committees. These are involved in the job modification process, as well as approval of teaching material, communication aids and selection of personal protective equipment (PPE).
Managers require that every job modification comply with Occupational Exposure Limits. These are approved by an occupational hygienist prior to their implementation. Supervisors are attentive to workers’ personal factors such as health problems or difficulties coping with hot/cool work cycles. Health problems are confidential, but they are handled by the employee himself, with appropriate medical assistance. These factors may require temporary workload adjustments.

All heat stress incidents requiring first aid treatment are investigated. These are considered as representing fatal accident potential. Availability of drinking water is increased through additional fountains throughout the workplace.

Job modification is performed by scheduling tasks on an hourly basis. This is carried out by taking the following aspects into consideration:

- WBGT index, workload, availability of micro-environments and safety garments. It is also advisable to pay special attention to disposable coveralls, specially those sealed at wrists and ankles, because many of these are considered as encapsulating suits, which may increase susceptibility to heat stress.

Each hour then has a workload equivalent, which allows some flexibility to cope with operational priorities. Modified jobs include recovery allowances through two different types of work schedules:

- Work in a hot environment / followed by a period of work in a cool environment;
- Work in a hot environment / followed by a period of rest in a cool environment.

In a recent study conducted by Alcan Occupational Health professionals and Laval University, physiological responses of two groups of potroom workers were compared for both schedules while performing similar jobs. In order to minimise interference with production, the following parameters were studies:

- Total heartbeats per shift;
- Mean heart rate per shift;
- Mean heart rates in the first hour and in the last hour of the shift.

The main conclusions were:

- The work schedule involving a period of work in a hot environment followed by light work in a cool environment does not cause additional physiological stress as compared to the same heat
exposure followed by rest in a cool environment. Moreover, neither schedule:

• Induces accumulation of physiological fatigue;
• Exceeds ceiling values of physiological demand proposed by Brouha or by the American Heat Association;
• Both work schedules effectively control heat stress among aluminium production workers.

TRAINING

Optimal prevention is achieved when workers are able to recognise the signs and symptoms of heat-related disorders. Training then really becomes the cornerstone of this prevention programme. This is provided by specially trained occupational hygiene technicians and nurses to the following categories of employees: managers, joint Occupational Health and Safety committees, workers, project managers and subcontractors. Annual refresher sessions are given prior to summer and are tailored to the workers’ knowledge base.

Training content includes: basic concepts of heat stress; Occupational Exposure Limits and their limitations; overview of heat stress monitoring procedures; results of previous monitoring campaigns; heat related disorders as well as recognition of their signs and symptoms; heat stress hygiene practices; importance of compliance with hot/cool work cycles; diseases, acute or chronic, drugs or personal factors affecting the body’s defence mechanisms; as well as other factors such as problems of conforming with hot/cool work cycles, new job appointment, obesity and effects of age (over 45) on heat stress tolerance.

Topics covered include a knowledge of heat related disorders:

• Heat rash;
• Dehydration, which is often potentiated by other problems;
• Heat cramps;
• Heat exhaustion;
• Heat syncope;
• Heat stroke.

Also, heat stress hygiene practices:

• Fluid replacement (we advise all workers to drink every 15 to 20 minutes, 150 to 200 ml of fresh water at a temperature of 10-15°C, and to realise that thirst is not a reliable indicator of hydration status);
• Diet;
• Life style compatible with work in hot environments, which means avoidance of alcoholic beverages, narcotics and excessive leisure-time heat stress exposure and adequate sleep and rest;
• Medication, advising the plant physician whenever medication, prescribed or not, is being used.

COMMUNICATION

This covers the same topics as above and we use a complete array of tools such as: slide shows, videotapes, facility newspapers, posters, place mats, etc.

MEDICAL COACHING

In summer, medical coaching is performed in the workplace by nurse(s). Special attention is paid to workers: taking medication(s), physically unfit, recently hired or in training, and those presenting other personal factors such as obesity or older than forty-five years of age. Nurses also carry out periodic reminders on the following topics: early recognition of signs and symptoms of heat stress disorders, hydration and the importance of compliance with hot/cool work cycles.

SUCCESS FACTORS

Factors for success required in the implementation of heat stress administrative controls are:

• Strong management commitment;
• Joint union-management approach;
• Consistent and repeated training and communication;
• Worker involvement.

All of the above activities and factors are essential in maintaining worker’s awareness and safe behaviour related to this significant and potentially fatal occupational hazard.
CONCLUSION

Our approach has proved its effectiveness in substantially decreasing the number of heat stress incidents throughout the facilities operated by Alcan Smelters and Chemicals, Quebec.
5. EMF AND HEALTH: OVERVIEW

Doreen G. Hill
Energetics Inc., 7164 Gateway Drive, Columbia, Maryland, 21046, USA

In the late 1970's and early 1980's, epidemiological studies were reported that suggested a possible relationship between exposure to electric and magnetic fields (EMFs) and the development of cancer. Most notable were studies concerning an increase in cancer, particularly leukaemia, in children who lived in homes close to certain kinds of power lines. Researchers also began to examine various national databases to explore whether men who had worked in certain industries or occupations exhibited differential risks in cancer mortality or incidence. It appeared that work that could involve electricity and possible electric and magnetic field exposure was associated with more leukaemia and brain cancer later in life. Extensive research efforts to investigate this issue ensued, including further epidemiological research and laboratory studies focused on investigating biological effects and identifying possible mechanisms whereby low levels of fields could interact in a way that might explain the epidemiological results.

Various expert reviewing bodies have found that the evidence developed to date does not indicate a causal relationship between EMF exposure and adverse impacts on public health. Thus far, the answer about whether EMFs could influence cancer development or other health endpoints is still uncertain. Any risk may never be fully clarified because of either the methodological difficulties of determining an environmental risk of low magnitude or because of the cessation of basic research. Also, it is possible there may be no risk.

Several more major studies will be reported in the coming year. In the United States, the research program established by the U.S. Congress, the EMF RAPID program, will be drawing to a close and will issue its own assessment of what the available scientific evidence means for public health and policy determination. Unfortunately, much of the available data does not directly bear on EMF concerns in the aluminium industry because of different exposures than those subjected to research examination. But generic concerns about EMF exposures and risks bear watching. The aluminium industry should continue to monitor emerging developments.
6. EMF MEASUREMENTS IN THE ALUMINIUM INDUSTRY

Greg Rawls
Alumax Primary Aluminum Corporation, PO Box 1000, Goose Creek, South Carolina, 29445, USA

SUMMARY

This paper describes the sources of EMF exposures within the aluminium industry and details the results of surveys conducted within smelters operated by a number of companies. The results show that EMF exposures are much below the 60 mT TLV set by the ACGIH. However, as expected they were higher for staff working close to bus bars and other conductors and in plants operating their pots at high currents.

WHAT IS EMF?

EMF, or electromagnetic fields, result from the flow of electrical current (measured in Amps) through a conducting material. This can be power lines, electrical connectors or the bus of a potline in an aluminium smelter. The existence of EMF depends upon the flow of current. If the current is switched off the electromagnetic field ceases to exist. The strength of the electromagnetic field will increase with increasing current. Aluminium smelters, with high amperage pots, produce intense EMFs which may result in high exposures to personnel resident within these fields. The strength of the field diminishes with distance, so the further away someone is from an EMF source (e.g., bus bars) the lower the relative exposure. EMF will pass through most materials and is very difficult to shield\(^1\).

The strength of magnetic fields is measured in units of either Tesla or Gauss (where 1 Tesla is equal to 10,000 Gauss). The Tesla is the more modern unit and defines the magnetic flux of the field per unit area. The Tesla was named after the Croatian-born electrical engineer and inventor Nikola Tesla (1856 – 1943) who was noted for his work with alternating electrical currents and magnetic fields.

There are two types of current: alternating current (AC) and direct current (DC). And with respect to the magnetic fields produced there are significant differences between them. Mains supply AC
produces time-varying fields which vary in strength and direction cyclically 60 times per second (in the USA) – that is they have a frequency of 60 Hz. Exposure to AC magnetic fields will induce electrical current flow within conductors within the field, including the human body. DC electricity produces static fields (frequency = 0 Hz) that cannot induce currents within the body unless it moves within the field (1). To put this in perspective, AC produces waves, but DC does not.

WHY IS EMF SIGNIFICANT WITHIN THE ALUMINIUM INDUSTRY

The process of making aluminium requires large amounts of electricity which produce EMFs. Due to its strong affinity for oxygen, aluminium does not naturally exist in its metallic (native) state. Aluminium is manufactured from its oxide, alumina, by an electro-thermal process where electrolysis takes place in a carbon-lined pot (2). This process consumes a great deal of power in the form of DC. In the aluminium industry, the alternating current produced by the generating source is transformed into DC before it enters the potline (Fig. 1). The current then flows in a series circuit through all the pots in the potline.

Figure 1. Alternating current is transformed into direct current within the rectifier and then is passed, in series, through the potline and back to the rectifier.

The current flows from the previous pot or the rectifier to the next pot. The current enters through the riser, passes through a bus bar to the anodes. The current then passes from the anode through the
molten cryolite and alumina to the cathode and out via the cathode collector bar. The current then flows through the bus to the next pot or returns to the riser (Figs. 2 and 3). It is along the pathways where the current flows (rods, buses and bars) that the EMF is created.

Figure 2. Basic potline configuration showing flow of electricity from rectifier to potline.

Figure 3. Basic potline configuration showing anode and cathode.
STANDARDS

There is a Threshold Limit Value (TLV) published by the American Conference of Governmental Industrial Hygienists (ACGIH) for static magnetic fields. The TLV refers to static magnetic flux densities to which it is believed that nearly all workers may be repeatedly exposed, day after day, without adverse health effects. The daily, time-weighted average exposure for the whole body is 60 mT, for the extremities it is 600 mT, and a ceiling for exposure of 2 T is stipulated (3). The whole body TLV accords to the minimum static magnetic field that would generate a 1 mV potential in the aorta of an adult human heart – 60 mT (4).

EMF MEASUREMENTS

Measurements of EMF are made in the aluminium industry in two ways: area measurements which determine the magnetic field at one location and at one specific time; dosimetry measurements which determine an employee’s time weighted average exposure to the magnetic field on a specific day. Data have been submitted by an Australian smelter, a Norwegian smelter, the Alcan Sebree smelter, the Reynolds Longview smelter, the Kaiser Tacoma Works smelter and the ALUMAX smelters: Mt. Holly; Lauralco; Eastalco; and Intalco. Owing to differences in monitoring protocols the data collected from these sites cannot be directly compared, but inferences can be drawn.

Table 1
EMF strengths (mT) measured at the Alcan Sebree smelter as a function of distance from the bus.

<table>
<thead>
<tr>
<th>Distance from bus</th>
<th>Start potline 3</th>
<th>End potline 2</th>
<th>Loop potline 2</th>
<th>Middle potline 4</th>
<th>Start potline 2</th>
<th>Riser pot 451</th>
<th>Riser pot 415</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 cm</td>
<td>23.4</td>
<td>19.9</td>
<td>32.7</td>
<td>21.1</td>
<td>22.3</td>
<td>23.0</td>
<td>29.0</td>
<td>24.5</td>
</tr>
<tr>
<td>60 cm</td>
<td>16.1</td>
<td>14.1</td>
<td>22.9</td>
<td>14.8</td>
<td>15.4</td>
<td>11.1</td>
<td>13.7</td>
<td>15.4</td>
</tr>
<tr>
<td>110 cm</td>
<td>13.9</td>
<td>11.0</td>
<td>17.3</td>
<td>11.7</td>
<td>12.2</td>
<td>6.3</td>
<td>6.9</td>
<td>11.3</td>
</tr>
<tr>
<td>160 cm</td>
<td>11.9</td>
<td>9.0</td>
<td>13.8</td>
<td>9.9</td>
<td>10.2</td>
<td>3.3</td>
<td>2.9</td>
<td>8.7</td>
</tr>
</tbody>
</table>
Australian Smelter

Area measurements were collected around various pots. These pots were operating at 185 kA and employed Pechiney technology. The field strengths measured ranged from 2 mT to 20 mT. The highest measurements were made in closest proximity to the risers and bus bars.

Norwegian Smelter

Dosimetry was performed and time-weighted average exposures to static EMF were determined to lie between 2 mT and 10 mT and exposures to AC magnetic fields were determined to lie between 1 and 5 µT.

Alcan Sebree Smelter

Dosimetry was performed and time-weighted average exposures were determined for a variety of potline jobs. This smelter operates at 178 – 180 kA. Table 1 shows the attenuation of static (DC) field strength with increasing distance from the buses.

Reynolds Longview Smelter

Dosimetry was performed and time-weighted average exposures to EMF were determined for a variety of potroom jobs. This smelter operates potlines at operating currents of 68 and 100 kA (Tables 2 and 3). Comparing similar jobs in potlines operating at different currents shows that field strength, for most jobs, increases with current (Fig. 3).

Table 2

Reynolds Longview smelter. Exposures to EMF (mT) for different jobs on 68 kA potline.

<table>
<thead>
<tr>
<th>Job</th>
<th>Mean Exposure (mT)</th>
<th>Geometric Mean Exposure</th>
<th>SD</th>
<th>Range (Largest − Smallest)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anodes – Pin Setter</td>
<td>3.9</td>
<td>3.9</td>
<td>0.2</td>
<td>0.4</td>
</tr>
<tr>
<td>Anodes – Channels</td>
<td>4.6</td>
<td>4.2</td>
<td>2.6</td>
<td>3.7</td>
</tr>
<tr>
<td>Pot Tender</td>
<td>4.6</td>
<td>4.6</td>
<td>0.4</td>
<td>1.0</td>
</tr>
<tr>
<td>Anodes – Pin Puller</td>
<td>5.5</td>
<td>5.4</td>
<td>1.1</td>
<td>1.5</td>
</tr>
<tr>
<td>Anodes – Rack and Plug</td>
<td>5.6</td>
<td>5.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Anodes – Flex Raiser</td>
<td>7.5</td>
<td>7.4</td>
<td>0.4</td>
<td>0.5</td>
</tr>
</tbody>
</table>
Table 3
Reynolds Longview smelter. Exposures to EMF (mT) for different jobs on 100 kA potline.

<table>
<thead>
<tr>
<th>Job</th>
<th>Mean Exposure (mT)</th>
<th>Geometric Mean Exposure</th>
<th>SD</th>
<th>Range (Largest – Smallest)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anodes – Pin Setter</td>
<td>6.9</td>
<td>6.8</td>
<td>1.2</td>
<td>2.4</td>
</tr>
<tr>
<td>Pot Tender</td>
<td>3.8</td>
<td>3.8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Anodes – Pin Puller</td>
<td>3.6</td>
<td>3.6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Anodes – Flex Raiser</td>
<td>4.3</td>
<td>4.2</td>
<td>0.7</td>
<td>1.5</td>
</tr>
<tr>
<td>Pot Helper</td>
<td>3.8</td>
<td>3.7</td>
<td>0.5</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Figure 3. Histogram showing the relative exposures of Reynolds Longview workers to EMF for similar jobs on potlines operating with a different current.
### Table 4
Potline exposures to EMF for potline workers on 60 kA and 90 kA potlines at Kaiser Tacoma Works.

<table>
<thead>
<tr>
<th>Job</th>
<th>Mean Exposure (mT)</th>
<th>Geometric Mean Exposure</th>
<th>SD</th>
<th>Range (Largest – Smallest)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supervisor Line I &amp; II</td>
<td>2.5</td>
<td>2.4</td>
<td>0.5</td>
<td>1.6</td>
</tr>
<tr>
<td>Anode Tender Line I &amp; II</td>
<td>2.9</td>
<td>2.9</td>
<td>0.6</td>
<td>1.9</td>
</tr>
<tr>
<td>Flex Operator Line I &amp; II</td>
<td>2.6</td>
<td>2.6</td>
<td>0.4</td>
<td>1.0</td>
</tr>
<tr>
<td>Pot Operator Line I</td>
<td>3.9</td>
<td>3.9</td>
<td>0.3</td>
<td>0.8</td>
</tr>
<tr>
<td>Pot Operator Line II</td>
<td>3.4</td>
<td>3.3</td>
<td>0.5</td>
<td>1.7</td>
</tr>
<tr>
<td>Pot Operator Line IV</td>
<td>4.7</td>
<td>4.7</td>
<td>0.8</td>
<td>2.6</td>
</tr>
<tr>
<td>Supervisor Line IV</td>
<td>3.4</td>
<td>3.3</td>
<td>0.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Anode Tender Line IV</td>
<td>3.4</td>
<td>3.3</td>
<td>0.7</td>
<td>2.4</td>
</tr>
<tr>
<td>Flex Operator Line IV</td>
<td>4.7</td>
<td>4.7</td>
<td>0.8</td>
<td>2.2</td>
</tr>
<tr>
<td>Crane Operator</td>
<td>1.3</td>
<td>1.3</td>
<td>0.3</td>
<td>0.6</td>
</tr>
<tr>
<td>Tapper</td>
<td>3.5</td>
<td>3.4</td>
<td>0.7</td>
<td>2.1</td>
</tr>
</tbody>
</table>

### Table 5
Potline exposures to EMF for maintenance workers on 60 kA and 90 kA potlines at Kaiser Tacoma Works.

<table>
<thead>
<tr>
<th>Job</th>
<th>Mean Exposure (mT)</th>
<th>Geometric Mean Exposure</th>
<th>SD</th>
<th>Range (Largest – Smallest)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Works Repairer – Potroom Maintenance</td>
<td>1.57</td>
<td>1.37</td>
<td>0.72</td>
<td>2.62</td>
</tr>
<tr>
<td>Maintenance / Service Supervisors</td>
<td>0.34</td>
<td>0.21</td>
<td>0.33</td>
<td>1.18</td>
</tr>
<tr>
<td>Rectifier Operator</td>
<td>1.94</td>
<td>1.93</td>
<td>0.22</td>
<td>0.63</td>
</tr>
<tr>
<td>Supervisor / Engineer Electric Shop Rectifier</td>
<td>0.26</td>
<td>0.26</td>
<td>0.03</td>
<td>0.09</td>
</tr>
<tr>
<td>Works Repairer – Electric Shop Rectifier</td>
<td>0.57</td>
<td>0.54</td>
<td>0.17</td>
<td>0.47</td>
</tr>
<tr>
<td>Works Repairer – Auto Shop</td>
<td>0.22</td>
<td>0.21</td>
<td>0.05</td>
<td>0.18</td>
</tr>
<tr>
<td>Works Repairer – Weld Shop</td>
<td>1.04</td>
<td>0.51</td>
<td>1.24</td>
<td>3.95</td>
</tr>
</tbody>
</table>
Table 6
EMF exposures determined for workers at the Alumax, Mt. Holly, smelter – 186 kA and 205 kA potlines

<table>
<thead>
<tr>
<th>Job</th>
<th>186 kA Mean</th>
<th>205 kA Mean</th>
<th>186 kA Geometric Mean</th>
<th>205 kA Geometric Mean</th>
<th>186 kA SD</th>
<th>205 kA SD</th>
<th>186 kA Range</th>
<th>205 kA Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon Setter</td>
<td>5.1</td>
<td>6.3</td>
<td>5.0</td>
<td>6.2</td>
<td>1.7</td>
<td>0.4</td>
<td>4.7</td>
<td>1.2</td>
</tr>
<tr>
<td>Equipment Operator</td>
<td>2.3</td>
<td>3.2</td>
<td>2.0</td>
<td>3.2</td>
<td>1.4</td>
<td>0.8</td>
<td>3.8</td>
<td>1.8</td>
</tr>
<tr>
<td>Pot Operator</td>
<td>5.6</td>
<td>7.4</td>
<td>5.5</td>
<td>7.2</td>
<td>0.9</td>
<td>1.8</td>
<td>1.6</td>
<td>4.7</td>
</tr>
<tr>
<td>Tapper</td>
<td>4.1</td>
<td>4.7</td>
<td>4.1</td>
<td>4.7</td>
<td>0.2</td>
<td>0.7</td>
<td>0.7</td>
<td>1.8</td>
</tr>
<tr>
<td>Trench Cleaner</td>
<td>4.5</td>
<td>6.0</td>
<td>4.4</td>
<td>6.0</td>
<td>1.0</td>
<td>1.0</td>
<td>2.9</td>
<td>2.3</td>
</tr>
</tbody>
</table>

Kaiser Tacoma Works Smelter

Dosimetry was performed and time-weighted average exposures were determined for a variety of potline jobs. This smelter operates potlines at 60 kA and at 90 kA. Kaiser collected data for both potline workers (Table 4) and potline maintenance workers (Table 5), which would be expected to have lower exposures due to the greater distance of their workplace from EMF sources.

Table 7
Dosimetry assessments of EMF exposure for workers at the Alumax Lauralco smelter operating at 316 kA.

<table>
<thead>
<tr>
<th>Job</th>
<th>Mean Exposure (mT)</th>
<th>Geometric Mean Exposure</th>
<th>SD</th>
<th>Range (Largest – Smallest)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anode Changer</td>
<td>5.4</td>
<td>5.3</td>
<td>1.0</td>
<td>3.3</td>
</tr>
<tr>
<td>Tapper</td>
<td>6.9</td>
<td>6.9</td>
<td>0.8</td>
<td>2.6</td>
</tr>
<tr>
<td>Raising Beam</td>
<td>9.2</td>
<td>9.2</td>
<td>0.5</td>
<td>1.3</td>
</tr>
<tr>
<td>Anode Changer / Raise Beam</td>
<td>6.7</td>
<td>6.7</td>
<td>0.8</td>
<td>2.1</td>
</tr>
</tbody>
</table>
Figure 4. Histogram showing the relative exposures of Alumax workers to EMF for similar jobs on potlines operating with either 186 kA or 205 kA.

**Alumax Smelters**

Dosimetry was performed and time-weighted average exposures were determined for a variety of potline jobs at all Alumax smelters. Of particular interest were the EMF surveys carried out before and after the operating current of the Mt. Holly smelter potline was raised from 186 kA to 205 kA. As expected the exposures to EMF were higher at the higher operating voltage (Table 6 and Fig. 4). Tables 7, 8 and 9 show data collected from the Lauralco, Eastalco and Intalco sites, respectively.

**CONCLUSIONS**

There are three factors that influence worker exposure to EMF:

- The operating current producing the EMF;
- The workers proximity to the field;
- The time spent by the worker within the field.
Workers who spend more time around the pot bus will have higher exposures. Workers at smelters operating with high working currents will also have higher exposures.

**Table 8**
EMF exposure assessment for workers in the Alumax Eastalco smelter – 142 kA.

<table>
<thead>
<tr>
<th>Job</th>
<th>Mean Exposure (mT)</th>
<th>Geometric Mean Exposure</th>
<th>SD</th>
<th>Range (Largest – Smallest)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pot Reline</td>
<td>2.6</td>
<td>2.4</td>
<td>1.2</td>
<td>3.9</td>
</tr>
<tr>
<td>Potline Operator</td>
<td>2.8</td>
<td>2.7</td>
<td>0.5</td>
<td>1.9</td>
</tr>
<tr>
<td>Hot Changeout</td>
<td>2.7</td>
<td>2.6</td>
<td>0.5</td>
<td>1.2</td>
</tr>
</tbody>
</table>

**Table 9**
EMF exposure assessment for workers in the Alumax Intalco smelter – 141 kA.

<table>
<thead>
<tr>
<th>Job</th>
<th>Mean Exposure (mT)</th>
<th>Geometric Mean Exposure</th>
<th>SD</th>
<th>Range (Largest – Smallest)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pot Operator – A Line</td>
<td>4.7</td>
<td>4.7</td>
<td>0.6</td>
<td>1.4</td>
</tr>
<tr>
<td>Pot Operator – B Line</td>
<td>4.1</td>
<td>4.1</td>
<td>0.4</td>
<td>0.8</td>
</tr>
<tr>
<td>Pot Operator – C Line</td>
<td>4.3</td>
<td>4.2</td>
<td>0.9</td>
<td>2.1</td>
</tr>
<tr>
<td>Rover – A Line</td>
<td>3.3</td>
<td>3.2</td>
<td>0.6</td>
<td>0.9</td>
</tr>
<tr>
<td>Rover – B Line</td>
<td>4.1</td>
<td>3.9</td>
<td>2.0</td>
<td>2.8</td>
</tr>
<tr>
<td>Rover – C Line</td>
<td>3.3</td>
<td>3.2</td>
<td>1.3</td>
<td>1.8</td>
</tr>
</tbody>
</table>

In spite of the variations in EMF exposure assessment, it can be concluded from these data that EMF exposures within the aluminium industry are most likely to fall well below the ACGIH TLV of 60 mT. This conclusion is based on the fact that field strength is directly proportional to current and the highest, 8 hour, time-weighted average exposure at the 316 kA smelter was 10 mT and no time-weighted averages exceeded 10 mT.

**ACKNOWLEDGEMENTS**

The author wishes to acknowledge the cooperation and help provided by Alcan Aluminium, Alumax Primary Aluminium Corporation, Kaiser Aluminium, Reynolds Metals and smelters in Norway and Australia.
REFERENCES

This paper discusses the issues related to the suggested production of health effects as a consequence of exposures to electromagnetic fields within the aluminium industry. The literature is reviewed, with particular reference to the effects of confounders, and recommendations for action by the industry are provided. The paper concludes that there is little evidence to suggest that exposure to Static EMF results in demonstrable health effects.
alternating power flow. Accordingly, the general public is mainly exposed to these Frequency Dependent (FD) EMF.

By contrast, static EMFs are generated when an electric current flows in one direction only through a conductor. The waves generated about such conductors thus are constant in amplitude and direction; accordingly these unmoving electromagnetic waves are referred to as “static”. It is such static wave forms which are of major significance in electrolysis-based industrial processes, e.g., aluminium electrolytic smelting.

THE WASHINGTON SÖDERBERG SMELTER COMPENSATION CLAIM

The claimant worked on a horizontal stud Söderberg line for 8 years followed by 10 more years of work in a crane cab; this cab was enclosed during his last 5 years of work. After retiring at age 46 in good health, six years later this male employee filed a claim alleging his lymphoid lymphoma had been caused by potroom EMF exposures. Claimant's belief in the rightness of his action was reinforced by discovery that 7 apparently similar cases had occurred during the previous 16 years at this smelter.

The claim was allowed by the first level claims examiner in mid-1994. The examiner was incorrectly persuaded that these 8 cases represented more cases of the same disease than would have been expected to have occurred by chance during - what has now become - 20 preceding years. The decision apparently sustained a contention that this group of eight all suffered a single disease. Contrarily, the record revealed that the 7 other cases at the smelter consisted of 4 lymphatic lymphoma of several different cell types and 3 other granulocytic leukaemia’s. Clearly, if 8 cases of the same disease occurred within a single plant, an inference that a common proximate causality was operating there is more credible than if several different diseases had occurred.

A rigorous defence and appeal led to reversal one year later of the 1994 lower level decision, despite an amendment added to the appeal claiming that Coal Tar Pitch Volatiles (CTPV) also produced claimant's disease. (This “denial” of an EMF effect was never reported in the popular media.)

The denial of plaintiff’s claim indicated that neither the excess disease incidence hypothesis nor the hemotologic or experimental literature supported a causal relationship between lymphoma and EMF and/or CTPV exposures. After this denial, a second appeal was filed by plaintiff, as of today, October 28, 1997, a decision in last appeal of August 1996 has not been returned. This long delay suggests the
difficulty of adjudicating science-laden actions. Analysis of these proceedings also reveals the common failure of the law, media and public to deal with significant relevant details inherent to scientific complexity. For example, one such detail – of which both public and media seem unaware - is the fact EMF exists in two different basic forms, i.e., Frequency Dependent and Static Fields (v.i.).

Although this case raises both scientific and legal issues, we shall address mainly the former. This discussion aims to clarify scientific understanding of Static EMF and its implications for employee health protection in smelters. This discussion will also indicate possible action options for aluminium industry consideration and possible implementation.

STATIC EMF HEALTH-EFFECT RESEARCH

HIGH INTENSITY ACUTE EXPOSURE HEALTH EFFECTS

It is well established that brief, short-term exposures to ultra-high (>4 T or 40,000 G) \(^{(9)}\) Static EMFs produce acute, almost immediate, annoying, mildly disabling biological effects. Fluxes between 1.5 and 4 T (15,000 G - 40,000 G) have been associated with similar acute, brief and transient symptoms \(^{(10)}\).

LONG-TERM, CHRONIC EMF EXPOSURES AND HUMAN HEALTH EFFECTS

Introduction

At the outset, it is apparent there is little information dealing with the question of possible health effects of static EMF exposures. Earlier concerns revolved about health questions in high-energy physics research installations; later, as those using NMR imaging devices have resulted in a few epidemiologic human health studies \(^{(11)}\) (v.i.). Other industrial populations working in long established electrochemistry-based undertakings have also provided little population based data (v.i.).

The world wide primary aluminium industry has exposed tens of thousands of workers to Static EMF environments for the past 110 years. Also, during the past two decades, multiple, epidemiologic retrospective cohort mortality studies of these workers have been made available to the scientific community. Although other health-related issues prompted these studies, long-term Static EMF exposures have been present in the course of all these investigations. Studying these populations might therefore assist in the resolution of Static EMF health effects.
questions. Once again, words of caution and an awareness of confounding work environments factors are absolute pre-requisites to any useful investigation.

Among these requirements are:

- Detailed, intimate knowledge of production technology. Recognition of important differences in health risks associated with Söderberg and prebake reduction cells is critical to the evaluation of epidemiologic health effect data. Both type electrolytic cells use anodes made up of mixtures of coal tar pitch and granular carbon powder; this mixture is baked at high temperature to form graphic anodes. The Söderberg process uses the resistive heating of the “pot” to bake this mixture. Thus, some of the Coal Tar Pitch Volatiles (CTPV) or polycyclic aromatic hydrocarbons components of the pitch are discharged into the working potroom environment \(^{(12)}\). Their ambient potroom presence has long \(^{(13,14)}\) been suspected of containing carcinogens which contributes a significant confounding variable (or possibly covariable?) to epidemiologic investigation. By contrast, electrolytic anodes in the prebake process are heated at sites well-removed from the aluminium potroom. Workers in this “pre-bake” aluminium reduction technology thus are virtually unexposed to these potentially carcinogenic CTPV vapours \(^{(7,8)}\).

- Work practices, exposures and job content. If the necessary facts are absent or not presented clearly, the readers’ understanding of worker/environment interactions inevitably is compromised; employee exposure classification biases inevitably supervene. Study populations not infrequently have worked where both types of reduction cells have coexisted simultaneously or over time. Unless clearly and unambiguously stated in research reports, job/exposure biases and competing variables inevitably supervene. These problems may arise because the existence of both types of reduction cells are minimally noted \(^{(15)}\), or the type of cell extant is barely mentioned \(^{(16)}\), or because of aggregation and common analysis of differing, heterogeneous exposure groups has occurred \(^{(17-20)}\).

- Determination of actual job experience of study subjects. Job and exposure classification bias may result from various causes, e.g., use of death certificates which simply reports the decedent was an employee of the “X Aluminium Company” \(^{(20,21)}\). Although the decedent may have been employed in an office, outside the plant at gate or guard post, as a sales representative, in anode fabrication \(^{(23)}\),
or even in a potroom, they nevertheless are aggregated and analysed as a unitary population assumed to have had common aluminium reduction environmental exposures. The potential for the introduction of erroneous exposure biases is self-evident.

We emphasise once more that thorough-going reading of many of the biomedical reports cited above will resolve some of the apparent ambiguities or biases discussed in those paragraphs. However, such clarification or resolution of ambiguities does require extensive, in-depth knowledge of the technology, exposures or work practices of the industry. Absent, these requisite knowledge details, imprecisely documented reports too easily lead general medical readers to erroneous attributions of worker risk or health harm. Ultimately these errors are embedded in the biomedical literature, most immutable in general reviews (24) and reference texts (25).

ANALYSIS OF INDUSTRIAL STATIC EMF HEALTH EFFECT RESEARCH

ALUMINIUM REDUCTION INDUSTRY

With the foregoing pitfalls in mind, it should be self-evident that only definitive, well documented and soundly designed epidemiological studies of prebake smelters can avoid major misconceptions caused by confounding (and collinear?) variables. Accordingly, we have focused mainly on the Rockette and Arena (26) analysis of prebake worker cohorts which most has clearly defined work exposure histories. Of the 14 smelters investigated, 7 of these had only utilised prebake cells throughout their life span. This singularity thus avoided almost all possibilities of job-selection bias found in other large (practically nation wide) aluminium industry studies. The other epidemiologic reports of prebake cohorts analysed by Mur et al (27) and Rønneberg and Andersen (28), though providing collateral support of the Rockette and Arena study, present some ambiguities in reporting or methodologies employed (v.i.).

In large part, our selection was premised on the basis Rockette and Arena provided the largest, most comprehensive, least ambiguous data regarding prebake workers exposed to possible risks of long-term, Static EMF exposures. Also, this choice reflects the reason why relatively few prebake mortality studies exist, i.e., the negative publication bias. Since Söderberg potroom studies quickly revealed whence research gold might be mined, the number of pre-bake related reports failed to grow.

The massive Rockette and Arena study (26) of the major elements of the U.S. industry was a historical retrospective cohort study
analysing the mortality experience among 21,829 workers who had worked five years or more at 14 aluminium smelters. Their study achieved 98.8% vital status ascertainment, and clearly defined and separately analysed each subject’s Söderberg, prebake or combined (1 smelter) exposures. Standardised mortality rates (SMR) for 60 diseases were calculated both on the basis of national and local county death rates. Although a number of SMR’s were greater than 100, none of these reached statistical levels of significance. The sporadically found but statistically insignificant elevated SMR’s outcome measures among some malignant and non-malignant conditions was expected to have occurred by chance, especially given this multiple comparison analysis. One question has been raised by Doll(29) concerned unusually low death rates occurring only in the early part of the cohort’s mortality experience; clearly, a follow-up study would probably clarify this matter. However, the weight of evidence here supports an inference that prebake work environments with significant Static EMF fluxes do not appear to be significantly associated with types of chronic health or mortality effects generally impugned to EMF exposures.

The Mur et al (30) retrospective cohort study included 6455 men employed one year or more in the French industry’s smelters. Four of these were uniquely composed of prebake reduction cells. Statistically insignificant excesses were noted for total and lung, bladder and leukaemia deaths. The total number of deaths from lung cancer was limited to short-duration employment and none of these occurred at prebake plants nor were associated with specific plant areas. The restricted follow-up and/or vital status ascertainment of the Mur et al study has been noted; unavoidably, French law governing death certificate access imposes severe constraints on extensive vital status ascertainments. Although mortality experience was separately analysed for prebake and Söderberg workers, it is not clear how subject job exposures were treated since a majority of the plants used both reduction techniques. Thus, while this report’s contribution in this analysis is limited, its general outcome provides some collateral support to the conclusions of Rockette and Arena.

The one other major epidemiologic study limited to prebake populations was reported by Rønneberg and Andersen (28). In contrast to all other aluminium smelter epidemiology, cancer morbidity analyses were calculated using the Norwegian National Cancer Registry. As noted by Doll (29) as well as these authors (28), use of this comparison population presented problems “…connected with the choice of appropriate reference populations”. And, as both also note, these reports are considered “…singular…” because they “…suggested associations between lung cancer risk and work in prebake plants”! Still another “singularity” is found in this Norwegian study: viz., excesses in lung
cancer rates were found only among workers engaged in these prebake potrooms for less than three years. By contrast, those working there for more than 4 years showed no excess lung cancer morbidity! Certainly, some generally unapparent problem exists in this study.

OTHER STATIC EMF EXPOSURES OF INDUSTRIAL WORKERS

In addition to aluminium reduction operations, other industries utilising electrochemical processes produce workplace exposures to static EMF. Such exposures occur among chlorine-caustic electrolytic cell operators where static EMF exposures (i.e., 40 to 300 G or 4 to 30 mT) are similar to those found in aluminium potrooms. It is noteworthy that there are no relevant confounding CTPV exposures in chlorine production facilities, particularly in Donora type electrolysis units. Unfortunately, despite a near absence of potentially confounding variables, the first population study of a chloralkali electrolytic cell room reported only simple, relatively short-term response parameters. That report was subsequently followed by a retrospective cancer mortality and morbidity study of a small population (157 exposed subjects) who had worked for 32 years in a Swedish chloralkali electrolysis cell room. Morbidity and mortality rates were determined on the basis of national and local county data and were compared with age-specific and calendar year specific rates at both five and ten year latency times. Vital status ascertainment remarkably was total. Mean static EMF fluxes exposures in these cells rooms were relatively low, i.e., 10 mT or 10 G. Although this was published as a letter to the editor, the carefully chosen elements of epidemiologic design, choice of comparison populations, and analytic adjustments lends more weight than ordinarily might be attributed to a non-peer reviewed publication.

Other occupations exposed to what are essentially static EMF often are also simultaneously exposed to other potentially noxious agents. Unless highly knowledgeable about the particular industry, investigators and reviewers may not fully appreciate or take into account biases introduced by confounding process variables, selection and stratification biases, etc. However, after appropriate adjustment(s), such population might well be worth further study. In this same category, one might consider populations engaged in electrolytic copper refining; unfortunately, no relevant epidemiologic studies have been reported to date.

Yet another large population of workers has been considered by some to be exposed to near-static or extremely low frequency EMF fluxes. This large group consists of electric arc welders whose exposure levels ranged from 100 µT to $10^4$ µT (1 to 100 G), at extremely-low
frequencies, i.e., >50 Hz. A large pooled epidemiologic mortality analysis of brain cancer and leukaemia frequencies indicated extremely weak evidence of excess health risk \(^{(32)}\). However, welders are clearly exposed to a wide variety of aggressively reactive chemical species presenting serious potential confounding variables. Still other working populations are found in “new” technology-based ventures presenting potential long-term, high flux static EMF exposure health risks, viz., high energy nuclear and fusion research. In addition, increasingly higher exposures are under consideration for use in nuclear magnetic resonance imaging (MRI) devices; such exposures will put medical personnel at increased Static EMF exposure risk. The available data have not demonstrated any apparent long-term health effects; they do require more rigorous improvement of follow-up and vital status ascertainment.

Finally, general population exposures to Static EMF will potentially be incurred as Maglev transportation modalities evolve. At present, epidemiologic design and treatment of these potentially available data on chronic human exposures require development.

**GENERAL ASSESSMENTS OF STATIC EMF HAZARD RISK**

Societal concerns regarding EMF during the last 10 to 15 years have prompted scientific analyses and assessments by governmental \(^{(33,34)}\) and international \(^{(35)}\) organisations. Review of such position statements dealing mainly with static EMF unanimously conclude that insufficient scientific evidence presently exists supporting belief that Static EMF exposure causes deleterious health effects. These reports also suggest that unduly strict protection standards presently can not be justified. All have suggested that a well-established exception applies to acute exposures and their annoying but non-debilitating effects occurring at flux levels two orders of magnitude higher than found in potrooms.

**SUMMARY AND CONCLUSIONS**

Strong inferences may be drawn that long-term exposure to static EMF does not lead to significant chronic disease, important biological effects or health impairments. This inference is drawn on the following basis:

- As a point of departure, there is no rational basis to assume that Static EMF exposures will (or will not) induce any of the potential or impugned health consequences associated with FD EMF exposure;
• There is a quantitative paucity of biomedical effect data relating to Static EMF exposures as compared to effects impugned to FD EMF exposures;

• Of such information as is available, long-term, chronic human exposures to static EMF fields encountered in prebake aluminium smelters constitutes the largest and most informative health effect information presently available;

• This information strongly suggests that such disorders impugned to Frequency Dependent EMF exposures do not occur consistently or reproducibly, particularly as has been studied in prebake potroom environments;

• Collateral evidence from other industrial static EMF exposed work-sites suggests a similar absence of long-term deleterious health outcomes. However, while such evidence requires augmentation, it also can not totally be discounted;

• Inter alia, presently diminishing scientific plausibility attached to concerns with community EMF (36) should be noted within the context of the Static EMF question.

Accordingly, especially taking into account prebake aluminium reduction studies, there is little consistent or coherent epidemiological evidence to support an association between Static EMF exposures particularly in the 40 G to 550 G (4 mT to 55 mT range) and deleterious long-term health effects.

For the foregoing reasons, and particularly as these draw significantly upon epidemiologic investigations of aluminium prebake smelters, we believe it reasonable to infer that little hazard is associated with EMF exposures therein. Obviously, further static EMF dose-response studies in prebake potroom workers might buttress or negate these inferences.

Furthermore, these are proposed with full cognisance of the problems inherent to epidemiological research attempting to prove absence of hazard. It is apparent that the breadth of presently available information could be enhanced. However, we suspect this is presently unlikely in view of diminishing scientific interest in further investment of efforts and resources in this area of investigation.

PRIORITISED ACTION RECOMMENDATION FOR THE PRIMARY ALUMINIUM INDUSTRY RE: EMF

Action Item #1. (Top Priority)
CONTINUE MONITORING AND SURVEILLANCE OF CASE LAW AND SCIENTIFIC LITERATURE RE: EMF HEALTH AND BIO-MEDICAL EFFECTS

Given the breadth and depth of the public concern with EMF, we can expect that new research reports, press coverage, and litigation will appear. Accordingly, at the very least, the industry should make an effort to follow relevant developments in law and science. From a practical point of view, such monitoring effort should be reviewed after five years to determine whether its continuation is warranted.

*Action Item #2. (Lower Priority)*

**USING DATA DERIVED FROM THE TRIPARTITE MORTALITY STUDY, LINK EACH WORKER DEATH TO THEIR JOB-SPECIFIC. RETROSPECTIVE ESTIMATE OF THE EMF DOSE EXPERIENCED BY EACH OF THOSE WORKERS.**

While we have largely focused upon static EMF exposures, we must recognise that potroom employees are also simultaneously exposed to time-varying and frequency dependent EMF. Although the magnitude of the cyclic (FD) fluxes are relatively low and thus of questionable health significance in the industry (except possibly in rectifier rooms), they nevertheless cannot be ignored. This combination of FD and Static EMF exposures peculiar to the aluminium reduction industry undoubtedly does exist elsewhere. Therefore, the possible health effects of this unique combination cannot be with great certainty extrapolated to the industry's health protection needs upon the basis of industrial health effect studies. This recommendation must certainly be contingent upon trends and directions taken by case law and science resulting from implementation of Action Item #1.

**REFERENCES**


8. BIOMONITORING OF ALUMINIUM IN PRODUCTION WORKERS

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Co-Authors: F. Diebold, and F. Baruthio

SUMMARY

The results of a study conducted using 335 workers from 7 aluminium industry plants are described. The 7 plants included bauxite mines and treatment plants, alumina production facilities and reduction plants. Plasma and urine levels of aluminium were measured for each worker – these being measures related to the level of aluminium intake by the worker. The amount of aluminium in plasma and urine varied considerably – depending on the industry sector and nature of employment. For plasma, the aluminium concentrations ranged from 6 ± 2 µg L\(^{-1}\) in bauxite mines up to 22 ± 7 µg L\(^{-1}\) in flake powder plant. For urine, the aluminium concentrations ranged from 13 ± 5 µg g\(^{-1}\) of creatinine in an alumina production plant to 87 ± 22 µg g\(^{-1}\) of creatinine in flake powder plant. In a second study 41 workers from these 7 plants participated in a week-long project. Pollutant concentrations were determined, daily, by personal air sampling and urine was collected during the week (7 or 8 samples per day). The individual urinary excretion kinetics of aluminium was found to be specific to the chemical nature of pollutants present in the workplace atmosphere. The impact of the results produced upon the design of appropriate biomonitoring protocols is discussed.

INTRODUCTION

Exposure to aluminium and aluminium compounds is common in metal industries and was long considered to be harmless. More recently concerns have been expressed regarding the possible toxic effects of aluminium. It follows that knowledge of aluminium intakes by workers is important, but to date, few studies have been carried out on the biomonitoring of workers occupationally exposed to this element.

The objective set at the onset of the present study was to define, by means of surveying a limited number of employees, the levels of aluminium in the urine and plasma of staff exposed to occupational aerosols containing aluminium. The study took place at seven
representative, industrial sites to give a comprehensive overview of the aluminium intakes for all major parts of the aluminium production industry from the mining of bauxite to smelting.

SUBJECTS AND METHODS

SUBJECTS

The central management team of the industrial group concerned had adopted a comprehensive protocol comprising two phases on seven industrial sites:

- an initial descriptive phase aimed at ascertaining the urinary and plasma concentrations encountered in the various occupational exposure situations,
- a second, more experimental phase intended to explore the kinetics of urinary elimination and the exposure-excretion relationship,

Contact was made with each establishment selected to participate in the study (senior management and occupational physician). The occupational health and safety committees were both informed and consulted.

Information was gathered from volunteers prior to the study getting underway. The toxicokinetics phase required the on-site presence of biologists and atmospheric sampling specialists on two occasions for periods of six or seven days. The invaluable assistance of the medical staff of the factories allowed this operation to run smoothly from start to finish.

Certain exposure situations were not unique to one site, and were encountered in several plants. To accomplish the initial phase, sites representative of a type of exposure were selected to accord with the following descriptions:

- Exposure to dust during bauxite deposit mining operations (underground mines);
- Exposure to dust when producing refined alumina (production of alumina (Al$_2$O$_3$) from bauxite);
- Exposure to dust when making fluoride compounds, production of aluminium fluoride (AlF$_3$) using alumina Al$_2$O$_3$;
- Exposure to the dust present during the production of aluminium by electrolysis:
  - Technology A : reduction plant with open potlines,
  - Technology B : reduction plant with enclosed potlines;
- Exposure to dust during smelting of the aluminium metal (smelting plant);
- Exposure to dust when producing aluminium powders (aluminium powder plant production of shot powder and flake powder).

In mixed aluminium / fluoride exposure situations, airborne and biological measurements relative to both types of exposure were carried out.

Dust containing aluminium was everywhere in the general environment. As result, the chief difficulty in carrying out this study in a working environment was to eliminate any possibility of contamination. On account of this difficulty, collection conditions were adapted to each situation, and analytical quality controls strengthened. Another difficulty, this time arising from the fact that the concentrations normally encountered in the biological environment, namely a few micrograms per litre, required powerful analytical techniques and decontamination procedures.

The protocols, particular to each site, took account of:

- the type of activity of the subjects (in the mine especially);
- the restrictions in obtaining uncontaminated samples.

These specific protocols were drawn up in detail in conjunction with the managers and the occupational physician concerned.

The initial phase consisted in establishing the levels of contamination of the employees at the different plants by measuring plasma and urinary aluminium - for 335 volunteers. The distribution of employees, by type of exposure, is given in Table 1. These groupings take account of the fact that the same type of exposure could occur in different plants. No airborne samples were taken during this phase, and the urine was collected at the end of shift.

The second phase of the study was undertaken in order to define the kinetics of urinary elimination. For each site, the assistance of several volunteers was utilised to determine, both the individual exposure to dust and the urinary excretion of aluminium over a period of a few days. The occupational physician at each plant contributed to the selection of volunteers free of renal pathology and who were not taking any aluminium-based medication. The volunteers (Table 2) were chosen to be representative of the exposure of each site. These subjects collected their own urine for a period of several days in accordance with a locally established protocol, which allowed several consecutive exposure / non-exposure periods to be monitored.
### Table 1
Distribution of staff volunteers (phase 1)

<table>
<thead>
<tr>
<th>Exposure group</th>
<th>Mine 1</th>
<th>Alumina Production 2</th>
<th>Al fluoride Production 3</th>
<th>Reduction Plant 4 A</th>
<th>Reduction Plant 4 B</th>
<th>Foundry 5</th>
<th>Al flake powder plant 6</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bauxite</td>
<td>18</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>28</td>
</tr>
<tr>
<td>Alumina + hydroxides</td>
<td>21</td>
<td>8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>29</td>
</tr>
<tr>
<td>Al fluoride</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>31</td>
<td></td>
<td>31</td>
</tr>
<tr>
<td>(Electrolysis) potroom dust</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>53</td>
<td>42</td>
<td></td>
<td>95</td>
</tr>
<tr>
<td>Foundry dust</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>15</td>
<td>37</td>
<td>31</td>
</tr>
<tr>
<td>Al powder</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>13</td>
</tr>
<tr>
<td>Other workers</td>
<td>10</td>
<td>2</td>
<td>22</td>
<td>9</td>
<td>8</td>
<td></td>
<td></td>
<td>51</td>
</tr>
</tbody>
</table>

### Table 2
Kinetics of urinary Al - Phase 2, Exposure and subjects (n = 41)

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>Factory</th>
<th>Number of subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bauxite</td>
<td>mine</td>
<td>5</td>
</tr>
<tr>
<td>Alumina</td>
<td>Al$_2$O$_3$ production</td>
<td>8</td>
</tr>
<tr>
<td>Al fluoride</td>
<td>AlF$_3$ production</td>
<td>2</td>
</tr>
<tr>
<td>Al potroom dust</td>
<td>Al production by electrolysis: A open potlines</td>
<td>5</td>
</tr>
<tr>
<td>Al potroom dust</td>
<td>Al production by electrolysis: B enclosed potlines</td>
<td>9</td>
</tr>
<tr>
<td>Foundry dust</td>
<td>Al foundry (Secondary smelting)</td>
<td>6</td>
</tr>
<tr>
<td>Al powder</td>
<td>Al flake powder production</td>
<td>6</td>
</tr>
</tbody>
</table>
The exposure of people during the period of work was assessed by means of sampling the particulate pollutants on a filtering device placed in the breathing zone. The activities of these 41 subjects were as follows:

- Bauxite mine: four miners, one day worker;
- Alumina production plant: one bauxite discharge worker, four production workers, three bagging workers;
- Aluminium fluoride: one production worker, one bagging worker;
- Aluminium reduction plant: plant A: with open potlines, one shift supervisor, one crane driver, three production workers; plant B: with enclosed potlines, nine multifunction production workers split into two teams;
- Aluminium foundry: four smelting workers, one slag treatment worker, one continuous rolling and casting shear operator;
- Aluminium powder: two Al shot powder bagging workers, four Al flake powder production and bagging workers.

**BIOLOGICAL SAMPLING AND ANALYSIS**

Blood and urine samples were collected in each factory, they were packed and frozen on site, and the analyses were carried out at the INRS Research Centre. “Vacutainer” vacuum sampling units were used to take the blood samples. All the material required was free of trace of aluminium. The materials required to collect urine was decontaminated before use. The procedure for collecting in the work premises (in most cases the infirmary) overcame the problem of contamination by using clean premises located outside the polluted zone, and by requesting the volunteers to remove their working clothes and to take a shower before collecting their urine, or at least to wash their hands thoroughly.

In the toxicokinetics phase of urinary excretion, the volunteers were requested to collect their urine according to an hourly schedule adapted to each situation. The first collection was taken on getting up before joining the shift, two more being taken at mid-shift and at the end of shift, with the other collections taken at home - these samples being returned the following day. The volunteers were requested not to change their normal eating and drinking habits, and depending on the individual, six to eight collections were obtained per day.

The analysis of aluminium in the biological samples was undertaken by atomic absorption spectrometry using a Zeeman effect Perkin Elmer 3030Z atomic absorption spectrophotometer, following a method of Oster (1), with calibration by standard addition. The quality of the analyses was controlled by means of a periodic external quality control conducted by the French interlaboratory quality assessment programme of the French Society of Clinical Biology (SFBC), and by a
daily accuracy check using commercially available products (Nycomed AS. Diagnostics. Oslo). Urinary aluminium concentrations were expressed with respect to mass of excreted creatinine. (Note: about 1 g of creatinine is excreted per day by normal adults.) The urinary fluoride analysis was carried out on site using a selective ion electrode (ORION 94-09) and the analytical method of Tüsli (2). External quality control was ensured by participating in an international programme of intercomparison (Laboratoire de Toxicologie de Québec).

AIR SAMPLES

Air samples were taken each day during the entire working period. For Al, airborne particulate sampling was performed on quartz fibre filters (Whatman QM-A) held in a three-piece, 37 mm-polystyrene cassette (Millipore). The filter holders were clipped to the collar of the work clothes in closed-face configuration allowing the selective sampling of inspirable particles. The sampling airflow rate of 1 L min$^{-1}$ was provided using Dupont® P-2500 pumps. Using the same cassette, both gaseous and particulate fluorides were sampled on a paper filter (Durieux) soaked with Na$_2$CO$_3$ and a membrane filter (DM 900 Metricel-Gelman), respectively. The air samples were analysed using methods described elsewhere (3).

For both aluminium and fluoride particulates, the water soluble fraction was obtained by dissolving the particles inside the holder with distilled water and mechanical stirring. Both the soluble and insoluble fractions of Al were analysed with a DCP-OES (Direct current plasma-optical emission spectrometry) apparatus (spectrametrics Spectraspan III B).

RESULTS AND DISCUSSION

FIRST PHASE

The results of the urinary concentration measurements are given in Figure 1. All the urinary excretion results were log-normally distributed.

Figure 1 presents the distribution of urinary aluminium concentrations in the form of Tukey boxes, grouped according to the type of homogeneous exposure, and there would appear to be a clear difference in urinary concentrations depending on the pollutants present. In this figure the central box covers the middle 50 percent of the data; the sides of the box the lower and upper quartiles, and the vertical line drawn through the box is the median. The wiskers extend out to the lower and upper values of the data (the range). The highest urinary
concentrations were found in the electrolysis reduction plants and in aluminium flake powder production plants.

A comparison of the same type of exposure in the seven sites studied is shown in Table 3. This shows the average concentrations of urinary aluminium differently. There would, therefore, appear to be a degree of homogeneity in the four foundry sectors studied, and a difference between the two reduction plants, the values being lower for the plant employing the more recent enclosed potline technology.

![Figure 1. Phase 1, Urinary Aluminium Concentrations by Exposure Groups (box plot - Tukey).](image)

It can be seen that the result for the foundry of plant 4A is higher than that of the other foundries, and this could be due to the fact that in this plant, the foundry and electrolysis workshops situated in the same building are close to one another. The distribution of the measured plasma concentrations also accord to a log-normal law. The distribution by exposure groups is presented in Figure 2. The aluminium concentrations in the plasma would appear to be lower than in the urine. These are detailed in Figure 2, which provides the results per exposure group, and which follows the same pattern of presentation as Figure 1. As for the urinary results, the highest concentrations were encountered in the electrolysis reduction plants and in aluminium powder production. The detailed results are given in Table 4, and take account of the exposure groups and the industrial sites.
Table 3

Arithmetic means of the urinary concentrations (Al) with respect to the sites and exposure groups, in µg g\(^{-1}\) creatinine.

<table>
<thead>
<tr>
<th>Exposure group</th>
<th>Mine 1</th>
<th>Alumina Production 2</th>
<th>Al fluoride Production 3</th>
<th>Reduction Plant 4 A</th>
<th>Reduction Plant 4 B</th>
<th>Foundry 5</th>
<th>Al flake powder plant 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plant</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bauxite</td>
<td>33.3 (23.1)</td>
<td>21.1 (11.9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alumina + hydroxides</td>
<td>15.8 (9.2)</td>
<td>27.8 (17.9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Al fluoride</td>
<td></td>
<td>13.4 (6.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Electrolysis)</td>
<td></td>
<td>31.4 (16.8)</td>
<td>20.2 (10.3)</td>
<td>19.2 (11.7)</td>
<td>22.1 (7.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>potroom dust</td>
<td></td>
<td>57.5 (27.4)</td>
<td>32.1 (10.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foundry dust</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Al powder</td>
<td></td>
<td>10.9 (6.1)</td>
<td>11.15 (3.0)</td>
<td>20.1 (10.3)</td>
<td>13.5 (6.5)</td>
<td></td>
<td>20.8 (6.2)</td>
</tr>
<tr>
<td>Other workers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SECOND PHASE

Assessment of exposure

Tables 5 and 6 list the individual measurements of exposure to aluminium and to fluorides for all the volunteers of the different sites: these are average concentrations, and maximum and minimum values per working day, expressed in mg m\(^{-3}\).
Table 4
Arithmetic means of the plasma concentrations with respect to the plants and the exposure groups.

<table>
<thead>
<tr>
<th>Exposure group</th>
<th>Mine 1 (3.3)</th>
<th>Alumina Production 2</th>
<th>Al fluoride Production 3</th>
<th>Reduction Plant 4 A</th>
<th>Reduction Plant 4 B</th>
<th>Foundry 5</th>
<th>Al flake powder plant 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bauxite</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alumina + hydroxides</td>
<td>6.9 (4.0)</td>
<td>12.8 (5.2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Al fluoride</td>
<td></td>
<td>12.3 (4.4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Electrolysis) potroom dust</td>
<td></td>
<td>21.9 (4.4)</td>
<td>14.9 (4.1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foundry dust</td>
<td></td>
<td>19.7 (7.3)</td>
<td>12.6 (3.5)</td>
<td>15.4 (18.6)</td>
<td>11.5 (4.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Al powder</td>
<td></td>
<td>5.4 (2.6)</td>
<td>10.5 (2.5)</td>
<td>15.0 (3.5)</td>
<td>13.1 (5.4)</td>
<td>9.0 (4.0)</td>
<td>21.6 (7.4)</td>
</tr>
<tr>
<td>Other workers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The airborne concentrations measured were, for aluminium - both soluble and insoluble parts - and for inorganic fluorides the soluble (gaseous or particulate) and the insoluble (particulate) parts. A great many different chemical forms in which aluminium was present were observed on all seven sites: in certain cases, one can speak of exposure to a mono-pollutant (Al₂O₃, AlF₃, aluminium metal) for numerous work stations, in other words exposure to a mixture of aluminium compounds.
Table 5
Individual exposure to aluminium and its compounds: average daily concentrations in mg m$^{-3}$.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Plant</th>
<th>Duration of Measurement, days</th>
<th>Activity</th>
<th>Mean Insoluble Al</th>
<th>Mean Soluble Al</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bauxite</td>
<td>1,2</td>
<td>30</td>
<td>Mining, unloading</td>
<td>1.45</td>
<td>≤0.005</td>
</tr>
<tr>
<td>Alumina</td>
<td>2,3</td>
<td>17</td>
<td>Production</td>
<td>0.98</td>
<td>0.001</td>
</tr>
<tr>
<td>Alumina</td>
<td>2,3</td>
<td>15</td>
<td>Bagging, Palletising</td>
<td>9.88</td>
<td>0.008</td>
</tr>
<tr>
<td>AlF$_3$</td>
<td>3</td>
<td>5</td>
<td>Production</td>
<td>0.33</td>
<td>0.03</td>
</tr>
<tr>
<td>AlF$_3$</td>
<td>3</td>
<td>5</td>
<td>Bagging</td>
<td>4.78</td>
<td>0.11</td>
</tr>
<tr>
<td>Potroom Compound</td>
<td>4A</td>
<td>20</td>
<td>Multiple</td>
<td>0.30</td>
<td>0.28</td>
</tr>
<tr>
<td>Potroom Compound</td>
<td>4B</td>
<td>27</td>
<td>Multiple</td>
<td>0.39</td>
<td>0.19</td>
</tr>
<tr>
<td>Smelting Compound</td>
<td>5</td>
<td>24</td>
<td>Foundary: All</td>
<td>0.15</td>
<td>≤0.005</td>
</tr>
<tr>
<td>Smelting Compound</td>
<td>5</td>
<td>6</td>
<td>Slag Treatment</td>
<td>4.34</td>
<td>0.10</td>
</tr>
<tr>
<td>Metal</td>
<td>5</td>
<td>6</td>
<td>Edge Cutting, Rolling</td>
<td>0.20</td>
<td>0.001</td>
</tr>
<tr>
<td>Metal</td>
<td>6</td>
<td>10</td>
<td>Shot Blasting, Casking</td>
<td>15.96</td>
<td>0.005</td>
</tr>
<tr>
<td>Metal</td>
<td>6</td>
<td>20</td>
<td>Powder Operations</td>
<td>0.88</td>
<td>0.003</td>
</tr>
</tbody>
</table>

An examination of Table 5 highlights the variability of exposure with respect to the activity at the work station; the only levels of exposure that can be qualified as high are those relative to packaging work of finished products, primarily bagging and crating the alumina and aluminium powder. Another important conclusion that can be drawn from the results presented in Table 5 concerns the strongly insoluble character of the aluminium compounds measured, with the exception of the compounds present in the air of the electrolysis rooms (plants A and B). At a total constant Al concentration it should be noted that there was a significant difference in the solubility of the aluminium compounds present in the air between these two sites. The ratio concentration soluble: insoluble aluminium was 0.93 for Site A and 0.48 for Site B.

In the absence of detailed analyses of both the nature and composition of the compounds present in the dust, an explanation for
this difference can be put forward by considering that the electrolysis units of the two plants use different technologies:

- Site B this was a recent enclosed series where the raw materials are added automatically;
- Site A, on the other hand, was an older unit that required the use of operators to feed the pot with raw materials;

In addition, the complex fluorine, sodium, and aluminium based substances produced in the pot were certainly more soluble than the initial products; these products were likely to be present in the air of plant A, whereas they were for the most part captured at site B.

![Exposure group](image)

**Figure 2. Phase 1, Plasma aluminium concentrations of exposure groups (box-plot Tukey).**

The differences in activities of the volunteers of the two plants (presence of a shift supervisor and a crane driver on site A) did not allow a more detailed comparison of the averages presented in Table 5.

Table 6 lists the results of the individual exposure measurements to fluoride, distinction being made between soluble gaseous and particulate fluorides. It was observed that the average gaseous fluoride concentration was approximately three times higher for the electrolysis unit at plant A than for the more modern units of plant B - this highlighting the significant improvement brought about by the introduction of enclosed tanks fitted with a pollutant extraction system.

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For the other site \(^{(3)}\), in the absence of soluble particulate fluoride, the results shown are those for insoluble particulate fluorides.

**Table 6**  
Individual exposure to fluoride compounds: average daily concentrations in mg m\(^{-3}\).

<table>
<thead>
<tr>
<th>Number of Measurements</th>
<th>Plant or Site</th>
<th>Fluoride Compounds</th>
<th>Activity</th>
<th>Soluble Gaseous Fluorides</th>
<th>Soluble Particulate Fluorides</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ave</td>
<td>Min</td>
<td>Max</td>
</tr>
<tr>
<td>27</td>
<td>4B</td>
<td>HF SiF4 AlF3 Na(_3)AlF(_6) NaAlF(_3) +</td>
<td>Electrolysis</td>
<td>0.26</td>
<td>0.09</td>
</tr>
<tr>
<td>20</td>
<td>4A</td>
<td>HF SiF4 AlF3 Na(_3)AlF(_6) NaAlF(_3) +</td>
<td>Electrolysis</td>
<td>0.72</td>
<td>0.27</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>AlF(_3)</td>
<td>Palletising</td>
<td>0.08</td>
<td>0.04</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>HF AlF(_3) CaF(_2)</td>
<td>Production F Products</td>
<td>0.26</td>
<td>0.07</td>
</tr>
</tbody>
</table>

**Biological results**

The magnitude of the variation in urinary concentrations, with respect to the exposure groups, are shown in Figure 3. This synthetic view was created, by grouping all the individual results of the subjects at the same site. To interpret this figure, it should be considered that the maximum concentration values taken into account correspond to the instantaneous peak values reached (maximum concentrations of the toxicokinetics curves of urinary elimination). A very clear hierarchy of personal
contamination by aluminium can be observed - comparable with that highlighted in the analysis of the results of the initial phase. The concentration gradient observed could be linked to the differences in solubility of the products in question, however water solubility and biological solubility should be differentiated. The latter was poorly defined, and the water solubility was only roughly assessed in the study. The measurement of the aluminium concentration stemming from these tests has only provided an indication of solubilisation capability.

In the present case, the solubility of oxide, hydroxide and fluoride type aluminium compounds was low. The dust sampled close to the electrolysis tanks was different in that it was 30 – 50% soluble in water, and this type of exposure corresponded clearly to higher aluminium excretion. However, the highest urinary concentrations were encountered in the case of exposure to aluminium powder whose aqueous solubility was very low (in the experimental conditions employed).

Figure 3. Phase 2, Urinary Aluminium Concentrations. All Results (n = 1,035) from 41 Volunteers in Seven Plants. The Results for the Unexposed Subject (Fig. 4) are provided for reference.

Also worthy of note in this graphic representation is the difference between the two electrolysis sites (A and B). After examining
the results of the air measurements, this difference would appear to correspond roughly to the divergence of exposure to soluble aluminium.

Table 7 presents, for each plant, the daily averages of the quantities of aluminium eliminated in the urine during the working days. Each result corresponds to the average of the quantities of urinary aluminium eliminated by one volunteer during the working days included in this study. This average quantity varies between 15 - 200 µg per 24 hour period. The highest values were found in the electrolysis reduction and aluminium powder production sectors. The efficiency of regularly wearing a disposable half-mask respirator (type 3M) was highlighted in one of the volunteers at plant 4B.

### Table 7

Average quantity of aluminium excreted per working day (µg).

<table>
<thead>
<tr>
<th>Compound</th>
<th>Plant</th>
<th>Activity</th>
<th>Al excretion µg / 24h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bauxite</td>
<td>1</td>
<td>Mining</td>
<td>17.7, 13.3, 30.1, 24.6, 15.0</td>
</tr>
<tr>
<td>Bauxite</td>
<td>2</td>
<td>Unloading</td>
<td>41.4</td>
</tr>
<tr>
<td>Alumina</td>
<td>2,3</td>
<td>Production</td>
<td>28.5, 27.4, 23.6, 14.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bagging</td>
<td>16.3, 17.1, 17.2</td>
</tr>
<tr>
<td>Al Fluoride</td>
<td>3</td>
<td>Production</td>
<td>18.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bagging</td>
<td>36.2</td>
</tr>
<tr>
<td>Potroom Compounds</td>
<td>4A</td>
<td>Shift Supervisor</td>
<td>80.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Crane Driver</td>
<td>32.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Potroom Workers</td>
<td>94.1, 133.7, 118.3</td>
</tr>
<tr>
<td>Potroom Compounds</td>
<td>4B</td>
<td>Multi. with Mask</td>
<td>36.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Multi. without Mask</td>
<td>34.5, 70.3, 60.0, 55.2, 58.6, 75.0, 85.8, 55.0</td>
</tr>
<tr>
<td>Smelting Compounds</td>
<td>5</td>
<td>Smelters</td>
<td>19.9, 27.6, 20.6, 22.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Treatment of Slag</td>
<td>25.9</td>
</tr>
<tr>
<td>Aluminium Metal</td>
<td>6</td>
<td>Edge Cutting Rolling Mill</td>
<td>21.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bagging Shot Powder</td>
<td>183.9, 58.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Flake Powder Production and Bagging</td>
<td>26.5, 219.0, 73.9, 161.7</td>
</tr>
</tbody>
</table>

The individual kinetics obtained on the various sites exhibit certain particularities that would appear to be specific to each site studied. The reference urinary elimination of a subject with no occupational exposure is given in Figure 4.
Figures 5 to 10 present the individual results of persons exposed to bauxite, alumina, aluminium fluoride, the dust of the potroom of plants 4A and 4B, and aluminium powders; the periods of work and the magnitude of the exposure measured have been indicated on each figure. In general, this information is presented in two parts corresponding to two 4-hour periods of air concentration measurement. The curves shown are the individual results chosen for each type of exposure. They are, to a great extent, representative of the kinetic results obtained for all the volunteers in the same conditions and exposed to the same pollutants, and monitored over the course of the study. The main differences noted were:

- The existence of consecutive elimination cycles of exposure periods of eight hours. Increases in urinary concentrations can be distinguished from the baseline to a greater or lesser extent depending on the sites. Exposure to aluminium powder gives a different kinetics from that of other exposures.
- The maximum concentrations reached, as well as the quantities excreted per 24 hours, are characteristic of the nature of the pollutants present on each site.
• Although difficult to quantify in the conditions of this study, the half-life time of aluminium elimination did not appear to vary with the nature of the compounds in question\(^3\).

![Graph showing urinary aluminium concentrations and airborne aluminium concentrations over time.](image)

**Figure 5. Urinary Aluminium Concentrations for Worker Exposed to Bauxite Dust in the Mine; each work period is shown with the airborne concentration of aluminium.**

The curve indicating exposure to aluminium powder (Fig. 10) shows the results of a powder production and crateing worker (the measured exposure was 0.2 - 2.3 mg m\(^{-3}\)). Here, the excretion cycles are different from those of the preceding figures, the minimum values remaining very high. In addition, there was an accumulative phenomenon over the course of the week. The other curves obtained in this plant are also difficult to interpret, but for the majority of the volunteers, the minimum weekly values were high (10, 50, 30, 70, 25 µg g\(^{-1}\) creatinine for the other subjects).

In the other situations where high urinary concentrations of aluminium were observed, the minimum values were also higher. Consequently, in reduction plant 4A, the minimum values recorded over one week were 25, 15, 40, 40, 30 µg g\(^{-1}\) creatinine. In plant 4B with the
more recent technology, the corresponding values were 10, 20, 25, 25, 20, 25, 20, 20, 10 µg g⁻¹ creatinine for the nine subjects monitored. Comparing the various curves obtained over the course of the study has highlighted the importance of new aspects of the kinetics of aluminium excretion. This is due to the fact that the modes of urinary excretion of an element such as aluminium or fluorine are linked to the nature of the element, but also to the physico-chemical nature of the corresponding compound. This specific excretion is expressed by the fact that the urinary concentration peak observed after a period of eight hours of exposure does not always occur after the same delay, and depends on the nature of the compound. Certain delays such as those observed for exposure to alumina produced an increased urinary concentration on starting work the next day. Here, a measurement at the start of the shift provided a result higher than that of the end of shift, and that should be taken into account in biological monitoring.

Figure 6. Urinary Aluminium Concentrations for Worker Exposed to Alumina Dust during the Production of Alumina; each work period is shown with the airborne aluminium concentrations.

It is not easy to state the value of this peak divergence with certainty with a view to characterising each type of exposure. An individual variability exists, and this could be due to differences between the activity and the time when the activity peaks occur over the
course of an eight-hour working day. These excretion characteristics are undoubtedly linked to the bioavailability of the compounds after penetrating the body. This bioavailability is linked to the physico-chemical characteristics of the substances present. It would, therefore, be important to determine the characteristics of the pollutants at the work station accurately when drawing up a prevention plan.

Figure 7. Urinary Aluminium Concentrations for Worker Exposed to Aluminium Fluoride (AlF$_3$) Dust during the Production of AlF$_3$; each period is shown with the airborne concentration of soluble aluminium.

The statistical relationships established in this study, and previously developed elsewhere (3), have demonstrated that a relationship exists between exposure and urinary elimination. This relationship, found only for soluble aluminium in the electrolysis plant, has yielded a mathematical model. According to this model, an elimination of 200 µg of aluminium per day corresponds to an exposure of 1.04 mg m$^{-3}$ of soluble metal, and a concentration of 200 µg g$^{-1}$ creatinine corresponds to an exposure of 1.36 mg m$^{-3}$.

In the other situations, it was not possible to find statistically significant relationships between urinary elimination and exposure, and the highly water-insoluble character of the majority of the compounds
encountered undoubtedly contributes to this. Studying the bioavailability of aluminium powder would provide a better understanding of the high biological concentrations indicated in the exposed workers.

Figure 8. Urinary Aluminium Concentrations for Workers Exposed to Aluminium and Fluoride in the Potroom of a Reduction Plant with Enclosed Potlines.

CONCLUSION

The results obtained from the first phase of this study have enabled exposure levels to be determined by means of biological assessment of the entire aluminium industry sector. In the second phase, aluminium excretion particularities were investigated and described for different exposure situations, and this information complements the studies already undertaken on the subject (4–18). It has been demonstrated that the excretion peak is delayed for certain compounds (AlF$_3$, Al$_2$O$_3$, bauxite). The kinetics obtained with aluminium powder were difficult to interpret.

The diverse situations encountered in this study demonstrate the necessity of taking into account the nature of the chemical substance in question when establishing biological monitoring methods based on analysing the urinary concentration of a chemical element that is an
indicator of occupational exposure. Understanding the real kinetics of elimination of an element is a determining factor for the occupational physician when choosing the moment of collection, knowledge of the elimination half life time normally employed being insufficient when an excretion delay exists.

Figure 9. Urinary Aluminium Concentrations for Workers Exposed to Aluminium and Fluoride in the Potroom of a Reduction Plant with Open Potlines.

The second point concerns setting biological limit values\(^{(19 – 21)}\) in accordance with the principle of a statistical relationship between exposure and excretion. Incorrect time scheduling of the collection or inadequate knowledge of multiple peaks during studies can lead to an incorrect assessment of the internal dose and an underestimation of the corresponding biological exposure index.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the contribution of Drs J.P. Goulon, F. Barbier, B. Buclez, M. Ducord, G. Lafitte-Rigaud and D. Sebban, of Aluminium Pechiney, to this study.
Figure 10. Urinary Aluminium Concentrations for Worker Exposed to Aluminium Flake Powder during Production and Bagging.

REFERENCES

SUMMARY

The ability of a biomarker to provide an assessment of the integrated individual dose following uptake through multiple routes is especially valuable for mixtures of PAH (polycyclic aromatic hydrocarbons). This is due to the methodological and practical difficulties of collecting and analysing samples from the various environmental compartments like air, water and soil and various media like diet, cigarette smoke and workroom air. Since 1980, a large variety of novel approaches and techniques have been suggested and tested, e.g. urinary thioethers, mutagenicity in urine, levels of PAH or metabolites in blood and urine, and methods for determination of adducts in DNA and proteins. A large research effort has been made to use the extent of binding of PAH to DNA as a biomarker of exposure. However, the levels of aromatic DNA-adducts may be subject to appreciable analytical and biological variation. The present technical complexity of the method makes it more convenient for research applications than for routine application in occupational health practice.

At the moment one approach is often reported: urinary 1-hydroxypyrene monitoring. Pyrene is a dominant compound in the PAH-mixture and is mainly metabolised to the intermediary 1-hydroxypyrene to form 1-hydroxypyrene-glucuronide, which is excreted in urine. Since the introduction of the determination of 1-hydroxypyrene in urine as a biomarker for human exposure assessment of PAH, in 1985, over 100 articles describing applications have confirmed the potential of this novel approach. The conclusion of the first international workshop on 1-hydroxypyrene in 1993 was that urinary 1-hydroxypyrene is a sound biological exposure indicator of PAH.

Studies with a comparison of several biomarkers confirmed that 1-hydroxypyrene in urine is a valid and sensitive indicator of exposure. Periodic monitoring of 1-hydroxypyrene appears to be a powerful method in controlling occupational PAH-exposure in the primary aluminum industry. The reference level and a biological exposure limit of 1-hydroxypyrene in urine are discussed.
INTRODUCTION

PACs (polycyclic aromatic compounds) are not present in the environment as single entities, but as mixtures of many PACs, in different concentrations. PAC-mixtures are mixtures of substituted and unsubstituted homocyclic and heterocyclic polynuclear aromatic hydrocarbons from the elements carbon and hydrogen, either modified with oxygen, nitrogen or sulphur-atoms in the aromatic ring, or substituted with methyl, amino or nitro-groups. PAC-mixtures consist of a broad range of compounds, present in smoke from charred food, exhaust gases from engines or emitted from several industrial processes. The relative contribution of each PAC (PAC-profile) may vary from source to source. Polynuclear aromatic hydrocarbons (PAH) are derived from the elements carbon and hydrogen and are a sub-family of the PAC. Workers from industrial settings with high airborne PAH-levels like gas works, coke works, primary aluminium industry show excess rates of cancers. Aluminium production, coke production, coal gasification and coal tar pitches/coal tar fumes are carcinogenic to humans according to IARC-classification (1). The PAH seems to be predominant in these mixtures.

Airborne PAHs in the working atmosphere are present both as gaseous compounds and as particulate matter. PAH with larger molecular weights (MW > approximately 228) are partly or fully bound to the airborne particulate matter. Comparative measurements of PAH of airborne particulate matter in certain work-sites have shown that the distribution of different PAH (the PAH-profile) is relatively constant in time, but the PAH-profiles of different work-sites may differ significantly (2,3).

The risks arising from the inhalation of PAH-mixtures have been recognised for many years, but only recently, have exploratory studies shown that uptake, due to dermal exposure, is very significant. The dermal absorption of pyrene among coke-oven workers and among creosote impregnating workers is 50-90% of the total daily pyrene-uptake (4,5). The large contribution of dermal exposure to the total uptake of PAH among workers was confirmed in studies among workers in coal liquefaction and in the timber impregnating industry (6,7).

Extensive knowledge is available on the metabolism of one of the carcinogenic PAH, benzo(a)pyrene (B[a]P). The intermediary epoxide-B[a]P and dihydrodiol-epoxide-B[a]P can covalently bind to nucleophilic sites in DNA to form benzo(a)pyrene-DNA-adducts. These type of metabolites are thought to be carcinogenic intermediate metabolites of B[a]P and, in general, of the PAH.

In rats, after inhalation of B[a]P, a small proportion of the total excreted metabolites of B[a]P is found in the urine (approximately 5-
15%). After dermal application of $^{14}$Cpyrene in rats, approximately half of the total was found in urine and half of the total was found in the faeces over 6 days, suggesting equal excretion in urine and faeces (8). In man, 1-hydroxypyrene is excreted in urine as a conjugated metabolite following exposure to pyrene (9).

A biomarker of exposure measures either the internal dose in body fluids or measures the dose at the target site in an exposed individual. Since PAH is a group of compounds, two approaches in developing a biomarker can be followed. The biomarker can be either a:

- marker of the whole group of PAH: a PAH-mixture marker;
- marker, specific for a single agent: a single PAH-marker.

Since 1980, a large variety of approaches and techniques have been tested. For example, PAH-levels in blood and urine, reduction of PAH-metabolites in urine, urinary thioethers, mutagenicity in urine and DNA-PAH adducts in white blood cells with a large range of different methods such as bacterial methods, UV- and fluorescence spectrometry, immunochemical methods, gas chromatographic-mass spectrometric and liquid chromatographic methods.

The presently available biomarkers are briefly reviewed from the point of view of exposure assessment in occupational and environmental health as a routine method.

**BIOMARKERS OF TOTAL PAH-MIXTURES**

When absorption of PAH leads to a reaction in the body that is similar for all PAH, this reaction can be used to develop a biomarker. A small proportion of the dose of PAH may react with nucleophilic sites in DNA, resulting in PAH-DNA-adducts. PAH may also react with glutathione and undergo further metabolism, finally resulting in the excretion of sulphur-containing compounds, known as thioethers. Another part of the metabolites may be excreted as mutagenic metabolites, which can be detected in the 'Salmonella/microsome' mutagenicity assay. Mutagenicity in urine is also a biomarker of exposure to a mixture of PAH.

**Aromatic DNA-adducts**

A large research effort has been made to use the extent of binding of PAH to DNA as a biomarker of exposure. DNA of white blood cells (WBC) is usually taken as surrogate target DNA. Agent-specific immuno-assays and non-agent specific $^{32}$P-post-labelling assays have been suggested (10). The $^{32}$P-postlabelling assay detects the total of
aromatic DNA-adducts and is more or less an indicator of exposure to the total PAH-mixture. The results of DNA-adduct studies in workers are not very clear; previous studies have produced conflicting results on adducts in WBC of smokers (11). Also results of the determination of aromatic DNA-adducts may be subject to appreciable variation, as was demonstrated in a recent trial (12). In some studies, an enhanced DNA-adduct level in highly exposed workers is not found (13,14), other studies, however, report on a positive relationship (15,16).

PAH-DNA-adducts in lung-tissue of lung cancer patients appeared not to be correlated with adducts in lymphocytes; in fact, an inverse relationship was found (17). Much research remains to be done to overcome the problems encountered in measuring and interpreting DNA-adducts. At the moment, the present technical complexity of the method makes it more convenient for research applications than for routine application in occupational health practice.

**Urinary thioethers**

The variation of the baseline-excretion of thioethers is high and tobacco smoking is a very strong interfering confounding factor. Occupational exposure to PAH in the range of 1 ng m\(^{-3}\) - 10 µg m\(^{-3}\) of PAH in workroom air does not lead to an increased level of thioethers (18-20). Therefore, monitoring of urinary thioethers, as a biomarker of exposure to mixtures of PAH, lacks sensitivity. The method is neither suitable for routine monitoring of workers at the presently found concentrations in the occupational environment, nor for the even lower environmental exposure level.

**Urinary mutagenicity**

Several studies showed that the urinary mutagenicity is hardly increased at the occupational exposure level of 1 ng m\(^{-3}\) - 10 µg m\(^{-3}\) PAH. Analysis of urinary mutagenicity as a biological monitoring method of exposure to PAH lacks sensitivity. Moreover, smoking is a very strong interfering/confounding factor (18,21,22) and results have a large variability. The method is neither suitable for routine application of monitoring of PAH in the occupational environment, nor in the environmental setting.

**Metabolites in urine of the PAH-mixture**

The determination of various PAH in urine has been suggested as a biomarker, either after ‘reversed metabolism’ to parent PAH (23) or by determining various hydroxylated-PAH (24). Analytical shortcomings
have been shown in the total PAH-assay, especially when a 'reversed metabolism' step is introduced \(^{(25,26)}\). The 'reversed metabolism' methodology has large analytical drawbacks and can not reproducibly be used for monitoring exposure to PAH.

The determination of urinary hydroxylated PAH in urine may be executed either as separated steps for each metabolite or in one run for all urinary hydroxylated-PAH. The determination of all hydroxylated metabolites in one run seems to be an informative method, but the experience is limited yet \(^{(24,27)}\).

**BIOMARKERS OF SINGLE PAH**

Benzo(a)pyrene, pyrene and phenanthrene have been selected as single indicator-PAH of the mixture of PAH. Benzo(a)pyrene is an example of a carcinogenic PAH and pyrene and phenanthrene are examples of dominant PAH in the PAH-mixtures.

*Blood protein-adducts of benzo(a)pyrene in subjects.*

Adducts of benzo(a)pyrene to blood proteins, including albumin and haemoglobin, have been reported as possible biomarkers of exposure. There is still little experience in humans and the first results show limited usefulness of benzo(a)pyrene-albumin adducts \(^{(28)}\) and benzo(a)pyrene-haemoglobin adducts \(^{(19,22)}\). The absence of association, as yet, of benzo(a)pyrene-haemoglobin adducts and early biological effects such as cytogenetic effects \(^{(29)}\) does not support the suitability of this approach.

*DNA-adducts of benzo(a)pyrene in subjects.*

Immuno-assays using monoclonal antibodies are applied to detect specific DNA-adducts. In occupationally exposed subjects DNA in white blood cells (WBC) have often been used as surrogate target DNA. Enzyme immunoassays as ELISA and USERIA \(^{(30)}\) with an antibody raised against benzo(a)pyrene-DNA have been applied. An extensive overview on PAH-adducts to macromolecules in the biological monitoring of PAH summarises the state-of-the-art and the present limitation of monitoring adducts \(^{(31)}\). Differences in purity of the benzo(a)pyrene-DNA-antibody causes a bias. The compound-selectivity of the antibody is of crucial importance. A clear relationship of PAH-exposure and B[a]P-DNA-adduct level is absent in many cases.
3-hydroxy-benzo(a)pyrene in urine of subjects.

Metabolites of benzo(a)pyrene are preferentially excreted via the bile. Traces of 3-hydroxy-benzo(a)pyrene in urine of coke-oven workers exposed to PAH have been detected with a sophisticated laser fluorescence technique at an ultra low level (0.5 - 20 ng L\(^{-1}\)). Simultaneous determination of 1-hydroxypyrene revealed 200-2000 fold higher concentrations of 1-hydroxypyrene \(^{(32)}\). As yet, the method is not available for routine application.

1-Hydroxypyrene in urine of subjects.

The metabolites originating from pyrene are more easily detected in the urine samples of workers. A metabolite of pyrene, 1-hydroxypyrene, is detectable with HPLC-separation and fluorescence detection. The level of pyrene in PAH-mixtures is significant. In 1985, 1-hydroxypyrene in urine was suggested as a biomarker of human exposure to PAH \(^{(33)}\). Pyrene is mainly metabolised to the intermediary 1-hydroxypyrene to form 1-hydroxypyrene-glucuronide, which is then excreted \(^{(9)}\). Since its introduction in 1985, many publications from different research groups from Europe, Japan, China, Canada and USA have confirmed the potential of the methodology \(^{(13,16,20,29,35-46)}\).

Community residents environmentally exposed to PAH, have also been tested for PAH-exposure using the 1-hydroxypyrene methodology. Several papers report on either the assessment of PAH-intake in urban areas \(^{(35,47,48)}\) or on dietary intake of PAH \(^{(37)}\).

Hydroxyphenanthrenes in the urine of subjects.

The measurement of various hydroxylated phenanthrenes has also been reported as a biomarker of exposure \(^{(24,27)}\) using a GC-MS method. However, the experience is still limited to a single research group.

COMPARISON OF BIOMARKERS OF PAH

Table 1 summarises the characteristics of the presently available biomarkers, some are merely tended for research applications and some are sufficiently informative to be used in routine application for the assessment of dose in occupational health practice or environmental health issues. Studies in which aromatic PAH-DNA-adducts and 1-hydroxypyrene in urine in workers are compared, confirm that 1-hydroxypyrene is a reliable indicator of exposure. Also, that monitoring of aromatic PAH-DNA-adducts in WBC has some value, but analytical and biological variation is substantial \(^{(14,17,19)}\).
Buchet and co-workers \cite{13} measured cytogenetic endpoints in lymphocytes, several tumour markers in serum and modified nucleosides in 150 workers exposed to PAH in coke-ovens and graphite electrode plants, and in 137 controls. It appeared that 1-hydroxypyrene was highly increased before biological effects were detected. Several studies, comparing the suitability of several biomarkers, underline the sensitivity of urinary 1-hydroxypyrene. Knowing the low cost requirement for large-scale application of the test, urinary 1-hydroxypyrene is the preferred biomarker for routine exposure assessment of workers and for PAH-exposure in the community environment.

**PREFERRED BIOMARKER:**

**1-HYDROXYPYRENE IN URINE**

**Analytical Performance of the HPLC-method.**

The original and most comprehensive description of the method has been given by Jongeneelen et al. \cite{9}. Recent adapted method descriptions are available \cite{49 - 52}. The recovery of the analyte from urine has been reported to be 80 - 100%. The within-day variation is typically $\lt 5\%$. The between-day coefficient of variation (CV) is approximately 10\%. The detection limit of urinary 1-hydroxypyrene is sufficiently low to quantify baseline levels (detection limit = 0.1 nmol L$^{-1}$, this is approximately 0.01 $\mu$mol mol$^{-1}$ creatinine). Fluorescence excitation and emission scanning of the HPLC-eluate of urine samples allows the identification of 1-hydroxypyrene. Parallel GC-MS analyses confirmed the absence of bias in the analytical method \cite{53}. An inter-method evaluation with HPLC, GC-FID and GC-MS showed that the HPLC-method is rapid and simple, with no quenching or interference \cite{53}. Angerer & Schaller \cite{54} performed an inter-laboratory test and the quality of the method was confirmed. Presently, urinalysis of 1-hydroxypyrene is a part of the current German quality assurance programme \cite{55}.

**Normal value among non-exposed referents**

Non-occupational uptake of PAH is reflected in urinary excretion of 1-hydroxypyrene: among community residents a trace amount of background excretion of 1-hydroxypyrene is found. Tobacco smoking affects the concentration of 1-hydroxypyrene in urine. It seems that background-values vary a little from country to country, probably due to variations in the environmental PAH background and/or dietary intake of PAH \cite{45}. The upper limit for normal values in residents from the Netherlands, defined as the 95-percentile in controls, is reported to be
0.7 in non-smokers and 1.3 µmol mol⁻¹ creatinine in smokers \(^{(56)}\) (1 µmol mol⁻¹ creatinine = 1.9 µg g⁻¹ creatinine).

**Veracity of 1-hydroxypyrene as an indicator of exposure to PAH.**

1-Hydroxypyrene is a metabolite of pyrene and pyrene is always present in PAH-mixtures. In fractionated human liver as the metabolic system, the activation of PAH in crude coal tar to mutagenic metabolites was closely correlated to the simultaneously formation of 1-hydroxypyrene; thus the formation of 1-hydroxypyrene is a good indicator for the activation of pre-mutagens from crude coal tar \(^{(57)}\). Urine of psoriatic patients, undergoing a dermal treatment with coal tar solutions, showed a highly increased concentration of 1-hydroxypyrene, showed an increased response in the Salmonella/mutagenicity assay and 1-hydroxypyrene and mutagenic metabolites were correlated \(^{(21)}\). These *in vivo* and *in vitro* experiments show clearly the representativeness of the biomarker 1-hydroxypyrene. However, the relative proportion of pyrene in complex mixtures or in emissions from PAH-sources is not constant. Therefore, the value of 1-hydroxypyrene as biomarker of PAH-exposure lies primarily in finding trends and comparing exposure within exposed subjects from one industrial location, rather than comparing results of different industrial work-sites.

**Biological exposure limit**

An authorised biological exposure index of hydroxypyrene (BEI of the USA-ACGIH or BAT-value of the DFG in Germany) has not yet been proposed, however, it is a new entry in 1996 for the German DFG-commission (Angerer, personal communication). Individual authors have reported on the relation of airborne PAH and 1-hydroxypyrene in urine in several work environments. The regression of airborne PAH-concentrations and urinary 1-hydroxypyrene concentrations in workers was used to estimate the biological exposure limit. Jongeneelen \(^{(58)}\) proposed an end-of-working week biological exposure limit of 2.3 µmol mol⁻¹ for workers at a coke oven. VanRooij *et al.*, \(^{(5)}\) proposed a limit of 3.2 µmol mol⁻¹ (end-of working week) as equal to an airborne concentration of 2 µg m⁻³ benzo(a)pyrene in coke ovens. Tjoe Ny *et al.*, \(^{(43)}\) suggested 4.3 µmol mol⁻¹ as maximal weekly increase for workers in a Söderberg potroom (primary aluminium production). Note that the proposed tentative limits are urinary concentration as found in workers exposed to the occupational exposure limit of either coal tar pitch volatiles or benzo(a)pyrene.
### Table 1.
Characteristics of Biomarkers of Exposure to PAH.

<table>
<thead>
<tr>
<th>Specific Parent Agent</th>
<th>Biomarker</th>
<th>Analytical Method</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total PAH-mixture</td>
<td>Aromatic PAH-DNA adducts in white blood cells</td>
<td>³²P-post-labelling</td>
<td>Indicator of exposure, laborious method with unexplained variability</td>
</tr>
<tr>
<td>Total PAH-mixture</td>
<td>Urinary thioethers</td>
<td>spectrophotometric</td>
<td>Low sensitivity, smoking a strong confounder</td>
</tr>
<tr>
<td>Total PAH-mixture</td>
<td>Mutagenicity in urine</td>
<td>Salmonella microsome assay</td>
<td>Low sensitivity, smoking a strong confounder</td>
</tr>
<tr>
<td>Parent PAH</td>
<td>PAH in urine after reduction</td>
<td>GC-MS</td>
<td>Very low analytical yield, analytical drawbacks</td>
</tr>
<tr>
<td>Parent PAH</td>
<td>Hydroxylated PAH</td>
<td>GC-MS</td>
<td>Limited experience</td>
</tr>
<tr>
<td>B[a]P</td>
<td>Adduct DNA-B[a]P in white blood cells</td>
<td>ELISA, USERIA</td>
<td>Method with unexplained variability</td>
</tr>
<tr>
<td>B[a]P</td>
<td>Adduct albumin-B[a]P</td>
<td>ELISA</td>
<td>Limited experience</td>
</tr>
<tr>
<td>B[a]P</td>
<td>3-Hydroxy-B[a]P</td>
<td>Laser-induced fluorescence</td>
<td>Limited experience</td>
</tr>
<tr>
<td>Phenanthrene</td>
<td>Hydroxyphenanthrenes in urine</td>
<td>GC-MS</td>
<td>Limited experience</td>
</tr>
<tr>
<td>Pyrene</td>
<td>1-Hydroxypyrene in urine</td>
<td>HPLC-fluorescence</td>
<td>Cost effective indicator of exposure, high sensitivity, sound method</td>
</tr>
</tbody>
</table>

Buchet et al., (29) measured cytogenetic endpoints in lymphocytes, several tumour markers in serum and modified nucleosides in 150 workers exposed to PAH in coke ovens and graphite electrode plants, and in 137 controls. The biomarkers of effects were related to the concentration of 1-hydroxypyrene in post-shift urine. It
was found that below 2.7 μg g⁻¹ (1.4 μmol mol⁻¹) no increased level of any of the biological effect markers was observed.

Table 2
Similar Exposure Groups of an Aluminium Smelter with Non-Compliance to Either the Reference or Tentative Limit Value of 1-Hydroxypyrene

<table>
<thead>
<tr>
<th>Similar exposure group</th>
<th>1-Hydroxypyrene in urine of end of week samples (range in μmol mol⁻¹)</th>
<th>% of group exceeding reference value of 1.3 μmol mol⁻¹</th>
<th>% of group exceeding the tentative limit value of 3.0 μmol mol⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pot relining</td>
<td>1.5 - 7.6</td>
<td>100</td>
<td>67</td>
</tr>
<tr>
<td>Pot rooms</td>
<td>0.1 - 5.7</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>Paste plant</td>
<td>1.3 - 5.7</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Bake oven</td>
<td>0.2 - 1.7</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Technical service cathode plant</td>
<td>0.2 - 3.3</td>
<td>14</td>
<td>14</td>
</tr>
</tbody>
</table>

The composition of the PAH-mixture in different work environments is not fixed, but varies. When a single compound is used as either an indicator or marker, one has to realise that the relative proportion of an individual PAH in the PAH-mixture can vary from time to time and place to place. Since the relative proportion of pyrene in the PAH-mixture of different work environments may vary, an industry-wide biological exposure limit of 1-hydroxypyrene in urine cannot be set. One must realize that the proposed biological exposure limits are yet solely valid for the referred work environment and that the biological exposure limit of 1-hydroxypyrene may be different for different industries.
Routine biological monitoring in aluminium smelters.

Routine sampling of PAH is necessary in high-exposure workplaces like coke ovens and primary aluminum industry. In the Netherlands there is experience with routine biological monitoring of workers of a prebake aluminum plant using urinary 1-hydroxypyrene. Results of periodic monitoring of 1-hydroxypyrene in urine are tested for compliance to the reference value and a tentative limit value.

The upper-limit of the reference-value of 1-hydroxypyrene in urine is known: non-smokers: 0.7 and smokers: 1.3 µmol mol\(^{-1}\). A tentative (in-company) biological limit-value was temporarily set, in the absence of a authorized value, at 3.0 µmol mol\(^{-1}\), mainly based on the data of the above section on biological limit value.

The recent result of the periodic monitoring program was as follows. The ‘blue-collar’ workers of the aluminum smelter were grouped as 20 ‘similar exposure’ groups. All 20 groups were sampled. Fifteen of the ‘similar exposure’ groups demonstrated compliance to the reference value and tentative biological limit value. Five groups were heavily exposed and did not comply. Table 2 shows the data of the groups, which did not comply. A surprise was that some mechanics of the technical service were highly exposed to PAH, see last line of the table. It is clear that the pot-relining department and paste plant are the sections with the highest exposure levels. Control measures are most urgently needed in these departments.

Table 3 lists tentative categories for medical action and a hierarchy of workplace controls for the means of similar exposure groups of workers from aluminum smelters as dependent from 1-hydroxypyrene in end-of-working week urine samples. It is used as a guideline for follow-up actions.

CONCLUSION

1-Hydroxypyrene in urine is the preferred biomarker of exposure assessment of PAH in the work and community environment. In less than 10 years this biological marker of exposure has become accepted, worldwide, as a reliable biological monitoring method for PAH. The biomarker 1-hydroxypyrene can be used for:

- exposure assessment in a specific situation;
- periodically controlling the base-line of the exposure-level;
- testing the efficiency of control measures.
The methodology cannot directly be applied for risk assessment covering a wide range of situations with different PAH-profiles, due to differences of the PAH-profile in the various sources of PAH.

### Table 3
Guide Line for Medical Action and Hierarchy of Work Place Controls for Means of Similar Exposure Groups of Workers from Aluminum Smelters as Dependent from 1-Hydroxypyrene in End-of-Working Week Urine Samples.

<table>
<thead>
<tr>
<th>1-Hydroxypyrene in urine (µmol mol⁻¹)</th>
<th>Category of alert</th>
<th>Medical action</th>
<th>Work place controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.75</td>
<td>Green</td>
<td>Minimum medical surveillance</td>
<td>Administrative controls</td>
</tr>
<tr>
<td>0.75 – 1.3</td>
<td>Orange 1</td>
<td>Enhanced biological monitoring</td>
<td>Engineering controls</td>
</tr>
<tr>
<td>1.3 – 3.0</td>
<td>Orange 2</td>
<td>Enhanced biological monitoring plus enhanced medical surveillance</td>
<td>Isolation / containment</td>
</tr>
<tr>
<td>&gt; 3.0</td>
<td>Red</td>
<td>Mandatory removal</td>
<td>Process modification</td>
</tr>
</tbody>
</table>

The value of 1-hydroxypyrene as a biomarker of PAH-exposure of subjects in the environmental and occupational setting lies primarily in detecting of uptake in PAH-exposed subjects compared to referents in order to determine the type of medical action and the level of intervening control measures at the work-site. Furthermore, periodic monitoring of 1-hydroxypyrene is valuable in tracing time-trends of the exposure level in longitudinal studies and thus in controlling exposure.
REFERENCES


10. INDUSTRY-SPONSORED STUDIES ON THE BIOKINETICS AND BIOAVAILABILITY OF ALUMINIUM IN MAN.

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Co-Authors: Don Newton, Bob Talbot, John McAughey, Philip Day and Keith Fifield

SUMMARY

In 1991 a series of industry-sponsored, human volunteer studies, employing the rare isotope $^{26}$Al were initiated. To date, 4 such studies have been undertaken. The first study compared the short-term biokinetics and metabolism of aluminium and gallium (using $^{67}$Ga) and then the long-term pattern of aluminium retention in the body. The second studied inter-subject variability in the short-term metabolism of aluminium. The third investigated the bioavailability of ingested aluminium compounds. The final study, which has yet to be completed, studied the solubility and retention characteristics of inhaled transitional aluminium oxides. These studies have confirmed that most aluminium is excreted in urine and that the fraction excreted in faeces is small. However, about 5% of aluminium is retained - such that chronic intakes of aluminium will lead to the accumulation of low levels within the body. Marked inter-subject variability was noted. The bioavailability, by ingestion, studies suggest that the range of uptake fractions for aluminium compounds span from 0.5 - 1.0% (citrate) to 0.001% (hydroxide). Co-administration of citrate increased the uptake of aluminium administered as a hydroxide. The inhalation studies have demonstrated that inhaled, $1.2 \, \mu$m aerodynamic diameter transitional aluminium oxide particles are very insoluble.

INTRODUCTION

A programme of industry-sponsored, biological research on the biokinetics and bioavailability of aluminium in man was initiated at the Harwell Laboratory of the United Kingdom Atomic Energy Authority in 1991. This programme was jointly funded by the Aluminum
Association and by the International Primary Aluminium Institute at a time when little precise information was available concerning the behaviour of aluminium within the body (see reviews (1 - 6)). At this time, it was well understood that aluminium could be toxic in patients with renal diseases - which inhibit the excretion of the metal. Dementia, aluminium-induced bone disease and microcytic anaemia had all been described in renal patients which had accumulated large body-deposits of aluminium as a consequence of the use of contaminated water for kidney dialysis. In addition, aluminium had been implicated in the causation of a variety of other conditions (including Alzheimer’s disease, impaired cognitive function and Parkinsonism dementia) in subjects exhibiting normal renal function. However, at that time it was not possible to derive evidence of causation as no methods were available which could be used to estimate the aluminium burdens / intakes of the metal by groups which claimed aluminium injury. Furthermore, by this time, while the aluminium industry had started to accumulate data on the levels of aluminium excretion by its workers, it did not have the necessary information to derive aluminium biokinetic models for the interpretation of this data.

The review of Wilhelm et al. (1) summarises the state of knowledge concerning the toxicokinetics of aluminium at this time. In 1990 the following information was available:

- aluminium intakes by adults within the western world normally ranged from about 2 to 20 mg day\(^{-1}\), but that the use of pharmaceutical preparations containing aluminium could result in the daily ingestion of greater than 5 g of the metal;
- both plasma aluminium levels and the quantity of aluminium excreted in the urine increased following the ingestion of aluminium - providing conclusive evidence that ingested aluminium is, to some extent, bioavailable;
- aluminium welders showed elevated urinary excretion of aluminium indicating the transfer of inhaled metal to blood;
- aluminium bioavailability (by ingestion), as determined either by balance studies, by aluminium excretion studies or by comparisons of integrated plasma aluminium concentrations lay within the uncertain range of 0.001 to 24%;
- estimates of the level of protein binding of aluminium in plasma ranged from 0 - 98%;
- measured clearance half-times for plasma aluminium in man ranged from 14 hours to 85 days and that the half-time measured was a function of the observation period;
- most aluminium, perhaps even 100%, in blood is excreted via the kidneys in urine, but evidence also existed to suggest that an unknown fraction was excreted by the biliary route in faeces;
• when aluminium was retained by the body the major sites of deposition were the liver, spleen, skeleton, kidneys and lungs.

It can be seen that for most biokinetic parameters the range of reported values was large, indicating substantial uncertainty. Indeed, the International Commission on Radiological Protection (7), a body which reviews the metabolic data for all elements in man (in order to specify mathematical models which can be used for dose calculation purposes following intakes of radioactive isotopes) found few unambiguous data to support the formulation of a metabolic model for use in calculating radiation doses from internal deposits of $^{26}$Al - aluminium’s only significant, but rare, radioactive isotope. The Commission proposed, as a working postulate, a model in which 30% of aluminium entering the body was deposited in the skeleton on bone surfaces and 70% became uniformly deposited throughout the remaining body tissues; systemic aluminium was assumed to be lost in urine, with a half-time of 100 days. Clearly, this model, which was considered conservative, could be justified on the basis of the wide range of available data, but equally the data was available to suggest a model which assumed that all aluminium intakes were rapidly excreted in urine.

To a large extent the uncertainty, pre-1990, in the various parameters was a function of:

• the ubiquitous presence of environmental aluminium in the diet and inhaled air;
• the low tissue, tissue fluid and excreta aluminium levels relative to environmental levels;
• the demanding analytical procedures for low-level aluminium determinations;
• the absence of convenient stable or radioactive aluminium isotopes for human studies (although the chemically similar isotope, gallium-67 ($^{67}$Ga) had been used for some).

Post-1990, the situation changed. Firstly, $^{26}$Al ($T_{1/2} = 7.16 \times 10^5$ years) had become available for studies, albeit at a very high cost and, secondly, a new analytical technique - accelerator mass spectrometry (AMS) - had become available which could allow the unambiguous measurement of this isotope down to levels as low as $10^{-16}$ g. Moreover, the methods for the determination of stable aluminium ($^{27}$Al) had improved substantially. Finally, the potential power of techniques employing $^{26}$Al in combination with AMS had been demonstrated, both in rats, by Meirav et al. (8) and in man by Day et al. (9). It follows, that in 1991 the aluminium industry was now in a position to sponsor strategic human studies, using $^{26}$Al.
To date, four studies have been undertaken on behalf of the industry:

- a study to determine the long-term biokinetics of $^{26}\text{Al}$ and $^{67}\text{Ga}$ in a single male volunteer \(^{(10)}\);
- a study of inter-subject variability in the short-term biokinetics of $^{26}\text{Al}$ \(^{(11)}\);
- a study to determine the likely range of values for the bioavailability of ingested $^{26}\text{Al}$-labelled, aluminium compounds by man \(^{(12)}\);
- a study of the lung retention and dissolution of inhaled $^{26}\text{Al}$-labelled aluminium oxide (unpublished).

These studies, and others conducted by the same research team and its collaborators (including a study of the bioavailability of aluminium in drinking water) \(^{(13,14)}\), have made a significant contribution to our understanding of aluminium toxicokinetics. The results obtained are described below.

All studies were approved by the independent AEA Technology Ethics Committee and were started following the receipt of a certificate issued by the UK, Departments of Health, Administration of Radioactive Substances Advisory Committee (ARSAC).

**DESCRIPTION OF STUDIES UNDERTAKEN**

**STUDY 1: METABOLISM OF ALUMINIUM-26 AND GALLIUM-67 IN A VOLUNTEER FOLLOWING THEIR INJECTION AS CITRATES.**

*Objectives*

This study was undertaken in order to:

- establish the early urinary and faecal excretion patterns of aluminium from an adult male human volunteer injected with high purity, carrier-free, aluminium-26 as a citrate, and to compare these patterns with those of gallium-67 injected concurrently, in the same chemical form;
- determine the pattern of translocation of these radionuclides from the blood-stream to the body and to measure the retention of aluminium in the body by whole-body, $\gamma$-spectrometry; to determine the retention of gallium in the body for as long as is permitted by the short half-life of its mass 67 isotope.
**Methods**

The volunteer was a white, Caucasian male, height 1.83m, who at the time of injection was aged 41 years 2 months and weighed 77.3 kg. The volunteer was injected with sterile, non-pyrogenic citrate solutions containing either 574 Bq of $^{26}$Al or 222 kBq $^{67}$Ga. Blood samples were withdrawn at times up to 18 months after injection to measure the levels of circulating radionuclide. Gallium measurements were possible only for times up to 14 days after injection, due to the relatively short half-life of the radioisotope ($T_{1/2} = 3.26$ days).

The volunteer collected total daily urinary and faecal excreta for two weeks after the injection. The $^{26}$Al and $^{67}$Ga contents of the samples were measured to determine their patterns of excretion and also, in conjunction with body radioactivity measurements of these radionuclides (made to 6 years and 21 days respectively), to establish the patterns of whole-body retention. The levels of $^{67}$Ga present at early times after injection were sufficient to permit investigations of its distribution within the body, but no such studies were possible for aluminium.

The levels of radionuclide present in the samples were determined using either $\gamma$-spectrometry or AMS ($^{26}$Al only). For $\gamma$-spectrometry samples containing $^{26}$Al were placed between two 150 mm, diameter, NaI crystal detectors and counted by employing a coincidence technique to measure the 511 keV positron annihilation radiations emitted by this isotope. Gallium-67 was determined by measurements of its 93 keV, 185 keV and 300 keV $\gamma$-emissions. Samples which contained insufficient $^{26}$Al activity for $\gamma$-spectrometry were chemically treated, at Manchester University, to produce ion sources for AMS. AMS measurements were made at the Australian National University using its 14 MV accelerator.

**Results and Conclusions**

This study confirmed the utility of $^{26}$Al and $^{67}$Ga as tracers to study the biokinetics of these elements in man. It has been possible to study the retention of aluminium in the volunteer to the present day (Fig. 1). In contrast, because of the short half-life of $^{67}$Ga, it was only possible to follow gallium biokinetics for about 3 weeks. The results showed that:

- the metabolism of $^{67}$Ga differs markedly from that of $^{26}$Al in all aspects studied;
- more than half of the $^{26}$Al had left the blood after 15 minutes and the decline continued, leaving <1% in blood after 2 days; the losses
occurred both to renal excretion and through uptake by body tissues; in contrast about 85% of gallium remained in the body at 1 day post-injection (a significant fraction in the liver) and even at 21 days 50 - 60% remained (Fig. 2);

- using AMS it was possible to measure $^{26}$Al in blood, even at 1000 days post-injection when its levels were about 100,000 times lower than those immediately after injection.
- estimated excretion of $^{26}$Al up to 13 days post-injection was 83% (urine) and 1.8% (faeces).
- whole-body retention of $^{26}$Al of 15% at 13 days post-intake declined to about 4% at 1178 days, when the daily reduction corresponded to a biological half-time of 7 years.

STUDY 2. INTERSUBJECT VARIABILITY IN THE SHORT-TERM METABOLISM OF ALUMINIUM-26 FOLLOWING INTRAVENOUS INJECTION AS CITRATE.

Objectives

The objectives of this study were:

- to investigate inter-subject variations in the early urinary and faecal excretion patterns of systemic aluminium in six healthy male volunteers receiving $^{26}$Al, injected as citrate;
- to determine the importance of fluid intake, as indicated by the volume of urine excreted, on the level of urinary excretion of aluminium.

Methods

The six male volunteers selected were aged between 20 and 32 years, weighed between 65 and 90 kg and ranged in height from 1.68 - 1.85 m. All were free from cardiac, hepatic, renal, pulmonary, neurological, gastrointestinal, haematological and psychiatric disease - as determined by history, physical examination and haematological screens. Normal kidney function was confirmed by standard tests for plasma urea, plasma potassium and plasma creatinine. None of the subjects was receiving either prescribed medications or self-administered OTC. pharmaceutical preparations.
Figure 1. Single volunteer study. A comparison of the whole-body retention of $^{26}$Al and $^{67}$Ga in the single volunteer.

The volunteers were injected with a sterile, citrate solution containing c. 60 Bq of $^{26}$Al. Levels of the tracer were determined, by AMS, in blood samples collected at periods up to 5 days after injection. The interventions and procedures employed were, in all important respects, the same as those developed for the single volunteer study. Complete daily collections were made of urine and faeces excreted up to 5 days post-injection for investigation of tracer levels by $\gamma$-ray spectrometry to determine, *inter alia*, the pattern of whole-body retention. However, unlike for the first experiment no whole-body $\gamma$-spectrometry was undertaken to determine body-retention of the radionuclide. The volume of urine excreted was recorded aliquots were analysed by atomic emission spectrometry (ICP-AES) to determine the excretion levels of significant metals including sodium, potassium, calcium, magnesium and phosphorus.

*Results*

The results obtained by this study were in broad agreement with those found for the previous, single volunteer study:
• the total content of $^{26}\text{Al}$ in circulating blood fell rapidly, averaging only 2% of that injected after 24 hours post-injection, and only 0.4% after 5 days;
• most of the tracer was excreted within a few days, with an average of 59% appearing in urine within 24 hours and $72 \pm 3\%$ (SE. mean) within 5 days (Fig. 3);
• faecal losses typically amounted to only 1% (range 0.6 - 1.7%) of total excretory output (Fig. 4);

Figure 2. Single volunteer study. The concentration of $^{26}\text{Al}$ and $^{67}\text{Ga}$ in the blood at different times after injection. It can be seen that gallium is cleared more slowly than aluminium.

• there were marked inter-subject differences between the early excretion patterns of $^{26}\text{Al}$, with fractions lost in the first 24 hours varying between 45 and 75% of the amounts injected; the total amounts excreted in the urine, during 5 days, varied from 62% to 83%;
• as a consequence of urinary excretion patterns, inter-subject variations in the derived whole-body retention exceeded a factor of two at all times between 1 day and 5 days;
• no relationships were evident connecting the variations in excretion patterns either with volumes of urine voided or with the daily output of sodium, potassium, calcium, magnesium or phosphorus.
Figure 3. Multi-volunteer study. Cumulative urinary excretion of $^{26}\text{Al}$ during the first 5 days after injection. Separate curves are shown for each of the volunteers in the multi-volunteer study (subjects A to G) and for the single volunteer (P).

STUDY 3. THE BIOAVAILABILITY OF ALUMINIUM-$^{26}$ LABELLED ALUMINIUM CITRATE AND ALUMINIUM HYDROXIDE IN VOLUNTEERS

Objectives

The study was undertaken to determine the:

- fraction of ingested aluminium that may be taken up via the gut of adult male volunteers, following the ingestion of either aluminium citrate or aluminium hydroxide;
- the effects of simultaneous citrate ingestion on the gastro-intestinal absorption of aluminium from its hydroxide;
- the kinetics of aluminium clearance from the intestinal tract.

The compounds were chosen since experience with a wide range of other metals suggested that the soluble, aluminium citrate
complex would be amongst the most bioavailable of ingested aluminium compounds, while the hydroxide, as a relatively insoluble suspension, would be amongst the least bioavailable. (Moreover, aluminium hydroxide is commonly ingested by adults as an OTC / prescribed antacid.) In the same way, the simultaneous investigation was undertaken because much evidence existed to suggest that the bioavailability of many metals could be enhanced by the co-administration of a complexing agent - such as citrate.

![Graph](attachment:image.png)

**Figure 4.** Multi-volunteer study, plus subject P. Volunteers’ cumulative faecal excretion of $^{26}$Al during 5 days post-injection. The amount excreted at the end of each 24 hr period is shown.

**Methods**

Two subjects aged 33 / 29 years were employed for the study. They were healthy males free from physical and psychological illness as determined by history, physical examination and laboratory screens. As for the other studies, neither of the subjects had recently used prescribed medicines nor OTC pharmaceutical preparations.

100 mL test solutions / suspensions containing $^{26}$Al-labelled aluminium hydroxide (pH 7.0) and $^{26}$Al-labelled aluminium trisodium citrate complex (pH 6.5) were prepared for administration to the subjects. Each solution / suspension contained 100 mg of stable
aluminium carrier in addition to c.115 Bq (1.62 x 10^{-7} g) of the $^{26}$Al label. Both preparations were prepared from an AlCl$_3$.6H$_2$O (analytical grade) stock solution to ensure correct speciation of the label. The doses were administered to the volunteers via a paediatric feeding tube.

For each volunteer the experiment spanned seven weeks. On day zero (the day prior to the administration of the first preparation), samples were collected to establish base-line levels for $^{26}$Al measurements in blood and excreta. On day 1 the $^{26}$Al-labelled hydroxide was administered, on day 21 the hydroxide followed by 100 mL of stable citrate solution (1% trisodium citrate, pH 6.5) was administered, then on day 49 the $^{26}$Al-labelled citrate was given. Following each dosing blood samples were removed from the volunteers at 1 hour, 4 hours and 24 hours. In addition, volunteers collected their total daily output of urine and faeces for six days following each dosing procedure.

Faecal samples were analysed by $\gamma$-spectrometry between the faces of two co-axially located, calibrated 152mm diameter scintillation detectors, as described for study 1. The blood and urine samples were analysed by AMS after the addition of a $^{27}$Al yield tracer and the preparation of ion sources.

**Results**

The results showed differences between the kinetics of aluminium uptake in the two volunteers. Similarly, $^{26}$Al was retained for about 1 day longer within the gastro-intestinal tract, prior to excretion in faeces, of one volunteer (Fig. 5). It follows that the higher aluminium uptake noted for this volunteer was probably due to the longer period available for uptake - a suggestion supported by his more protracted period of aluminium excretion and higher blood concentrations at 24 hours post-intake.

As a consequence of inter-subject differences in the kinetics of $^{26}$Al transfer to blood (Fig. 6), it was not possible to derive, as others have attempted, gut transfer factors from the $^{26}$Al in blood data.

Using urinary excretion data (Fig. 7), it was found that the uptake of aluminium was greatest following its administration in the citrate form and was least following intake as the aluminium hydroxide suspension. The co-administration of citrate with the aluminium hydroxide suspension was found to enhance the uptake of the radiotracer in both volunteers. Using a urinary excretion factor based on the results of the above injection studies, the absorbed fraction for each of the doses was calculated, as follows:

- aluminium as aluminium citrate $\quad 5.2 \times 10^{-3}$;
- aluminium as aluminium hydroxide $1.0 \times 10^{-4}$;
- aluminium hydroxide with citrate $1.4 \times 10^{-3}$.

Figure 5. Ingestion study. Cumulative faecal excretion of $^{26}$Al for volunteers A and B for times up to 6 days post-administration of labelled aluminium hydroxide (1), labelled hydroxide in the presence of citrate (2) and labelled citrate (3). It can be seen that compared with A volunteer B consistently retained aluminium within his gut for 1 to 2 days longer.

STUDY 4. THE CLEARANCE KINETICS AND BIOAVAILABILITY OF INHALED $^{26}$AL-LABELLED ALUMINIUM OXIDE IN MAN.

Objectives

The objectives of the study were to:

- develop and validate a method for the production of a transitional aluminium oxide aerosol, the composition of which is relevant (and applicable) to (but not necessarily identical to) aerosols encountered by workers within the aluminium industry;
• determine the retention and absorption characteristics of inhaled $^{26}$Al-labelled transitional oxide deposited in the respiratory tract of male human volunteers;

![Diagram](image)

Figure 6. Ingestion study. Blood concentrations of $^{26}$Al for volunteers A and B following the ingestion of either labelled aluminium hydroxide (1), labelled aluminium hydroxide in the presence of citrate (2) and labelled aluminium citrate (3).

• determine the fraction of the inhaled aluminium that is transferred from lungs to blood and then excreted in the urine;
• estimate, by assay of faeces, the fraction of the inhaled aluminium that is mechanically removed from the lung via the upper respiratory tract, swallowed and excreted.

**Methods**

Aluminium oxide particle production was undertaken using a RETEC nebuliser, to produce monodisperse droplets of an aluminium nitrate solution containing $^{26}$Al. These droplets were dried, with subsequent calcination of the particles in an alumina-tube flow-through furnace operated at 1500°C in a vertical configuration. Particles produced were collected on to a PTFE filter for subsequent re-suspension.
Figure 7. Ingestion study. Cumulative urinary excretion of $^{26}$Al following the ingestion of labelled aluminium compounds. Data are presented for volunteers A and B following the administration of either labelled aluminium hydroxide (1), labelled aluminium hydroxide in the presence of co-administered sodium citrate (2) or labelled aluminium citrate (3).

Aerodynamic particle size was determined, on line, with an API Aerosizer instrument (Amherst Process Industries, Mass., US). The particles collected were then examined using a fully automated Siemens D500 diffractometer employing Cu Ka radiation ($\lambda=0.15406\text{nm}$) and a secondary monochromator. Analysis was achieved by comparison of the XRD data, collected from the sample, with standard data collated by the Joint Council for Powder Diffraction Standards (JCPDS) for different aluminium oxides.

As for the previous studies, the two subjects chosen for the study were selected from the list of prospective volunteers held by the AEA Technology plc ethics committee. The volunteers were free from cardiac, hepatic, renal, pulmonary, neurological, gastrointestinal, haematological and psychiatric disease as determined by history, physical examination and laboratory screens. In addition, neither
volunteer was receiving regular medications including prescribed drugs and OTC preparations.

For administration the $^{26}$Al-labelled alumina particles were re-suspended from an ethanol / water mixture, by nebulisation, into a 100 L chamber, from which the subjects subsequently inhaled the particles, via a computer-controlled valving system. The inhalation rig used consisted of a computer-controlled shuttle valve providing separate pathways for inhalation and exhalation, allowing either the collection of exhaled particulate matter, or rebreathing into the chamber. In this case, rebreathing was used until the final two minutes of exposure when an exhale capture sample was taken - to validate deposition efficiency versus predicted. Volunteers breathed according to a pre-programmed pattern of 6 x 1000 mL breaths per minute displayed on a computer monitor. The suspension half-time of particles in the box had previously been shown to be 45 minutes.

Immediately after exposure, estimates of $^{26}$Al in the whole-body were made inside a shielded whole-body monitor with an array of NaI(Tl) scintillation counters, each 152 mm dia. x 89 mm thick, positioned four above and two below the supine subject. In the standard configuration, the centres of the six detectors were located in the mid-sagittal plane with a longitudinal separation of $c. 300$ mm. Such an arrangement invites calibration errors where the radioactive deposit is essentially confined to a specific anatomical region, as would be the case following the inhalation of an insoluble aerosol; in this situation a more uniform coverage of the body is required. To achieve this an initial gamma-ray spectrum was recorded in the standard arrangement, followed by eight additional spectra for each of which all detectors were displaced longitudinally and/or laterally, relative to their normal locations, by $150$ mm in each direction; the count time in each of the nine dispositions was 5 min. Combining the spectra simulated the effect of a 5-min measurement with a 54-counter array, providing a response that was essentially independent of the distribution of the aerosol. A 1 kBq $^{26}$Al standardised point source, placed in several locations along the mid-coronal plane of a water-filled elliptical cylinder, was employed to calibrate the counting system.

The subjects commenced faecal collections two days before the exposures and continued for seven days afterwards, for assessment of the $^{26}$Al excretion by $\gamma$-ray coincidence spectrometry. Each sample was ashed at $500^\circ$C and counted between two shielded 150-mm-diameter NaI(Tl) scintillation counters. The response from 0.51 MeV coincident positron annihilation quanta was recorded and compared with that from an appropriate reference standard. Subsequently, each subject provided additional 24 hour faecal samples at 1 month, 2 months and 3 months post-inhalation. The ash from these samples was insufficiently
radioactive for assessment by γ-ray spectrometry. Instead, arrangements are being made for their future assessment by AMS.

Venous blood samples were taken for analysis at approximately logarithmically spaced intervals ranging from 1 hour to 82 days post-inhalation. In all, 11 blood samples were collected and analysed for $^{26}$Al by AMS.

Volunteers collected their total daily output of urine for six days, and then at spaced intervals up to 3 months following each dosing procedure - bulked 24-hour samples were collected. Each urine collection bottle had 10 mL of concentrated nitric acid added to act as a preservative. No lost or missed samples were reported. The samples were transferred to the Department of Chemistry, University of Manchester for the preparation of ion sources for AMS. Prepared ion sources were despatched to the Department of Nuclear Physics, Australian National University, Canberra, Australia, where they were analysed to determine the ratio of $^{26}$Al: $^{27}$Al in each source by AMS. The $^{26}$Al content of each urine sample was then determined.

**Results**

The particles inhaled by the subjects had an aerodynamic diameter (MMAD) of 1.2 $\mu$m as determined by an API Aerosizer time-of-flight instrument. Evidence of the presence of transitional oxides and the absence of $\alpha$-alumina was confirmed by X-ray diffraction. Overall yield for the process was approximately 40%. Solubility of the particles (determined by $^{67}$Ga tracer) was less than 0.2% per day.

Filters used for exhale capture for the final 2 minutes of the exposure period estimated deposition efficiency in the region of 65-70%, values consistent with estimated deposition for 1.0 $\mu$m aerodynamic diameter particles, under the chosen breathing pattern of 63%. On this basis, concentration samples taken from the breathing box during the inhalation allow estimates of deposition, which were 12 Bq for Subject A and 10 Bq for Subject B.

Given that the amount of $^{26}$Al deposited in the lungs of the volunteers was only a small fraction of the intended deposit (c. 250 Bq), whole body gamma spectrometry of the subjects had insufficient sensitivity to allow an accurate determination of the deposit size. Consequently, the random counting errors (1σ) determined for the measurements undertaken were very large - when expressed as a percentage of the estimated deposited activity. Nevertheless, multiple γ-measurements undertaken during the first 7 days post-exposure and these in association with the known quantity of aluminium excreted in the faeces proved sufficient to derive a best estimate of the $^{26}$Al deposited: 14.4 Bq (20.2 ng) and 3.8 Bq (5.3 ng) for subjects A and B respectively.
Blood samples were collected from each of the volunteers both prior to the aluminium oxide administration and at four times post-administration. A known quantity of stable, $^{27}$Al, tracer was added to these and then they were prepared for $^{26}$Al determination by AMS. The $^{27}$Al content of each sample was determined by GF-AAS prior to AMS and the level of $^{26}$Al was estimated from the measured ratio $^{27}$Al : $^{26}$Al. However, the results produced were judged to be unreliable - the levels detected approximating the detection limit of the AMS technique.

Analysis of the collected faecal samples by $\gamma$-spectrometry showed that levels excreted within the first day post-exposure and after seven days post-exposure were too low to be determined without the use of AMS. These samples will be measured at a later date, however, given the low levels of $^{26}$Al present in these, the AMS results will little change estimates of the total amount excreted by this route. $\gamma$-Analysis of the remaining samples showed that Subject A voided a total of 6.9 Bq of $^{26}$Al and Subject B 1.5 Bq during the period 1 - 7 days post-exposure - with most aluminium voided within days 2, 3 and 4. Previous experiments and data in the literature suggest that during this period about 40% of a 1µm MMAD deposit within the respiratory tract will be lost by mechanical clearance to faeces. Using this fraction the estimated initial lung deposits for the subjects are 17.3 Bq (24.2 ng), for subject A, and 3.8 Bq (5.3 ng), for subject B. These values, given the uncertainties, agree well with those derived by whole body $\gamma$-spectrometry and with those determined by exhal capture.

Measurements of $^{26}$Al in urine showed, that except for the first few days immediately following exposure, the masses of $^{26}$Al excreted by both volunteers were little changed over the period of measurement - this finding indicating that the particles inhaled were essentially insoluble. Overall, the results show that an average of about 0.015% of the initial respiratory deposit (calculated as the mean value of the estimates made using whole-body gamma spectrometry, faecal excretion data and exhaled breath monitoring) was excreted each day - equivalent to approximately 0.025% of the retained lung deposit (after mechanical clearance). This percentage fraction is equivalent to a clearance half-time, due to dissolution of the retained, inhaled deposit, in the order of 2000 days (5.5 years).

**DISCUSSION**

All the studies described above are radioactive tracer studies. In all such studies, the assumption is made that the body is unable to differentiate between stable and radioactive isotopes of the same element and that as a consequence they behave identically in the body. For the
bioavailability studies it is further assumed that the fraction of the radioactive isotope absorbed will be the same as the fraction of stable isotope carrier. This will be true provided that the aluminium carrier and tracer are similarly speciated within the administered solution / suspension / aerosol. It follows that for the present studies great care was taken to ensure that the tracer was evenly dispersed throughout the volume of administered carrier. In all cases this required the preparation of doses from aluminium solutions containing the tracer.

**BIOKINETICS OF INJECTED ALUMINIUM**

The studies undertaken confirmed the utility of research procedures employing $^{26}$Al as a radiotracer for stable aluminium in man. The results of the two biokinetic studies undertaken, to date, support suggestions that systemic aluminium is lost mostly *via* the kidneys (16) and would appear to resolve the controversy concerning the importance of the biliary route of aluminium excretion (1). These have shown that, as in the rat (8), most aluminium entering the blood-stream is rapidly cleared from the body - the majority being lost within the first 24 hours post-intake (59.1% with a SD. of 9.9%), most of the remainder being cleared within one week, but with a small fraction retained by the body and cleared with a long biological half-time. In the single volunteer study this fraction amounted to about 5% of the injected activity at several hundred days post-injection. It follows, that under normal intake conditions the daily systemic aluminium intake will approximate the daily aluminium excretion in urine. It was observed that the pattern of aluminium clearance from the single volunteer was very similar to the clearance of barium, as determined in another study. (This similarity probably arises from the low binding strength of these elements to blood proteins and to their common deposition in the skeleton.) Similarly, the inter-subject variability in the short-term clearance of aluminium and barium are similar. This being so, then it is possible to speculate that the fraction of aluminium retained for long-term clearance might range from c. 3 - 9%. The single volunteer study showed that aluminium loss from the body could be represented as a power function of time:

$$R_t = 35.4 t^{-0.32} \quad (t \geq 1)$$

where $R_t$ was the fraction remaining within the body at time $t$ days.

A consequence of the above is that, under conditions of continuous intake, aluminium will accumulate in the body. With certain assumptions, the data produced may be used to predict the levels of long-term aluminium accumulation in the body from data which exists on the normal levels of aluminium excretion. The data of Kaehny et al. (17) indicate a typical daily urinary excretion level of 15 µg of
aluminium; this, given our results, must correspond roughly to the daily systemic uptake. Applying the range of factors (160 - 440) derived from our studies\(^{(10)}\) would suggest a total accumulation during adult life of 2 - 7 mg. This is much less than published estimates based on the chemical analysis of tissues: 35 - 40 mg\(^{(18)}\) and 60 mg\(^{(19)}\). Defects in our various assumptions may have contributed to this discrepancy, but seem unlikely to be solely responsible. Possibly, the reported analyses\(^{(18)}\) were subject to extrapolation errors and/or affected by contamination of the samples with environmental aluminium. In contrast, if these factors are employed to calculate accumulated body burdens by aluminium flake workers over a 50 year period, with daily aluminium urinary excretion levels of about 300 \(\mu g\) d\(^{-1}\)\(^{(20)}\) then the predicted burdens would range from about 50 mg to 100 mg.

Power function expressions were also derived for the average levels of aluminium in blood and urine\(^{(11)}\):

\[
C_t = 0.37 \, t^{-0.90} \, \% \, L^{-1}
\]

(where \(C_t\) is the blood concentration at time \(t\) days);

\[
U_t = 13.4 \, t^{-1.69} \, \%\]

(where \(U_t\) is daily percentage excreted at time \(t\) days).

Such power functions provide a convenient empirical representation of metabolic data over long periods and may be applied with caution in the absence of sufficient metabolic data to undertake multi-compartmental analysis.

The speciation of aluminium in blood remains uncertain, although some blood samples were fractionated prior to analysis. Rahman et al\(^{(21)}\) have suggested that most of this element is bound to transferrin and this suggestion is supported by our analyses\(^{(13)}\) and earlier analyses of Day et al.\(^{(9)}\). However, our data also suggest a fraction associated with citrate and with a small molecular weight protein. Moreover, we found a partial association with red blood cells, established at late times (14% at 880 days post-injection). This probably results from the incorporation of aluminium into the cells during haematopoiesis and suggests a possible mechanism both for long-term hepatic accumulation due to the release of aluminium along with iron when red blood cells break down in the liver and for enhanced biliary (faecal) excretion at late times after intake.

The finding that \(^{67}\)Ga and \(^{26}\)Al behaved differently with respect to their patterns of body-retention, body distribution and excretion pathways suggests that the former should not be used as an aluminium surrogate for metabolic studies.
Until our studies, all $^{26}\text{Al}$ and many stable aluminium bioavailability studies have employed blood and/or plasma aluminium determinations, often at fixed, single time points, to derive gut uptake factors. The results of the above Study 3, and a similar study conducted using radiolabelled drinking water, demonstrated the difficulties in this approach. It was concluded that such data are insufficient to derive estimates of bioavailability, largely because of the diverse kinetics of aluminium transfer from gut to blood and because aluminium blood levels reach no convenient plateaux for such assessments.

In contrast to the above, when urine data, collected over 1 week post-administration, were employed to determine gut uptake factors, the values derived were more reliable. This is because most of the absorbed aluminium is excreted during the first few days following intake (see Studies 1 and 2). The results of our studies showed that even when aluminium uptake is delayed, a week’s collection of urine is sufficient to derive a meaningful result. Nevertheless, some uncertainties exist due inter-subject variability in the fraction of aluminium excreted during the collection period, but such errors are much less significant than the unavoidable errors associated with the use of blood data and can be quantified. It follows, that the suggested precision of the values reported is about ± 10%, allowing for such inter-subject variability, and the mean for both the volunteers employed is likely to be more precise.

The chemical species employed for the industry studies were chosen because previous experience, with other polyvalent metals, suggested that they would be either relatively bioavailable (citrate) or relatively unavailable (hydroxide) and would represent the likely range of bioavailabilities. In addition, citrate is a common component of food and beverages and aluminium hydroxide is the active ingredient of many antacid preparations.

In our study the calculated fraction of aluminium uptake when ingested as a citrate was c. 0.5%. This is a factor of two lower than that independently published by our collaborator, Day (9); however, his experiment involved a single volunteer and the quantity of citrate ingested was unrealistically high. Moreover, the result was based on restricted blood data, the limitations of which are discussed above. Nevertheless, our study indicated no reason why Day should have overestimated aluminium uptake and it was concluded that under some conditions aluminium absorption must equal at least 1%. Nevertheless, experience with other polyvalent metal ions (22) suggests that the 0.5 - 1% fraction range is likely to be close to the maximum bioavailability range in weaned children and adults under normal ingestion exposure conditions - such as the ingestion of aluminium in orange juice - and that
the bioavailability of other, less soluble, ingested species, including aluminium hydroxide, will be lower. The measured result for aluminium hydroxide (absorbed fraction = 0.01%) is consistent with this suggestion. It is also consistent both with a similar fraction of 0.1% derived from published data on normal aluminium intakes and on average levels of aluminium excretion\(^{(14)}\) and with the fraction of 0.2% derived for aluminium in drinking water\(^{(15)}\) - see Table 1. The latter study was conducted with \(^{26}\)Al-labelled, Sydney drinking water and used similar methods to those employed in the industry-sponsored studies.

**Table 1.**

A comparison of uptake fractions calculated for different ingested aluminium species.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Fed or Fasted</th>
<th>% Uptake</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aluminium hydroxide</td>
<td>fed</td>
<td>0.01</td>
<td>(12)</td>
</tr>
<tr>
<td>Aluminium hydroxide with citrate</td>
<td>fed</td>
<td>0.14</td>
<td>(12)</td>
</tr>
<tr>
<td>Aluminium in Sydney drinking water</td>
<td>fasted</td>
<td>0.22</td>
<td>(15)</td>
</tr>
<tr>
<td>Aluminium citrate</td>
<td>fed</td>
<td>0.52</td>
<td>(12)</td>
</tr>
<tr>
<td>Aluminium citrate</td>
<td>fasted</td>
<td>~1.0</td>
<td>(9)</td>
</tr>
<tr>
<td>Aluminium in total diet</td>
<td>fed</td>
<td>0.1</td>
<td>(14)</td>
</tr>
</tbody>
</table>

Despite the low absorbed fraction measured for aluminium hydroxide and the even lower retained fraction (5 % of 0.01 % = 0.0005%) our results suggest that the consumption of multi-gram amounts of this compound within OTC pharmaceutical preparations could result in significant, compared with normal, excess body burdens of the element. For example, if 1 g of aluminium hydroxide was ingested each day for a year the resulting increment in the aluminium body burden could be as high as c. 20 mg and protracted treatment with larger doses could result in body burdens much higher than those predicted for workers in the aluminium industry. Moreover, our results showed that the co-administration of citrate with aluminium hydroxide, a not uncommon medical practice, will result in even greater body burdens (absorbed fraction = 0.01%). Given that symptoms of aluminium toxicity are seldom seen in such patients with normal kidney function it might be concluded that dietary aluminium intakes, or even enhanced industrial aluminium intakes are most unlikely to result in the classical symptoms of aluminium toxicity.
While for most individuals ingestion will be the major source of body aluminium it is possible, that for some individuals, inhalation will also be important. Within the general population the most likely sources of inhaled aluminium will be environmental dusts (> 10 µg m$^{-3}$ in urban atmospheres) and aerosol antiperspirants - the latter comprising particles of aluminium chloride / chlorohydrate. Nevertheless for most individuals, even though a large, compared with ingested aluminium fraction of inhaled aluminium will be transferred to blood, it is unlikely that it would account for more than a minor fraction of their life-time accumulated body-burden. In contrast, workers in the primary aluminium industry, and probably others exposed to industrial aluminium aerosols (e.g., aluminium welders and aluminium arc sprayers), may accumulate significant body-burdens of the element as a consequence of their occupational exposure. The high levels of aluminium excreted by such workers, even after periods of vacation, being a testament to the veracity of this statement$^{(20,23)}$.

The final study in the Harwell series (Study 4) was undertaken in order to more fully appreciate the consequences of the inhalation of aluminium aerosols within the primary, smelting industry. In particular, the project aimed to determine the retention kinetics of inhaled transitional aluminium oxides - these being the most widely used oxides within the industry. Following inhalation two main clearance mechanisms operate to remove inhaled particles: a rapid mechanical clearance of particles deposited within the nasopharynx and respiratory airways; a slower clearance, by dissolution, of particles deposited within alveoli. The relative importance of these mechanisms depends upon the aerodynamic diameter of the particles (a function of the geometric size and density) and on their solubility. In general, very small particles (such as those comprising molten metal fumes) will deposit by diffusion mechanisms in the nose and alveoli, medium sized particles will deposit preferentially in the alveoli and large particles will deposit by impaction and sedimentation in airways. The particles used for our study were of intermediate size, mass median aerodynamic diameter (MMAD) 1.2 µm, and about 40% of those inhaled would have deposited in alveolar regions of the lungs.

While not yet complete, sufficient data have been accumulated to show that transitional aluminium oxides are extremely insoluble (estimated T½ = 5.5 years). Accordingly, it should be expected that workers with accumulated lung deposits of such materials will show enhanced, aluminium excretion, relative to normal population levels, at all times, to death. Where such levels are seen to fall rapidly following the cessation of exposure then two possibilities exist: exposures were recent (for the first few days after exposure aluminium excretion levels
are high, presumably, due to the “wash off” of loosely bound aluminium); exposures were to another aluminium aerosol - perhaps aluminium metal fume which, due to its small size (c. 10 nm) and very high surface to volume ratio, may be expected to dissolve much more rapidly than the transitional oxide.

**CONCLUSION**

Post-1990, the industry-sponsored studies, and other allied studies, using the radiotracer $^{26}$Al have substantially added to our knowledge of the biokinetics and bioavailability of aluminium and aluminium compounds in man. In particular these studies have established that:

- while most aluminium entering the blood-stream is rapidly excreted a small fraction, c. 5%, is retained and that under conditions of continuous intake the metal will accumulate within the body;
- the fraction of aluminium excreted in the faeces is small, less than 2%;
- within the blood-stream most aluminium is bound to transferrin, but that significant fractions may also be found complexed to citrate and low-molecular weight proteins;
- at long times after intake some circulating aluminium is associated with red blood cells and such deposits provide a possible explanation of the mechanism of aluminium accumulation by the liver;
- ingested aluminium compounds are poorly absorbed by the gut, with the bioavailabilities of common compounds (in normal adult males) ranging from about 0.01% (hydroxide) to about 0.5 - 1.0% (citrate);
- aluminium added to drinking water (fraction absorbed c. 0.25%) will contribute little to the average body burdens of members of the public (even where levels of aluminium in water approach the permitted maximum);
- inhaled transitional aluminium oxides are very insoluble.
- The significance of the contribution of these studies, to our knowledge of aluminium toxicokinetics, may be deduced from the frequent reference to them within the recent International Programme on Chemical Safety / WHO review of aluminium $^{24}$.

**ACKNOWLEDGEMENTS**

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11. RESPIRATORY TRACT TRANSLOCATION AND BIOAVAILABILITY OF ALUMINIUM

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SUMMARY

This paper describes plans for a study of the dissolution and translocation of aluminium oxide in rat lungs. The relevance of the study to the human situation is highlighted. Aluminium oxide will be administered to the rats by either serial intubation or by, nose-only, inhalation. Animals will be sacrificed at different times post-exposure and tissues analysed by GF-AAS to determine the subsequent behaviour of the metal.

INTRODUCTION

Little published information is available concerning the kinetics and translocation of aluminium following its inhalation and subsequent deposition within the respiratory tract. This is because almost all studies of aluminium kinetics involved administration of the metal via injection or ingestion. However, systemic aluminium has been found in occupationally exposed individuals (1,2) and in a laboratory study of animals inhaling aluminium oxide (3), clearly suggesting the respiratory tract as a potential route for systemic uptake and resulting in concern regarding this pathway of occupational human exposure. These studies, however, generally did not address the issue of accumulation of respiratory tract-derived aluminium in critical target organs, such as bones and brain. Thus, if in fact the lung is a significant portal of entry for systemic uptake of aluminium, questions concerning the ultimate fate of inhaled metal need to be resolved in order to determine the true health significance of occupational exposures.

Following inhalation, particulate aluminium may follow various pathways, depending upon the region in which the particles deposit and the solubility of the inhaled material (4). The clearance of insoluble particles deposited in the non-olfactory portion of the nasal passages occurs via mucociliary transport and the general flow of mucus is backwards towards the nasopharynx where the material is swallowed. Soluble material deposited on the nasal epithelium will be accessible to
The bloodstream if it can diffuse to them through the mucus lining prior to removal via mucociliary transport. The nasal passages have a rich vasculature, and uptake into the blood from this region may occur rapidly. Clearance of insoluble particles deposited in the oral passages is by swallowing into the gastrointestinal tract, while soluble particles are likely rapidly absorbed after deposition.

Insoluble particles deposited within the tracheobronchial tree are cleared primarily by mucociliary transport, with the net movement of fluid towards the oropharynx, followed by swallowing. As in the nasal passages, soluble particles may be absorbed through the mucus layer of the tracheobronchial airways and into the blood. In any case, the relative contribution of direct transport of aluminium across the lung tissue vs. uptake via the gastrointestinal tract is not resolved.

Clearance from the pulmonary (alveolar) region occurs via a number of mechanisms and pathways. Particle removal by specialised cells, namely alveolar macrophages, comprises the main process for clearance of insoluble particles from this region. These cells reside on the epithelium, where they phagocytose and transport deposited material that they contact. Particle-laden macrophages may then be cleared from the pulmonary region along a number of pathways. One route is cephalad transport via the mucociliary system after the cells reach the distal terminus of the mucus blanket or passage through the alveolar epithelium and the interstitium. Some cells that follow interstitial clearance pathways are likely resident interstitial macrophages that have ingested particles transported through the alveolar epithelium.

Macrophages that are not cleared via the bronchial tree may migrate within the interstitium to a nearby lymphatic channel or, along with un-ingested particles, be carried into the lymphatic system. Particles within the lymphatic system may be translocated to tracheobronchial lymph nodes, which often become reservoirs of retained material. Particles penetrating the nodes and subsequently reaching the post-nodal lymphatic circulation may enter the systemic circulation.

Un-ingested particles or macrophages in the interstitium may traverse the alveolar-capillary endothelium, directly entering the blood. Once in the systemic circulation, transmigrated macrophages, as well as un-ingested particles, can travel to extrapulmonary organs. Un-ingested particles and macrophages within the interstitium may travel to perivenous, peribronchiolar or subpleural sites, where they become trapped, increasing the lung particle burden.

Clearance, by an absorptive mechanism, involves dissolution in the alveolar surface fluid, followed by transport through the epithelium and into the interstitium, and diffusion into the lymph or blood. Some soluble particles translocated to and trapped in interstitial sites may be
absorbed there. Although the factors affecting the dissolution of deposited particles are poorly understood it is influenced by the particle's surface to volume ratio and other surface properties. Thus, materials generally considered to be relatively insoluble may have high dissolution rates and short dissolution half times if the particle size is small.

Of special interest, regarding metal particles, is that deposited particles may undergo dissolution in the acidic _milieu_ of the phagolysosomes after ingestion by macrophages, and such intracellular dissolution may be the initial step in translocation from the lungs for these particles. Following dissolution, the material can be absorbed into the blood. Dissolved particles may then leave the lungs at rates, which are more rapid than would be expected, based upon their normal dissolution rate in lung lining fluid. Because of this, the clearance rate of such a material can vary with the form in which it is inhaled. Since both free Al\(^{3+}\) and simple A1-complexes tend to hydrolyse at pH <7, if some aluminium translocates directly to the bloodstream from the lungs, it may occur in a different form than if it is translocated via macrophages with subsequent incorporation of the aluminium into acidic phagolysosomes.

Because of the lack of information regarding pathways of clearance of aluminium from the lungs and potential translocation to other organs, a study was designed to provide information on the fate of aluminium deposited in the lungs. The study will involve a kinetic analysis of aluminium following introduction into the lungs and the development of equations describing the distribution and clearance of aluminium from the lungs and various other organs.

**APPROACH**

Given the current state of knowledge, the question of aluminium bioavailability cannot be adequately addressed by epidemiological or controlled clinical studies, where biological endpoints are necessarily limited. However, the question can be addressed using an animal model. Accordingly, this study will assess the fate of aluminium delivered to the respiratory tract of the rat. The form of aluminium will be aluminium oxide (Al\(_2\)O\(_3\)).

While one of the problems inherent in the use of any animal model involves extrapolation to humans, there are available empirical models that can be used to compare the deposition of particles in rats and humans. These can be applied to the particles to be used in this study such that relative exposure doses in rats can be related to those that would occur in humans.

The first stage of the project involves repeated intubations into the lung (a series of 20 intubations over a 20 wk period) to simulate
chronic exposure. The advantage of such a delivery technique is that it allows exact determination of deposited dose, which can then be related to subsequent tissue distribution. This facilitates development of a model for aluminium distribution from the lungs. However, since intubation is an artificial exposure route, the next stage of the project will involve actual inhalation of aluminium. Exposures will be for 4hr / day, 5d / week, so as to obtain the same deposited dose as in the intubation study above. Exposure will employ a nose-only system to avoid problems of direct ingestion of aluminium by preening, a problem inherent in reported whole-body chamber exposures \(^{(3)}\). The median size of the particles used in both phases of the study will be about 1 µm.

Aluminium content in the lungs and other organs (brain, bone, blood, stomach, liver, spleen and kidney) of the rats will be determined using graphite furnace atomic absorption spectroscopy (GF-AAS). Immediately after the first exposure, at 1, 4, 8, 12, 16 and 20 weeks post-intubation or inhalation, at 1, 3 and 5 days after the last exposure and weekly thereafter for 20 weeks. This protocol will allow determination of initial deposition and of aluminium translocation with repeated exposures.

**SUMMARY**

This study is designed to provide the first kinetic analysis of aluminium translocation in the body, including the development of equations for the distribution and clearance of aluminium from the respiratory tract and various other organs. Such information will provide a needed insight into the translocation and bioavailability of aluminium when the respiratory tract is the portal of entry, and will help in the interpretation of occupational exposures.

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12. OCCUPATIONAL CANCER OVERVIEW: ALUMINIUM REDUCTION

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SUMMARY

Workers within the aluminium reduction industry are exposed to a variety of possible carcinogens. In turn, exposures may lead to a variety of tumour-types. Possible cancer excesses have been described including respiratory cancer, stomach cancer, and skin cancer in Soviet workers. In addition, some evidence exists to suggest that workers may also exhibit excess levels of other tumour types, but the evidence is far from compelling. By monitoring the exposures and health status of the workforce it is possible, over a long period, to estimate the risk of these diseases. However, the start of the aluminium reduction industry is too recent to evaluate risks with any precision – due to the long latency period for many cancers. Nevertheless, such evaluations are essential for cancer prevention, medical intervention and worker compensation. The paper reviews current knowledge concerning the risk of tumours in reduction workers.

INTRODUCTION

An understanding of the aetiology and risk of cancer are fundamental to cancer prevention, medical intervention and worker's compensation.

Preventive action, medical intervention and compensation decisions can either be guided by information about health outcome [e.g., direct evidence of an increased cancer risk in the specific workplace, same or similar industry], or by a knowledge of the workplace agents and their potential to pose a risk for workers in that specific industrial setting. Generally both approaches are used. The latter approach works well when the agents and effects are well established and exposure parameters well known (e.g., high exposure to lead). However, there remain in the primary aluminium reduction industry many situations where the risks are far from well established and the specific agents to control are inadequately known.
In order for prevention to be effective, it is necessary to control exposure to the specific aetiological agent(s) or a reliable surrogate for the aetiological agent(s). Preventive actions can involve considerable investment and workers remain at risk if the incorrect exposure parameters are eliminated. This probably demands at a minimum, evidence that risk increases with increasing exposure and information on whether and to what extent other workplace exposures or lifestyle factors (e.g., smoking alcohol, diet) modify (e.g., act synergistically) or confound risk estimates and biological plausibility.

THE CANCERS UNDER SCRUTINY

The first published reports of a cancer risk in workers in the primary aluminium industry appear to be those from the former Soviet Union (1,2). Increased rates of respiratory cancer, stomach cancer and skin cancer in Söderberg plant workers, but not in prebake plant workers were reported. Unfortunately the published data were inadequate to fully evaluate the findings3.

More than 20 years later, the list of cancers includes sites such as lung, bladder, pancreas, kidney, brain, stomach as well as non-Hodgkin's lymphomas and leukaemias. Most of these have been noted in earlier reviews (3-6). However, the evidence that they are causally linked to reduction processes, in many instances is not consistent. In this overview, an attempt will be made to identify and perhaps clarify some of the issues and hopefully stimulate efforts to resolve them.

RESPIRATORY CANCER

The evidence that lung cancer risks are increased in workers employed in Söderberg potrooms is now reasonably well established. However, it is useful to examine apparent data inconsistencies, remaining issues and reported increases in risk in prebake facilities.

In the late 1960's studies were initiated at McGill University to determine if the risk of lung cancer was increased in Quebec aluminium reduction plants. In the early 1970’s the lung cancer risk reports from the former USSR appeared (1-2). Subsequently, there was increasing evidence demonstrating or supporting an aluminium reduction industry-related lung cancer risk.

Milham (7) in 1976 reported on the occupational mortality of more than 300,000 men who died in Washington State in the period 1950-71. Occupations were taken from the death certificate and a proportionate mortality ratio (PMR) analysis was performed. A slightly elevated PMR of 1.3 was found (7). While such studies have serious limitations (3), a cohort study of 2103 workers at a prebake plant in the same State showed "exposed" prebake workers (essentially potroom and
carbon plant workers) to have an elevated standardised mortality ratio (SMR) for respiratory cancer of 129 (observed (O) deaths = 16) \(^{(8)}\). There was also a tendency for risk to increase with period from first exposure to death with a statistically significant mortality excess 15 - 19 years after first exposure. It would have been useful to know if this increased risk was in prebake potroom or in carbon plant workers. The cohort study undertaken by Milham \(^{(8)}\) most likely included at least some of the deaths from the Washington State PMR study and it is possible that workers from Washington State were also included in the studies by the US Aluminum Association study \(^{(3)}\) and Rockette and Arena \(^{(9)}\) described below. Hence it must be considered that the US studies may not be totally independent of one another when evaluating cancer risks.

The U.S. Aluminum Association multi-plant study involving over 20,000 workers \(^{(3)}\) did not identify any overall significantly increased risk of lung cancer. However, the relative risks of lung cancer for workers in various types of plant, 30 years after first exposure were: horizontal Söderberg (HS) = 2.2; prebake (PB) = 1.4 and carbon plants (CP) = 1.2. Two years later, Rockette and Arena \(^{(9)}\) reported on the mortality experience of 21,829 workers with five or more years employment in 14 US reduction plants. This population was in large part that included in the US Aluminum Association study, so results can not be considered to be totally independent. Their study also failed to demonstrate an increased risk of lung cancer although a non-significant increase in lung cancer risk was observed for Söderberg plant workers employed for more than 25 years (O = 5, E = 2.4). This risk is similar to that found in the Quebec smelters. There was no increased risk in prebake workers employed for more than 25 years.

The cohort mortality studies in Quebec \(^{(10,11)}\) were the first to incorporate an index of coal tar pitch volatile (CTPV) exposure. Based on more than 5000 workers and more than 1000 deaths, the study showed a definite exposure-response relationship between tar-years of exposure and lung cancer mortality. The SMR for persons exposed for more than 21 years to the highest level of tars was 2.3 times that of non-exposed persons.

In Norway an SMR of 2.4 was reported in workers with more than 25 years of employment in the old [mixed prebake and Söderberg] plants \(^{(12)}\). In 1991, a non-statistically significant association between lung cancer and employment in a vertical Söderberg plant was also reported in British Columbia \(^{(13)}\).

When all the data are considered it is clear that lung cancer risks are increased in plants which have used Söderberg technology. The failure of other studies to demonstrate a statistically significant increase in lung cancer mortality is almost certainly due to the smaller numbers of long-term highly exposed Söderberg plant workers and shorter
follow-up periods. However, none of the above studies took smoking into account in their analyses, so the very valid question had to be asked - is this due to smoking? When the Quebec studies were first undertaken (10,11) information on smoking was not available. However, this has now been investigated (14) and established, as originally suspected (10), that smoking does not explain the increased lung cancer risk in the Quebec cohorts. The small number of non-smokers means that the additive or multiplicative effect of smoking and CTPV exposure risks are still debated.

A quantitative relationship between lung cancer mortality and benzo[a]pyrene [BaP] indices of exposure acting as surrogates for CTPV exposures has now been demonstrated for the Quebec data (14). While benzene soluble matter [BSM] also related well, the B[a]P index turns out to be very important as risk estimates using the Quebec data resemble very closely those derived from other coal tar derived polycyclic aromatic hydrocarbon (PAH) exposures (15). Exposure estimates should now be further refined and comparisons made between vertical and horizontal Söderberg plants. Recent works on PAHs (16) suggest that certain polycyclic aromatic hydrocarbons PAHs, because of their potency may be more important than others to control. If this is the case, these same PAHs are not the major contributors to cigarette smoke carcinogenicity, so cell type differences may exist. To date, the distribution of lung cancer cell types in smokers and non-smoking, potroom, lung cancer cases has not been reported.

The prebake evidence is confusing. While the US studies did not detect an increased lung cancer risk, an increase in the standardised incidence ratio (SIR) for lung cancer with period since first exposure, reaching 2.4, 30 years from first exposure has been reported in Norway (17). The Norwegian authors do not consider smoking to be responsible. Such a finding would not be anticipated unless the prebake population included a good proportion of workers from the carbon plant, other lung carcinogen exposures occurred or the prebake exposures were more potent. As the finding is based on small numbers this may prove to be a chance observation. However, it should be examined further. If the findings, as seems unlikely, really are due to prebake potroom exposures the results may have great importance for modern prebake operations.

BLADDER CANCER

A high rate of bladder cancer in the region of Quebec serving the reduction industry led to a case-control study in which non-smoking aluminium plant workers had relative risk of 1.9 and smokers a relative risk of 5.7 (18). The finding of a high mortality rate from bladder cancer in persons exposed to more than 21 tar-years (SMR = 666.7) was also a clear indication of a bladder cancer problem (11). In this predominantly
horizontal Söderberg industry, bladder cancer risk increases with increasing B[a]P and BSM exposure with the predicted relative risk of 1.72 for persons exposed for 40 years at 1 µg m\(^{-3}\) of B[a]P as an index \(^{(19,20)}\). This compares to a relative risk of 1.11 for lung cancer at the same exposure \(^{(14)}\).

The number of observed bladder cancers exceeded that expected in the mixed Söderberg and prebake exposed workers in Norway \(^{(12)}\), in US Söderberg and carbon plants \(^{(9)}\) and bladder cancer was statistically in excess in a vertical Söderberg plant in BC, Canada \(^{(13)}\). While bladder cancer incidence was also reported to be increased at a prebake plant in Norway \(^{(15)}\) there was no indication of increased mortality from bladder cancer in prebake plants in the USA \(^{(8,9)}\). This may be due to the fact that bladder cancer is not always fatal. On the other hand, the finding of an increased risk in prebake operations would not be anticipated unless workers had higher exposures than generally assumed to date or if the aetiological agent were more potent. While the Norwegian findings may be due to chance they require further investigation, as clearly a long latency is important. While B[a]P and BSM serve as indices of exposure which predict bladder cancer risks the actual aetiological factor is still unknown. Research to identify such an agent could be very important in prevention. Acetylation rates and other factors which might potentially put workers at increased risk also deserve investigation.

**PANCREATIC CANCER**

In Norway, the overall incidence of cancer of the pancreas in mixed Söderberg and prebake plants was at or below expected levels (O = 15; SIR = 93.8) \(^{(12)}\). There was also a deficit of pancreatic cancer in workers with more than 3 years of cumulative employment in a Norwegian prebake smelter (O = 4; SIR = 69) \(^{(17)}\).

In the USA, Milham \(^{(7)}\) first reported increased mortality from pancreatic cancer in workers who had been employed in the industry based on the PMR study in Washington State. He then studied a prebake plant. Mortality from pancreatic cancer in the period 1946-1976 was increased (O = 9, SMR = 180). When examined in relation to exposure in the potrooms, the SMR's for cancer of the pancreas were higher for men in the non-exposed group. The pancreatic cancer mortality of persons with less than 15 years of employment compared with that of persons with more than 15 years of employment was also essentially the same (Table 1).

In the multi-plant study there were indications of a higher than expected mortality from pancreatic cancer \(^{(9)}\). In that study there were 5
plants using the horizontal Söderberg technology, one using the vertical Söderberg technology, seven using the prebake process and one plant used all three processes with no indication of the process in which workers were employed. At the mixed technology (prebake & Söderberg) plant there were 11 cases of cancer of the pancreas with 8.9 expected. There were no deaths from pancreatic cancer in the vertical Söderberg plant. There were 13 deaths with 10.2 expected (SMR = 128) in the horizontal Söderberg plants and 39 with 30.3 expected (SMR = 132.9) in the prebake plants. Thus, there was no suggestion that risks were higher in the plants where one might expect higher CTPV exposures.

Table 1
Mortality from Pancreatic Cancer in Relation to Duration of Employment and Period from First Exposure in a Pre-Bake Plant (from Milham (8))

<table>
<thead>
<tr>
<th></th>
<th>&lt; 15 years</th>
<th></th>
<th>&gt; 15 years</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Obs.</td>
<td>Exp.</td>
<td>SMR</td>
<td>Obs.</td>
<td>Exp.</td>
</tr>
<tr>
<td>Duration of Employment</td>
<td>5</td>
<td>2.74</td>
<td>183</td>
<td>4</td>
</tr>
<tr>
<td>Period from Hire</td>
<td>4</td>
<td>1.6</td>
<td>25</td>
<td>5</td>
</tr>
</tbody>
</table>

As shown in Table 2 there was an apparent deficit of pancreatic cancer in men, with less than 15 years of cumulative exposure, in the Söderberg potrooms (O = 1 SMR = 20) and an apparent excess (O = 7, SMR = 233.3) in men with 15 or more years of cumulative employment in the Söderberg potrooms. The published paper (9) reported a statistically significant (p<0.05) excess of pancreatic cancer with an SMR of 271.3 in the horizontal Söderberg plants (i.e., after removing the vertical Söderberg data). However, the mortality from pancreatic cancer in men employed for more than 15 years in prebake plants was not dissimilar (SMR = 222.2). The study did not take into account smoking. However, there is clearly increased risk of pancreatic cancer.

In France a study of predominantly prebake plants resulted in a statistically significantly increased SMR of 149 based on 9 deaths from pancreatic cancer (21).

While the US cohort of horizontal Söderberg employees (6534) (9) was marginally larger than the combined Quebec cohorts (5891) (11), the number of deaths in the Quebec cohort was 1185 compared to only 797 in the US study. The pancreatic cancer mortality experience of the
5406 men in Cohort A and 485 in cohort B for the period 1950-77 is shown in Table 3. There was no definite indication of an increased pancreatic cancer risk for persons exposed to tars and no pattern of increasing risk of pancreatic cancer with duration of exposure, tar years of exposure or years since first exposed.

Table 2
Observed and Expected Deaths from Pancreatic Cancer by Process and Jobs by Duration of Employment (from Rockette and Arena (9))

<table>
<thead>
<tr>
<th></th>
<th>All durations of employment</th>
<th>&gt; 15 years employment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Obs.</td>
<td>Exp.</td>
</tr>
<tr>
<td>SÖDERBERG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potrooms</td>
<td>8</td>
<td>7.9</td>
</tr>
<tr>
<td>Carbon</td>
<td>1</td>
<td>3.3</td>
</tr>
<tr>
<td>Non Potroom</td>
<td>5</td>
<td>4.5</td>
</tr>
<tr>
<td>PREBAKE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potrooms</td>
<td>21</td>
<td>15.2</td>
</tr>
<tr>
<td>Carbon</td>
<td>13</td>
<td>9.2</td>
</tr>
<tr>
<td>Non Potroom</td>
<td>11</td>
<td>10.9</td>
</tr>
</tbody>
</table>

In the British Columbia cohort, there were 338 deaths, 8 from pancreatic cancer with 6.36 expected (SMR = 126). Based on incidence there were 8 cases with 5.72 expected (SIR = 140). These numbers are small and as the authors note "At this time, chance cannot be ruled out as an explanation for these excess risks."

In conclusion, there are several studies mentioning that pancreatic cancer risks are increased and other studies clearly negative. If there is an increased risk the aetiological factor does not appear to be CTPVs unless the CTPVs in prebake plants are more potent than those in Söderberg plants, but this does not fit with the Norwegian finding of no increased risk of pancreatic cancer. Present evidence is clearly inadequate to conclude that there is an association between exposure in the reduction industry and cancer of the pancreas. However, mortality update studies should examine this further.

Special attention needs to be directed at distinguishing carbon plants, quantifying exposures and gathering quantitative smoking data.
KIDNEY CANCER

There was a slight increase in kidney cancer mortality in workers employed in a horizontal Söderberg plant in Quebec (O = 8, SMR = 130) (11) and an slight increase in kidney cancer in a vertical Söderberg (O = 6, SMR = 170) plant (13) in Canada. However, there was no indication of an increase in kidney cancer mortality in the Söderberg operations in the USA (Rockette & Arena) where only 3 cases were reported.

Table 3
Mortality from Cancer of the Pancreas in Relation to Various Indices of Exposure (from Gibbs (11))
Arvida Isle Maligne Cohort

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>&lt;1 - 10</th>
<th>11 - 20</th>
<th>21+ years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total SMR</td>
<td>22.3</td>
<td>92.1</td>
<td>89.5</td>
<td>183.2</td>
</tr>
<tr>
<td>Exp.</td>
<td>4.5</td>
<td>6.5</td>
<td>2.2</td>
<td>1.1</td>
</tr>
<tr>
<td>Obs.</td>
<td>1</td>
<td>6</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>&lt;1 - 10</th>
<th>11 - 20</th>
<th>21+ years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total SMR</td>
<td>22.3</td>
<td>104</td>
<td>78.7</td>
<td>131.0</td>
</tr>
<tr>
<td>Exp.</td>
<td>4.5</td>
<td>5.8</td>
<td>2.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Obs.</td>
<td>1</td>
<td>6</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>&lt;1 - 10</th>
<th>11 - 20</th>
<th>21+ years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total SMR</td>
<td>22.3</td>
<td>0</td>
<td>143.4</td>
<td>92.9</td>
</tr>
<tr>
<td>Exp.</td>
<td>4.5</td>
<td>0.6</td>
<td>2.8</td>
<td>6.5</td>
</tr>
<tr>
<td>Obs.</td>
<td>1</td>
<td>0</td>
<td>4.0</td>
<td>6.0</td>
</tr>
</tbody>
</table>

Slight increases in kidney cancer risk in prebake operations have been suggested by data in the USA (O = 19, SMR = 151) (9) and Norway (O = 8, SMR = 120) (17). However, when kidney cancer mortality data from both the Söderberg and prebake operations were examined in relation to CTPV exposure indices, there was no clear evidence of an exposure-response relationship (11, 5). The observation by Ronneberg and Andersen (17) that 4 of their 6 kidney cancer cases with more than 3 years of exposure were in the highest heat stress category is interesting and should perhaps be examined in plants with greater numbers of cases. However, it is noted that heat exposure in an aluminium reduction plant is likely to be confounded by many other exposure and lifestyle factors.
NON-HODGKIN’S LYMPHOMA (NHL)

The term "non-Hodgkin's lymphoma" is a clumsy negative definition referring to those neoplasms of the lymphoreticular system other than Hodgkin's Disease (22). As mentioned by Davis (23) "Lymphomas of the non-Hodgkin's type represent a heterogeneous group of tumours, probably comprised of groups of related diseases each with a distinct aetiology". This is likely to be a very important issue when attempting to unravel the NHL risks in the primary aluminium reduction industry.

One of the main difficulties encountered in understanding the patterns of occurrence of NHL and their aetiology relates to their classification and the major changes that have occurred in both histological and cause of death coding. Greiner et al. (24) discussing the US Surveillance, Epidemiology and End Results (SEER) data, noted. "With the enhanced ability of pathologists to delineate new clinicopathologic entities by immunophenotypic and molecular biologic studies, future modification to the SEER data will be appropriate. Such an approach will address the limitations of the Working Formulation and lead to a more accurate base for the evaluation of epidemiological trends". Referring to lymphosarcoma and reticulum cell sarcoma (ICD9 200), Boyle et al (25) noted that "Following changes in histological classification, data for this group of tumours are rather unreliable and many which would have been previously coded to this rubric are now to be found in ICD9 202 as non-Hodgkin's lymphomas”.

Researchers often analyse leukaemia, aleukaemia, myeloma, Hodgkin's Disease and the range of non-Hodgkin's lymphomas together as neoplasms of lymphatic and haematopoietic tissues. Another complication is the fact that the overall rate of non-Hodgkin's lymphoma has increased but not in the same way for all non-Hodgkin's lymphomas (25).

The list of claimed links with NHL is long, ranging from viruses and immunodepressants (the increasing incidence of AIDS is potentially important), smoking for some lymphomas, radiation, electromagnetic fields, numerous occupational links especially those linked to agriculture (26-30), diet (31) and Helicobacter pylori infection (31) among others. These factors explain why interpreting potential links between NHL and exposure in aluminium reduction is extremely difficult.

Vertical Söderberg Plants

In the vertical stud Söderberg aluminium reduction plant in British Columbia, there was no overall excess of deaths from this cause (O = 4 and E = 3.58) (13). When incident cases in BC were examined in relation
to BSM years of exposure, it was found that as a group they occurred more frequently than expected in men with more than 5 BSM-years of exposure. The apparent increase in the number of NHL in the higher categories of coal tar pitch volatile (CTPV) exposure did not involve a statistically significant excess of deaths in either of the two highest exposure categories of BSM exposure. A test for trend was apparently statistically significant at the 5% level of probability. However, it is likely that the trend achieved significance due in part to a deficit of NHL deaths (SMR = 41% and 0%) in the lowest two exposure categories. These authors reported "no significant associations were observed between mortality or cancer incidence and exposure to electromagnetic fields" (13).

Table 4
Summary of the Study Results Relating to Non-Hodgkin’s Lymphoma and Leukaemia (from Rockette and Arena (9))

<table>
<thead>
<tr>
<th></th>
<th>Lymphatic and Haematopoietic Cancer</th>
<th>Lympho-sarcoma and Reticulo-sarcoma</th>
<th>Leukae-mia and Aleukae-mia</th>
<th>Other Lympho-poietic Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prebake</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMR</td>
<td>103.2</td>
<td>132.2</td>
<td>127.6</td>
<td>60.6</td>
</tr>
<tr>
<td>Exp.</td>
<td>51.1</td>
<td>11.7</td>
<td>20.2</td>
<td>18.7</td>
</tr>
<tr>
<td>Obs.</td>
<td>51</td>
<td>15</td>
<td>25</td>
<td>11</td>
</tr>
<tr>
<td>Söderberg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMR</td>
<td>138.1</td>
<td>116.7</td>
<td>130.8</td>
<td>157.3*</td>
</tr>
<tr>
<td>Exp.</td>
<td>22.7</td>
<td>5.2</td>
<td>8.5</td>
<td>9.0</td>
</tr>
<tr>
<td>Obs.</td>
<td>31</td>
<td>6</td>
<td>11</td>
<td>14</td>
</tr>
<tr>
<td>Remainder</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMR</td>
<td>83.7</td>
<td></td>
<td>123.5</td>
<td>76.4</td>
</tr>
<tr>
<td>Exp.</td>
<td>14.5</td>
<td>3.3</td>
<td>5.7</td>
<td>5.3</td>
</tr>
<tr>
<td>Obs.</td>
<td>12</td>
<td>1</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>All plants</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMR</td>
<td>109.1</td>
<td>111.4</td>
<td>127.9</td>
<td>90.3</td>
</tr>
<tr>
<td>Exp.</td>
<td>88.3</td>
<td>20.2</td>
<td>34.4</td>
<td>32.9</td>
</tr>
<tr>
<td>Obs.</td>
<td>94</td>
<td>22</td>
<td>43</td>
<td>29</td>
</tr>
</tbody>
</table>

*Within this category, Hodgkin’s Disease accounted for 6 deaths with 3.4 expected (SMR = 178.4). When these are removed, the observed = 8 and expected = 5.6 (SMR = 142.8). Neither of these represent a statistically significant excess (<0.05).

Information provided to me by Dr. Spinelli (personal communication) indicated that three of the four deaths were classified as ICD9 = 202.8 (i.e., other lymphoma) and 1 was 200.1 (lymphosarcoma). The classification of these 4 cases translated to edition 2 of the ICD-0 differed in respect to site [(1963, 1968, and 1969 (2) and histology (96703, 96953, 96963, 95923)]. The three additional incident cases were classified as occurring at sites 1691, 1968 and 1960 and were classified as having histology (96723 (2) and 95903). It is evident that there is no
clear concentration of lymphomas of a particular type or site in this workforce. Unfortunately data to examine the other studies in this detail do not appear to exist, but are needed.

In the US multi-plant study \(^9\), there were two plants using the vertical Söderberg process. One of these had also used prebake and horizontal Söderberg processes. Although the plant had been operating since 1914 there was no increased risk of non-Hodgkin’s Lymphoma based on quite reasonable numbers of deaths (Table 4).

**Horizontal Söderberg Plants**

In the Quebec study \(^{11}\) non-Hodgkins lymphomas were combined with other malignancies. This category of combined deaths (a "catch all category") was statistically in excess at the 5% level of probability compared to the Province of Quebec. Examination of the original files used in the study identified 11 deaths which might be classified as non-Hodgkins lymphoma - 4 reticulum cell sarcoma (ICD 200.0); 6 lymphosarcoma (200.1) and 1 other primary neoplasm of lymphoid tissue (202.2). If it assumed that none of the other causes in this "catch all" category were in excess, there would have been 7.4 deaths expected for an estimated SMR of 149. This might suggest the possibility of a slightly increased risk of non-Hodgkin’s lymphoma overall. However, it is also not known whether these cases occurred in the CTPV exposed or non-exposed workers. There were more Hodgkin’s disease deaths than expected in the ever exposed to tars workers.

In the British Columbia study \(^{13}\) three of the four deaths were classified as ICD9 = 202.8 (other lymphoma) and 1 was 200.1 (lymphosarcoma). In the Quebec study 6 of the 11 deaths were classified as ICD8 200.1 (lymphosarcoma). This contrasts with the BC data. This is important because the data lack consistency, which detracts from a credible association.

**Washington State**

There are six aluminium reduction plants in the US State of Washington \(^8\). In a report on occupational mortality in Washington State, in the period 1950-1989 Milham noted that among aluminium workers (Occupational Code 526) there were 2300 deaths. He stated “Lung cancer, kidney cancer, the other lymphomas, acute leukaemia, ASHD and machinery-related accidents at work have elevated PMRs”. It can be seen from Table 5 that based on malignant neoplasms of all lymphatic and haematopoietic tissues there was an apparent increased mortality in all the periods studied and overall a statistically significant excess of deaths for the total study period 1950-1989. It is also noteworthy that:
• There was no overall increased mortality from lymphosarcoma and reticulosarcoma (200.0 and 200.1). There were 5 deaths observed and 5 expected and there was no indication of an increased risk in any of the three periods analysed.

• There were 3 deaths from reticulum cell sarcoma (200.0) and 3 expected...i.e., no evidence of any increased risk.

• There were 3 lymphosarcoma deaths observed and 5 expected for a deficit of deaths from this cause overall.

Table 5
Proportionate Mortality Ratios (PMRs) in Washington State, White Males 1950 – 1989 Aluminium Workers (526) (from Milham (32))

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>All malignant Neoplasms</td>
<td>146** (63)</td>
<td>110* (137)</td>
<td>105 (308)</td>
<td>110 (580)</td>
</tr>
<tr>
<td>Malig. Neoplasms of Lymphatic and Hemopoietic Tissues (200 – 205)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphosarcoma and Reticulosarcoma (200.0 – 200.1)</td>
<td>- (E = 1)</td>
<td>115 (3)</td>
<td>64 (5)</td>
<td>71 (6)</td>
</tr>
<tr>
<td>Reticulum Cell Sarcoma (200.0)</td>
<td>- (E = 1)</td>
<td>-</td>
<td>133 (3)</td>
<td>90 (3)</td>
</tr>
<tr>
<td>Lymphosarcoma (200.1)</td>
<td>- (E = 1)</td>
<td>165 (3)</td>
<td>- (E = 2)</td>
<td>59 (3)</td>
</tr>
<tr>
<td>Hodgkin’s Disease (201)</td>
<td>250 (3)</td>
<td>53 (1)</td>
<td>128 (2)</td>
<td>129 (6)</td>
</tr>
<tr>
<td>Other Lymphomas (202, 200.2)</td>
<td>- (4)</td>
<td>432 (5)</td>
<td>120 (9)</td>
<td>200** (18)</td>
</tr>
<tr>
<td>Multiple Myeloma</td>
<td>- (E = 1)</td>
<td>214 (4)</td>
<td>112 (7)</td>
<td>126 (11)</td>
</tr>
</tbody>
</table>

** p<0.01, * p<0.05. E = expected (provided when no deaths were observed). Number of observed deaths shown in parenthesis.

• As the classification did not change in a major way between the 7th and 8th revisions, it might be noted that cancers classified as
reticulum cell sarcoma and lymphosarcoma represented 10 of the 11 deaths in the Quebec study mentioned earlier. There was one more death than expected from Hodgkin's Disease (O = 6, E = 5) and from various leukaemias.

- All of the apparent excess mortality from non-Hodgkin's lymphomas in these Washington State data are in the "other lymphoma" category of disease with 18 observed and 9 expected (SMR = 200). These include "other lymphoid" -7th Revision - ICD 202 and 200.2. As the codes 200.0 - reticulum cell sarcoma and 200.1 lymphosarcoma existed in the 7th revision, it seems that in the Quebec study there was only 1 of the 11 deaths which could be considered "other" in contrast to 18 of 24 in the Washington study.

This indicates the very clear lack of consistency between studies and the complexity of comparing study results.

**Prebake Plant Workers in Washington State**

In his study of a prebake plant (8) Milham reported that lymphatic and haematopoietic cancers for the period 1946 - 1976 were in excess (SMR = 184) and indicated that the relation with duration of employment and latency "suggests that some of the lymphatic and haematopoietic cancers (especially malignant lymphoma), may be of occupational origin in this worker population." The results were as shown in Table 6.

There seems to be little doubt that in this prebake plant, there was an excess of certain NHLs. In 4 cases the cause of death was "malignant lymphoma" and in two cases, malignant lymphoblastoma". The estimated SMR for these causes was said to be 1395. When examined by job-exposure category, there were 6 lymphosarcoma / reticulosisarcoma deaths with 0.9 expected (SMR = 643) in the exposed group of workers (p<0.05), while there was only 1 in the "non-exposed" workers with 1.3 expected. When all lymphatic and haematopoietic cancer deaths were examined in relation to duration of employment, it was seen that the SMRs increased from 60 to 515, but with no consistent pattern of increase. The number of observed deaths and expected numbers of death in each category of exposure were relatively small. Unfortunately, it is not possible to determine whether this apparent increase in risk with duration of employment was due to non-Hodgkin's lymphomas or the other causes included in the "Lymphatic and Haematopoietic" category.

As prebake plants have low levels of CTPVs compared to Söderberg plants, the increased risks of non-Hodgkin's lymphoma at this plant cannot be explained by exposure to CTPVs, otherwise the risks in
Kitimat, Quebec and the US Söderberg plants would be exceedingly high. The increased risk in the "exposed workers" is also unlikely to be explained by magnetic fields as non-Hodgkin's lymphoma were not related to magnetic field exposures at Kitimat.

Table 6
Mortality from all Lymphatic and Haematopoietic Neoplasms Combined in Prebake Reduction Plant Workers by Duration of Employment (from Milham(8))

<table>
<thead>
<tr>
<th>Years Employed</th>
<th>Deaths</th>
<th>SMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 - 4</td>
<td>1</td>
<td>60</td>
</tr>
<tr>
<td>5 - 9</td>
<td>4</td>
<td>187</td>
</tr>
<tr>
<td>10 - 14</td>
<td>1</td>
<td>220</td>
</tr>
<tr>
<td>15 - 19</td>
<td>3</td>
<td>147</td>
</tr>
<tr>
<td>20 - 24</td>
<td>3</td>
<td>247</td>
</tr>
<tr>
<td>25+</td>
<td>2</td>
<td>515</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>184*</td>
</tr>
</tbody>
</table>

As this Table combines all lymphatic and haematopoietic neoplasms, conclusions cannot be reached concerning non-Hodgkin’s lymphomas alone. * = p <0.05

Other US plants

In the multi-plant study of prebake plants (9), there were slightly more deaths from lymphosarcoma and reticulosarcoma than expected (O = 15, E = 11.7) and fewer "other lymphopoietic cancers "than expected (O = 11, E = 18.7). Combining them there were 26 deaths observed and 30.4 expected, i.e., no excess of non-Hodgkin's lymphomas.

In the Söderberg plants, there was essentially the same number of deaths from lymphosarcoma and reticulosarcoma as expected (O = 6, E = 5.2) and slightly more than expected in the "other lymphopoietic cancer" category (O = 14, E = 9). Within this "remainder" category there were 6 Hodgkin's disease deaths with 3.4 expected. Thus there would have remained 8 "other non-Hodgkins" with 5.6 expected (SMR = 143).

The mortality from lymphosarcoma and reticulosarcoma was slightly higher in the prebake than in the horizontal Söderberg plants, but the other lymphopoietic cancers were less frequent in the prebake plants.
When the various NHL were examined in relation to employment in the potroom and carbon plant, there was no evidence that men ever employed for more than 5 years in the potrooms had an increased risk of lymphosarcoma and reticulosarcoma or of other lymphopoietic cancers compared to those with less than 5 years (SMRS 98.3, 97.4, 93.7, 108.4 respectively). This would suggest that neither exposure to CTPVs or potroom electromagnetic fields are important in the occurrence of these cancers.

Rockette and Arena (9) recorded that of the total of 94 deaths from haemolymphopoietic cancers in all plants, 22 were coded to ICD 200 - lymphosarcoma and reticulosarcoma - 3 were reticular cell carcinoma, 10 were lymphosarcoma, 8 were malignant lymphoma and 1 was carcinoma of bone marrow.

In the study by Milham (8) 6 of 7 (86%) in the ICD 200 category were coded as other primary neoplasm of lymphatic tissue. In the multi-plant study there could have been 8 out of 22 (36%).

It was noted that 13 of the 22 deaths from NHL occurred in plants 1 and 11 where SMRs were 176.5 and 282.3 respectively and at plant 11 the SMR for potroom workers was 340.3 (p<0.05). These plants were both prebake.

In the Norwegian primary aluminium industry, there were fewer than expected deaths from cancer of the lymphatic system in both the "old" (O = 5, E = 6.2) and "new" (O = 7, E = 10.1) plants in the period 1953 -1979 (12). In a Norwegian prebake plant, there were 4 lymphoma (ICD 200-202) with a SIR = 196 for men with less than 3 years cumulative employment and 2 (SIR = 0.51) for men with more than 3 years of cumulative employment in the smelter (17). When all haematopoietic cancers were examined in relation to static magnetic fields, there was a higher SIR (2.79) in men with the lower magnetic field exposure than in men more highly exposed (SIR = 0.85).

In summary, the epidemiological study results present a very confusing picture. There is no single non-Hodgkin's lymphoma associated with the industry potroom or electromagnetic exposures. High risks are found in some prebake industries where CTPV exposures would be expected to be low. However, several of the studies involved the same or some of the same cases. There appears to be a widespread occurrence of slightly elevated rates of lymphohaematopoietic neoplasms. However, they appear to be significantly in excess only in prebake plants and primarily in Washington State.

The lack of specificity of risk to a disease subgroup detracts from the existence of a link with an environmental factor in the industry. The fact that several studies have identified small increases in the frequency of NHLs may in the future after detailed evaluation of tumour types and sites identify the existence of an increased risk of a more
specific entity. However, the present data are inadequate to confirm or even to speculate substantively on such a possibility.

Simonato (33) in 1981 concluded that "Data suggesting an association with.... and lymphomas do not however seem to be conclusive and require further confirmation." While more data have been gathered since, the question of non-Hodgkins lymphoma in this industry is still in need of further investigation.

**BRAIN CANCER**

While brain cancer has been raised as an issue for several years, the evidence for an increased risk of brain cancers in the industry is limited. Milham (8) reported a significant excess of benign brain tumours in prebake plant workers [O = 5, SMR = 391]. However the excess was restricted to the non-exposed workers. He also reported 2 deaths from brain cancer in exposed (carbon plant and potroom production-related) workers with 1.3 expected. In the Quebec industry, the SMR based on 10 brain cancer deaths was 9711. Benign tumours were not examined separately. Spinelli et al (13) reported an excess of brain and nervous system cancers for a SMR = 2.17 (O = 10). However, these were not related to their BSM exposure index or electromagnetic field exposure estimates, although these were noted to be crude. There was no increase in brain cancer or nervous system cancers reported from the prebake plant in Norway or US multi-plant study (9).

A difficulty in studying brain tumours is that they are often a secondary site for cancer. It is interesting to note that the original cases described by Milham were benign and these have not been reported by others. Clearly brain tumours, malignant and benign will receive further investigation, but on present evidence seem unlikely to be related to work in the primary aluminium reduction industry.

**LEUKAEMIA**

Milham (8) showed no clear increased risk in the prebake plant studied. Ronneberg and Andersen (15) observed only a slight increase [O = 5, SMR = 153] in persons exposed more than 3 years. Spinelli et al (13) found slightly increased mortality [O = 7 SMR = 175], but not morbidity. Andersen et al (12) reported an increase but no clear excess for mixed prebake and Söderberg plant workers. Gibbs (11) found no statistically valid increase in risk [O = 9, SMR = 112.4] in the Quebec smelters and Rockette & Arena (9) reported a slight increase in both prebake (O = 25 SMR = 127.6) and Söderberg [O = 11, SMR = 130.8] plants.

In summary, the evidence for an increased risk, especially in Söderberg plants is extremely weak. However, there appear to be consistent indications of slightly greater number of deaths from
leukaemia than expected but these may be chance observations. As chemically linked leukaemias are often associated with certain cell types, examining the various types of leukaemia may ensure that the consistent "blips" are not due to an increased risk for workers of developing one certain type of leukaemia.

**STOMACH CANCER**

Gibbs \(^{(11)}\) found a statistically significant increase in oesophageal and stomach cancer in workers "ever exposed to tar" in the Quebec cohort and an exposure-response relationship with tar-years of exposure but it was less clear with years of exposure and period from first exposure. Konstantinov mentioned stomach cancer in their studies. On the other hand increases in the risk of stomach cancer has not been reported by Spinelli et al (vertical Soderberg) \(^{(13)}\), Ronneberg & Andersen (prebake) \(^{(15)}\), Milham (prebake) \(^{(8)}\), Rockette & Arena (prebake and Söderberg) \(^{(9)}\) or Andersen (mixed Söderberg and prebake) \(^{(12)}\). The reason for the Quebec and Russian observations remains unknown.

**THE FUTURE**

The diseases and risks that we observe today have their origins in conditions of past high exposure. In addition cigarette smoking has been an important parameter. For some years to come the results of past exposure will contribute claims for worker's compensation. Claims may also arise for the cancer endpoints for which the current data are inadequate to make rational decisions as to cause. Carefully planned updates of the existing cohorts might go a long way towards clarifying many of these issues. From a prevention standpoint, it is very evident that for some of the cancers examined, if they prove to be linked with employment in the industry seems unlikely to be related to CTPV exposures. This can be resolved if reliable exposure estimates are included in the various studies and criteria for assigning workers into various groups well defined. Perhaps, some international agreement on criteria would greatly facilitate the interpretation of data from different sources.

Risk estimates based on additive or multiplicative models have rarely taken account of the effect of "quitting smoking" on risk. Changes in workplace exposures and smoking rates will impact lung and bladder cancer risks. Data to monitor these reductions and ensure that the predicted reductions are happening must be built into health monitoring programs today.

The studies of prebake plants have raised a number of important issues that must be resolved.
Finally, systematic epidemiological studies of workers in the modern prebake operations should be integrated into company health surveillance programs in a way that comparisons can be made with other companies and perhaps in some cases data combined. This will become increasingly important as cancer risks would be expected to be extremely low and small populations will be incapable of detecting risks even if they exist. For this reason, it may be necessary to conduct multi-centre studies.

The industry knows much more about its cancer risks today than 30 year ago. Unfortunately 30 years is approximately the latency of some cancers. Decisions made today need to be made on the basis of sound scientific knowledge to prevent cancers 30 years from now.

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13. HOW TO EVALUATE BENZO(A)PYRENE EXPOSURE IN COMPENSATION CLAIMS FOR LUNG OR BLADDER CANCER

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Alcan Smelters, 1955 Mellon Blvd., Jonquiere, Quebec, G7S 4L2, Canada.

SUMMARY

This morning you have received a benzo[a] pyrene-induced bladder cancer claim from one of your workers; yesterday you received a lung cancer claim from another worker. How do you deal with these? This paper shares Alcan’s experience - with emphasis on the practical aspects of managing either bladder or lung cancer claims in the Province of Quebec, Canada. The paper describes how to build a benzo[a]pyrene (B[a]P) exposure profile for such claimants. It also describes Alcan’s protocol for the early detection of bladder cancer. In conclusion, it indicates which elements are essential for success.

INTRODUCTION

In Quebec it is the Commission de la Santé et de la Sécurité du Travail (CSST) that deals with worker compensation claims. This organisation is the Quebec equivalent of a workers compensation board (WCB). The law “Loi sur les accidents et les maladies professionnelles” provides the legal framework (1).

Given that both lung cancer and bladder cancer are recognised as compensable diseases by the CSST, then Alcan has needed to develop a framework for the assessment of claims. Various epidemiological studies on employee health have been undertaken at Alcan since the seventies. It is not appropriate to describe them in this paper, but their results have provided a valuable input into the assessment process. Specifically, they have impacted upon the relationship between exposure to B[a]P, the disease and the compensation decisions of the CSST (WCB) (2,3).

Bladder cancer was recognised as a compensable disease by the CSST in 1986. It has identified two conditions that must be satisfied prior to a successful claim:

- Confirmation of the diagnosis of bladder cancer;
• A minimum level of work-place exposure to B[a]P equivalent to 19 B[a]P µg m\(^{-3}\) y\(^{-1}\).

A little later lung cancer was recognised as a compensable disease, by the CSST, in 1993. As for bladder cancer conditions are specified which must be satisfied for a successful claim:

• Confirmation of the diagnosis of primary lung cancer;
• An excess exposure to B[a]P as calculated using a matrix which takes account of both B[a]P years and the claimants smoking habits.

Given the frequency of tobacco-induced lung cancer in the working population it is necessary to establish the excess risk, due to B[a]P exposure, that is the “work-relatedness” of the lung cancer. The interaction between two principal factors are considered:

• Workplace tar (coal tar pitch volatiles - CTPVs) dose. CTPVs, which contain B[a]P, are generated in the process of the production of aluminium and constitute a risk factor directly related to work. B[a]P is the index of exposure employed to assess risk;
• Tobacco tar dose, expressed in pack-years: the use of tobacco is a personal pollution risk factor which is important, but unrelated to work.

RECONSTRUCTION OF JOB HISTORY

Following receipt of a worker’s claim for workplace B[a]P-induced lung or bladder cancer we must, as a first step, reconstruct the job history of the claimant. Our objective is to identify all occupations undertaken since employment commenced, their duration and all periods of absenteeism. Sometimes we have difficulties because we may have to retrace occupations back to the opening of the plant when records were poorer. Also, we have to consider all organisational modifications that could have impacted upon the workers exposure to CTPVs over the period of his occupation. Within Alcan the reconstruction of the worker’s job history is undertaken by the personnel department. For this purpose, it is very important to conserve all job-history data.

ALLOCATION OF B[A]P EXPOSURE LEVEL TO JOBS

Once the job profile history has been reconstructed then one must next allocate the appropriate exposure levels to each of the worker’s jobs.
These are then aggregated to provide an estimate to the total exposure of the claimant to B[a]P.

This is possible for jobs undertaken after the late 1970’s, because since this time B[a]P concentration / exposure data has been collected in our aluminium reduction plant. The industrial hygenists supply the claims department with the data required - these being kept on a computer system. However, for exposures prior to 1970 this is not possible because no environmental monitoring for B[a]P was undertaken. For such exposures a computer model is employed. This takes account of a variety of factors including:

- Processes and equipment employed, e.g., the introduction of drier anode paste and the computerisation of the production process;
- Workers schedule, including job task descriptions, personal data and the results of interviews;
- Engineering controls including ventilation, overhead crane modifications, the introduction of new generation mobile equipment and mechanisation;
- Documentation, including annual production reports, plant photographs, technical reports, engineering drawings and the company newspaper.

Data on these parameters (both measured and estimated) are fed into the computer which then generates an appropriate B[a]P exposure profile.

**EXPOSURE PROFILE**

After entering the appropriate data a B[a]P exposure profile is printed out for each claimant worker (example overleaf).

In this example, if the claimant had bladder cancer, he would have been compensable, given that the minimum exposure level stipulated for a successful claim is 19 B[a]P years.

If the claimant had made a case for compensation for lung cancer then a different procedure is used. This takes account of the claimants smoking history. After cases have been filed with the CSST, with the co-operation of the medical centre, we estimate the claimants exposure from cigarette smoke. We estimate how many pack-years he has smoked. We then consult the matrix presented in Table 1 and determine the probability of causation. It can be seen from this Table that if he had smoked 20 pack-years he would be compensable. On the other hand, if he had smoked 40 pack-years he would not be compensable.
PROFILE

BILAN (plant name)
No. of years at Alcan          39 year(s)    1 month(s)
No. of years - absenteeism    1 year(s)      11 month(s)

EVALUATION
27 years 5 months of exposure
19 years 9 months B[a]P

FORMULA

The following is the formula (as adopted by the CSST following the study of Armstrong and Thériault\(^{(4)}\)) upon which Table 1 is based. This formula was derived from epidemiological studies into the degree of lung cancer risk inherent in smoking cigarettes in the Quebec population, and the degree of lung cancer risk associated with B[a]P exposure in Quebec aluminium production workers.

\[
P = 1 + \frac{(0.0476 \text{ B}[a]P) \times 100\%}{(0.33 \text{ p-y}) + (0.0476 \text{ B}[a]P)}
\]

where \(P\) = probability that lung cancer was caused by exposure to CTPV (B[a]P) in \% (the upper 95\% confidence limit of the assessment used for risk increment), \(B[a]P = \mu g \text{ m}^{-3} \text{ y}^{-1}\) total career exposure to B[a]P, \(\text{p-y}\) = estimate of cigarettes smoked in pack-years.

EARLY DETECTION OF BLADDER CANCER

Our data are also used for the early detection of bladder cancer. Each year we update our list of workers who have attained a cumulative career exposure of 19 B[a]P years and are also 50 years of age or older. They are identified on a confidential list which is distributed to our medical officers. Then our doctors can make specific health examinations for detecting either pre-cancerous changes in the bladder or signs of early cancer - before it has reached an invasive stage.
Table 1
Percentage Probability that Lung Cancer Caused by Exposure to CTPV (B[a]P, µg m⁻³ y⁻¹): Linear Models

<table>
<thead>
<tr>
<th>BaP</th>
<th>Multiplicative Model</th>
<th>Additive Model</th>
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<tr>
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<tr>
<td>50</td>
<td>12.7 (5.5,20.8)</td>
<td>56.9 (34.6,70.4)</td>
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<tr>
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<td>22.6 (10.5,34.5)</td>
<td>72.6 (51.4,82.6)</td>
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<tr>
<td>150</td>
<td>30.5 (14.9,44.1)</td>
<td>79.9 (61.3,87.7)</td>
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<td>36.9 (18.9,51.3)</td>
<td>84.1 (67.9,98.5)</td>
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<td>250</td>
<td>42.2 (22.6,56.8)</td>
<td>86.9 (77.6,92.3)</td>
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<td>300</td>
<td>46.7 (25.9,61.2)</td>
<td>88.8 (76.0,93.5)</td>
</tr>
<tr>
<td>350</td>
<td>50.6 (29.0,64.8)</td>
<td>90.3 (78.8,94.3)</td>
</tr>
<tr>
<td>400</td>
<td>53.9 (31.8,67.8)</td>
<td>91.4 (80.9,95.0)</td>
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</table>

Additive Model

<table>
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<tr>
<th></th>
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<th>50PY</th>
<th>60PY</th>
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<tr>
<td>50</td>
<td>8.5  (3.6,14.4)</td>
<td>7.0  (2.9,12.0)</td>
<td>6.0  (2.5,10.3)</td>
<td>5.2  (2.1,9.0)</td>
<td>4.6  (1.9,8.0)</td>
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<tr>
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<td>15.7 (6.9,25.1)</td>
<td>13.1 (5.7,21.4)</td>
<td>11.3 (4.8,18.6)</td>
<td>9.9  (4.2,16.5)</td>
<td>8.8  (3.7,14.8)</td>
</tr>
<tr>
<td>150</td>
<td>21.8 (10.0,33.5)</td>
<td>18.5 (8.3,29.0)</td>
<td>16.0 (7.1,25.6)</td>
<td>14.1 (6.2,22.9)</td>
<td>12.6 (5.5,20.7)</td>
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<tr>
<td>200</td>
<td>27.1 (13.0,40.1)</td>
<td>23.2 (10.8,35.2)</td>
<td>20.3 (9.2,31.4)</td>
<td>18.0 (8.1,28.3)</td>
<td>16.2 (7.2,25.8)</td>
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<td>400</td>
<td>42.7 (22.9,57.3)</td>
<td>37.7 (19.5,52.1)</td>
<td>33.7 (16.9,47.8)</td>
<td>30.5 (14.9,44.1)</td>
<td>27.9 (13.4,41.0)</td>
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</table>
CONCLUSION

As you can see the occupational hygiene data that is collected by Alcan provides an extremely valuable resource for our organisation. They have many uses including: occupational health research; ill health prevention; early detection of occupational disease; processing CSST (WCB) claims. It follows that the company needs to carefully maintain the historical inventory of our plants. Without proper archives it would have been impossible to reconstruct B[a]P exposure levels for workers.

Communications between the various players is also of utmost importance. Hygienists, engineers, physicians, nurses, personnel officers and others must all be able to obtain and manage information. They must also respect the confidentiality rights of the workers, aim to further reduce workplace risks and handle any compensation claims in a just, equitable and respectful manner. Our experience has shown that the maintenance and proper management of reliable data is of paramount importance - good data is worth its weight in gold. So, perhaps it is time for you in your organisation to think about it!

REFERENCES

SUMMARY

While extrapolation from epidemiological studies of workers to the community has been quite widespread, limited attention has been given to the uncertainties and assumptions associated with extrapolation, other than those related to the shape of the dose-response relationship and risk estimation at levels well below those at which risk was initially measured.

This study has shown that there are many uncertainties and assumptions which must be made in extrapolating risks from a workforce to the general population. The gathering of additional data may permit closer definition of some of them and improve the reliability of risk estimates. Without an adequate consideration of these factors, extrapolations are likely to have little if any validity.

In relation to the specific example examined, assumptions and uncertainties should be quantified as carefully as possible, prior to using the lung cancer experience of aluminium smelter workers to assess community PAH related lung cancer risks. Most of these are likely to be of equal importance in any situation involving extrapolation from workplace to general population risks.

Experimentally based data could play an important role in extrapolating PAH related risks for persons exposed to one PAH profile to those exposed to another, also perhaps in targeting those PAH contributing most to risk. They, like proposals to estimate community cancer risks from smelter based risks must first examine the parameters affecting validity and the assumptions implicit in applying them to assess community risks.

INTRODUCTION

The increasing emphasis on environmental factors as determinants of disease has stimulated the demand for reliable methods of assessing risks for the public exposed to pollutants from specific sources. In practice, the direct measurement of community health risks is extremely
difficult and often impossible. Study populations (human or animal) of adequate size to measure risks of the order of $1 \times 10^{-6}$ increasingly discussed as "Society's norm" for chemical pollutants are rare or non-existent (1). As a consequence, risks can only be derived by extrapolation.

This report describes factors to be taken into account in such extrapolations. The estimation of polycyclic aromatic hydrocarbon (PAH) related lung cancer risks for the general population using risk estimates measured for PAH exposed aluminium smelter workers (2,3) will be used to illustrate some of these factors.

**ESTIMATES OF PAH RELATED LUNG CANCER RISKS**

Several lung cancer mortality studies in which workers have been exposed to PAHs have been used to derive public health risk estimates (4,5). Based on recent compilation and recalculation of risk estimates (6) risk estimates based on coal tar pitch exposed workers appear to fall in a relatively narrow range ($10^{-5} - 10^{-6}$ per ng m$^{-3}$ benzo[a]pyrene (B[a]P)). However, large differences in risk have been reported for PAHs from different sources. For example, Pott & Heinrich (7) estimated that the amounts of B[a]P inhaled to produce the same lung tumour rate of 1.6 - 1.7% were 100mg for coke ovens, 1mg for cigarettes and 0.1 mg for diesel exhaust. Thus lung cancer risks extrapolated from one incomplete combustion source to another could be quite wrong.

In light of the complexity of coal tar pitch volatiles (CTPVs), an approach increasingly proposed is to estimate risks using animal studies (8) and risk assessment grids taking account of individual compound carcinogenic potentials. Recently two approaches to risk estimation have been proposed in Ontario (9). One of these assumes that the potency of a PAH fraction is proportional to its B[a]P content. This assumption would appear to be fully in line with the recent findings of Gibbs (6) that there is not a major deviation in risk estimates for workers exposed to coal tar pitch derived PAHs from different sources. The other approach sums the risks attributable to each compound in the mixture based on potencies relative to B[a]P. Their analysis suggests that absolute risks differ between animal species, but are similar within an animal species. This would explain why attempts to validate animal derived risk estimates based on rodent potencies have uniformly failed. On this basis they have used rodent assays to estimate potencies in humans. Both these methods depend on the reliability of the epidemiological data.

The association between lung cancer mortality and an index of CTPV exposure in workers employed in aluminium smelters in Quebec
was first published in 1979 \(^{(10)}\). At that time, smoking was considered unlikely to explain the observed increased risk, but as smoking data were not available, they could not be taken into account in the analysis.

More recently, a case-cohort study of lung cancer was carried out extending the size, follow-up and exposure assessment of the previous study \(^{(2,3)}\). This study will be referred to as the "Armstrong study". The analysis concerned 338 lung cancer deaths and 1138 controls selected from the 16,297 persons in the cohort. This new study took smoking into account using data available in company medical records, and quantified PAH exposures using benzene soluble material (BSM) and B[a]P concentrations as exposure indices. The B[a]P concentrations were derived from extensive BSM measurements using a B[a]P/BSM ratio measured in the period 1976-1983 for each of 19 broad occupational groups. In line with the assumptions of other researchers, the authors considered B[a]P, as an indicator of PAH exposure to be "a priori" likely to be most related to lung cancer risk. After taking account of smoking, an increased lung cancer risk remained \(^{(2,3)}\). The results showed that the relative risk of lung cancer mortality increased with increasing B[a]P exposure. This latter finding provided the basis for considering the possible use of these study results in assessing PAH related lung cancer risks due to smelter emissions in the region.

**PREDICTION OPTIONS**

There are essentially three options available for predicting lung cancer risks for persons living in the region surrounding the aluminium smelter. While only one will be considered in detail in this report, all deserve mention. These use:

a. Risk estimates extrapolated from industries other than the aluminium industry (i.e., coke ovens, gas works etc.).
b. Experimentally derived estimates using animal carcinogenic potency models.
c. Lung cancer risk estimates for workers in the aluminium smelter \(^{(2,3)}\) with extrapolation to the community.

**EXTRAPOLATION FROM OTHER INDUSTRIES**

Extrapolation from other industries is not needed in this instance, as the data available for the aluminium smelter in the region is more substantial and immediately pertinent.
Experimentally derived estimates

If such a model, taking account of the PAH profile and carcinogenic potencies of the individual PAHs can be shown to provide reasonable predictions of risk for workers in the aluminium industry, the method may be helpful in several ways.

First, it may be possible to generalise results from one area with one PAH profile to another with a different profile by adjusting risk estimates to take account of PAH profile differences.

Second, a well-validated model might be used to directly derive human lung cancer risk estimates by combining the risk estimates for individual or key PAHs. The recent work in Ontario \(^9\) in combination with the finding of a similarity in risk estimates from coal tar sources \(^6\) suggests that such an approach is likely to be valid if based on ratios of PAHs to B[a]P. Importantly this approach might suggest the relative contribution of PAHs in the mixture to the overall risk; very useful information, at least for within-plant and perhaps external plant preventive purposes.

Third, the aluminium smelter study \(^2,3\) showed that the excess lung cancer risk for workers related well to a B[a]P exposure index. However, this alone, does not establish that B[a]P or associated PAHs are the etiological agents. An experimental approach may confirm or otherwise whether the lung cancer excess in the smelter is due, (at least in part) to the PAH exposures. In an extreme scenario, the excess risk in smelter workers could relate well to the B[a]P concentrations in the plant because the latter relate well to the profile of carcinogens present in the plant air. If these carcinogens were absent from outside air, it is easy to see that in-plant risk estimates based on B[a]P would be meaningless for community lung cancer risk assessment.

EXTRAPOLATION USING THE EXPERIENCE OF THE SMELTER WORKFORCE

This is a logical approach but requires careful evaluation of the assumptions and factors that must be taken into account when extrapolating from occupational to community settings.

Assumptions and uncertainties

Extrapolation involves the original studies on which occupational risk estimates are based, the population to which the risk is to be extrapolated and assumptions.
Reliability of in plant risk estimates

The Armstrong study \(^{(2,3)}\) probably provides the most comprehensive data in which B[a]P exposure estimates have been made and where smoking has been taken into account. Nevertheless, there are a number of important factors that have an impact on the reliability of the risk estimates derived from that study. While most of these were addressed in the study reports, \(^{(2,3)}\) key factors which must be critically evaluated before accepting the risk estimates include the reliability of the B[a]P exposure estimates; the reliability of the conversion of BSM to B[a]P indices; the errors associated with use of hybrid arithmetic and geometric mean concentrations and factors to "convert" these to arithmetic mean equivalents; the effect of respirator usage on actual exposures, the reliability of extrapolating exposures into the past, effects of exposure misclassification on the shape of dose-response relationships and risk estimates, temporal changes in lung cancer risks, smoking data reliability and the issue of additive or multiplicative smoking - PAH interactions \(^{(6)}\). Regardless of the validity of using these data to assess community risks, the assumptions and uncertainties associated with the risk estimates for the workers \(^{(3,4)}\) will need to be recognised in any risk extrapolated from them to persons living in the region.

Absolute and relative risks

In the case-cohort study \(^{(2,3)}\) the actual rates of disease cannot be directly calculated as risks are compared to the non-exposed workers whose risk is set at 1. Assumptions must be made that this risk of "1" is the same as that of some other non-exposed external population in order to calculate an absolute lung cancer rate. Armstrong et al., \(^{(3)}\) used both a lifetime risk of lung cancer of 9% and Quebec lung and all cause mortality rates for 1980-1984 to predict absolute risk levels in hypothetical populations exposed at various levels.

The risks for workers have been measured over an almost 30 year period (1950-88). During that time, there have been changes in lifetime lung cancer risks ranging from less than 1% in the early 1950s to more than 9% in the mid-late 1980's. Future lung cancer risks, might more closely match those based on present-day lifetime lung cancer risk estimates or be even lower as smoking rates diminish. It is evident that the choice of rate will affect the estimated risk. Using late 1980 rates will overestimate the actual risk of the cohort by approximately 25% when compared to the risk using the rate for the triennium containing the mean year of death for the persons in the study \(^{(11)}\).
An issue in epidemiology is always whether to use local, provincial or national rates. As Armstrong et al., estimated absolute risks using Canadian (2) and Quebec (3) rates with similar results, using one or the other is unlikely to give widely different results. However, under ideal circumstances, it is desirable to use the lifetime risk from lung cancer for the community in which the plant is located as this takes into account factors affecting the workers by virtue of living in the community. However there are several reasons why the use of such local data is difficult or even undesirable in this situation, even if they existed!

1. Lifetime risks of dying from lung cancer or age & sex-specific lung cancer rates are not usually calculated for small regions.

2. Many of the men living in the community work in the aluminium smelter. As a consequence, any increased lung cancer risk among workers in the smelter will be reflected in community rates if the workers make up a significant proportion of the community. In order to evaluate the likely impact of the plant on community rates over the years, it is necessary to know the proportion of workers by age/sex and exposure to the total community population.

3. Because a small region may have a small population size relative to a province or country, local rates if available may not be as reliable. It is possible to obtain an idea of the extent to which local rates differ from provincial or national rates by comparing the expected number of lung cancer deaths at the latter rates with the observed number of deaths.

This has been examined for Jonquiere and Chicoutimi, the main regions providing the workforce for the smelter (12). The results showed that lung cancer death rates in men were about 17% and 35% above death rates in the Province of Quebec respectively (6). This may reflect a high proportion of men who are at an increased risk of lung cancer from employment; from community exposure, from differences in smoking or other risk factors between the community and Province. These results provide an idea of the upper limit of the extent to which risks might be overestimated if Provincial male rates were used. This is an upper limit because approximately 33% of deaths in these two communities had worked in the aluminium smelter, so it was not possible to know whether the plant rate increased the community rate or vice-versa.

Women in Jonquiere and Chicoutimi had death rates from lung cancer higher than women in the Province of Quebec by approximately 32% and 19% respectively (6). As women did not work in potrooms, this
increased risk was most likely due to cigarette smoking. Women in this area are reported regularly smoking about 8% more often than women in Canada as a whole. If the risks in women had not been confounded by such unusual smoking rates or such a high proportion of the male deaths had not worked in the plant, the reference rate used in calculating absolute rates might have been scaled up or down to match the difference between the local and Provincial rates.

It should be noted that when the smoking rates of men in the community were compared with those of the workers studied by Armstrong et al., they showed that for the men the effect of smoking differences if anything would be small. The percentage of the 696 men in the Armstrong sub-cohort, who survived to 1983, were 40 years and over and had ever smoked was 84.5%. The percentage of men who had ever smoked in the community was 70.8% (CV 10.7%). As the mean age of the cohort was 66 and that the community sample was 57, this difference could well have been due to age differences. However, for women, the percentage of women who had ever smoked in the community was 46.6% (CV 17.3%). Estimates of lung cancer risk based on the Armstrong study (a male population) would be greatly overestimated if applied to women in the community (13, 6).

KEY FACTORS IN EXTRAPOLATION

The main factors involved in the production of an occupational or environmentally induced disease are: 1. The nature of exposure; 2. The level of exposure; 3. The duration of exposure; 4. The pattern of exposure; 5. The period from first exposure; 6. Individual factors such as hobbies, habits (e.g., smoking) which might enhance (synergism) or diminish (antagonism) the risk; 7. Pre-existing diseases, genetics, age etc. that might put the individual or group at greater or lesser risk.

The nature of exposure

The nature of exposure includes the chemical substances to which the workers are exposed; their chemical and physical properties (e.g., phase - vapour or particle, particle sizes, adsorption on other particles, bioavailability); their carcinogenic potency, initiating, promoting or other relevant properties of the substances; physical agents.

Chemical substances

As noted earlier, it has been assumed that B[a]P concentrations reflect the concentrations of other PAHs present in the air of the workplace. If risks are indeed increased, due to the concentrations of PAHs in the smelter atmosphere, it is important to know:
• if the profile of PAHs to which residents are exposed in the outside air is similar to that in the smelter.
• if, at least, key recognised carcinogens are not missing from the outside air which are present in the smelter atmosphere.
• the relationship between B[a]P and other workplace airborne substances which have the potential to enhance or reduce lung cancer risk.

The use of an index of exposure assumes that the index, if it is not specifically the "causal" agent, reflects, at least to some degree, the concentrations of the agents responsible for increasing risk. This is satisfactory when the most probable causal agent is known, where a dose-response relationship has been demonstrated and where the risk estimates are to be used to establish controls for the same work environment as that in which the risk was established. When extrapolating to other environments, it is important to know that the index of exposure used in the occupational setting is reflective of the same qualitative mix of agents in the general environment. At least two scenarios are possible:

• the index of exposure (eg: B[a]P) in the plant is highly correlated with the agents responsible for the increased lung cancer risk, eg: certain high molecular weight PAHs.

The fact that prebake workers who are not highly exposed to PAHs do not appear to have the same risk of lung cancer but are also exposed to several of the same agents other than B[a]P and PAHs is supportive of such an aetiology.

• the index of exposure (eg: B[a]P) in the plant is highly correlated with the agents responsible for the increased lung cancer risk, which may be PAHs or other agents to which workers are exposed or PAHs whose effects are modified by the other substances or agents present.

This is not far-fetched, because B[a]P concentrations may reflect close contact with the electrolytic cells and certain jobs involving fluoride and heat exposures. Indeed, all other CTPV populations studied such as coke oven gas workers are exposed only to the distillates of coal plus heat. In an aluminium smelter exposures can include, CTPV's with PAHs and heterocyclics, sulphur dioxide, fluorides in various forms, alumina dust, carbon monoxide, carbon dioxide, coke/carbon and in the past, exposure in some jobs to asbestos\textsuperscript{(14,15)}. 

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Are the PAHs inside the plant attached to particles while those outside are not, whereby modifying their bio-availability? Some PAHs present in particulate form may not be in that form when at low concentrations such as in community air, which may have an important impact on the distribution of the dose in the lung. If not known, the assumption is made that differences inside and outside the plant do not influence lung cancer risk. This may be erroneous. If the agent(s) change (e.g., oxidised), persons outside the plant would be exposed to different chemicals than those within the plant.

Information is needed concerning the situation inside and outside the plant, to identify differences that may have significance in relation to enhancing or reducing lung cancer risks.

Physical agents

Workers at higher risk for lung cancer have been exposed to heat and low humidity. These might be hypothesised as changing the extent to which workers might breath in particles/vapours. While no data currently exist to suggest any relevance to lung cancer risks, workers in the plant are exposed to electric and magnetic fields and in the past, many of them to vibration. Most physical factors will not be present in the external environment at least not as the result of smelter activities.

LEVEL OF EXPOSURE

The validity of extrapolating risk estimates from one population to another population depends on:

- The validity of the exposure assessments and risk estimates for the working population studied;
- The shape of the dose-response relationship between the chosen "index of exposure" and the disease outcome, in this case lung cancer;
- The evidence in support of extrapolating from high exposure levels to low exposure levels.

Validity of exposure assessments

In the aluminium smelter study (2,3), exposures were analysed as cumulative lifetime exposures and recalculated as average exposures over a 40 year period using B[a]P and BSM indices. The appropriateness of these indices, precision of exposure assessments, measurement errors, changes in B[a]P / BSM ratios over time etc. should be part of a detailed critique of the study methodology.
The fact that lung cancer risks increased with increasing cumulative B[a]P BSM indices suggests validity. This is perfectly adequate for demonstrating exposure-response relationships within the smelter. However, the question is how reliable are the exposure assessments as the basis for establishing absolute levels of exposure for control purposes. Limitations in measurements and confidence in the exposure estimates in absolute terms should be identified and clearly stated as a caveat affecting any extrapolated risk estimates.

**Shape of the exposure-response curve**

Armstrong *et al.*, (2,3) attempted to fit their exposure-response data to a number of curves. Their conclusion is that the data fit both a linear and a power curve. However, they were not able to distinguish which was the better predictor of risk. The problem is that the power curve will estimate greater risks per unit exposure at low concentrations than at higher ones. Even at concentrations of 0.1 µg m\(^{-3}\) B[a]P the predicted risks are 6 fold greater than predicted by a linear model.

It seems unlikely that risks at low levels of exposure will be the same as those at higher levels, as the body is efficient in removing particles from the lung. Pharmacokinetic considerations and indeed DNA repair mechanisms would also be expected to be working at low levels where risks would be virtually eliminated. This is contrary to the power model concept. The possibility of an S curve might also be considered, that is, no detectable risk below a certain level, a high risk per unit exposure that diminishes reaching a plateau at which risk is not increased further. This might be compatible with what we know about smoking and other risks where 100% of the population is never affected even when they are very heavy smokers. The data are inadequate in the opinion of this author to adopt a non-linear model unless clear pharmacokinetic or other mechanistic reasoning supports such a model.

A second major difficulty lies in the fact that risks have been measured at high concentrations where risks are high. For example, the estimated lifetime lung cancer risk of employees with past exposure as high as 20,000 ng m\(^{-3}\) B[a]P was 20.2%. One of the highest 1992 concentrations of B[a]P in the area surrounding the smelter, based on results from a sampling station where the profile of PAHs was similar to that of the smelter emission (16,17) was 7.5 ng m\(^{-3}\) (annual arithmetic mean) and 1.8 ng m\(^{-3}\) (annual geometric mean) (6).

The actual environmental concentrations are also about 1/50th of the lowest concentration category for which risks were measured in workers (100 ng m\(^{-3}\)). This raises the serious question about the shape of the curve below the bottom end of the measured dose-response curve. It might be noted also that even within exposure response curves for...
Occupationally exposed workers, confidence intervals surrounding risks measured at low concentrations are already considerably wider than those at high concentrations - adding to the uncertainties.

Extrapolation using a linear model has been an accepted method of dealing with PAH risk estimates. However, it must be remembered that the uncertainty increases with the extent to which the extrapolation is extended below measured levels. A recent meeting on linear extrapolation (18) made it evident that the possibility of a threshold cannot be ruled out even though a linear exposure-response extrapolation may be used for convenience.

**Arithmetic vs. geometric mean conversions**

Ideally inhalation exposure estimates should be expressed as arithmetic means (19). In the Armstrong study, a hybrid of arithmetic and geometric means was used. As these will not strictly reflect the concentration of BAP inhaled that is essential for community risk extrapolation, the exposures must be adjusted to provide data in a form for such analyses. The conversion factors mentioned in the study report would increase the exposure estimates based on geometric mean exposures by about 17%.

**DURATION OF EXPOSURE**

The maximum duration of exposure of workers is limited to 8 or 12 hour shifts worked over at most a working life-time of 50 years. In most instances the duration of exposures are less and in the Quebec smelter the mean number years of service was 26.96 (standard deviation = 10.82).

In the analyses that have been carried out, the importance of exposure has been examined as cumulative exposure. It is not known whether the excess risk is being mainly predicted by duration or by level of exposure. In fact the dose rate was shown not to be a statistically significant additional contributor to risk (2). Whether this is because this factor was already taken into account in the cumulative exposure computation is not clear. If it was not, this might suggest that duration of employment is a very important exposure variable.

Duration of employment in the Söderberg pots and carbon plant both produced significantly elevated rate ratios even after taking account of smoking. The fact that rate ratios for workers with less than 20 years of employment in either the potrooms or carbon plant were of the same order of magnitude as for prebake potroom workers, in all categories of years of exposure, suggests that very long term employment may be necessary to increase risk. This does not appear to be a latency effect as no clear latency effect was observed in the study. This prompts the question as to whether the risk associated with long exposure to low
levels is indeed equivalent to short periods of exposure at high concentrations.

This becomes important because the major determinant of the cumulative exposure at low levels of exposure such as encountered by the public will be duration, while for workers, the level of exposure will be the significant contributor. For example a lifetime exposure for a member of the public involves 40 years of 24 hour exposures. A worker in the smelter could theoretically acquire such the same cumulative B[a]P equivalent in a few months. Extrapolation on the basis of a lifetime cumulative exposure or average lifetime concentration model, involves a clear assumption that long term low level exposures carry the same risk as short term high level exposures (6).

An assumption routinely applied in the literature (in tune with a cumulative exposure model) is that the total quantity of B[a]P or PAH inhaled is responsible for the increased risk. In order to determine this "total quantity" for workers and for the general public several assumptions are possible:

- Workers and the general public breathe in the same volumes of air per day;
- Workers breathe in more air per day during their working hours. Members of the general public are assumed to inhale 23 cubic metres of air per day and a hard working worker, 10 m$^3$ of air over an 8 hour work day.

The cumulative exposure-lung cancer relationships make no allowance for breathing rate as it is irrelevant for internal plant use (unless there are major differences in breathing levels between workers on different jobs). Various studies have used different breathing rates. This could have an important effect on risk estimates when the results are extrapolated to the public.

A second "duration of exposure" consideration is duration of residence in the community. The selected duration of exposure in the community is a basic assumption. It could be based on criteria such as community life expectancy or the real residency times of people in the region that would make estimates more realistic.

A 24 hour exposure is usually assumed for the general public. This assumption means that all people for their whole lives are considered to be exposed continuously to the external air pollutant levels 24 hours per day. This is probably a gross overestimate of exposure as some persons work in buildings or homes with air cleaners and spend some of their lifetime outside the region.
PATTERN OF EXPOSURE

If very high exposure to particles occur, the lung may become over burdened with particles, called overload, and particles may not be removed from the lung. The metabolism of a compound may be such that if the load exceeds the amount that the body can adequately detoxify, then there may be an accumulation of a toxic agent in the lung/system. This depends on assumptions concerning the actual carcinogen and the pharmacokinetics for the class of compounds suspected as responsible for the lung cancer. These factors are not likely to be important for community residents. However, if the mechanism of disease causation in workers were related to such an effect, extrapolation to the community would be in doubt.

PERIOD FROM FIRST EXPOSURE TO DISEASE OUTCOME (LATENCY)

In their report (2), Armstrong et al., suggest that there was no evidence for latency. However in their published report (3), they noted the possibility of a long latency. Exposure in the last 10 years prior to death did not give rise to a significant excess of lung cancer, while exposure in the last 20 years and especially in the last 40 years did. This might be interpreted as showing a latency of at least 10 years and probably longer which would fit more closely with conventional wisdom.

The use of a latency or lag period, would potentially reduce the period of exposure of workers, increasing their risk per unit exposure and reduce the exposure of the public and taken into account in any risk estimate. The adoption or otherwise of a latency period and the length of that latency period on present evidence will involve an assumption which will affect estimated risk.

Relationship between latency and exposure level

The period from first exposure to cancer occurrence is important in assessing the practical impact of a risk. For example, if persons exposed to low levels of carcinogen took longer to acquire their cancer than persons of the same circumstances exposed to high levels of carcinogen, then it would be reasonable to anticipate levels of exposure such that the period since first exposure would be sufficiently long that any excess lung cancers would not be seen during life. Such a situation appears to exist for mesothelioma and certain asbestos exposures. This remains to be investigated.
INDIVIDUAL FACTORS

The importance of smoking lies in the extent to which smoking has contributed to the excess cancer in the plant and impact on the workforce and public in the face of changing smoking rates. Two questions might be asked:

- Does the population used as the background rate for establishing absolute risk have the same smoking habits as the aluminium smelter workforce studied? Differences in smoking histories would lead to the underestimation or overestimation of absolute risk for the workforce due to smoking effects alone.
- Are risks multiplicative or additive for smokers? The study by Armstrong was unable to determine whether the interaction between smoking and CTPV exposures was additive or multiplicative for the lung cancer risk. Without this information, assumptions will need to be made, which depending on the approach taken could lead to errors in the estimation of risk for smokers and for the community.

If smoking and CTPV risks are additive, calculation of the real excess risk for workers due to CTPV exposure would be straightforward if the risks for non-smokers can be determined. This excess cancer risk would then be directly extrapolatable to the community as an additional risk due to PAH or CTPV exposures. Unfortunately the data to date have proven inadequate to evaluate the risk for non-smokers.

If risks are multiplicative, then the observed excess risk is reflective of the smoking habits of the workforce and the interactions between their smoking and CTPV exposures. The use of these data will only reflect the community lung cancer risk if the smoking habits of the community are the same as those in the smelter and if the multiplicative model is valid at all levels of exposure.

In the absence of information, assumptions about the smoking histories of residents compared to workers, whether the interaction of smoking and CTPV exposures are additive or multiplicative, the risk for non-smokers will need to become assumptions.

There has been a decline in smoking and a move towards low tar cigarettes. In view of this, risks for the future would be expected to be considerably less on a multiplicative model than would be extrapolated from the workforce experience. An assumption has been implicit, that the risk of smoking cigarettes today and the future is the same as in the past.
PRE-EXISTING DISEASES ETC.

When the general population is used to establish background rates, one must recognise that this population is already a population which is likely to have a less favourable health experience than that of an industrial population. This is because it contains people who are unable to work because of illness, people in hospital etc. As a result, the baseline experience is generally worse than that of unexposed workers and even exposed workers - this is known as the healthy worker effect. This will affect the absolute risk assigned to the CTPV exposures. The extent of this effect for lung cancer is really not known.

The risk estimates based on the Armstrong study are derived from a study of male workers. Direct extrapolation to the community would assume no sex differences in the risks associated with CTPV exposures. It would also assume that the persons living in the community do not have other risk factors that might enhance or diminish risk. An example of such a factor might be other occupational exposures that may put them at a higher risk of lung cancer.

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SUMMARY

A study of the cancer incidence within the environs of Norwegian aluminium smelters was undertaken. Compared to the national average, no increased incidence of any form of cancer was found in the register-based cancer incidence study for the populations resident within aluminium plant municipalities.

INTRODUCTION

The research described in this paper was undertaken by Alf Rønneberg as a part of a study concerning the Norwegian aluminium industry and the effects of its emissions on the local environment. The paper is based on Alf Rønneberg’s evaluation.

As early as 1959 it was suggested that employees in the Norwegian aluminium industry might run a greater risk of developing lung cancer as a result of exposures to coal tar pitch volatiles (CTPV) containing considerable amounts of carcinogenic PAHs. During the years since 1959, several epidemiological studies have been performed both in Canada, Norway, USA and in other countries. Altogether 47,000 workers at 35 aluminium plants in five countries have been included in epidemiological studies. These studies have revealed a definite connection between exposure to coal tar pitch volatiles and an increase of cancer in the urinary bladder. A higher incidence of lung cancer also seems to be documented.

The question has, therefore, been raised whether people who live near aluminium plants, and who are thus exposed to small amounts of such substances, may constitute an at risk group.
METHODS OF RISK ASSESSMENT

In this study, two approaches were used to evaluate the potential risk. First, data from the cancer registry was used to chart the incidence of different types of cancer in municipalities with an aluminium plant. Second, an indirect approach was used to estimate the potential increase in cancer risk by extrapolation of the dose-response relationship from high exposed occupational groups to the much lower exposed residential population living near the aluminium plants.

CANCER STATISTICS FOR THE NORWEGIAN ALUMINIUM PLANT MUNICIPALITIES

Environmental factors may influence the incidence of most types of cancer. Of these, smoking probably has the greatest impact, but diet and pollutants may also be of importance. Cancer statistics for the communities around four of the existing Norwegian aluminium plants (Høyanger, Årdal, Sunndal and Mosjøen) which have been in operation for more than 30 years, was studied. The communities around the other three aluminium plants in Norway (Lista, Husnes and Karmøy) were excluded as they had been in operation for a shorter period than the time it usually takes for the relevant types of cancers to develop.

The observed and expected number of new cancer cases diagnosed in men and women between 1960 and 1991 were compared. The expected numbers were calculated from national age and sex specific incidence rates.

Table 1 shows the number of observed and expected cases of cancer in the aluminium plant municipalities between 1960 and 1992. The comparison showed that the incidence of cancer as a whole, in both men and women, was lower in the aluminium municipalities than in the rest of the country. Lung cancer among men and stomach cancer among women were significantly lower in the aluminium plant municipalities than in the rest of the country. The incidence of other types of cancer was as expected. The study did not show any unusually high incidence of cancer in children.

ESTIMATION OF RESIDENTIAL CANCER RISK DUE TO PAH IN AMBIENT AIR

Although no unusually high incidence of any form of cancer compared to the national average was found in the register-based study, the
possibilities cannot be excluded that PAH emissions do contribute to cancer risk. The alternative approach was to estimate the potential increase based on the increased incidence of cancer found in high exposed occupational groups, using a linear dose response model.

The PAHs represent a large group of substances occurring in pitch volatiles, some of which have been classified as probably or possibly carcinogenic for human beings (CPAH). One does not know for certain the etiological agents, so for the time being, and for practical reasons, benzo(a)pyrene (B[a]P) is often used as an indicator of CPAHs in the working environment, in the ambient air or in food.

**Table 1.**

**Number of Observed and Expected Cases of Cancer in the Aluminium Plant Municipalities Between 1960 and 1992.**

<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Obs.</td>
<td>Exp.</td>
</tr>
<tr>
<td>All cancers</td>
<td>1598</td>
<td>1754</td>
</tr>
<tr>
<td>Stomach</td>
<td>140</td>
<td>164</td>
</tr>
<tr>
<td>Intestines</td>
<td>234</td>
<td>224</td>
</tr>
<tr>
<td>Lung</td>
<td>156</td>
<td>201</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>125</td>
<td>114</td>
</tr>
<tr>
<td>Cancer among children</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;15 year</td>
<td>21</td>
<td>19</td>
</tr>
</tbody>
</table>

* Less than 1% probability that the differences between observed and expected is by chance ** RR = Relative Risk = Observed/Expected

In the working environment, exposure to potentially carcinogenic substances is far greater than in the ambient air, often 100-1000 times greater. If there is any risk connected with certain substances there is, therefore, a better chance of detecting it in a highly exposed industrial population than in the general population.

Table 2 shows some levels of B[a]P in the working environment and in ambient air. In the past, exposure to B[a]P in many of the plants included in the studies was 20-50 times as high as that found in modern Söderberg potrooms. Concentrations of B[a]P in the
ambient air in the aluminium plant municipalities were also considerably higher in the past.

A group of Canadian researchers led by Ben G. Armstrong carried out an extensive survey of aluminium workers in the province of Quebec, Canada and arrived at a relationship between dose (concentration of B[a]P in the working environment length of employment) and relative risk of bladder cancer and lung cancer \(^{(6 - 8)}\). By correcting this for the difference in degree of exposure between workers in the industry and the local community, an attempt was made to calculate the risk to people living near the aluminium plants.

Table 3 shows the lifetime risk of cancer of the bladder and lung in aluminium municipalities in Norway and Table 4 the estimated number of excess cancers in the aluminium plant municipalities during one decade.

### Table 2
Concentration of Benzo(A)Pyrene (B[a]P) in the Working Environment and in Ambient Air (ng m\(^3\))

<table>
<thead>
<tr>
<th>Working environment</th>
<th>B[a]P (ng m(^3))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Söderberg potrooms before 1980</td>
<td>5,000 –50,000</td>
</tr>
<tr>
<td>Söderberg potroom 1990-</td>
<td>250-1000</td>
</tr>
<tr>
<td>Prebake potroom 1990-</td>
<td>50</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ambient air</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Aluminium municipalities 1960</td>
<td>4-30</td>
</tr>
<tr>
<td>Årdal 1990</td>
<td>6</td>
</tr>
<tr>
<td>Aluminium municipalities 1990</td>
<td>2</td>
</tr>
<tr>
<td>Norway 1990</td>
<td>0.1-1</td>
</tr>
</tbody>
</table>

The risk estimates indicated an increase in absolute lifetime risk of approximately 0.02 - 0.05% for cancers of the lung and bladder due to exposure to PAH in the ambient air near aluminium smelters. This risk may result in one excess case of cancer of the bladder in 30 years for men and one in 100 years for women. The corresponding figures for lung cancer are one case in 100 years for men and one in 300
years for women. By comparison, 200 - 220 cases of these forms of cancer will occur regardless of ambient PAH exposure, every decade, in the aluminium municipalities, if they follow the national average hereafter.

Table 3

Lifetime Risk of Cancer of the Bladder and Lung in Aluminium Plant Municipalities in Norway. Based on the Exposure Level, the Age Distribution and the Population Size as in 1990, the Norwegian Average Mortality and Cancer Incidence in 1988 and Armstrong’s Linear Dose-Response Model\(^{(6 - 8)}\)

<table>
<thead>
<tr>
<th>Type of Cancer</th>
<th>Lifetime risk for the Norwegian population</th>
<th>Excess risk with B[a]P exposure of 2 ng m(^{-3}) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer of the bladder</td>
<td>2.92%</td>
<td>0.016% (0.006-0.037)</td>
</tr>
<tr>
<td>Cancer of the lung</td>
<td>4.71%</td>
<td>0.004% (0.002-0.007)</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer of the bladder</td>
<td>1.02%</td>
<td>0.006% (0.002-0.013)</td>
</tr>
<tr>
<td>Cancer of the lung</td>
<td>1.76%</td>
<td>0.001% (0.001-0.003)</td>
</tr>
</tbody>
</table>

These estimates are based on multiple assumptions that make the estimation results prone to error. Some of the most important and debatable assumptions are the following:

- The results from the studies upon which the dose-response relationship is based are valid and transferable to the residential population;
- The exposure is qualitatively similar in the high exposed occupational group and in the low exposed residential population;
- The linear-risk model applied is relevant for the relationship between exposure, dose and effect;
- There is no safe level of exposure.
CONCLUSIONS

Compared to the national average, no increased incidence of any form of cancer was found in the register based cancer incidence study for the aluminium plant municipalities.

The risk estimation indicated an increase in absolute lifetime risk of 0.02 - 0.05% for cancers of the lungs and bladder due to exposure from PAH (B[a]P = 2 - 6 ng m\(^{-3}\)) in the ambient air near aluminium smelters. These estimates also suggest that cancer risk associated with environmental PAH exposure at this level is too small to be detected in an epidemiological study.

It must be emphasised that there are great uncertainties attached to these estimates, and the validity of extrapolating such a dose-response relationship from high to very low concentrations is questionable. However, it seems to be the best method available for estimating such risk. Despite uncertainties, one can probably conclude that the increase in risk is low.

### Table 4.
Estimated Number of Excess Cancers in the Aluminium Plant Municipalities in Norway during One Decade. Based on the Exposure Level, the Age Distribution and the Population Size as in 1990, the Norwegian Average Mortality and Cancer Incidence in 1988 and Armstrong’s Linear Dose-Response Model\(^6\)\(^-\)\(^8\).

<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>Expected number of cancers</th>
<th>Excess cancers B[a]P =2 ng m(^{-3}) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer of the bladder</td>
<td>60.9</td>
<td>0.3 (0.1 – 0.8)</td>
</tr>
<tr>
<td>Cancer of the lung</td>
<td>94.6</td>
<td>0.1 (0.0 – 0.1)</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer of the bladder</td>
<td>18.1</td>
<td>0.1 (0.0 – 0.2)</td>
</tr>
<tr>
<td>Cancer of the lung</td>
<td>34.8</td>
<td>0.0 (0.0 – 0.1)</td>
</tr>
</tbody>
</table>
REFERENCES

SUMMARY

For epidemiological studies it is often necessary to determine the incidence / prevalence of disease as a function of exposure to a potential toxin over a long period. However, in many industrial situations data for some years of exposure are missing. This paper describes a method to estimate past area concentrations of fluorides and PAH in VSS-potrooms, as a supplement to traditional methods, using statistical modelling based on process parameters.

INTRODUCTION

In retrospective epidemiological investigations, exposure often has to be assessed in total or partial lack of representative measurement data. The use of multiplicators, subjective evaluation and extrapolation of measurement data has traditionally served as methods to estimate probable levels of exposure in such cases \(^{1-4}\). An alternative may be to use process data to indicate levels of exposure in the pre-measurement period \(^{4-7}\). The aluminium smelters have traditionally recorded various process data throughout their period of operation. In the present study we wanted to find out whether such data could be used to estimate the area concentration of polycyclic aromatic hydrocarbons (PAHs) and fluorides in vertical stud Söderberg (VSS) potrooms before industrial hygiene monitoring started.
MATERIALS

This study concerns three Norwegian aluminium smelters. The first has operated at Sunndal from 1954, the second at Årdal since 1948 (VSS-potrooms since 1959) and the third at Mosjøen since 1958.

Industrial hygiene measurements collected routinely in the VSS potrooms at the three smelters included about 9,000 area samples of total fluorides and 2,500 samples of particulate PAH. Area concentrations of total fluoride (gaseous + particulate) have been monitored at the Sunndal smelter since 1961, at the Mosjøen smelter since 1980 and at the Årdal smelter since 1962. PAH has been sampled routinely since 1980 at the Sunndal smelter and since 1978 at the Mosjøen smelter. There also exists measurement data of benzene soluble material (BSM) from the Sunndal smelter sampled in 1956 - 58, in 1964 and in 1971 - 72. These latter measurements were transformed to PAH estimates based on parallel sampling of PAH and BSM at a fourth Norwegian VSS-smelter at Høyanger. The fraction of PAH in BSM was estimated to 160 µg PAH per mg BSM.

Particulate fluorides had been collected on membrane filters. Hydrogen fluoride had been collected in an absorption bottle with an alkaline solution or on a filter impregnated with sodium formiate. Fluorides had been analysed by Willard-Winther distillation followed by filtration with thorium nitrate until around 1970, when this method was replaced by potentiometry with ion-selective electrodes. PAH samples had been analysed by thin-layer chromatography and gas chromatography, and the BSM samples had been analysed by gravimetric methods.

The aluminium smelters have recorded various process data. We were restricted to use the ones recorded from the start of operation for the VSS-potrooms included. Table 1 shows the process parameters used in the analyses.

METHODS

We used the proportion of cells in operation (operating rate) as an indicator of production volume and defined a dummy variable for each potroom to account for differences in ventilation rates, sampling strategy and other differences specific for each potroom. Dichotomous variables were also defined based on the method used for crust breaking (pneumatic hammer or wheel breaker) and for periods with poor ventilation. The specific consumption of fluorides and anode paste, the average cell age, the current efficiency, and the relative change in current from the previous year were also included in the analyses. We restricted our analyses to the operation period before 1986 to assure relatively stable process conditions. After 1986/87 the industry converted
to dry anode-technology, which led to major changes in the process conditions and to reduced emissions in the potrooms.

The association between process parameters and area concentrations in VSS-potrooms in the three smelters was investigated by multivariate linear regression using the statistical software package SPSS for Windows v 6.

The natural logarithm of the arithmetic mean of area concentration was used as the dependent variable, since this transformation produces a multiplicative effect for each of the process parameters and prohibits negative estimates. The regression analysis was performed by the stepwise entering and removal of variables. Each model's explanatory value was assessed through the coefficient of determination (adjusted $R^2$). The level of significance was set at $p<0.05$ for entering a variable and at $p>0.1$ for removing a variable.

For validation and sensitivity analyses of the model we removed 25% of the observations at random and ran the regression on the remaining 75% to gain new prediction coefficients for the model. Based on these new regression coefficients we predicted the concentrations for the 25% of observations removed. The predicted concentrations were plotted towards the actual measured concentrations and Pearson's correlation coefficients were calculated. The procedure was repeated ten times, each time randomly removing 25% of the sets of observations.

### Table 1.
Annual process parameters and transformed variables used in the regression analyses

<table>
<thead>
<tr>
<th>Process parameter</th>
<th>Unit</th>
<th>Transformed variable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consumption of raw materials</td>
<td>kg fluoride per t Al</td>
<td>Specific fluoride consumption</td>
</tr>
<tr>
<td>Cryolite + AlF$_3$ + CaF$_2$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anode paste</td>
<td>kg paste per t Al</td>
<td>Specific anode consumption</td>
</tr>
<tr>
<td>Production data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of cells in operation</td>
<td>(ratio)</td>
<td>Operating rate</td>
</tr>
<tr>
<td>Number of relined cells</td>
<td>(ratio)</td>
<td>Proportion of cells relined</td>
</tr>
<tr>
<td>Average age of active cells</td>
<td>Year</td>
<td>Age of cells</td>
</tr>
<tr>
<td>Energy parameters</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ratio between actual and theoretical metal production</td>
<td>(ratio)</td>
<td>Current efficiency</td>
</tr>
<tr>
<td>Cell current</td>
<td>kA</td>
<td>Proportional current change</td>
</tr>
</tbody>
</table>
RESULTS

Table 2 describes the regression models developed for the prediction of area fluoride concentration and area PAH concentration in the VSS-potrooms.

<table>
<thead>
<tr>
<th>Agent (number of observations)</th>
<th>Coefficient of determination (adjusted $R^2$)</th>
<th>Explanatory variables</th>
<th>Regression coefficient</th>
<th>Standard error</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAH (n=29)</td>
<td>0.66</td>
<td>Specific anode consumption</td>
<td>0.011</td>
<td>0.002</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Poor ventilation</td>
<td>0.44</td>
<td>0.10</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(constant)</td>
<td>-0.82</td>
<td>1.05</td>
<td>0.44</td>
</tr>
<tr>
<td>Fluorides (n=79)</td>
<td>0.76</td>
<td>Current efficiency</td>
<td>-7.20</td>
<td>1.05</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pneumatic crust breaking</td>
<td>-0.38</td>
<td>0.09</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Proportional current change</td>
<td>4.58</td>
<td>1.44</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Operating rate</td>
<td>1.60</td>
<td>0.38</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Poor ventilation</td>
<td>0.39</td>
<td>0.11</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Potroom EAM 3-5</td>
<td>0.53</td>
<td>0.06</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Potroom HA-Su 1/2</td>
<td>0.83</td>
<td>0.11</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(constant)</td>
<td>4.10</td>
<td>0.98</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

The PAH model explained 66% of the variation in the area PAH concentration. In the sensitivity analyses of the PAH model the correlation coefficient (Pearson's $R^2$) between the observed and
predicted values (in the original scale) varied between 0.69 and 0.95 with a mean of 0.85 for the ten runs.

The fluoride model explained 76% of the variation in the area fluoride concentration. In the sensitivity analyses of the fluoride model the correlation coefficient (Pearson’s $R^2$) between observed and predicted values (in the original scale) varied between 0.81 and 0.87 with a mean of 0.84 for the ten runs.

In Figure 1 the predicted levels of PAH are compared with the actual measured levels of PAH for the Sunndal plant. In Figure 2 the predicted levels of fluorides are compared with the actual measured levels of fluorides for the Sunndal plant.

Pearson’s correlation coefficient = 0.91

**Figure 1.** Predicted levels of area concentration of PAH (µg m$^{-3}$) compared with measured levels for the VSS potrooms at the Sunndal smelter.

**DISCUSSION**

Emissions of pollutants into the atmosphere of a potroom depend on many factors. Potential explanatory variables are those related to material balances, ventilation, process temperatures, type of equipment
used, material handling, maintenance and cleaning. The experience and the motivation of the workers and their way of handling materials and equipment are also of importance.

In this study we intended to predict area concentrations in periods with no industrial hygiene data. The available data were restricted to the ones recorded for economical and technical reasons. As a consequence, we were not free to choose the explanatory variables that might be considered most important according to an á priori analysis of the anatomy of the emission process. We did not necessarily expect to identify causal relationships between process parameters and area concentrations, but hoped to find parameters that correlated with area concentrations. Based on these restrictions our explanatory variables might reflect some, but certainly not all, of the variations in the area concentration in periods without measurements. The sensitivity analyses indicated that the models were robust at least in the investigated period. The validity of extrapolating such models over time is, however, uncertain due to a multifactorial relationship between emissions and the running conditions at the potrooms. A relatively stable process technology is therefore necessary for extrapolation of such models over time.

![Figure 2. Predicted levels of area concentration of fluoride (mg m$^{-3}$) compared with measured levels for the VSS potrooms at the Sunndal smelter.](image)

Pearson's correlation coefficient = 0.57

Figure 2. Predicted levels of area concentration of fluoride (mg m$^{-3}$) compared with measured levels for the VSS potrooms at the Sunndal smelter.
To estimate job specific exposure, the estimates of area concentration have to be supplemented with knowledge about the association between personal samples and area concentrations. If one assumes that the ratio between job specific exposure and area concentration remains constant over time, this ratio may be used to estimate job specific exposure in periods where only estimates of the area concentration exist.

CONCLUSIONS
Statistical modelling based on process parameters may serve as a method to estimate past area concentrations of fluorides and PAH in VSS-potrooms as a supplement to traditional methods.

REFERENCES

17. OCCUPATIONAL ASTHMA: OVERVIEW AND MANAGEMENT

Thomas V. O'Donnell
Physician Consultant to Comalco, 32A Simla Crescent, Wellington, New Zealand.

SUMMARY

Among industries in which occupational asthma arises the aluminium industry is very low on our international incidence list. It has been observed especially among workers engaged in the reduction cell areas or exposed for several hours each working day to reduction cell “bath material” within plants. Guidelines for the diagnosis of Occupational Asthma within the primary aluminium industry (Potroom Asthma) have been agreed by the IPAI Health Committee.

A specific cause has not been established. An irritant inflammatory mechanism is favoured rather than an allergic one. Gaseous and particulate fluorides are likely to play a role. Among one group of 90 cases close to half have symptoms of asthma at least weekly after 2 years or more of treatment and after removal from production areas.

Preventative measures include regular workplace hygiene monitoring with feedback to employees, good ventilation and dust/fume removal, minimising exposure to hot used anode butts and “bath” material, a well managed respiratory protection programme and pre-employment respiratory assessment. Careful workplace health surveillance has the objective of preventative advice on early diagnosis of cases in the interests of a favourable outlook.

CONDITIONS OF INTEREST

The occupational respiratory disorders of interest to the aluminium industry are asthma, chronic bronchitis and chronic obstructive pulmonary disease (COPD). These disorders - the obstructive disorders - affect breathing by limiting one's ability to move air in and out through our breathing passages.

Asthma is usually episodic with wheeze, difficulty in breathing, a sense of tightness within the chest, and shortness of breath, which may ease spontaneously or in response to medication. Asthmatic breathing
passages are usually very reactive and may narrow rapidly in response to sudden temperature changes, inhaled dust, fume, smoke or physical exercise (bronchial hyper-responsiveness).

Occupational asthma refers to asthma induced in the workplace. It is to be differentiated from pre-existing asthma aggravated at work. It may be difficult and is likely to depend on the information recorded at a pre-employment assessment. It is usually taken also to embrace the Reactive Airways Dysfunction Syndrome or RADS, which may follow a single exposure to a high level of an irritant, fume or smoke. Chronic bronchitis: persistent cough and phlegm and some wheezing at times when breathing is obstructed.

Chronic obstructive pulmonary disease (COPD or chronic airflow obstruction): there may be some frequent cough with some phlegm, shortness of breath and often wheeze. It is most commonly due to tobacco smoking. There is a slowly progressive deterioration over years and usually only mild improvement following the medication used for the relief of asthma.

INCIDENCE

Occupational asthma occurs in many industries. The aluminium industry is very low on an international incidence list of occupational asthma. Anecdotal reports suggest a different incidence between some countries. The data available for such a conclusion may not be comparable. In some areas there may be diagnostic confusion also between asthma and chronic obstructive pulmonary disease especially where that has a greater recognition as a health problem.

The term bronchial hyper-responsiveness refers to the increased sensitivity of asthmatic air passages to the inhalation of a range of agents from allergens to irritants. This is assessed by studying the effects of standardised inhalations of chemical agents such as methacholine or histamine. In general, the more severe the asthma at a particular time, the greater the bronchial responsiveness. It must be noted that at least five percent of community populations may show such bronchial hyper-responsiveness, usually mild\(^1\) and although they have reported having had no symptoms of asthma. In diagnosed cases of occupational asthma, the recovery in symptoms and objective findings such as bronchial hyper-responsiveness which may be found after removal from work exposure, provides evidence that the association between the occupational asthma and the smelting process is a real one.

My brief is to deliver a concise review of occupational asthma within the primary aluminium industry. It was described first in 1936 and has been referred to as a “potroom asthma”. Time does not permit
me to detail many of the published reports about this condition. They
have come from several parts of the world, especially Norway\(^2\),
Australia\(^3\), Canada\(^4\), the former Yugoslavia\(^5\) and New Zealand\(^6\).

**HOW COMMON IS OCCUPATIONAL ASTHMA WITHIN THE PRIMARY ALUMINIUM INDUSTRY?**

As I have noted, there may be variation country to country. I shall
present data from the South Pacific. Over the recent decade, the Health
Committee of the Australian Aluminium Council has collected annually
from each smelter in Australia and New Zealand, details of those cases
diagnosed as having developed occupational asthma. The recent
incidence has been around 1% among those working in reduction cell
areas or exposed to “bath material” (Tables 1 and 2).

### Table 1

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of cases</th>
<th>Incidence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1992</td>
<td>3065</td>
<td>2.00</td>
</tr>
<tr>
<td>1993</td>
<td>3132</td>
<td>1.25</td>
</tr>
<tr>
<td>1994</td>
<td>3365</td>
<td>1.40</td>
</tr>
<tr>
<td>1995</td>
<td>2746</td>
<td>1.06</td>
</tr>
<tr>
<td>1996</td>
<td>2938</td>
<td>0.50</td>
</tr>
</tbody>
</table>

**WHAT LENGTH OF SERVICE WITHIN THE INDUSTRY HAD BEEN SERVED BEFORE SYMPTOMS WERE NOTED?**

Just over 6% of cases have occurred within the first three months of
employment (Table 3). Among this group may be individuals from
among the five percent or so in the general community who have shown
bronchial hyper-responsiveness without any symptoms, or some in
whom asthma existed but was not disclosed or detected at pre-
employment assessment.
DIAGNOSIS

In order to facilitate a uniformity of approach, guidelines for the diagnosis of occupational asthma in the primary aluminium industry have been agreed on by the IPAÏ Health Committee in 1996, for recommended use in workforce surveys or relevant epidemiological studies (Table 4).

Table 3
(Aust. & NZ)

<table>
<thead>
<tr>
<th>Length of Service</th>
<th>Fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 3 months</td>
<td>6.3%</td>
</tr>
<tr>
<td>3 months - 1 year</td>
<td>22.6%</td>
</tr>
<tr>
<td>&gt; 1 year - 2 years</td>
<td>22.6%</td>
</tr>
<tr>
<td>&gt; 2 years</td>
<td>48.4%</td>
</tr>
</tbody>
</table>

Because of the episodic occurrence of asthma, objective tests for obstructed breathing may intermittently give normal results. Peak expiratory flow rate measurements which can be made and recorded by an individual using a small portable meter, may show differences in results at work compared with at home. These differences are helpful in the diagnosis of occupational or work-related asthma, but do not provide a gold standard of certainty. If one is to get reliable information from such measurements, good employee understanding and co-operation are required to try to ensure good technique and appropriate frequency of measurement. Dr Moira Chan-Yeung and her colleagues (7), have found
in a study using a logging device attached to the peak expiratory flow meter, that 55% of readings were correct, but 23% were inaccurate. The remaining 22% of records were obviously fabricated (not recorded by the attached mini-log). However, the use of the peak expiratory flow rate measurements may be the only means of obtaining the objective evidence which may be often required by a compensatory authority to demonstrate a work relationship of the asthma.

Table 4
Guidelines for the diagnosis of occupational asthma (potroom asthma) in the primary aluminium industry.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms comprising difficulty in breathing, chest tightness and/or wheezing, often with a cough and which may be brought on by physical exercise.</td>
<td>A period of initial work exposure of two weeks or longer before the onset of symptoms occurring for the first time in the individual.</td>
</tr>
<tr>
<td>Symptoms or evidence of airflow obstruction related in time to exposure; onset of symptoms may occur immediately, after several hours, or during sleep.</td>
<td>Symptoms improve when the subject is away from work for days or longer.</td>
</tr>
</tbody>
</table>

The symptoms are to be supported by objective evidence of significant reversible airflow obstruction - a diurnal variation trough to peak amplitude of 15% or more of the mean peak expiratory flow rate associated with work exposure and resolving at other times - measurements being made four times each day; or an increase in FEV$_1$ of at least 12% and $>$200ml from the baseline value following inhalation of bronchodilator, and/or evidence of bronchial hyper-responsiveness (histamine or methacholine inhalation challenge) which will indicate also the severity of the syndrome.

*Current objective guidelines of The American Thoracic Society and of The European Respiratory Society.*

CAUSE

A specific cause has not been established. Attention is focussed on the contents and emissions from the reduction cells. Some of these can be distributed to other plant areas as dust or through the transportation of the hot used anode butts with their attached bath material. There are many potential respiratory irritants in that work environment. However, research has produced no evidence of an allergy as a cause (8).
Particulate fluoride has received particular attention because occupational asthma does occur in plants manufacturing or involved with aluminium fluoride (9), or sodium or potassium tetrafluoride (10). Further, Søyseth and Kongerud have demonstrated an association among smelter workers in Norway (11), between the prevalence of work-related asthmatic symptoms and higher exposure levels of total fluoride. There are several chemical compounds of sodium, aluminium and fluorine within the reduction cell contents that may be incriminated. To progress research into the cause of asthma, the Norwegian aluminium industry has provided, to the University of Oslo, an environmental testing chamber for asthma research. Here Dr. Kongerud and his colleagues, have shown, so far, that inhalation exposure to low concentrations of hydrogen fluoride can induce inflammation of the breathing passages - although asthma symptoms have not occurred in their subjects (12).

Table 5
Outlook: Diagnosed Cases Followed Two Years or More after Removal From Production Area - 1980 – 1997, n = 90

<table>
<thead>
<tr>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>19% recovered</td>
</tr>
<tr>
<td>Further 33% - occasional asthma</td>
</tr>
<tr>
<td>Further 28% - asthma symptoms at least weekly, &lt; daily</td>
</tr>
<tr>
<td>Further 20% - continuing daily asthma symptoms</td>
</tr>
</tbody>
</table>

THE EMPLOYEE-ASSOCIATED RISK FACTORS FOR DEVELOPING OCCUPATIONAL ASTHMA

No one factor has been identified consistently. Within our 110 New Zealand cases over almost 20 years, the percentage who were current tobacco smokers, or who had positive skin tests to common domestic allergens (atopic), were similar to the percentages found within the general population. Kongerud and colleagues (2), however, reported an association between work-related asthmatic symptoms and tobacco smoking, and a slightly increased one with a family history of asthma.
WHAT IS THE OUTLOOK AFTER DIAGNOSIS?

Among 90 cases within New Zealand with whom follow-up has been possible for at least two years following removal from their production areas, 19% have recovered; a further 33% report only occasional asthma, especially at the time of any upper respiratory infection; a further 28% report asthma symptoms recurring at least weekly but less than daily; a further 20% continue to experience daily asthma symptoms on a regular basis (Table 5).

Among our cases, there has been a greater risk of continuing daily asthma symptoms and with a greater risk of having persisting bronchial hyperresponsiveness among those in whom cough and phlegm persisted or developed. In 70% of our cases, the bronchial hyperresponsiveness changed to normal levels, mostly within one year of removal from the production work areas, although in some cases this took two years. Persisting bronchial hyperresponsiveness showed no relationship with positive allergen skin tests (atopy) or previous, or current tobacco smoking. However, those with a family history of asthma had double the risk of persisting bronchial hyperresponsiveness.

MANAGEMENT

The principles of management of this condition include:

• treatment of individual cases
• preventive measures –
  minimising work place exposures
  pre-employment respiratory assessment
• regular employee health surveillance

OCCUPATIONAL ASTHMA - MANAGEMENT

Individual Cases:

• Remove from exposure/reduction area
• Medication - symptom relief
• Trial - at least three months anti-inflammatory inhaler, corticosteroid with personal instruction re: medication
• Cessation of tobacco smoking
• Respiratory and general exercise advice

Subsequent - Monitor monthly - symptoms and objective tests
• Recovery to at least trivial symptoms state - consider trial of return to reduction area work after 6 months with insistence on compliance with supervised respiratory protection practices.

Inhaler Administered Corticosteroid Medication

This may have a disappointing benefit in the treatment of this type of asthma in contrast to its effect in the more common community asthma. Dr Malo and colleagues in this city \(^{(13)}\), have concluded from their carefully controlled study that such treatment does induce a small but definite improvement in occupational asthma caused by many agents and following withdrawal from exposure. In their study, the beneficial effect was more pronounced if the medication was started early after the diagnosis was made. This observation provides support for pursuing early diagnosis among the production work force.

Some of those affected can recover sufficiently to return to their former smelter work, provided strict respiratory protection measures are in place. In 1996, within Australia and New Zealand, there were 86 employees who had been previously diagnosed with occupational asthma who were working in the reduction areas of smelters and reported no, or only, mild occasional asthma symptoms. Presumably in these, the damage to the lining of the breathing passages has healed. I should say that in my own clinical experience, I have not followed such a policy.

OCCUPATIONAL ASTHMA - PREVENTION

The strategy is to minimise workplace exposure by:

• regular hygiene monitoring with feedback to employees and with data review at health staff/plant management meetings
• ventilation and dust/fume removal
• engineering improvements to minimise exposure to hot used anode butts and “bath” material - aim is particularly to achieve a prompt removal from potrooms to a separate facility
• well administered respiratory protection programme will be covered later by Linda Kissane.

Pre-Employment Respiratory Assessment

Can those at risk of respiratory impairment be selected out?
• Previous asthma or sustained respiratory symptoms or wheeze detected at clinical exam.

• Functional - Vital capacity/Forced vital capacity
  > 80% predicted normal required
  - FEV1 - forced expired volume 1 sec.
  > 80% predicted normal required
  - FER (FEV1/FVC) > 90% predicted

There has also been discussion as to whether an assessment of bronchial responsiveness among employees has a place:

• In routine pre-employment or pre-placement assessment to detect persons with a potentially greater risk of developing asthma or suffering aggravation of pre-existing asthma which has not been disclosed. The value of such a practice would depend on the incidence of occupational asthma within a particular plant - an input/benefit assessment. There could, of course, be legal difficulty in excluding an asymptomatic person in spite of their having some level of bronchial hyperresponsiveness.

• Does it have a place in ongoing employee health surveillance? The question here is, would this provide an early warning for the development of asthma?

  I do know that such a programme has been implemented in a few smelters.

**Employee**

• pre-employment respiratory health assessment - ? urinary check for bronchodilator drug use suppressing asthma at assessment

• bronchial responsiveness assessment

**EXPOSED EMPLOYEE RESPIRATORY HEALTH SURVEILLANCE - 6 MONTHLY**

Regular health surveillance of employees especially in reduction areas, with the following aims:

• Prevention;

• Early diagnosis with milder disease and favourable outlook following treatment and removal from work exposures.
OCCUPATIONAL ASTHMA: THE FUTURE

There is a need for research to guide prevention and management programmes:

- Cohort Studies with relevant exposure measurements in the areas of:
  - respiratory health;
  - respiratory function including bronchial responsiveness;
  - natural history of diagnosed cases.

- Environmental chamber studies to determine relevant exposure effects.
  - Induced sputum - studies of the nature of the inflammation of the air passages in diagnosed cases and those developing hyperresponsiveness.

REFERENCES


18. CHRONIC OBSTRUCTIVE PULMONARY DISEASE: PREVENTION BY REPETITIVE SPIROMETRY

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SUMMARY

This paper describes the results of spirometry undertaken over a period spanning 1982 to 1996 on potroom workers within three Canadian aluminium smelters. During this period marked changes were seen both in the environmental conditions within the smelters and in the smoking habits of the workers. Chronic obstructive pulmonary disease (COPD) was identified in workers using measurements of forced expiratory volume in one second (FEV$_1$) and forced vital capacity (FVC). In 1982 COPD was especially prevalent in potroom workers that smoked (~28%), but was also common in non-exposed workers (~19%). The results of serial spirometry measurements are used to define the population at particular risk of COPD within the potroom workers.

INTRODUCTION

In recent years numerous studies have been published dealing with industrial bronchitis in general and industrial bronchitis has been described in the aluminium industry. The first reported studies, notably those of Roholm in 1937 (1), Papoyan in 1963 (2), Kaltreider in 1972 (3) and Coulon in 1975 (4), found a greater prevalence of clinical signs of bronchial obstruction; however, none of these studies were correlated with function, and only the work of DeVries et al. in 1974 (5) combined clinical with objectives studies. In this study, clinical bronchitis was observed but spirometric variables were within normal range. In 1976, Discher (6) found no prevalence of clinical or functional chronic bronchial obstruction among the same workers. Field, in different studies, the most recent in 1984 (7) and based on just over 100 potroom workers and Chan Yeung, in a study of 797 potroom workers and 713 control (8) described clinical signs of chronic bronchitis and statistically confirmed the effect of exposure and smoking on the forced expiratory volume in one second (FEV$_1$) and the maximal mid-expiratory flow
(MEF 75-25). The differences reported by Chan Yeung et al. between potroom workers and the control group were slight and only observed among highly exposed workers. Smoking doubled these differences. These same workers were re-evaluated in 1989 (9) and 586 participated in both studies: there were no exposure effects in the annual decline of the FEV_1, but she observed a significant effect of ageing and smoking.

Kongerud in 1990 (10) reported the development of asthma symptoms and reduced respiratory function, while Bakke et al (11) described an association between exposure to aluminum production and airway obstruction.

In 1991 Carta et al (12) stated that symptoms of cough and sputum production were high and that the annual decline in FEV_1 was also greater. Finally Soyseth et al (13) reported an association between low metacholine PC_{20} and high annual decline in FEV_1; however after correction for age, smoking habit, gender and FEV_1, this association was no longer significant.

It must be kept in mind that frequently all the potroom workers, without restriction for their length of exposure, were included in these studies whose main objectives were the determination of a chronic effect of exposure on lung function. There was also a large individual variability in the frequency and/or the degree of obstruction more or less mimicking the situation observed in a smoking population where subgroups at high risk of developing obstructive airways disease have long been recognized.

In the last 20 years or so, we have been involved in different population surveys in the potroom environment designed to:

- describe the respiratory status of potroom workers;
- help the early detection of workers at risk of developing chronic airways obstruction.

In this paper we use results from two of these surveys to attempt to place apart among actual workers, through analysis of their repetitive spirometry in the last 15 years, those with an exacerbated annual decline in FEV_1. Thus, these workers will either display fully established airways obstruction, (FEV_1/FVC below 82 % predicted) or be associated with the higher rate of FEV_1 decrease (> 31 mL y^{-1}).

**STUDY POPULATION**

The first study was performed at the Jonquières Industrial complex in 1982. The cohorts consisted of:

- 324 non-exposed workers, with a mean age 43, employed by Sécal for an average of 19 years;
• 357 potroom workers from the prebake and / or Söderberg environment, mean age 44, employed by Sécal for an average of 20 years.

Because, in previous reports, we did not observe significant functional differences between prebake and Söderberg workers, their results are combined in this analysis.

The second group of workers originates from two surveys, performed during the summer of 1996, one at the Laterrière complex of Sécal, the other at the Shawinigan complex. The cohorts consisted of:

• 129 non-exposed workers, with a mean age of 44 and employed by Sécal for an average of 21 years.

Exposure for the 324 potmen varies somewhat in between groups: we find prebake type pots in the Laterrière complex while Söderberg type pots are in use in the Shawinigan complex. However, most of the employees of the Laterrière complex, built in 1990, originated from the Jonquière complex where their exposure had been to mixed prebake and Söderberg emissions. With a mean age of 44, they also have been in the potroom for an average of 20 years.

**MATERIALS AND METHODS**

For the 1981 study in Jonquière we used a Hewlett Packard 47804S system, which, for purposes of forced expiration testing, included a pneumotachograph (HP21073B) and a flow sensor (HP47304A). The analog signals were converted into digital ones and then processed by a HP9825 calculator. Finally the data as well as the individual tracings were stored on floppy disks which were also used to store test control software. For the 1996 studies in Shawinigan and Laterrière we used a Morgan Spiroflow PK 136 automated spirometer, coupled to the S&M pulmonary software.

Finally, where repetitive spirometric measurements were obtained, i.e., in the 1984-1994 interval, these tests were performed at the medical centre, by the company personnel with a Spirotec S400 automated spirometer or a Morgan spiroflow PK 1330 also coupled to the S&M pulmonary software. The company personnel had received a specific training in spirometry by our chief technician and were regularly re-evaluated.

In both surveys, we employed pulmonary function technicians trained for epidemiological studies. The ATS criteria were always used in the calibration and performance of the test either for the specific
surveys or for the yearly evaluation undertaken at the medical centre by
the company personnel.

When spirometry was done as part of a specific project, (i.e.
Jonquière, Shawinigan and Laterrière studies) measurements were
always made on the first day of work, after a minimum of two days of
absence from the exposure area, and before any exposure to the potroom
environment. Also, because there was a risk of exaggerating the
presence of obstructive syndromes during winter months, for the
different surveys, no data were collected between November 1st and
May 15th.

The first measurement does not always represent the first day
of employment. These employees could have been working for 5 to 10
years in 1984, when the company started doing spirometry as part of the
annual medical evaluation.

The results of all the pulmonary variables, (forced vital
capacity (FVC), forced expiratory volume in one second (FEV₁) and the
FEV₁/FVC ratio are expressed as a percentage of the predicted value (%
pred.) The regression obtained in the Province of Quebec and recently
accepted for publication (Martin et al., La Revue Francaise des Maladies
Respirales) was used. Using these predicted the lower limit level
containing 95% of the population was 80% for the FVC and the FEV₁
and 82.5 for the FEV₁/FVC.

RESULTS

In the 1982 study the FEV₁/FVC ratio is reported in % of predicted
values, for the non-exposed and exposed population subdivided
according to smoking habit (Fig. 1). A significant smoking effect is
observed irrespective of the exposure, but comes out larger in the
exposed group where current and ex-smokers differ form the non-
smokers. (Anova, F = 9.14; d of f = 5/675) An exposure effect can also
be seen in the current and ex smokers.

The prevalence of FEV₁/FVC ratio below the 95% confidence
interval (82.5% for that set of predicted values) is displayed in figure 2.
Once more the analyses of variance shows significant differences
between the subgroups (F = 8.3; d of f = 5/675) again with a significant
smoking effect and an exposure effect for the current and ex-smokers.
Note that the exposed workers displaying a low FEV₁/FVC also
displayed a longer exposure (25 vs. 18 years; t = 4.71; d of f = 355) That
was, however, not the case in the non-exposed group where the
respective mean working duration at Alcan was 19.7 and 18.8 years (t =
0.54; d of f =321). Smoking was more prevalent in this sub-group with a
low FEV₁/FVC.
Smoking habits changed drastically from 1982 to 1996; smoking fell from around 50% to 31%, mainly by an increase in the non-smoking population from 19% to 34% as shown in figure 3. These changes were constant irrespective of exposure. Note that even if we are looking at two different populations, Jonquière in 1982, Shawbridge and Laterrière in 1996, they are quite representative of the smoking habits in the Province of Quebec for these two periods. We also observe a slight increase in the proportion of ex-smokers probably less than expected from the anti-smoking campaigns.

Figure 1. Original study, 1982. FEV$_1$/FVC in the non-exposed and exposed workers. Mean and standard errors. Anova, F = 9.14; d of f = 5/675. NS = non-smokers, Ex = ex-smokers, S = smokers.

If we compare the FEV$_1$/FVC ratio of these two different populations at 14 years interval, we can have an estimation of the respiratory status of the potroom populations of workers in each period (Fig. 4). It is manifest that irrespective of the exposure, lung function has significantly improved by about 4% during the interval. While the equipment changed, calibration was always the same using ATS criteria, so was the performance of the test. The overall pattern remains similar, however, with a significant exposure effect in the current but not in the

Nevertheless, 38 workers (6 non-exposed and 32 exposed) or 8% of the population exhibit definite signs of airways obstruction ($\text{FEV}_1/\text{FVC} < 82.5 \%$ pred.); we possess spirometric evaluation for these employees since approximately 1984; we must keep in mind that at their first evaluation in the medical centre these workers had already been subjected to some exposure if we reckon that in 1996 their total work at Alcan averaged $21 \pm 6.7$ years.

![Graph showing prevalence of $\text{FEV}_1/\text{FVC}$ ratios lower than 82% of predicted.](image)

**Figure 2.** Prevalence of $\text{FEV}_1/\text{FVC} < 82.5 \%$ predicted. Anova, $F = 8.3$: d of $f = 5/675$.

Original and actual $\text{FEV}_1/\text{FVC}$ are displayed in figure 5 for both class of workers i.e. $\text{FEV}_1/\text{FVC}$ smaller or larger than 82.5 % pred. Length of exposure differs mildly in the two sub-groups of $\text{FEV}_1/\text{FVC}$ ($22.84 \pm 7.7 \ n = 38$ vs. $20.4 \pm 7.06 \ \text{years} \ n = 415$; $t = 1.85$) but not age or smoking habits. Still, potroom workers presenting now with low values were already significantly different then ($t = 7.04$; d of $f = 308$). There is a similar trend in the non-exposed workers but the numbers are too small ($n = 6$) for valid comparison.

On an individual basis, 15 out of the 38 revealed a $\text{FEV}_1/\text{FVC}$ below 82.5% pred. at that first evaluation as shown in figure 6.
Furthermore, not only did they show low values in 1984, but since then, their annual rate of change in FEV\textsubscript{1} are higher as found in figure 7, where the annual decline in FEV\textsubscript{1} expressed in millilitres per year is displayed according to the actual FEV\textsubscript{1}/FVC. This annual fall is around 17 mL in the 301 workers whose actual FEV\textsubscript{1}/FVC ratio is within normal limits and is within expected range in relation to the predicted equations based on cross-sectional studies. However it increases to 31 mL in the 29 subjects with the low FEV\textsubscript{1}/FVC ratios. Only 29 of the 38 workers had the minimum of 4 repetitive spirometry to allow calculation of annual changes. In other words they started with low values and continued worsening since. Repetitive spirometry allows for the detection of these individuals at risk.

![Figure 3. Smoking habits 1982 vs. 1996.](image_url)

When this annual decline in FEV\textsubscript{1} is examined individually, (Fig. 8) we observe that in 14 it exceeded 30 mL, to reach 100 mL in one. This individual aged 44, had spent 23 years in the potroom, and gives a smoking history of 50 pack-years. His actual FEV\textsubscript{1}/FVC is 54% of predicted and his FEV\textsubscript{1} has gone from 3.56, to 2.6, 2.4 L and finally 2.04 L respectively in 1985, 1991, 1994 and 1996.

Figure 5. Actual study (1996). Initial FEV$_1$/FVC given actual FEV$_1$/FVC. $t$ for exposed workers = 7.04; d of $f = 308$. 

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Figure 6. Individual FEV\textsubscript{1}/FVC in 1982 of workers whose actual FEV\textsubscript{1}/FVC is < 82.5 % predicted.

Figure 7. Annual decline in FEV\textsubscript{1} in mL / year. Workers with FEV\textsubscript{1}/FVC < or > 82.5 % predicted.
Figure 8. Individual annual decline in FEV₁ if FEV₁/FVC is below 82.5 % predicted.

Figure 9. Annual decline in FEV₁ for workers with normal FEV₁/FVC. (> 82.5% predicted.)
While detection of abnormal workers is important, detection of individuals at risk is essential. In figure 9 we find that in the 301 workers with an FEV$_1$/FVC ratio larger than 82.5% predicted 63 demonstrated no changes in the FEV$_1$ through the period, while it was between 0 and 30 mL or as predicted in 158. Still, 80 subjects (27%) displayed changes beyond the maximum predicted level of 30 mL y$^{-1}$. Already their FEV$_1$/FVC is slightly but significantly ($t = 3.07$; d of f = 299) lower than the rest of the population (Fig. 10) and in 21 the annual decline exceeded 60 mL y$^{-1}$. 70% of these were current or ex-smokers, and the majority originated from the potroom environment. Length of exposure was identical in the two groups.

![High Risk Group (> 30 mL / year Drop in FEV1)](image)

Figure 10. Functional description of the high risk group. Mean FEV$_1$/FVC according to an annual decline in FEV$_1$ $<$ or $>$ than 30 mL / year, and the annual decline for that latter group. $t$ on FEV$_1$/FVC = 3.07; d of f = 299.

**CONCLUSION**

We must remember that the survey of 1982, in a population of workers with a mean exposure of 21 years, mainly represented the conditions of the late sixties. The last 15 years or so have been marked by important
environmental changes and anti-smoking campaigns have resulted in significant modifications of smoking habits.

The actual study based on a cross sectional evaluation and a retrospective analysis of spirometry done, as part of the yearly medical evaluation, is highly dependent on the so-called “healthy workers effects”. Throughout the sixteen years period, there could and must have been work cessation due to respiratory complaints, but the recovery of information about these is impossible. However, as stated, the objective was to define among a population of actual workers the population at risk of developing airway obstruction. Thus, even if the actual prevalence is underestimated, the presence of such individuals at higher risk confirms airway obstruction due to environmental exposure, and indicates that significant deterioration may be prevented by the early detection of those individuals whose annual decline in FEV$_1$ exceeds predicted limits.

By modifying their smoking habits and exposure, as well as assessing repetitively their respiratory status, we might reduce the occurrence of serious obstruction in the future.

REFERENCES

19. A PROSPECTIVE STUDY OF RESPIRATORY HEALTH IN ALUMINUM SMELTER WORKERS

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Co-Authors: Feroza M. Daroowalla, Nancy A. Nelson, Susan R. Sama, Noah S. Seixas, Martin A. Cohen

SUMMARY

Kaiser’s Mead facility and the Washington State Department of Labor and Industries initiated a multi-year longitudinal study in August 1995 to address the reported association between occupational asthma and exposures in primary aluminum reduction.

Newly hired employees are assessed with questionnaire, spirometry, methacholine challenge, and skin tests for common antigens, prior to beginning smelter work in this prebake facility. These tests (except skin testing) are repeated at regular intervals. Exposures are assessed using air sampling and urine fluoride measurements, with a focus on potroom exposures. A subset of employees, including those who have shown an increase in non-specific bronchial responsiveness or new asthma-like symptoms, underwent a two-week assessment of airflow during work- and non-work periods using data-logging pulmonary function equipment and two days of concurrent exposure assessment using direct reading (real-time) instruments. Subject recruitment, data collection, and data analysis are still underway.

171 newly hired potroom employees (>95% participation) have been recruited into the study thus far; 117 of these remain in the cohort following attrition. At least two examinations have been completed on 113, and three examinations on 85. Following one year of follow-up, 14 of 93 have met our criteria for an increase in nonspecific bronchial responsiveness, based on a change in methacholine slope. We have identified workers who report new asthma-like symptoms and have increased airway responsiveness.
Further study to determine the significance and work-relatedness of our findings is underway. This presentation will discuss the findings of the study to date, including both respiratory health and exposure assessment.

INTRODUCTION

The development of lung disease in aluminum smelter (electrolytic reduction) workers has been reported for 60 years, and investigators in Australia, Norway and New Zealand have reviewed the issue of asthma in potroom workers \(^1-3\). Writing in a comprehensive 1989 review, Abramson and colleagues found that "there is inadequate evidence to resolve the question of whether potroom exposure initiates asthma or merely precipitates asthma-like symptoms in a predisposed individual \(^1\)". Despite several investigations concerning "potroom asthma," significant controversy persists regarding the existence of the condition, and if it exists, its natural history, pathogenesis (immunologic vs. non-immunologic irritant-induced), non-occupational risk factors (including atopy, family history, childhood asthma, and smoking), and causative agent(s).

Respiratory health was one of the issues of interest when the Safety and Health Assessment and Research for Prevention (SHARP) program of the Washington State Department of Labor and Industries began collaborating with labour and management at the Kaiser Mead Works regarding key occupational health and safety issues in 1992. When the Mead Works undertook large scale hiring of new workers during the summer of 1995, plans were made to recruit these workers into a longitudinal study of respiratory health. All parties understood that this represented an important opportunity to understand the relationship between smelter exposures and respiratory health. The collaboration has included investigators from the University of Washington and the University of British Columbia.

METHODS


STUDY POPULATION RECRUITMENT

New hires to the plant were approached for recruitment into the study during the first week of orientation. Participation was voluntary and institutional review board-approved informed consent was obtained.
Confidentiality of individual results was guaranteed; no one other than the research team has access to information that would identify an individual. Prior to orientation for potroom employment, each employee had successfully completed a job interview, security and criminal history check, testing for aerobic conditioning and strength, medical examination including spirometry, and urine testing for illicit drugs. Approximately 30% of applicants passed this screening with most being eliminated by physical capacity testing, followed by security/criminal clearance and drug testing. New hire orientation was a two-week process during which the new employee was familiarised with processes and procedures, and trained in the basics of potroom work. Regular potroom work followed the orientation period. For purposes of analysis at this time, potential subjects included all individuals who completed orientation and at least one subsequent day of potroom employment. For this report, only subjects recruited in 1995 are included.

BASELINE HEALTH ASSESSMENT

At the initial evaluation each subject had: 1) allergy skin testing to common antigens; 2) interview for occupational and health history, including respiratory symptoms; 3) spirometry; and 4) methacholine bronchoprovocation challenge.

Allergy skin testing

Skin prick testing was performed according to standard protocol, with histamine (positive control), negative control, cat allergen, mixed grass antigen, and Dermatophagoides pteronyssinus (dust mite) antigen. The tests were read 15 minutes after application and the size of erythema and wheal were noted. A test was considered positive if at least one non-control test response was greater than or equal to the histamine response; one positive among the three non-control antigens was considered evidence of likely atopy.

Interview

Trained interviewers conducted all interviews. The initial interview includes demographic, personal health, family health, habits (including tobacco use), occupational history, and symptom information. The American Thoracic Society respiratory symptom questionnaire was administered, along with a supplementary validated instrument on asthma-like symptoms developed by Venables for epidemiologic
investigations,\(^{(6)}\) and questions on rhinitis and other upper respiratory symptoms.

**Spirometry and methacholine challenge**

Spirometry was performed using American Thoracic Society standards,\(^{(7)}\) using a dry rolling seal spirometer (SM Instruments, PA, USA), with the subject in a seated position, wearing nose clips. FEV\(_1\), forced vital capacity (FVC), FEV\(_1\) / FVC ratio, mid-expiratory flow rate (FEF\(_{25-75}\)), and PEFR were calculated, along with percent predicted using prediction equations described by Crapo and colleagues.\(^{(8)}\) Methacholine challenge was administered in a standardised format, with oxygen nebuliser administration at a flow rate of 5 L min\(^{-1}\), Puritan-Bennett Twin nebulisers and mask delivery.\(^{(9)}\) At each stage, solution was administered during tidal breathing for a two-minute period, with forced expiratory manoeuvres at 30 seconds and 3 minutes after each inhalation. Escalating methacholine concentrations, to a maximum of 32 mg mL\(^{-1}\), followed saline baseline. If FEV\(_1\) reached 80% of the lowest post-saline value, the test is stopped. Bronchodilators are administered to reverse any airway reactivity elicited. The provocative concentration of methacholine that induces a 20% fall in FEV\(_1\), or PC\(_{20}\), is determined by extrapolation of the log dose-response curve. The linear least squares slope of the relationship between FEV\(_1\) and methacholine concentration (methacholine slope) is also calculated.

Methacholine challenge represents a measure of non-specific bronchial airway responsiveness. Asthmatics demonstrate more responsive airways, indicated by a response at a low dose concentration of methacholine, usually much less than 8 mg mL\(^{-1}\).

**PERIODIC HEALTH ASSESSMENT**

At approximately 6 months and annually following recruitment into the study, participants are asked to repeat the interview, spirometry, and methacholine challenge. An attempt was made to repeat the interview with subjects at 2 and 4 months following recruitment.

**PHASE ONE EXPOSURE ASSESSMENT**

Initial exposure assessment investigation was conducted over the period of one week. Exposures were measured on the first and last day of each participating employee’s three (12-hour) day workweek, from both the day and night shifts.

A sample of employees was selected from the cohort for the initial assessment with equal representation from the four shift groups.
During the first and last day of the shifts, personal 12-hour average air samples for total particulate matter, particulate fluorides, and hydrogen fluoride gas were collected for each of these employees. For analytical purposes, two consecutive six-hour air samples were collected instead of a single 12-hour sample. Pre- and post-shift urine samples were collected on the first and last day of their shift and analysed for fluoride and creatinine content.

Throughout the sampling periods, observations were made of the employees' activities and work habits including task duration and respirator usage.

EXPOSURE ASSESSMENT AND REPEATED AIRFLOW MEASUREMENT SUB-STUDY

In the spring and summer of 1997, 20 subjects were recruited from the overall cohort to participate in a 14-day assessment of repeated pulmonary function (peak-expiratory flow-rates and FEV$_1$) measurements, and a 2 day detailed exposure assessment sub-study. Airflow measurements were performed using a data-logging pressure-sampling device (VM-1, Clemente Clarke, Inc.). Participants were instructed to take three consecutive expiratory manoeuvres at least five times per day. The highest value at each time was kept for future analysis. For two full work-shifts during this period, participants wore personal sampling equipment for sulphur dioxide (continuous reading), particulate (by both traditional filter and continuous reading aerosol monitor), and fluoride (by filter).

DATA ANALYSIS

Data analysis, along with data collection, is still underway. The information presented here should be viewed as preliminary. As data are most complete for the baseline and initial follow-up visits on the cohort that started in 1995, only their data are included. Inclusion of comprehensive data on any portion of this study is beyond the scope of these conference proceedings, so limited results from each portion are included. Data are not included from the exposure assessment and repeated airflow measurement sub-study, as completed analysis is too preliminary.

Based on the methacholine challenge, a subject was characterised as having increased non-specific airway reactivity if their PC$_{20}$ dropped two or more dose-doubling categories (e.g., from $\geq 16$ and $< 32$ mg mL$^{-1}$] to $[\geq 4$ and $< 8$ mg mL$^{-1}$]). They could also achieve
this by a 2-fold change in the methacholine slope (if the follow-up PC$_{20}$ is < 32 mg mL$^{-1}$).

RESULTS

BASELINE SUBJECT CHARACTERISTICS

161 newly hired employees for the carbon (anode) setter position were eligible for participation and 153 (95.0%) agreed to participate in 1995. One subject was subsequently excluded as he did not complete the orientation process or begin potroom work. The remaining 152 subjects completed all of the initial testing. (Since 1995, an additional 19 employees have been recruited into the study.)

Of the 152, 99.3% were men. 13 subjects (8.6%) were non-white, 6 were African-American. 44 (28.9%) were current smokers. The mean age was 28.7 years (range 18-49). 15 (9.9%) reported wheezing apart from a cold. 5 (3.3%) reported a current diagnosis of asthma.

Allergy Skin Testing

71 (46.9%) of the subjects had at least one positive skin test, meeting our criteria for likely atopy.

<table>
<thead>
<tr>
<th>Dose(mg mL$^{-1}$)</th>
<th>Number of Subjects (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2</td>
<td>8 (5.2%)</td>
</tr>
<tr>
<td>&gt;2 and ≤8</td>
<td>13 (8.6)</td>
</tr>
<tr>
<td>&gt;8 and ≤16</td>
<td>13 (8.6)</td>
</tr>
<tr>
<td>&gt;16 and ≤32</td>
<td>14 (9.2)</td>
</tr>
<tr>
<td>&gt;32</td>
<td>104 (68.4)</td>
</tr>
<tr>
<td>Total</td>
<td>152 (100)</td>
</tr>
</tbody>
</table>

PC$_{20}$=provocative concentration achieving 20% drop in FEV$_1$
Spirometry and Methacholine Challenge

The mean FEV\textsubscript{1} was 4.31 litres, with the mean percent predicted being 97.6 and 8 subjects (5.3 %) less than 80 % of predicted; 36 (23.7 %) of the subjects had an FEV\textsubscript{1}/FVC ratio less than or equal to 0.75.

Methacholine challenge results are shown in Table 1. Current asthmatics, those reporting wheezes, and those with atopy as indicated by at least one positive skin test to common antigens all were more likely to have increased bronchial reactivity (p<0.0001). Current smokers, as a group, had similar non-specific bronchial responsiveness to the overall cohort.

Table 2.
Results from Phase One Exposure Assessment

<table>
<thead>
<tr>
<th>Type of sample</th>
<th>Number of Samples</th>
<th>GM (GSD)</th>
<th>PEL or BEI (per 8-hr shift)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air--Total Particulate 12-hr TWA (mg m\textsuperscript{-3})</td>
<td>52</td>
<td>12.4 (2.3)</td>
<td>10.0 (PEL)</td>
</tr>
<tr>
<td>Air--Total Fluoride 12-hr TWA (mg m\textsuperscript{-3})</td>
<td>52</td>
<td>3.3 (2.2)</td>
<td>2.5 (PEL)</td>
</tr>
<tr>
<td>Urine Fluoride Pre-Shift Spot (mg g\textsuperscript{-1} creatinine)</td>
<td>58</td>
<td>1.1 (1.8)</td>
<td>3.0 (BEI)</td>
</tr>
<tr>
<td>Urine Fluoride Post-shift Spot (mg g\textsuperscript{-1} creatinine)</td>
<td>50</td>
<td>2.6 (1.8)</td>
<td>10.0 (BEI)</td>
</tr>
</tbody>
</table>

notes: PEL is US Occupational Safety and Health Administration's Permissible Exposure Level. BEI is American Conference of Governmental Industrial Hygienists' Biological Exposure Index. 12-hour shifts actually worked. Respiratory protection used. GM is geometric mean; GSD is geometric standard deviation.

PHASE ONE EXPOSURE ASSESSMENT

34 individuals were monitored for two days of their working week. Air and urine measurements are summarised in Table 2. Despite the magnitude of fluoride exposures, fluoride absorption (documented in the urine results) was fairly modest, likely due to the use of respiratory protection.
RESPIRATORY SYMPTOMS

Some subjects reported new symptoms over the first 6 months of employment, while others reported fewer symptoms on later inquiry, as shown in Table 3.

LONGITUDINAL PULMONARY FUNCTION AND AIRWAY REACTIVITY

Of the original cohort, at least two examinations have been completed on 100, and three examinations on 85. Simple spirometry (FEV₁, FVC, FEV₁ / FVC) has not revealed changes in this cohort’s airway function. Table 4 shows categorical methacholine challenge results from the first two examinations.

By spring of 1997, at least two examinations were completed on 113 total cohort members, and three examinations on 85. Fourteen participants have demonstrated increased nonspecific bronchial responsiveness, according to our criteria. Those 14 include some individuals who have reported new asthma-like symptoms and some individuals with baseline bronchial responsiveness in the “normal” range.

Table 3
Longitudinal Analysis of Symptoms Through Six Months, n=118

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Baseline (% with symptom)</th>
<th>New Symptom (%)</th>
<th>Symptom Lost (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheeze (not associated with cold/ not clearing with cough)</td>
<td>18.6</td>
<td>23.7</td>
<td>8.5</td>
</tr>
<tr>
<td>Shortness of Breath</td>
<td>7.6</td>
<td>11.0</td>
<td>2.5</td>
</tr>
<tr>
<td>Cough</td>
<td>10.2</td>
<td>26.3</td>
<td>5.9</td>
</tr>
<tr>
<td>Chest Tightness</td>
<td>5.1</td>
<td>6.8</td>
<td>3.4</td>
</tr>
<tr>
<td>Any of these</td>
<td>28.8</td>
<td>36.4</td>
<td>16.8</td>
</tr>
<tr>
<td>Sx which improve away from work</td>
<td>3.4</td>
<td>9.7</td>
<td>2.4</td>
</tr>
</tbody>
</table>

note: "New symptom" indicates symptom present at 6 months follow-up but not at baseline. If no 6 mo. follow-up data was available, then the last date (4- or 2- month) was used. "Symptom lost" indicates the symptom was present at baseline, but not at follow-up.

DISCUSSION
By collecting baseline data on bronchial responsiveness, this study has the potential to answer important questions about respiratory health in the primary aluminum industry. Thus far, the preliminary results indicate that bronchial responsiveness may be increasing among newly-hired employees. The first-year findings support the thesis that the asthma noted among aluminum smelter workers is due to new bronchial hyperresponsiveness, rather than an exacerbation of underlying hyperresponsiveness.

More data collection and analysis are required to understand these findings. As the study progresses, the relationship between exposures and respiratory health will become clearer.

**FUTURE STUDY PLANS**

We plan to continue to collect data for this project to complete five years of follow-up of the original cohort. This is possible due to the continued interest and commitment to the project from plant management and labor, and the availability of grant funding to support the project. During the planned study period, new employees will be recruited into the cohort if available.

**Health Assessment**

Annual follow-up of all employed cohort members will be conducted, including interview, spirometry, and methacholine challenge. In addition, an attempt will be made to evaluate employees leaving employment at the facility.

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Methacholine Responsiveness in Calculated PC_{20} (mg mL^{-1}) Among Subjects Tested at Baseline and at 6 months of Employment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose</td>
<td>Baseline</td>
</tr>
<tr>
<td>≤2</td>
<td>3</td>
</tr>
<tr>
<td>&gt; 2 and ≤8</td>
<td>11</td>
</tr>
<tr>
<td>&gt;8 and ≤16</td>
<td>7</td>
</tr>
<tr>
<td>&gt;16 and ≤32</td>
<td>10</td>
</tr>
<tr>
<td>&gt;32</td>
<td>69</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
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</tbody>
</table>
Percent in each category, n=100

**Exposure Assessment**

An effort will be made to characterise or estimate each cohort member’s individual exposure levels. As the cohort gains seniority, they will be working in a variety of positions throughout the plant. Administrative records will be supplemented by periodic air sampling and semi-annual (winter and summer) urine fluoride measurements.

**Assessment of Exposure-Effect Relationships**

In addition to epidemiologic analyses of the cohort-wide data, more detailed assessment of selected workers will be conducted. The sub-study described above is an effort to determine if certain measurable exposures, including peak irritant exposures, can be linked to respiratory health effects. The substudy methods will be refined and additional cohort members, both with and without possible exposure-associated health effects, will be recruited to participate.

**ACKNOWLEDGMENTS**

This study has been made possible by tremendous contributions of time and support from many individuals. We would not have been able to launch the project without generous and timely assistance from our collaborators at the University of British Columbia, especially Susan Kennedy, PhD, Barbara Karlen, and Moira Chan-Yeung, MB, FRCPC. Many hours of work have been invested into this project by University of Washington students and staff including Martha Horike, Patrick Moore, Rhonda Pariser, and Brian Zevenbergen. Many SHARP program staff have contributed immeasurably, including Michael Cotey and Deborah Moore. Our collaborators at the University of Washington, Scott Barnhart, MD, MPH, and Harvey Checkoway, PhD, are critical to the projects’ successes.

Above all, this study owes its very existence to the management and staff of the Kaiser Mead Works and the leadership of USWA local 329, who have shown unstinting support for the project, despite its unavoidable intrusion into their activities. The study investigators and staff are especially indebted to Carl Larson, Ray Perdue, Dave Kjos, and Tom Franklin for their endorsement of this research. Support from the plant medical clinic including Patty Cox and Dr. Judy Huesner has been very important. Thanks are also due to Chris Laszcz-Davis, Kaiser Aluminum’s Corporate Director for Risk Assessment Strategy & Compliance, for her ongoing assistance.

Finally, this research belongs to the workers who have volunteered to be studied. We are grateful for their contribution. The Washington State Department of Labor and Industries, SHARP Program provided primary funding for the study. The National Institute for Occupational Safety and Health Division of Respiratory Disease Studies provided funding for the peak-flow/exposure assessment sub-study. Dr. Daroowalla is the recipient of a National Research Service Award from the National Institute for Environmental Health Sciences.

**REFERENCES**

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20. HEALTHWISE: A STUDY OF HEALTH IN ALUMINIUM WORKERS

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SUMMARY

Objectives - To investigate the relationship between respiratory symptoms and changes in lung function, all causes mortality and cancer morbidity, and occupational exposures to specific chemical and physical agents at three bauxite mines, three alumina refineries, two smelters and a rolling mill.

Methods - Mortality and cancer morbidity will be assessed using a retrospective and prospective cohort. Demographic and workplace information has been collected from all employees who have worked for more than three months at any site and were employed on or after 1/1/83. Names will be matched with National death and cancer registers and a standardised incidence ratio will be calculated for all employees and for different jobs.

To assess the prevalence of respiratory conditions, a cross-sectional study has been undertaken: current employees were invited to complete a questionnaire and perform a lung function test whilst to investigate the incidence of these conditions a cohort of new employees have undergone similar questions and tests and have, in addition, performed a non-specific bronchial challenge procedure.

Detailed job information and quantitative assessments of occupational exposures have been combined to produce an accurate individual job exposure matrix. These will be used to indicate whether exposure to certain substances induce or exacerbates respiratory disease and whether or not a risk analysis is possible.

Results - The response rate for the cross sectional study was over 89%: 5095 employees were surveyed. Ages ranged from 15 - 69 whilst smoking and alcohol usage patterns were similar to the Australian community. Stage one analysis shows that chest tightness and wheeze was present in 10 - 20% of the workforce and at least one work related chest symptom was reported in 15% of those surveyed. These symptoms were more common in both smelters but only one refinery. Currently there are 367 participants in the inception cohort. Registry matches for the mortality and cancer morbidity study will commence late 1997.
Conclusions - Results to date suggest that occupational exposures have not produced an adverse effect on the respiratory health of workers in the bauxite mines, two refineries and the rolling mill. The excess of symptoms in the smelters are largely confined to some work groups in the older plant. A second stage analysis will determine whether this is linked to specific exposures or if it is a chance finding.

INTRODUCTION

Alcoa of Australia is a fully integrated aluminium producer operating three bauxite mines, three alumina refineries and two shipping terminals in Western Australia, and an aluminium smelter, power station and brown coal mine in Victoria. It is the major shareholder and manager of another smelter at Portland, Victoria, and was owner at the commencement of the study of a rolling mill, now KAAL Australia.

Previous studies in the aluminium industry world wide, dominated by historical or retrospective studies triggered by belated recognition of disease clusters, have concentrated on employees in reduction plants exposed to the Söderberg rather than the prebake process often however to both \(^{(1)(2)(3)}\). These have identified excesses of certain malignancies notably cancers of the lung, urinary tract and the lymphohaemopoetic system \(^{(4)(5)}\). Coal tar pitch volatiles have been identified at the exposure of most concern \(^{(6)}\).

Due to the exposures from varying process, results have been difficult to analyse and extrapolate to Australian smelters, which only utilise the prebake process.

No cancer studies have examined employees in bauxite mines or alumina refineries.

Aluminium smelter employees have also been shown to have an increased risk of occupational asthma probably due to exposure to respiratory irritants, and possibly an increased risk of chronic lung disease \(^{(7)(8)(9)}\). There have been few investigations of respiratory disease in employees in bauxite mines or alumina refineries, none in Australia.

In occupational epidemiology the most frequently applied criteria for the establishment of causation put forward by Bradford Hill are: strength of association; consistency; dose response; and a temporal relationship of exposure and disease outcome. Assessing the coherence of the various studies has proved difficult: populations have differing geographic and demographic characteristics; differing levels of frequently unrecorded potential compounding variables e.g. most studies of chronic obstructive lung disease have been cross sectional with attendant problems of bias and confounding by cigarette smoking; and
differing levels of workplace exposure often based on final, less exposed, jobs.

Accordingly, the management of Alcoa of Australia contracted the Department of Epidemiology and Preventive Medicine at Monash University Melbourne and the Department of Respiratory Medicine, University of Western Australia to carry out a feasibility study for a long-term health surveillance project within the company. The present paper outlines the development of this project and preliminary results of the cross sectional study of respiratory morbidity.

SUBJECTS AND METHODS

Many previous studies have been limited by inadequate exposure data and follow up of subjects. The Healthwise study has been designed to try to overcome these major limitations and comprises three separate sections, all of which have been approved by ethical committees of the investigating universities.

1. An historical and prospective mortality and cancer incidence study of former, current and future employees employed on or after 1st January 1983 with a minimum of three months service with the company. The main aims of this study are to investigate the relationships between deaths and the development of specific cancers, e.g. cancers of the urinary systems and lung, and occupational exposures to coal tar pitch volatiles and electromagnetic fields.

New, current and former workers recruited to this study are now in excess of 10,000 and matches of these with the National Death Index (N.D.I.) and the National Cancer Statistics Clearing House (N.C.S.C.H.) will commence within the next three months.

2. A cross sectional study of respiratory morbidity in current employees at each site. The main aim of this section is to investigate relationships between respiratory symptoms and lung function and occupational exposure to fluorides, coal tar pitch volatiles, bauxite dust, caustic mist, oil mist and alumina dust.

All employees were invited to participate and 5095 (89%) agreed to the completion of the questionnaire containing questions on demographic characteristics, respiratory symptoms, life style and work history, a lung function test using identical Graseby-Anderson Spirotech rolling seal spirometers at all sites, and a skin prick to test for atopic tendency. The survey was completed in July 1996.
The questionnaires and tests were conducted by fully trained personnel. Sixty employees did not wish to take part in the respiratory part of the survey but did enter the cancer incidence study.


The main aims of this study are to investigate developments of respiratory symptoms, changes in lung function and changes in bronchial hyper reactivity and their relationship to exposures to chemicals outlined in the cross sectional study of respiratory morbidity. Recruitment into this cohort is still ongoing and has proved to be slower than anticipated. There are currently 367 employees recruited to this study. Two rounds of follow up have been completed but meaningful results are not projected for at least two years.

![Figure 1. Participation rates for each centre in the cross-sectional survey.](image-url)
RESULTS

Demographic data

The total number of employees who agreed to take part in the cross sectional study was 5095 (89%). There were slight differences between sites (fig. 1). Participants ranged in age from 15 to 69 years with a mean age of 39 years, and were mainly men (92%). In this survey 78% were married, over half had spent at least 11 years at school, of those 53% had further qualification mainly trade certificates (fig 2), and 70% were born in Australia. English was the language spoken at home in 95% of participants.

A quarter of surveyed employees said they currently smoked cigarettes, the majorities smoking either 20 or fewer per day, 34% were ex-smokers (fig 3). About 86% of those surveyed currently drank alcohol. The percentages of male drinkers in the no or low, medium and high-risk groups were 94%, 4% and 2% respectively. For females there were no high-risk drinkers but 1.8% were considered at moderate risk.

These data indicate that the Healthwise Study population is very similar in most demographic and lifestyle variables to the Australian population (census 1991).

Employment characteristics

Participants have worked with the companies for between one and 34 years with a third of the workforce having been employed for between five and nine years. Most have had one or two jobs. The two newest sites had a lower average of years-worked (fig 4).

Respiratory health

The first stage of analysis used job titles. The next phase will use a more specific quantitative exposure classification, which is a more sensitive method of establishing a possible causal link.

Fourteen per cent of participants reported that they had been diagnosed as having asthma by a doctor, whilst 16% reported being diagnosed as having bronchitis. Rhinitis was reported in 27% and it was common for participants to report a positive family history of asthma and rhinitis.
Figure 2. Education level of the participants.

Figure 3. Percentage of current smokers by site.
In response to questions designed by the British Medical Research Council to investigate the prevalence of respiratory disease, wheeze in the previous year was reported by 21% of participants although only 5% reported a frequency of at least once a week. It was associated with shortness of breath in 17%. Waking at night with wheeze, chest tightness or shortness of breath and all symptoms of possible asthma, were reported by 5%, 3% and 1.5% of participants respectively.

Chronic bronchitis, using the definition of cough or sputum for three months in each of the past two years was reported by 12%. Perennial rhinitis was present in 11% whilst there was seasonal rhinitis reported by 20% of participants. Atopy or allergy measured by skin prick test to common allergens was common, 45% being positive (fig 5).

These results are not dissimilar to responses evoked by a respiratory survey carried out in Busselton Western Australia 10 years ago. There about 8% of male adults said they had asthma, 25% reported wheeze, 25% said they had hayfever and chronic bronchitis was found in 15%.

The distribution, by work site, for the more common respiratory symptoms and tests does however differ from site to site.
Reported asthma, wheeze, shortness of breath and chest tightness were most common at the oldest smelter (fig 6).

Figure 5. Histogram showing the percentage of participants with atopy (>3mm), by site.

Atopy and shortness of breath were most common at a mine site. Chronic bronchitis was marginally more common at another mine site whilst perennial rhinitis was commonest at the newer smelter (figures 7 and 8).

Participants were asked whether any respiratory symptoms were better at the start of the day, at the start of the working week or during holidays to assess the work-relatedness of their symptoms.

Work related wheeze was reported by 5% and work related chest tightness, shortness of breath wheeze and chest tightness were reportedly most frequent at the smelters (fig 9).

The remaining analysis of the results is reported for three separate groups - smelters, refineries and mines. Participants are grouped according to their current job into process groups at each site, similar sites having broadly similar exposures. Administration and maintenance employees were separated from production employees in each area.
Figure 6. Percentage of participants reporting wheeze in the previous twelve months, by site.

Because of the small number of women working in the production areas, the analysis is for men only. There is no reason to assume that these results would not be applicable. A number of issues need to be considered in the interpretation of the data.

**Confounding factors**

Respiratory symptoms are more common in certain groups of people than in others e.g. chronic bronchitis is more common in cigarette smokers than in non-smokers. It is possible that one process group has more smokers than another and that the prevalence of chronic bronchitis in this group is high. This could have nothing to do with the industrial process but is what is called confounding by smoking.
Figure 7. Percentage of participants reporting chronic bronchitis (from MRC questions), by site.

It has been accounted for by use of a statistical technique known as multivariate analysis, which adjusts the symptoms rate to reflect confounders. Whilst data will contain important factors there is the risk that others may have been missed.

Systematic errors

A cross sectional study can only give information on what is happening at one point in time. It is impossible to quantify the influence of previous events on the present situation and this may create a systematic error or bias an important one being selection bias. For example known asthmatics may not be assigned to a particular job group and this could result in a process group having a very high rate of reported asthma whilst in another there is very little. We cannot say that the process causes the high rate. Survival bias is another cause of misleading results. Individuals who develop symptoms in one process group in response to a particular exposure may be moved to a non exposed group or may in fact quit the employer leaving the highest exposed group with
the least symptoms. Different people may assign different causes for their symptoms and this is another form of bias.

Figure 8. Percentage of participants reporting perennial rhinitis, by site.

*Chance*

When a large number of analyses are performed some of the results may be significant by chance. There are a number of ways to assess the importance of a statistically significant finding and one way is to consider the consistency of the results across different sites. In this study there is data across several different sites for each industry. It is less likely to be chance for example if the same symptom arose in the same process group across the three refineries. The size of the effect is also important. Large differences in rates between two groups are less likely to be due to chance than small differences. Similarly results are less likely to be chance if based on large numbers of subjects.

**ANALYSIS OF RESPIRATORY SYMPTOMS**

In the multivariate analysis for the smelters, the model adjusted for age, previous work in the potrooms, smoking, schooling and atopy. For
refineries and mines, the model adjusted for age, smoking and atopy and these results were compared, for the smelters, to a combined group of administration employees to give an odds ratio with confidence intervals.

Figure 9. Percentage of participants reporting work-related wheeze, by site.

ANALYSIS BY PROCESS GROUPS

Smelters

Whilst nine process groups formed the smelters, two of these (rolling mill and power generation) were only present at the oldest smelter. Administration, green mill, carbon bakes, rodding, potroom, ingot mill and maintenance groups were common to both. After adjusting for confounding factors in the multivariate analysis, in the older smelter potroom, green mill, and ingot mill employees had statistically significant increased rates of wheeze, work related wheeze and chest tightness compared to the newer smelter where only rhinitis and work related rhinitis were raised to statistical significance.
Lung function results

For each process group, the lung volumes were similar or slightly lower at the older smelter than the newer. The differences however were not large (fig 10).

Refineries

There were nine process groups within refineries, but within these, due to differences in employee grouping, residue employees at one refinery are included in the clarification process group and precipitation employees are in the calcination/shipping group.

Respiratory symptoms and work related symptoms were more common at Pinjarra, the middle aged refinery but the differences were not as clearly marked as in the comparison between smelters. Precipitation employees at this refinery had, after multivariate analysis statistically increased rates of wheeze, chronic bronchitis, rhinitis, work...
related wheeze and work related rhinitis, the latter finding being quite common throughout work groups in all refineries.

**Lung function results**

Employees at the refinery with most reported respiratory symptoms tended to have the highest lung function values whilst the oldest refinery had the lowest. Job groups with lower lung function were not the same as those reporting the most symptoms and this will be explained in further analysis (fig 11).

**Mines**

Three process groups at the mines comprised administration, production and maintenance. Farmland and nursery at Willowdale is included as a separate group.

Some respiratory symptoms appear more common in the mine process groups but the pattern is not consistent. Multivariate analysis showed statistically increase rates at the one mine for asthma and chest tightness in production employees, and at another chronic bronchitis was increased in a maintenance group. There was no statistically significant increase in work related symptoms for any group. The calculated FEV\textsubscript{1} and FVC showed very little difference between groups at all mines.

**DISCUSSION**

Frostad published the first report of respiratory irritation in aluminium smelter workers in 1936. A number of cross sectional studies of 'potroom asthma' have appeared in the literature some of which have suggested that smelter workers also have an increased risk of developing chronic obstructive lung disease.

In the initial analysis of the cross sectional study data ingot mill and potroom employees at the older smelter have been shown to have the most consistent findings of work-related symptoms suggestive of asthma whilst ingot mill employees had a marginal decrease in lung function. There were no significant differences between these groups and administration for chronic bronchitis.

The unexpected finding of the elevated rate of several respiratory symptoms amongst ingot mill workers could be explained by different screening procedures, different processes and the production of alloys at the older plant. The method used to assign employees to exposure groups was quite simple and results might well be affected by
selection bias. These issues will be further examined when exposure-monitoring data is available.

Figure 11. Spirometry (refineries), illustrated for a 40 year old male, non-smoker, height 1.77m.

The results of lung function testing are shown in fig. 10. Lung volumes were similar or slightly lower at the older smelter. Further analysis is
planned to see if decreases in lung function are associated with symptoms and workplace exposures.

Analysis of data from refineries has so far produced somewhat conflicting results. Generally symptoms were more common amongst Pinjarra employees whilst they tended to have the highest lung function values. The oldest refinery had the lowest. The groups with lower lung function are not the same as those reporting symptoms, contrary to the smelters and this finding will be explored in more detail in further analysis. Whilst some groups of refinery workers reported more work related rhinitis and these were statistically significant compared to the administration group it is not yet possible to link this with a specific exposure. There is no evidence that employees in any of the mining process groups have more work related respiratory symptoms or poorer lung function than administration employees.

ACKNOWLEDGEMENTS

This paper is based in part, on the first triennial report prepared for Alcoa, Portland and KAAL by the Monash University and University of Western Australia study team. It is their efforts that have yielded the results that I have described.

REFERENCES

SUMMARY

Several important issues have to be considered when planning and implementing respiratory surveillance of potroom workers. These are the:

- task types undertaken by the worker;
- personal protection-related habits of the worker;
- individual susceptibility of the worker to respiratory disease;
- non-occupational exposures of the worker e.g., weekend work, hobby exposures, smoking;
- concentration of inhalable pollutants and the temporal pattern of worker exposure to them.

Such information can only be obtained when a person that is able to follow in his “foot steps” throughout the day monitors the worker. In addition, national laws and corporate rules influence the medical surveillance of the plant. In contrast most research undertaken employs superficial exposure models which are little practical use. However, the plant occupational health physician has to make practical decisions, particularly when faced with a new job applicant. The method of work of occupational physicians is an important issue discussed by Norwegian aluminium plant physicians. These physicians co-operate closely and, as a consequence, common medical surveillance procedures have evolved within the Norwegian industry.

INTRODUCTION

Methods employed for respiratory surveillance among the workforce of the aluminium reduction industry are, in many respects, controversial. Each year the decisions made by occupational health physicians become topics of discussion within the workforce, their families, their trade unions and management. This is particularly true in the area of pre-employment medical screening. The applicants, who are determined to work in the industry, do not wish to be rejected on the basis of medical advice. Similarly, there is pressure on the occupational physician to
accept an applicant from a management that has problems in hiring qualified workers – there being little unemployment in Norway. A conservative workforce that has been working in the industry for a long time and resists job change also causes problems. It follows that the occupational health physicians within the industry are often pleased to fall back upon the protection afforded them by regulatory frameworks and corporate rules.

With respect to the respiratory surveillance of existing workers, particularly potroom workers, the practice of physicians is hampered by a lack of knowledge concerning individual susceptibility and the relationship between specific exposures and health effects. Little practical help is provided by research projects undertaken by the industry and others. Occupational physicians commonly find these to be of theoretical rather than practical value. Most research undertaken is concerned with the effects of pollutants within ambient aerosols and too little attention has been focused on the confounding effects of smoking. Moreover, the data analysed is often superficial. Similarly, almost no reports describe the influence of individual task performance, what respiratory protection should be employed and its best method of usage. Studies of such issues, if they are to be of practical use to the occupational physician, need to employ “real data” collected in the workplace by researchers who track workers throughout the day.

Plant physicians make decisions at the level of the individual employee. In this they are aided by a considerable level of co-operation which exists between them and their colleagues throughout the Norwegian Industry. Close co-operation, annual meetings, frequent telephone calls and social contacts have resulted in very uniform practices within the Norwegian aluminium industry.

WORKFORCE RESPIRATORY SURVEILLANCE PRACTICES

All potroom workers are examined each year during the months September to November. The annual surveillance procedures are standard. These include:

- the completion of questionnaires (American Thoracic Society and smoking questionnaire);
- the establishment of a thorough occupational exposure history;
- a clinical examination;
- spirometry;
- a radiographic examination of the chest.
According to the results of the above, some workers may either receive more frequent examinations or be referred to lung specialist. Particular attention is paid to the results of the spirometry. Further action may be required if an employee has shown a marked drop in FEV\textsubscript{1} or if the FEV\textsubscript{1} value recorded for that employee falls to 80% of the expected value for that person. Where poor FEV\textsubscript{1} performance has been detected the employee will be required to perform an additional test 15 minutes after the administration of Salbutamol. A more detailed occupational exposure history may also be indicated. Issues of particular importance are:

- task types undertaken by the worker;
- personal protection-related habits of the worker;
- individual susceptibility of the worker to respiratory disease;
- non-occupational exposures of the worker e.g., weekend work, hobby exposures, smoking;
- concentration of inhalable pollutants and the temporal pattern of worker exposure to them.

The physician has to: decide whether the worker is fit for the job; are there any underlying conditions which make the worker particularly susceptible to job-exposures; are there signs of a deterioration in the health of the worker; are there any non-occupational exposures (e.g., smoking) that increase the risk of an occupational disease? The history obtained, combined with the clinical observations / measurements are used to decide what further steps need to be taken. The worker has the right to be informed of any clinical findings and an overview of any actions that need to be taken is normally provided. Such actions might include:

- advising the employee of an occupational illness / disease;
- personal steps that need to be taken by the employee – these might include advice to stop smoking, advice on personal hygiene, job performance, the use of ventilators, etc;
- relocation and / or re-education of the worker;
- plans for follow-up and referral;
- plans for economic compensation.

It has been found that a simple graph showing the employees personal lung function measurement results over a long period is a particularly useful tool in discussions.

Experience has shown that such actions, particularly relocation, are effective in the management of occupational asthma. For example, a follow-up study of 33 workers with potroom asthma at the Karmøy plant...
in 1981 showed that 8 years after relocation > 30% still showed asthma symptoms.

Clinical findings are not communicated to management without the signed approval of the worker. In all cases, the actions of the physician are to approved, written procedures. These procedures are approved by the trade union and the management and conform to legal requirements. Information passed to management comprises a notification of an occupational illness / disease (this information is also required, by law, to be passed the Norwegian Directorate of Labour Inspection), notification of required actions (as agreed by the worker) and required management actions relating to relocation, re-education, improved respiratory protection, etc. Copies of all documents are sent to the employee.

**CHOICE OF RESPIRATORY PROTECTION**

![Figure 1. The numbers of inhaled particles (1 μm diameter or less / cm³) within Söderberg plants with no protection and using different respiratory protectors.](image_url)
It is well established that ventilators provide good respiratory protection of the worker. Our own investigations have shown that worker exposures to airborne particulates with a diameter less than 1 µm may be reduced from 170,000 particles cm\(^{-3}\) to 50 particles by the use of a ventilator fitted with an ABCP3 filter. After tests with paper filters and air-stream hoods, we regard this filter to be unbeatable for daily use within the aluminium potroom environment (figure 1).

![Figure 1](image_url)

**Figure 2.** The number of Karmøy workers with asthma symptoms reported to the Directorate of Labour Inspection, by year since 1988.

**NEED FOR CONTINUED RESPIRATORY SURVEILLANCE**

The Karmøy plant is a large aluminium plant producing about 270,000 tonnes of primary aluminium and re-melting about 70,000 tonnes of the metal. The plant employs about 1000 workers and uses both Söderberg and prebake technologies. Within this population an average of 10 - 11 persons per year, since 1988, have been reported to management as showing symptoms of asthma (figure 2). Most of these workers were employed in the Söderberg plant, with smaller numbers reported in the prebake plants and among maintenance and foundry workers. In addition, significant levels of reduced lung function / chronic obstructive
lung disease (COLD) are present within the Karmøy workforce (figure 3). The continued presence of asthma and COLD illustrate the importance of continued respiratory surveillance within the aluminium industry.

![Histogram showing the prevalence (number of employees with disease) and incidence (number of new employees with disease) of COLD in Karmøy workers.](image)

Figure 3. Histogram showing the prevalence (number of employees with disease) and incidence (number of new employees with disease) of COLD in Karmøy workers.
SUMMARY

In the work environment of an aluminium smelter, employees may be exposed to a variety of atmospheric contaminants capable of causing harm if not adequately controlled. Primarily, control of exposure should focus on removal of the hazard at the source by engineering methods or by implementing work practices aimed at reducing exposure. Where this is not practicable, control of an atmospheric hazard may need to rely on the use of personal respiratory protection. If respiratory protection is used as a method of exposure control, the purchase and supply of respirators is only a small part of employer responsibility. In order for respirators to be effective in controlling exposure, a comprehensive respiratory protection programme must be developed and implemented as an integral part of the plant's hazard control strategy.

Simply purchasing the best respirator will not necessarily result in an adequate level of protection for an exposed employee. Effective protection will only be afforded with the support of a comprehensive management programme that addresses selection, fit, inspection and maintenance, training and regular review.

This paper presents a case study of the progressive development of a respiratory protection programme through the 10 year history of a primary aluminium smelter. Changes in the programme through time have contributed to a reduction in respiratory illness at the smelter, while at the same time resulting in significant cost reductions in the supply of respirators as an exposure control initiative.

INTRODUCTION

Portland Aluminium is located on the Victorian coast about 375 km east of Melbourne and 500 km west of Adelaide. Known as “Smelter in the Park”, Portland Aluminium is one of the world's largest and most modern aluminium smelters. Set amongst some of Victoria's most beautiful coastal heathlands, the smelter has become a benchmark for environmentally harmonious industrial development. Portland
Aluminium is a joint venture operation of which Alcoa of Australia is the major shareholder. Alcoa of Australia manages the smelter on behalf of the joint venture participants.

The Portland aluminium smelter commenced operation in October 1986. The two potlines, consisting of 408 smelting pots have a production capacity exceeding 300,000 tonnes per year. All aluminium produced is cast into 22.5 kg ingots and the majority is exported through the Port of Portland to markets in Southeast Asia. Portland Aluminium currently employs around 680 people.

In the early years, Portland Aluminium operated with a young and relatively inexperienced workforce. Most new operators had not worked in heavy industry before and the smelter experienced high staff turnover rates. Despite the modern technology and state of the art exposure controls, the health of many people was affected by work-related asthma.

Extensive occupational hygiene exposure assessments revealed that the risk of exposure was low when compared to documented health standards and in comparison to known exposures in older smelters which were less automated. Respiratory protection provided was of the standard accepted throughout the industry. The provision of respirators was supported by fit testing and training in the importance of facial seal, care and maintenance of re-usable respirators and in the potential health effects of over-exposure to known workplace atmospheric hazards. While there was a gradual reduction in the incidence of respiratory illness after the first years of operation, it became evident that exposure control initiatives, including personal respiratory protection, were not preventing the onset of work-related asthma.

Clearly, more needed to be done to understand the respiratory health issues experienced among the workforce and to develop and implement a strategy that would prevent further new cases of asthma and adequately control symptoms in those people already affected.

This paper makes reference to literature reports of respiratory health studies in the aluminium industry and describes strategies for exposure control through the use of personal respiratory protection. The experience at Portland Aluminium will demonstrate that effective respiratory protection will only be achieved through the implementation of a comprehensive respirator management programme.

**INDUSTRY EXPERIENCE**

Frostad published the first report of “respiratory irritation” in aluminium smelter workers in 1936 (1). In subsequent years, numerous reports on “potroom asthma” have appeared in the scientific literature. The question of whether exposures in aluminium smelting cause airways
disease has been reviewed in some detail by Abramson et al. (2). In his review, Abramson concluded that the relationship between respiratory disease and workplace exposure was unclear. It was not known whether exposure initiated asthma or precipitated symptoms in employees with sub-clinical asthma. This review of the literature revealed that the strength of association between the occurrence of asthma and potroom work varied considerably. However, it was concluded that there were a number of chemicals in the smelter environment that were capable of precipitating exacerbations of asthma, lending biological plausibility to the association.

Several reports in the literature suggest that aluminium industry employees with higher fluoride exposures are at increased risk of respiratory disease (3)(4). However, while reporting an association with fluoride exposure, none of these studies can exclude the possibility that fluoride is acting as a marker for some other constituent in the smelter environment. A study by Kongerud and Samuelsen suggests that cumulative irritant exposure may be responsible for asthmatic symptoms in the potroom workforce studied (5).

The literature provides good evidence that aluminium smelter employees have an increased risk of work-related asthma, however no definite cause has yet been identified. While the cause of this condition remains unclear, the provision of appropriate personal respiratory protection continues to challenge health professionals charged with managing health programmes within the workplace.

Although there are many reports on studies of respiratory health in the aluminium industry cited in the literature, reports on respirators appropriate to control exposure and prevent respiratory illness are infrequent. Disposable respirators were evaluated for their suitability for use in aluminium smelting by Archer in 1981 and again by Fergin in his presentation to the American Industrial Hygiene Association Conference in 1985 (6)(7). In 1991, Kongerud and Rambjor investigated the short-term effect of a helmet-style-powered air-purifying respirator on peak flow measurements when compared with a disposable mask (8).

Manufacturers provide technical data on the filtration capabilities of their products and on their suitability to protect against the various irritants present in the smelter environment. However, little information is available that links this laboratory data with actual respirator performance in the field. An abundance of different respirators are available on the market and are being used throughout the industry worldwide. These range from disposable dust masks to cartridge-style gas/vapour/fume respirators and powered air helmets with various filter combinations.

However, smelters that report ongoing respiratory health issues are all providing respiratory protection for their employees. If smelter
employees at risk of exposure are wearing appropriate respirators, why are they experiencing respiratory illness related to their work?

RESPIRATORY PROTECTION PROGRAMMES

The answer to this question lies in the effective management of respiratory protection in the workplace.

It has been established that in the work environment of an aluminium smelter, employees may be exposed to a number of atmospheric contaminants capable of causing harm if not adequately controlled. Occupational hygiene monitoring programmes have characterised exposure profiles of smelter employees performing jobs and tasks typical of the aluminium smelting operation. Primarily, control of exposure should focus on removal of the hazard at the source by engineering methods or by implementing work practices aimed at reducing exposure. However, where this is not practicable, reliance on personal protection may be the only available option for exposure control.

There are numerous respirators available that are capable of filtering the airborne contaminants in question. However, simply purchasing and issuing the best respirator will not necessarily result in an adequate level of protection for an exposed employee. Effective protection will only be achieved with the support of a comprehensive management programme that addresses selection, fit, inspection and maintenance, training and regular review.

Standards in various countries outline the requirements for the implementation of a respirator programme. While there are some minor differences, the fundamental principles are consistent throughout. All concur that if respiratory protection is to be used as a method of exposure control, the purchase and supply of respirators is only a small part of employer responsibility. In order for respirators to be effective in controlling exposure, a respirator management strategy must be developed and implemented as an integral part of the plant's hazard control programme. The following key elements form the basis of the respirator programmes detailed in the above referenced standards:

- Management responsibility
- Selection of equipment
- Medical screening
- Issue of respirators
- Facial fit-testing
- Inspection and maintenance
- Training
Programme evaluation

Although these key elements are common to respiratory protection standards world-wide, a recent review of respiratory protection programmes in 18 aluminium smelters revealed vast inconsistencies in the implementation of these requirements.

THE PORTLAND EXPERIENCE

During the early years of operation, Portland Aluminium experienced a high incidence of work-related asthma among a new and relatively inexperienced workforce. Most operators had never worked in heavy industry before and high turnover rates exacerbated the problem. While modern and highly automated technology maintained the risk of exposure to airborne contaminants at a very low level, it became clear that the exposure control initiatives implemented were not preventing the onset of work-related asthma. Moreover, respirators worn were not effective in controlling exposure so that some people with asthma could not continue to work in the smelter environment.

In an effort to better understand and control the respiratory health issues confronting the organisation, an asthma prevention strategy was developed and implemented. The strategy was broad in scope and attempted to address all aspects of the smelter operation that could impact the respiratory health of employees. The main components included:

- Source control
- Work practice modification
- Respiratory protection
- Medical surveillance
- Education / training
- Research

Initiatives to reduce the potential for exposure through engineering modifications and review of work practices were ongoing and were approached aggressively across all areas of the operation. Research to assist in understanding the cause and to identify better control and management opportunities was initiated. Implementation of the strategy sought and achieved involvement and commitment of people across all areas of the plant and throughout all levels of the organisation.

Respirators with approved gas/vapour/fume cartridges, both in re-usable silicon face pieces and in powered air helmet styles were introduced in place of disposable masks. Potentially, these would
provide a higher level of protection through more efficient filtration and superior fit compared with the “one size fits all” disposable mask. A quantitative fit-testing programme was implemented for all employees and this was supported on an ongoing basis by annual qualitative fit testing. Efforts in respiratory education and training were escalated with the introduction of respiratory protection workshops for all employees. Respirator maintenance rooms were established in each operating area of the plant so that people had convenient access to all spare parts and cleaning facilities for the daily care of their respirator.

Over time, the incidence of new cases of work-related asthma decreased. Results of surveys conducted showed an increase in awareness of respiratory issues, an increase in knowledge of how and when to wear respirators and of how to maintain them. Compliance with wearing requirements had significantly improved. Positive progress had been made, but it was obvious that there were still issues that could be addressed to further improve the effectiveness of our programme.

While the incidence of asthma was decreasing, there were still new cases being diagnosed and people with existing asthma were still having difficulty in managing their condition in the workplace. Although respirators were being worn, the question of the effectiveness of the protection and the cost effectiveness of the programme needed to be analysed.

Although intensive training and convenient facilities were provided, an audit of routine maintenance and inspection showed vast inconsistencies in the level of daily care employees were providing to ensure optimum protection from their respirator. While some people were extremely diligent, others were less enthusiastic leading to some respirators being poorly maintained. There was no easy way to track usage patterns or identify common faults. When a respirator failed, the tendency was to dispose of it and get a new one, rather than identify the problem and fix it. Not only were respiratory protection costs still significant, it became obvious that the quality of routine maintenance was affecting the level of protection afforded.

The need to continue to build on education and awareness programmes already in place was recognised. In addition, continuing to promote individual accountability for daily cleaning and inspection of personal respirators was seen as fundamental to the success of the programme. However, while more attention to these areas would bring about incremental improvement, this would not achieve the step change that was necessary to prevent asthma in the workplace. The introduction of a Respiratory Support Centre was seen as the way forward to realise the step change that we were seeking.
The Respiratory Support Centre was established as a central facility that supported people within the plant to achieve the best performance from their respirator. While routine daily inspection and care remains the responsibility of the wearer, the Centre provides a higher level of maintenance for all respirators twice per month. In addition to routine servicing, the staff of the Centre is available across all shifts to provide expert advice to people who have concerns about their respiratory protection. Faults are now tracked and taken up with the manufacturer for continuous improvement and warranty issues are addressed. Annual fit-testing and respiratory training is performed by the staff of the Respiratory Support Centre and fit-testing, training and service history records are maintained for each person on site, thus providing total support and co-ordination of the respiratory protection programme.

The improvements realised from the operation of the Respiratory Support Centre are summarised as follows:

- Improved maintenance and better protection
- Increased accessibility to problem solving expertise
- Common faults identified and continuous improvement
- Record keeping improvements
- Respirators and parts available only through the Centre
- Accountability remains with the individual
- Overall respiratory programme co-ordination

Since the introduction of the Respiratory Support Centre in 1994, significant improvements have been seen in the respiratory health of employees and in the cost effectiveness of the respiratory protection programme. The number of new cases of work-related asthma have decreased steadily since the introduction of the Respiratory Support Centre and more people with existing asthma are able to remain at work symptom free. While these results are the net effect of the synergism of all aspects of the asthma prevention strategy, the Respiratory Support Centre has made a significant contribution. Twenty new cases of work-related asthma were diagnosed during 1994. This decreased to eight in 1995 and four in 1996 and no new cases presented in 1997.

In addition to the pleasing results in the decline in respiratory illness at the plant, the cost of running the programme has decreased significantly since the introduction of the Respiratory Support Centre. Annual respiratory protection costs have reduced by more than 60% compared with costs incurred in the early 1990's. This trend continues to decrease. The programme is achieving the desired results in terms of preventing the occurrence of work-related respiratory illness with the added benefit of significant cost advantage.
CONCLUSIONS

The successful control of respiratory illness at Portland Aluminium has not been achieved by respiratory protection alone. The overall asthma prevention strategy is broad in scope and addresses all issues which may contribute to the control of respiratory disease through workplace exposure. The successful implementation of the strategy has involved a wide range of people across the site and has required commitment from all levels of the organisation.

Improvements in the respiratory protection programme over time have contributed significantly to the control of work-related asthma and to the cost effectiveness of this exposure control initiative.

In order for respirators to be an effective exposure control option, they must be well fitted, well maintained and worn. This will only be achieved by the successful implementation of a comprehensive respiratory protection management programme.

REFERENCES

23. CAN WE CHANGE SMOKING HABITS?

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SUMMARY

This paper describes a scheme initiated by Alcan to help discourage staff from smoking. Plant specific programmes were initiated. To date, the scheme claims a 33% success rate in helping staff to quit.

THE ALCAN PROGRAMME

In order to maintain our momentum towards continuous improvement of working conditions and health of its employees, a few years ago, Alcan initiated a program aimed at preventing employees from being exposed to cigarette smoke.

Supported by the senior management of the company, a committee worked towards establishing the objective and strategies to be used to deal with this problem. Afterwards, each plant made arrangements to reach the set objective. The joint working committees, thus formed in each plant organised their action plan and defined its characteristics: policy for the reimbursement of transdermic patches, choice of assistance program etc.

To support and stimulate these local efforts, a provincial work group formed with delegates from every plant in the province of Quebec to co-ordinate and organise promotional and awareness activities. In January 1997, during the National Non-Smoking Week, the group launched a Sponsorship Challenge to all Alcan employees in the province of Quebec and their immediate family. This challenge, which was due to end in January 1998, requires the creation of duos, that is a smoker wishing to quit and willing to take up the various steps of the challenge, and a non-smoker as sponsor during this year of abstinence. At the end of each step, the duos that are still refraining from smoking are eligible for a draw.
RESULTS

The results so far of the 983 teams who signed up to the 48 hour challenge, 334 were still refraining from smoking after the fourth month challenge. That represents a fraction of 33%. The Sponsorship Challenge and the efforts are ongoing since results will only be interesting if long term and extra long term follow-ups are ensured. Needless to say; our motivation lies in the high smoking ratio of our youth, our future employees.

Yes, we can change smoking habits, but a lot of energy and humanity need to be devoted to reach our objective.
SUMMARY

Our knowledge about Alzheimer’s disease (AD) is rapidly expanding. This review outlines new trends in the diagnosis, natural history, pathophysiological hypothesis and therapy of AD for this disease.

DIAGNOSIS AND NATURAL HISTORY

The diagnosis of AD requires a combination of decline of intellectual performance in comparison with previous levels, involving memory and at least one other cognitive domain such as language, spatial orientation or executive functioning, in an alert person. Furthermore this cognitive loss must interfere significantly with social or occupational functioning (1). Diagnosis of AD thus requires a medical history with a reliable informant (2), supplemented by serial mental status assessment using tools such as the Mini Mental State Examination (3). Few laboratory tests are usually required if the clinical history is clear and physical examination normal (4) (5). As stated in a recently published consensus statement, the laboratory assessment is performed to identify uncommon treatable causes and common treatable comorbid conditions (6). None of the biological markers from spinal fluid has yet shown enough specificity for routine use in clinical diagnosis (7).

There has been an increased recognition of the sequence of milestones in AD that may be used as end-points for stabilisation therapy. One of them is progression from mild cognitive impairment to diagnosable dementia (8), requiring detection of changes in functional abilities for instrumental tasks such as handling money, using the phone and planning an outing (9). This early milestone of AD will be used in new studies that aim at delaying progression in very early stages of AD (10). Other milestones include appearance of neuropsychiatric symptoms, institutionalisation, loss of autonomy for self-care activities, and death. The latter three have been used as end-points for a stabilisation study using alpha-tocopherol and selegiline (11).
PATHOPHYSIOLOGICAL HYPOTHESIS

The pathology of AD has been extensively studied and the most important feature appears to be loss of synapses and neurons in the cerebral cortex \(^{(12)}\). The relative importance of extra-cellular and peri-vascular amyloid deposition, and of tau hyperphosphorylation in intracellular neuro-fibrillary tangles is under debate. More recently, cellular inflammation associated with acute phase reactants has attracted attention, from both pathological and epidemiological perspectives \(^{(13)}\).

A number of genetic mutations have been identified and lead to AD symptoms appearing at ages as varied as 40 to 90 \(^{(14)}\). The mutation that has been the most studied and is relevant to the more common sporadic AD is that of apolipoprotein E4 (apoE4) \(^{(15)}\), which alters the brain ability to maintain synaptic plasticity \(^{(16)}\). ApoE4 genotyping is not recommended as a routine diagnostic nor as a presymptomatic test \(^{(17)}\), but it may allow prediction of responsiveness to therapy since persons with AD without the apoE4 mutation do better on cholinergic replacement than those who carry this mutation \(^{(18)}\).

Factors other than genetic mutations clearly alter the risk of developing AD symptoms at a given age. Epidemiological studies have documented the protective role of anti-inflammatory drugs and higher education \(^{(19)}\). In the latter study, aluminium exposure was found to be of no relevance.

THERAPY

The treatment of AD has so far been supportive, paying attention to common comorbid conditions such as depression, hypothyroidism, malnutrition, and misuse of sedatives or tranquilisers. The health and well-being of the caregiver also requires close attention throughout the illness.

New medications designed to treat symptoms of AD in early to intermediate stages have been developed, most of them bolstering acetylcholine activity by slowing down its degradation by acetylcholinesterase (cholinesterase inhibitors, CI), or acting as substitutes and stimulating selectively post–synaptic muscarinic receptors (muscarinic agonists, MI). The latter have proven so far difficult to tolerate because of autonomic side-effects such as sweating and syncope \(^{(20)}\), whereas the former include widely used drugs such as tacrine (Cognex), donepezil (Aricept) and rivastigmine (Exelon). There is hope of additive beneficial effects from combining a CI and a MI.
Clinicians are currently developing utilisation guidelines for the CI, taking into account data generated from phase III studies\(^{(21)}\).

There is hope of stabilisation therapy by targeting a number of pathophysiological mechanisms such as amyloid deposition, inflammatory response and oxidative stress \(^{(22)}\). The regulatory requirements for a claim of disease progression have been recently clarified \(^{(23)}\).

Finally, a preventive approach for the ageing population at large is feasible, taking into account the wealth of risk and protective factors being uncovered with each large-scale epidemiological study. Aetiology-driven hypothesis will soon allow testing in well-defined populations at different level of genetic risk with agents such as alphatocopherol and estrogens. It has indeed been estimated that delaying the symptoms of AD by five years would result in a 50% reduction in prevalence in one generation, and a delay of ten years would reduce prevalence by 75% \(^{(24)}\).

**CONCLUSION**

Careful optimism is warranted in our ability to treat AD by understanding its complex and multiple aetiologies converging towards a core clinical syndrome and pathology, whatever the age of onset. Refinements in the selection of symptomatic and stabilisation agents may be possible by careful observations in phase IV studies correlating clinical profiles, genotypes and therapeutic responses.

**REFERENCES**

It has been 17 years since we first detected excess aluminium in association with the neurofibrillary tangle (NFT)-bearing neurons of cases of Alzheimer’s disease \(^1\). Subsequent studies detected evidence of prominent aluminium accumulation in NFT bearing neurones of cases of amyotrophic lateral sclerosis / Parkinsonism-dementia complex (ALS/PDC) of Guam \(^2\). The subsequent introduction of laser microprobe mass analyser (LAMMA) instrumentation provided more precise sub-cellular localisation as well as more detailed and sensitive trace elemental data. This confirmed the presence of excess aluminium, as well as increased iron concentrations specifically in association with the NFT of cases of Alzheimer’s disease \(^3\) as well as Guam ALS/PDC. Similar findings of increased concentrations of both aluminium and iron have also been detected in the neuromelanin granules of the substantia nigra of cases of Parkinson’s disease and in the Lewy body inclusions \(^4\).

This growing body of data has stimulated our interest in the consequences of increased intraneuronal iron concentrations. Through its actions in the Fenton reaction it would be anticipated that excess iron, if not properly modulated by intracellular protective mechanisms, might induce hydroxyl radical formation resulting in oxidative damage. Most recently we have shown that the very cellular populations in which we have demonstrated excess iron and aluminium also contain evidence for the presence of nitrotyrosine formation \(^5\). Peroxynitrite, formed through the action of the superoxide radical with nitric oxide (and the presence of iron), binds to tyrosine residues of proteins and forms a stable protein-modifying bond, which remains as a permanent marker that oxidative damage has taken place. This important piece of evidence suggests that oxidative damage to vital intracellular macromolecules in target neurons may underlie the progressive cellular destruction associated with the category of disease entities. What of aluminium and
its possible role in this mechanism for neuronal damage? Aluminium, with a single 3+ valence state, does not itself play a role in oxidative reactions. However, several pieces of evidence indicate that aluminium, when present with iron, can enhance the latter element’s capacity to induce oxidative damage. In this way, the combined presence of both iron and aluminium in cells that normally employ a high level of oxidative metabolism might overwhelm the normal available antioxidant mechanisms leading to progressive damage and ultimately cell death.

Finally, we have attempted to explore the means by which aluminium (and iron) might gain access to the central nervous system. We recognise that the brain is normally carefully sequestered against environmental exposure to aluminium and normally has a very stable content of iron. In this work we have turned to the model of manganese poisoning. For many years it has been known that manganese can induce selective damage to the putamen, globus pallidus and substantia nigra pars reticulata (SNr) and through the resultant damage to post-synaptic dopaminergic target fields induce a Parkinsonian state. We have exposed rhesus monkeys to oral doses of manganese compounds, inducing a Parkinsonian state. Magnetic resonance imaging has revealed evidence of selective manganese accumulation in the putamen and globus pallidus\(^9\). On sacrifice, evidence of neuronal loss and gliosis was seen in the globus pallidus and SNr along with prominent perivascular and parenchymal mineralisation in these regions. Laser microprobe studies have revealed that these mineral deposits contain high concentrations of both iron and aluminium\(^10\). This indicates that exposure to a third element, namely manganese, is capable of interfering with the normal mechanisms which keep the brain sequestered from access by both aluminium and iron. In addition, it suggests that entry of both elements to the brain is linked to the neuronal degeneration, which underlies this condition. Whether this precise mechanism plays a role in the entry of iron and aluminium in the human neurodegenerative disease above is currently under investigation.

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26. THE ROLE OF ALUMINIUM IN ALZHEIMER’S DISEASE

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SUMMARY

The demonstration that the introduction of aluminium (Al) into the brains of rabbits induced neurofibrillary tangles gave rise to the hypothesis that aluminium played an important role in the aetiology of Alzheimer’s disease. In the three decades following these initial findings, a variety of different types of studies, including post-mortem analyses of Alzheimer’s brains, epidemiological investigation of disease risk with aluminium exposure, assessment of renal insufficiency patients and a clinical trial of chelation, have been addressed determining the possible involvement of this metal in Alzheimer’s disease. The present paper reviews this literature and concludes that, although aluminium is clearly neurotoxic, there is no evidence indicating that it causes Alzheimer’s disease.

INTRODUCTION

Although it has been known since 1897 that aluminium (Al) is neurotoxic (1), three research findings, reported between 1965 and 1976, led to the idea that this metal contributed to the aetiology and pathogenesis of senile dementia of the Alzheimer’s type (SDAT). First, introduction of aluminium salts into the brains of rabbits was shown to induce cognitive deficits in association with the formation of neurofibrillary changes that, with conventional silver staining, appeared similar to the neurofibrillary tangles of SDAT (2-5). Shortly after this, it was discovered that dialysis encephalopathy, a rapidly lethal disorder characterised in part by profound dementia, was caused by aluminium (6) and that aluminium levels were elevated in the brains of patients with SDAT (5). The present paper will critically evaluate these findings in the context of current information concerning SDAT and, in addition, will address more recent reports concerning occupational and dietary exposure to aluminium as well as the effects of chelation on the progression of SDAT.
ALUMINIUM AND THE BIOCHEMISTRY AND NEUROPATHOLOGY OF SDAT

The neuropathological hallmarks of SDAT are intraneuronal neurofibrillary tangles, extracellular β-amyloid plaques, amyloid angiopathy and neuronal loss. While aluminium in the rabbit brain produces neither β-amyloid plaques, nor amyloid angiopathy nor extensive cell loss, it does cause neurofibrillary pathology. It is therefore crucial to ask if aluminium-induced tangles as seen in the brain of the rabbit are similar to the neurofibrillary pathology of SDAT?

Consideration of biochemical, ultrastructural and immunohistochemical data indicates that the answer to this question is unequivocally in the negative (vide infra). Under light microscopy, aluminium-induced tangles and SDAT pathology appear similar with silver staining. However, only SDAT tangles show strong florescence when stained with thioflavin-S and birefringence associated with a β-pleated sheet after staining with Congo red. Aluminium-induced tangles differ from those of SDAT in their distribution on both gross and ultrastructural levels. While both types of tangle are found in the cortex and hippocampus, only aluminium-induced pathology is also found in the spinal cord. Indeed, the spinal burden appears to exceed that of the brain itself. Within single neurons, aluminium-induced tangles are found in the perikaryon and the proximal parts of the dendrites and axon. In contrast, SDAT tangles are found throughout the neuron including the entire length of the dendrites and throughout the axons including the terminals. Aluminium-induced tangles are made up of straight 10nm diameter neurofilaments while SDAT tangles are 20-24 nm paired helical filaments. The protofilament building blocks of aluminium-tangles also differ from those of SDAT with the diameter of the former ≈ 2.0 nm and the latter ≈ 3.2 nm. The peptide composition of aluminium-induced tangles is chiefly neurofilament protein while SDAT paired helical filaments are composed primarily of hyperphosphorylated tau, a microtubule associated protein, and ubiquitin. Although a few investigators have reported that tau is also found in the aluminium-induced tangles of rabbits (7,8), it should be noted that the majority of investigators failed to confirm the presence of tau (9 – 12). Moreover, those that did find this protein reported that it is primarily in non-phosphorylated form (8). Accordingly, aluminium-induced tangles fail to react with the 5-25 monoclonal antibody to SDAT tangles (13).

Thus, aluminium introduced into the brain of rabbits produces neuropathology that superficially resembles the neurofibrillar pathology of SDAT. Upon closer scrutiny, however, aluminium-induced tangles differ qualitatively from SDAT paired helical filaments. Moreover, aluminium in the rabbit brain produces none of the other
neuropathological stigmata of the human disorder. In addition, aluminium introduced into the brain of other species (mouse, rat, monkey) not only fails to produce plaques and angiopathy but also is unable to produce neurofibrillary tangles of either the type found in SDAT or in rabbit brain. In addition, as will be discussed, aluminium introduced into the brain of humans, while certainly toxic, does not produce any of the neuropathological changes associated with SDAT.

It is of interest that there does appear to be one effect of aluminium that is caused in both rabbits and also in those species of animals that are resistant to aluminium-induced fibrillary changes. Indeed, this same symptom is also observed in humans after aluminium accumulation in the brain (vide infra). Aluminium is a potent epileptogenic agent and seizures are seen in virtually all species as a result of brain aluminium build-up. It should be noted with respect to the aluminium hypothesis of SDAT, seizures are only seen in a small minority of patient’s with Alzheimer’s disease.

EFFECTS OF ALUMINIUM ON THE HUMAN BRAIN

There is one well-documented case in which the effects of metallic aluminium on the human brain were assessed (14). In this instance, a 14 years old boy sustained a small injury in the left occipital region after a hand grenade, with which he was playing, exploded. Although he experienced dizziness and transient visual problems in the immediate aftermath of the injury, he apparently recovered sufficiently to complete high school and then law school. Fifteen years later, he began to experience grand mal seizures which, over the next four years increased in frequency in association with developing problems of language and cognition. He died at age 34 in status epilepticus. Post-mortem studies showed local scarring in the left occipital region, generalised thinning of the cortex and mild dilatation of the fourth ventricle. Although no other anatomical abnormalities were observable with gross inspection, there was evidence of metallic deposits that, upon analysis, proved to be metallic aluminium. Notable with respect to the implication of aluminium in SDAT were two points. First, the clinical presentation of the disorder was seizure activity rather than the behavioural changes that herald the onset of SDAT (see below). Second, microscopic analysis revealed neither neurofibrillary tangles nor plaques.

While it is unwarranted to generalise from this one case report, there is another clinical condition associated with aluminium accumulation in the brain that is far more common and, therefore, allows more general conclusions. Dialysis encephalopathy, a rapidly progressing fatal disorder characterised in part by severe dementia, was found to be caused by the accumulation of aluminium in the brain (6).
Consideration of the clinical symptoms of dialysis encephalopathy and the associated neuropathology sheds light on the possible role of aluminium in SDAT.

In its most typical form, SDAT shows a characteristic presentation and pattern of decline (15) with the initial symptom most typically an impairment of recent memory that is often neither acknowledged nor noticed by the patient. In addition, executive functioning also suffers early with the patient showing a lack of flexibility and deficits of planning ability frequently accompanied by depression. As the disorder progresses, memory impairments become severe, the patient becomes disoriented and language abilities are also affected. Finally, about 5-10 years after the initial symptoms, profound impairment affects all areas of cognition and movement, which was relatively untouched in the earlier stages, now is also severely affected. Death usually is secondary to pneumonia.

The clinical picture of dialysis encephalopathy radically differs from that of SDAT in its presentation, clinical progression and time course. Unlike SDAT, the initial symptoms of dialysis encephalopathy are motoric and most often take the form of dysarthria. More generalized motor disruption and seizures follow with memory and other cognitive functioning only being affected subsequently. Death usually occurs due to status epilepticus about 6 months after the initial symptoms were noticed. It is important to note that seizures are seen only rarely in SDAT. In addition, post-mortem examination of the brains of patients with dialysis encephalopathy revealed none of the neuropathological hallmarks of SDAT (i.e. neurofibrillary tangles, neuritic plaques and amyloid angiopathy).

With the recognition that dialysis encephalopathy is caused by aluminium contamination of dialysates, use of appropriate safeguards has virtually eliminated this disorder. However, since the primary route for eliminating ingested aluminium is through the kidneys, some patients with renal insufficiency who are exposed to high levels of dietary aluminium accumulate this metal in their brains. Unlike patients with dialysis encephalopathy, the levels of brain aluminium are not so high as to induce an acute neurotoxic reaction. Indeed, since the exposure is at a lower concentration and over a much longer time span (i.e. years), consideration of the clinical and neuropathological sequelae may be more relevant to the question of aluminium involvement in SDAT than is dialysis encephalopathy.

Neuropsychological testing of dialysis patients with significant body burdens of aluminium reveals memory impairments restricted to the visual domain unlike the more general memory deficits that characterise the initial stages of SDAT. In addition, dialysis patients have problems with attention and concentration, difficulties only seen in the later stages of SDAT (16). CT scans demonstrated evidence of frontal
cortical atrophy in about 25% of patients \(^{(17)}\). In contrast, the earliest and most severe cell loss in SDAT occurs first in the entorhinal cortex, subsequently in hippocampus later in limbic structures and temporal gyrus and only in the final stages is there widespread cortical atrophy \(^{(18)}\); cell loss restricted to frontal areas is not seen. In addition, post-mortem examination of the brains of renal insufficiency patients did not indicate increased frequency of neurofibrillary tangles or the presence of neuritic plaques \(^{(19,20)}\).

**ELEVATION OF ALUMINIUM IN BRAINS OF PATIENTS WITH SDAT**

Initial reports that the bulk concentration of aluminium was elevated in the brains’ of patients with SDAT \(^{(5)}\) lent further support to the idea that this metal was involved in the aetiology and/or progression of the disorder. However, the studies that were stimulated in the wake of this initial study were contradictory and led to no unequivocal statement concerning the putative bulk elevation of aluminium. For example while some investigators found elevated aluminium in some regions of SDAT brain \(^{(21 - 25)}\), several studies failed to replicate these findings \(^{(26 - 29)}\). The presence of these negative findings has to be given serious consideration for two important reasons. First, negative findings are more difficult to publish and, to make it through editorial review, are typically quite solid methodologically. Second, Bjertness et al., \(^{(30)}\) have pointed out that measurements made with neutron activation analysis, the technique used to measure aluminium in two of the studies reporting elevated concentrations \(^{(22,24)}\) are subject to contamination by phosphorus. This point is particularly relevant since the authors of these studies \(^{(22,24)}\) did not indicate that they had taken appropriate precautions to ensure accurate measurement.

In general, studies of aluminium concentration in SDAT have been criticised for “...methodological problems” such as inadequate neuropathological assessment of the AD (Alzheimer’s Disease) and/or control patients. These may result in: a risk of misclassifications; lack of appropriately age-matched control patients; too few cases analysed, leading to risk of type II errors; and lack of geographical homogeneity of the AD and control populations, resulting in a selection bias due to possible differences in aluminium exposure.” \(^{(30)}\). In the most recent investigation of this question, efforts were made to correct the methodological inadequacies of the previous studies concerning selection of controls, sampling bias, aluminium exposure, and SDAT diagnosis \(^{(30)}\). Aluminium measurements were made with graphite furnace atomic absorption in frontal and temporal cortex, areas most heavily involved in SDAT pathology. The authors reported that their
data “...show conclusively that in AD, bulk aluminium concentration is not increased in two cortical brain regions that are selectively vulnerable to the neuropathological changes associated with this disorder.”

While SDAT does not appear to be associated with bulk aluminium elevations in brain, the picture is less clear concerning more localised accumulations. Although several investigators have reported aluminium concentrated in the neuritic plaques of SDAT (31,32), the preponderance of reports fail to find such accumulations (see review (33)). In contrast, there is much more convincing evidence that aluminium is found, along with iron, in SDAT neurofibrillary tangles. However the presence of aluminium in tangles does not indicate whether the accumulation is a cause or an effect of neurodegeneration. Indeed, the fact that similar co-concentrations of aluminium and iron are found in tangles associated with a host of other neurodegenerative diseases, including those in which aluminium clearly plays no aetiological role (e.g., dementia pugilistica - see Perl, this volume, Chapter 26) favours the latter interpretation.

**Epidemiological Studies of SDAT and Aluminium Exposure**

The relation between SDAT and aluminium has been investigated in epidemiological studies of occupational, dietary and other modalities of exposure. While some studies have reported elevated risk with increased aluminium exposure, contradictory results have also been published and no consensus exists to date (see review (34)). Valid epidemiological studies are methodologically difficult and those that assessed the role of aluminium exposure suffered from a number of problems that precluded generalisation based on their results (35). In this context, two recent studies, one of occupational exposure and the other of dietary intake, are particularly interesting because efforts were made to avoid methodological confounds. In addition, each consisted of a comprehensive evaluation of data that had earlier served as the basis for publications implicating aluminium exposure in the aetiology of SDAT (36,37).

The first study concerned miners from northern Ontario who were exposed to aluminium as part of a prophylactic program against silicotic lung disease. These individuals inhaled air containing a dust (McIntyre Powder) said to be composed of 15% elemental aluminium and 85% aluminium oxide (20,000-34,000 ppm.) for 10 minutes preceding each work shift. This program began in 1944 and was ended in 1979 on the conclusion of a medical panel that the conditions in mines had changed such that silicosis risk had declined to the extent that prophylaxis was no longer necessary. The Ontario Ministry of Labor, in 1987, commissioned studies of miners who had been exposed to
McIntyre Powder to determine if there was any long-term negative impact on health. In the initial study, Rifat et al., (36) reported that, although there was no increased incidence of neurological disorders in exposed miners, a higher proportion showed impairment on cognitive testing than did the control group of unexposed miners. However, there were significant methodological concerns that were prompted by the cross-sectional design of the study, sampling procedures and statistical analysis. Consequently, the investigators designed a more comprehensive assessment incorporating methodological changes that corrected the weaknesses of the initial study. In contrast to their earlier findings, this follow-up investigation revealed no statistically significant differences between exposed and non-exposed miners with respect to neurological disease or cognitive impairment (38).

The second study concerned the risk of SDAT as a function of aluminium concentrations in drinking water. A case-control study was conducted in eight regions of England and Wales as a follow-up of an earlier investigation in which these same authors found that risk varied among populations according to the aluminium concentration in their water supplies (37). A subsequent confirmatory study was deemed necessary due to weaknesses in the initial investigation including inadequate estimation of aluminium exposure. This second study, improved through the incorporation of important methodological changes, contradicted the earlier report and found no evidence of increased risk of SDAT according to aluminium concentration in the water supply (34).

Since there are a number factors that mitigate the likelihood that negative findings, such as those reported by Rifat et al., (38) and Martyn et al., (34), are published, these papers must be given considerable weight in considering aluminium’s possible role in SDAT. “Not only is it more difficult to get negative results published than positive ones, but negative results are discouraging to the investigators, who may fail to complete the study or to write it up.” “...it is possible that preliminary results of long-term studies have been reported when they accorded with an association which would not have been published if they did not.” (see review by Doll (39)).

**EFFECTS OF CHELATION ON THE PROGRESSION OF SDAT**

McLachlan and associates (40,41) reported that the trivalent chelating agent desferrioxamine (DFO), used in what was described as a single-blind placebo controlled trial, significantly slowed the progression of SDAT. Post-mortem analysis of the brains of DFO-treated patients who died during the study indicated that chelation lowered cortical
aluminium concentrations without significant effect on iron, manganese, and copper. The authors concluded that the “…therapeutic effect of DFO is likely due to the lowering of aluminium concentration in brain rather than some other effect” \(^{(41)}\). However, consideration of the methods used in this trial as well as the effects of the chelating agent indicate that the results of this trial are open to several interpretations.

DFO was injected intramuscularly twice daily while controls received either oral lecithin once daily or no treatment. Clearly, neither non-DFO group was comparable to the treatment group and, if placebo effects reflect the degree of patient manipulation, such influences would be greater with a twice-daily injection. Furthermore, the likelihood of a placebo effect was further enhanced by the fact that the DFO-treated patients (and their caregivers) were informed as to the nature of their treatment. Moreover, the unblinding of the treated patients, in addition to increasing the possibility of non-specific effects, also destroyed the single blind design of the trial. Specifically, the administrators of the behavioural assessment, the primary outcome measure of the trial, were testing individuals who knew if they were being treated with DFO. Thus, the test administrator may well have known the nature of the treatment of the subject who was being assessed. It has been well established that performance on psychometric tests can be influenced, either intentionally or unconsciously, by the expectations of the tester.

In addition to the methodological shortcomings of the chelation study, consideration of the actions of DFO itself indicate that attributing its beneficial effects to removal of aluminium is unwarranted in the absence of additional information. The post-mortem findings notwithstanding, DFO removes other trivalent cations, including physiologically important iron. Iron mediates the formation of neurotoxic hydroxyl radicals; DFO’s lack of effect on bulk iron levels does not preclude redistribution on a cellular or sub-cellular level. DFO also has anti-inflammatory effects, both through influences on iron and also via other biological pathways \(^{(42,43)}\). Anti-inflammatory agents have been demonstrated to have a beneficial effect on persons with SDAT. That chelation can have positive effects on the brain apart from any influences on aluminium is illustrated in a recent experiment assessing recovery from traumatic brain injury in rats \(^{(44)}\). Those animals submitted to a controlled cortical impact that also received DFO showed significantly better spatial memory performance than similarly injured animals that received only saline injection.

**CONCLUSIONS**

Investigation of the aluminium hypothesis of Alzheimer’s disease has drawn upon studies of neurofibrillary tangle formation in rabbits, post-mortem assessment of SDAT brain, dialysis encephalopathy,
epidemiological investigations of aluminium exposure and a clinical trial employing chelation of trivalent cations. In each of these areas, the pattern of results were similar; early findings suggested that aluminium played a role in the aetiology of SDAT but further research ultimately failed to support this suggestion. After a similar review of the extant literature five years ago, it was concluded that “...extensive studies of the pathology of AD (Alzheimer’s disease) and aluminium-induced encephalopathy by our group and others have revealed that aluminium does not cause AD neuropathology” (45). Investigations published in the intervening years continue to support that conclusion.

REFERENCES


Several studies have focused on effects on the nervous system in workers exposed to different compounds of aluminium and at the same time measured aluminium in biological fluids as an estimate of exposure. A very tentative dose-response relationship could be observed in these studies, but the results were not totally consistent and more studies are needed to establish a firm dose-response relationship.

INTRODUCTION

During the last two decades aluminium exposure has been assessed by the blood and urine sampling of industrially exposed workers. The highest concentrations of aluminium were found in welders and flake powder producers. Lower concentrations were found in workers in electrolytic aluminium production, aluminium sulphate production and in grinders. Occupational exposure and its effects have recently been reviewed (1).

In 1962 the first case report was presented regarding occupational aluminium exposure and neurotoxic effects. Difficulty with speech was an important symptom in a worker who was exposed to aluminium powder for 13 years. He became forgetful, and he also had attacks of clonic jerking of his left leg and later also his left arm, even though conscious (2).

This paper will concentrate on studies with biological exposure information.

Aluminosis

Five Swedish men suffered from pulmonary aluminosis due to exposure to pyrotechnic flake powder during the late 1940s. Two men were investigated 40 years after exposure. One of the two survivors had...
developed a dementia with motor disturbances. This man had a very high level of aluminium in his cerebrospinal fluid. The other survivor had a normal concentration and was not demented\(^{(3,4)}\).

**Welders**

A group of aluminium-exposed welders (\(n = 38\)) were compared with a referent group of iron-exposed welders (\(n = 39\)). Subtle disturbances in motor function were observed among the welders with the highest urine concentrations of aluminium. All these 19 welders had a urine level above 24 \(\mu g\) L\(^{-1}\). Their median urine concentration was 59 \(\mu g\) L\(^{-1}\) and five welders had a urine level above 100 \(\mu g\) L\(^{-1}\). These welders were slower when they performed a test composed of alternately clenching and stretching the left hand in 10 seconds. Their right hand was also slower but not significantly so. Tapping speed (non-dominant hand) was also slower. No disturbances of memory or attention could be observed among these welders\(^{(5)}\).

Seventeen Finnish aluminium-exposed welders performed normally on a battery of neuropsychological tests when compared with the clinical norms for these tests. They had been exposed for four years and their mean urine aluminium concentration was 76 \(\mu g\) L\(^{-1}\) (range 24 - 165 \(\mu g\) L\(^{-1}\)). Despite the fact that these aluminum-exposed welders displayed normal performances according to test norms, negative relationships were found between performance on tests of short-term memory, learning, and attention and the concentrations of aluminum in urine\(^{(6)}\). The mean urine aluminium concentration was based on four weekly urine samples taken during the summer vacation from 11 welders and on urine samples taken on the day of examination from six welders. The estimated post shift urine concentration of aluminum was based on a logarithmic excretion of aluminium\(^{(7)}\). If the interval between exposure and sampling is assumed to be seven or ten days, the mean post shift excretion would be approximately 100 or 110 \(\mu g\) L\(^{-1}\). These levels might well be an underestimation of exposure. The calculated post shift concentration derived from the highest value is 210 or 230.

**Foundry and smelter workers**

A total of 119 men with a minimum of five years of occupational aluminium exposure in foundries and in a primary smelter were studied. No disturbances of motor function, memory, or attention could be observed among these workers with a calculated post shift concentration of aluminium below 40 \(\mu g\) L\(^{-1}\)\(^{(8)}\).
In a Norwegian study of retired aluminum exposed potroom workers a test for tremor discriminated significantly between exposed and referents. The mean urine aluminium concentration of the 14 potroom workers was 13 µg L\(^{-1}\), but the interval from last exposure to examination was on average 22 days. The post shift urine concentration was probably higher as the mean urine aluminium level of the non-retired colleagues working in the same factory was 54 µg L\(^{-1}\) \(^{(9)}\).

**Powder producers**

In a German study 32 powder-exposed workers were compared with 30 referents. The median exposure time was 13 years and the median urinary concentration of aluminium was 110 µg L\(^{-1}\). No differences were observed between the groups regarding the tests performed, which included some sub-tests of WAIS and trail-making \(^{(10)}\).

### Table 1

A tentative dose-response relationship between approximate post shift urine concentrations of aluminium and effects.

<table>
<thead>
<tr>
<th>Post shift urine concentrations (µg L(^{-1}))</th>
<th>Effects on the nervous system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Below 40</td>
<td>No Observable Adverse Effect Level (NOAEL)</td>
</tr>
<tr>
<td>50-60</td>
<td>Subtle disturbances in motor function and sub-clinical tremor</td>
</tr>
<tr>
<td>100-200</td>
<td>Effects on short-term memory, learning, and attention</td>
</tr>
</tbody>
</table>

**OCCUPATIONAL EXPOSURE LIMITS**

Germany has adopted 200 µg aluminium per litre urine as a post shift limit value \(^{(11)}\). This concentration is higher than the level at which subtle disturbances in motor function were observed in welders \(^{(5)}\) and sub-clinical tremor was seen in potroom workers \(^{(9)}\). Several countries, e.g., the USA and UK, have adopted 5 mg m\(^{-3}\) as an occupational exposure limit for respirable aluminium dust. The
Swedish National Board of Occupational Safety and Health lowered the occupational exposure limit for respirable aluminium dust from 4 to 2 mg m$^{-3}$ in July 1997 and this decision was mainly based on the presented studies.

**CONCLUSIONS**

A very tentative dose-response relationship could be observed in these studies (Table 1) but the results are not totally consistent and more studies are needed to establish a firm dose-response relationship. It should be remembered that the differences found in these groups of workers are group differences. It means that the levels presented in table 1 are not associated with a clinical disease. On the other hand the presented studies are cross-sectional which means that workers with a clinical disease might have left their work. It should also be emphasised that knowledge is lacking whether these observed effects are reversible or not.

**REFERENCES**

SUMMARY

Performance on neurobehavioral tests serves as a surrogate measure for determining central nervous system (CNS) integrity. High aluminium levels in dialysis patients have been associated with decrements in neurobehavioral performance. However, reports of neurobehavioral effects have been inconsistent in workers occupationally exposed to aluminium. Discrepancies in results may be due to differing methodologies, such as differences in sample demographics, level of exposure, and selection of tests administered. Limitations are presented for the interpretation of neurobehavioral test results. For example, neuropsychological techniques are sensitive but not specific. Therefore, caution must be exercised when interpreting aberrant test results. For instance, clinically significant impairments may be noted in both neurotoxicant exposure cases and other CNS disorders. Furthermore, the pattern of performance exhibited by patients with neuropsychiatric conditions, such as depression and anxiety, is often similar to the pattern noted in toxic exposure cases. Finally, caution must be used when attributing decrements in performance to exposure to an element such as aluminium, rather than considering possible alternative differential diagnoses.

INTRODUCTION

Neurobehavioral test performance is a surrogate measure of the integrity of the central nervous system (CNS). The field of behavioural neurotoxicology applies neuropsychological methods to individuals with potential exposure to neurotoxicants. Patients are primarily referred to determine if there is CNS damage, and if this damage is related to exposure to a specific chemical. Evidence indicates that high levels of exposure to aluminium, lead, organic solvents, mercury manganese, carbon disulphide, carbon monoxide, herbicides, and pesticides can adversely effect the CNS in susceptible individuals.

To determine an association between exposure and CNS effects, a reliable biomarker of the exposure must be readily available. The lack of a biomarker prevents the clinician from reliably determining
if a known exposure is sufficient to cause alterations in CNS functioning. Without this knowledge, it can be difficult to determine if the source of the patient's symptoms is physiological or psychological. For the most part, the effects of neurotoxicants on the CNS are subtle. In addition, these subtle changes are usually not detectable with routine physical or neurological evaluations. Many neurodiagnostic tests, such as EEG, CT, and MRI, also fail to discern neurotoxic exposure. Since a neuropsychological evaluation is sensitive to CNS effects, the evaluation of cognitive functioning using neuropsychological techniques provides an indirect method for determining the integrity of the CNS. However, neuropsychological test results must be interpreted with caution, as this technique is extremely sensitive, but not specific.

**NEUROPSYCHOLOGICAL METHODS**

A well-designed neuropsychological test battery assesses a number of cognitive domains (e.g., orientation, intelligence, language, remote memory, verbal and visual short-term memory, visuoconstruction, perception, executive ability, psychomotor functioning, manual dexterity, and mood). Also, multiple tests measuring the same cognitive domain are administered to obtain convergent validity. For example, if abnormal test results are obtained on one out of three verbal memory tests, it is less likely that the patient has a true verbal memory deficit. There are a number of available, standardised tests that measure performance ability in each cognitive domain. These tests are detailed in two excellent sources(1)(2).

**INTERPRETATION – LIMITATIONS / CAUTIONS**

Although limited, neuropsychological assessment is the best method for detecting adverse effect of chemicals on the CNS. Nevertheless, interpretation of the aetiology behind performance decrements must be made with caution. Firstly, in order to determine if an individual's scores fall outside the normal limits, adequate norms must be used for comparison. Unfortunately, there is a paucity of appropriate norms currently available for individuals with low or very high levels of intellectual functioning. Since intellectual ability predicts test performance to a large extent, the use of normative values based on a more highly intelligent group than the person tested would lead to the erroneous conclusion of CNS insult where none exists. Conversely, if inappropriate norms are applied, a highly intelligent person's performance decrements may be missed since their performance may very well be at the upper limits when compared to the normative group.
with average level of intellectual functioning. Since cognitive performance is influenced by age and sex, as well as intellect (3), appropriate norms must be developed and utilized to ensure an accurate judgement of the normality of test results.

Furthermore, when abnormal test results are found, the most critical duty of the neuropsychologist is to determine the validity of these results. For example, as previously mentioned, a deficit is truly a result of an alteration in brain functioning, abnormal performance should be noted on more than one test of the same cognitive domain (e.g., verbal memory). Also, performance on a more difficult, complex task should not be superior to that of a simpler test. Finally, overall patterns of performance provide information on the nature of brain injury (e.g., static versus progressive, acute versus chronic, diffuse versus localised). More specifically, performance deterioration after removal from the source of chemical exposure is uncharacteristic of brain injury secondary to neurotoxicants. In these cases, a progressive brain disorder, such as Alzheimer’s disease, would be suspected.

Because neuropsychological tests have high sensitivity but low, specificity, every effort should be made to determine if abnormal results are related to neurotoxicant exposure or to another aetiology. For example, persons with documented significant exposures often complain of poor concentration and short-term memory loss, as well as symptoms indicative of major depression including: depressed mood, anxiety, restlessness, loss of interest in work and hobbies, decreased libido, irritability, headaches, weakness and sleep disturbances ranging from insomnia to somnambulism (4,5). Since symptoms associated with disturbances of affective state can mimic the symptoms associated with neurotoxicant effects, it is extremely important to rule out the presence of anxiety or depression. This is accomplished through the use of the clinical interview and a variety of standardised questionnaires (6). In addition, while patients may report a recent onset of cognitive difficulties, review of school and prior employment records could indicate long standing problems (i.e., subnormal intelligence or a learning disability). Furthermore, cognitive decrements may be symptomatic of many CNS disorders (e.g., medication side effects, multiple sclerosis, Parkinson’s disease, systemic lupus erythematosus, cerebrovascular disease, Alzheimer’s disease, chronic alcohol use, previous head injury). In addition, certain tasks will be individually affected by a specific disorder. For instance, motor tasks involving timed responses will be affected by peripheral nerve problems, such as those seen with carpal tunnel syndrome. Due to job requirements, this syndrome is very common in workers and can be easily evaluated with nerve conduction studies.

Depression or anxiety will also produce decrements in neuropsychological test performance. These decrements are usually
observed in the areas of attention, learning and memory, and psychomotor speed. Since similar cognitive domains are affected by both neurotoxicants and alterations in mood, it is often difficult to determine the relative contribution of each to neuropsychological test performance decrements. More specifically, such symptomatology could be related to neurotoxic exposure, the emotional state and personality characteristics of the patient, or an interaction of the two. In order to determine the true aetiology of complaints, patterns of performance and inconsistencies during testing (such as superior performance on harder tasks, with poor performance on simpler ones, or lower than chance performance on all of the tasks) must be carefully examined.

While epidemiological studies have reported decrements in attention/concentration, new learning and memory, executive functioning, psychomotor speed, and manual dexterity in individuals exposed to neurotoxicants (7), neurotoxicants have not been associated with decrements in any aspect of language (reading, writing, naming, speech), nor in remote memory. Remote memory is assessed by asking questions concerning significant early life experiences. With the exception of acute high level exposure, disorientation is not characteristic of neurotoxicant exposure. Therefore, it is unlikely that patients complaining of the above mentioned symptoms have a toxin-induced encephalopathy.

As with any diagnostic process, making a differential diagnosis between neurotoxicant exposure neurologic disease, psychiatric disturbance, or malingering is based on the combined evidence taken from the medical, social, and academic histories, physical and neurologic exams, biological monitoring nerve conduction studies, EEG, CT/MRI, and the neuropsychological evaluation.

In order to further assist with the differential diagnosis, workers should be tested repeatedly. If psychological mechanisms are suspected, repeat testing over a short time interval (days) will provide information on the stability of the findings. If there are large discrepancies between test battery results alterations in affective state are probably responsible. If the performance decrements are believed to be purely physiological, then re-testing after a longer interval (months to years) and after the patient has been removed from any potential exposure, should show equivocal findings, or even an improvement between the two testing sessions. If performance deteriorates significantly without re-exposure, then a progressive disease or secondary psychological reaction to the exposure may be the cause of any difficulties.

In clinical settings, psychological disturbances are common in workers and may be a primary or secondary sequela of chemical exposure. Emotional reactions to exposure may be as important as the
direct physiological effects of the chemicals, especially when considering aetiology and persistence of symptoms. The fear associated with suspected exposures can be so stressful as to cause severe psychological disorders, adjustment disorders, and typical and atypical post-traumatic stress disorders. In addition, specific inherent personality characteristics may predispose an individual to develop physical, cognitive, and psychological symptoms. These personality characteristics must be considered when determining the diagnosis.

The neuropsychological evaluation provides unique information on the functional integrity of the CNS. However, the results must be used in combination with the information obtained from medical, social, and occupation histories. In addition, findings from physical and neurologic examinations as well as auxiliary laboratory tests (nerve conduction studies, MRI’s) must also be integrated in order to make a differential diagnosis between neurotoxicant exposure, other CNS pathology, or psychiatric (affective) disorder.

REFERENCES

SUMMARY

Aluminium is known to be a neurotoxic element, and since it is used widely as a coagulant in water treatment the issue of safe levels of aluminium in drinking water is of considerable interest to public health officials and regulatory agencies. Although acute exposure to high doses of aluminium are well tolerated, several epidemiological studies have reported an increased relative risk of dementia associated with aluminium concentrations in drinking water. However, as all of these studies have some inherent methodological weaknesses, it is believed that relying on these studies alone to assess the drinking water guideline for aluminium is not sufficient. A number of animal studies exist, but these studies have limitations. None of these studies are sufficient for setting the drinking water guideline for aluminium on health grounds. Therefore, Health Canada in co-operation with United States Environmental Protection Agency (US EPA) held a workshop in Ottawa on September 3rd and 4th, 1997. In the workshop international experts on the toxicology, bioavailability and speciation of aluminium discussed the critical issues concerning the conduct of a chronic neurotoxicity study of aluminium administered in the drinking water of animals and approaches for addressing these issues.

All participants recommended that a study of the neurotoxicity of aluminium in the drinking water of animals would provide useful information for agencies in developing guidelines for human exposure. The study should focus on the consequences of life-span exposure on neurotoxicity assessed in young and aged adults. The appropriate species of animals are (in order of priority) mouse, rabbit, and the transgenic mouse carrying risk factors for Alzheimer's disease.
INTRODUCTION

Aluminium is used widely as a coagulant in water treatment and the issue of safe levels of aluminium in drinking water is of considerable interest to public health officials and regulatory agencies. Although acute exposure to high doses of aluminium are well tolerated, chronic exposure to aluminium has been shown to produce encephalopathy in patients undergoing renal dialysis. Aluminium may be a contributing factor in certain neurodegenerative diseases such as Alzheimer’s disease (AD), amyotrophic lateral sclerosis (ALS) and in the dementia associated with Parkinson's disease (PD). Several epidemiological studies have reported an increased relative risk of dementia associated with aluminium concentrations in drinking water. However, as all of these studies have some inherent methodological weaknesses, it is believed that relying on these studies alone to assess the drinking water guideline for aluminium is not sufficient. In experimental animal studies aluminium at higher levels in drinking water has also produced neurotoxic effects in animals. However, none of these studies are of sufficient quality for setting a health-based drinking water guideline for aluminium. Therefore, Health Canada convened a Workshop consisting of international experts on aluminium toxicology, availability and speciation.

OBJECTIVE

The objective of the Workshop was to investigate the feasibility of a chronic neurotoxicity study of aluminium administered in the drinking water of animals, which could then be used for the purpose of establishing a health-based drinking water guideline for aluminium.

METHODOLOGY

The following international experts participated in the workshop:

- Dr. Kenneth Bailey, Water Research Centre, Medenham, Marlow, Buckinghamshire, SL7 2HD, United Kingdom.
- Dr. Trond Peder Flaten, Department of Chemistry, The Norwegian University of Science and Technology (NTNU), Jarleveien 4, NTNU,N-7034 Trondheim, Norway.
- Dr. Donald R. Crapper-McLachlan, 59 Sutherland Drive, Toronto, Ontario, Canada M4G 1H5.
- Dr. William F. Forbes, Clinical Epidemiology Unit, University of Ottawa, 43 rue Bruyere, Ottawa, Ontario, Canada K1N 5C8.,
Some of the critical issues concerning a neurotoxicity study of aluminium administered in the drinking water of animals were highlighted. Participants were asked to contribute papers addressing one or more of the following critical issues:

- What are the problems in assessing the toxicity of aluminium in drinking water for humans?
- How important is aluminium speciation and the effect of substances which affect speciation, such as silica, fluoride, and pH?
- Is an animal study crucial in human risk assessment; that is, is an animal study an appropriate next step?
- Which is the best animal model and what are the appropriate end points to be measured, such as neurotoxicity, behavioural changes, and aluminium transfer to the serum and the brain?
• In an animal study with Al$^{26}$, how much aluminium is absorbed? Where does it accumulate? What are the pathways for accumulation? What are the effects of age?
• What are the appropriate methods to avoid contamination from aluminium, which is present ubiquitously in nature, during an animal study?

The workshop was held in Ottawa on September 3rd and 4th, 1997, with support from the Environmental Health Directorate of Health Canada and the United States Environmental Protection Agency. Written papers of the invited experts were circulated to the Workshop participants prior to the meeting, and presentations were made on the first day of the Workshop. Each paper was discussed after its presentation. The proceedings will be available from the Environmental Health Directorate and on the Health Canada World Wide Web site.

DISCUSSIONS

On the second day of the Workshop the following issues arising from the papers were discussed and, where possible, a consensus reached:

• Is an animal study needed, or should reliance be placed on further epidemiological studies?
• Should the focus of such a study be directed to the problem of the relationship between aluminium and dementia, or should it encompass the general neurotoxicity of aluminium, including effects on neural development?
• What is the most appropriate species of animal to study: mice, rats, rabbits, transgenic mice?
• Which chemical compound of aluminium should be used: inorganic (sulphate, chloride); organic (citrate, lactate, maltolate)?
• How should the aluminium be administered: drinking water, gavage, intracisternally?
• What range of dose should be used, and at how many levels?
• At what ages should the animals be exposed: young, old, lifetime?
• Which end-points should be studied: behaviour, histology, tissue levels?
• Should other constituents of drinking water be incorporated: silicate, fluoride, pH?
• How should aluminium in the diet and the environment be controlled?
• Should kinetic studies be incorporated, perhaps using $^{26}$Al?
A consensus was obtained on all these questions, except on the use of a single species of animal. Arguments were made for the use of mice, rabbits and transgenic mice carrying risk factors for Alzheimer's disease, if sufficient funding can be obtained. However there was a consensus that if funding is restricted then the species should be given priority in the order listed above.

RECOMMENDATIONS

Recommendations were drafted, discussed and agreed upon as follows.

• A study of the neurotoxicity of aluminium in the drinking water of animals would provide useful information for agencies in developing guidelines for human exposure.

• The study should focus on the consequences of life-span exposure on neurotoxicity assessed in young and aged adults. Exposure should begin in utero (at implantation) and continue throughout life.

• The appropriate species of animal are (in order of priority) mouse and rabbit. The transgenic mouse carrying risk factors for AD and premature ageing should also be considered.

• Aluminium should be administered in the drinking water after a pilot study to determine the maximum tolerated dose (MTD). Subsequently control, maximum tolerated and two intermediate doses should be used. Based on epidemiological studies one dose level might be that equivalent to 200 ppb in human drinking water.

• Although the use of an inorganic compound such as aluminium sulphate would be desirable, solubility considerations, stability in solution and ability to dissociate in the stomach of the animals will probably require the use of an organic compound such as aluminium maltolate. The solution should be made with deionized water and then filtered through a 0.22 µm filter to eliminate particulates. To simulate patterns of human consumption some of the water should also be given in the absence of food.

• Purified diet (NRC recommended nutrient composition), with less than 7 mg kg⁻¹ Al food should be given to mothers (beginning 2 weeks before mating) and their offspring.
• The end-points employed by the US EPA neurotoxicity testing guidelines should be used for behavioural testing, with the addition of delayed alternation and multiple fixed interval-fixed ratio performance. Behavioural tests should be conducted beginning at age 50 days and 18 months (in mice). Behavioural tests should be those which are not confounded by repeated experimentation. Brain histopathology - examination of at least three coronal sections of fore-, mid- and hind-brain should be taken, using appropriate stains such as H&E, Bielschowsky and immunohistological staining for amyloid and phosphorylated tau. Blood specimens should be obtained for biochemical and haematological studies. Biochemical assessment should be carried out of aluminum, beta amyloid, and a cholinergic marker.

• Sufficient dams should be treated to provide 20 animals per sex per group (1 male and 1 female per litter) for functional neurotoxicity testing in young and aged adults. The pathology / chemistry assessment at the end for the study should be performed on those animals undergoing behavioural assessment. An additional 5 male and 5 female animals per group (1 male and 1 female per litter) should be performed for additional pathology / chemistry assessment at the same age that first behavioural testing is concluded.

• It was recommended that kinetic studies using Al\textsuperscript{26} should be included to determine if aluminium accumulates in brain from the drinking water.

• Proper control of contamination with aluminium is essential and should be demonstrated. The study should be conducted under Good Laboratory Practice conditions.

• A lifetime exposure study of rabbits is recommended to take advantage of their sensitivity to aluminium-induced encephalopathy and related neuropathological features seen in this species. The protocol suggested for the mouse neurotoxicity studies could be modified for this species which has a life expectancy of approximately 8 years. Modified behavioural testing using the classically conditioned defensive eye blink reflex should be considered.
30. MONOMERIC ORGANIC ALUMINIUM AS A RISK FACTOR FOR ALZHEIMER’S DISEASE

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SUMMARY

To investigate the relation between different physicochemical forms of aluminium (Al) in drinking water and Alzheimer’s disease (AD), we carried out a case-control study in Saguenay-Lac-Saint-Jean Region (Quebec). The study participants were randomly selected, and the sample was equally stratified for age (70 - 74, 75 - 79, 80 and over) and sex. The AD diagnostic was established in three steps within the recognised criteria. 122 cases were diagnosed with those cases 68 case-controls pairs were formed. For each one a non-demented control was paired for age (± 2 years) and sex. Al speciation was studied in 54 drinking water supplies with an established standard analytical protocol along with quality control procedures. Potential exposure to Al forms (total dissolved Al, monomeric organic Al, monomeric inorganic Al, polymeric Al, Al$^{3+}$, Al-OH, Al-F, AlH$_3$SiO$_4$$^{2-}$, Al-SO$_4$) in drinking water was estimated by juxtaposing the subjects’ residential history with the physicochemical data of the municipalities. The results showed that when risk is adjusted for education level, presence of family cases and presence of the ApoE $\varepsilon 4$ allele, the long-term exposure (1945 to onset) to all Al forms in drinking water indicates no significant risk of AD development. But at the onset, exposure to monomeric organic form of Al seemed to increase the risk of developing AD (OR 2.67; 95% CI 1.04 – 6.90).

INTRODUCTION

In industrialised countries, Alzheimer’s disease (AD) is the fourth largest cause of death in the elderly. The prevalence rate is more than five percent among people who are 65 years old and over, which indicates that more than 161,000 Canadians and four million Americans carry the clinical signs of the disease. Actually, AD has been linked to at least five chromosomes: 1$^{(1)}$, 12$^{(2)}$, 14$^{(3)}$, 19$^{(4)}$, and 21$^{(5)}$. Furthermore, many studies have observed
a strong association between family history and AD development \(^{(6)}\). However, the genetic components account only for a part of AD cases \(^{(7)}\), indicating that other genes or risk factors such as environmental exposure could be involved in the aetiology of the disease.

Several epidemiological studies have observed a positive association between aluminium (Al) in drinking water and AD \(^{(8-14)}\) while some others did not \(^{(15-18)}\). Critical evaluation of these studies reveals certain limitations. Firstly, all epidemiological studies used total aluminium (Altot) as an indicator of aluminium exposure. However, Altot may not be a good measure of exposure since it incorporates particulate, colloidal and dissolved Al forms (Altd), including highly and weakly bioavailable forms \(^{(19)}\). Furthermore, several studies determine the exposure at the onset of the disease. Evaluation of exposure at the onset assumes that the subjects stayed at the same residence during their whole life. But subjects can move during their life, which means that there will be changes in the physicochemical properties of the water they drink. Consequently, exposure is not necessarily constant throughout life. Migration from one city to another with different drinking water supplies could introduce a bias and reduce considerably the strength of the association between AD and exposure to aluminium. Therefore, epidemiological studies should take into account the residential history of the subjects before the onset to obtain an adequate measure of exposure over time. Second, the diagnostic of AD is not very accurate in many epidemiological studies. In many cases, AD is not specifically defined and the neuropsychological tests performed only evaluate the cognitive deficit or dementia. Furthermore, in several studies, the selection of the subjects was not performed from a randomized sample, introducing a selection bias. Thirdly, most epidemiological studies have not considered potentially confounding factors such as age, sex, education level, occupation as well as genetic factors that might influence the relationship between Al and Alzheimer’s disease \(^{(20-21)}\).

The objective of the study described was to evaluate the influence of long-term exposure to soluble Al forms on AD development while considering the potentially confounding factors (genetic, occupational and socio-demographic factors).

MATERIALS AND METHODS

This study was conducted in the Saguenay-Lac-St-Jean (SLSJ) region in the province of Quebec, Canada. The 1924 study participants were randomly selected, and the sample was equally stratified within their age range (70 - 74, 75 - 79, 80 and over) and sex. Structured questionnaire addressed to proxy respondents allowed a description of the socio-demographic characteristics and of residential, occupational and medical history. To assess the quality of data provided by proxy respondents, an
analysis of agreement between the controls and their respondents was conducted. AD diagnostic was established in three steps according to recognised criteria (figure 1).

Water samples were collected in high-density polyethylene bottles and stored at 4 ºC. Samples were sent on the day of collection by courier and reached the laboratory within 24 hours. They were analyzed within 48 hours of reception. A survey was also carried out to obtain precise information on water supply history: type of supply, type of treatment, chemicals used, sequence of operations, site of water intake, duration of water supplies, pollution problems, and distribution system. In addition, the status of each distribution system before sampling was obtained (defect, spill, treatment, etc.) in order to take into account all abnormalities that might affect the physicochemical properties of the sample. Aluminium speciation in drinking water (Altot, Altd, monomeric organic Al, monomeric inorganic Al and polymeric Al) was analysed with a standard protocol and following established procedures (QA/QC) (23-25).

Figure 1. The main steps followed to diagnose Alzheimer’s disease
Blood samples were collected for ApoE genotyping. A total of 122 cases were diagnosed. With those cases, 68 case-control pairs were formed. For each case, a non-demented control was paired for age (± 2 years) and sex.

The speciation of Al in drinking water was performed for 54 municipalities of the SLSJ. Aluminium speciation was measured in 1995 - 1996 at four different periods to take into account the seasonal variation in aluminium chemistry. Water samples were collected by technicians, specialised in water treatment, within a standard protocol and quality control procedures (QA/QC) (22). Monomeric inorganic forms (Al³⁺, Al-OH, Al-F, AlH₃SiO₄²⁺, Al-SO₄) were estimated by using the geochemical model ALCHEMI (26). The seasonal variation are greatly responsible for changes in Al speciation in drinking water and it is probable that the speciation did not significantly fluctuate over a long period of time if the variables involved in Al speciation were similar over the years (27-28). To verify if the 1995 - 1996 sampling campaign could be used to estimate the Al speciation over a long period of time, we compared the variables involved in Al speciation (pH, SO₄, F, DOC) with historic data (1978 - 1994) (29) on the physicochemical characteristics of drinking water as measured in 1995 - 1996 from those 54 municipalities. Potential exposure to Al forms in drinking water was estimated in combining the subjects' residential history with the physicochemical data of the municipalities (see equation below).

\[
\frac{[\text{Al}]}{[\text{Al}]}_1 + \frac{[\text{Al}]}{[\text{Al}]}_2 + \frac{[\text{Al}]}{[\text{Al}]}_3 + \frac{[\text{Al}]}{[\text{Al}]}_i \rightleftharpoons \frac{[\text{Al}]}{[\text{Al}]} \times \frac{[\text{Al}]}{[\text{Al}]}_i ^ t \text{ total} \\
[\text{Al}]= \text{Al concentration in municipalities residences} \\
t_i = \text{residence period}
\]

This equation is used to evaluate the different periods of potential individual exposure according to residential itinerary, while adjusting for the available information in time. Logistic regression was used to estimate the relationship between Al exposure and AD considering different potential confounding factors such as education level, the presence of family cases, ApoE ε4 allele, and occupational exposure. In the data presented, the exposure to Al forms was defined as a binary variable, considering as exposed the upper quartile of the subjects.
RESULTS

The comparison between the historical data (1978 - 1994) and the data collected during the study (1995 - 1996) showed that the variables involved in Al speciation (pH, DOC, SO₄, F) followed similar patterns ($p < 0.05$). The exposure before 1945 was included in the analysis because of the low number of subjects using the municipality water supplies and of the lower quality of the exposure estimation. A relation has been observed between education level, presence of family cases and presence of ApoE ε₄ allele and AD. However occupational exposure was not related to AD (Table 1).

![Table 1: Distribution of Cases and Controls](image)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cases (n = 68)</th>
<th>Controls (n = 68)</th>
<th>$\rho$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>49</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>19</td>
<td>19</td>
<td>Paired</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70-74</td>
<td>6</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>75-79</td>
<td>17</td>
<td>17</td>
<td>Paired</td>
</tr>
<tr>
<td>over 80</td>
<td>45</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td><strong>Education level</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 7 grade</td>
<td>43</td>
<td>30</td>
<td>0.025†</td>
</tr>
<tr>
<td>≥ 7 grade</td>
<td>25</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td><strong>Family cases</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence</td>
<td>33</td>
<td>58</td>
<td>0.001†</td>
</tr>
<tr>
<td>Presence</td>
<td>35</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td><strong>Presence of ApoE ε₄</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>27</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>One ε₄</td>
<td>35</td>
<td>16</td>
<td>0.001††</td>
</tr>
<tr>
<td>Two ε₄</td>
<td>6</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Ratio of occupational exposure to neurotoxic substances</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High exposure</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Medium exposure</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Low exposure</td>
<td>1</td>
<td>0</td>
<td>(1.0^{††})</td>
</tr>
<tr>
<td>Very low exposure</td>
<td>61</td>
<td>62</td>
<td></td>
</tr>
<tr>
<td><strong>Occupational exposure to aluminium for at least 10 years</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>65</td>
<td>65</td>
<td>(1.0^{††})</td>
</tr>
<tr>
<td>No</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

† Used Chi- square test; †† used Fisher’s exact test

No relation was observed between the long-term exposure (1945 to onset) to all Al forms in drinking water and AD development (Table 2). During
this period, the subjects lived on average, in 1.86 (± 1.4) different residences and stayed on average, 32 years (± 14 years) in each. At the onset, exposure to monomeric organic form of Al (Almo) appeared to increase the risk of developing AD (OR 2.67; 95% CI 1.04 - 6.90). On average, the subjects have lived for 43.6 years (± 25.7) in the residence where they lived at the time of the onset. The mean Altd concentration for the 54 supplies is 1.43 µM L^{-1} (± 1.61 µM) and the mean pH value is 6.91 ± 0.60. The surface waters have a higher Altd annual mean concentration (2.51 µM L^{-1} ± 1.92 µM) and contain mostly Almo (36%) and polymeric Al (45%). Waters treated with Al sulphate have a lower Altd annual mean concentration (1.36 µM L^{-1} ± 1.28 µM) than those that were not treated. Treated waters also have a lower proportion of Almo (22.6%) than other type of supplies. Groundwater has low Altd concentration (0.33 µM L^{-1} ± 0.302 µM) and contains mostly Almo (54%) and inorganic forms (32.2%). The relations between AD and Al^{3+} and Al-SO_4 were not considered because their concentrations were below the detection limit in all drinking water samples. Furthermore, we have not observed a significant protective effect against Al toxicity due to Si and fluoride.

**DISCUSSION**

The results of this study suggest the existence of a relationship between onset exposure to Almo and the development of AD. No significant relation was observed between long-term exposure (1945 to onset) to Almo and AD. This result could possibly be due to the inclusion of some cumulative elusive information between 1945 to onset in equation 1. In fact, when we compare the average exposure of cases and controls to organic monomeric Al for each year preceding the onset, we observed that the cases were significantly more exposed to Almo than the controls (ρ=0.01). Furthermore, the onset period seem to represent a long-term exposure because the subjects have lived for 43.6 years (± 25.7) in the residence where they lived at the time of the onset. We observe also that the subjects were exposed to small Al concentrations compared to the level previously reported in epidemiological studies.

It is possible that Almo is more bioavailable than other forms through the gastrointestinal tract. Some toxicokinetic studies involving animals and humans revealed that in drinking water low molecular weight organic complexes like Al-citrate were absorbed to a greater extent in the gastrointestinal tract than other (organic and inorganic) forms of Al. The absorption mechanism through the gastrointestinal tract is not yet clear and various hypotheses were proposed. One of them suggests that Al is fixed to some functional groups over the epithelium membrane and alters the permeability of it. This may favour a quick intracellular accumulation
of Al (33-36). Results have shown that Almo was most available in untreated water and that the concentration of Altd and Almo were lower in municipalities which used Al-based coagulants. Several studies on aluminium chemistry suggest that Al forms such as Al-citrate represents a greater proportion of Altd at pH value between 4.0 and 7.0 (37-39). The use of Al-based coagulants reduces the concentration of organic matter in drinking water and decreases the formation of Al organic complexes (40-42).

### Table 2

Adjusted odd ratios for the development of Alzheimer’s disease among subjects exposed to aluminium forms and variables involved in aluminium speciation in drinking water

<table>
<thead>
<tr>
<th>Variables [threshold] moles L⁻¹ (M)</th>
<th>Onset exposure (n=68 pairs) adjusted* OR (CI95%)</th>
<th>Longtime exposure (1945 to onset) (n = 68 pairs) adjusted* OR (CI 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altot [2.84E-6 M]</td>
<td>2.10 (0.83-5.35)</td>
<td>1.52 (0.59-3.88)</td>
</tr>
<tr>
<td>Altd [1.44E-6 M]</td>
<td>1.93 (0.79-4.67)</td>
<td>1.31 (0.52-3.29)</td>
</tr>
<tr>
<td>Almo [4.53E-7 M]</td>
<td>2.67 (1.04-6.90)</td>
<td>1.84 (0.73-4.68)</td>
</tr>
<tr>
<td>Almi [3.1 E-7 M]</td>
<td>0.71 (0.29-1.72)</td>
<td>0.87 (0.32-2.31)</td>
</tr>
<tr>
<td>Al-OH [2.96E-7 M]</td>
<td>0.53 (0.20-1.42)</td>
<td>0.65 (0.21-2.04)</td>
</tr>
<tr>
<td>Al-F [1.03E-8 M]</td>
<td>0.67 (0.26-1.67)</td>
<td>0.65 (0.25-1.63)</td>
</tr>
<tr>
<td>Al-Si [1.4E-9 M]</td>
<td>0.67 (0.26-1.69)</td>
<td>0.68 (0.28-1.70)</td>
</tr>
<tr>
<td>Alpoly [5.4E-7 M]</td>
<td>1.98 (0.79-4.98)</td>
<td>1.31 (0.52-3.29)</td>
</tr>
<tr>
<td>F [4.29E-6 M]</td>
<td>1.08 (0.46-2.58)</td>
<td>1.00 (0.40-2.52)</td>
</tr>
<tr>
<td>Si [1.42E-4 M]</td>
<td>1.88 (0.79-4.49)</td>
<td>1.37 (0.55-3.43)</td>
</tr>
<tr>
<td>DOC [2.35E-4 M]</td>
<td>1.13 (0.48-2.69)</td>
<td>1.58 (0.63-3.92)</td>
</tr>
<tr>
<td>pH [7.19]</td>
<td>1.64 (0.68-3.93)</td>
<td>1.26 (0.46-3.44)</td>
</tr>
</tbody>
</table>

OR = odds ratio; (CI95%) = confidence interval with a significance level of 95%; DOC: dissolved organic carbon; Altot: total aluminium; Altd: total dissolved aluminium; Almo: monomeric organic aluminium; Almi: monomeric inorganic aluminium; Alpoly: polymeric aluminium; [threshold] = cutpoints are the upper last quartiles ; *adjusted for education level (<7, >7 years of education), presence of family cases (no, one or more) and presence of at least one ApoE ε4

Contrary to earlier studies, we have not observed a significant protective effect due to silicate (43-45) and fluoride (45-47). Since the concentration of these elements was higher than our studies and that the high pH condition did not favourise the formation of these complexes. We observed a relationship between Al and AD in a system characterised by low Al concentration and high pH values. Drinking water supplies in SLSJ are, in most part, localised in areas where the soils have the ability to neutralise the acidic loading. This might explain why we observed
relatively neutral pH conditions in drinking waters together with low Al concentrations. Furthermore, the results suggest that Almo was more important than total aluminium in the relation between Al and AD. Thus, Al speciation could better define the risk associated with Al in the development of AD. Our study allowed us to:

- identify AD cases and pair controls with a rigorous protocol;
- determine the aluminium speciation in drinking water within a recognized standard protocol with QA/QC procedures;
- estimate longtime exposure to Al species according to residential histories and historic data of drinking water;
- control certain confounding variables such as ApoE 4, education level and presence of family cases.

Our work presents certain limitations. First, individual exposure could not be measured exactly because the amount of drinking water consumed by the subjects and the concentrations of aluminium at the point of delivery (tap water) were not quantified. Thus, it is more a potential exposure index then a direct measure of aluminium intake. Second, the evaluation of long term exposure to aluminium forms has limitations. The calculated annual average does not include extraordinary hydrological events such as floods or spills that could have modified the physico-chemicals properties of drinking waters. In our study, the annual average is considered as a good indicator of conditions in drinking water supplies and we calculated no temporal trend from 1945 to 1996. So, the Al data form 1995 - 1996 can be used to estimate the historical exposure to Al. Finally, we could not established the dose / response relationship because the population studied was to small for statistical purposes.

Further investigations will be necessary to confirm our results using similar and different geochemical settings (acidic condition). Finally, it could be interesting to determine the chemical nature of the organic monomeric Al compounds present in drinking waters and to evaluate a dose/response relationship between Almo and AD.

DISCUSSION

The results of this study suggest the existence of a relationship between onset exposure to Almo and the development of AD. No significant relation was observed between long-term exposure (1945 to onset) to Almo and AD. This result could possibly be due to the inclusion of some cumulative elusive information between 1945 to onset in equation 1. In fact, when we compare the average exposure of cases and controls to organic monomeric Al for each year preceding the onset, we observed that the cases were significantly more exposed to Almo than the controls
Furthermore, the onset period seem to represent a long-term exposure because the subjects have lived for 43.6 years (± 25.7) in the residence where they lived at the time of the onset. We observe also that the subjects were exposed to small Al concentrations compared to the level previously reported in epidemiological studies.

ACKNOWLEDGEMENTS

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REFERENCES


31. IS ALUMINIUM IN DRINKING WATER A NEUROTOXIC RISK TO HUMANS?

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Co-Author: Nicholas D. Priest

SUMMARY

The apparently positive relationship between aluminium and Alzheimer’s disease that has been demonstrated in several epidemiological studies cannot be totally dismissed. However, strong reservations about inferring a causal relationship are warranted in view of the failure of studies to account for demonstrated confounding factors and for aluminium intake from all sources. It follows that, any published risk estimates are likely to be imprecise for a variety of methodological reasons. An hypothesis that exposure of an elderly population in some regions to high levels of aluminium in drinking water may either exacerbate or accelerate Alzheimer’s disease is not supported by available data. It has also been hypothesised that particular exposures via drinking water may be associated with non-specific impaired cognitive function. Again, the data in support of this hypothesis are currently inadequate to justify concern. It was concluded by a WHO task group that there is insufficient health-related evidence to justify revisions to existing WHO Guidelines for aluminium exposure in healthy, non-occupationally exposed humans. Also, that there is an inadequate scientific basis for setting a health-based standard for aluminium in drinking water.

INTRODUCTION

Aluminium sulphate is commonly added to surface waters during the treatment and production of drinking water. While most of this is subsequently removed from the water by filtration, prior to its release for consumption, residual levels of aluminium remain. Currently, International standards, in this case based upon aesthetic qualities, limit the amount of aluminium in drinking water to 200 µg L⁻¹. While, in some countries this limit has been / is exceeded, in most average aluminium levels are much below the limit e.g., in the United Kingdom average levels are 20 µg L⁻¹. While these levels are small and, assuming normal rates of water consumption, would account for only a
few percent of daily aluminium intake anxiety exists regards possible health detriments resulting from consumption. These are recognised to be a cause of concern within the aluminium industry.

**NEUROTOXICITY OF ALUMINIUM**

Compared to most heavy metals, aluminium is relatively non-toxic and exposure to it, at environmental levels, produces no proven adverse effects in man\(^{(1,2)}\). There is a little evidence to suggest that aluminium may produce adverse effects under conditions of chronic, excess, occupational exposure. Under conditions of high medical exposure, resulting in large aluminium body-burdens, the metal is toxic. Aluminium intoxication is characterised by a number of conditions including encephalopathy.

Most information concerning these has been produced by the study of dialysed renal failure patients\(^{(3,4)}\). These had lost their ability to excrete aluminium and accumulated large body burdens of aluminium, mostly, by transfer of the metal from contaminated dialyzates during haemodialysis, but also as a consequence of the use of large quantities of aluminium hydroxide as an oral phosphate binder. The amount of transfer, and resultant body-burdens, depended upon the duration of treatment and the concentration of aluminium in the dialyzate. In addition, toxic effects of aluminium have been demonstrated in four groups of patients with normal kidney function: patients supported by total parenteral feeding; patients with hepatic insufficiency receiving aluminium antacids; premature infants receiving prolonged intra-venous therapy; other patients receiving parenteral therapy. Aluminium-induced neurotoxicity has also been claimed in some occupationally exposed groups, but the evidence supporting these claims is not conclusive\(^{(2)}\).

**ENCEPHALOPATHY**

Several neurological effects have been attributed to aluminium intoxication. Aluminium-induced impairment of cognitive function, following the occupational exposure of gold miners to inhaled aluminium, and the exposure of members of the general public to ingested aluminium sulphate has been claimed, but not proved\(^{(1,5)}\). To date, no convincing evidence has been produced to either support or refute the existence of neurological effects at low levels of aluminium uptake. Even so, sufficient evidence exists to show that such effects could occur in man at some levels of uptake. For example, dialysis patients exposed to lower than average levels of aluminium sometimes
demonstrate disturbed cerebral function, as compared to controls. In one study of dialysis patients, correlations were sought between cognitive function and exposure to aluminium in both dialysis source water and administered oral gut phosphate binders. The results of the study were confusing since it found negative correlations between the cognitive measures and source water aluminium, but positive correlations with the level of orally administered phosphate binder. Again, in a gold miner study, some results indicated cognitive impairment while others were less conclusive. The comment has been made that most studies, undertaken to date, are flawed, in that they have failed to include normal ageing controls. Attempts to improve cognitive scores by chelation therapy have met with very limited success.

The most important neurological effects, produced by aluminium, occur at large body-burdens \(^{(5,6)}\). These include apraxia, dysarthria, dysphagia, myoclonia, convulsions and dementia. Epidemiological studies have shown that aluminium-induced encephalopathy (dialysis dementia) was absent at those dialysis centres using water with aluminium concentrations less than 50 µg L\(^{-1}\). In contrast, encephalopathy was common in those that employed water with aluminium concentrations greater than 200 µg L\(^{-1}\). At these centres the prevalence of the disease rose significantly with increasing cumulative exposure to aluminium and was often a direct cause of death. In terminal cases, facial grimacing, myotonic spasms and dysphagia interfere with eating and lead to inhalation pneumonia and death. The recorded concentrations of aluminium in the brains of such patients are highly variable, but values in the region of 15 - 100 mg kg\(^{-1}\) are typical. Experience has shown that chelation therapy with desferrioximine is effective in reversing neurological effects.

There is no evidence to suggest that aluminium causes neurological effects of the type described above as a consequence of the consumption of drinking water.

**EVIDENCE FOR A ROLE FOR ALUMINIUM IN ALZHEIMER’S DISEASE**

Alzheimer’s disease (AD) is a progressive, often insidious, dementing disease occurring in mid to late life \(^{(7,8)}\). Its incidence increases with age, such that at age 85+ about 20% of people suffer from the condition. Alzheimer’s disease causes neurone death and a reduction in brain volume. The progress of the disease (which, in most cases, means about 7 years of intellectual and personal decline until death) cannot, currently, be arrested and eventually patients become bed-ridden. At this stage concomitant bedsores, feeding difficulties and pneumonia result in death.
The diagnosis of Alzheimer’s disease is made on the basis of the histological examination of brain tissues. These show the presence of widespread accumulations of β-amyloid senile plaques and neurofibrillary tangles throughout the limbic system, and in parts of the cerebral isocortex and brainstem. β-Amyloid plaque formation occurs in the majority of non-demented elderly individuals, but neurofibrillary tangles are rare. Consequently, it has been suggested that in Alzheimer’s disease plaque formation precedes and may predispose to neurofibrillary tangle formation.

The aetiology of the disease is complex and incompletely understood. Two risk factors for the disease have been identified, and confirmed: old age and family history. The aetiology of non-familial, sporadic AD is unknown. However, cases have been attributed to head injury and to environmental factors - including aluminium. An involvement of aluminium in AD has been suggested because:

- of the similar symptomologies of AD and dialysis dementia;
- the administration of aluminium to animals produces histological changes within the brain that are, in some respects, similar to those seen in the brains of Alzheimer patients;
- of some reports indicating the presence of aluminium within the cores of senile plaques;
- of the results of some epidemiological studies that have linked AD incidence either with aluminium levels in drinking water, or with its consumption as medicines;
- a disease, similar to Alzheimer’s, is prevalent in some Pacific islands (Guam) where the levels of aluminium in soils and water are high.

However: the pathologies of AD and dialysis dementia are different; the histomorphological changes seen in experimental animals differ, in important respects, from those seen in the brains of Alzheimer patients; not all studies have indicated the presence of aluminium within the cores of senile plaques, and attempts to demonstrate enhanced levels of aluminium in the brain of Alzheimer patients have mostly failed; the results of the epidemiological studies are conflicting and have been criticised on methodological and logical grounds; Guam disease, which may be associated with both aluminium and iron uptake by the brain, and Alzheimer’s disease are clinically different.

It follows, that most reports, including the recently published IPCS Environmental Health Criteria for Aluminium, now suggest that, in the absence of a clear association between exposure to aluminium and the disease and/or an identified mechanism for disease induction by the
metal, there is insufficient evidence to suggest that aluminium is causative with respect to AD\textsuperscript{(1,11,12)}. Most reports now suggest that the causation of sporadic Alzheimer’s disease may be multifactorial and involve a number of different genetic and environmental factors - one of which may be aluminium.

**ALZHEIMER’S AND DRINKING WATER**

It can be seen from the above that one of the reasons given for suspecting a link between aluminium and Alzheimer’s disease was the results of some epidemiological studies that linked AD incidence with aluminium levels in drinking water. Concerns regarding this possible linkage were greatest during the early years of the current decade, but have not completely disappeared.

Between 1986 and 1991, eight papers were published\textsuperscript{(13 – 20)}, seven of which suggested that Alzheimer’s disease was linked to aluminium in drinking water. One of these studies was a particularly influential study conducted by Martyn et al\textsuperscript{(15)}. This was conducted in eight regions of the United Kingdom. It appeared to show both a higher incidence of AD in regions where levels of aluminium in drinking water were highest and an indication of a dose response, such that the highest number of AD cases were reported for the area with the highest aluminium residuals in drinking water. All the studies undertaken employed ecological techniques and no attempts were made to assess either total aluminium intakes or aluminium body-burdens. Similarly, no attempts were made to identify the influence of known risk factors for the disease and often the exposure data and AD incidence data were collected for different periods. Furthermore some studies were uncompleted. It follows that some have suggested that little reliance should be placed on the conclusions made. A review of these studies has been published elsewhere\textsuperscript{(12,21)}.

More recently, other studies have been published which have indicated no link between aluminium levels in drinking water and AD. These include a re-analysis of data by Martyn et al\textsuperscript{(22)}. Using improved methodologies no evidence of increased risk of AD according to the level of aluminium in the drinking water supply was found. Another study conducted in North East England\textsuperscript{(23)} also failed to show a linkage. Subsequently, the authors speculated that the reason for their failure was due to poor control for the silicon content of the water - it being suggested that the \textit{in situ} formation of aluminosilicate compounds in the gut\textsuperscript{(24)} would prevent the uptake of the aluminium in some areas. However, a re-evaluation of the data after controlling for this confounder also failed to demonstrate a link\textsuperscript{(25)}. In view of both the results of later human volunteer experiments, using \textsuperscript{26}Al, which indicated that only a few percent of the bodies aluminium intake was sourced
from drinking water (26) and the failure to demonstrate excess AD in high exposure situations it may be concluded that a linkage has not been established.

**IPCS CONCLUSIONS**

The, recently published, World Health Organization, International Programme on Chemical Safety (IPCS) Report (1): Environmental Health Criteria 194, Aluminium lists the following conclusions with respect to the health effects of aluminium in the general population:

“Hazards posed by aluminium to intrauterine and neurological development and brain function have been identified through animal studies. However, aluminium has not been shown to pose a health risk to healthy, non-occupationally exposed humans.

There is no evidence to support a primary causative role of aluminium in Alzheimer’s disease (AD). Aluminium does not induce AD pathology in vivo in any species, including humans.

The hypothesis that exposure of the elderly population in some regions to high levels of aluminium in drinking-water may exacerbate or accelerate AD is not supported by the available data.

It has also been hypothesized that particular exposures, either occupational or via drinking-water, may be associated with non-specific impaired cognitive function. The data in support of this hypothesis are currently inadequate.

There is insufficient health-related evidence to justify revisions to existing WHO Guidelines for aluminium exposure in healthy, non-occupationally exposed humans. As an example, there is inadequate scientific basis for setting a health-based standard for aluminium in drinking water.”

**REFERENCES**


SUMMARY

The management of Occupational Health services within Hydro Aluminium is described. While occupational health in general has become highly regulated the services provided by the company are diverse and include many non-standard aspects. These include elements of social and economic services. The approach taken by Hydro Aluminium has allowed the occupational health service to maintain focus in a decentralised medical organisation. Similarly, it has been able to demonstrate its economic value in ways that are understood in an otherwise industrial production-oriented organisation. It has become a strategic target to demonstrate the cost-effectiveness of the medical / health service, in addition to the demonstration of its more value-based qualities.

INTRODUCTION

Seen from a regulatory point of view, occupational health is far more regulated and defined, through International standards, than Safety, Health and Environment. Logically, this should have led to occupational health being reduced to a technical matter of industrial hygiene, involving day-to-day operations - supplemented with a hired medical service secured on an hourly basis. However, this has not been the case in Hydro Aluminium, even if we see such tendencies in some other Norwegian companies. There are several reasons for this:

- Norsk Hydro, of which Hydro Aluminium is a division, has a long tradition of having an active medical service as an integral part of the organisation. The lesson learned is that the medical profession is a cohesive factor in many of the relations between employees and management. This is specifically so in difficult periods.
- Even if OSHA and other organisations, supported by our national occupational health authorities, have set standards for almost all facets of occupational health, we still find that we have something
to learn about our working environment. Matters related to specifications in the way we operate our plants, and to specific important factors, like fluorine and PAH, still need attention and better understanding.

- More and more, matters that cannot be given standardised answers, need additional attention and better understanding. This relates to muscular and skeletal diseases; to questions of lifelong occupation and an increasing number of possible liabilities due either to earlier releases or to other causes of acquired malfunctions.
- Traditionally our medical officers have, to a limited degree, also had the role of giving general medical advice to employees.

Several of these points will have to be re-evaluated:

- We have increasingly reached an understanding that enables us to run our plants with practically no industrial hygienic threats.
- The general practitioner has become a specialist, as for almost all other branches of the medical profession. It is questionable if our medical officers, being certified specialists in occupational health, can be permitted to give general medical advice.

At the same time, new challenges have been raised with regard to matters related to work safety, to high quality in the constant development of the organisation and its members - from blue collar workers to presidents - and an increasingly demanding international working climate. Occupational health becomes a matter of health, personal development for all parties incorporated in our organisation and organisational health. A lot of travelling - many by members of the organisation - places new demands on our medical officers, too.

The international competitive climate demands steady improvements in the way we run our business. The understanding that this goes back to every individual in our organisation has become very clear. At least theoretically, our organisation and management understands that, with the changes indicated, the medical profession will also be an important factor in the future economic success of our operation.

As of today we are, therefore, faced with some strategic challenges in our organisation related to the way we get the most from occupational health services.

The understanding of - and experience with - the occupational health service as the cohesive factor in a very labour- / employee-oriented organisational culture is well established. This leaves us with a decentralised occupational health service. We have no chief medical officer, the medical service being where the people are.
A prime strategic target is to maintain focus in a decentralised medical organisation with a change in focus from just occupational health to what I will call an expanded definition of occupational health, that includes a strong element of social and economic factors.

Even if we theoretically can understand the economic importance of an occupational health service, it has to be demonstrated in terms and ways that are understood in an otherwise industrial production-oriented organisation. It becomes a strategic target to demonstrate the cost-effectiveness of the medical / health service in addition to its more value-based qualities.

This paper deals with how we in Hydro Aluminium attack these two prime strategic targets, partly through a network organisation of the occupational health service itself, and partly through the development of broad based projects with defined improvement targets.

THE OCCUPATIONAL HEALTH STRUCTURE

We have structured our Safety, Health and Environment work along almost identical lines to many other organisations. The structure is characterised by:

- Line responsibility;
- Continuous improvement through goal-setting, planning, performance and auditing / measuring.

Along these lines we have defined our medical / occupational health services as being part of plants and corporate offices. We have no corporate medical staff apart from a few staff that have a co-ordinating function. The medical expertise in the company is decentralised. To take care of and develop our expertise, we have defined a medical council with our medical officers as members. It is more than ten years since Hydro had a corporate chief medical officer. The model with the council has worked very well. With the growth of our aluminium business, we have for several years also had a separate aluminium medical council. As we see it today, there is no need to change the model.

As indicated above, the challenge is to maintain focus on a moving target. Statistically, the change in target can be demonstrated by the following numbers from one of our plants.

- In 1985, we found 12 new cases of asthmatic symptoms - 9 of these were smokers. In 1996 we found 6 new cases of asthmatic symptoms - 5 of these were smokers.
• In the period 1994-1996, more than 113 of all registered sick days were related to muscular and skeletal diseases. In addition more than 1 in 10 were related to mental disorders.
• If we look at the total number of occupational health related diseases, we find a general decline from 1985-86 to 1995-96.

The general observation is that we see a relative increase in socio-related challenges and reasons for absence. What we do not as easily observe, but instinctively understand, is that socio-related challenges often represent matters that also have a direct influence on the effectiveness of our organisation. This signals a need for a wider focus, including both the chemically-related occupational health and the more socio-related occupational health. This change in focus represents a challenge for the medical officer, but even more - I think - for management. As a more personal observation, I think it is right to say that management in most corporations today uses its own personal experience, and the personnel departments more formal know-how about labour-relations to solve organisational matters. The probably vast field in terms of social and psychological insight between just occupational health and the more vague concept organisational health, is generally uncovered or partly covered by the occupational health profession and consultants or specialised research organisations on industrial psychology. As far as my observations go, and as far as this brief analysis takes us, I expect that the needed adjustment in focus will have as a consequence the expansion of the remit of the occupational health service. I expect that industrial psychology and / or sociology will be added to our future manning in the occupational health department or as a start of an upgrading of the occupational health profession. At one of our bigger office complexes, the occupational health department, under guidance from the medical officer, has carried out interviews on a departmental basis. The results clearly indicate that an expansion of our occupational health department as indicated will be useful.

A development and expansion of focus, as indicated, will move the occupational health profession or the redefined occupational health profession more towards being a part of management - in addition to its role as a form of authorised auditor of the working environment and medical officer for each single employee. This leaves us with two different challenges:

• One related to the definition of rules for and content of the occupational health profession;
• One related to building and expanding the bridge between occupational health as a specialised profession and general management.

Since this is a discussion of managing, I will leave the first of these law points and go on to the last one. How do we bridge the professions of occupational health and general management? This takes us to the last of my two strategic points.

**HOW DO WE DEMONSTRATE THE COST-EFFECTIVENESS OF OCCUPATIONAL HEALTH**

Based on our experience of the last 10-15 years of efforts to improve in our SHE work, we have found that improvements come through demonstrations of success in clearly defined cases. If we can demonstrate through a defined project that we can improve our performance, we will indirectly also learn how to define the next project, and so on.

As already mentioned, 113 or more of "sick days" were related to muscular and skeletal diseases. In 1986 muscular and skeletal diseases were related to 8,000 work days lost at one of our plants. The plant has about 1,550 employees. The average number of days lost per case was about 14. In total, about 570 employees were struck by "muscular and skeletal" diseases. It is easy to agree that this form of sickness means:

• A huge economic loss to the company;
• More than every third employee or in reality all departments at the plant were affected by sick days relating to “muscular and skeletal diseases”;
• The expected potential for improvement is great enough to expect improvements by organised efforts to improve.

One of the reasons this form of illness is so visible is that we do not know enough about it. What we do know is that there is a multifactorial set of reasons, both physical and socio-psychological. We know enough to do something to improve the situation. To do this we need to both deploy existing expertise and develop new insights.

Put in other words - muscular and skeletal-related illness represents a case that should be attacked because it represents:

• A disease/illness that harms our employees;
• A huge economic loss;
• A challenge for all lines of management;
A challenge for the occupational health profession.

Moreover, the problem can only be solved by the active participation of all involved - employees, management and the occupational health profession. As a consequence, we have decided to attack the challenge through an organised programme. We are currently in the process of establishing a programme comprising:

- a project studying causes and methods of improvement;
- a management-driven project at each plant;
- a support effort established through each occupational health department.

The project, that shall study causes and ways, will be made accessible to all aluminium plants in Scandinavia, while each plant in principle will be autonomous with its own separate project. Each plant will also have to set its targets for improvement. There will also be an improvement target for Hydro Aluminium Metal Products - I also predict we will see a target for Elkem and other participating aluminium companies.

Going back to the title of this paper “Managing Occupational Health”, you can see that by choosing this project and by setting a corporate target for improvement that is later reflected in each plant, each plant's different departments, etc., we have installed a common goal, a common yardstick and a common challenge to improve. To put it another way, we have defined a common unit that can help us to unfold the complexity of causes and ways related to muscular and skeletal illnesses. To my mind this is in essence an example of how we can develop management and also the economic dimension of occupational health in a decentralised organisation.
SUMMARY

Traditional Occupational Health programmes do not typically address the specific needs of the employee population to be served. Most traditional programmes allocate resources to tertiary prevention methods, which have the least cost benefit to the organisation and the least health benefit to the employee. A site specific needs assessment is critical in identifying the physical, chemical, ergonomic and lifestyle risk behaviour of the employee population.

At Alcan Rolled Products: Oswego Works, a non-traditional approach has been utilised in the implementation of Occupational Health Service guidelines for the 750 employees and their families. This process is based on a mission statement and goals that add value to the organisation. Cost avoidance, cost management and optimising employee and family wellness are the keys to the Occupational Health strategy. The prevention pyramid is used in development of core process components with resources appropriated accordingly. Components include: establishing the responsibilities of the team members; health risk assessments of employees and families; identification of group trends in health and safety risks and establishing dynamic health education processes to decrease the risks.

An Occupational Health Service can provide benefits for employers and employees, while decreasing health care costs. A dynamic process provides opportunities for decentralised plant sites to service their employees and to benchmark and share successful programme components with other locations.

STRATEGY

The strategy for managing Occupational Health programmes must begin with a mission statement of what is to be accomplished. Adding value to the company through cost avoidance, cost management and service to the employees is a reasonable goal. The greatest opportunity for cost avoidance lies in primary prevention. Preventable illness costs
approximately 70% of health care dollars. Secondary prevention or early detection is the next area for saving health care dollars. Routine screenings for cancer, heart disease and hypertension can help us to treat these diseases before they progress to more severe consequences such as MI and stroke. The final opportunity to decrease medical costs is through early return to work programmes and worker's compensation and disability management.

Traditional approaches in occupational health consist of regulatory mandated programmes such as blood borne pathogens and hearing conservation programmes, post event treatment; and early return to work programmes. There is an opportunity for savings in this approach, through decreased absenteeism, avoidance of government fines and avoidance of worker's compensation claims. Utilisation of in-house medical treatment can further defray costs by avoiding high emergency care costs.

**PREREQUISITES**

Before setting up the Occupational Health programme available resources (personnel, space and budget) need to be identified. The Alcan Occupational Health team consists of:

- Medical Staff
- IH / Safety/ Environmental
- Administrative support
- Dietician
- Occupational/ Physical Therapist
- CAP
- Wellness Centre Instructors
- Human Resources/Benefits

**OCCUPATIONAL HEALTH PROGRAMME**

The Occupational Health Team plans the programme to fit the needs of the site. If resources are not available on site the corporate Health and Safety group could perform the needs assessment and help plan the Occupational Health Programme. When planning, each site could use benchmarking techniques looking at programmes that work well in other sites. They could then tailor those programmes to fit their needs. (Alcan Nurse's group forms a network to share information.)

To avoid Health care costs we must focus on prevention. To accomplish this task a site specific needs assessment must be performed. The needs assessment should determine:
• Average age  
• Cost and availability of health care  
• Community culture  
• Labour situation  
• Workplace stresses (chemical, physical, ergonomic)  
• Environmental and behavioural risks (smoking, weight, cholesterol levels, stress levels, cumulative trauma, accident trends, drug/alcohol abuse)

The mission of the proactive approach that we now use is to promote physical, emotional and social wellness to employees and their families while reducing employer health care costs. The goals include: reducing health care costs by 25% over one year; providing quality education for the prevention and early detection of illness and injury; and providing quality medical care to employees and their families.

ECONOMICS

The 1996 expenditures for active employee and family medical claims were 3.5 million dollars. The Prescription drug costs were 460 thousand and the retiree medical claims were 1.7 million dollars. This reflects the cost for medical care for approximately 750 employees and their families and approximately 250 retirees and spouses. To reduce those costs we have:

- Negotiated with local laboratory and X-ray for special pricing. Frequently ordered laboratory panels = 50% savings; single laboratory tests = 25% savings; X-rays and X-ray interpretation costs = 15% savings.
- Negotiated prices with local pharmacy - cut out administrative fee and negotiated for 14% savings over the AWR price through our RX drug plan. Also developed a local clinic based formulary allowing prescriptions for non-prescription drugs at a much cheaper rate (e.g. Zantac 75 mg 2 tabs bid vs. Zantac 150 mg bid. Saving = $42 per month per patient).
- Established primary care on site for family and employees who choose the clinic as their Primary Care Provider. Visits = 900 - 1300 per month. Savings for past 3 months = $186,100.00 (care given by CPT code = $242,000.00 - cost of running medical department $60,500.00 = $186,100.00).
- Established an extensive Health Education Process to decrease illness and injuries.
HEALTH EDUCATION PROCESS

The Health Education Process consists of:

- Trend Analysis - allows you to determine in which area of safety and health you need to expend your energy. For example: if hand injuries are the dominant injury, hand safety should be the target of safety education and protective equipment.

- Medical Monitoring - allows for early detection of disease. (Examples: Routine urine screening led to detection of bladder cancer in a 31 year-old male and routine BP screening led to renal cancer detection in a 48 year old at very early stages of disease. Neither person needed chemotherapy or long term treatment that would be extremely costly. It also saves lives.)

- Health Risk Appraisal - Through use of a questionnaire, medical testing and fitness testing, the employee is given a detailed report of where their particular health risks are. We then enroll them in classes to educate and modify their behaviour to reduce those risks. (Weight control; cholesterol countdown; smoking cessation; healthy back; diabetes control; aerobic classes; hypertension control; stress reduction).

- Wellness Centre - Aerobics; Circuit Training; Weight Equipment are offered with the instruction of trained individuals that are subcontracted through the YMCA.

- Functional Capacity Exams - performed for an objective measurement of an employee's physical capability - This allows fitting the employee to the job. Used for RTW or pre-placement.

- Physical Therapy - On site treatment decreases time away from work; early intervention offers faster resolution of problem; closer follow up of progress for earlier access to light duty programme and return to work.

- Nutrition - On site programmes include; Cholesterol Countdown; Diabetes Control; Weight Loss; Hypertension Control which aid in lifestyle changes to decrease disease risk factors.

- Employee Assistance Programme - Onsite programme allows for confidential crisis management and early access into mental health or chemical dependency programmes.

- Ergonomics Programme consists of a team including: Occupational Therapist; Occupational Health nurse; Department co-ordinator and facilitator.
• **Scope:** (2-year project): To provide videotape, a written job description that identifies the essential job functions of every job and intervention to change high-risk tasks.

• **Format:** Videotaping of each task on the team is done over 2 separate shifts. The team views the tape and uses videoworks to identify any high stress lifts based on the NIOSH lifting equation. The tape is then presented to each shift on the team at their monthly safety meeting. The employees provide feedback on how they feel jobs can be modified to create less physical stress on the employee and also validate that the team has accurately captured the job. Recommendations from the employees and the ergonomic team are presented to department management and an action plan is developed to make the changes. The job is then re-taped and employees are interviewed to determine if the changes are beneficial. Any change in the manufacturing process is conveyed to the team to keep an up to date file on all jobs.

**BENEFITS**

• Educates employees on proper techniques of lifting, bending and carrying.

• Employee involvement gets their buy-in on the safe way to perform tasks.

• The medical providers in the community can see the job on video and make a better determination for return to work in light duty programmes.

• The job description and the functional capacity use the same format for ease in matching jobs to employees.

• If the employee does not fit into any job based on physical limitations we use work hardening and rehabilitation to decrease their limitations.

These programmes work toward the goal of decreasing workers compensation claims; disability claims; absenteeism and improving employee's job satisfaction.

**REFERENCES**


More and more companies over the last 10 years have moved to outsourcing. As with all approaches, strengths and limitations exist with this one as well. The following presents some thoughts for those considering a move towards the outsourcing of select occupational health services.

Generally there are two types of services offered by consulting organisations - preventive services and ameliorative services. Occupational health preventive services include the following:

- Physical exams;
- Screening tests;
- Wellness;
- Health promotion;
- Safety;
- Industrial hygiene;
- Ergonomics.

Ameliorative services include:

- Acute care;
- Emergency response;
- Case management;
- Employee assistance.

Whether or not a company should consider outsourcing is often contingent upon several parameters - corporate versus facility perspective; facility size considerations; and need for special expertise.

Approaches to outsourcing are several. They range from outsourcing few, if any, services - to management's outsourcing of all services. Outsourcing examples include - services frequently outsourced, those seldom outsourced and those which are many times
optional. Services frequently outsourced include wellness / health promotion and employee assistance. A service seldom outsourced is safety. Optional outsourcing services include:

- Physical Exams / Screening Tests
- Industrial Hygiene
- Ergonomics
- Acute Care / Emergency Response
- Case Management

Outsourcing can come in various forms. As a first case, reviews and medical follow ups can all be done by an outside resource. As a variation on this, a facility can conduct the tests and choose to outsource the data, management and reviews. As another variation on this, a facility can utilise test vans for a turnkey service.

The advantages of outsourcing are several:

- Increases flexibility in staffing
- Provides access to special expertise
- Management focus on core business
- Less costly in many situations

The management issues in outsourcing are generally three:

- Selection of service providers
- Time and attention to assure quality
- Risks not assumed by service providers

Whether or not a company chooses to outsource is a function of many things. It is the best solution for some, but must be weighed against a company's culture, resources and ability to manage services that are not within their present existing infrastructure.
35. MANAGING OCCUPATIONAL HEALTH, INDUSTRIAL HYGIENE AND SAFETY: A GLOBAL PERSPECTIVE

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SUMMARY

Within this paper: managing occupational health, industrial hygiene and safety in a global context, "Visible" and “invisible” factors, which heighten the challenge presented by this issue, are discussed. A case study is used to describe the approach used to resolve the need for a consistent global record keeping system for workplace related health and safety outcome statistics. The question of “different country - different standard?” is also brought forth and discussed briefly as a lead - in to further panel and audience discussion. In conclusion, the author believes those factors of geography, language, culture, resources, skills and regulation add extra dimensions to the challenge of managing occupational health and safety on a global basis. Through the use of modern communications, consensus, and teamwork many of these differences can be overcome and, in the final analysis, will add value to the global organisation.

THE CHALLENGE: “VISIBLE” FACTORS

Alcan is a Canadian based multinational company with major operations in over 20 countries, on five continents. This geographic diversity is further compounded by the need to work in at least 10 languages and respond to over 25 different sets of occupational health, industrial hygiene, and safety, regulatory requirements.

Throughout the organisation, there also exists considerable variation in available professional and technical resources and a paucity of head office resources. To manage occupational health and safety needs requires the sharing of skills and competencies between different operating areas.
THE CHALLENGE: "INVISIBLE" FACTORS

A number of qualitative factors also impact the overall management approach. These include considerable cultural variations between different countries and different sites and a decentralised management style and levels of commitment to health and safety which varies from individual to individual. These "invisible" factors can constitute unknowns in implementing a global approach to the management of occupational health and safety.

MEETING THE CHALLENGE - A CASE STUDY OF A GLOBAL OPPORTUNITY

A record keeping system for the statistical analysis of work related data on serious injuries (AIRS - Alcan Injury Record Keeping System) has been in use for the past 10 years. The details of that system are not reviewed in this paper - the focus is on the global approach undertaken to respond to a recognised need to update the system. Fortunately, this need was recognised by one division in 1996 and considerable discussion was undertaken with divisional personnel to arrive at consensus for a revised AIRS system. As a result, a drafted version of the revised system was available by the end of 1996. The question was then raised of whether this system should be applied on a global basis.

Once the opportunity was identified and a decision made to manage the opportunity on a worldwide basis, senior safety representatives from each division were asked to join a management advisory committee. Teleconferences were held to outline the opportunity and to determine the path forward - global standardisation of record keeping approaches was deemed essential. The teleconferences led to a determination by the committee to hold a consensus building exercise.

This exercise involved a senior safety group (8 persons) representing various geographic and functional areas. The decision was taken to meet at four Alcan sites in Germany. The format used was designed to "add value". A combination of short site visits, to exchange health and safety expertise, and discussion of the new record keeping system, resulted in benefits for the sites and the committee members. Site based formal discussions, as well as informal discussions during travel periods, were held.

Three positive outcomes were identified. The team accomplished their goal of obtaining consensus on a new record keeping system for workplace injuries and illnesses. In addition, the exchange of information between health and safety professionals on the team and site
professionals proved to be of considerable value. Finally, a functioning safety management resource team is now in place and continues to work on other topics requiring a global approach.

**CONCLUSIONS**

Teleconferences are an ideal method for planning and following up global management opportunities. Face to face meetings build the team and achieve consensus - there may also be "added value" options to these opportunities. A functioning global team is a global resource. Factors of geography, language, culture, resources, skills, and regulation add extra dimensions to the challenge of managing O.H. & S. on a global basis. Through the use of modern communications, consensus, and teamwork many of these differences can be overcome and, in the final analysis, add value to the global organisation.
Alcoa has recently undergone a transition from a highly centralised corporation, through a highly decentralised corporation, to a new structure in which a Business Services Group was established to assist both the Corporate Groups and the Business Units in handling administrative, transactional and expert services. Included in the new Business Services Group is an Environment, Health and Safety Services Group. This possesses considerable occupational health, industrial hygiene, toxicology, and other medical and health-related expertise. In addition, Alcoa has developed a partnership with Yale University's School of Medicine and both organisations now work together on issues related to occupational and environmental health.

Global committees, teams and advisory boards were set up to support the organisational goals and objectives. The activities of these are considered essential. During the reorganisation the main lessons learned were:

- The necessity of keeping corporate values and goals in perspective;
- The need for common purpose and teamwork throughout the organisation;
- The importance of never underestimating the power of communication;
- The realisation that there is no substitute for "good" people;
- The finding that a "good" plan, backed by organisational acceptance and understanding, achieves more traction, in implementation, than a "perfect" plan lacking either organisational acceptance or understanding.