SIERRA CLUB The Florida Chapter

3120 38th Ave. E.
Bradenton, FL 34208
April 27, 1998

Martin Costello
FL Department of Environmental Protection
Twin Towers Office Building
2600 Blair Stone Road
Tallahassee, FL 32399-2400

Dear Mr. Costello,

Re: FPL Manatee Orimulsion Project, Application No. 94 - 35

Orimulsion is reputed to contain high amounts of vanadium and nickel. I plan to send you copies of research reports that detail the effects of vanadium in causing cancer.

What powers does the FL Department of Environmental Protection have to protect the public from fine Orimulsion particulates containing vanadium?

Was your section of the FL Department of Environmental Protection provided with copies of this research which I believe were submitted to Administrative Law Judge in January 1998 during public comment?

What actions has the FL Department of Environmental Protection taken as of April 27, 1998 to address the protection of Florida's citizens from the health threats posed by vanadium and nickel in Orimulsion should it receive a permit to be burned in Florida ?

What actions can the FDEP take to protect Florida's residents from air pollution containing vanadium and nickel?

Thank you for your attention to these questions.

Sincerely,

Mary E. Sheppard

Mary Sheppard
Clean Air Chair for
Florida Sierra Club

cc. Mr. E. Timothy Oppelt (MD-235) EPA
File
C. Fancy
D. Beason

The Whistle

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Campaign Project

ASTHMA & INDUSTRIAL AIR POLLUTION

A Failure of Regulation

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Freedom to Care
Campaigning for Ethical, Open & Accountable Organisations

Important Notice

Every effort has been made to ensure accuracy and fairness in this report. It is made purely in the public interest (the interest of Pembrokeshire children in particular) in order to provide a *prima facie* case for an independent inquiry into regulatory breaches in the management of industrial emissions in Pembrokeshire and elsewhere in the UK. If any inaccuracies or misleading propositions remain we apologise for them and sincerely hope that an inquiry will uncover the whole truth. We do not believe confidentiality has been breached at any point; but if it has then this will be due to the paramountcy of the public interest in our thinking on this matter.

Acknowledgements

Freedom to Care wishes to thank **The Body Shop Foundation** for generously covering the cost of producing this report. Dr van Steenis gratefully acknowledges the support of the **Campaign for the Protection of Rural Wales,** the hard work done on industrial air pollution in Wales by **Dr Max Wallis** of FOE Cymru (Friends of the Earth Wales), the help given by **Mrs Mary Horner** in the Clitheroe research, and the support of **Ken Coates MEP** (NE Derbyshire).

Related literature is available from **FOE Cymru**, 33 The Balcony, Castle Arcade, Cardiff CF1 2BY, Tel. 0222 229577.

Membership & Subscriptions

FREEDOM TO CARE is a voluntary organisation and a company limited by guarantee. Its patrons are John Hendy QC and Allan Levy QC. It supports employees victimised for speaking up with a public concern and campaigns for ethical, open and accountable organisations. It is organised into a number of occupational networks which meet regularly, for example, a healthcare network and a scientific & medical research network. Membership costs £18 per annum (£3 for those on low income) and members are entitled to attend meetings and receive two issues of 'The Whistle' (special reports) and three issues of the 'Campaign Report' per year. For information contact :

FREEDOM TO CARE PO Box 125 WEST MOLESEY SURREY KT8 1YE UNITED KINGDOM.

Technical terms

Asthma = breathing difficulty from inflammation of the lungs due to allergens, irritants and toxic material leading to airway constriction; can become chronic.
BATNEEC = Best Available Techniques Not Entailing Excessive Cost
Baseload fuel = the main fuel for continuous operation
Bitumen bottoms = A tar-like substance left over from oil refinery
BPEO = Best Practicable Environmental Option
COSHH = HSE regulations on the Control of Substances Hazardous to Health
Cumulative sequelae = a piling up of medical problems in a patient
Dioxin = a very dangerous cancer-causing chlorinated hydrocarbon
Flue gas desulphurization (FGD) = removal of most polluting sulphur dioxide gas
Heavy metals = nickel, lead, arsenic, chromium, cadmium, vanadium many of which cause cancers, asthma and other disease
Ingestion = taking into the body through mouth, swallowing
Inhalation = breathing into the lungs
Immune-compromised patients = patients who have a weakened resistance to infection due to drugs or disease, so get sick easily
Nitrogen oxides (NOx) = nitric oxide, nitrogen dioxide; which affect breathing
Opencast coal mining = the mining of coal from above ground, which throws up a lot of coal dust into the air
Orimulsion ® = Bitor's trade name for bitumen/water emulsion
Ozone = a form of oxygen, a gas which in the upper atmosphere helps block radiation, but too much at ground level harms health
Particulates = tiny particles, fragments, dust in the air
Peak-low meter = measures how rapidly air is breathed out
Petcoke = a toxic processed bitumen bottoms fuel
Plume dispersion = spreading cloud of chimney fumes
Plume grounding = the fall of a cloud of chimney fumes to the ground
PM1 = particles of a diameter of 1 micron, that is, one thousandth of one millimetre. The monitoring standard is PM10. There will be 1,000 PM1 particles in the space of one PM10 particle. [redacted] particles SMALLER THAN PM 4 pass into the lungs. Many pollen grains are about PM10.
Pollution abatement equipment = devices to reduce pollution at source
Polycyclic aromatic hydrocarbons = carbon-hydrogen compounds such as benzene
SLF = secondary liquid fuel. Waste oils, solvents, etc. mixed into an emulsion
Sulphur dioxide = an acrid polluting gas which can turn to acid rain
Temperature inversions = weather causing warm emissions to be held near ground
Ugm/m3 = micrograms per cubic metre; measure of how much matter in a space

The Participants

Agenda 21 = principles agreed by UK at conclusion of Rio Summit on environment & sustainable development, with which County advisers should comply
Ainger, Nick MP (Labour, Pembroke)
Bitor = Bitúmenes Orinoco, S.A. Venezuelan company marketing bitumen emulsion (Orimulsion) from Orinoco oil fields.
CCW = Countryside Council for Wales
CPRW = Campaign for the Protection of Rural Wales
Delahunty, Dr. = Doctor who produced report for Dyfed Health Commissioning Authority in May 1995
DoE = Department of the Environment
DoH = Department of Health
DTI = Department of Trade & Industry
EA = Environment Agency (ex HMIP), started April 1996
EPAQS = Expert Panel on Air Quality Standards, DoE
Ferrers, Lord Earl - Environment Minister
FOE Cymru = Friends of the Earth Wales
Gummer, John MP - Secretary of State for Environment
Harrison, Mr Keith = retired BP technical manager
HMIP = Her Majesty's Inspectorate of Pollution, founded 1987, and later incorporated in Environment Agency
HSE = Health & Safety Executive, implements legislation such as Health & Safety at Work Act 1974
MAFF = Ministry of Agriculture, Fisheries & Food
National Power = privatised company which owns Pembroke power station
PCC = Pembrokeshire County Council, Dyfed County Council existed prior PCC, that is until 31 March 1996
Pembrokeshire CHC = Pembs Community Health Council, representing patients
PHD = Public Health Department, a department in every health authority
PowerGen = a privatised company operating power stations
PCC = Pembrokeshire County Council, formed 1st April 1996
PPDC = Preseli Pembrokeshire District Council, now PCC
QUARG = Quality of Urban Air Review Group, DoE
Queenborough, Dr J = Director of Dyfed Health Commissioning Authority until 31st March 1996, then consultant to Dyfed/Powys Health Authority from 1st April 1996
Seal, Mr. = Director of the SPDC's Environmental Health Department
SEEC = Sea Empress Enquiry Committee
SPDC = South Pembrokeshire District Council, now PCC
WDA = Welsh Development Agency

A Breath of Fresh Air

Geoff Hunt
FTC National Coordinator

Asthma out of Control?

Until the 1960s there were about 100,000 cases of asthma a year in the UK. Today there are **three million** cases and 1,600 deaths a year. There is hardly a school in any urban area in which children have no need for inhalers. In 1994 the NHS spent £380m on prescriptions for asthma drugs, an increase of 20% in two years.

Now new maps drawn up by a retired Pembrokeshire doctor, on the basis of his own research done without official funding, provide very strong evidence for the idea that air pollution causes asthma in schoolchildren. Three of his maps are published here. Dr Dick van Steenis, is a member of **Freedom to Care**'s 'Fairness & Accountability in Science & Technology Network', and thinks the public ought to see the maps for themselves since the responsible authorities have not been taking them seriously.

The maps cover three quite separate parts of the UK and show a striking pattern of increased numbers of children taking inhalers to school downwind of industrial plants, particularly power stations. The nearer to the polluting industry the more inhalers are used; over one third of schoolchildren use them in one downwind locality. (Inhaler use is a good measure of asthma incidence.)

Since 1992 a great deal of poisonous waste, British and imported, has been incinerated in UK plants not designed to cope with it, such as power stations and cement works. The result has been a trebling of the asthma incidence locally and downwind of such plants in certain weather conditions.

Cheap and Dirty

A specific worry addressed in this issue of **The Whistle** is National Power's proposal to burn in a power station a natural bitumen mix imported from Venezuela and called Orimulsion®. This new fuel is cheap, and would save National Power money, but is dirty. It is planned to burn four to five million tonnes a year of this at Pembroke power station - making it the world's largest such plant, in fact twice all the other plants put together. Dr van Steenis' has produced a map for the area which shows that it already has very serious asthma problems downwind of the power station and oil refineries. The burning of Orimulsion without the most stringent pollution control could make matters worse. Orimulsion contains cancer-causing heavy metals such as nickel and vanadium which get into the air. (It also contains an additive called 'nonylphenol' which, if there was an oil spill, would cause great harm to fish and other sea life and probably human beings. The additive is known to damage the reproductive ability of marine animals. It is, of course, in this very same area that the tanker *Sea Empress* recently did so much damage.)

Communities in the USA have already rejected Orimulsion. There were demonstrations in Florida and the state government finally decided that the environmental harms outweighed the benefits.

The British Ostrich

The attempts by this conscientious doctor to gain the attention and action of the responsible authorities have been ignored or frustrated by these authorities. The Health & Safety

Executive has not prosecuted where they could and should have done, the Environment Agency (previously HM Inspectorate of Pollution) has allowed the Orimulsion application to proceed without due thought for the consequences, the local Public Health Department ordered Dr van Steenis to stop his surveys of schoolchildren, the local Environmental Health Department won't measure the very fine particles being emitted by local industry and has published misleading counter-information, and National Power (the power company involved) refuses to be open with its information and plans.

Yet Dr van Steenis has gained the support of no less than forty one community doctors in his area. Local environmentalists (such as The Council for the Protection of Rural Wales, Friends of the Earth, and the Phoenix group) are also very concerned and are opposing the proposal to burn of Orimulsion. **Freedom to Care** is particularly concerned about the failures of openness, ethics and public accountability. It is so typical of our secretive and closed political culture that once again a whistleblower has to risk everything in order to let the public know what it is their right to know anyway.

The Departments of Health and the Environment have recently woken up to the disease-causing impact of the dust (particulates) thrown into the air by power stations, waste incineration and other industrial combustion. The trouble is that they are not monitoring small enough particles - ones that get deep into the lungs - and they are not looking hard where they should be - downwind of industries burning dangerous substances. Although particles of size PM10 (see Glossary) have become an international standard for air pollution monitoring, the Americans are already questioning this and thinking about much smaller ones. Perhaps we should now be monitoring particles which are one-quarter that size or even less. It seems that 85% of the particles in the emissions from Pembroke Power Station have been less then PM1, far below the current monitoring standard.

It is vital to get the balance right between economic demands and environmental ones. But one cannot even begin if one is not prepared to look hard in the right place and face the truth. Does it make economic sense to save on pollution control and waste on NHS bills for the treatment of asthma and other diseases caused by air pollution? Litigation from thousands of poisoned people looms on the horizon. The prima facie case for localised particulate emissions causing asthma and other diseases, such as cancer, is now so strong that it would be negligent not to proceed with concentrated research followed by the necessary action. It appears that we are very far from meeting the recommended levels of the government's Expert Panel on Air Quality Standards (EPAQS).

'There is no evidence..'

The official UK government position is still that there is no evidence that air pollution can cause asthma, (although they say there is proof it can make it worse for existing sufferers). No doubt readers will remember similar announcements about the connection between BSE and CJD in humans. In October 1995 the DoH said 'asthma has increased in the UK over the past 30 years but this is unlikely to be the result of changes in air pollution.' In November 1995 the DoH said its recent work 'confirms that there is no evidence that healthy people are likely to be affected by airborne particles.'

Yet academic researchers working in occupational epidemiology have long established hard evidence that inhaled pollutants in the workplace can cause asthma in people who did not have the disease and would not otherwise have developed it. Then there is the evidence of ordinary people all over the country. It is surely quite unethical to ignore this background in dealing with the issue of whether outdoor air pollutants can cause asthma.

Public accountability, openness and the honesty and boldness to look hard in the right place would certainly bring a breath of fresh air

INDUSTRIAL AIR POLLUTION AND ASTHMA
A Failure of Regulation

Dick van Steenis MBBS

Let the people know the facts,
and the country will be safe
Abraham Lincoln 1861

PART ONE: ASTHMA IN PEMBROKESHIRE

INTRODUCTION

The Fresh Air of Wales?

With clean Atlantic air blowing in on the prevailing wind one might expect no major problem with asthma in Pembrokeshire, West Wales. However, the incidence of diagnosed asthma in the primary school children locally due to temperature inversions and downwind of the power station and three major oil refineries appears overall to be the highest in the UK along with one school near Greenwich and one at Arkwright, Derbyshire. As many as 37.9% of four and five year olds are using inhalers (FOR CHRONIC ASTHMA?) in the power station pollution footprint. It is postulated that emissions of particulates smaller than PM1 of vanadium, nickel, other heavy metals, and possibly polycyclic aromatic hydrocarbons are to blame, potentiated in summer by high levels of ozone associated with the nitrous oxides emitted from the complex. Levels of nitrous oxides in Pembroke in April/May have been at peak London traffic levels.

American public health studies of over half a million people confirmed an increase of asthma and cardiac deaths due to health damage from sulphate particulates being the products of combustion of various fuels. Environmental Health departments in Dyfed, West Wales refused to monitor particulates prior to mid-1996. Since the hospital was built in Haverfordwest in 1979 asthma admissions had been second highest in the UK. The power station opened in 1973. After privatisation , with the oil refineries utilising the maximum extraction from crude oil, the power station was left with residuals comprising what might be described as "bitumen bottoms" which could be mixed with oils like waste vehicle engine oil or even solvents, to be called "residual fuel oil", or could be emulsified with water like the bitumen/water mix called Orimulsion® that comes from Venezuela, marketed by Bitor. The previous oil burned was called "heavy fuel oil". Bitor's

data sheet for the Health & Safety Executive (HSE), which had been available to no one but was extracted by Mr Keith Harrison (a retired BP technical manager) from HMIP, states that inhaling the products of combustion poses health damage such as asthma from the vanadium, cancers from the nickel etc, which applies not only to Orimulsion but also to heavy fuel oils. The power station had been since 1992 operating on and off burning residuals supplied, we understand, by Texaco and maybe British Petroleum.

Using a cold chimney, in the circumstances, emissions would not rise in the air on most days but descend almost undiluted on local populations. They did not have any pollution abatement equipment.

In 1991 the power company tried to push through an application for baseload Orimulsion without abatement which was withdrawn after opposition. In October 1994 a new proposal was put forward with initial consent to apply from HMIP. The power company made a presentation to the Health Authority, councillors and others, but the public were not told until early January 1995 The Health Authority leaders made a further visit to the power station and then approved the application without further ado.

UNCOVERING THE TRUTH

Finding out for Myself

About the same time the CPRW (Campaign for the Protection of Rural Wales) had invited me to join their Pembrokeshire Executive, so I was asked to look into the matter as the proposal had major health implications.

At the outset I was not aware of these background matters and have had to delve. Having prayed for insight and wisdom I determined to ascertain the incidence of primary school children taking inhalers to school for asthma, having previously observed that my wife and huge numbers of adults and children had developed asthma in the locality during and since 1992, mostly without previous history. My technique I later discovered had been previously used by Public Health in Derbyshire and County Durham and by Environmental Health in Bristol. (It is a pity that GPs' software cannot yet print out disease, age and postcode correlations.)

When mapped out the results were extremely clear cut with over one in seven children taking inhalers to school in the high zone downwind of the power station for over 40 miles, with one in fifteen to the north and south of the hills delineating the high zone, with only one in thirty on clear coastal areas. When initial results were presented at a public meeting in Martletwy and published on the front page of the 'Western Mail' newspaper on 3rd March 1995, the effect on the local district councils and health authority was electrifying.

Shutting out the Truth

The power company was thrown off balance by the challenge to their claims of safety. The Director of Public Health and relevant Director of Environmental Health, without having read my report, issued a press release to try and "calm asthma fears" and the Director of Public Health ordered me and CPRW to cease contacting primary schools forthwith. They later said that our sample was not large enough, when we were in the process of contacting every school in Dyfed. I had already obtained results from 30 schools and doctors' surgeries in three towns where manual searches of practice records had been done.

'The Lancet' published on 8th April 1995 a letter of mine, highlighting the findings. Claire Williams, secretary to Mr Jackson of Pembroke Power Station, wrote to 'The Lancet' disputing the contents of my letter without evidence, hence the editor declined to publish her letter.

The Public Health Department later produced a report in the name of a trainee registrar as their official response to the planning proposal for the use of the local district council (SPDC) and HMIP, which was actually published by the manager of the power station before being issued to councillors. The report was full of misinformation, incorrect claims and data, graphs had been deliberately relabelled with what they were not, to come to conclusions about the relabelled headings that were hence not valid (rather like plotting prescription data for paracetamol and relabelling it prescriptions for appendicitis to conclude that there was a lower rate of appendicitis in Pembrokeshire than in the rest of Wales). The report did not cover many relevant issues at all, and mixed up data relating to primary and secondary schools. If the primary school alleged data was mapped out, it coincided largely with my map. Nobody had referred to the Bitor Orimulsion data sheet which also admits that 85% of the particulates of heavy metals etc. are of a size less than PM1, which would cause maximum health damage.

During subsequent months public meetings and articles in the press revealed vehement opposition to my findings and their implications by the power company, Environmental Health, the Health Authority and the local MP. The Public Health Director even wrote to GPs declining to seek data but instead backing the power company with lots of misinformation. This included a map of rural SO_2 (sulphur dioxide) deliberately instead of a town SO_2 map which would have shown Milford Haven as being the fourth highest in the UK.

Seventeen Times the National Average

The local Community Health Council (PCHC), however, did pursue my claims and arranged a special meeting. The Director of Medical Services at the local hospital checked hospital admission data on the hospital computer and printed out asthma coded admissions (ICD 9.493.9) per 1000 people per area of Pembrokeshire. The results concurred with my primary school asthma inhaler map and revealed that hospital admissions for asthma (which in published studies have shown a correlation with asthma incidence) to be 17 times the national average in Pembroke and Pembroke Dock and some 14 times the national average in Milford Haven, Neyland and Haverfordwest.

One local newspaper declined to print my case for the two years. Both local newspapers constantly carried major articles and editorials promoting National Power, mostly using the "local jobs" argument. At one stage an advert had to be bought by environmentalists at the cost of hundreds of pounds to enable just a few aspects of the case to be presented. Elsewhere a newspaper had been threatened that if it dared print anything against the polluting company they would be sued. At two public meetings I was deliberately prevented from being allowed to ask questions.

However, a representative of the 41 Pembrokeshire GPs backed by a public health consultant and university senior lecturer on an S4C (Channel Four Wales) TV programme castigated Public Health and totally agreed with my warnings. Meanwhile BBC television declined to broadcast a programme in English, in Wales or nationwide. The 41 GPs wrote a letter on 23rd July 1996 to the County Council, Welsh Secretary, local MP, Environment Agency and John Gummer MP (Secretary of State for Environment) demanding a public enquiry as well as warning of impending health damage.

Following the 'Sea Empress' oil spill in February 1996 off the Pembrokeshire coast the

public perception of the inherent dangers altered, and the MP now called for a public enquiry, which the power company had been desperate to avoid. I continued to investigate industrial air pollution and was asked to assist in other problem areas: toxic waste burning cement works, power stations and opencasting of coal and toxic waste sites where investigation revealed clusters of asthma, heart deaths and cancers of the breast, lung, bowel and renal tract. Government policy had previously been to dump waste on landfill sites with consequent dangers of local air and water pollution, but in 1992 with shortage of land they began to incinerate waste without dedicated plants (i.e. not fitted with adequate pollution abatement systems), leading to wide spread air and agricultural pollution. Also toxic waste is being moved so affected sites can be redeveloped, again sometimes causing major dangers to those living locally and downwind, threatening food chain safety.

Are Pollution Laws respected?

The suffering public, you and me, are supposed to be protected by the Health and Safety at Work Act 1974, the Environment Protection Act 1990, various European directives such as the Incineration of Toxic Waste and air and water pollution guidelines. But these seem to be blatantly disregarded by the regulators who comprise the Environment Agency (ex HMIP), the HSE, public health departments of the health authorities, and Environmental Health departments of local councils. As long ago as 1988 secret trials with burning emulsified hydrocarbons (Orimulsion) were carried out at Pembroke Power Station, using specially developed burners. No record of monitoring or safety precautions has been found.

My experiences during the past two years, some of which I discuss in the following pages, bring me to the sad and alarming conclusion that there is a need to investigate whether collusion has been taking place between the regulators and the polluters at the expense of the public. A colleague of mine was told that his small company would be bankrupted if he did not cease immediately opposing the power company's plans. British Telecom told me that with my "sensitive asthma research" I must expect the company to be tapping my telephone. Bitor, the Orimulsion supplier, is prepared to issue writs to prevent publication.

The Mayor of Dalhousie's Letter

The Mayor of Dalhousie, Canada, runs a consultancy introducing new business to his town. Apparently he introduced Bitor's Orimulsion to their oil/coal power station of 315 MW. After initial major problems of air pollution, the scrubbers were rebuilt and he has been happy since, especially as emissions blow out to sea. Recently an application for an extension was refused by the Canadian authorities on the grounds of excessive anticipated pollution. Meanwhile Pembroke power station's application is for 2,000 MW with emissions blowing onto land and people.

The Mayor wrote to the Florida authorities in April 1996 promoting Orimulsion, and Bitor copied this letter to key people in Pembrokeshire some months later. Orimulsion was refused in Florida and has not been allowed to be burned anywhere in the U.S.A. With tight controls those in Florida did not want a huge rise in NOx (polluting gases) as would ensue in Pembrokeshire with consequent increases in toxic algae, and an experimentation on the population. The PCHC asked me to investigate the Mayor's letter. Following a long telephone conversation with him and subsequent fax I wrote a report to the PCHC on 23rd October 1996, which by 1st November 1996 had been faxed around the country by Lowe Bell Good Relations (PR company acting for National Power and Bitor). It transpires that they contacted the Mayor who was prompted to

write a letter to the Pembrokeshire County Council Chairman (dated 7th November 1996) to limit the damage of my PCHC report. Lowe Bell Good Relations then faxed the Mayor's letter between 13th and 20th November 1996 with press releases, but I was leaked copies.

In fact all the Orimulsion-fired power stations in the world put together add up to less than half the Pembroke application. Furthermore, National Power are building one in Spain by the gasification process which is much safer than their Pembroke proposal. The UK desperately needs a gasification plant to cope safely with oil-based waste, some toxic coking plant waste, etc. HMIP agreed in 1993 that this was the best way forward but nothing has been done though Mr. Budge has proposed a coal fired gasification power station in Yorkshire (Feb. 97.)

PART TWO: THE NATIONAL EVIDENCE

most of the available evidence does not support a causative role for outdoor air pollution in the initiation of asthma...
Department of Health 19th October 1995

SUMMARY

Background

Studies into the health affects of UK air pollution have been few and almost entirely confined to the issue of traffic pollution, despite extensive documentation overseas. Evidence published confirms pollution exacerbating existing asthma, but investigations into consequences of UK industrial practices since 1992 of opencasting coal; waste sites; incinerating toxic waste and secondary liquid fuels in cement works, incinerators and power stations reveal health damage crying out for detailed study and action.

Method & Results

As existing GP computers mostly are unable to print out details of disease linked with ages and postcodes, I ascertained the proportion of primary schoolchildren taking inhalers to school for asthma over large areas in seven counties, mapping out the results with prevailing wind directions and fixed point pollution sources and various controls elsewhere, including results of manual searches of GP records.

I discovered, in broad terms, a trebling of the incidence of children taking inhalers to school for asthma, both locally due to temperature inversions and downwind of point sources burning toxic fuels without adequate pollution abatement with the incidence rising from zero to 10 percent in at least two schools, and a continuing steep rise year after year in the case of the worst sources. Local upwind areas remained at very low levels.

I discovered that many adults as well as primary schoolchildren, even those without a previous or family history, developed asthma for the first time only following a switch in fuel at the point sources. Results were identical in all areas surveyed which included over 23,000 children, which also revealed similar cumulative rises in prevalence of asthma in children within

three miles of opencast coal mines, where findings of PM1 size coal particulates within and outside buildings confirm exposure.

General Conclusions

The use of toxic waste/waste oils and solvent mixes in non-dedicated plants with inadequate pollution abatement, and also opencast coal mining, were found to cause a sharp rise in the prevalence of asthma in primary schoolchildren and others, with the rise including new cases of asthma associated with the pollution.

It is postulated that particulates of certain heavy metals such as vanadium, nickel, cadmium and arsenic and certain organic compounds are the causative mechanism, especially at times of concurrent high zone levels (associated with increased NOx and sunshine).

It is recommended that the method be used by community or public health officials to ascertain the current state of affairs, allowing investigations at a particular school which has exceptionally high levels (peak flow readings, history and tests). Local weather conditions and the temperature and nature of emissions determine outfall and consequent health damage. Cancer clusters have been discovered around toxic waste sites, confirming American findings.

RESEARCH DETAILS

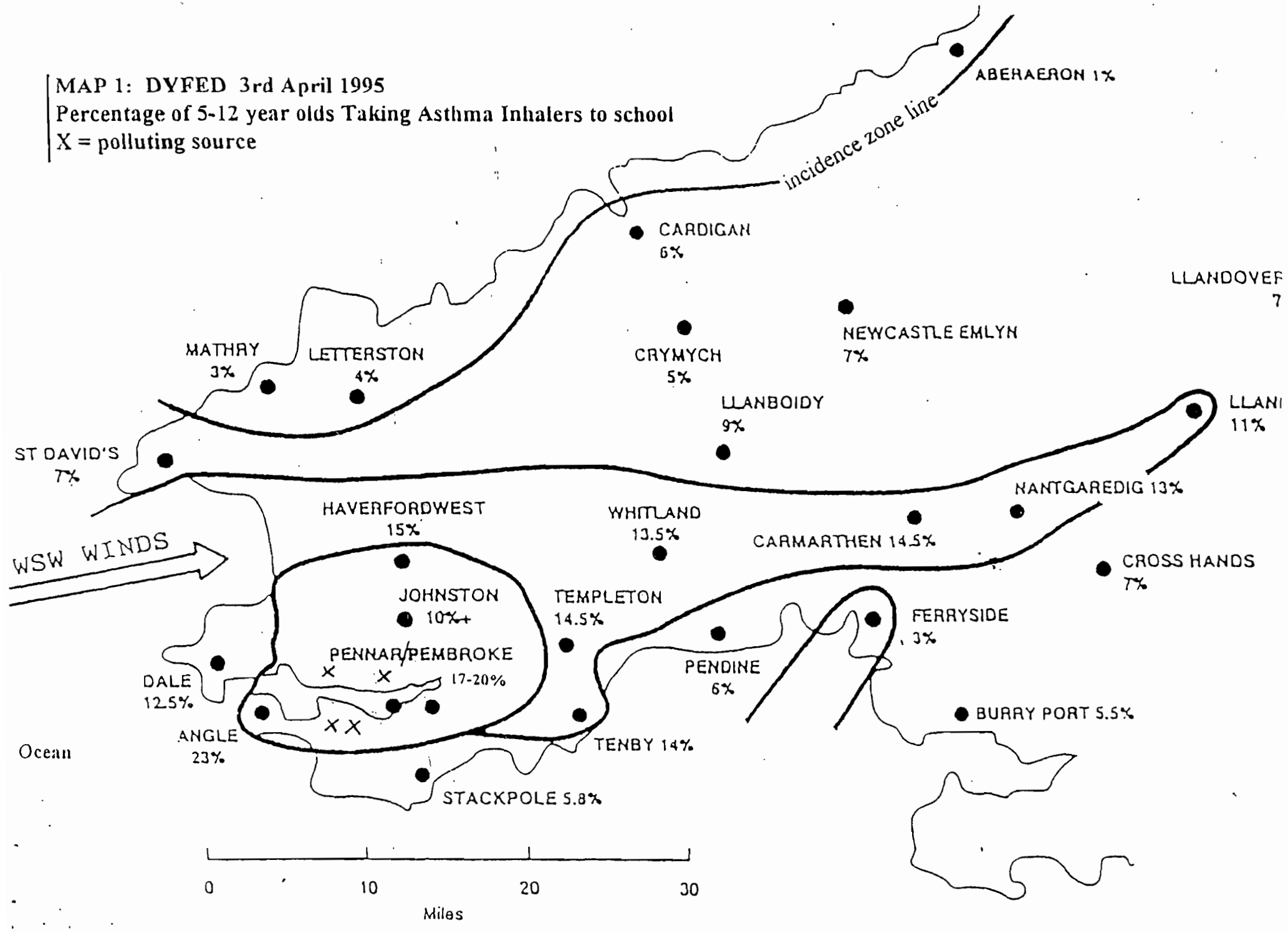
Dyfed (Map 1)

In January to March 1995, I researched the incidence of asthma in 5 to 12 year old primary schoolchildren in Dyfed, Wales, obtaining carefully counted statistics of incidence of inhalers taken to school for asthma and mapped-out the results (**Map 1**). I telephoned head teachers repeatedly and in three towns, due to lack of co-operation, I was able to obtain figures from GP surgeries which had done manual searches of their records. Subsequent surveys were also carried out by telephone, sometimes backed up with letters, which allowed discussions about local problems and provided further information. With my system the response rate averaged around 80%.

Around the Pembroke greater area, with temperature inversions estimated at over 60 days annually, the prevalence of children taking inhalers to their primary schools averages 18%. Downwind with prevailing WSW winds the prevalence is some 14% as far as 45 miles. The adjacent area north and south of this long valley has a prevalence of about 6% whilst on the unaffected coastline prevalence was only about 2%.

Similar results were obtained by Dr J Irving Spur of Weardale, County Durham, where upwind of the Eastgate cement works, only 1% of primary schoolchildren had asthma, whilst two miles downwind 7.1% had asthma, at four miles 12.5% had asthma and at eight miles downwind 9.1% had asthma. He analysed his surgery records. These effects would be expected from plume dispersion. Soil levels of heavy metals downwind from the cement works were double upwind levels.

In the Dyfed survey the lowest rate was 1% at Aberaeron and the highest at Angle of 22.7%, both on the seacoast. Cumulative effects of the bitumen waste burning power station along with asthma since 1992 beginning in babies resulted in a steep rise of prevalence of chronic asthma in infant school children by January 1997 typified by Whitland where 37.9% of four and five year olds now are asthmatic and the overall prevalence in the school of severe asthma is now


MAP 1: DYFED 3rd April 1995
Percentage of 5-12 year olds Taking Asthma Inhalers to school
X = polluting source
incidence zone line
ABERAERON 1%
CARDIGAN
6%
LLANDOVER
7
NEWCASTLE EMLYN
7%
CRYMYCH
5%
MATHRY
3%
LETTERSTON
4%
LLANBOIDY
9%
LLANI
11%
ST DAVID'S
7%
NANTGAREDIG 13%
HAVERFORDWEST
15%
WHITLAND
13.5%
CARMARTHEN 14.5%
CROSS HANDS
7%
WSW WINDS
JOHNSTON
10%+
TEMPLETON
14.5%
FERRYSIDE
3%
PENNAR/PEMBROKE
17-20%
PENDINE
6%
DALE
12.5%
BURRY PORT 5.5%
ANGLE
23%
TENBY 14%
Ocean
STACKPOLE 5.8%
0
10
20
30
Miles

20.8% compared with 13.3% two years previously. Many asthmatics noticed an improvement in their condition during the months when the power station was closed. (Similarly in Derbyshire 27 to 34 percent of nine year olds were using inhalers where plumes or open cast dust appeared to ground.)

Analysis of 1,252 asthma hospital admissions (coded ICD 493.9) for 1993/94 at the Pembrokeshire NHS Trust Withybush Hospital (Haverfordwest), analysed into rates per 1000 population and into specific areas, confirmed my survey of inhaler usage at schools. On this basis hospital admission rates per 1000 were found as follows:

- Pembroke/Pembroke Dock 17.65
- Milford Haven/Neyland 14.49
- Haverfordwest 14.05
- Southeast Pembrokeshire 10.42
- North Pembrokeshire 6.74.

These figures are many times the national average, typified by Worcester Health Authority where rates per thousand annually between 1989 and 1993 averaged 1.07.

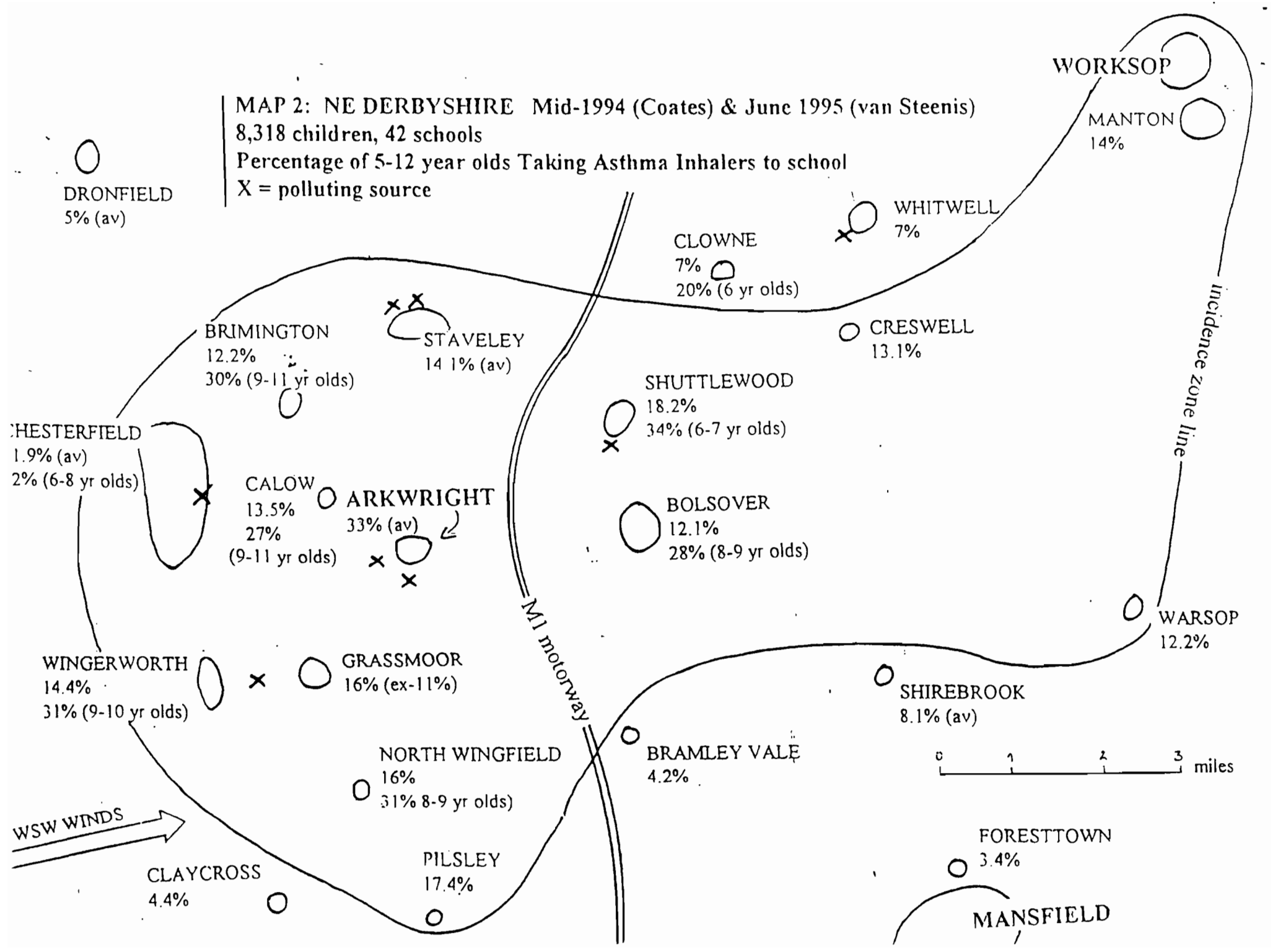
The Pembrokeshire high zone of primary school inhaler use is overall the worst in the UK yet found (apart from the two schools mentioned earlier). The Director of Public Health in March 1995 ordered me to cease contacting schools in Dyfed and this prevented the survey from covering a higher proportion of schools. Considerable opposition has been encountered in my research due to my "opening a can of worms" (BBC TV comment).

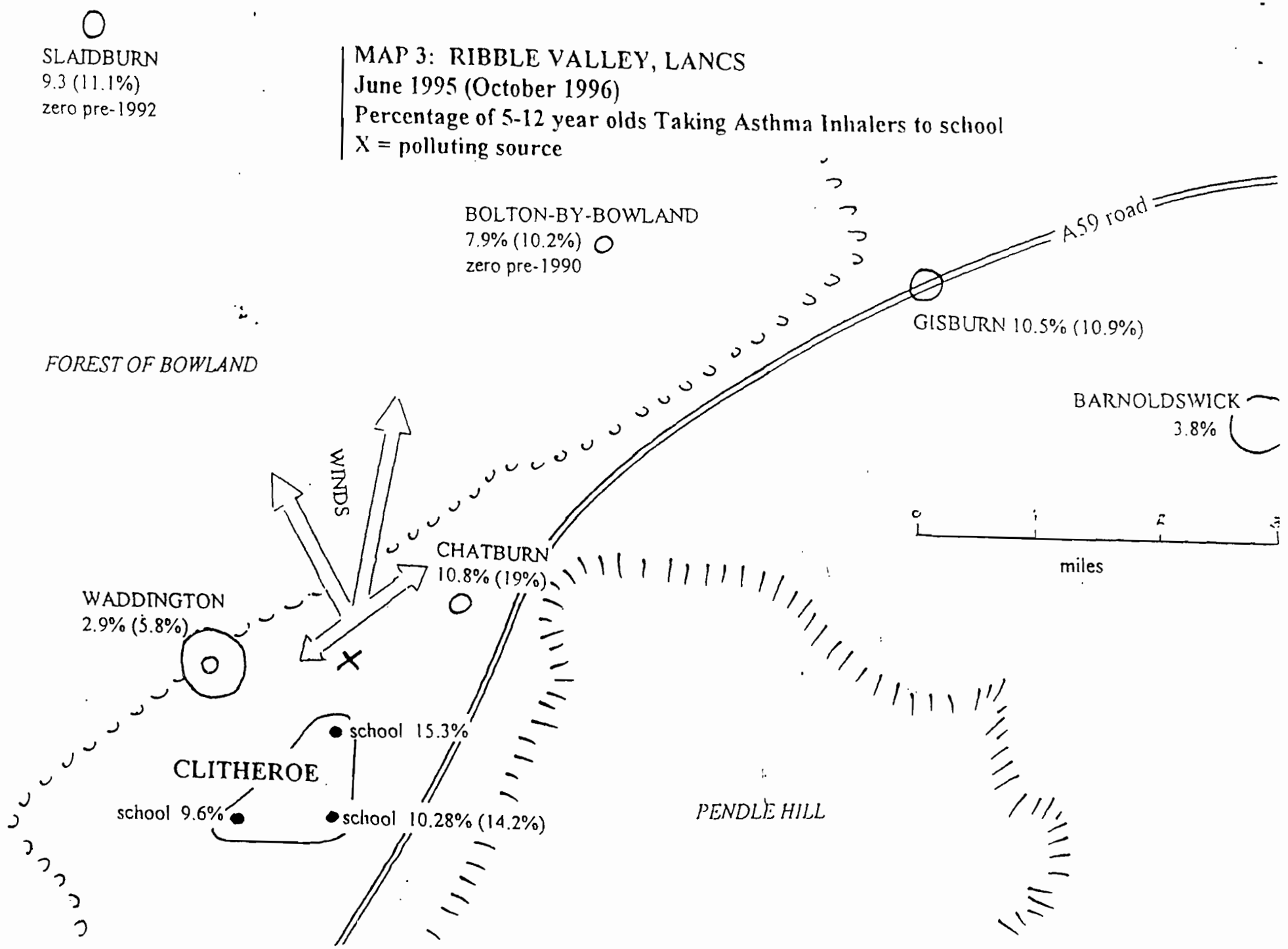
An investigation at three local schools near Gwaun-cae-gurwen affected by open cast coal mining, by the Welsh Office in 1993, revealed 12 percent of primary school pupils to have been taking inhalers to school for asthma, a further eight percent who had asthma symptoms undiagnosed. But when all the pupils were tested with peak low meters before and after exercise the actual numbers diagnosed asthmatic amounted to 33 percent with most living one mile from the centre of the open cast. At Glynneath Dr Temple noted a cumulative rise in weekly new episodes of asthma in his practice following commencement of a new open cast mine, the rise being from 4.4 to 7.9 episodes (p less than 0.001) (13).

Northeast Derbyshire (Map 2)

Another study in Northeast Derbyshire in mid-1994 by Ken Coates MEP, with my own extra data added in June 1995, on a total of 8,318 children from 42 primary schools, revealed inhaler usage for asthma local and downwind from polluting chimneys and open cast mining at between 12 and 18 percent, dropping to seven percent under one mile from the high band, then to a more normal 4.5 percent clear of the pollution in North Mansfield, Clay Cross and the southern edge of Sheffield (**Map 2**).

At Arkwright primary school inhaler incidence was 33 percent near the centre of a huge open cast coal mine with brand new housing and school affected by the surface soil and coal dust churned up by diesel exhaust emitting machinery. The area affected by the coal mining particulates had a radius of some 3 miles (see **map 2**). At Grassmoor primary school just over two miles from Arkwright open cast, the inhaler usage rose from 11 percent after the open cast opened to 16 percent during the second year and 21 percent by October 1996, confirming the cumulative damage caused by particulate inhalation, with usage of inhalers varying with the daily weather.


MAP 2: NE DERBYSHIRE Mid-1994 (Coates) & June 1995 (van Steenis)
8,318 children, 42 schools
Percentage of 5-12 year olds Taking Asthma Inhalers to school
X = polluting source
WORKSOP
MANTON
14%
DRONFIELD
5% (av)
WHITWELL
7%
CLOWNE
7%
20% (6 yr olds)
BRIMINGTON
12.2%
30% (9-11 yr olds)
STAVELEY
14 1% (av)
CRESWELL
13.1%
SHUTTLEWOOD
18.2%
34% (6-7 yr olds)
CHESTERFIELD
1.9% (av)
2% (6-8 yr olds)
CALOW
13.5%
27%
(9-11 yr olds)
ARKWRIGHT
33% (av)
BOLSOVER
12.1%
28% (8-9 yr olds)
incidence zone line
M1 motorway
WARSOP
12.2%
WINGERWORTH
14.4%
31% (9-10 yr olds)
GRASSMOOR
16% (ex-11%)
SHIREBROOK
8.1% (av)
NORTH WINGFIELD
16%
31% 8-9 yr olds)
BRAMLEY VALE
4.2%
0 1 2 3 miles
WSW WINDS
FORESTTOWN
3.4%
CLAYCROSS
4.4%
PILSLEY
17.4%
MANSFIELD


SLAIDBURN
9.3 (11.1%)
zero pre-1992
MAP 3: RIBBLE VALLEY, LANCS
June 1995 (October 1996)
Percentage of 5-12 year olds Taking Asthma Inhalers to school
X = polluting source
BOLTON-BY-BOWLAND
7.9% (10.2%)
zero pre-1990
A59 road
GISBURN 10.5% (10.9%)
FOREST OF BOWLAND
BARNOLDSWICK
3.8%
WINDS
CHATBURN
10.8% (19%)
WADDINGTON
2.9% (5.8%)
miles
school 15.3%
CLITHEROE
school 9.6%
school 10.28% (14.2%)
PENDLE HILL

Microscopy of dust samples within and outside buildings at Calow, Grassmoor and Bolsover revealed copious PM1 size coal particulates which would inevitably be inhaled by those exposed For example at Calow, where 27 percent of 9 to 11 year olds took inhalers to school, PM1 coal was even discovered inside the local hospital building and at the bus shelter outside. With the prevailing wind, amounts of the PM1 coal particulates were slightly higher at Bolsover where 28 percent of 8 and 9 year olds took inhalers to school. Council SO_2 monitoring revealed that the highest levels in the county were at Staveley near a factory, which strongly suggests that the asthmatic problem is due to the particulates.

Preliminary results from some 125 schools surveyed in Greenwich/Bexley by the CHC in early 1996 reveal an ambient rate of 11.9 percent children taking inhalers to school with just one school at 30 percent at one at 20 percent in an area of heavy traffic and some 120 point sources of pollution. The latter two schools are being investigated as we go to press.

My surveys in primary schools in East Kent in 1995 showed an ambient rural rate of inhaler usage around six percent but at one school near Ramsgate downwind of the Orimulsion fired Richborough Power Station (closed March 1996) the incidence of children with inhalers rose from three percent before the switch to Orimulsion to 12 percent in the following three years. At Ellesmere Port near the Ince Power Station fired by Orimulsion, there have been so many complaints of asthma, a full survey of every 10th house is being undertaken by Liverpool University. Yet, Ellesmere Port receives downfall from Ince Power Station on about two days per week and the proportion of primary school pupils taking inhalers to school was found to be 13 percent. At Runcorn downwind of Ince, with downfall three or four days per week the proportion of those on inhalers was 17 percent. At Tranmere inhalers dispensed by the chemist trebled following the switch to Orimulsion at Ince. Of extreme concern was the admission by the Environment Agency dealing with Ince that they did not have the current Orimulsion data sheet which specifically warns that inhalation of the vanadium pentoxide and nickel compounds causes asthma, skin and eye irritation, respiratory tract cancers and other toxic reactions. Subsequently Powergen announced that Ince would be closed early 1997.

Emissions from coal fired plants have larger size particulates which are easier to trap in pollution abatement systems on flues and chimneys than smaller size particulates from secondary liquid fuels fired plants. Coal fired plants have flyash to absorb heavy metals and organics while oil based products, including petcoke, do not have adequate flyash, thus are a bigger hazard.

Ribble Valley, Lancashire (Map 3)

My study in June 1995 in the Ribble Valley, Lancashire, revealed a sharp rise in incidence of inhalers taken to primary schools in Clitheroe (with temperature inversions), and northeastwards into the Forest of Bowland and as far as Gisburn (**Map 3**). From an ambient rate of zero to five percent, we noted a higher band of 7.9 to 15.3 percent in relation to the cement works. This cement works began burning waste SLF mixes in 1992. The upwind village of Waddington had a rate of 2.9 percent usage, whilst near the chimneys, the Brookside school reveals a rate of 15.3 percent usage of inhalers, with a peak of 22 percent of 8 and 9 year olds. A survey of SO_2 levels by HMIP in March 1995 showed that no emissions from the cement works, near Clitheroe, were reaching Waddington, the Forest of Bowland was receiving emissions two or three days weekly, whereas Clitheroe was suffering daily. A milk dioxin level survey by the Ministry of Food, Agriculture and Fisheries (MAFF) revealed low levels at Waddington but levels four times higher at Clitheroe.

An analysis of prescribing for asthma by a large Clitheroe practice showed a steep rise following the switch of fuel at the cement works, including a 50 percent rise in steroid inhalers, 25 percent rise in oral steroids with 12 percent rise of total prescriptions. This again correlates with a rise in heavy metal emissions from the cement works including an 800 percent rise in nickel emissions. In August 1995 near Brookside mobile monitoring of PM10 particles revealed a peak of 490ugm/m3 compared with a peak of 75ugm/m3 at Waddington school. Unusually there had been easterly winds. Even NPL staff suffered health damage.

Lord Earl Ferrers, Environment Minister, has written that plume grounding at Clitheroe is not in dispute. Temperature inversions are more frequent at Clitheroe because it lies in a valley, averaging 16 days a month. In 1995 conditions were so dangerous that the Environment Agency (ex HMIP) declined to publish the results of the cement works chimney emissions onto the public register. The Public Health Department discovered that deaths in people under 75 years of age in four Clitheroe wards had risen to 40 percent above the national average, and a repeat primary school asthma inhaler usage survey around 1st October 1996 showed a steep rise in the local schools to almost double the 1995 figures, for example Chatburn school had risen from 10.8 percent in June 1995 to 19.0 percent October 1996, St James Clitheroe from 10.2 percent to 14.2 percent and Bolton by Bowland (zero until 1990) from 7.9 percent to 10.2 percent. By comparison Great Harwood school (industrialised Accrington, outside Ribble Valley) is 9.3 percent, and Barnoldswick, protected from the cement works by Pendle Hill, has a rate of only 3.8 percent. Even Waddington was affected by easterly winds and the rate doubled from 2.9 to 5.8 percent. This shows, I believe, that the effects of SLF burning plant emissions are cumulative, even from sub-lethal prolonged exposure. For example their lead, industrial solvent and halogenated hydrocarbon content are cardiotoxic quite apart from other health damage (14).

Cancers

Current investigations in the vicinity of coking plants in the UK at Wingerworth (Chesterfield), Abercwmboi (Aberdare) and Coed Ely are revealing not only an excess of cancer of the lung and other cancer deaths among the workers, but also clusters of breast and other relevant cancers among the population in the immediate vicinity of the waste sites, as would be expected following American studies (11). The scale of breast cancer incidence uncovered is particularly alarming, but should have been anticipated following warnings by Professor Epstein of Chicago who claimed in 1994 that as many as 70% of breast cancers were of environmental causes and hence preventable. At Wingerworth 12 women were discovered with breast cancer in 45 houses in 10 years, half of whom have already died. Nearby in Tupton another 10 have died of cancer. At Coed Ely out of 82 houses in the past eight years 24 people have died of cancers, comprising six gastro-intestinal tract, nine breast and nine lung, plus those not yet surveyed. This is more than 12 times the American incidence (11).

Ozone

Ozone has a further depressive effect on breathing ability (up to 25 percent) by setting up a lung cell inflammation for 24 hours which then would exacerbate the action of particulates such as vanadium, nickel, cadmium, as well as pollen, moulds, house dust mite and airborne viruses. A study among cyclists suggested antioxidant vitamin daily supplements, decrease airway hyperactivity (as does indomethacin) after exposure to ozone, but not the influx of white cells, which are reduced by prophylactic corticosteroid inhalers (5, pp 34-35). Several months exposure

to moderate concentrations of ozone leads to fibrotic and other changes in the lung lining (3, p 4). An editorial with associated papers in the 'British Medical Journal' (15) showed a logarithmic increase in asthma with six hour ozone levels above 80ug/m3 with a concomitant increase in daily mortality above 100/m3, especially when relevant particulate levels were also elevated. In Dyfed when ozone was monitored mid-1995 weekly averages in the high zone of **Map 1** were as high as 140ug/m3 near Haverfordwest. Many locals and others moving into this zone developed asthma for the first time in 1992/93, and this might be explained by the toxic residual fuel being burned by the power station from that time onwards. Local councils deliberately refused to monitor particulates in Dyfed until after the power station closed.

General Conclusion

While most research in the UK has investigated the effects of traffic and diesel emissions, my work indicates that industrial pollution is actually causing asthma in previously unaffected children and adults, explaining much of the surge in asthma incidence over recent years. Readers must note that the incidence of diagnosed asthma in the primary schoolchildren surveyed is about 1.3 times the school inhaler rate, as I have done controlled checks in several areas.

PART THREE: IS ANYONE REGULATING?

These issues are too important to ignore ...
As GPs, our duty is to highlight these potential health risks and
we strongly believe that a Public Inquiry is vital to ensure a balanced debate
We ... question the validity of the Dyfed Health Authority
1995 report on local disease patterns.
Letter from 41 Pembrokeshire doctors to Welsh Secretary, 23rd July 1996

LOCAL COUNCILS: PLANNING & ENVIRONMENTAL HEALTH

Preseli Pembrokeshire District Council (PPDC) Planning Department passed the power station proposal in January 1995 as quickly as they could. As they were not statutory consultees their decision was not binding on South Pembrokeshire District Council in whose area the application was sited. However, PPDC did cover a large area and population who would be directly affected by the proposal, and when the two councils amalgamated in April 1996 the early decision was used as an excuse by the new County Council to avoid any discussions whatsoever concerning the safety of the proposal.

When I saw the Environmental Health Department of PPDC concerning the very high asthma zone downwind of the power station in 1995, the Director said that the asthma was caused by gas cookers. I pointed out that gas was not available in many streets where asthma had arisen from 1992 onwards in the high zone. Other comments followed, all of which had been disproved by public health studies elsewhere. PPDC adamantly refused to monitor particulate

emissions in 1995/6. Furthermore Mr Watts of that Environmental Health Department had written to the Health Authority on 17th October 1994 asking whether the perceived increase in asthma incidence locally was not due to the pollution Yet we have the response of the director in July and September 1995 deliberately trying to rubbish my report with unfortunate comments and deliberate misinformation taken from the March 1995 press release. This director took early retirement in March 1996. It was very interesting to note that Milford Haven SO_2 levels measured by his council were the fourth highest in the U.K. in 1994, and ozone levels when they dared to measure them in summer 1995 were in excess of critical health damage levels at all sites in the high asthma zone of my map (but below the critical level in the intermediate zone). SPDC Environmental Health Department also refused to monitor particulates in 1995/6.

The Director, Mr Seal, without reference to his chairman, issued the misleading press release on 23rd March 1995 in the names of himself, his press officer and Dr Queenborough, following a meeting in his office with G Davies, Drs Queenborough and Delahunty and me and Mr G Sinclair of CPRW. The press release made unreferenced, unsubstantiated and derogatory allegations about my findings. Mr Davies pressed the Health Authority for an alternative report to mine. That HA report was produced in the name of Dr Delahunty in May 1995 but was published by the manager of the power station before councillors were allowed to see it (at a special council planning meeting at which the HMIP officer was present). Councillors were very angry they had not been given opportunity to read the document and formulate questions. At a subsequent report for the power station liaison committee it was clear that all particulate emissions since its inception had been estimates. Furthermore the compilers of the council report assume that the vanadium and nickel content of the fuel being burned remained constant since 1973 when it was quite obvious that this is not the case. Even the fuel oil authorization sheet issued by HMIP dated 1st October 1970 allowed for the vanadium content in one batch to be 30 times higher than in another batch, without even contemplating further increments as the fuel became residual fuel oil since about early 1992.

Mr Seal in 1996 appointed the power station's PR secretary to be the Agenda 21 Coordinator for the new county council. At the first main Agenda 21 meeting discussions were held about future projects and areas of involvement, and the new Coordinator wrote up the minutes and without having these approved as a true and accurate record gave them to the newspapers. Non-council members were not invited to the second meeting, but found out unofficially.

When the new Pembrokeshire County Council was formed the Department of Trade & Industry (DTI) instructed them that they were the new relevant planning authority for the Section 36 (Electricity Act) application. The planning committee were determined to pass the power station proposal without mentioning any health matters or ensuring shipping safety or removing from the final vote all those who had a pecuniary interest in the application. The DTI, Countryside Council for Wales, and the Welsh Office put a holding order on the council at their first efforts to bulldoze an approval through. But on 12th December 1996, Councillor Hall (who had previously organised a public meeting to promote the power company's application to which only those who were in favour were invited) proposed a motion that the DTI's advice and the previous holding order be ignored and that the proposal be passed forthwith. The motion was passed. The formal letter of the 41 practising GPs of Pembrokeshire of 23rd July 1996 which had been sent to the council chairman and council members, was totally ignored and health dangers of the Orimulsion proposal were not even mentioned at the council meeting. When the DTI complained, a special

meeting of councillors was held to discuss the holding order later on 18th December 1996.

In accordance with new legislation four particulate PM10 monitors were installed by the county council in mid-1996. As some 85% of emissions would be below PM1 this exercise might be described as a waste of taxpayers' money as at least PM2.5 heads should have been used and preferably PM0.5 heads. Furthermore, the siting of these monitors avoided the peak pollution areas such as Neyland, Johnston, Milford Haven and Pennar. Despite challenge they refused to alter them.

On 7th January 1997 reporters from a national Sunday newspaper who were researching asthma were refused access to any school in the county by Pembrokeshire County Council Education Department refused. This is hardly surprising following my experiences and previous prohibitions.

Officers of Dyfed County Council (prior to Pembrokeshire CC) in mid-1995 deliberately omitted to mention "particulates" in their planning report for the Pembroke power station, even though I had warned them of health risks from particulates. Similarly in 1996 when the Welsh Development Agency (WDA) proposed Tesco's meat plant be sited 700 yards north of the Trecatty toxic hazardous waste site, the environment report and planning reports referred to Trecatty (one of Europe's largest) as "disused works" and "landfill". This was despite a 6,000 signature petition objecting to the siting in such close proximity to the waste being dumped (plus the problems of the road planned to be widened).

HEALTH AND SAFETY EXECUTIVE

The Health & Safety Executive was set up to implement the Health and Safety at Work Act 1974 and related functions, which involve monitoring of the responsibilities of employers to ensure the safety of their staff. It puts a duty on employers not to harm the public and specifically not to emit poisonous substances into the air (see box). Where hazardous substances are used in an industrial plant factory data sheets are obligatory under the Control of Substances Hazardous to Health (COSHH) regulations.

HEALTH & SAFETY AT WORK ACT 1974

Section 3(1) of the Act says, 'It shall be the duty of every employer to conduct his undertaking in such a way as to ensure, so far as is reasonably practicable, that persons not in his employment who may be affected thereby are not thereby exposed to risks to their health or safety.' Section 3(3) requires that such employers give information about health effects to those who may be affected. Section 5(1) of the Act says, 'It shall be the duty of the person having control of any premises ... to use the best practicable means for preventing the emission into the atmosphere from the premises of noxious or offensive substances and for rendering harmless and inoffensive such substances as may be so emitted.'

Mr Keith Harrison discovered that the regulations are being flouted in that National Power are and have been burning bitumen bottoms waste without a data sheet at Pembroke Power Station. Castle Cement also declined to produce a data sheet at times when the public were being made ill

by their emissions at Clitheroe when they were using up to 90% SLF (oil and solvent industrial waste) as fuel. It remains to be established why the HSE are so reluctant to prosecute. At Clitheroe last year when a spill of a toxic fuel occurred and staff were affected, HSE was contacted, but a prosecution was handed over to the Environment Agency, when it was really an HSE matter. The absurd situation arose that court adjournments resulted from vital submissions not having been exchanged by the EA. Then one of the company managers boasted that the company would not be fined much, if at all. Eventually a £4,000 fine was imposed

Regarding the coking industry the HSE has not itself carried out any studies into cancer among workers but they claimed that they regularly monitored research by others. These include reports published in 1983 and 1987 leading to a 1993 review which confirmed increased risks of lung and genito-urinary and kidney cancer mortality in workers dealing with coke ovens (Circular from HSE Director General, 8th March 1996). What alarms me is that the population exposed around the plants have not been considered worthy of a study anywhere (despite Section 5 of the Act, see Box).

In 1984 the HSE had no comment to make concerning an application for a waste disposal licence at Abercwmboj at an area called the White Horse Stocking Site. The previous waste tip represented a pond into which all the toxic rubbish was dumped until 1987, that is, 13 years after the Control of Pollution Act 1974. No licence has ever existed for that tip. There were clear dangers of pollution of the River Cynon from the 1984 application but it was passed. In 1991 the phurnacite works were demolished and the demolition waste was dumped on the White Horse (1984) site despite no planning or licence existing for that demolition waste. What was the HSE doing between 1974 and 1991?

Proposed reclamation has now in consequence become a nightmare scenario with the Welsh Development Agency involved in Wales, and English Partnerships in England. The HSE does not appear fully to comprehend the dangers not only to workers but to the surrounding public affected by bulldozing and transporting hazardous waste in open vehicles. Sites to which the waste is moved are being protected only by plastic sheeting and clay, which is almost certain to result in leaching of the contaminated products into the local water, both surface and underground, hence putting some present and future water supplies at risk. For example at Coed Ely in 1994 some residents developed asthma for the first time in their lives due to the particulate matter thrown in the air by partial clearance of the site. No doubt there will be a cancer risk in years to come.

The HSE is also unwilling to prosecute National Power in spite of massive health damage probably having resulted from its burning of bitumen bottoms without any pollution abatement equipment, and trying to pass the buck to the Environment Agency. When data sheets on North Sea crude oil were not used by local councils and the 'Sea Empress' incident team (SEECC) in protecting workers following the 73,000 ton oil spill from the tanker 'Sea Empress' again the HSE refused to prosecute the councils. Yet some workers became ill from lack of stipulated protection, and the Pembrokeshire County Council refused follow-up medical examinations on the workers and refused to supply names and addresses of the workers for medical surveillance.

The question must be asked why the HSE declines to prosecute following breaches of the Act? Following further correspondence between the HSE and Mr Keith Harrison and myself the HSE wrote on 20th December 1996 to say that Sections 1(1)d and Section 5 of the 1974 Health and Safety Act (covering industrial emissions) were repealed in parliament with effect from 16th December 1996. Both Mr Harrison and I had been informed by the HSE helpline of the

contents of Section 5 within days of 16th December 1996 (see box below).

ACT'S SECTIONS TRANSFERRED

Freedom to Care is inquiring into this repeal of sections 1(1)d and 5 of the Health & Safety at Work Act. So far it has been told by the HSE that the sections have been transferred to the Environmental Protection Act 1990 (EPA), that the transfer is determined by committee and not by any parliamentary discussion and that statutory instrument 3056 (1996) was employed. Freedom to Care is curious about the effect of the transfer and has written to Dr Douglas Bryce at the Department of the Environment and Mrs J Willis at the Health & Safety Commission. As a result of our concern the office of Austin Mitchell MP has written to John Gummer, Secretary of State for the Environment, asking for clarification. In particular we want to know if the new sections in the EPA will have the same force, scope and effectiveness as the previous sections in the Health & Safety at Work Act. The timing of the transfer is also interesting.

With legal aid becoming more difficult to obtain and the Environment Agency failing to act effectively the prospects for the affected public are bleak. I have now discovered that Sun Alliance Insurance Company has issued a notice to policy holders of an important change to their policies entitled 'Pollution Exclusion' which means the insurers will no longer [illegible] any claims or expenses caused directly or indirectly by pollution which could or should have been expected, were intentional and not a sudden incident, or were not during any period of insurance. My fear is that the HSE, the Government and insurance companies are well aware of the consequences of current industrial air pollution and are taking preemptive action to deny the public proper channels of protection and recompense.

HMIP (NOW ENVIRONMENT AGENCY)

As a result of the 1976 Royal Commission on Environmental Pollution (Fifth Report), Her Majesty's Inspectorate of Pollution (HMIP) was established in 1987 It was followed by the Environmental Protection Act 1990 which specifically instructs HMIP to curtail or neutralise emissions so that they do not cause any damage to human health, senses or property. The underlying principle for authorising or insisting upon modifications of industrial plant should be the "Best Practicable Environmental Option (BPEO)". In the field of air pollution control within the general context of integrated pollution control (IPC) HMIP was the enforcement agency for about 2,000 works with the greatest pollution potential. For those polluting the air, as a concession, the Government allowed a dilution of standards to that of "Best Available Techniques Not Entailing Excessive Cost (BATNEEC)". Publication of the WHO Report in October 1995 led to a Government response in recognition of the need for tighter limits on certain items contributing to air pollution such as a limit of 50ugm/m3 of PM10 particulates at ground level.

By mid-1994, following detailed American studies and the advice of the White Report (an independent report to HMIP), the leadership of HMIP agreed that the safe and best way forward for dealing with industrial oil waste including residual fuel oil and Orimulsion was by gasification. The oil is first turned to gas, which means pollutants can be much more effectively controlled. Yet today no such plant exists or is proposed in the UK. The Spanish Government is building such

plant. Despite this knowledge HMIP Cardiff in late 1994 allowed National Power to go ahead with an application to convert their Pembroke power station to Orimulsion and oil refinery waste residues, using inadequate electrostatic plates and flue gas desulphurization (FGD). By July 1995 HMIP guidance to IPC (Integrated Pollution Control) was that the addition of ceramic or fabric filters would represent current best technology standard and fabric filters were to be considered for all scales of operation. However, the Cardiff Inspector had not told National Power this fact.

It was further clear that the extremely fine particulates from Orimulsion penetrate through FGD systems and would accumulate in humans by inhalation and the food chain. In the public HMIP record I found a comment that the proposed air levels of nickel and chromium anticipated by the National Power application would be "intolerable". The HMIP officer insisted he did not know that asthma could be caused by inhalation of nickel particulates even though it is described in the medical literature (for example, on page 693 of Casarett and Doull's 'Toxicology' 5th Edition. The same textbook also describes its role in producing lung cancer.) Yet the Environment Agency still persist in pressing on with the application process.

National Power produced an environmental report about October 1994 without local weather maps, without local heavy metal air or soil surveys and without ancillary jetty arrangements. The HMIP officer gave presentations sometimes with National Power or in their company at various venues between October 1994 and May 1996. Despite complaints from 41 local GPs and myself, and the evidence of a public health consultant and university senior lecturer that the Health Authority 'Delahunty Report' of May 1995 was flawed and full of misinformation and alleged scientific medical fraud, the HMIP (now Environment Agency) Officer has written that he is determined to stick to that report. The officer thus dismisses complaints and comments by the doctors as anecdotal instead of heeding these 44 doctors and calling for a public enquiry or, even better, dismissing the National Power application as not being up to the required standard for protecting the health of the public according to the 1990 Act.

When Keith Harrison asked the Environment Agency officer covering Ince power station about their Orimulsion data sheets they had an obsolete version and not the December 1993 one, which stipulates that inhalation of the products of combustion would be expected to cause asthma and cancers (as with heavy fuel oil, perhaps to a lesser extent). A few weeks later Powergen announced that they were closing Ince in early 1997. Why did the HMIP officers in Cardiff not pass on the Orimulsion data sheets produced by Bitor to the Health Authority and relevant councils and order the health warnings to be printed in the environmental assessment? (One notes health warnings on cigarette packets!) It was only due to persistence by Mr Keith Harrison that he was able to prise out the data sheet from HMIP.

What is the Power Station Burning?

Although HMIP allege they knew the ingredients of the product being burnt at Pembroke Power Station, they allowed huge variations from batch to batch, did not insist on a data sheet for HSE laws and when challenged by me repeatedly refused to sample the contents of the fuel tank at the power station. An HMIP Officer even told me there was no fuel tank because it was piped in direct from Texaco. When the power station admitted their tanks were nearly empty when containing 10,000 tons the falsehood was blown wide open. The power station manager admitted at a public meeting that he was also receiving ship loads of fuel from elsewhere. Mr Harrison investigated this and it could well have been from BP who produce bitumen and they would also have waste, including spent oils collected by Swansea Council such as motor vehicle oils (which

apparently are not recycled at Llandarcy refinery but are disposed of [redacted]"). The Environment Agency Officer wrote to Mr Harrison that BP did not produce fuel oil and anyway, it was now owned by Mobil. I telephoned the Llandarcy refinery and was told they still produce every grade of fuel oil and that BP was still producing bitumen.

When the power station resumed operations in November 1996, having been closed since 31st March, I was told backdated authorization was given at a subsequent date. The MP (Mr Nick Ainger) then wrote to Mr Harrison that the power station were burning No 3 fuel oil. When I questioned a refinery about No 3 it was described in a 1950 American textbook as being the next grade down from domestic heating oil and had been obsolete in the UK for some 30 years and had not been for sale in the UK for at least 15 years. From the descriptions given one might have expected the power station to have been burning No 3 or 4 oil in the 70s, No 5 in the 80s and No 6 since 1992 (the worst). Why was it not possible to locate in the Public Register details of the fuel burnt at Pembroke Power Station and detailed emissions coming out of the chimneys? Equally worrying is the lack of information concerning the 1988 secret trials of Orimulsion at the power station.

The Public Relations line

Following the incorporation of HMIP into the Environment Agency on 1st April 1996, an office was opened in Swansea and a free complaints phone number was supplied. A number of complaints about health and smell damage of emissions were fobbed off by officers with comments such as: the dark orange/brown emissions were steam seen in poor light (even though photographed), emissions were due to sprays on the field adjacent to my house (never sprayed), due to coal fires (only three in adjacent 120 houses), "in the mind" (even when another person complained from another part of the town).

Secret Agendas?

HMIP covering Cambridge is also interesting. When the cement company wished to switch to SLF (industrial oil/solvent waste) the local Medical Research Council said that a full survey of the health of the children in the area expected to be polluted by the plant should be undertaken plus 25 independently monitored unannounced readings of details of air pollution over a period of 5 months before any authorisation for permanent use be given. Instead HMIP, and now Environment Agency, has been giving authorisation based on one sheet of readings done by the polluter itself. This has applied to SLF in cement works, tyre burning in cement works and no doubt many other sites and situations. At Thrislington the Agency gave approval for permanent SLF use based on one day's results out of a three year trial.

Why did HMIP Cardiff not call for these health surveys and unannounced independent monitorings local and downwind of Ince and Richborough where small amounts of Orimulsion were being burnt, and the same around Pembroke following the burning of bitumen bottoms residual fuel oil before contemplating allowing stage one for an application by National Power using what they knew was the wrong process? This is a very important question. Two experts told me how decimal points were conveniently moved in self-regulation one-sheet reports to mislead. After two months notice of a site visit it is easy for a company to fiddle by switching fuel tank contents, and invoices can be worded appropriately. Comments concerning new fuels claimed to be less polluting need to be carefully checked out as to what they really mean, because

in some areas a slight reduction in SO_2 emissions has been interpreted as meaning a cleaner fuel while deliberately hiding massive increases in heavy metal, dioxins, and/or toxic organic compounds, which would really cause massive health damage.

Secrecy prevails under the guise of commercial confidentiality concerning the truth of emissions and fuel composition. Why is the Environment Agency not revealing exactly what "special" waste is being dumped next to homes in various areas? At Nantgwyddion Refuse Site (near Tonypandy) the Environment Agency allowed the dumping of industrial toxic filter cakes on a site only licensed for domestic and inert waste. This resulted in vociferous complaints of health damage including sore throats, also noxious odours due to the hydrogen sulphide etc. produced, clearly a breach of the Environment Protection Act by the Environment Agency. The same waste was refused by Trecatty (Merthyr Tydfil) following complaints to the Merthyr Council.

Clitheroe

Following the pleas from sufferers at Clitheroe, I undertook a survey of the incidence of inhalers for asthma at the primary schools in the area and managed to obtain results from every school in the 'Yellow Pages'. The results were incorporated into my report. Following a public meeting the HMIP carried out independent air monitoring as well as chimney emissions from the plant they had authorised to burn up to 90% toxic waste based on one sheet of company's own figures. The results of chimney emissions in August 1995 have still not been published. Results in the school play grounds were appalling with one school having PM10 levels of 490ugm/m3 compared with a new U.K. limit of 50ugm/m3. My report caused consternation and the area HMIP obtained a copy (together with the Dyfed Health Authority rubbishing press release) via the Cardiff HMIP Within days my report was with the managing director of the company and the HMIP wrote that they no longer had it.

Even more interesting was the observation that at a second public meeting I took in Clitheroe none of the 17 executives of the company nor Environment Agency experts were able to present faults with my findings and presentation. Following further complaints from the public the HMIP covering Clitheroe ordered the company to reduce Nickel, Chromium and Lead emissions plus various other orders/variations in early 1996. The company appealed and the Department of the Environment appointed an inspector to adjudicate. A prehearing meeting was arranged for sorting out the details. With colleagues I was allocated one and a half days to give evidence, the Environment Agency one and a half to two days and the company three days (with a QC). Weeks later just before all the evidence had to be with the Inspectorate, the company's solicitor wrote that the hearing was off. This was not because the company were now going to fully comply with the demands, but they appeared to say that the Environment Agency had suddenly, after secret discussions, become quite happy with everything so there was no longer a problem or need for appeal. It was noted that the company were willing to install scrubbers on one of the three kilns only (the one not burning SLF), but even that would not be in operation until December 1998 due to new electricity supply required etc. Why did the Agency not require scrubbers and special filters on the other two kilns burning SLF and why did they allow toxic waste to be burnt before scrubbers were in operation plus filters? As the company were and still are being paid money to burn SLF it should not be such a problem to recoup the expense of the scrubbers and filters. It is now clear that the Agency's interpretation of BATNEEC appears to be "the cheapest systems they dare get away with".

During the prehearing meeting I asked the Environment Agency whether they were

authorising the cement works as a toxic waste burning plant or as a cement works. After discussion their solicitor said "as a toxic waste burning cement works". I further asked why it was then not being brought under the European Directive for Incinerating Toxic Waste mandatory in the UK by 31st December 1996. I further asked why PM10 levels were way above the UK limit in the school play ground. The Agency claimed they had never heard of these two laws, nor had they heard of a third law quoted by my colleague. I wrote to Dr Maynard (Chairman of WHO) of the U.K. Department of Health and asked whether these matters revealed local corruption or were Government orders. It was alleged the letter never arrived, but the Environment Agency weeks later, I understand, did order the company to reduce the toxic waste to under 40% to escape the European Directive I had quoted.

The company had also asked the Agency in mid 1996 to approve their scrubber plans before they went to the borough council, to avoid third party comment on the application. The Agency wrote that it could not but many weeks later complied with the company request. The Agency had demanded action by 31st December 1996 but, as one might expect, nothing had been achieved by that date. One is reminded of the refusal of anybody to date to call a public enquiry into the Orimulsion application at Pembroke.

Serious Breaches of EC Law

Barristers' opinion from County Durham was compiled into a report which revealed serious breaches of EC and UK law by the UK Government, UK agencies such as the Environment Agency and companies, allowing an excess of heavy metal and other toxic pollutants to be released into the air we breathe and pollute water, soil and food chain. Health damage is already resulting with epidemics of asthma and cancers and premature deaths from heart problems. The Environment Agency covering Clitheroe has also allowed the kiln dust containing huge excesses of lead, mercury and arsenic to be mixed with cattle feed and spread on the crops and fields. The disposal of the toxic ash from the power station at Pembroke has not been sorted properly either, some having been sent to Trecatty.

Surveys are now proceeding in the vicinity of various waste sites in England and Wales which confirm American findings in the vicinity of 593 waste sites of increased deaths from cancers of the breast, lung, bowel and bladder. Already clusters of breast cancer patients have been discovered in four affected UK areas. These waste sites represent waste dumps and areas around closed coking and other plants. The Environment Agency should be investigating around every hazardous waste site such as Trecatty and Nantgwyddion where solicitors and I are investigating complaints from those living in the vicinity of health damage including three recent cases of gastroschisis (exposed intestines in newborns).

Even the Agency's Chief Executive, Ed Gallagher, admitted that the matter of the Environment Agency's incompetent regulation of cement kilns burning secondary liquid fuel (SLF), the controversial fuel made from industrial wastes; was a "serious embarrassment to the Agency" ('ENDS Report' December 1996).

PUBLIC HEALTH (HEALTH AUTHORITIES)

With subtle but major changes in fuel content and waste management taking place since 1992 one might understand some public health directors not keeping themselves adequately informed of the

nature and implication of changes and their effects on human health. At Clitheroe by 1996 the Director discovered that the death rate of those under 75 years of age had soared to 40% above the national average in wards affected by plume grounding of the cement works which had switched to burning toxic waste.

In North East Derbyshire, without examining postcode data or journal articles, the public health consultant alleged that the breast cancer cluster in Wingerworth was a coincidence and had nothing to do with pollution. On 'Radio 5 Live' she commented that just a few workers at the coking plant may have died of cancer without ascertaining the facts that some 300 workers had died of cancers of the lung etc. at that plant and a similar one at Abercwmboi, when the carcinogenic dangers of coking plants have been well publicized. The same consultant is quoted in the opencast industry's house magazine as saying "there is no proof that opencasting triggers asthma". The validity of this comment is jeopardized by findings of her MEP (Ken Coates), my journal article and maps (in this issue of **The Whistle**) and even the published findings concerning industrial point sources of pollution by her own department and a letter from her Director.

In Pembrokeshire we find the letter from the consultant to PPDC of 29th November 1994 stating that no health authority "is in a position to say what their local incidence of any disease is." Yet the necessary data for the calculations resides within General Practice. Why then did the Health Authority, without seeing my report, determine in March 1995 to counter my findings with a very widely publicized press release with scurrilous comments without evidence or references, and send the Director to South Pembrokeshire DC who ordered me to cease surveying Dyfed schools? Their motives should be investigated.

My introduction discusses some of the events of 1995. Returning to the letter of the Director to Pembrokeshire GPs of 16th May 1995, he alleged that only SO_2 is a relevant measure of air quality regarding asthma, but the 'British Medical Journal', other journals and textbooks and my findings confirm that ozone and particulates are the relevant parameters. Particulate levels have never been properly measured and when ozone was checked in 1995 levels in the high zone of my map were greatly in excess of danger levels. The Director also commented on asthma prescribing, but prescription graphs in his registrar's report relate to all respiratory conditions and not asthma and had been deliberately relabelled to deceive readers and come to conclusions based on the false relabelling. The Director claimed that pollutants from the power station had decreased steadily, making no mention of changes in fuel content or the effects of emissions from a cold chimney with on/off operation leading to earlier plume grounding at much higher concentration of particulates due to less dilution. The Director alleged that all pollutants at ground level would remain well within the guide levels, but WHO has concluded that there is no safe lower limit of PM2.5 and smaller particulates. The Bitor data sheet and power station report both state that 85% of particulate emissions would be below PM1, that is the most dangerous size and would contain carcinogenic heavy metals. The Director claimed there was no pattern of inhaler use in school children, but deliberately mixed up primary and secondary schools, hiding the fact that the registrar's alleged primary school results when mapped out coincided almost exactly with my map.

The Director's registrar's report consists almost entirely of misinformation. Hospital admission figures do not agree with those published in Hansard, nor with those printed off the hospital computer. Toxicology figures and comments do not agree with the current textbooks and we have comments such as "air concentrations much less than in 50s and 60s" referring to

"respirable fine dust" (tiny particulates), while readers may be interested to learn that the power station opened in 1973, Elf Refinery in 1973 and Gulf Refinery in 1968. Referring to incidence of asthma in polluted South and Mid Glamorgan of between 9 and 15% of children quoted in the report it then alleges "we can, therefore, expect a similar background level in Pembrokeshire." Why?

Claims are made that "asthma has increased as air pollution has decreased, and its incidence is higher in least polluted areas such as ... the Isle of Skye." When I phoned primary schools in the Isle of Skye there was not a single child with asthma on the west coast and around 4% taking inhalers around the port. Comments are made about toxic heavy metals, alleging "with Orimulsion still lower than rural background level", without mentioning that rural background was measured immediately downwind of the large nickel factory in Clydach and nickel was measured in England, and Pembrokeshire soil samples of heavy metals have shown a relentless recent rise.

The Health Authority continually refused to ask Pembrokeshire GPs for relevant data. So 41 GPs, representing almost all Pembrokeshire GPs from 10 practices, finally wrote a joint letter to the County Council, Community Health Council, MP, the Welsh Secretary and others on 23rd July 1996, highlighting the detrimental health effect of ultra-fine carcinogenic heavy metal dust particles, anticipated increased NO_2 and ozone that would result from the Orimulsion proposal. They wrote, "These issues are too important to ignore ... As GPs, our duty is to highlight these potential health risks and we strongly believe that a Public Inquiry is vital to ensure a balanced debate... We ... question the validity of the Dyfed Health Authority 1995 report on local disease patterns." Contrast this with the unreferenced allegations of the Health Authority: "No adverse health impact from the burning of Orimulsion is predictable". Friends of the Earth (FOE Cymru) also saw and wrote to the Director and registrar.

On 19th September 1996 a colleague and I saw the new Director of Public Health for the new amalgamated Dyfed/Powys Health Authority and pleaded with him to withdraw the May 1995 report and revise it. I explained and discussed many relevant matters with him. He remains intransigent and refuses to discuss or remove the report from the public arena for revision. He did suggest that he might ask for finance which would be given to do a small pilot study, but this would consist of looking at one small site of his choosing and no control, hardly what one would call a valid study. He has refused to respond to follow-up letters from FOE Cymru and me.

CONCLUSION

My research strongly suggests a link between industrial air pollution and asthma in primary schoolchildren and adult cancers. My efforts to draw the attention of the authorities to the significance of my research has demonstrated a failure by the Environment Agency to monitor independently and without warning, and to regulate and to punish breaches of the Environmental Protection Act 1990; and a failure by the Public Health Department of Dyfed Health Authority, along with other public health departments elsewhere in the UK, to protect the health of the public.

RECOMMENDATIONS

In consultation with **Freedom to Care**, I now recommend the following:

- Present proposals for Pembroke Power Station should be scrapped as unsafe
- National and properly resourced epidemiology of health damage by waste burning power stations, cement works, incinerators, waste sites and opencast coal sites should be conducted by the Department of Health
- The Department of the Environment should institute a thorough inquiry into the ineffectiveness and failures of the Environment Agency in policing and enforcing the regulations of the Environment Protection Act 1990. Funding of the agency should be independent of the polluters.
- The General Medical Council should use an independent investigative team to examine the actions of Dyfed Health Authority's public health doctors and their dissemination of gross misinformation.

APPENDIX: Other Research Findings

Extensive research since 1974 by Dr D W Dockery et al (1) of Harvard School of Public Health and Dr Joel Schwartz (2) has documented the adverse health effects of air pollution with particulates comprising soot, acid condensates, sulphates, nitrates and compounds of heavy metals; the range of metals being determined by the content of the items burned or processed. Particulates of a size under PM10 are inhaled, the critical sizes being PM0.03 to PM6 which go to the alveoli at the bottom of the lungs. Heavy metals could stay there indefinitely. Vanadium, cadmium, nickel and arsenic in particular will in some children and adults cause an inflammatory reaction leading to asthma, which may lead to chronic obstructive pulmonary disease.

Particulates in general also may restrict activity due to illness and even at a level of PM2.5 as low as 10 micrograms per cubic metre, may lead to premature death, especially in those patients on the borderline with pulmonary and cardiac disease (3, pp 16 & 28), partly because of the platelets becoming more sticky with the inflammation caused, leading to problems with circulation to the heart. Professor A Seaton found such effects in relation to emissions from diesel powered vehicles (4). Hence, it is not surprising that some 9 percent of people develop asthma from heavy diesel traffic fumes as found in Japan and as confirmed in Egham, Surrey, adjacent to the M25 motorway and airport, where a team from St George's Hospital, London, measured peak low in children at the primary school and found 10 percent to have clinical asthma. I found 7.5 percent (that is 75 percent of these) to be taking inhalers to school for asthma. At Spaghetti Junction, Birmingham, some 9.5 percent of primary schoolchildren took inhalers to school. At

Walsall, alleged to have severe asthma problems, 13 percent of the primary schoolchildren took inhalers to school, the level dropping sharply less than a mile away. The critical distance appears to be within 500 metres of the road (5, p 167).

In addition to diesel vehicle emissions American research has included studies of tyre dust particulates from wear on the highways with 60% of tyre dust being smaller than PM10 and microscopy by Dr M Straight of Denver, Colorado, has revealed the sticky latex attaching to the diesel particulates at sizes around PM1.5 upwards. Further studies in America have shown that latex from the guayule plant does not cause the usual allergy that results from regular latex used in gloves and car tyres. Hence a switch in latex source and active use of "city diesel" should have a beneficial effect in reducing traffic related asthma.

Furthermore, WHO has published tables of extra deaths, hospital admissions and exacerbation of asthma in the short term due to only 3 days of moderate particulate air levels, the severity being directly related to the air particulate concentration (3, pp 16-20). A further study in Seattle of all hospital casualty attendances at all eight hospitals over a 12 months period, showed a statistically significant positive correlation between asthma visits and PM10 particulate levels outdoors for the previous 4 days. This relationship was graded with no evidence of a threshold in all ages up to 65 years. The reason for the delay would be the time for an inflammatory reaction to get going and home treatment to fail (5, p 141). A further study of 552,138 residents between 1980 and 1989 proved an association of fine particulate air pollution, especially sulphates from fossil fuel combustion, with heart and lung mortality not attributable to tobacco smoking (6). A study of casualty attendances for asthma in Philadelphia revealed increases up to 9 fold on stagnant days associated with high levels of pollution irrespective of pollen counts or epidemics of upper respiratory infection (5, p 139).

A Bristol city study of inhaler usage in primary school asthmatic children by McMahon and Fryer (7) indicated that PM10 air pollution primarily from traffic when directly influenced by the weather resulted in a high use of inhalers at the school up to 14 days later paralleled by a large increase in hospital admissions. Insufficient attention has been paid to local weather causing plume grounding from industrial point sources during temperature inversions (K Harrison), noting that cool emissions from cold chimneys or Scrubbers/FGD could be prone to ground almost undiluted.

Apart from asthma, arsenic (8, 14), chromium (8, 14), nickel (9 p 19 S116 & 14) and coke-oven particulates (8) and polycyclic aromatic hydrocarbons (14) all can cause respiratory cancers (9, pp 267/573 and 14). Cadmium, coal-dust, rock-dust, graphite, iron-dust, etc, can cause pneumoconiosis (8). Cadmium can cause prostate cancers (14), arsenic can cause liver cancer (14) and chromium and nickel are also alleged to cause gastrointestinal tract cancers (14) and aromatic amines such as 2-naphthylamine found in coking plants can cause urinary bladder cancer (14). Arsenic, cadmium, lead, mercury and thallium and certain aromatic hydrocarbons have been proven to be vasculotoxic with effects on brain, heart and kidneys (14). Dioxins and PCBs present in much hazardous waste, can cause endocrine, immunological and reproductive system effects (10) e.g. endometriosis, sperm loss, susceptibility to viral infections, diabetes, reduced testosterone levels in males. Other reported dangers of dioxin exposure include chloracne and cancers (only if a high body burden is evident), and even learning disorders were noted in laboratory monkeys following exposure. Exposure to benzene can result in leukaemia (14).

In some cases body metabolites are more dangerous than the items inhaled, ingested or absorbed (14). The EC issued a directive 94/67/EC on 12th December 1994 which was

mandatory in the UK by the end of 1996, limiting emissions from burning hazardous waste; exhaust dust to be a maximum daily average output of 10mg/m3 and limiting heavy metals to 1.1mg/m3 total in existing plant (0.55mg/m3 for new plant). Some of the exclusions are a grey area and need legal decisions, such as Cemfuel® and emulsified or remnant residuals (bitumen bottoms made into residual oil, ex-refinery).

The UK on 8th November 1995 accepted 50ug/m3 as a 24-hour average maximum for PM10s, but as the WHO report revealed no safe lower limit for PM2.5s it would seem much wiser for environmental health departments to be using PM2.5 heads or even PMO.5 heads on their monitors especially as most of the most troublesome emissions are in the 0.1 to 1.0PM range. Many particulates are too small and gaseous to be trapped by electrostatic precipitators and even FGD/Scrubbers (M Hubbard *Energy World* Nov 1991).

Dangers exist not only from chimney emissions but from hazardous waste sites, noting that open-casting of coal may involve open-casting of hazardous waste above or adjacent to coal deposits. A study of 593 waste sites in the USA with evidence of associated contaminated ground drinking water revealed clusters of excess cancers of the lung, bowel, bladder, breast and gastrointestinal tract (11).

In the USA, asthma prevalence in the under-10s is stated at 2.5% and in the under 18s at 4.1% for ethnic whites and 5% for ethnic blacks, the increase being blamed on teenage smoking. Of course, we have many allergic causes such as cow's milk allergy (age 3 to 18 months onwards), house dust mite allergy (age 3 onwards when children are in the house most of the day or at an older age following triggering of the immune system and lung cells), allergy to other foods or food additives, allergy to dog or cat hairs, allergy to pollens such as cedar trees and oilseed rape crops, moulds, some grasses, reactions to diesel traffic emissions, reactions to particulates of vanadium and nickel found in air pollution emissions from oil refineries and power station, cocktails of heavy metals from SLF burning cement, brick and lime works and dust from open cast coal mining and coal fired cement and other works. If sulphuric acid coated vanadium is inhaled, the corrosive inflammatory effect in the lungs in 30 times greater than inhaling dry vanadium particulates. More studies are required on the effects of inhaling particulates from vehicle tyres both due to wear and tear and following incineration in cement works. Special filters are now available to reduce emissions of volatile organic compounds in certain industries but one wonders whether they are being used as widely as conditions would indicate. Some women are allergic to nickel from jewellery and would hence respond immediately to a nickel particulate challenge.

The study in Derbyshire by Singleton et al 1995 (12), confirmed that physical factors such as overcrowding, double glazing, type of heating, pets or parental smoking had no statistical effect on asthma prevalence in young children, but there was some association with traffic fumes, damp in the house and family history (24). Singleton's mapping was concentric hence only showed up temperature inversion effects and not downwind.

A German university study measured outside PM10, PM2.5, PM0.5 and PM0.03 particulates and correlated the results with daily diaries and daily peak flow measurements and concluded the PM10 and PM0.03 were most strongly associated with decreased peak flow, increased prevalence of feeling ill, shortness of breath and cough (8).

References

[1] D W Dockery et al 'An association between air pollution & mortality in six US cities' *New Eng J Med* Dec 9/1993, 329, 1753-59 [2] J Schwarz 'Particulate air pollution & daily mortality in Steubenville' *Am J Epidem* 1992, 135/1, p 12-19 [3] WHO Revision of the Air Quality Guidelines for Europe October 1995 [4] A Seaton et al 'Particulate air pollution & acute health effects' *Lancet* 21st Jan 1995, 345, 176-177 [5] Asthma and Outdoor Air Pollution, DoH, Oct 1995 [6] Pope et al 'Particulate air pollution as a predictor of mortality, *Am J Respir Crit Care Med*, 151, 669-674, 1995 [7] *Environmental Health* July 1995, 'Asthma in children', p 160-161 [8] *Harrison's Principles of Internal Medicine*, 13th Edition, p 1880, 1994 [9] *Epidemiology* Volume 6 No. 4 Jul 1995 [10] Meharg and Osborn *Nature* Vol 375, 1/6/1995 p 353 [11] Griffith et al, 'Cancer mortality in U.S. counties with hazardous waste sites, *Archives of Env Health*, Mar/Apr 1989 Vol 44 (no 2) pp 69-74 [12] Singleton et al 'Prevalence of asthma and related factors in primary school children in an industrial part of England, *J Epidemiol. Comm. Health* 1995, 49: 326-327 [13] Temple and Sykes, *Brit Med J* 305, 15 Aug 1992, 'Asthma and open cast mining', p 396-397 [14] Casarett & Doull's *Toxicology* 5th Ed 1996 [15] Editorial, and Buchdahl and Anderson, *Brit Med J* 16 Mar 1996, Volume 312 pp 649, 650, 661-669.

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The spasmogenic effects of vanadate in human isolated bronchus.

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1. Inhalation of vanadium compounds, particularly vanadate, is a cause of occupational bronchial asthma. We have now studied the action of vanadate on human isolated bronchus. Vanadate (0.1 microM-3 mM) produced concentration-dependent, well-sustained contraction. Its -logEC50 was 3.74 +/- 0.05 (mean +/- s.e.mean) and its maximal effect was equivalent to 97.5 +/- 4.2% of the response to acetylcholine (ACh, 1 mM). 2. Vanadate (200 microM)-induced contraction of human bronchus was epithelium-independent and was not inhibited by indomethacin (2.8 microM), zileuton (10 microM), a mixture of atropine, mepyramine and phentolamine (each at 1 microM), or by mast cell degranulation with compound 48/80. 3. Vanadate (200 microM)-induced contraction was unaltered by tissue exposure to verapamil or nifedipine (each 1 microM) or to a Ca2+-free, EGTA (0.1 mM) containing physiological salt solution (PSS). However, tissue incubation with ryanodine (10 microM) in Ca2+-free, EGTA (0.1 mM)-containing PSS reduced vanadate-induced contraction. A series of vanadate challenges was made in tissues exposed to Ca2+-free EGTA (0.1 mM)-containing PSS with the object of depleting intracellular Ca2+ stores. In such tissues cyclopiazonic acid (CPA; 10 microM) prevented Ca2+-induced recovery of vanadate-induced contraction. 4. Tissue incubation in K+-rich (80 mM) PSS, K+-free PSS, or PSS containing ouabain (10 microM) did not alter vanadate (200 microM)-induced contraction. Ouabain (10 microM) abolished the K+-induced relaxation of human bronchus bathed in K+-free PSS. This action was not shared by vanadate (200 microM). The tissue content of Na+ was increased and the tissue content of K+ was decreased by ouabain (10 microM). In contrast, vanadate (200 microM) did not alter the tissue content of these ions. Tissue incubation in a Na+-deficient (25 mM) PSS or in PSS containing amiloride (0.1 mM) markedly inhibited the spasmogenic effect of vanadate (200 microM). 5. Vanadate (200 microM)-induced contractions were markedly reduced by tissue treatment with each of the protein kinase C (PKC) inhibitors H-7 (10 microM), staurosporine (1 microM) and calphostin C (1 microM). Genistein (100 microM), an inhibitor of protein tyrosine kinase, also reduced the response to vanadate. 6 Vanadate (0.1-3 mM) and ACh (1 microM- 3 mM) each increased inositol phosphate accumulation in bronchus. Such responses were unaffected by a Ca2+-free medium either alone or in combination with ryanodine (10 microM). 7. In human cultured tracheal smooth muscle cells, histamine (100 microM) and vanadate (200 microM) each produced a transient increase in intracellular Ca2+ concentration ([Ca2+]i). 8. Intracellular microelectrode recording showed that the contractile effect of vanadate (200 microM) in human bronchus was associated with cellular depolarization. 9. It is concluded that vanadate acts directly on human bronchial smooth musole, promoting the release of Ca2+ from an intracellular store. The Ca2+ release mechanism involves both the production of inositol phosphate second messengers and inhibition of Ca-ATPase. The activation of PKC plays an important role in mediating vanadate induced contraction at values of [Ca2+]i that are close to basal.

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Effects of vanadium upon polyl:C-induced responses in rat lung and alveolar macrophages.

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Hosts exposed to vanadium (V) display a subsequent decrease in their resistance to infectious microorganisms. Our earlier studies with rats inhaling occupationally relevant levels of V (as, ammonium metavanadate, NH4VO3) indicated that several nascent/inducible functions of pulmonary macrophages (PAM) were reduced. In the present study, V-exposed rats were examined to determine whether some of the same effects might also occur in situ. Rats were exposed nose-only to air or 2 mg V/m3 (as NH4VO3) for 8 h/d for 4 d, followed, 24 h later, by intratracheal (it) instillation of polyinosinic:polycytidilic acid (polyl:C) or saline. Analysis of lavaged lung cells/fluids after polyl:C instillation indicated that total lavageable cell/neutrophil numbers and protein levels, while significantly elevated in both exposure groups (as well as in saline-treated V-exposed rats), were always greater in V-exposed hosts. Exposure to V also affected the inducible production of interleukin 6 (IL-6) and interferon gamma (IFN gamma), but apparently not that of tumor necrosis factor-alpha (TNF alpha) or IL-1. Although polyl:C induced significant increases in lavage fluid IL-6 and IFN gamma levels in both exposure groups, levels were greater in V-exposed rats. If calculated with respect to total lavaged protein, however, V-exposed rats produced significantly less cytokine. Following polyl:C instillation, there were no marked exposure-related differences in basal or stimulated superoxide anion production by pooled lavaged cells or PAM specifically. With V-exposed rats, pooled cells recovered 24 h after saline instillation displayed reduced production (in both cases) compared to the air control cells; PAM-specific production was affected only after stimulation. In both exposure groups, polyl:C caused decreased superoxide production in recovered cells. Though less apparent with pooled cells, there was a time post polyl:C instillation dependent decrease in stimulated PAM-specific superoxide production; this effect was greater in PAM from V exposed rats than in PAM from air controls. Phagocytic activity of PAM from rats in both exposure groups was significantly increased by polyl:C instillation, although total activity in cells obtained from V-exposed rats was always significantly lower compared to air control cells. Our results indicate that short-term, repeated inhalation of occupationally relevant levels of V by rats modulates pulmonary immunocompetence. Modified cytokine production and PAM functionality in response to biological response modifiers (such as lipopolysaccharide, IFN gamma, or polyl:C) may be, at least in part, responsible for the increases in bronchopulmonary disease in humans occupationally exposed to V.

MeSH Terms:

.Administration, Inhalation
.Animal
.Bronchoalveolar Lavage Fluid/cytology

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Vanadium(IV)-mediated free radical generation and related 2'-deoxyguanosine hydroxylation and DNA damage.

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Free radical generation, 2'-deoxyguanosine (dG) hydroxylation and DNA damage by vanadium(IV) reactions were investigated. Vanadium(IV) caused molecular oxygen dependent dG hydroxylation to form 8-hydroxyl-2'-deoxyguanosine (8-OHdG). During a 15 min incubation of 1.0 mM dG and 1.0 mM VOSO4 in phosphate buffer solution (pH 7.4) at room temperature under ambient air, dG was converted to 8-OHdG with a yield of about 0.31%. Catalase and formate inhibited the 8-OHdG formation while superoxide dismutase enhanced it. Metal ion chelators, DTPA and deferoxamine, blocked the 8-OHdG formation. Incubation of vanadium(IV) with dG in argon did not generate any significant amount of 8-OHdG, indicating the role of molecular oxygen in the mechanism of vanadium(IV)-induced dG hydroxylation. Vanadium(IV) also caused molecular oxygen-dependent DNA strand breaks in a pattern similar to that observed for dG hydroxylation. ESR spin trapping measurements demonstrated that the reaction of vanadium(IV) with H2O2 generated OH radicals, which were inhibited by DTPA and deferoxamine. Incubation of vanadium(IV) with dG or with DNA in the presence of H2O2 resulted in an enhanced 8-OHdG formation and substantial DNA double strand breaks. Sodium formate inhibited 8-OHdG formation while DTPA had no significant effect. Deferoxamine enhanced the 8-OHdG generation by 2.5-fold. ESR and UV measurements provided evidence for the complex formation between vanadium(IV) and deferoxamine. UV-visible measurements indicate that dG, vanadium(IV) and deferoxamine are able to form a complex, thereby, facilitating site-specific 8-OHdG formation. Reaction of vanadium(IV) with t-butyl hydroperoxide generated hydroperoxide-derived free radicals, which caused 8-OHdG formation from dG and DNA strand breaks. DTPA and deferoxamine attenuated vanadium(IV)/t-butyl-OOH-induced DNA strand breaks.

MeSH Terms:

- Chelating Agents/pharmacology
- Chromatography, High Pressure Liquid
- Deoxyguanosine/metabolism*
- Deoxyguanosine/analogs & derivatives
- DNA Damage/drug effects*
- Electron Spin Resonance Spectroscopy
- Free Radicals
- Hydrogen Peroxide/metabolism
- Hydroxyl Radical/metabolism
- Hydroxylation
- Kinetics
- Lipid Peroxidation
- Peroxides/metabolism
- Spectrophotometry, Ultraviolet
- Vanadium/toxicity*

Substances:

- Deoxyguanosine

Toxicol Appl Pharmacol 1997 Mar;143(1):152-166

Carcinogenicity assessment of selected nickel compounds.

Oller AR, Costa M, Oberdorster G

Nickel Producers Environmental Research Association, Durham, North Carolina 27713, USA.

The early epidemiological data indicated different carcinogenic risks from inhalation of different nickel compounds, but it was not clear what characteristics governed the intrinsic carcinogenic hazard of the various nickel compounds. Based on the earlier results, all soluble and insoluble nickel compounds were assumed to have the same carcinogenic mechanism albeit different potencies. Recent in vivo and in vitro studies challenged this assumption. In this paper an attempt is made to integrate the most relevant human, animal, and in vitro data into a general model that can help understand the different carcinogenic potentials of the various nickel compounds. In this perspective, it is recognized that there are two main components that could contribute to the development of lung cancer via exposure to certain nickel compounds. The first component corresponds to the heritable changes (genetic or epigenetic) derived from the direct or indirect actions of nickel compounds. The second component may be the promotion of cell proliferation elicited by certain nickel compounds. The different contributions of three nickel compounds to these two components are presented. This paper emphasizes the importance of recognizing the individuality of the different nickel species in reaching regulatory decisions and the fact that different risk assessment considerations may apply for compounds that appear to produce immortality and cancer by genetic/epigenetic mechanisms (like nickel subsulfide), compounds that may present a threshold for the induction of tumors in rats (like high-temperature nickel oxide), or compounds that may only have an enhancing effect on carcinogenicity (like nickel sulfate).

MeSH Terms:

- Administration, Inhalation
- Animal
- Carcinogens/toxicity*
- Cell Division/drug effects
- Environmental Pollutants
- Human
- In Vitro
- Lung Neoplasms/genetics
- Lung Neoplasms/chemically induced*
- Maximum Permissible Exposure Level
- Nickel/toxicity*
- Nickel/pharmacokinetics
- Rats
- Risk Assessment

Substances:

- Nickel
- Environmental Pollutants
- Carcinogens

PMID: 9073603, MUID: 97236984

Mutat Res 1997 Apr;386(2):163-180

DNA methylation, heterochromatin and epigenetic carcinogens.

Klein CB, Costa M

Nelson Institute of Environmental Medicine, New York University Medical Center, NY 10016, USA.

This paper will explore emerging concepts related to alternative carcinogenic mechanisms of 'non-mutagenic,' and hence epigenetic, carcinogens that may heritably alter DNA methylation without changing the underlying DNA sequence. In this review, we will touch on the basic concepts of DNA methylation, and will elaborate in greater detail on related topics including chromatin condensation, and heterochromatin spreading that is well known to induce gene silencing by position effect variegation in Drosophila and other species. Data from our model transgenic G12 cell system will be presented to support our hypothesis that certain carcinogens, such as nickel, may be carcinogenic not primarily because of their overt mutability, but rather as the result of their ability to promote DNA hypermethylation of important cancer-related genes. We will conclude with a discussion of the broader relevance of our findings and its application to other so-called 'epigenetic' carcinogens.

MeSH Terms:

- Animal
- Carcinogens/toxicity*
- Carcinogens/classification
- Chromatin/genetics*
- Chromatin/drug effects*
- Diethylstilbestrol/toxicity
- DNA Methylation/drug effects*
- Evolution
- Forecasting
- Gene Expression/drug effects
- Human
- Mutagens/toxicity
- Mutation
- Neoplasms/genetics
- Neoplasms/drug therapy
- Neoplasms/chemically induced
- Nickel/toxicity
- Oxidation-Reduction
- Support, Non-U.S. Gov't
- Support, U.S. Gov't, P.H.S.
- Telomere/genetics

Substances:

- Nickel
- Diethylstilbestrol
- Mutagens
- Chromatin
- Carcinogens

Biol Trace Elem Res 1997 Apr;57(1):79-90

Catalase activity in erythrocytes from colon and gastric cancer patients. Influence of nickel, lead, mercury, and cadmium.

Martin Mateo MC, Martin B, Santos Beneit M, Rabadan J

Biochemistry Department, Faculty of Sciences, Universidad de Valladolid, Spain.

Catalase (CAT) is an enzyme that is involved in antioxidant defense, cell growth, and is possibly associated with tumoral processes. In this paper, the results of experiments designed to determine the influence of metallic carcinogens such as nickel (Ni), lead (Pb), mercury (Hg), and cadmium (Cd), on CAT activity are reported. CAT activity was measured in erythrocytes from three groups: a group of colon cancer patients, a group of gastric cancer patients before clinical treatment, and a-control group of healthy blood donors. Concentrations of this enzyme are significantly higher than controls in the colon cancer group, but lower in gastric neoplasia. By generating highly reactive oxygenated species, Ni, Pb, Hg, and Cd alter catalase activity. Solutions of Ni, Cd, and Pb at 0.2 mM concentrations inhibit CAT activity in colon cancer, but increase it in gastric neoplasia. Hg activates CAT in colon cancer, and causes a slightly increased activity in gastric cancer. No complete deactivation of the enzyme was observed.

PMID: 9258471, MUID: 97403102

Environ Res 1997 Feb;72(2):162-172

Metal and sulfate composition of residual oil fly ash determines airway hyperreactivity and lung injury in rats.

Gavett SH, Madison SL, Dreher KL, Winsett DW, McGee JK, Costa DL

Pulmonary Toxicology Branch, U.S. Environmental Protection Agency, Research Triangle Park, North Carolina 27711, USA.

The biological effects of particulate matter (PM) deposition in the airways may depend on aqueousleachable chemical constituents of the particles. The effects of two residual oil fly ash (ROFA) PM samples of equivalent diameters but different metal and sulfate contents on pulmonary responses in Sprague-Dawley rats were investigated. ROFA sample 1 (R1) had approximately twice as much saline-leachable sulfate, nickel, and vanadium, and 40 times as much iron as ROFA sample 2 (R2), while R2 had a 31-fold higher zinc content. Four groups of rats were intratracheally instilled with a suspension of 2.5 mg R2 in 0.3 ml saline (R2), the supernatant of R2 (R2s), the supernatant of 2.5 mg R1 (R1s), or saline only. By 4 days after instillation, 4 of 24 rats treated with R2s or R2 had died, compared with non treated with R1s or saline, and pathological indices were greater in both R2 groups compared with the R1s group. In surviving rats, baseline pulmonary function parameters and airway hyperreactivity to acetylcholine challenge were significantly worse in R2 and R2s groups than in the R1s group. Numbers of bronchoalveolar lavage neutrophils, but not other inflammatory cells or biochemical parameters of lung injury, were greater in both R2 groups compared with the R1s group. These results reinforce the hypothesis that the composition of soluble metals and sulfate leached from ROFA, an emission source particle, is critical in the development of airway hyperreactivity and lung injury.

MeSH Terms:

- .Acetylcholine/pharmacology
- .Animal
- .Bronchial Hyperreactivity/chemically induced*
- .Carbon/toxicity*
- .Carbon/chemistry
- .Lung/pathology
- .Lung/drug effects*
- .Male
- .Metals/chemistry*
- .Petroleum
- .Pneumonia/chemically induced
- .Rats
- .Rats, Sprague-Dawley

Other Formats: [redacted]

Links: [redacted]

Am J Physiol 1997 Mar;**272(3 Pt 1)**:L426-L432

Disruption of protein tyrosine phosphate homeostasis in bronchial epithelial cells exposed to oil fly ash.

Samet JM, Stonehuerner J, Reed W, Devlin RB, Dailey LA, Kennedy TP, Bromberg PA, Ghio AJ

Center for Environmental Medicine and Lung Biology, University of North Carolina at Chapel Hill, 27599-7310, USA.

Residual oil fly ash (ROFA) is a toxic air pollutant that we have previously shown induces inflammatory mediator expression in human bronchial epithelial cells. To identify intracellular signaling mechanisms activated by ROFA, we studied its effect on protein tyrosine phosphate metabolism in the human bronchial epithelial cell line BEAS. Noncytotoxic levels of ROFA induced significant dose- and time-dependent increases in protein tyrosine phosphate levels in BEAS cells. ROFA-induced increases in protein phosphotyrosines were associated with its soluble fraction and were mimicked by vanadyl [V(IV)]- and vanadate [V(V)]-containing solutions. Ferrous, ferric, and nickel (II) ion solutions failed to increase phosphotyrosine levels. Tyrosine phosphatase activity, which was known to be inhibited by vanadium ions, was markedly diminished after ROFA treatment. Tyrosine kinase activity was unaffected. We conclude that ROFA exposure induces vanadium ion-mediated inhibition of tyrosine phosphatase activity, leading to accumulation of protein phosphotyrosines in BEAS cells. These findings demonstrate that ROFA exposure disrupts protein tyrosine phosphate homeostasis in BEAS cells and suggest a possible mechanism that leads to increased synthesis of proinflammatory proteins in airway epithelial cells exposed to PM10.

MeSH Terms:

.Air Pollutants, Environmental/toxicity*
.Bronchi/enzymology
.Bronchi/drug effects*
.Bronchi/cytology
.Carbon/toxicity
.Cells, Cultured
.Epithelium/drug effects
.Homeostasis/drug effects
.Human
.Industrial Waste
.Molecular Weight
.Oils
.Phosphoproteins/metabolism*
.Phosphotyrosine/metabolism*
.Protein-Tyrosine Kinase/metabolism

Other Formats: [redacted]

Links: [redacted]

Am J Physiol 1997 Mar;272(3 Pt 1):L426-L432

Disruption of protein tyrosine phosphate homeostasis in bronchial epithelial cells exposed to oil fly ash.

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Center for Environmental Medicine and Lung Biology, University of North Carolina at Chapel Hill, 27599-7310, USA.

Residual oil fly ash (ROFA) is a toxic air pollutant that we have previously shown induces inflammatory mediator expression in human bronchial epithelial cells. To identify intracellular signaling mechanisms activated by ROFA, we studied its effect on protein tyrosine phosphate metabolism in the human bronchial epithelial cell line BEAS. Noncytotoxic levels of ROFA induced significant dose- and time-dependent increases in protein tyrosine phosphate levels in BEAS cells. ROFA-induced increases in protein phosphotyrosines were associated with its soluble fraction and were mimicked by vanadyl [V(IV)]- and vanadate [V(V)]-containing solutions. Ferrous, ferric, and nickel (II) ion solutions failed to increase phosphotyrosine levels. Tyrosine phosphatase activity, which was known to be inhibited by vanadium ions, was markedly diminished after ROFA treatment. Tyrosine kinase activity was unaffected. We conclude that ROFA exposure induces vanadium ion-mediated inhibition of tyrosine phosphatase activity, leading to accumulation of protein phosphotyrosines in BEAS cells. These findings demonstrate that ROFA exposure disrupts protein tyrosine phosphate homeostasis in BEAS cells and suggest a possible mechanism that leads to increased synthesis of proinflammatory proteins in airway epithelial cells exposed to PM10.

MeSH Terms:

.Air Pollutants, Environmental/toxicity*
.Bronchi/enzymology
.Bronchi/drug effects*
.Bronchi/cytology
.Carbon/toxicity
.Cells, Cultured
.Epithelium/drug effects
.Homeostasis/drug effects
.Human
.Industrial Waste
.Molecular Weight
.Oils
.Phosphoproteins/metabolism*
.Phosphotyrosine/metabolism*
.Protein-Tyrosine Kinase/metabolism

Biometals 1997 Apr;**10(2)**:119-122

Hydroxyl free radicals generated by vanadyl[IV] induce cell blebbing in mitotic human Chang liver cells.

Bay BH, Sit KH, Paramanantham R, Chan YG

Department of Anatomy, National University of Singapore, Kent Ridge, Singapore.

Vanadium has recently been reported to induce interphase and M-phase (mitotic) programmed cell death via the generation of hydroxyl free radicals (OH*). In this paper, the effects of antioxidants on: (a) vanadyl[IV]-generated OH* free radical levels; and (b) cellular glutathione in vanadyl [IV]-treated Chang liver cells were evaluated. The surface morphology of vanadyl-treated mitotic cells was studied by confocal and scanning microscopy. The free radical scavengers zinc chloride, glucose and thiourea reduced the levels of vanadyl-induced OH* free radicals and partially prevented the depletion of cellular glutathione. Concurrent with OH* free radical production, vanadyl treated telophase cells exhibited excessive cell blebbing and cell shrinkage. The morphological features demonstrated in vanadyl-induced mitotic programmed cell death as a consequence of oxidative stress is novel.

MeSH Terms:

.Apoptosis/drug effects
.Cells, Cultured
.Chlorides/pharmacology
.Free Radical Scavengers/pharmacology
.Glucose/pharmacology
.Glutathione/metabolism
.Human
.Hydroxyl Radical/toxicity*
.Liver/ultrastructure
.Liver/drug effects*
.Liver/cytology
.Microscopy, Confocal
.Microscopy, Electron, Scanning
.Mitosis/drug effects
.Oxidative Stress
.Spectrophotometry, Ultraviolet
.Support, Non-U.S. Gov't
.Telophase
.Thiourea/pharmacology
.Vanadates/toxicity*
.Vanadates/metabolism

Chem Res Toxicol 1997 Apr;10(4):393-400

Generation of putative intrastrand cross-links and strand breaks in DNA by transition metal ion-mediated oxygen radical attack.

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Generation of putative intrastrand cross-links and strand breaks was investigated in salmon sperm DNA exposed to Fenton-type oxygen radical-generating systems. 32P-Postlabeling analysis of DNA treated with hydrogen peroxide and either copper(II), chromium(VI), cobalt(II), iron(II), nickel(II), or vanadium(III) resulted in the detection of between four and eight radioactive TLC spots that are probably hydroxyl radical-mediated oxidative DNA lesions. The copper Fenton system generated the highest total yield of these DNA lesions (75.6 per 10(8) nucleotides), followed by cobalt (47.5), nickel (26.2), chromium (25.1), iron (21.7), and vanadium (17.1). Two spots, common to all these Fenton systems, were the major oxidation products in each case. Similar Fenton-type treatment of the purine dinucleotides dApdG and dApdA resulted in products that were chromatographically identical on anion-exchange TLC and on reverse-phase HPLC to the two major products generated in DNA. These results extend our earlier studies suggesting that these products were the result of a free radical-mediated intrastrand cross-linking reaction. Incubations involving cadmium(II), chromium(III), or zinc(II) ions with hydrogen peroxide did not generate DNA oxidation products at levels greater than in incubations with hydrogen peroxide alone. Generation of the putative intrastrand cross-links increased in a concentration-dependent manner up to 1 mM cobalt, nickel, or chromium(VI) ions. However, in experiments with copper, iron, or vanadium ions, maximum levels were obtained at 250, 150, and 150 microM, respectively, and the yield declined with higher concentrations of these three metal ions. Agarose gel electrophoresis demonstrated extensive DNA strand breakage with copper, iron, chromium(III), or vanadium, but not with nickel, chromate(VI), cobalt, cadmium, or zinc Fenton systems. The results demonstrate that generation of the putative intrastrand cross-links and strand breaks in DNA, mediated by Fenton reactions, occurs by independent mechanisms.

MeSH Terms:

.Animal
.Cross-Linking Reagents/pharmacology*
.DNA/drug effects*
.DNA Damage*
.Electrophoresis, Agar Gel
.Oxidative Stress
.Reactive Oxygen Species*
.Salmon

J Biol Chem 1997 May 16;272(20):12968-12977

Activation of HIV-1 long terminal repeat transcription and virus replication via NF-kappaB-dependent and independent pathways by potent phosphotyrosine phosphatase inhibitors, the peroxovanadium compounds.

Barbeau B, Bernier R, Dumais N, Briand G, Olivier M, Faure R, Posner BI, Tremblay M

Centre de Recherche en Infectiologie and Departement de Microbiologie, Centre Hospitalier Universitaire de Quebec, Pavillon CHUL, Faculte de Medecine, Universite Laval, Ste-Foy (Quebec), Canada G1 V 4G2.

Replication of human immunodeficiency virus type 1 (HIV-1) is increased by different cytokines and T cell activators, also known to modulate tyrosine phosphorylation levels. A novel class of protein tyrosine phosphatase (PTP) inhibitors, peroxovanadium (pV) compounds, were tested for a putative effect on HIV-1 long terminal repeat (LTR) activity. We found that these PTP inhibitors markedly enhanced HIV-1 LTR activity in 1G5 cells, a stably transfected cell line that harbors an HIV-1 LTR-driven luciferase construct. A direct correlation between the extent of tyrosine phosphorylation and the level of HIV-1 LTR inducibility was seen after treatment with three different pV compounds. Transient transfection experiments were carried out in several T cell lines, and after addition of pV, a marked increase in HIV-1 LTR activity was measured. Monocytoid cells were tested using U937-derived cell lines and were also found to be sensitive to the pV-mediated potentiating effect on HIV-1 LTR activity. A significant reduction of the pV-mediated increase in HIV-1 LTR activity was seen in cells transiently transfected with an HIV-1 LTR-driven luciferase construct bearing a mutation in both NF-kappaB binding sites although detectable levels of induction remained. Electrophoretic mobility shift assays allowed the identification of the nuclear translocation of the NF-kappaB p50.p65 heterodimer complex induced by pV compounds. A dominant negative version of the repressor IkappaBalpha mutated on serines 32 and 36 impeded pV-induced NF-kappaB-dependent luciferase activity. Western blot analysis showed a clear diminution in the protein level of IkappaBalpha starting 30 min after pV treatment of Jurkat E6.1 cells which is indicative of its degradation. On the other hand, no increase in tyrosine phosphorylation was observed on IkappaBalpha itself. Finally, we tested the PTP inhibitors on four cell lines latently infected with HIV-1 and showed a consistent pV-mediated increase in virion production. Thus, our studies suggest that pV-mediated activation of HIV-1 LTR activity is controlled by the nuclear translocation of the NF-kappaB transcription factor, which is mediated by IkappaBalpha serine phosphorylation and degradation, but also by a still undefined NF-kappaB-independent pathway.

MeSH Terms:

- Cell Line
- Gene Expression Regulation, Viral/drug effects

Other Formats: 

Links: 

Mol Cell Biochem 1997 May;170(1-2):53-63

Influence of vanadate on glycolysis, intracellular sodium, and pH in perfused rat hearts.

Geraldes CF, Castro MM, Sherry AD, Ramasamy R

Biochemistry Department, Faculty of Science and Technology, University of Coimbra, Portugal.

Vanadium compounds have been shown to cause a variety of biological and metabolic effects including inhibition of certain enzymes, alteration of contractile function, and as an insulin like regulator of glucose metabolism. However, the influence of vanadium on metabolic and ionic changes in hearts remains to be understood. In this study we have examined the influence of vanadate on glucose metabolism and sodium transport in isolated perfused rat hearts. Hearts were perfused with 10 mM glucose and varying vanadate concentrations (0.7-100 microM) while changes in high energy phosphates (ATP and phosphocreatine (PCr)), intracellular pH, and intracellular sodium were monitored using 31P and 23Na NMR spectroscopy. Tissue lactate, glycogen, and (Na+, K+)-ATPase activity were also measured using biochemical assays. Under baseline conditions, vanadate increased tissue glycogen levels two fold and reduced (Na+, K+)-ATPase activity. Significant decreases in ATP and PCr were observed in the presence of vanadate, with little change in intracellular pH. These changes under baseline conditions were less severe when the hearts were perfused with glucose, palmitate and beta-hydroxybutyrate. During ischemia vanadate did not limit the rise in intracellular sodium, but slowed sodium recovery on reperfusion. The presence of vanadate during ischemia resulted in attenuation of acidosis, and reduced lactate accumulation. Reperfusion in the presence of vanadate resulted in a slower ATP recovery, while intracellular pH and PCr recovery was not affected. These results indicate that vanadate alters glucose utilization and (Na+, K+)-ATPase activity and thereby influences the response of the myocardium to an ischemic insult.

MeSH Terms:

- .Adenosine Triphosphate/metabolism
- .Animal
- .Energy Metabolism/drug effects
- .Glucose/pharmacology
- .Glucose/metabolism
- .Glycogen/metabolism
- .Glycolysis/drug effects*
- .Heart/drug effects*
- .Hydrogen-Ion Concentration*
- .Hydroxybutyrates/pharmacology
- .In Vitro
- .Kinetics
- .Lactates/metabolism

Other Formats: [redacted]

Links: [redacted]

Biometals 1997 Apr;10(2):127-133

Proliferative and morphological changes induced by vanadium compounds on Swiss 3T3 fibroblasts.

Cortizo AM, Salice VC, Vescina CM, Etcheverry SB

Catedra de Bioquimica Patologica, Facultad de Ciencias Exactas, Universidad Nacional de La Plata, Argentina.

Vanadium compounds are shown to have a mitogenic effect on fibroblast cells. The effects of vanadate, vanadyl and pervanadate on the proliferation and morphological changes of Swiss 3T3 cells in culture are compared. Vanadium derivatives induced cell proliferation in a biphasic manner, with a toxic-like effect at doses over 50 microM, after 24 h of incubation. Vanadyl and vanadate were equally potent at 2.5-10 microM. At 50 microM vanadate inhibited cell proliferation, whereas slight inhibition was observed at 100 microM of vanadyl. At 10 microM pervanadate was as potent as vanadate and vanadyl in stimulating fibroblast proliferation, but no effect was observed at lower concentrations. A pronounced cytotoxic-like effect was induced by pervanadate at 50 microM. All of these effects were accompanied by morphological changes: transformation of fibroblast shape from polygonal to fusiform; retraction with cytoplasm condensation; and loss of lamellar processes. The magnitude of these transformations correlates with the potency of vanadium derivatives to induce a cytotoxic-like effect: pervanadate > vanadate > vanadyl. These data suggest that the oxidation state and coordination geometry of vanadium determine the degree of the cytotoxicity.

MeSH Terms:

- .Animal
- .Cell Division/drug effects
- .Cells, Cultured
- .Enzyme Inhibitors/toxicity*
- .Mice
- .Oxidation-Reduction
- .Structure-Activity Relationship
- .Support, Non-U.S. Gov't
- .Vanadates/toxicity*
- .3T3 Cells/pathology
- .3T3 Cells/drug effects*
- .3T3 Cells/cytology

Substances:

- .Vanadates
- .Enzyme Inhibitors
- .pervanadate

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Toxicology 1996 Jan 8;106(1-3):27-38

Vanadium(IV)-mediated free radical generation and related 2'-deoxyguanosine hydroxylation and DNA damage.

Shi X, Jiang H, Mao Y, Ye J, Saffiotti U

Laboratory of Experimental Pathology, National Cancer Institute, NIH, Bethesda, MD 20892, USA.

Free radical generation, 2'-deoxyguanosine (dG) hydroxylation and DNA damage by vanadium(IV) reactions were investigated. Vanadium(IV) caused molecular oxygen dependent dG hydroxylation to form 8-hydroxyl-2'-deoxyguanosine (8-OHdG). During a 15 min incubation of 1.0 mM dG and 1.0 mM VOSO4 in phosphate buffer solution (pH 7.4) at room temperature under ambient air, dG was converted to 8-OHdG with a yield of about 0.31%. Catalase and formate inhibited the 8-OHdG formation while superoxide dismutase enhanced it. Metal ion chelators, DTPA and deferoxamine, blocked the 8-OHdG formation. Incubation of vanadium(IV) with dG in argon did not generate any significant amount of 8-OHdG, indicating the role of molecular oxygen in the mechanism of vanadium(IV)-induced dG hydroxylation. Vanadium(IV) also caused molecular oxygen-dependent DNA strand breaks in a pattern similar to that observed for dG hydroxylation. ESR spin trapping measurements demonstrated that the reaction of vanadium(IV) with H2O2 generated OH radicals, which were inhibited by DTPA and deferoxamine. Incubation of vanadium(IV) with dG or with DNA in the presence of H2O2 resulted in an enhanced 8-OHdG formation and substantial DNA double strand breaks. Sodium formate inhibited 8-OHdG formation while DTPA had no significant effect. Deferoxamine enhanced the 8-OHdG generation by 2.5-fold. ESR and UV measurements provided evidence for the complex formation between vanadium(IV) and deferoxamine. UV-visible measurements indicate that dG, vanadium(IV) and deferoxamine are able to form a complex, thereby, facilitating site-specific 8-OHdG formation. Reaction of vanadium(IV) with t-butyl hydroperoxide generated hydroperoxide-derived free radicals, which caused 8-OHdG formation from dG and DNA strand breaks. DTPA and deferoxamine attenuated vanadium(IV)/t-butyl-OOH-induced DNA strand breaks.

MeSH Terms:

- Chelating Agents/pharmacology
- Chromatography, High Pressure Liquid
- Deoxyguanosine/metabolism*
- Deoxyguanosine/analogs & derivatives
- DNA Damage/drug effects*
- Electron Spin Resonance Spectroscopy
- Free Radicals
- Hydrogen Peroxide/metabolism
- Hydroxyl Radical/metabolism
- Hydroxylation
- Kinetics
- Lipid Peroxidation
- Peroxides/metabolism
- Spectrophotometry, Ultraviolet
- Vanadium/toxicity*

Substances:

- Deoxyguanosine

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=NOTE=

ndam Appl Toxicol 1996 Nov;34(1):67-72
e of the Syrian hamster embryo cell transformation assay for determining the
rcinogenic potential of heavy metal compounds

rckaert GA, LeBoeuf RA, Isfort RJ

rporate Professional & Regulatory Services, Procter & Gamble Company, Miami
lley Laboratories, Cincinnati, Ohio 45253-8707, USA.

balt sulfate hydrate, gallium arsenide, molybdenum trioxide, vanadium pentoxide,
d nickel sulfate heptahydrate were tested in the Syrian hamster
bryo (SHE) assay in order to increase the SHE assay database for heavy metals.
l five compounds produced significant morphological
ansformation at one or more doses in a dose-responsive manner. Cobalt sulfate
drate, gallium arsenide, molybdenum trioxide, and nickel (II)
lfate heptahydrate were all positive with a 24-hr exposure, suggesting direct DNA
turbation. Vanadium pentoxide was negative with a 24-hr
posure, but positive with a 7-day exposure. This pattern of response (24-hr SHE
gative/7-day SHE positive) has been seen with other chemicals
ch have tumor promotion-like characteristics. Since the inception of the use of
e SHE cell transformation assay for detecting the neoplastic
ansformation potential of chemicals, over 42 heavy metal compounds have been
ted in this assay. Based on the 24 metal compounds which have
n tested in the SHE, Salmonella, and some type of rodent bioassay, the SHE assay
92% concordant with rodent bioassay carcinogenicity
ults, including a sensitivity of 95% (21/22) and a specificity of 50% (1/2). At
s time, the measure of SHE assay specificity for rodent
cinogenicity of metals is limited by the paucity of metal compounds which are
ent noncarcinogens. The Salmonella assay results are only 33%
cordant with the rodent bioassay for these same chemicals. This relatively high
cordance between the SHE assay and the rodent bioassay
cinogenicity results demonstrates the utility of the SHE assay for determining
carcinogenic potential of heavy metal compounds in rodent cancer
assays.

iron Health Perspect 1996 Oct;104 Suppl 5:1011-1016

PACT and molecular structure in toxicity assessment: a prospective evaluation of
chemicals currently being tested for rodent carcinogenicity by the NCI/NTP.

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ew series of 30 miscellaneous National Toxicology Program chemicals has been
luated prospectively for carcinogenicity and overt toxicity by
PACT (Computer Optimised Molecular Parametric Analysis for Chemical Toxicity.
1A and CYP2E1). Evaluations were also made by
ardexpert, and for metal ion redox potentials; and these, together with COMPACT,
e compared with results from the Ames test for
agenicity in Salmonella, the micronucleus test, and 90-day subchronic rodent
iology. Seven of the 30 chemicals (nitromethane, chloroprene,
enesulphonic acid, furfuryl alcohol, anthraquinone, emodin, cinnamaldehyde) were

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positive for potential carcinogenicity in the COMPACT evaluation; xylenesulphonic acid and furfuryl alcohol were only equivocally positive. Four of the 30 chemicals-scopolamine, D&C Yellow No. 11, citral, cinnamaldehyde-were positive by Hazardexpert; 6 of 30-D&C Yellow No. 11, 1-chloro-2-propanol, anthraquinone, emodin, sodium nitrite, cinnamaldehyde-were positive in the Ames test; 2 of 30-phenolphthalein and emodin-were positive in the in vivo cytogenetics test; and 3 of 30-molybdenum trioxide, gallium arsenide, vanadium pentoxide-were metal compounds with redox potentials of the metal/metal ion indicative of possible carcinogenicity. The overall prediction for carcinogenicity was positive for 12 of 30 chemicals: nitromethane, chloroprene, D&C Yellow No. 11, molybdenum trioxide, 1-chloro-2-propanol, furfuryl alcohol, gallium arsenide, anthraquinone, emodin, sodium nitrite, cinnamaldehyde, vanadium pentoxide). This overall prediction has been made on the basis of the results of the computer tests and from consideration of the information from bacterial mutagenicity, together with likely lipid solubility and pathways of metabolism and elimination.

Fundam Appl Toxicol 1996 Oct;33(2):254-263

Pulmonary immunotoxicity of inhaled ammonium metavanadate in Fisher 344 rats.

Cohen MD, Yang Z, Zelikoff JT, Schlesinger RB

Department of Environmental Medicine, New York University Medical Center, Tuxedo 10987, USA.

Male Fisher 344 rats were exposed to 2 mg vanadium(V)/m3 (as ammonium metavanadate NH4VO3, 0.32 micron MMD) atmospheres for 8 hr/day for 4 days in a nose-only exposure system. In exposed rats, lung V burdens increased in a time-dependent fashion. Analysis of lung cells and lavage fluid 24 hr after the final exposure suggested that tissue damage and a strong inflammatory response was elicited; numbers of neutrophil and small macrophages (Mo), as well as levels of lavageable protein and lactate dehydrogenase, were significantly elevated as compared with levels observed with air-exposed rats. Vanadium also affected pulmonary alveolar Mo (PAM) capacities to produce and respond to immunoregulating cytokines. Inducible PAM production of tumor necrosis factor-alpha was significantly inhibited, as was the ability to increase cell surface Class II/I-A molecule expression in response to interferon-gamma (IFN gamma). PAM from V-exposed hosts were also inhibited in their ability to be primed by IFN gamma to produce superoxide anion and hydrogen peroxide in response to stimulation with opsonized zymosan. These studies indicate that short-term repeated exposure of rats to atmospheric V, at levels encountered in an occupational setting, can alter host pulmonary immunomocompetence, with one major effect occurring at the level of cytokine-related functions. These alterations may be underlying mechanisms for the well-documented increases in bronchopulmonary infections and cancers in workers chronically exposed to V-containing atmospheres.

From:
To:
Subject:

===NOTE===

Experientia 1996 Aug 15;52(8):778-785

Induction of vanadium accumulation and nuclear sequestration causing cell suicide in
human Chang liver cells.

Sit KH, Paramanantham R, Bay BH, Wong KP, Thong P, Watt F

Department of Anatomy, National University of Singapore, Kent Ridge, Singapore.

Very little is known about the modulation of vanadium accumulation in cells, although this ultratrace element has long been seen as an essential nutrient in lower life forms, but not necessarily in humans where factors modulating cellular uptake of vanadium seem unclear. Using nuclear microscopy, which is capable of the direct evaluation of free and bound (total) elemental concentrations of single cells we show here that an NH4Cl acidification prepulse causes distinctive accumulation of vanadium (free and bound) in human Chang liver cells, concentrating particularly in the nucleus. Vanadium loaded with acidification but leaked away with realkalinization, suggests proton-dependent loading. Vanadyl(4), the oxidative state of intracellular vanadium ions, is known to be a potent source of hydroxyl free radicals (OH). The high oxidative state of nuclei after induction of vanadyl(4) loading was shown by the redox indicator methylene blue, suggesting direct oxidative damage to nuclear DNA. Flow cytometric evaluation of cell cycle phase-specific DNA composition showed degradation of both 2N and 4N DNA phases in G1, S and G2/M cell cycle profiles to a solitary IN DNA peak, in a dose-dependent manner, effective from micromolar vanadyl(4) levels. This trend was reproduced with micrococcal nuclease digestion in a time response, supporting the notion of DNA fragmentation effects. Several other approaches confirmed fragmentation occurring in virtually all cells after 4mM V(4) loading. Ultrastructural profiles showed various stages of autophagic autodigestion and well defined plasma membrane outlines, consistent with programmed cell death but not with necrotic cell death. Direct intranuclear oxidative damage seemed associated with the induction of mass suicide in these human Chang liver cells following vanadium loading and nuclear sequestration.

Reprod Toxicol 1996 May;10(3):175-182

Vanadium: a review of the reproductive and developmental toxicity.

Domingo JL

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While the essentiality of vanadium for living organisms has yet to be established with certainty, vanadium has become an increasingly important environmental metal. Moreover, in recent years pharmacological interest in vanadium has also increased because of the hypothetical utilization of oral vanadium as an alternative therapy to parenteral insulin in diabetic patients. Adverse effects of vanadium depend on the circulating levels of this

element. Among those effects, it is now well established that vanadate (V+5) and vanadyl (V+4) may be reproductive and developmental toxicants in mammals. Decreased fertility, embryolethality, fetotoxicity, and teratogenicity have been reported to occur in rats, mice, and hamsters following vanadium exposure. The reproductive vanadium toxicity, the maternal and embryo/fetal toxicity of this trace element, the perinatal and postnatal effects of vanadium, as well as the prevention by chelating agents of vanadium-induced developmental toxicity are reviewed here. The developmental effects of vanadium in pregnant diabetic rats are also summarized.

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Bioaccumulation of vanadium and other trace metals in livers of Alaskan cetaceans and pinnipeds.

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Concentrations for 38 elements are routinely measured in the marine mammal liver tissues archived in the National Biomonitoring Specimen Bank (NBSB). Results show that hepatic concentrations of vanadium, selenium, silver, cadmium, and mercury are positively correlated with age for beluga whales (Delphinapterus leucas) and of vanadium, selenium, cadmium, and mercury with length for ringed seals (Phoca hispada). Many researchers have reported linear correlations of hepatic selenium, cadmium, and mercury with marine mammal age; however, there is only one other report of a linear correlation of hepatic vanadium with marine mammal age. Vanadium levels are at or below detection limits (< or = 0.01 micrograms/g) in liver tissues of U.S. east coast marine mammals from the NBSB but are present at levels ranging from 0.02 to 1.2 micrograms/g of wet weight in the tissues of Alaskan marine mammals. Although only three bearded seal (Eriganthus barbatus) and three bow-head whale (Balaena mysticetus) liver samples have been analyzed, hepatic vanadium levels also increased with animal size for these species. The presence of relatively high levels of vanadium in the livers of these Alaskan animals may reflect a unique dietary source of vanadium, a unique geochemical source of vanadium, or anthropogenic input to the Alaskan marine environment.

oxicol Appl Pharmacol 1996 May;138(1):110-120

Vanadium affects macrophage interferon-gamma-binding and -inducible responses.

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Mouse WEHI-3 cells were exposed overnight to vanadium [V; ammonium metavanadate (NH4VO3) or vanadium pentoxide (V2O5)] to determine whether documented V-induced immunomodulation might arise from altered macrophage (M phi) interactions with interferon-gamma (IFN gamma) or altered IFN gamma-inducible responses. Binding studies performed at 22 degrees C indicated that although NH4VO3-pretreated cells had approximately 48% fewer actively-binding Class I IFN gamma receptors, binding affinities were 1.5-fold greater than that of control cell receptors; Class II expression was unaffected but affinities were reduced 2-fold. Postbinding IFN gamma-receptor complex internalization was unaffected by V

pretreatment. Spontaneous production of both hydrogen peroxide and superoxide anion was significantly increased by treatment with both V compounds. Total hydrogen peroxide and superoxide production was increased by stimulation of IFN gamma-primed cells with zymosan, but relative increases in primed V-treated cells were lower than that in controls. Vanadium-treated cells also displayed decreased rates of IFN gamma-induced changes in [Ca2+]i levels secondary to increased resting [Ca2+]i levels. Although V-treated cells did not display significant increases in I-A expression after IFN gamma treatment, increased numbers of I-A+ cells (irrespective of priming) and lower maximal antigen densities than observed on I-A+ control cells were evident. Results from this study show that V exposure may produce alterations in M phi-mediated functions, in part, by modifying cell interactions with IFN gamma and subsequent IFN gamma-dependent functional parameters.

Vanadium-induced chemokine mRNA expression and pulmonary inflammation.

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Occupational exposure to vanadium is common in petrochemical, mining, steel, and utilities industries and results in toxic effects largely confined to the respiratory system. Vanadium exposure has been associated with inflammatory changes in the upper and lower respiratory tracts in addition to changes in pulmonary function. We investigated the abilities of several vanadium compounds to increase mRNA levels for selected cytokines in bronchoalveolar lavage (BAL) cells and also to induce pulmonary inflammation. Rats (200-250 g) were intratracheally instill

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nonyl phenols - see p 3
see PAH also

Health, Hormonal, and Reproductive Effects of Endocrine-Disrupting Chemicals in the Food Chain: Dioxins, PCBs, Other Organochlorine Chemicals,etc.- Summary of Health Effects, Incidence, Areas Affected, and Sources (07-1-96)

Large quantities of endocrine system disrupting chemicals that have adverse effects on the hormonal and reproductive systems of animals and humans have been released into the environment since WWII and are accumulating in the food chain, animals, and humans. These chemicals have been found to act as estrogens, anti-estrogens, androgens, anti-androgens,or to interfere with thyroid hormone, cortisol, insulin, or growth regulators. Evidence that they are having widespread catastrophic effects on wildlife and domestic animals is growing, and serious widespread effects on humans are now also being seen.

TCDD dioxin is the most toxic of a class of organochlorine chemicals including chlorinated dibenzo-p-dioxins(CDDs),dibinzofurans(CDFs), polychlorinated biphenals(PCBs), brominated dibenzo-p-dioxins(BDDs), brominated dibenzofurans(BDFs), and polychlorinated pesticides. This group have been found to have hormonal effects that disrupt the endocrine system of wildlife and humans resulting in adverse effects on reproductive system development and hormones, fetal development, and the immune system at extremely low levels of exposure (10,11,12,32). Dioxins have been found to have both estrogenic and antiestrogenic effects depending on the organ or tissue affected. The toxic metals mercury, lead, and cadmium as well as phenols have also been found to have reproductive and endocrine system disrupting effects(10,11,12,32). Exposure to relatively low levels of these chemicals have been documented to have had catastrophic effects on populations of Beluga whales, alligators, turtles, mink, otters, bald eagles, osprey, cormorants, terns, herring gulls, migratory birds, chickens, lake trout, chinook and coho salmon, etc. throughout the U.S. and Canada (5,6,7,8,9,10,11,12,32,34).

Animals and human fetal development is dependent on hormonal levels at various phases of development and the endocrine, reproductive, neurological, and immune systems are all being impacted, often seriously or catastrophically.

These chemicals are being found to have estrogenic effects(10) and/or antiandrogenic effects(48,49,50) on the hormonal/endocrine systems of fish, birds, and animals- resulting in effects at very low levels on the male and female reproductive organs and systems (9,10,12,32,34). Some of the effects are immediate and acute, but other effects are less obvious and are not recognized until years later or in the next generation. Male animals and humans in industrial countries appear to be becoming feminized through exposure to these estrogenic and antiandrogenic chemicals. Estrogenic chemicals cause cells to produce surplus levels of estrogen, which has been linked to breast cancer, testicular cancer, lowered sperm counts, and malformation/mutations of male sex organs(63,29,31). Studies have found that the combined synergistic effects of such estrogenic organochlorine chemicals such as endosulfan, dieldrin, toxaphene, and chlordane are much stronger than would be expected(63). The combined estrogenic effect of combinations of these chemicals was found to be as much as 500 to 1000 times as much as simply adding the effects of individual chemicals. Similar synergistic estrogenic effects were observed when small levels of estrogenic pesticides were combined with 2 types of PCBs(84).

The widespread effects observed in wildlife found to have accumulated these chemicals have now been confirmed in experimental animal studies, and a long list of additional chemicals that have estrogenic effects have been identified. Table 1 gives a list of 46 chemicals documented to have serious endocrine system disrupting effects- including 27 insecticides or fungicides, 8 herbicides, 3 toxic metals, and 7 industrial chemicals or by products(10). Very low levels of these chemicals are required to produce reproductive problems, birth defects, and development problems compared to even the low levels found to produce cancer. For example only 60 parts per billion(ppb) of DDE are required to cause antiandrogenic effects on male test animals. Lake Apopka alligators and many other populations including people have been found to have much higher levels.

(1)

DDT is still a widely used chemical throughout the developing world and is dispersed all over the world by atmospheric and oceanic transport. Low levels of vinclozolin, a widely used fungicide, have similar anti-androgenic effects(49), and even lower levels of TCDD have endocrine disrupting effects on animals. The herbicide atrazine similarly blocks testosterone binding(87), and another group of common pesticides, pyrethrins, also have been found to have anti-androgenic effects(83) and to be the likely cause of enlarged breasts in men in some populations such as one in Haiti in 1981.

Health Effects of Dioxins and Related Chemicals

Dioxin is the most acutely toxic chemical and the most potent carcinogen ever tested according to the U.S. Center for Disease Control(5,9). Dioxin causes cancer, birth defects, learning disabilities, endometriosis, depression and behavioral problems, lower sperm counts and other sexual abnormalities, atherosclerosis and heart disease, and damage to the immune system, endocrine system, liver, skin, and neuromuscular system(1,2,3,4,9,10,11,29,32,36,37,38,45). Industrial pesticide plant workers exposed to dioxin have been found to be more than 3 times as likely to die from cancer and more than 2.5 times as likely to die from ischemic heart disease as workers of similar characteristics working in a nearby gas plant(61). And the risk of dying was found to be dose related- increasing directly with increased exposure to dioxins and furans.

Dioxin along with other related organochlorine chemicals are very widespread in the environment and food chain in all areas of the country and is found in the blood, semen, breast milk, and fatty tissues of humans throughout the country (1,11,26,33,38). Infants receive the highest dose and are also the most vulnerable(11,33). Large numbers of people are being adversely affected by dioxins and other members of its chemical family, and very small levels of dioxin cause serious adverse health effects. Dioxin is still found in the bodies and sperm of Vietnam veterans 20 years after exposure(average of 49 ppt in 1987 compared to 5 ppt for controls), and Vietnam veterans children have experienced much higher levels of birth defects and learning disabilities than normal(4,11). Furans, PCBs, DDT/DDE, and other organochlorine pesticides such as endosulfan, methoxychlor, dicofol, and lindane have also been shown to be endocrine-disrupting chemicals that have health effects and adverse reproductive impacts on wildlife similar to dioxins(1,10,11,12,82,85). Polyaromatic hydrocarbons(PAHs) and toxic metals like mercury, cadmium, and lead also are highly neurotoxic and strong cancer promoters- in addition to being endocrine-system disrupting chemicals(1,10).

Effects of Organochlorines and Other Endocrine-disrupters on Wildlife and Animals

Studies(5,6,7,8,9,10,11,12,32,45,46,51) have found organochlorine chemicals to be the cause of widespread catastrophic effects on wildlife including:

(1) egg shell thinning, deformities and high mortality in birds and eagles of the Great Lakes area, West Coast, New England, Florida, etc.
(2) abnormal thyroid function in fish and birds of the Great Lakes area.
(3) abnormal hormone levels in birds, alligators, and mammals in the Great Lakes area, Florida, etc.
(4) decreased fertility in birds, fish, shellfish, otters, and minks in the Great Lakes area, west coast, Florida, etc.
(5) emasculation and feminization of male fish, birds, turtles, alligators, otters, minks, and panthers in the Great Lakes area, Florida, west coast, Europe, etc.
(6) defeminization and masculation of female fish, gastropods, turtles, birds, and mammals in the Great Lakes area, Florida, west coast, Europe, etc.
(7) alteration of immune function in birds and mammals of the Great Lakes area
(8) birth defects and high infant mortality in mammals of the Great Lakes area
(9) behavioral changes in birds of the Great Lakes and west coast areas
(10) abnormal sex organs and intersexed birds, turtles, alligators, sturgeon, etc. in the Great Lakes, west coast, Florida, Mississippi and Missouri Rivers, etc.
(11) low testosterone levels and undescended testes in alligators and

panthers in Florida

(12) strongly significant dose related relationship to endometriosis in monkeys.

(13) production of vitellogin, a female protein, by male fish living near sewer outfalls.

(14) doubled rate of testicular cancer and reproductive defects in military dogs used in Vietnam and their offspring.

Studies have found these chemicals to be the cause of large numbers of egg mortality, infant deformities, sexual abnormalities, and population decline among birds and fish eating animals in the Great Lakes area, Florida, Arkansas, Oregon, Canada, Great Britain, etc.(5,6,7,8,9,10,11,12,32). One type of deformity commonly caused among bird populations and in millions of commercially raised chickens exposed to low levels of dioxin or other dioxin-like chemicals is chick-edema disease, which causes twisted beaks, crooked legs, deformed claws and feathers, and other abnormalities(9). More than 50 horses and hundreds of birds, chickens, dogs, and cats died after a horse practice area was sprayed with oil contaminated with relatively low levels of dioxin at the Shenandoah Stables near Moscow Mills, Missouri(9).

The most extensive study of organochlorine related effects are the widespread cases of egg thinning, reproductive problems, and other health effects observed in the Great Lakes area as a result of DDT, PCBs, and dioxin levels for the last 3 decades. These effects have also been observed and studied in other more isolated cases. David Best of the U.S. Fish & Wildlife Service has been seeing increased deformities in eagles, high mortality, and reduced hatching rates(12). He indicates no successful reproduction in the Great Lakes area and that this area acts as a "black hole" for eagles migrating from other areas. He found eagle reproduction falls when PCBs in the body exceed 4 parts per million(ppm) or DDE levels exceeds 1 ppm. Much higher levels are common in the Great Lakes area, with PCBs in eggs found as high as 120 ppm. The levels of PCBs in Great Lakes fish has also been found to be the cause of reproductive system abnormalities and population declines in fish eating animals like otters and minks(12). PCBs have been found to cause developmental and reproductive effects on wildlife at levels similar to the average levels of PCBs found in human breast milk in industrial nations like the U.S.(34,46). PCBs have been shown to turn turtles that should have been males into "females" and females into feminized males at levels as low as 10 micrograms per egg. PCBs have also been found to interfere with transport of thyroid hormone which is necessary for normal growth and development(74). Higher levels of PCBs in breast milk were found to be correlated with lower levels of thyroid hormone in infants(76). A relationship has been demonstrated between decreased thyroid in infants and increased risk of neurological disorders. Humans are accumulating PCBs since they bioaccumulate and the food chain contains PCBs. Fish collected nationwide show PCB residues at a level of .53 ppm, and many marine species have levels thousands of times higher(72). Inuit mothers in the Arctic have extremely high levels of PCBs in their milk due to a diet high in fish(37).

T.M. Gross of the Univ. of Florida indicates PCBs appear to have synergistic effects with those of other estrogenic chemicals like dioxin, DDT, mercury, etc.(34) Dioxin has been found to have effects at extremely low levels(parts per trillion), but much less historic testing has been done for low levels of dioxin due to technical difficulty and expense. Some of the wildlife effects attributed to PCBs and DDT/DDE could have been contributed to by dioxins, though laboratory studies have confirmed each of these cause effects on animals of the types seen in wildlife at levels of the pollutants observed in wildlife.

Production of a female protein, vitelloginin, in males is turned on by estrogen and has a feminizing effect on the male reproductive system(77). Therefore vitellogenin production in males serves as a good marker for estrogenic chemical effects. Extremely high levels of vitelloginin and estrogen are being found in trout and carp in England, Wales, and other locations(51). The main sources appear to be ethynlestradiol(EE-the main estrogenic chemical in birth control pills) and nonylphenols, a breakdown chemical of alkylphenol

polyethoylates which are widely used in dishwashing fluids, paints, pesticides, plastics, food wraps,etc. The main source of these in streams in the U.S. and other industrial countries appears to be sewage effluent, but they are also found in food and drinking water(78). Lab studies on animals find reproductive systems effects at levels similar to current levels of human exposure.

Some of the Phthalates (plasticizers) which are the most widespread chemicals in the environment have also been found to be estrogenic, carcinogenic, and reproductive toxins in animal studies(51,79). The effects on the 2nd generation are more than on the generation exposed(79). While phthalates are found in fish in fresh or marine waters exposed to sewage, the most common human exposure is likely from food packaging where DBP levels of 50 to 500 micrograms/kg are common(80). Others include BHA(a commonly used food preservative), BBP, DEHP, and diphenyl phthalate. These and other xenoestrogens also stimulated the growth of breast cancer cells in culture, and a strong case has been developed by studies that such chemicals are a significant factor in the rapid increase in breast cancer that has been observed(47,51,86). DBP is widespread in insect repellents, plastic plumbing pipes, and plastic food wraps. BBP is found in adhesives and paper products used in food wrapping. BBP is often found in levels exceeding 45 mg per kg in butter and margarine(52). Another estrogenic chemical commonly found in food is bisphenol-A, which is leaching from plastic resins coating cans in supermarkets. About 50 % of cans surveyed had significant levels of BPA which has been shown to cause health problems(55). Beta-sitosterol, a phytoestrogenic chemical produced by tree bark and found in waters below paper mills, has been shown to affect the endocrine and reproductive systems of fish and animals below pulp plants(60). It has been found to significantly alter male and female reproductive hormones. Since sitosterol is found in the bark, much of this effect of pulp mills might be reduced by debarking pulp trees prior to grinding them up. However other chemicals which affect fish hormones such as dioxin are also found in pulp effluent. While some of the common phthalates of weakly estrogenic, they have also been found to have more adverse synergistic effects when combined with other chemicals found in the environment and food chain. For example, DEHP has been found to have synergistic effects with trichloroethylene and heptachlor for prenatal loss of fetus and maternal mortality in rats(81).

Organo Chlorines and Population Dieoffs of Marine Mammals

Catastrophic declines in mammals at the top of the marine food chain such as dolphins and seals throughout the world have been traced to buildup of these chemicals in fish and the animals at the top of the marine food chain(6,10). Fish in the North Sea and Baltic Sea have been found to have high levels of PCBs and dioxins, and a Dutch study found that seals eating fish from these areas have significantly damaged immune systems compared to seals eating less polluted fish. Over 20,000 harbor seals died in infectious epidemics in recent years(6).

Native groups eating these marine mammals have also been found to have high levels of PCBs and dioxins, and to have related health problems(27,37).

Organochlorines and Endocrine-disrupting Chemicals Effects in Florida

Florida is one of the states most at risk from organochlorine and endocrine-disrupting chemicals due to its large and growing population with much higher than average emissions and sources than most other states. Florida has the most incineration of any state(which is the number one source of dioxins and furans), and likewise has the highest per capita use of pesticides, herbicides, and fungicides, along with a large number of paper mills with dioxin in effluent. Widespread problems in wildlife populations in Florida related to such chemicals have already been documented. Little is known about the effects on humans in Florida as there has been virtually no testing of meat and dairy products, dioxin levels in humans or mother's milk, or of high risk populations as in some other states and countries where data is referenced.

Lake Apopka, Florida's 3rd largest lake, is polluted with organochlorine pesticides from a chemical spill of DDT and pesticide runoff from citrus farms and muck farms. Studies of bass, alligators, and turtles in Apopka found

population densities less than 10 % that of less polluted lakes(7,8,12), with sexual infertility and sexual abnormalities of males appearing to be the main cause. Both alligators and bass were found to have abnormally high levels of estrogen and males to have very low levels of testosterone and very small penises. This has resulted in very low levels of successful reproduction, with spermless males, intersexed gators with testes and ovaries, and gator eggs where 90% do not survive and the rest are sexual mutants(8,12,48). Dr. Guillette of the Univ. or Florida said that "if organochlorine chemicals are detrimental to embryos of other species, they are going to be detrimental to human embryos". Bass and other fish have also been found to be unable to reproduce and to be vanishing from other formerly highly productive Florida Lakes such as in the Ocklawaha chain of Central Florida(7). Like in Apopka, the cause of reproductive failure in the fish appears to be estrogenic effects of pesticides from runoff. The levels causing reproductive failure in fish and animals are more than 1000 times less than the level that current EPA standards for pesticide residues in food indicate is dangerous(7).

Similar findings have been seen in dioxin or organochlorine chemically contaminated fish and wildlife of the Great Lakes region, other areas throughout the U.S. and Canada, and in dioxin or pesticide contaminated Florida rivers (8,9,10,12,1). Animal studies have confirmed that PCBs have similar feminizing and sexual mutation effects, and that there are synergistic effects between different organochlorine congeners that produce effects at lower levels than for one toxic chemical alone(12,20). According to the U.S. EPA, there have been over 4000 listings of health bans or restrictions on eating fish due to food chain contamination in millions of lakes and rivers throughout the U.S., with over 30 states having such bans due to organochlorine chemical pollution(23 states including Florida with bans due to dioxin, 30 states for PCBs,& 26 states for pesticides).

In addition to seven Florida rivers and portions of St Andrew Bay and Perdido Bay that have been documented to be contaminated with dioxin, over 20,000 acres of St Joseph's bay have been found to be contaminated by dangerous levels of dioxin from 2.9 to 10.9 ppt in sediments of the bay(16). Dioxin was also found to be bioaccumulating in fish, crabs, and shellfish. The levels in bay sediments are similar to those in other areas studied where biomagnification occurred in adult cormorants, gulls, and mergansers to levels that caused birth defects and reproductive failure(16,19). A study of bioaccumulation of dioxin and PCBs in a bay in Lake Huron with sediment levels similar to those in St Josephs Bay found biomagnification occurred on a logarithmic scale as you go up the trophic food chain scale. The biomagnification at the fifth trophic level of fish eating birds was 31 times the sediment levels in TCDD-equivalence and 14.2 times for PCB levels. These levels resulted in widespread birth defects and reproductive failures. A non-viable bald eagle egg had even higher levels, 1065 ppb TCDD-Eq and 58.9 ppm PCBs. The source of the dioxin in St Josephs Bay is effluent from a pulp and paper mill. Due to the widespread contamination in the bay, which was one of the most pristine and productive fish, shellfish, and wildlife areas in Florida, the Fish & Wildlife Service has recommended that dioxin emissions into the bay should be eliminated by switching to a non-chlorine process that does not produce dioxins. They have also recommended more stringent controls on dioxin than currently exist in Florida. However these recommendations have not been approved by regulatory agencies.

In addition to the dioxins, other similar highly toxic and carcinogenic chlorinated organic chemicals have been found in the sediments of most bays and estuaries in Florida. A Dept. of Environmental Protection survey found polycyclic aromatic hydrocarbons(PAHs) in 70 percent of coastal sediments sampled, PCBs in 55% of sediments sampled, and chlorinated pesticides in 28% of sediments sampled(17). These chemicals have been identified in studies as being responsible for widespread fish cancer and fish disease by scientists who participated in a Congressional Hearing on "the fish cancer epidemic in the U.S."

In addition to bioaccumulation of toxic organic chemicals in fish and

shellfish, the levels of highly toxic contaminants in much of the sediments sampled have been found to be toxic to marine biota and fauna in the area with many dead zones or areas with greatly reduced diversity resulting(the number of species found in sampling was less than 5 at 17% of Gulf Coast sites). Florida Gulf Coast estuarine sediments were found to be at levels toxic to marine organisms in 20 percent of areas sampled in 1992(22), and PAHs exceeded the EPA ERL criterion (total PAH>4 ppm)in 14 % of the sediments. Pesticides such as dieldrin,endrin,chlordane, and DDE(ERL=2.2ppb) exceeded the EPA criteria in 23-32 percent of sediments(21,22), and heavy metals such as mercury, chromium,nickel,lead, and cadmium exceeded the standard in 11 to 22 percent of sediments. The Effects Range Low(ERL) is the concentration of a contaminant that is above 10% of the ranked contaminant levels that resulted in toxic effects. Along with the many dioxin congeners, PCBs, chlorinated PAHs and pesticides found in the sediments of Panama City Harbor in St Andrew Bay, elevated levels of toxic metals and sulfides were also found(19). The sediments were found to be toxic to bottom feeding amphipods.(PCB ERL=22.7ppb)

These chlorinated chemicals and toxic metals are also being found in fresh water sediments and are affecting fish and wildlife throughout Florida in drainage ponds, lakes, and other inland waters(41). Studies found widespread contamination of drainage ponds and lakes in Tallahassee and Orlando by PAHs and toxic metals from atmospheric deposition and runoff. In a survey of the Indian River Lagoon, PAHs were found to be up to 29.4 ppm with many sites above the ERL level and 2 sites above the AET level(22 ppm-level above which biological effects always occur)(24). PAHs are primarily the result of incomplete combustion of coal, oil, gas, and garbage. The Indian River survey also found phthalate esters from plasticizers and highly toxic levels of tributyltin to be widely distributed in the lagoon(24) and referenced studies that have also found PCBs and chlorinated pesticides in the system. Pesticides in rivers, lakes, and coastal areas come primarily from agricultural or lawn runoff.

Pyrogenic PAHs such as benzo(a)pyrene(ERL=.43ppm,dry weight) have been shown to be highly carcinogenic, mutagenic, and teratogenic to a wide variety of organisms (21,22,24,25,53), as well as estrogenic(51). PAHs are thought to be a major factor in the increased cancer rates found in industrial countries. In animal studies on mammals,PAHs have been shown to cause skin cancer, leukemia, breast cancer, lung cancer, lymph system cancer, and reproductive system cancers(25). They also cause cancers in fish and other marine organisms, along with causing high chick mortality and abnormalities in birds feeding in areas with high PAHs. PAHs have also been found to cause eye damage, cataracts, and reproductive toxicity(53).

PAHs are not very soluble and tend to concentrate in sediments, organic materials, and the plant or animal food chain. Aquatic invertebrates, fish, and amphibians collected in areas with high PAHs in sediments show elevated levels of tumors and disease(25). Lower molecular weight PAHs such as naphthalenes are more acutely toxic but less carcinogenic than the high molecular weight pyrogenic PAHs. Atmospheric emissions are responsible for at least 75% of pyrogenic PAHs in aquatic environments. The main sources of emissions are burning of organic materials in forest fires, incinerators, power plants, and home heating equipment. Car exhaust is a lesser but very widespread source as well. PAHs are found in plants grown in areas with high PAH deposition rates- in such cases fruits and vegetables may have up to 100 times normal levels.

Toxic metals like mercury and cadmium have high levels of emissions in Florida and have also been found to have estrogenic effects at very low levels(10). Mercury appears to be responsible for feminization and reproduction problems of panthers in Florida(12,40,NIEHS 29). In recent years 67% of male panther cubs born have had undescended testicles, low testosterone levels, abnormal sperm, and very high estrogen levels. Recent tests show some males have estrogen levels twice as high as testosterone levels and some females have higher testosterone levels than estrogen levels(12). Levels of mercury in

Florida are also sufficient to have contaminated lakes and bays in Florida to levels where fish in over half the lakes and streams tested have levels of mercury dangerous to wildlife or humans eating the fish, and where birds and panthers in South Florida are dying as a result of mercury levels in the fish(1,40). Panters eat racoons and other fish predators.

Organochlorine and Endocrine-disrupting Chemicals Effects on Humans

The first generation of humans widely exposed to synthetic chlorinated organic chemicals in the womb began reaching reproductive age in the 1970s. Lab experiments and studies of human exposures have demonstrated that exposures of fetuses to endocrine-disrupting chemicals can profoundly disturb organ differentiation and development of the endocrine, immune, neurological, and reproductive systems of the fetus(1,10,11,13,20,28,29,32). Many chemicals that have estrogenic effects that disrupt the endocrine system have been identified (see Table 1), as well as a large group of chemicals that affect the reproductive systems of male fish and animals through antiandrogenic effects (47,48,49,50).

Studies have found mother's pass hormone-mimicking chemicals to a fetus or child through blood before birth and through breast feeding after birth, with widespread serious consequences(10,29,31,33,38).

International data from industrial countries using thousands of men show average sperm densities have fallen over 40% along with an additional drop in sperm volume of 20% and increased sperm abnormalities in the last 50 years (over 50% decline in overall sperm counts) (10,29,31). The largest declines have been seen in urban areas. A study of sperm counts at a Paris sperm bank found a large decline of 33% in sperm density over the last 20 years in a group of men followed in a carefully controlled study, with the decline averaging over 2.5 % per year and an increase in abnormal sperm of 0.7% per year(NEJM,31). Researchers at Florida State Univ. reported similar findings(1). Occupational exposure to certain pesticides have been found to result in reduced sperm counts and infertility(65). There has been a more than 200% increase in male reproductive problems such as cryptorchidism(undescended testicles), hypospadias, abnormal sperm, and testicular cancer in the U.S. and England since 1969(10,29,31). In a group of London men, these problems were also accompanied by significant increases in sperm abnormalities including a twelvefold increase in the number of men producing mostly abnormal sperm in the 1980s compared to the 1970s(29).

A factor in this increase appears to be increased estrogenic chemicals in river drinking water in the London area. During this period there has also been a significant increase in breast cancer,testicular cancer, and prostrate cancer in the U.S., and an over 400% increase in ectopic pregnancies (outside the womb) and increased endometriosis in women. Follow up studies and laboratory animal studies have confirmed a relation of these conditions with hormone mimicking estrogenic chemicals such as DES, dioxin, PCBs, DDT, etc. which have been increasing widely distributed in the environment since the 1950s.

A strong case has been developed that xenoestrogens in the food chain are a major factor in the increase in breast cancer in the U.S. and industrial countries(51,86). 16-alpha-hydroxyestrone, a metabolite of the human estrogen estradiol, has been found to be strongly linked to breast cancer. Xenoestrogenic chemicals have been found to promote breast cancer by several mechanisms-including: promotion of the bad 16-alpha form of estrogen as opposed to the good 2-alpha form; binding to estrogen receptors and inducing proliferative signals to cells; generation of new blood vessels that aid tumor growth; damaging DNA. Corn oil and polyunsaturated or hydrogenated fats also appear to have such estrogenic effects, while indole-3-carlinol found in plants of the broccoli family and soy products retard cancer by favoring the 2-alpha form of estrogen(51). A synergistic effect of low levels of estrogenic chemicals has also been documented. Mixtures of low levels of organochlorine chemicals were found to cause a significantly greater proliferation of tumor cells than when exposed individually. This could also explain why the distribution of toxic-waste sites in the U.S. closely parallels the sites of highest breast cancer mortality(59) and increased birth defects().

Several populations of boys in Taiwan and Michigan have been monitored whose mothers were exposed to endocrine system disrupting chemicals such as dioxin and PCBs through contaminated rice oil and eating meat grown with contaminated feed or PCBs from Lake Michigan fish(10,11,75,88,96). These boys have developmental, psychomotor, and cognitive disfunction, along with reproductive system deformities and problems similar to some of the animal populations. The Michigan groups effects were found to be related in a dose-dependent manner to umbilical cord serum level. Another group whose mothers ate 2 to 3 fish per month from Lake Michigan prior to birth were found to have lower birthweight, growth retardation, low IQs, and cognitive, motor, and behavioral deficits compared to a control group. The group having high level of PCBs later was found to display disruptive and intractable behavior. The group with the highest prenatal exposure to PCBs had averge IQ 6 points below controls and other persistent harmful developmental effects(88). Other studies on children with prenatal exposure to PCBs or DDT/DDE have found similar neurological problems and learning disabilities(36,53,75,88),some in populations with no known special exposure. Studies indicate at least 5% of the babies born in the U.S. are exposed to quantities of PCBs sufficient to cause neurological effects, learning disabilities, and behavioral problems. According to EPA and other studies this is true for an even higher percentage due to toxic metals such as lead, mercury, and cadmium(1).

Another similar well documented case is the experience with DES(a synthetic estrogenic chemical used to prevent spontaneous abortions from 1948 to 1971). Daughters whose mothers took DES have been found to suffer reproductive organ disfunction, abnormal pregnancies, lowered fertility, immune system disorders, and depression(10). These effects are similar to those documented for animal populations with similar exposures to endocrine-disrupting chemicals.

The rate of depression and other similar neurological problems has increased substantially since 1945(54). In a given year approximately 13% of women and 6% of men suffer major depression in the 1990s(54), and over 20% of all U.S children have their learning ability adversely affected by endocrine system disrupting chemicals including toxic metals (62). Many of the organochlorine chemicals and toxic metals have been found to adversely affect the levels of brain neurotransmitter uptake of serotonin, dopamine, acetylcholine, and norepinephrine which control the brain and body's neurologic functions. Low levels of serotonin have been shown to result in depression, anger, anxiety, aggression, violence, insomnia, obesity, sexual deviance, and other impulse disorders(62).

EPA conducts an annual survey of chemicals building up in the adipose(fatty) tissue of humans autopsied throughout the U.S. and has found levels of dioxin and organochlorine chemicals found in scientific studies to cause serious harm to wildlife and humans(10,11,26). The average body burden in the U.S. is 9 parts per trillion(ppt), and the average dietary background exposure level of CDDs, CDFs, and PCBs is 200 to 400 picograms TEQ/ day (3 to 6 pg TEQ/ kilogram/day) (pico=1 trillionth). A group suffering from Chronic Fatigue Immune Dysfunction Syndrome was found to have significantly higher levels of orgaochlorine chemicals than a matched control group(57). The CFIDS group averaged 100% higher levels of DDT and hexachlorobenzen than the controls. They were also found to have a chemical in their blood similar in structure to pesticides and which appeared to have been caused by mutation of natural body bacteria. The breasts of Quebec area women with breast cancer and other groups of women with breast cancer have been found to have much higher levels of DDE than those without estrogen responsive cancer(37,51). There is now a strong case that estrogenic chemicals are a significant factor in the increase in hormone responsive cancers(1,51).

Relatively high concentrations of dioxins and furans have been documented in human milk in industrial countries such as those of Europe(33). The average daily dose of infants through breast milk is 60 pg TEQ/kg body weight/day- 10 to 20 times that of average adult exposure levels. In a recent study of infants with average dioxin levels in this general range, the infants were divided into a high exposure and low exposure group based on mother's blood level before birth(38). Total thyroxine and mean thyrotropin levels were somewhat higher at

birth for high exposure group infants than for the low exposure group, but were significantly higher at 11 weeks old after both groups were breast fed. Both prenatal and post natal exposures appear to produce abnormal thyroid hormone levels and affect thyroid system function. Thyroid system function has broad effects on developing infants. Studies have found that the timing of fetal exposures is as important to effects as the magnitude of the dose; very low maternal exposures in critical window periods of fetal development can catastrophic effects(66).

Scientific studies on animals have found as a result of dietary intake of dioxin-like compounds- at dietary intake of 1 to 1.5 parts per trillion: altered enzyme induction response and altered lymphocytes in mice(11); at dietary intake of 4 to 25 ppt: chloracne in rabbits, endometriosis and decreased object learning ability in monkeys, skin tumor promotion in mice, increased reproductive disorders in fetally exposed male rats, and immune system deficiency(enhanced viral susceptibility)(11,67); general inability of monkeys to produce viable offspring at 25-50ppt dietary intake(11,68); decreased fertility in mice at 100 ppt(69); physical birth defects in mice at 1-4 ppt(70); and lower testosterone levels in rats at 15 ppb(71) In terms of body burden of dioxin-like compounds studies found: altered enzyme induction, altered lymphocytes, and enhanced viral susceptibility in animals at body burdens of 7 ppt(11); decreased human testis size and altered glucose tolerance at 14 ppt(11), decreased monkey object learning ability at 19ppt body burden; mortality to lake trout eggs at 65 ppt, mortality to chicken embryo at 250 ppt egg wt, and mortality to rainbow trout embryos at 400 ppt(72). These study results and body burden information do not include the many other endocrine-disrupting or estrogenic chemicals not included in the EPA study of dioxin-like chemicals. Thus many are currently exposed to levels of endocrine-disrupting chemicals already proven to cause serious adverse effects.

The currently used EPA and DEP risk assessment for dioxin and dioxin-like chemicals has been found to be greatly flawed and inaccurate due to the use of 1970s fish consumption data(44.1 grams/week) and failure to take into account the high risk of children, pregnant women, and groups that consume more than average amount of fish such as Native Americans, sport fishermen's families, etc. (3,7,10,14). The average health risk from eating fish has more than quadrupled since the 1970s and is much higher for groups eating more than the average amount of fish. According to a state survey, Florida adults eat an average of 253 grams per week of fish and 69 grams per week of shellfish(23). Additionally the EPA risk assessment does not include the endocrine-disrupting and reproductive system effects on humans, domestic animals, and wildlife that have been widely documented. Similarly the EPA currently does not include any of the endocrine system mediated effects discussed in this paper or food chain source effects in air emission risk assessments used in setting air emission regulations- even though EPA scientists have pointed out that these effects that are not taken into account represent over 90% of health risk to humans(1,14,42,43).

Sources

The U.S. uses over 178 billion kilogram of synthetic organic chemicals per year(196 million tons), of which approx. 318 million kg is pesticides(35). The largest source of dioxins, furans, PCBs, PAHs, mercury, and cadmium is air emissions. Dioxins and furans are chlorinated pollutants that can form during combustion of materials containing chlorine or in several industrial activities(30). Approx. 90% of dioxins and furans are from air emissions, with incinerators and cement kilns being the largest sources(64,30,3,11,33). Total emissions are approx. 12,500 kg per year(64), with municipal incinerators responsible for approx. 28% of known emissions and cement kilns 25%. Incinerators have been found to produce from 514 to 5140 ng TEQ PCDD/DF gas emissions per ton of MSW(58). Likewise about 90 % of PCBs in the Great Lakes come from air emissions(34). PCBs historically were primarily used in electrical equipment.

According to the U.S. EPA, Minnesota Pollution Control Agency, and World

Health Organization, the main source of dioxins in humans are contaminated dairy and beef products, along with fish and other parts of the food chain contaminated by emissions from incinerators and other combustion of chlorine compounds (3,11,14,15,30,33,42,43). Widespread emissions containing large amounts of dioxins, mercury, cadmium and other toxics result from the over 6000 medical waste incinerators, municipal incinerators, hazardous waste incinerators, and sewer sludge incinerators. Significant portion of hospital waste are chlorine based plastics or compounds, MSW incinerators are the second largest source, and 40% of the waste burned in hazardous waste incinerators is chlorine compounds that produce large amounts of dioxin emissions.

The largest cause of dioxin emissions in incinerators is combustion of PVC plastics which are extremely widespread in building materials and hospital equipment(3,11). Burning 1 kilogram of PVC produces approx. 50 micrograms of dioxin. The large amounts of dioxin emissions in Europe and serious health effects have caused many European countries to phase out or reduce PVC usage in packaging and other applications. Some dairy farms in areas around incinerators have also had to be closed due to high levels of dioxins in the milk. In addition to dioxin emissions, combustion of PVC produces over 75 other toxic emissions including vinyl chloride, PCBs, chlorobenzene, benzene, hydrogen chloride, lead, cadmium, etc. HCl and other emissions cause acid rain, metal corrosion, and destruction of the ozone layer. Significant levels of dioxin is found in incinerator ash which has been found to produce dangerous levels of exposure to workman, in addition to the exposure to toxic metals in the ash. Workers and others exposed to ash or ash piles have had a high incidence of serious neurological problems. PVC feedstock plants also emit large amounts of dioxin with high cancer rates among workers and those living around the plant. Additionally the PVC in buildings causes many deaths or serious injuries from building fires that emit dioxins and other toxic gases.

While the majority of dioxins in the food chain including fish come from atmospheric sources, high dioxin or PCB levels are also found in fish in localized areas near industrial effluent sources such as pulp mills, where fish have been found to have dangerous levels of dioxin and reproductive abnormalities in 7 Florida rivers. Approx. 110 grams of dioxin is released by U.S. paper mills into rivers and steams each year. This is a small fraction of that released by incinerators according to EPA(30). Other sources of dioxins include incinerator ash, diesel vehicles, manufacturing of chlorine-rich chemicals, wood burning, and paper making(30).

Government Actions to Ban or Restrict Chlorinated Chemicals

Due to the growing and well documented serious health problems being seen in animal and human populations, many Government agencies, public health, and environmental organizations have called for phasing out or severely limiting the use of chlorinated chemicals(28,13). The International Joint Commission on the Great Lakes, the 1992 Paris Commission for the Prevention of Marine Pollution, and many U.S. or international environmental organizations have called for phasing out chlorinated chemicals. The Society of Environmental Toxicology and Chemistry has called for restricting or banning chlorinated chemicals that are highly toxic, persistent, and bioaccumulative. These include dioxins, furans, PCBs, and many chlorinated pesticides. The Canadian Government announced that Canada is moving aggressively to implement this policy. Germany and other European countries have placed severe restrictions on use of chlorinated chemicals and plastics such as PVC, Studies also show that use of chlorine dioxide by paper mills rather than chlorine for bleaching would greatly reduce dioxin emissions, as most European countries have done(30). In the U.S., the American Public Health Association has called for strict regulations and phaseout or cutbacks in all non-essential chlorinated chemicals, and the U.S. EPA has recommended examining chlorines impact on health and the environment- with the possible goals of banning or restricting it use.

A recent study has found that Trichlorophenols(TCPs) can be biodegraded in some situations by a combination of hydrogen peroxide and a catalyst (2,9,16,23-tetra sulfopha thalocyanine)(56).

References

(1) B.Windham, "Health Effects of Toxic Metals: Annotated Bibliography", 9-1-94.

(2) U.S. EPA, Hazardous Air Pollutants: Profiles of Noncancer Toxicity from Inhalation Exposures, EPA/600/R-93/142, 1993.

(3) Office of Technology Assessment, "Facing America's Trash, Whats Next for Municipal Solid Waste?", OTA-O-424, USGPO, 1989.

(4) Birth Defect/Learning Disability Registry, New Jersey Agent Orange Commission- Association of Birth Defect Children, Fall 1993; & J.D.Erickson et al, Journal of the American Medical Assoc., 252:903-912, 1984.

(5) B. Windham, "Health Effects of Pesticides: Annotated Bibliography", 6-1-95.

(6) Science News, Vol 146, July 1994, "Something's Fishy",p 8-9 & Study by Seal Rehabilitation and Research Centre and Netherlands National Institute of Health, in Science, Vol 266, Nov 18 1994, p1162.

(7) T.Gross & F.Perival(Univ. of Florida) &W.Johnson(Fla. Game & Freshwater Fish Commission), study reviewed in Science News, Vol 146, Aug 13, 1994; & L.J.Guillette et al,Environmental Health Perspectives, 102(8):680-688,1994; & Human and Ecological Risk Assessment, 1(2):25-36.

(8) Science News, 1-8-94, p145; & Tallahasse Democrat, 8-5-94 & "Lake Apopka: Gator sexual mutations likely caused by organochlorine chemicals" L.Guilette, Univ. of Florida, in Tallahassee Democrat, 8-29-94.

(9) "Dioxins Toll on Wildlife", National Wildlife, Aug/Sept, 1994, p4-12.

(10) Dr.T. Colborn(Ed.),Chemically Induced Alterations in Functional Development-The Wildlife,Human Connection , Princeton Scientific Press, 1992 & T. Colburn et al, "Developmental Effects of Endocrine-Disrupting Chemicals in Wildlife and Humans", Environmental Health Perspectives, Vol 101, No5, Oct 1993; & T.Colburn et al, "Environmentally Induced Alterations in Development, Environmental Health Perspectives, Supplement 4, May 1995.

(11) U.S. EPA, Health Assessment for 2,3,7,8-Tetrachlorodibenzo-p-dioxin and Related Compounds, Volume III, External Review Draft, August 1994(2000pages).
& L.S. Birnbaum, "The Mechanism of Dioxin Toxicity", Environmental Health Perspectives, 1994, Nov: 102, Suppl 9: 157-67.

(12) "Are Environmental Hormones Emasculating Wildlife", Science News, Volume 145 1994, p24-27 & "Another Emasculating Pesticide Found", Science News, Vol 146, 1994,p16 & Science News, 1-22-94,p56 & Science News, Vol 145, 1994,p27.

(13) International Joint Commission, Supplemental Information to the Seventh Biennial Report, 100 Avenue Ouellette, Windsor Ontario, 1994.

(14) Minnesota Pollution Control Agency, Supplemental Health Risk Assessment Technical Working Paper, Vol I: Dioxins/Furans, Wisconsin County Resource Recovery Facility Report, April 1988.

(15) World Health Organization, "PCDD & PCDF Emissions from Incinerators-Evaluation of Human Exposure", Copenhagen, 1987.

(16) G.A. Carmody et al, U.S. Fish and Wildlife Service, Preliminary Report on Dioxin Contamination in St Josepths Bay to U.S. Environmental Protection Agency, May 27, 1994

(17) Florida Dept. of Environmental Protection, Florida Coastal Sediment Contaminant Atlas, A Summary of Coastal Sediment Quality Surveys, 1994.
& E.R.Long et al, "Incidence of Adverse Biological Effects Within Ranges of Chemical Concentrations in Estuarine Sediments", Envir. Management, Vol 1(3)

(18) Batelle Marine Sciences Laboratory, "Ecological Evaluation of Proposed Dredged Material from St Andrew Bay", Batelle/Pacific Northwest Laboratory, October 1993.

(19) P.D. Jones et al, Biomagnification of Bioassay Derived TCDD-Dioxin Equivalents", U.S. Fish & Wildlife Service, July 1992.

(20) J.M. Bergeron et al, Environmental Health Perspectives, Sept 1994 & "Gender Bending PCBs", Science News, Volume 146, Oct 8, 1994, p239 & D.E.Tillet et al,"...PCBs..." Environ Toxicol Chem 11:1281-1288, 1992.

(21) U.S. EPA, Contaminated Sediments News, EPA-823-N94-003, September,1994.

(22) U.S. EPA, Environmental Monitoring and Assessment Program-Estuaries-Louisianian Province-1992 & 1991.

(23) Fla. Agricultural Market Research Center, Per Capita Fish and Shellfish

Consumption in Florida, Fla.Dept. of Environmental Protection, August 1994.
(24) J.G. Windsor & J.M. Surman, Toxic Substances Survey for the Indian River Lagoon System", Vol 2, Organic Chemicals, St Johns Water Mmgt Dist, 1993.
(25) J.M.Neff, "Polycyclic aromatic hydrocarbons", in Fundamentals of Aquatic Toxicology, Hemisphere Publishing Corp., New York, 1979, p416-454; & R. Eizler, "Polyaromatic Hydrocarbon Hazards to Fish, Wildlife, and Invertebrates", U.S. Fish & Wildlife Service, Contamination Hazard Reviews Biological Report 85(1.11), May 1987.
(26) U.S. EPA, Broadscan Analysis of Human Adipose Tissue, annual report, 1987 ... & M.J.DeVito et al, Environ Health Perspectives, 103(9): 820-831,1995.
(27) "Organochlorines lace Innuit breast milk", Science News, Vol 145, Feb 12, 1994 & P. Ayotte et al, Environmental Health Perspectives, Dec 1993, p618.
(28) "The Role of Chlorine and Its Future", Science News, Vol 145, June 1994, p59 & Science News, Vol 146, Sept 10, 1994, p56-59 & Science News, 1-22-94, p59.
(29) C.Chivers et al, "Apparent doubling of frequency of undescended testicles in England and Wales, 1962-1981",Lancet i:330-332, 1984; & M.B. Jackson et al, British Medical Journal, 293:1401-4,1986 +"The Epidemiology of Cryptorchidism", Hormone Research, Vol 30, 1988,p153-156; & Science News, Vol 145, Jan 22, 1994, p56-59; & A.Giwercman et al, Environ Health Persp 101(Sup2):1993 & Science News, 1-8-94, p 24; & Science News, 2-26-86, p264; & "Sperm changes linked to River Drinking Water", Science News, Vol 145, 1994, p142; & A.Giwercman et al, "The human testis: an organ at risk", International Journal of Andrology, vol 15, 1992; & A.Osterlind, "Trends in testicular cancer in Denmark", British J of Cancer, Vol 53, 1986, p501-503; & A.R. Moss et al, "Hormonal Risk Factors in in testicular cancer", American J of Epidemiology, Vol 124, 1986; & M.B. Jackson et al, "The Epidemiology of Cryptorchidism", Hormone Research, Vol 30, 1988; & J.Toppari et al, NIEHS, Envir. Health Perspectives, Vol 104, Supp 4, August 1996, p741-803.
(30) "Dioxins Dominate Denver Gathering of Toxicologists", Science, Vol 266, Nov 18, 1994, p1162 & Science News, Vol 146, p206.
(31) E.Carlsen et al, Brit Med Journal, 305:609-613, 1992; & Lancet,i:1311,1985. & J.Auger et al, "Decline in Sperm Quality Among Men in Paris", New England Journal of Medicine, Vol 232, Feb 2, 1995; & Science News, Vol 145, 1-22-94, p56; & C.M.K.Nelson, Fertil Steril, 25:503-7,1974 & J. Ginsberg et al, London's Royal Hospital School of Medicine, Lancet, 1994. & D.Rajpert et al, Eur Urol 23:54-61, 1993; & C.A. Kimmel, Environ Health Perspectives, 101(Suppl 2): 137-143,1993; & U.S. GAO, Reproductive and Developmental Toxicants, Washington D.C. 1993.
(32) "Dioxins are more than carcinogens", Vol 146, Sept 17, 1994, p181, & Science News, 1-11-92 & Science News, 11-27-93 & Science News, 1-8-94.
(33) WHO Environmental Health Series 34, "Levels of PCBs, PCDDs, and PCDFs in Breast Milk", World Health Organization, Copenhagen, 1989; & A.H.Smith, "Assessment of Infant Exposure to Dioxins in Breast Milk from Incineration Emissions", Risk Anal 7(3): 347-353,1987 .
(34) "Gender Bending PCBs", Science News, Vol 146, Oct 8,1994; & Science News, 1-22-94, p56; & Science News, Vol 145, 1994, p27; & Science News, Vol 146, p206; & J.M. Bergson, Environmental Health Perspectives, Sept 1994; & "PCB Hazards to Fish, Wildlife, and Invertebrates", U.S. Fish & Wildlife Service, Contamination Hazard Reviews Biological Report 85(1.7), 1987.
(35) Environmental Health Perspectives, Aug 1993, p215.
(36) J.L. Jocobson et al, "Effects of in utero exposure to PCBs on cognitive functioning in young children", Journal of Pediatrics, Vol 116, 1990, p38-45 & W.J. Rogan et al, "Neonatal effects of transplacental exposure to PCBs or DDE", Journal of Pediatrics, Vol 109, 1986, p335-341.
(37) E. Dewailly et al, Journal of the American Cancer Institute, Feb 2, 1994; & Environ Health Perspective, 101:618-620, 1993.
(38) J.P. Hendricks et al, "Effects of Pre- and Postnatal Exposure to Chlorinated Dioxins and Rurans on Human Neonatal Thyroid Hormone Concentrations", Environmental Health Perspectives, Vol 101, No 6, Nov 1993, p504-508.
(39) H.A. Tilson et al, "PCBs and the developing nervous system", Neurotoxicology and Teratology, Vol 12, 1990.(at U.of Fla.)

(40) "Mercury found in dead Florida Bay cormorants",Tallahassee Democrat, 1-5-95.
(41) "Troubled Water: Many Question Drainage Ponds' Impact on Toxins", Wall Street Journal, 1-18-95 & "Are we poisoning our lakes?",Tallahassee Democrat, Dec 11, 1994.
(42)M. Lorber et al, U.S. EPA Office of Research and Development, Exposure Assessment Group, "Screening estimate of indirect impacts from the Columbus, Ohio incinerator", August, 19, 1994.
(43) W. Farland et al, U.S. EPA Office of Research and Development, "Screening Analysis for WTI Incinerator", Washington D C, March 8, 1993.
(44) Representative John Breaux, Chairman of U.S. House Committee on Fisheries, Committee Meeting on the "Fish Cancer Epidemic in the U.S."
(45) Endometriosis Association, Milwaukee, Wisconsin,1995. (414-355-2200)
(46) Canadian Dept. of Health and Welfare, 1985, from (45).
(47) Science News, 7-3-93, p10 & 7-15-95, p44 & 5-12-90, p303.
(48) Science News, 1-8-94 & 7-15-95,p44.
(49) W.R. Kelce & L.E. Gray, EPA, Science News, 7-2-94,p15 & 7-15-95, p45 & W.R. Kelce et al, EPA, Nature, 375:581-585,June 15, 1995; & L.E.Gray et al, Biol Reprod.48(suppl1): p97,1993.
(50) W.R. Kelce et al, Toxicology and Applied Pharmacology, March 1995 & Science News, 7-15-95, p46.
(51) S.Jobling et al, Environmental Health Perspectives, 103(6):582- , 1995 & R.E. Menzer, Casarett and Doull's Toxicology, 4th ed., McGraw-Hill, 1991; & Science News, 7-15-95, p47 & D.L. Davis et al, "Can Environmental Estrogens Cause Breast Cancer?" Scientific American, October, 1995, p166-
(52) Danish Environmental Protection Agency, "Male Reproductive Health and Environmental Chemicals with Estrogenic Effects", Copenhagen, Denmark, 1995.
(53) U.S. EPA, Hazardous Air Pollutant Hazard Summary Fact Sheets, In Risk Information System, 1995.
(54) M.N.Weissman, Columbia Univ., Science News, 12-5-92, p391.
(55) N. Olea et al, Environmental Health Perspectives, June, 1995.
(56) Science News, 5-27-95.
(57) T. Roberts t al, Newcastle Univ., ABDC News, Vol 25, No. 4, 1995.
(58) P. Dyke et al, ETSU, AEA Technology, "PCDD/PCDF Releases from Various Waste Manangement Strategies", Warmer Bulletin 46 (UK), August 1995, p22-23.
(59) Scientific American, October 1995, p32.
(60) D.L. McLatchy et al, Toxicology & Applied Pharmacology, Oct 1995; & Science News, Vol 148, Nov 4, 1995, p295; & M.E. McMaster et al, Ecotoxicol Environ Safety 23:103-117,1992.
(61) D. Flesch, American Journal of Epidemiology, Dec 1, 1995; & Science News, Vol 148, Dec 9, 1995, p399; & Science News, 9-4-93, p149.
(62) Science News, Sept 13, 1986, p164; & NRDC Newsline, April, 1991; and Science News,Vol 149, Feb 10, 1996; & H.L. Needleman,Journal of American Medical Association, Feb 7, 1996; & R.L. Siblerud et al, Psychological Reports, 74, p67-80, 1994..
(63) J. McLachlan,S.K.Arnold, et al, Science, June 7,1996, 272:1489-1492.
(64) L.P.Brzusy et al, Environmental Science & Technology, June, 1996.
(65) P.S. Larson et al, Toxicol Appl Pharmacol, 48:29-41, 1979.
(66) L.A. Couture et al, Teratology, 42: 619-627, 1990; & T.A. Mably et al, Toxicol Appl Pharmacol 114: 108-117, 1992.
(67) S.E.Rier et al, Fund Appl Toxicol 21:433-441, 1993; & T.A. Mably et al, Toxicology and Applied Pharmacology, Vol 114, May 1992, p118-126..
(68) J.R. Allen et al, Ann NY Acadamy Sci, 320:419-425, 1979; & D.S. Barsotti et al, Bull. Environ. Contam Toxicol. 21:463-469, 1979.
(69) F.J.Murray et al, Toxicol Appl Pharmacol 50:241-252, 1979.
(70) H.Weber et al, Toxicol Letters, 26:159-167,1985.
(71) R.W.Moore et al, Toxicol Appl Pharmacol 109:85-97, 1991.
(72) J.B. Grieg et al, Food Cosmet Toxicol 11:585-595, 1973.
(73) C.J. Schmitt et al, National Pesticide Monitoring Program, Arch Environ Contam Toxicol, 14:225-260, 1985; & Leifer et al, EPA-560/83-025, 1983;
(74) J.D. McKinney et al, Environ Health Perspect 102(3): 290-297, 1994.
(75) CC Hsu et al, Chemosphere, 1991; & J.L. Jacobson et al, (Lake Michigan)

Journal of Pediatrics, 116(1): 38-45, 1990; & M.S.Golub et al, (...PCBs-

N. Carolina:neurobehavioral effects), Environ Health Persp 103(S2):1995,151-
(76) D.C.Morse et al, Pediatric Research 36: 468-473, 1994; & J.H. Kok et al, Pediatr Res 39:142-145, 1996.
(77) C.E. Purdom et al, Chem Ecol, 8:275-285, 1994; & R.M.Sharpe et al, Lancet, 1993,341:1392-; & Environmental Health Perspectives, 103(12): 1136-1143, 1995.
(78) R.White et al, (alkylphenolic estrogenic compounds), Endocrinology, 135(1): 175-82,1994; & L.B.Clark et al, Intern J Environ Anal Chem 47:167-180,1992; & G.A. Junk et al, Environ Sci Technol 8:1100-1106, 1974.
(79) S.Jobling et al, Environ Health Perspectives, 103(6): 582-587, 1995; & D.K.Gulati et al, NTIS Technical Report/PB92-111996, Sept 1991(279pp).
(80) ATSDR, Toxicological Profile of DBP, Atlanta, Ga., 1991.
(81) M.G. Narotsky et al, Fund Appl Toxicol 27:203-216, 1995.
(82) P.S.Guzelian, (chlordecone), Annu Rev Pharmacol Toxicol 22:89-113,1982.

(83) M.J.Ronis et al, Abstracts of the 13th International Neurotoxicology Conference, Hot Springs, Ark., 1995,p16- & C. Eil et al, J Steroid Biochem 35(3-4): 409-414, 1990.
(84) A.M.Soto et al, Environmental Health Perspectives, 102:380-383, 1994.
(85) P.S.Cooke et al, Biol Repro 42(3)573-583; & L.E. Gray et al, Toxicol Appl Pharmacol, 96(3): 525-540; & L.E.Gray et al, Fund Appl Toxicol,12(1):92-108.
(86) M.S.Wolff et al, J.National Cancer Inst, 85(8):648-652,1993; & H.Mussslo et al, Cancer, 66:2124-2128,1990; & F. Falck et al, Arch Env Health, 47(2): 143-146,1992.
(87) J.Kniewald et al, J Appl Toxicol 15(3): 215-218, 1995.
(88) J.L.Jacobson et al, "Intelectual Impairment in children exposed to PCBs in Utero", New England Journal of Medicine, V 335, Sept, 1996, p783- .
(89) L.Crpem et al, Epidemiology, July 1997 & Science News, Vol 151, 6-21-97.

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