350 YEARS OF AIR POLLUTION: WHAT WE THINK WE KNOW AND WHAT WE DON'T.

Anthony Seaton

JOHN EVELYN AND FUMIFUGIUM (1661)

A PLEA TO KING CHARLES II

FUMIFUGIUM:

OR,

The Inconvenience of the AER,

AND

SMOAKE of LONDON

DISSIPATED

TOGETHER

With some REMEDIES humbly proposed

By John Evelyn Esq;

To His Sacred MAJESTIE,

AND

To the PARLIAMENT now Assembled.

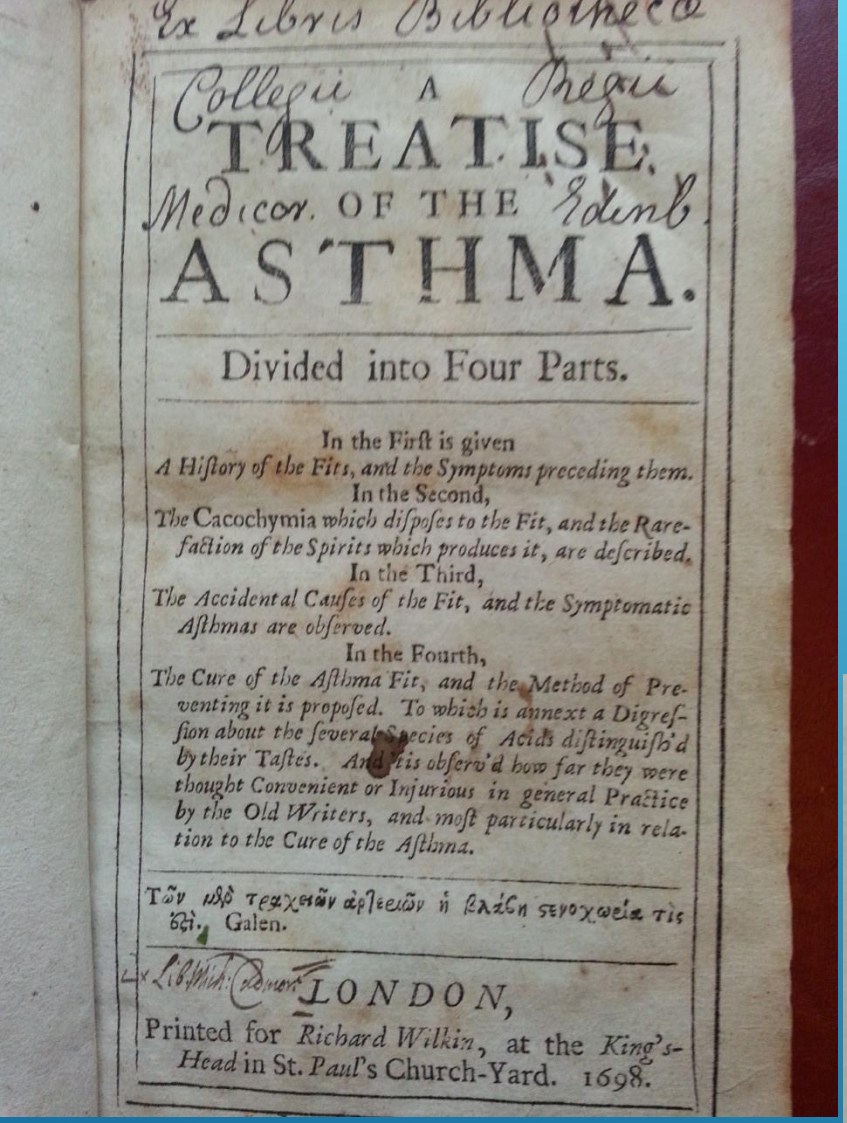
Published by His Majesty's Command.

Lucret. l. 5.

Carbonumque gravis vis, auque odor insinuatur.
Quam facile in Cerebrum?——

SIR JOHN FLOYER
1649-1734

A TREATISE OF THE ASTHMA
1698



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TREATISE

Medicor. OF THE Edinb.

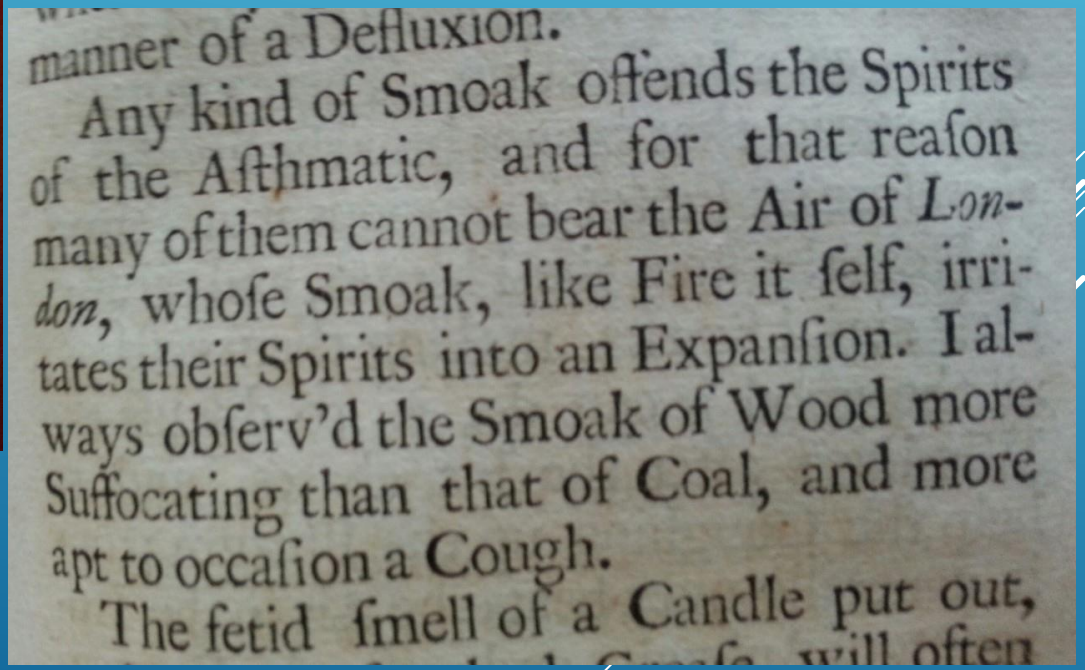
ASTHMA.

Divided into Four Parts.

In the First is given
A History of the Fits, and the Symptoms preceding them.
In the Second,
The Cacochymia *which disposes to the Fit, and the Rarefaction of the Spirits which produces it, are described.*
In the Third,
The Accidental Causes of the Fit, and the Symptomatic Asthmas are observed.
In the Fourth,
The Cure of the Asthma Fit, and the Method of Preventing it is proposed. To which is annext a Digression about the several Species of Acids distinguish'd by their Tastes. And 'tis observ'd how far they were thought Convenient or Injurious in general Practice by the Old Writers, and most particularly in relation to the Cure of the Asthma.

Τῶν ὑπὸ τραχείαν ἀρτηρίαν ἡ βλάβη στενοχωρίαν τίς ἐστι. Galen.

LONDON,
Printed for *Richard Wilkin*, at the *King's-Head* in St. *Paul's* Church-Yard. 1698.

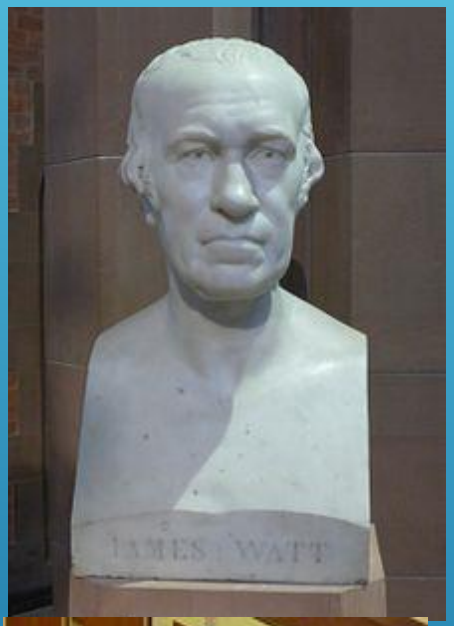


manner of a Defluxion.

Any kind of Smoak offends the Spirits of the Asthmatic, and for that reason many of them cannot bear the Air of *London*, whose Smoak, like Fire it self, irritates their Spirits into an Expansion. I always observ'd the Smoak of Wood more Suffocating than that of Coal, and more apt to occasion a Cough.

The fetid smell of a Candle put out, will often

GLASGOW 1776 – THE YEAR THE WORLD CHANGED



- James Watt and his improved steam engine

- Adam Smith and The Wealth of Nations

CLAUDE MONET
THE HOUSES OF PARLIAMENT
1904

LONDON SMOG

TRAFALGAR SQUARE
NOON, DECEMBER 1952

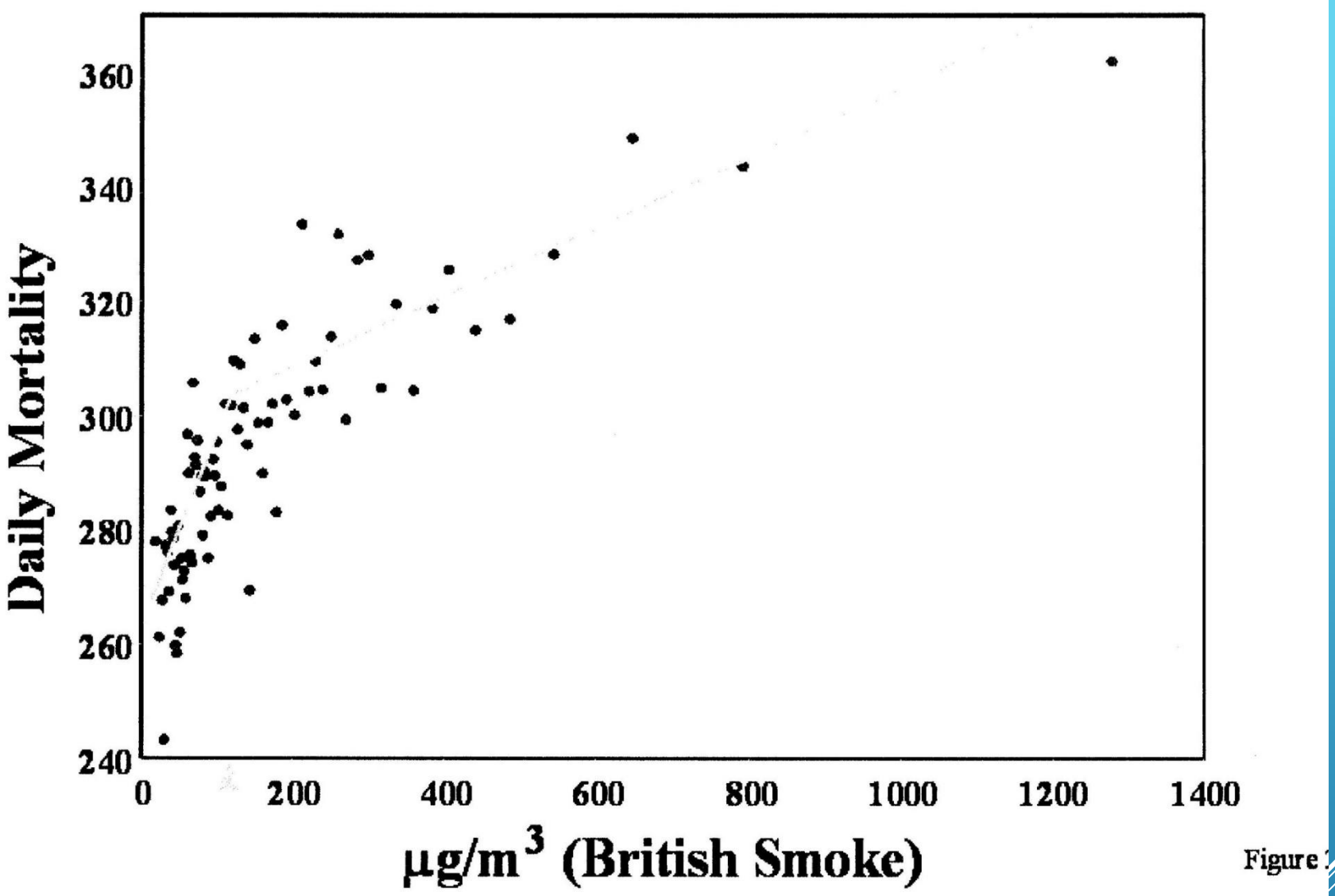
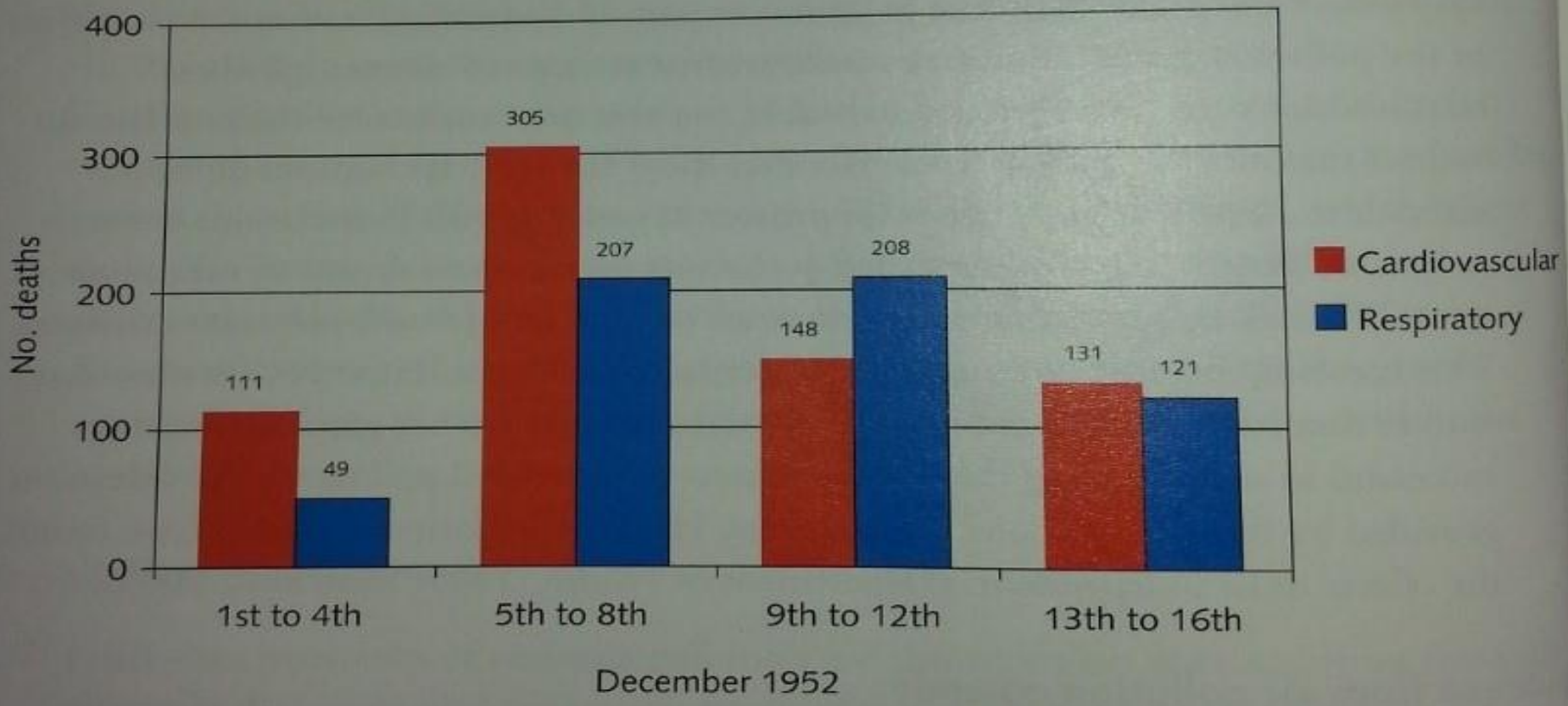


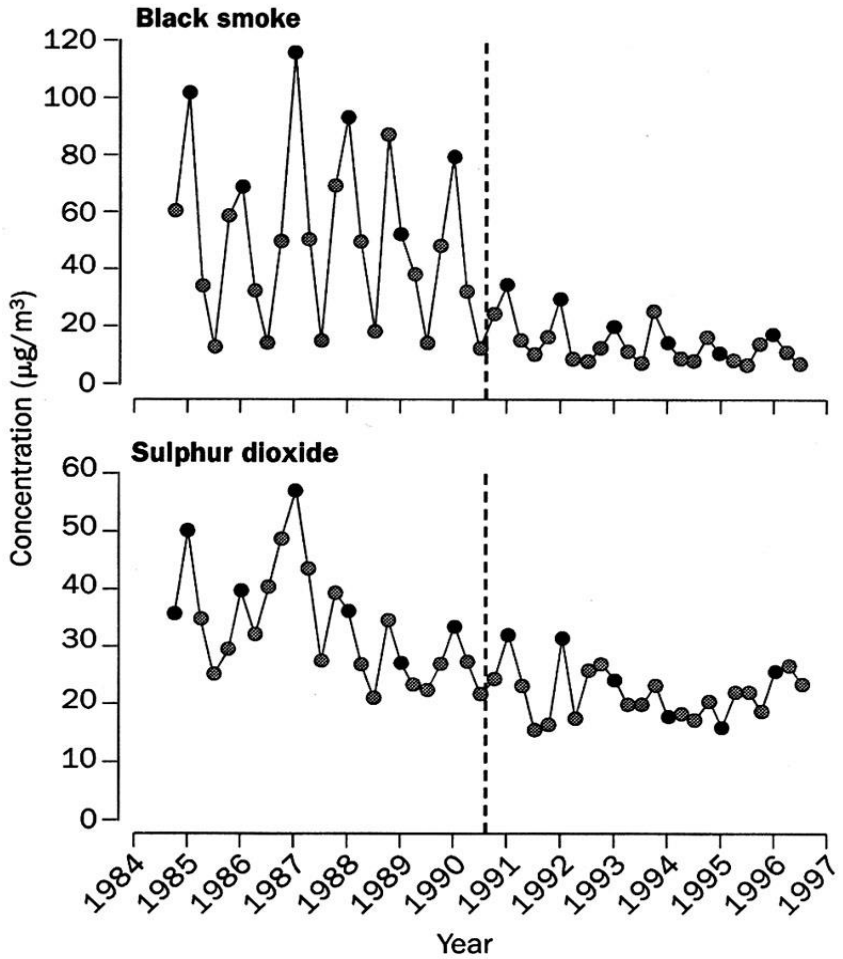
Figure 1

DEATHS IN 1952 LONDON SMOG: LED TO UK'S CLEAN AIR ACTS

Figure 2.1: London air pollution episode, December 1952. Changes in deaths for respiratory and cardiovascular disease



CARDIAC VS RESPIRATORY DEATHS LONDON DECEMBER 1952



Air pollution declined by an average 35.5µg/m^3 black smoke

Respiratory death rates (adjusted) fell by 15%

Cardiac deaths (adjusted) fell by 10%

c359 fewer cardio-respiratory deaths per year

DOES REDUCTION IN POLLUTION MAKE A DIFFERENCE? DUBLIN 1984-96

CLANCY ET AL, *LANCET* 2002;360:1210

LATE 20TH CENTURY: THE ERA OF OIL.
GROWTH OF TRANSPORT, INDUSTRIAL COMBUSTION, HEATING ETC.

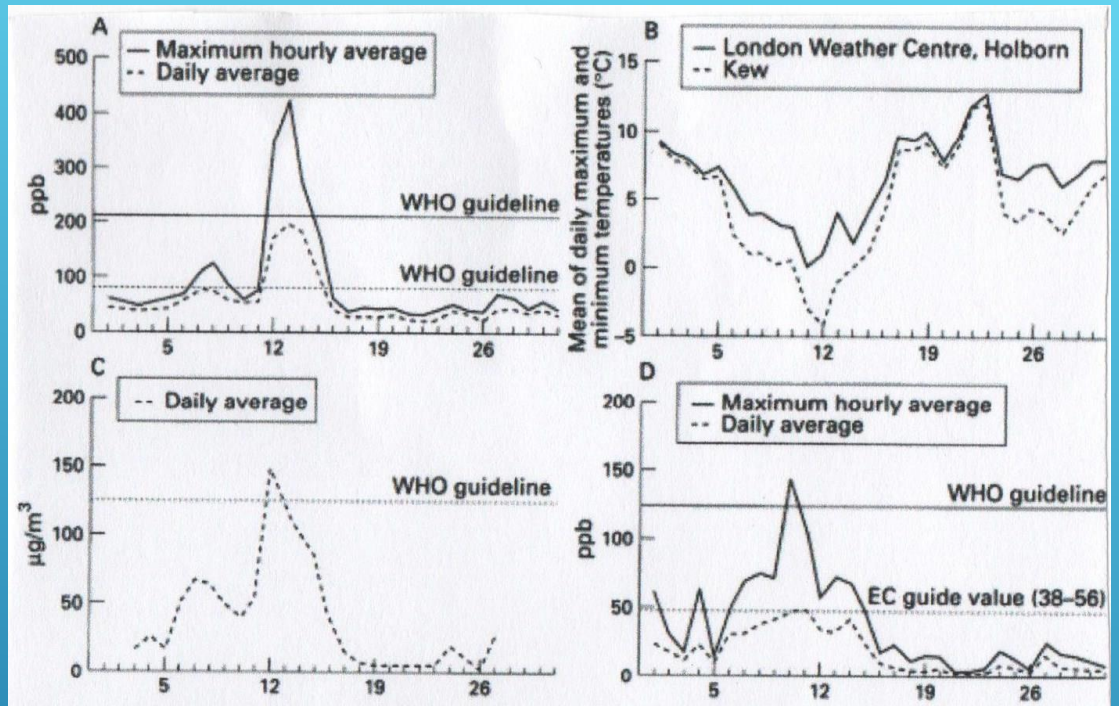


Figure 1 Concentrations of (A) nitrogen dioxide, (C) black smoke, and (D) sulphur dioxide recorded in central London during December 1991. (B) Mean of daily maximum and minimum temperatures in London during December 1991.

POLLUTION EPISODE DECEMBER 1991

Thorax 1995;50:1188–1193

Health effects of an air pollution episode in London, December 1991

H Ross Anderson, Elizabeth S Limb, J Martin Bland, Antonio Ponce de Leon, David P Strachan, Jonathan S Bower

Abstract

Background **– In December 1991 London experienced a unique air pollution episode during which concentrations of nitrogen dioxide rose to record levels, associated with moderate increases in black smoke. The aim of this study was to investigate whether this episode was associated with adverse health effects and whether any such effects could be attributed to air pollution.**

Methods **– The numbers of deaths and hospital admissions occurring in Greater London during the week of the episode were compared with those predicted using data from the week before the episode and from equivalent periods from the previous four years. Relative risks (RR) (episode week versus predicted) for adverse health events were estimated using log linear modelling and these were compared with estimates from control areas which had similar cold weather but without increased air pollution.**

Results **– In all age groups mortality was increased for all causes (excluding accidents) (relative risk = 1·10) and cardiovascular diseases (1·14); non-significant increases were observed for all respiratory diseases (1·22), obstructive lung diseases (1·23), and respiratory infections (1·23). In the elderly (65+ years) the relative risk of hospital admission was increased for all respiratory diseases (1·19) and for obstructive lung diseases (1·43), and a non-significant increase was observed for ischaemic heart disease (1·04). In children (0–14 years) there was no increase in admissions for all respiratory diseases and only a small non-significant increase for asthma. When compared with control areas the relative risks became non-significant but remained increased.**

Conclusions **– The air pollution episode was associated with an increase in mortality and morbidity which was unlikely to be explained by the prevailing weather, a coincidental respiratory epidemic, or psychological factors due to publicity. Air pollution is a plausible explanation but the relative roles of nitrogen dioxide and particulates cannot be distinguished.**

(*Thorax* 1995;50:1188–1193)

Keywords: air pollution episode, mortality, hospital admissions, particles, nitrogen dioxide.

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Received 15 March 1995
Returned to authors 16 June 1995
Revised version received 28 June 1995
Accepted for publication 24 July 1995

In December 1991 an anticyclone lay over most of Britain and Western Europe, creating the cold and stagnant air conditions typically associated with long lasting fogs and air pollution episodes in London.[1,2] Emissions from motor vehicles and power sources were trapped by a temperature inversion which prevented the normal circulation and dispersion of pollutants.[3] On Thursday 12 December 1991 nitrogen dioxide (NO_2) levels in inner London exceeded the WHO hourly average guideline of 210 ppb[4] and, early on 13 December, the urban background monitoring site at Bridge Place, Victoria recorded an hourly average level of 423 ppb NO_2. This was the highest hourly average concentration ever recorded at a background site in London since measurements began in 1972. Levels remained high until Sunday 15 December, four days in all. Levels of black smoke during this period increased at the nearby Westminster site to a maximum daily average of 148 μg/m^3, well above the monthly mean for that station of 43 μg/m^3. Sulphur dioxide (SO_2) levels did not increase to the same extent. London was the only city in Britain to experience a major air pollution episode at that time.

The episode was publicised at the time and there was widespread public and medical concern about its possible health effects with reports from hospital doctors of an increase in hospital attendances, for asthma in particular. Our investigation aimed to determine whether the episode was associated with adverse health effects and, if so, to evaluate the possible role of air pollution. This paper reports the results concerning mortality and hospital admissions. Fuller details may be found in our report to the Department of Health.[5]

Methods

For the purpose of analysis the episode period was defined as the seven day period from Thursday 12 December to Wednesday 18 December ("episode week"). The episode week was compared with the week prior to the episode (5–11 December) ("previous week") and with the corresponding dates (5–11 and 12–18 December) of the preceding four years ("control years"). The study area was all District Health Authorities in Greater London (population 7·2 million). Three control areas were defined: (1) the rest of England (population 40·6 million): (2) the rest of the south east of England (population 10·2 million); and (3) Manchester (population 2·6 million), another large conurbation for which pollution data were available. The episode period and comparison weeks and areas were defined *a priori* and adhered to throughout.

- Rise in deaths overall and from heart attack
- Rise in hospital admissions from lung disease in elderly
- Non-significant rise in asthma admissions in children
- Non-significant rise in lung disease admissions overall

ROSS ANDERSON ET AL. *THORAX* 1995;50:1188

Many studies had shown PM to be associated with both:

- short-term increases in cardiac mortality and admissions, and
- increases in cardio-pulmonary mortality in relation to historic exposure.

THE 1990S - WHAT NEEDED EXPLANATION: THE ASSOCIATION OF AIR POLLUTION WITH *CARDIAC* DISEASE

It takes c100mg arsenic to kill!

Why were these very low particle masses, <1mg inhaled over 24 hours, associated with such consistently adverse effects?

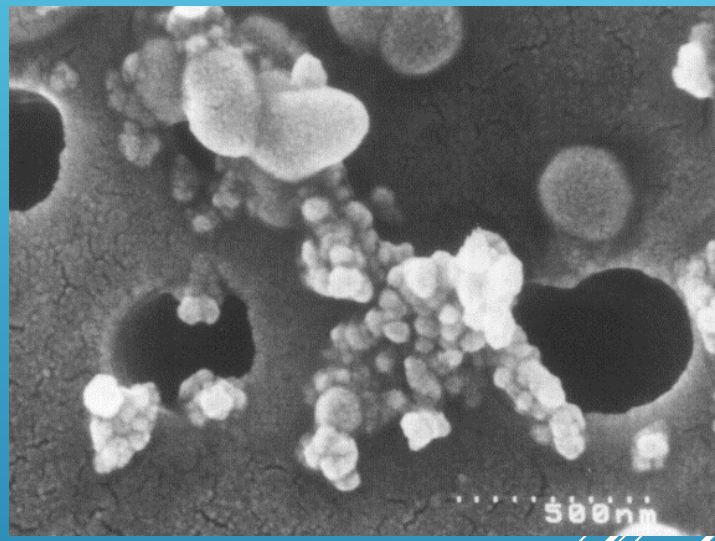
PLAUSIBILITY PROBLEM

- Hypothesised that:
- it is not the mass but the number;
- the ultrafine particles are important, as they
  - penetrate readily indoors
  - cause local lung inflammation
    - which in turn results in release of mediators
    - which alter blood coagulability
    - which increases risk of heart attacks

PARTICULATE AIR POLLUTION AND ACUTE HEALTH EFFECTS

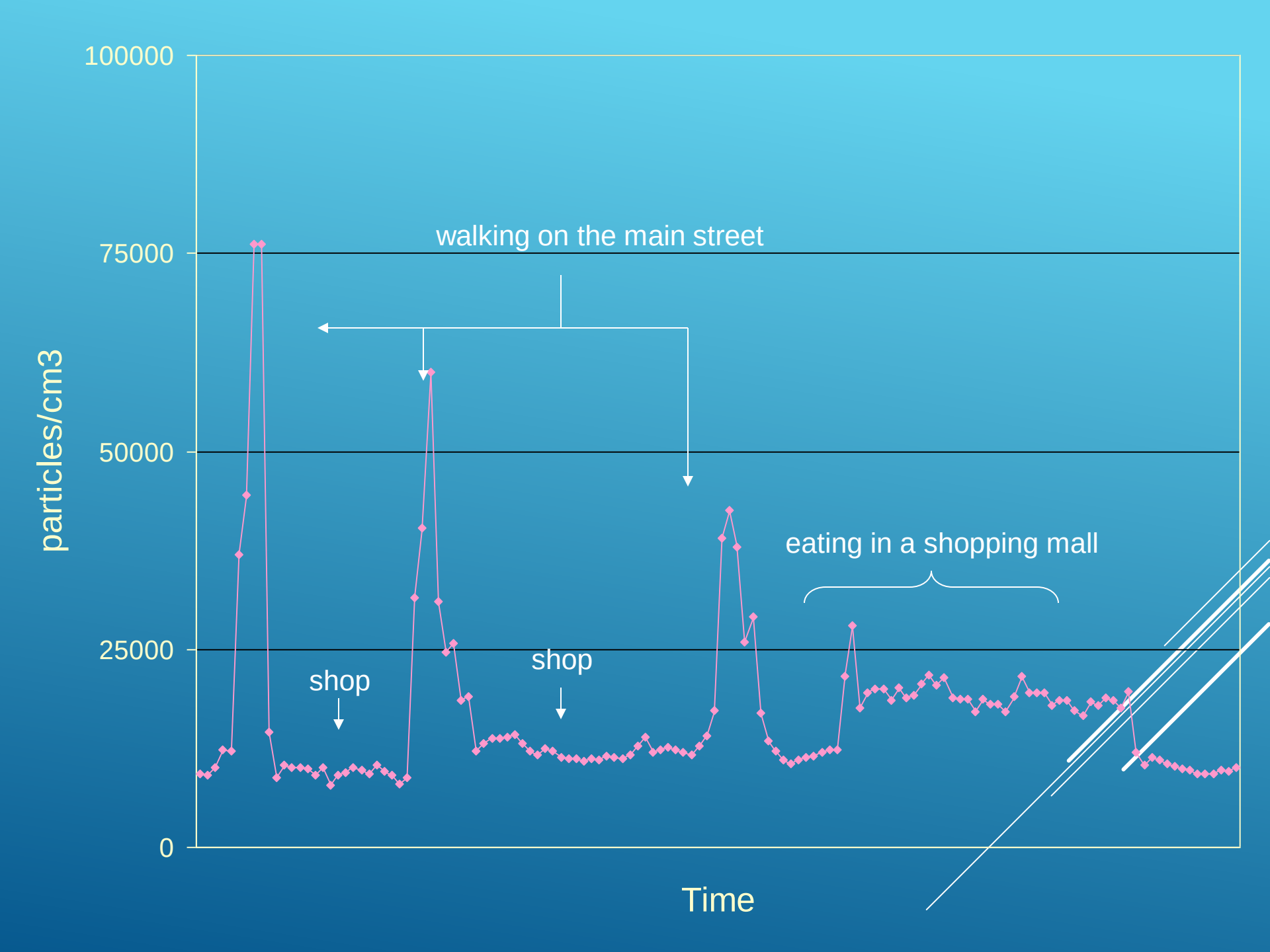
SEATON A ET AL. *LANCET* 1995;**345**:176

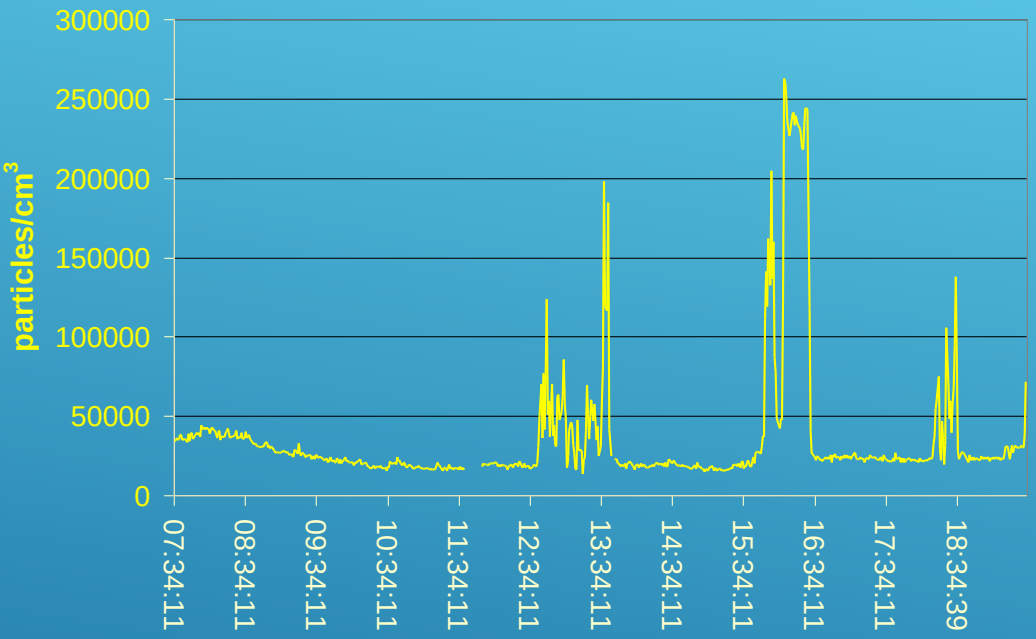
- Each tiny particle is a potential invading micro-organism, requiring
  - local macrophage defence and
  - a systemic reaction
- The more particles above background, the greater the systemic reaction,
- and the greater the chance of adverse effects from inflammation.



DOES THE LUNG COUNT PARTICLES?

SEATON AND DENNEKAMP *THORAX* 2003;**58**:1012-5


100000
75000
50000
25000
0
particles/cm3
walking on the main street
shop
shop
eating in a shopping mall
Time



PARTICLE NUMBERS IN OXFORD CIRCUS STATION

- 112 healthy subjects aged 60+
- Belfast and Edinburgh
- Monthly blood samples
- 3-day diaries pre-sampling
- One 24hr personal PM_{10} sample on each

PARTICULATE AIR POLLUTION AND THE BLOOD

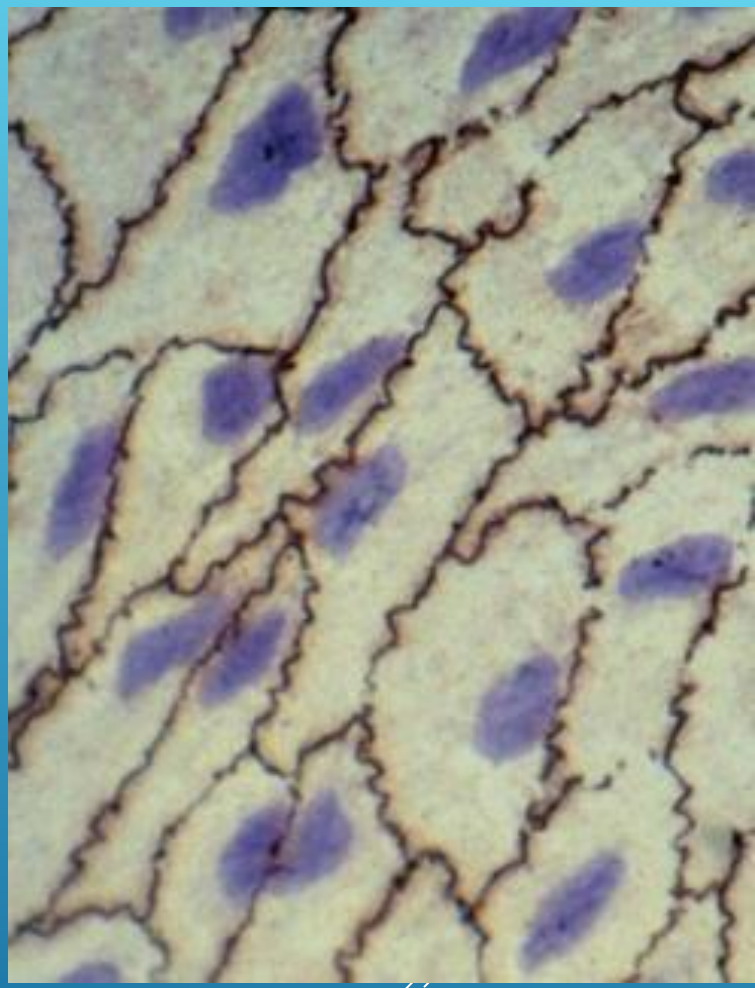
SEATON *ET AL* THORAX 1999;54:1027

	mean	95%CI	p
Haemoglobin g/dl	-0.44	-0.62, -0.26	<0.001
PCV ratio	-0.016	-0.022, -0.01	<0.001
RCC $x10^{12}/l$	-0.14	-0.2, -0.08	<0.001
Platelets $x10^{12}/l$	-10.8	-21.2, -0.4	0.039

CHANGE IN RELATION TO RISE OF 100μG/M^3 PM_{10} IN ESTIMATED 3 DAY EXPOSURE

INTERPRETATION

- Changes in red cells and platelets most likely to be related to sequestration
- Thus, activation of endothelial factors likely explanation

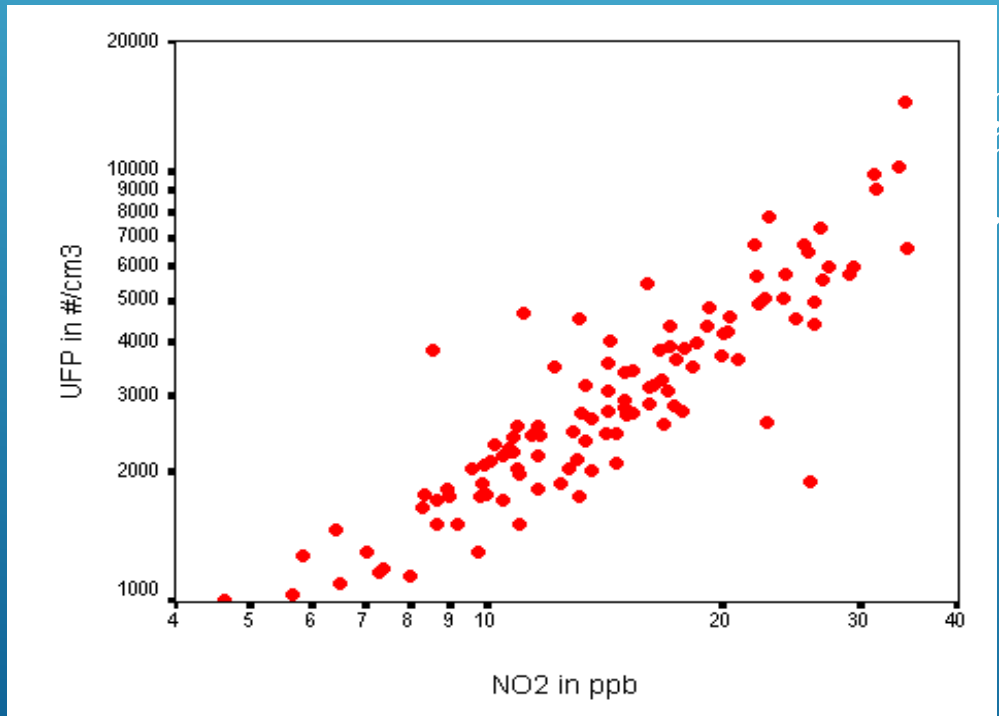


THE 21ST CENTURY

- 1% increase in risk of cardiac death or admission per 10μg/m^3 rise in PM_{10}
- 6-7% higher long-term risk of cardiac death per 1μg/m^3 city difference in $PM_{2.5}$
- Small increases in risk of stroke and venous thrombosis
- Possible increase in risk of cot death

- Particles are a likely *cause* of cardiovascular disease and exacerbations of lung disease
- NO_2 is also *associated* with similar risks, but this seems less plausibly causative.
- NO_2 is a good marker of vehicle combustion and nanoparticle numbers

WHAT WE THINK WE KNOW, 2016



"CARBONUMQUE GRAVIS VIS, AUQUE ODOR INSINUATOR QUAM FACILE IN CEREBRUM"

HOW EASILY THE STRONG, HEAVY FUME OF CARBON MAY INFILTRATE THE BRAIN!

LUCRETIUS. *DE NATURA, LIBER VI c60 BC*

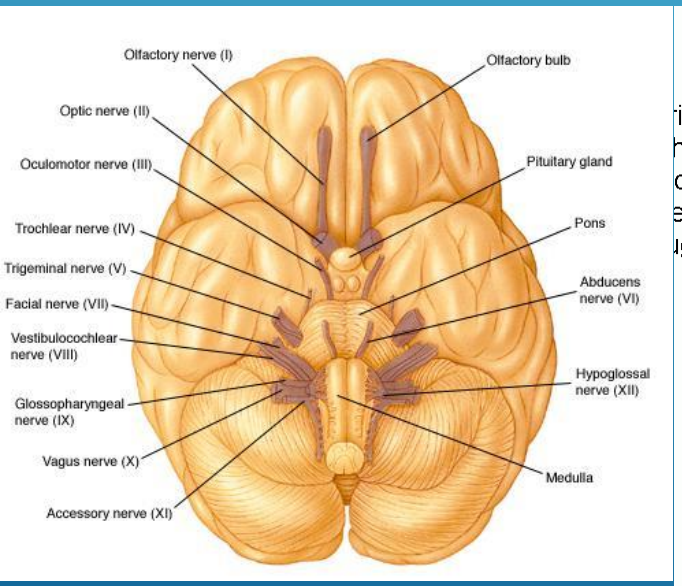
So far, weak evidence of:

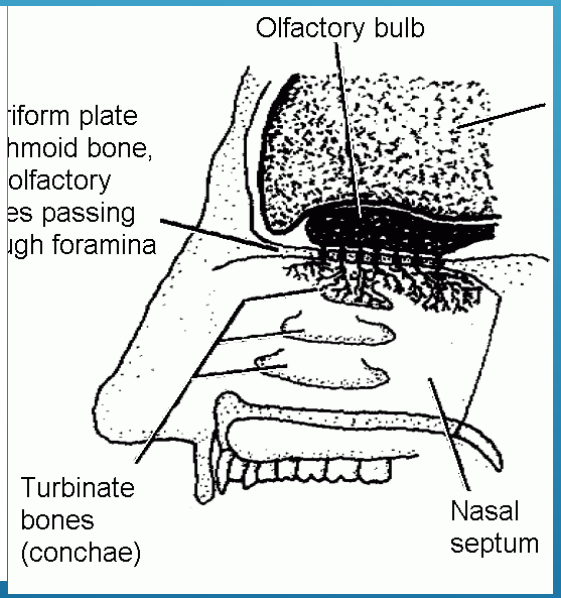
- Delayed development with *in utero* exposure.
- Impaired neurocognitive performance in children
- Accelerated cognitive decline in adults

DOES AIR POLLUTION AFFECT THE BRAIN?

CLIFFORD A ET AL. *ENV RES* 2016;**147**:383-98

- **Direct action of nanoparticles?**
  - Several viruses can access and be transmitted along olfactory nerve
  - Air pollution particles have been found in brains of dogs and people in Mexico City
- **Mediated effect on endothelial blood-brain barrier?**





HOW CAN THIS BE?

WHAT WE DON'T KNOW 2016

- How the message is transmitted
- If/how pollution affects the brain
- Does NO_2 do anything or is it just a marker of nanoparticles?

SOME THOUGHTS FOR THE FUTURE

- Cardiac and thrombotic effects are explicable on basis of general change in blood and/or endothelial function.
- So is cot death - ask me how!
- And cognitive change?
- Is a unitary hypothesis conceivable? Clue: red cells, endothelial cells contain ChAT, ACh receptors and AChE.

Institute of Occupational Medicine

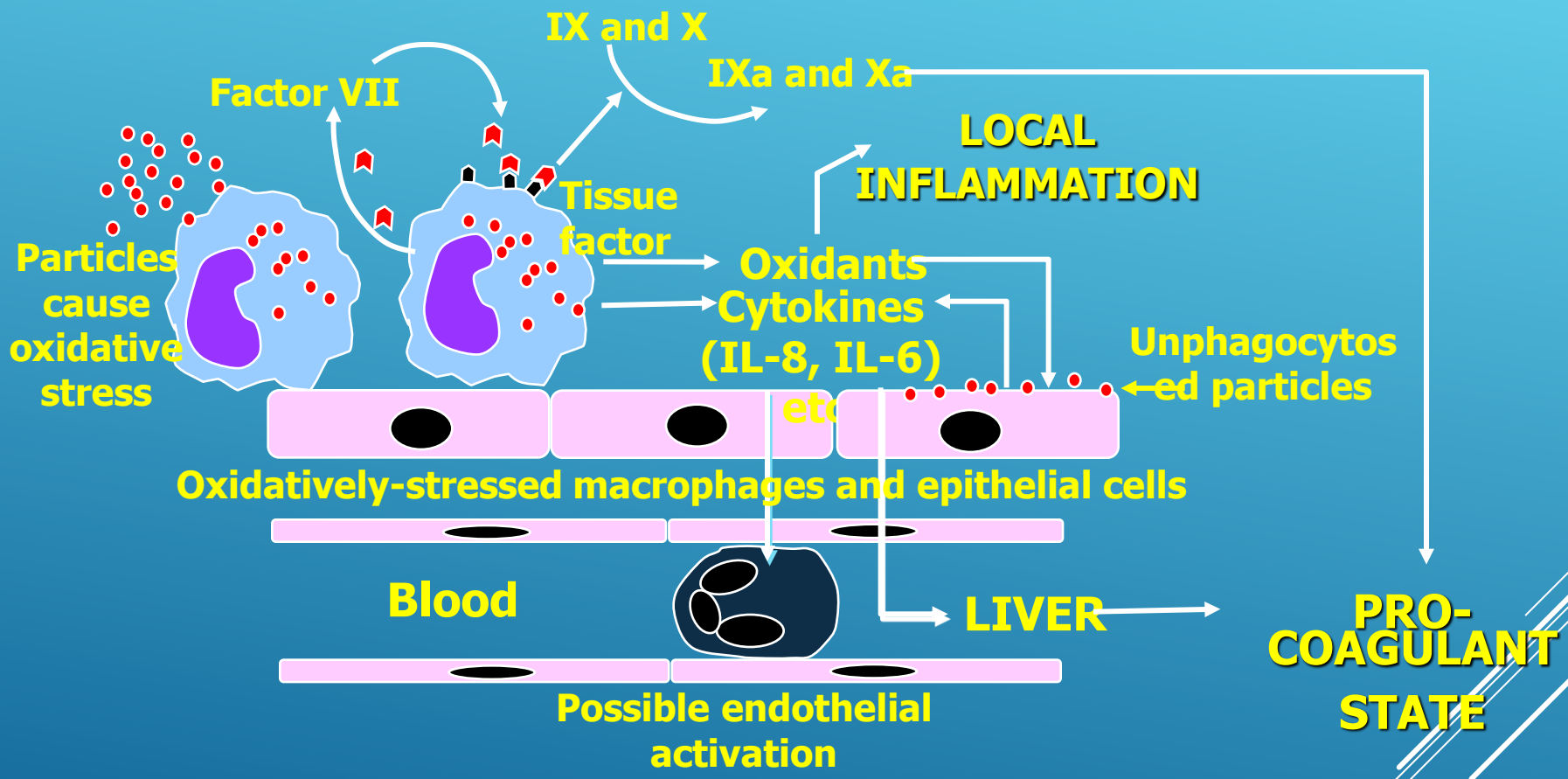
THANK YOU.

ANTHONY SEATON

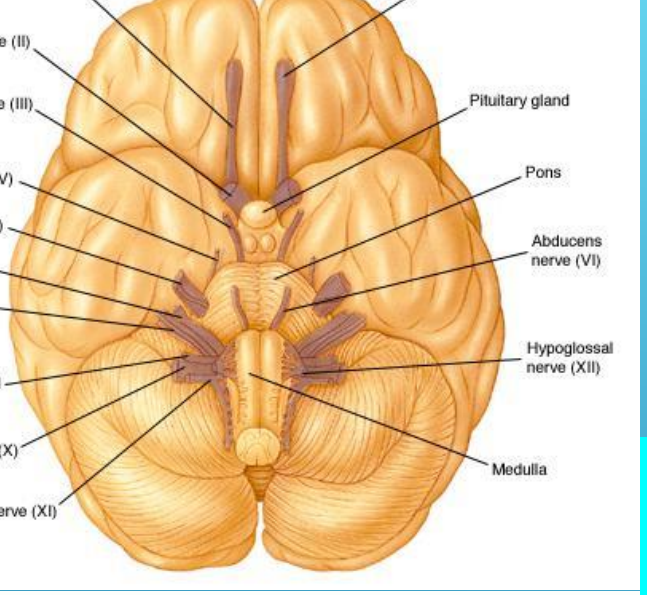
	Lung	Blood vessels	Brain
Pathological mechanisms	Inflammation - Fibrosis and tissue breakdown	Thrombosis, endothelial dysfunction, inflammation	Neurovascular bundle disruption, inflammation, leaky blood-brain barrier
Diseases	Silicosis, IPF, emphysema	Atheroma, plaque breakdown, heart attack	Impaired cognition, dementia

LUNG, BLOOD VESSELS AND BRAIN: ANALOGOUS EFFECTS OF PARTICLES

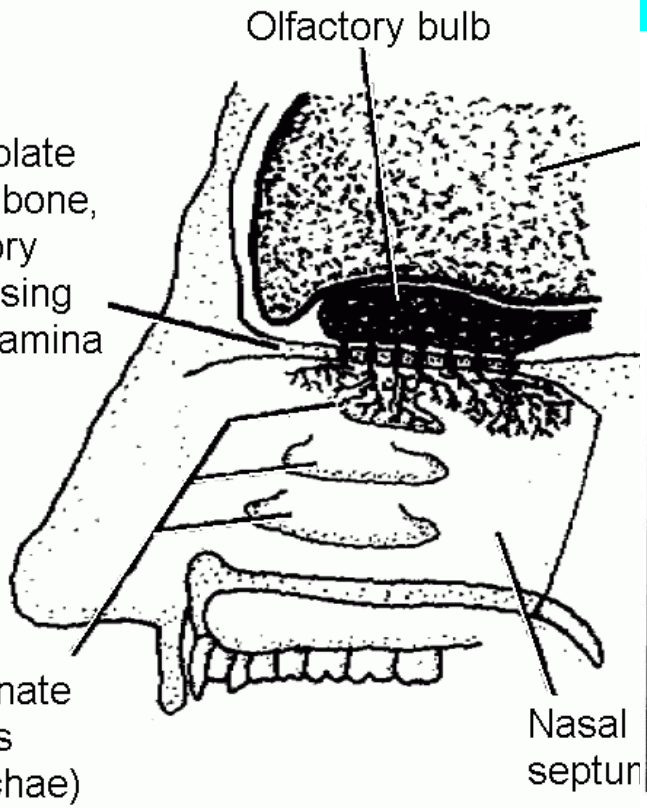
Possible mechanisms for the production of local inflammation and a systemic pro-coagulant state after PM10/2.5 exposure

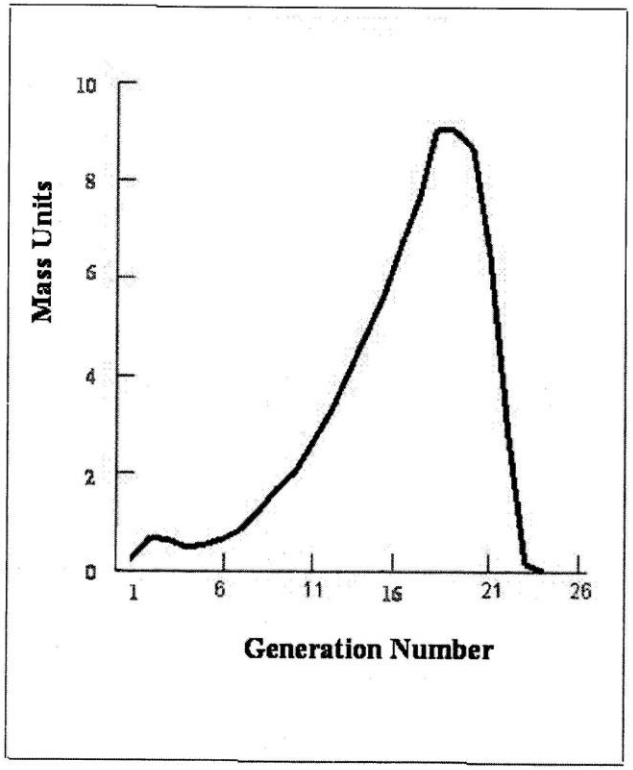


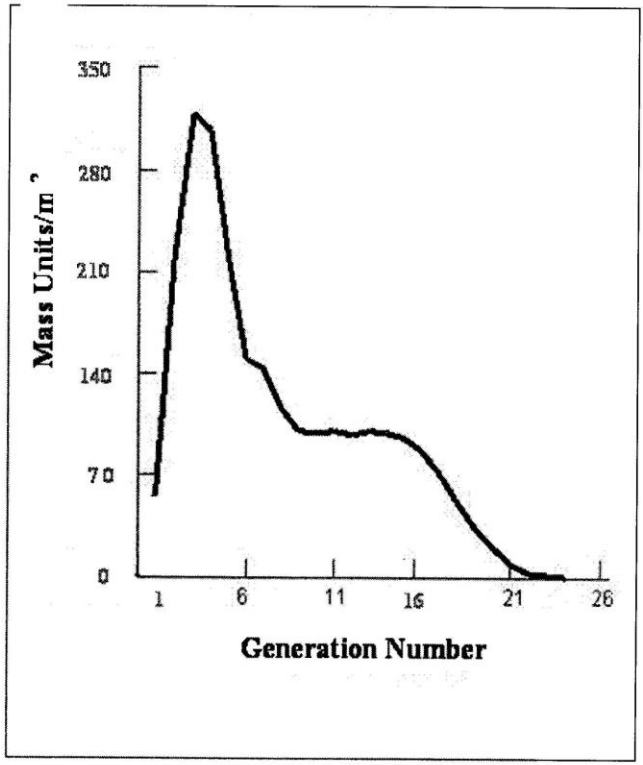
NANOPARTICLES, THE NOSE AND THE BRAIN



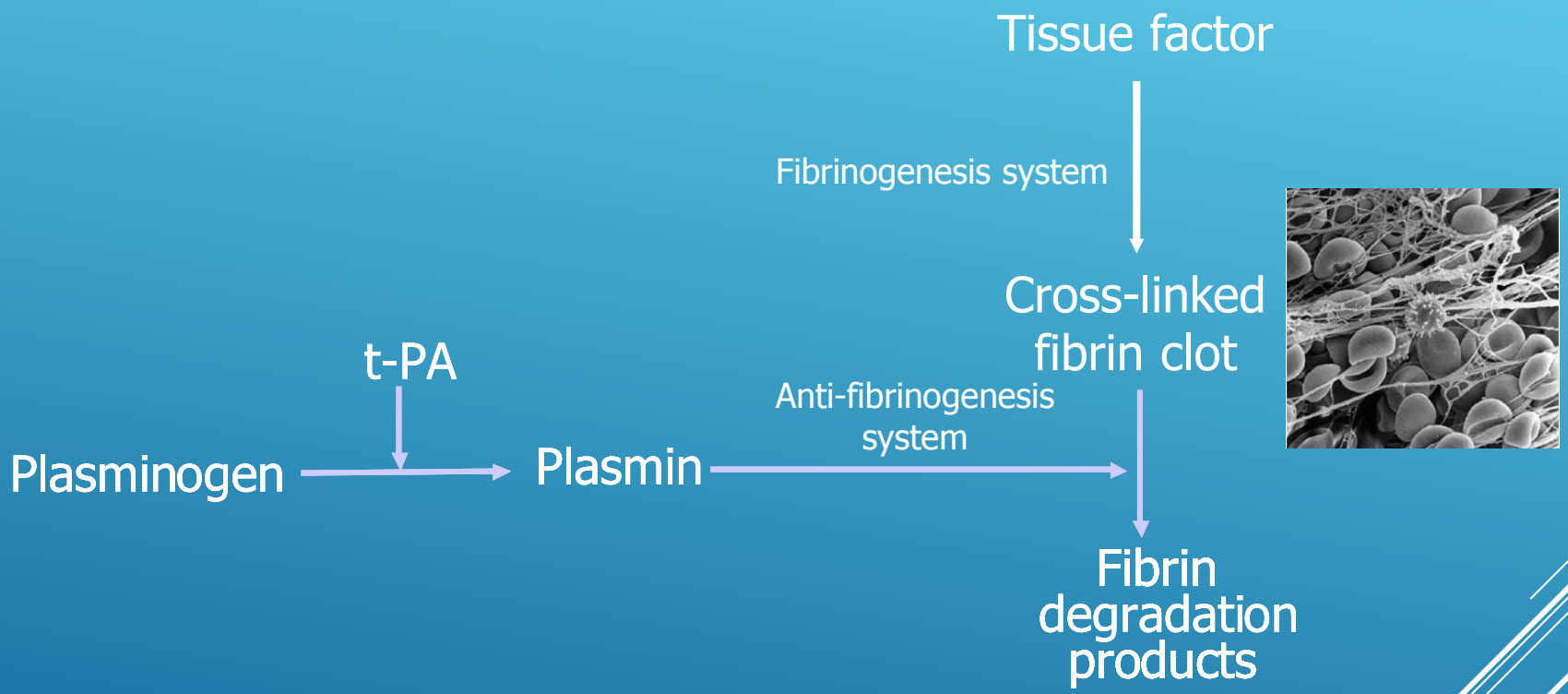
Estimates of deposition of 20nm particles in human respiratory tract (from Oberdörster *et al* 2004)



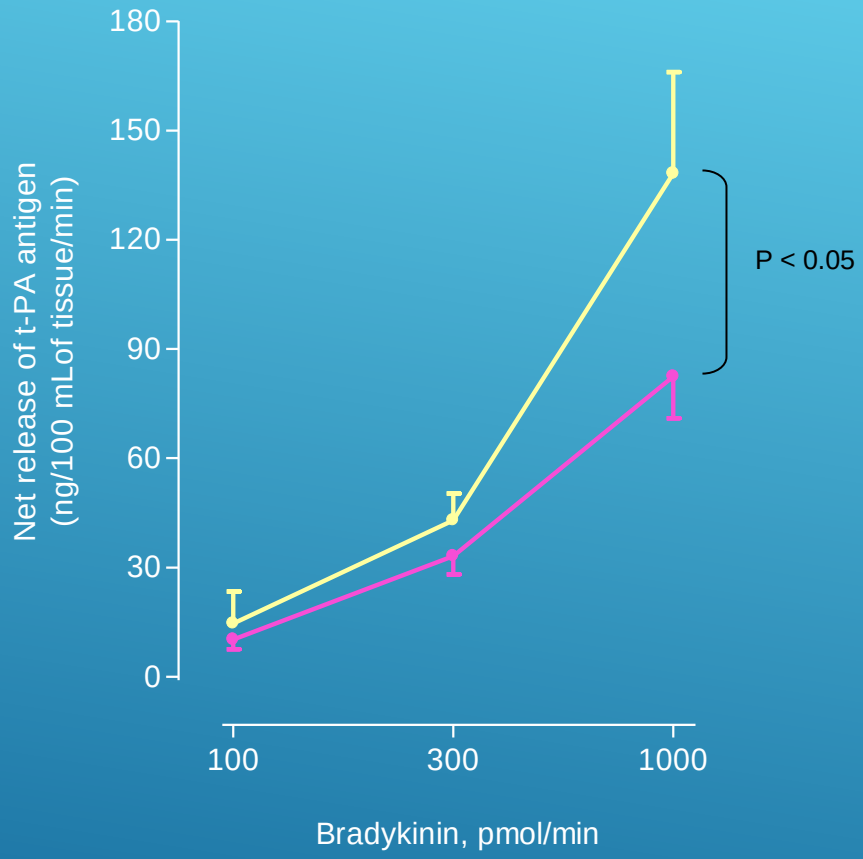




The clotting and fibrinolysis systems



ENDOGENOUS FIBRINOLYSIS – TISSUE PLASMINOGEN ACTIVATOR (T-PA) RELEASE



t-PA antigen following diesel (●) and air (●) during brachial artery infusion of bradykinin.

Area under the curve for t-PA release was reduced by 33.6% following diesel exhaust exposure

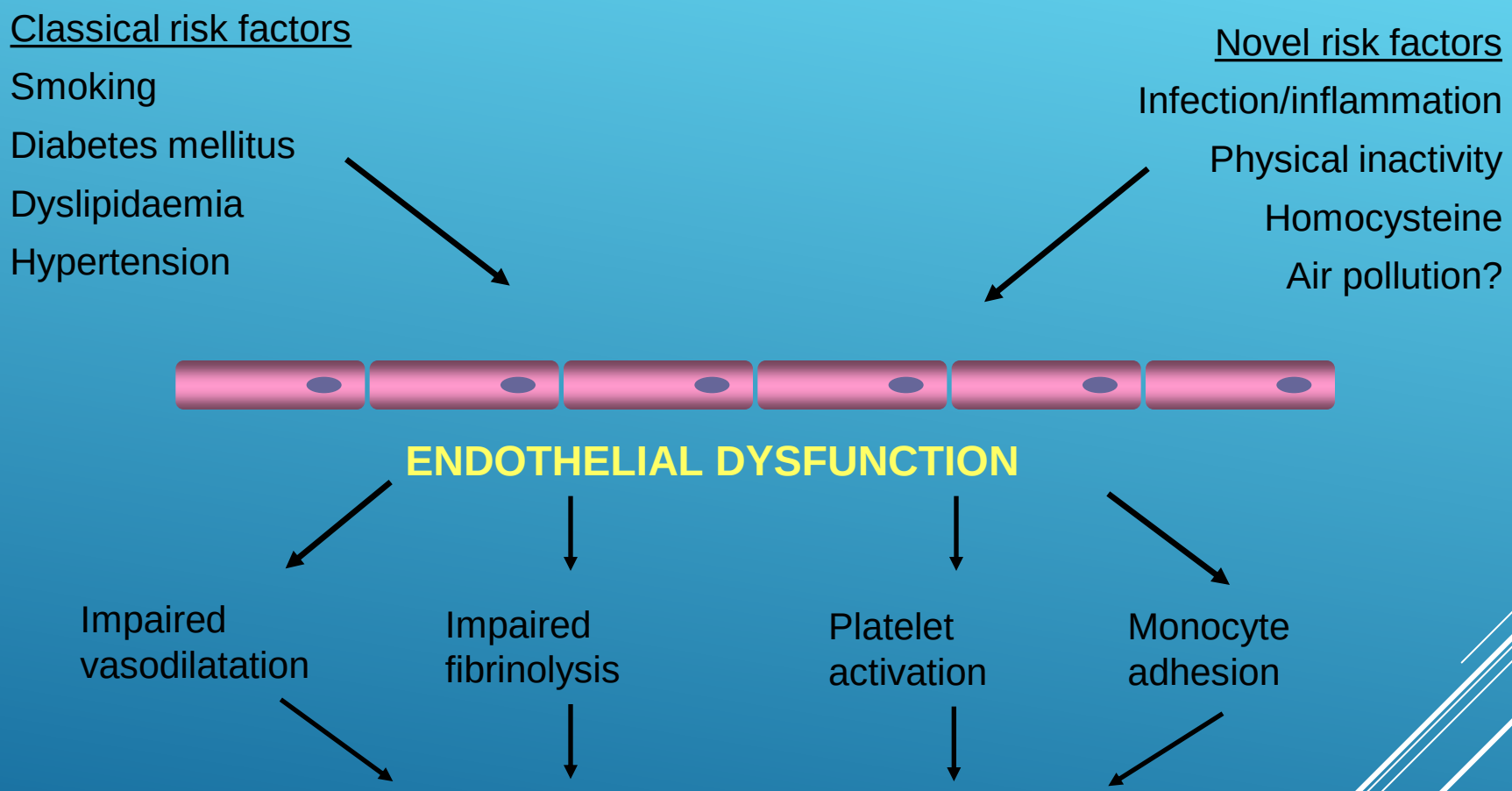
79 concurrent counts in and outside lab, door and windows closed, no internal source, 2 months

- Correlation 0.94
- Indoor = 0.527 x outdoor +1468

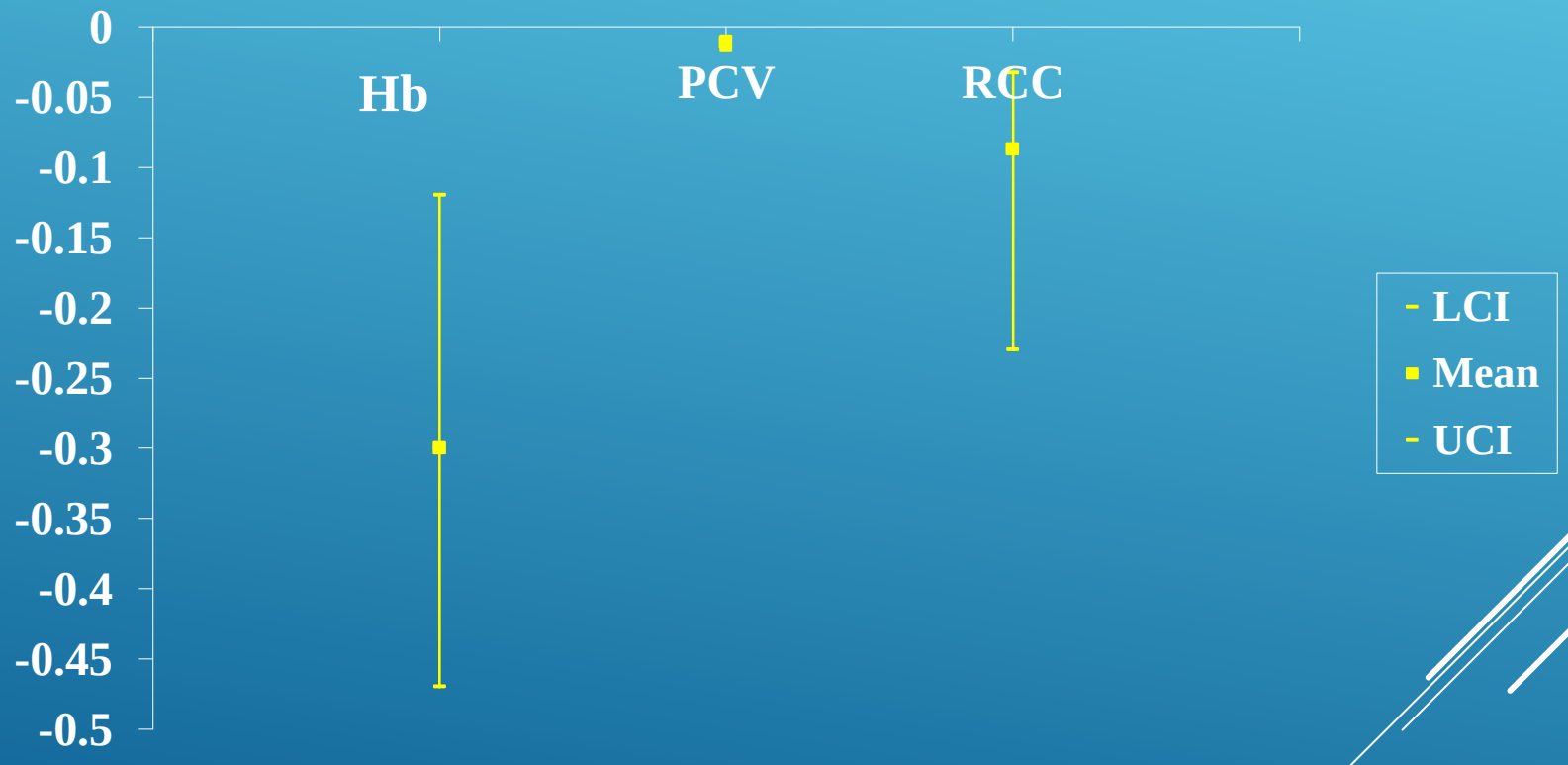
DO ULTRAFINE PARTICLES TRAVEL INDOORS?

OSUNSANYA ET AL OEM 2001;58:154

Vascular endothelium

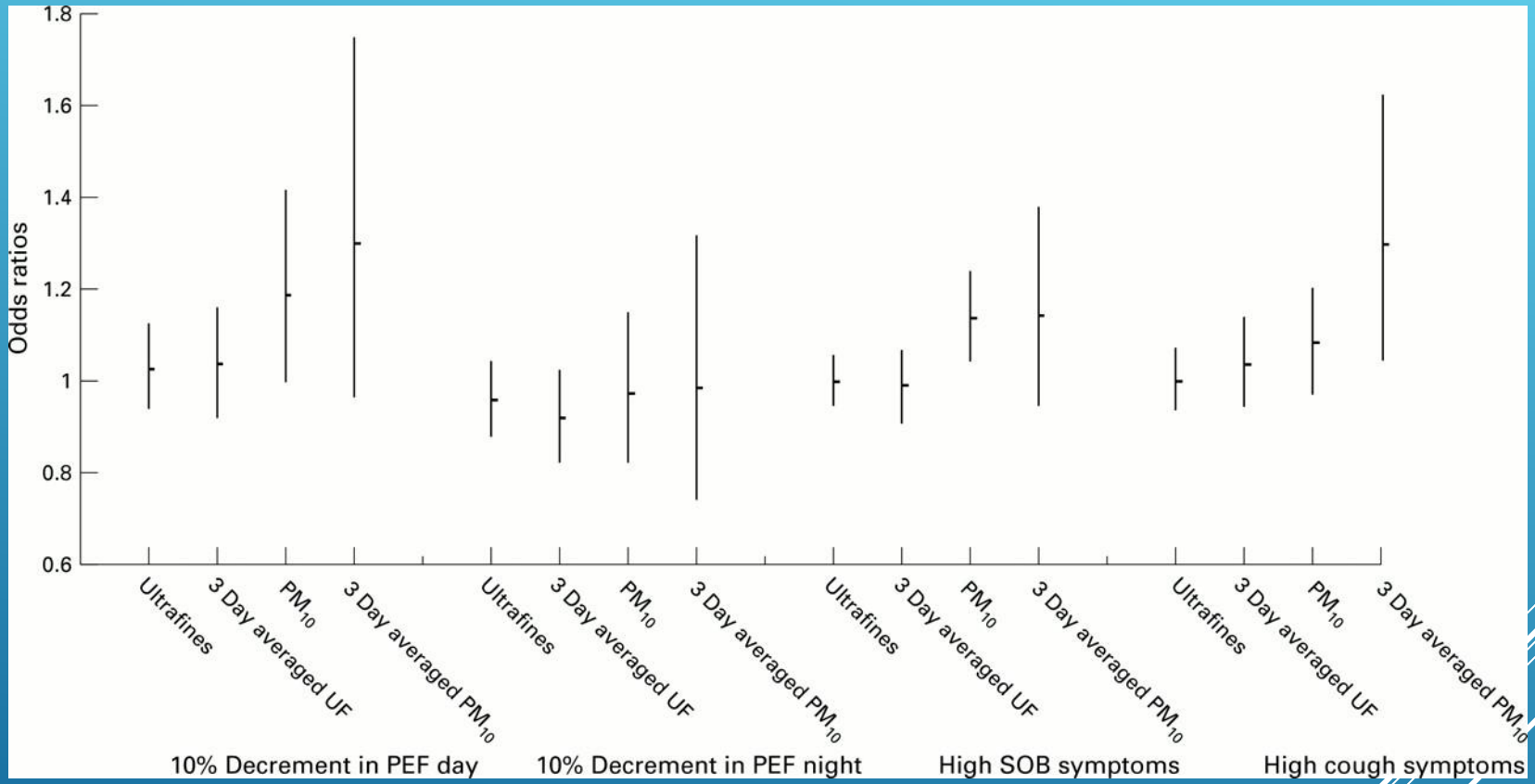


RELATIONSHIP BETWEEN BLOOD MEASUREMENTS AND PREVIOUS 3 DAYS ESTIMATED EXPOSURE - CORRECTED FOR ALBUMIN



Hb - g/dl, PCV %, RCC - $x10^{12}$/dl

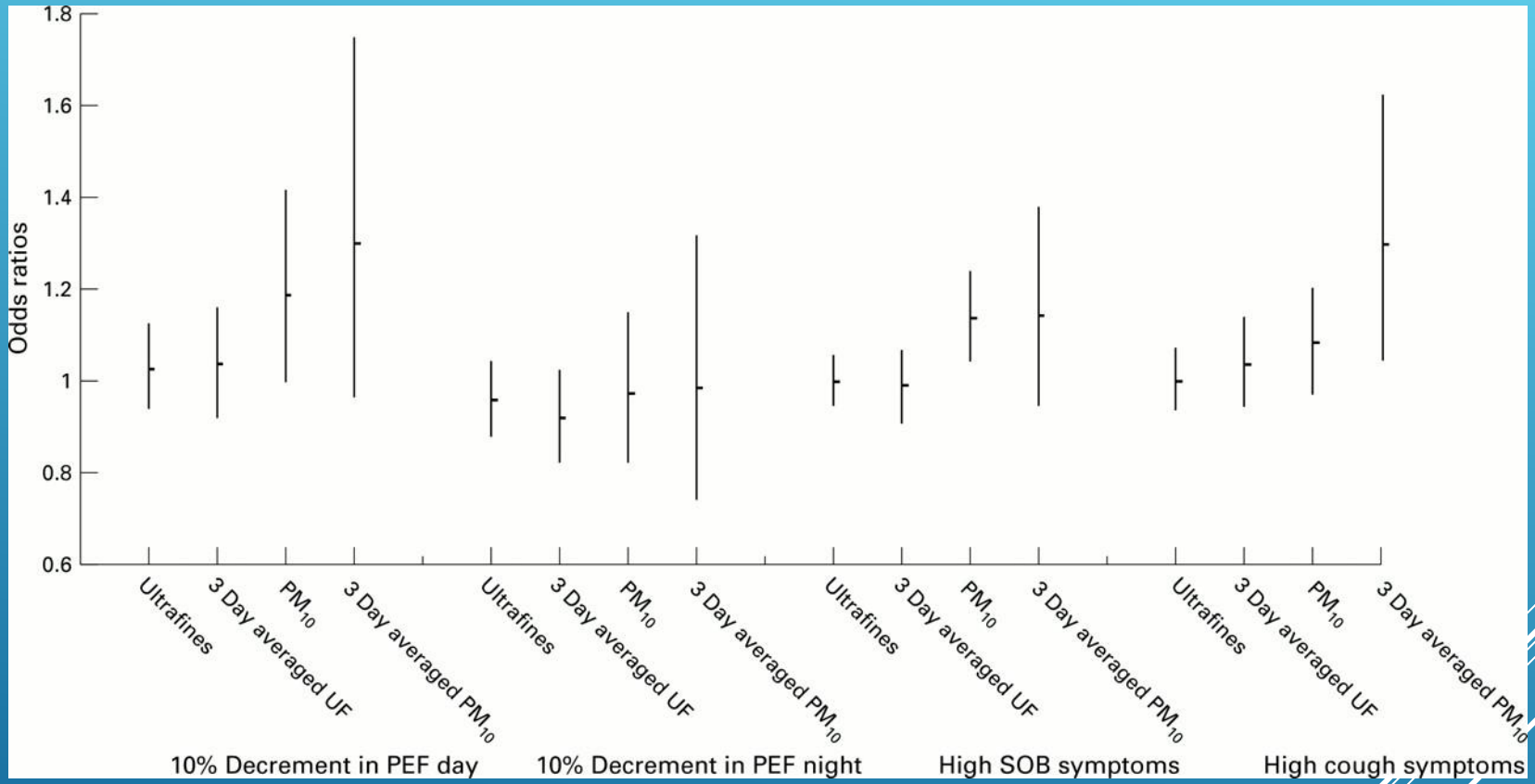
Results from regression model, allowing for wind speed, humidity, temperature, and serial association, showing odds ratios for changes in PM10 from 10–20 µg/m3or in ultrafine counts from 10 000–20 000/cm3.



T Osunsanya et al. Occup Environ Med 2001;58:154-159

OEM

Results from regression model, allowing for wind speed, humidity, temperature, and serial association, showing odds ratios for changes in PM10 from 10–20 µg/m3or in ultrafine counts from 10 000–20 000/cm3.



T Osunsanya et al. Occup Environ Med 2001;58:154-159

OEM

ORIGINS OF THE HYPOTHESIS

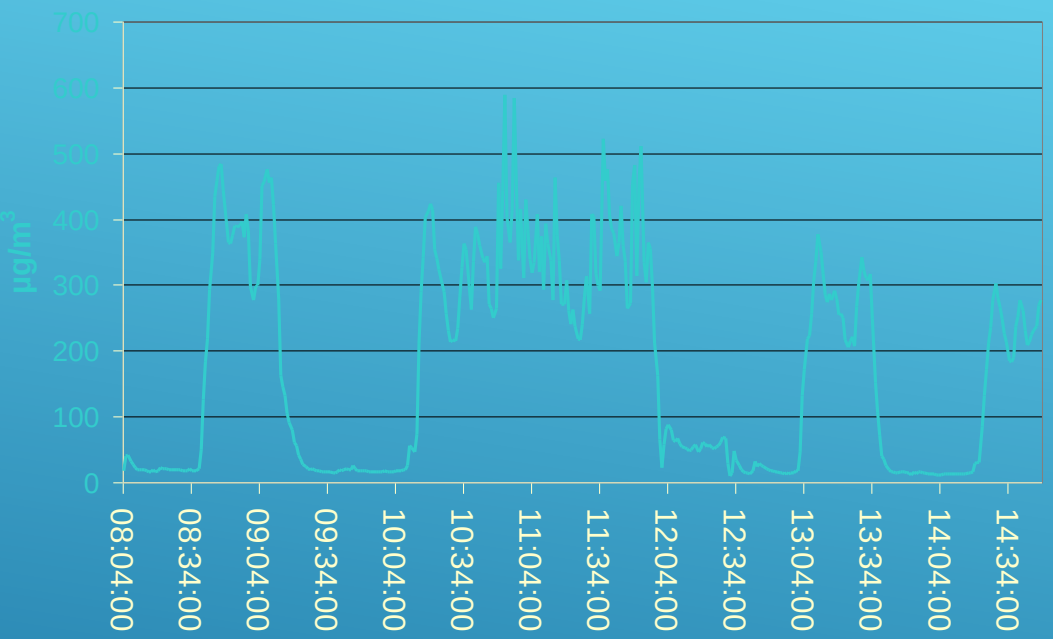
- COMEAP discussions early 1990s
- Associations with cardiac episodes
- Low exposures - $\mu g/m^3$
- People spend most of their time indoors
- Must be some confounder – social factors, temperature?

- How does pollution harm health? Which components are harmful?
- Emphasis on black smoke and acid aerosol, leading to control of coal burning in cities.
- Recognition of concomitant effects of weather – cold, still periods,
- Resulted in dramatic reductions in urban pollution – problem solved?

1950S TO 1980S
PROF PAT LAWTHER AND THE MRC

WHAT WE KNOW, 2016

- Air pollution increases risk of cardiac and chronic respiratory disease, and of ischaemic stroke, embolism and cot death
- It is associated with exacerbations of asthma
- The main cause of pollution is combustion of fossil fuels
- Reduction of pollution is associated with reduction of cardiorespiratory deaths



$PM_{2.5}$ IN CENTRAL LINE - DRIVER'S CABIN

WHAT WE KNEW BY 1990

- In spite of great reduction in levels, pollution was still associated with cardio-respiratory deaths and admissions
- Composition of pollution had changed – less SO2, less black and acidic
- Associations were detectable at very low concentrations

	% increase in risk per 10μg/m^3 rise in:		
	PM_{10}	$PM_{2.5}$	Black smoke
Cardiovascular deaths	0.9 (0.7-1.2)	1.4 (0.7-2.2)	0.6 (0.4-0.7)
Cardiac admissions	0.9 (0.7-1.0)	-	1.0 (0.4-1.5)
Cerebrovascular deaths	0.4 (0.0-0.8)	-	-

COMBINED EFFECT ESTIMATES OF DAILY MEAN PARTICULATE POLLUTION (COMEAP 2004)

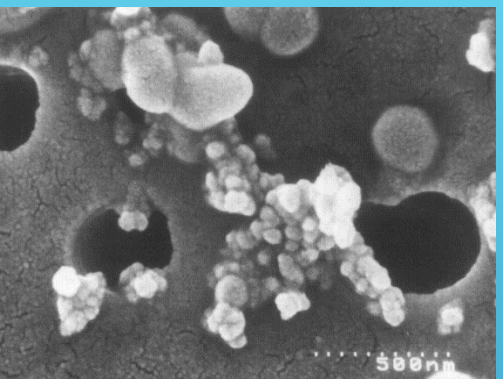
LONG-TERM CARDIO-PULMONARY EFFECTS

- 6% increase in *cardio-pulmonary mortality* in relation to historic exposure differences of 10μg/m^3 $PM_{2.5}$, in US adults

  (*JAMA* 2002;287:1132)

- 7% increase in risk of *cardio-pulmonary mortality* in relation to 10μg/m^3 estimated average personal exposure to black smoke in The Netherlands

  (*Lancet* 2002;360:1203)



PARTICLE NUMBERS IN DIFFERENT ENVIRONMENTS