UNIVERSITÀ DEGLI STUDI DI PERUGIA

Dipartimento di Medicina Clinica e Sperimentale

Sezione di Medicina del Lavoro, Malattie Respiratorie e Tossicologia Professionali e Ambientali

Direttore Prof. Giacomo Muzi

Effetti biologici precoci delle esposizioni ambientali sull'apparato respiratorio

Terni 14 Settembre 2018

SENTIERI DA PERCORRERE

SALUTE E AMBIENTE A TERNI: CONOSCENZE ATTUALI E PROSPETTIVE DI STUDIO E INTERVENTO

Nicola Murgia

Broncopneumopatie professionali e ambientali

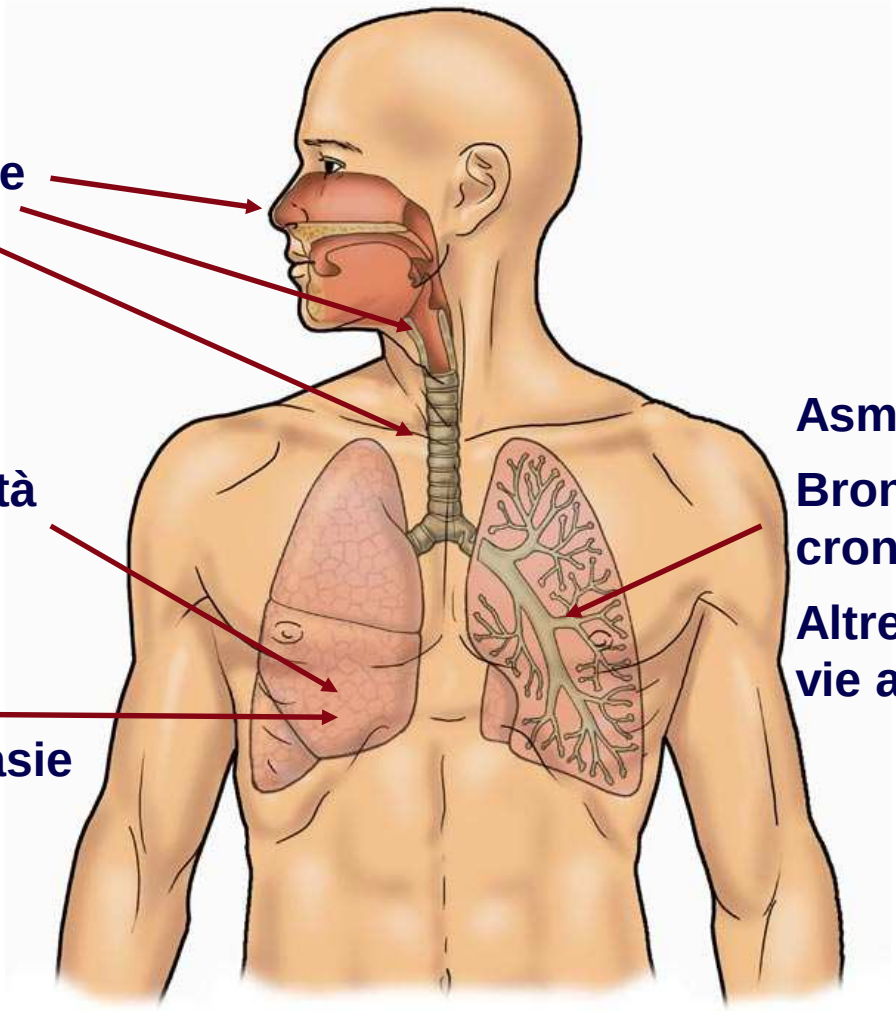
Rinite, faringite, tracheite

Asbestosi, Silicosi

Polmoniti da ipersensibilità

Altre pneumopatie

Carcinomi polmonari,
Mesotelioma, altre neoplasie



Asma bronchiale

Broncopneumopatia cronica ostruttiva

Altre malattie delle vie aeree inferiori

Spirometria

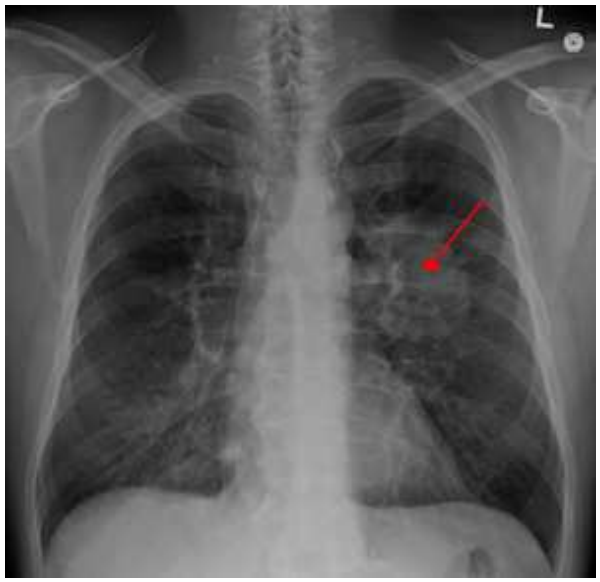
II secolo

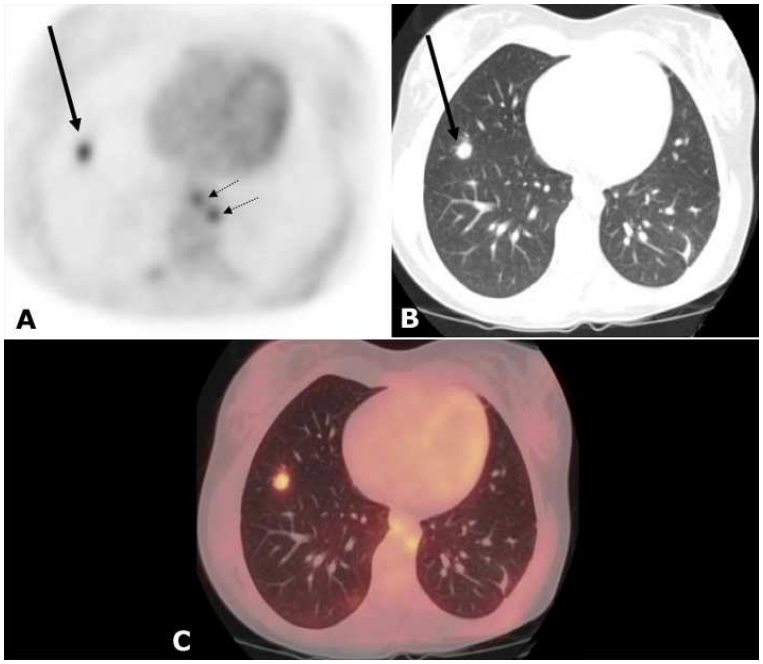
XVII secolo

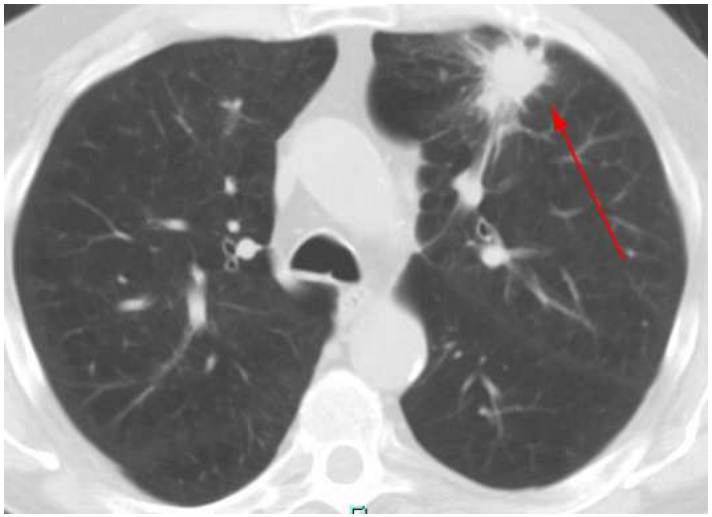
XIXsecolo

XX secolo

XXI secolo


L


A
B
C



UNIVERSITA' DEGLI STUDI DI PERUGIA - AZIENDA OSPEDALIERA DI PERUGIA
DIPARTIMENTO DI MEDICINA CLINICA E SPERIMENTALE
MEDICINA DEL LAVORO, MALATTIE RESPIRATORIE E TOSSICOLOGIA
PROFESSIONALI ED AMBIENTALI

Ospedale S. Maria della MIsericordia - Perugia - Loc. S. Andrea delle Fratte
Lab. Fisiopatologia Respiratoria - Tel. 075/5784444 - 5784466

---

paz.: PAOLO sesso: M d.n.:

c.f.: g.e.: alt.: 165 eta':

cod.: peso: 85.0 c.r.:

ind.: amb.

---

data: 25/10/2012 cartella n: 34025

VALORI SPIROMETRICI BASALI

		oss.	teorici	%	lim.
VC	l	4.08	3.06	133	2.14-3.98
FVC	l	4.08	2.97	137	1.97-3.97
FEV1	l	2.51	2.17	116	1.33-3.01
FEV1/VC	%	61.45	72.17	85	60.4-84.0
FEF25-75	l/s	1.06	2.29	46	0.58-4.00
FEF25-75/VC	l/s	0.26			
PEF	l/s	5.97	6.68	89	4.69-8.67
MEF75	l/s	4.74	6.10	78	3.29-8.91
MEF50	l/s	1.50	3.30	46	1.13-5.47
MEF25	l/s	0.33	0.78	42	-0.50-2.06

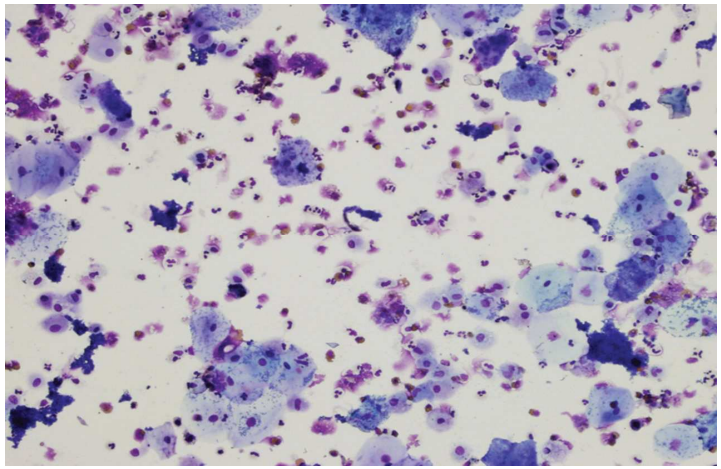
Teorici di Riferimento: Polgar 71 (6<eta'<18) ERS93 (18<=eta')

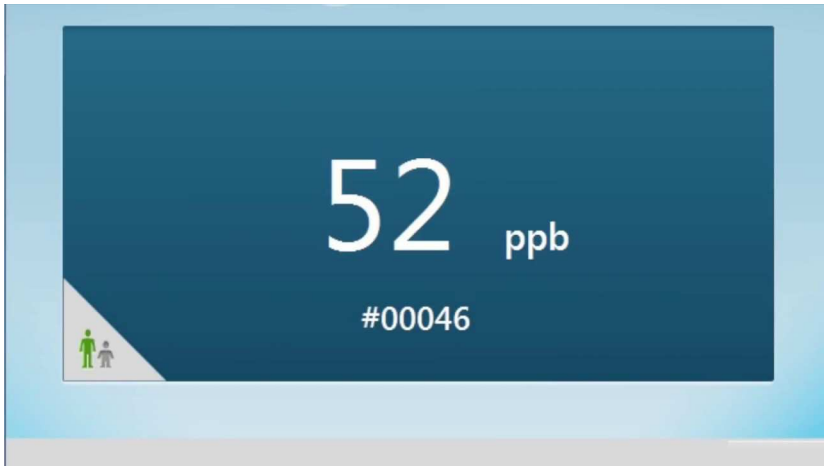
Valutazione degli effetti precoci e reversibili sull'apparato respiratorio

- Espettorato indotto
- Ossido nitrico esalato
- Condensato dell'aria espirata
- Ricerca mutazioni in sangue e urine
- Citologia nasale e e buccale

Valutazione degli effetti precoci e reversibili sull'apparato respiratorio

- **Espettorato indotto**
- **Ossido nitrico esalato**
- **Condensato dell'aria espirata**
- Ricerca mutazioni in sangue e urine
- Citologia nasale e buccale




52
ppb
#00046

<A7>

Parma 11-14 September 2011

Breath Analysis Summit 2011 - International Conference on Breath Research

Oxidative stress and airway inflammation in workers exposed to crystalline silica and in patient with silicosis assessed by lung function tests and exhaled breath condensate

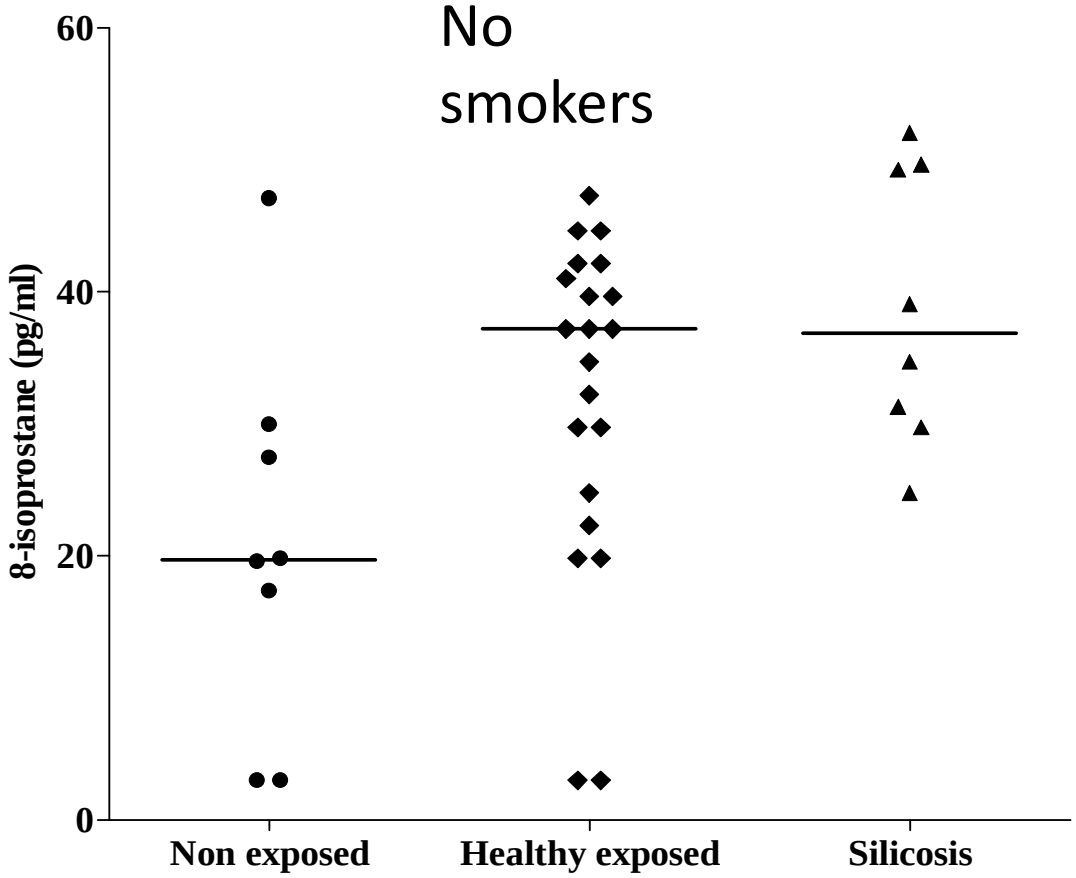
Murgia N.[1], Montuschi P.[2], Gambelunghe A.[1], Dell'Omo M.[1], Ciabattoni G.[3], Abbritti G.[1], Muzi G.[1]

[1]Section of Occupational Medicine, Respiratory Diseases and Occupational and Environmental Toxicology, University of Perugia, Italy. [2]Department of Pharmacology, Faculty of Medicine, Catholic University of the Sacred Heart, 00168 Rome, Italy.[3]Department of Drug Sciences, School of Pharmacy, University of Chieti "G. d'Annunzio", Chieti, Italy

Characteristics of subjects – no smokers

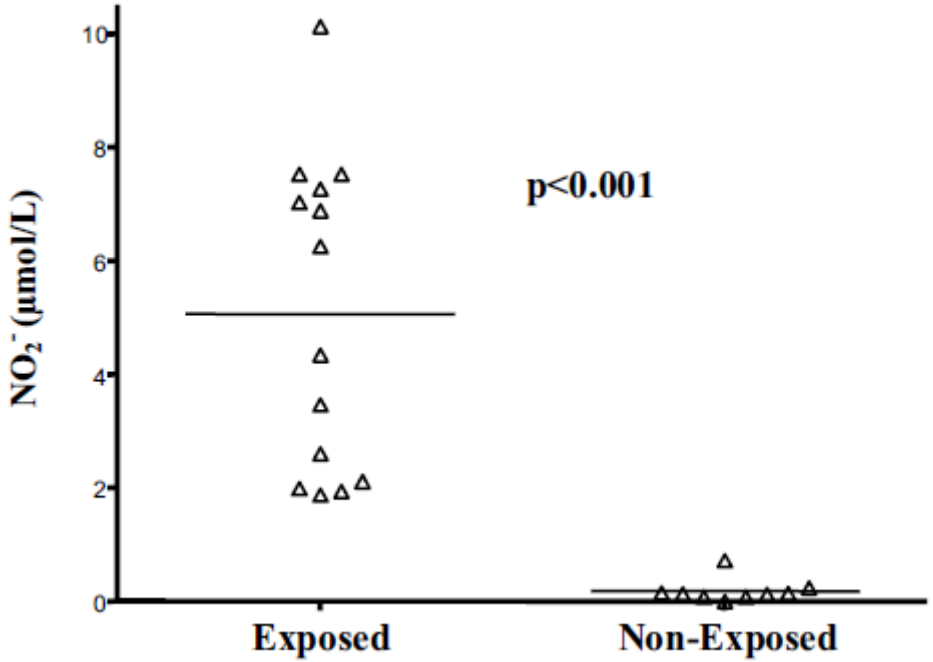
	Non smokers (n=37)						
	Non exposed n=8		Healthy exposed n=21		Silicosis n=8		p
	median	min-max	median	min-max	median	min-max	
Age (yrs)	31	26-42	34	23-52	36.5	30-53	NS
Silica exposure (yrs)	/	/	12	1-22	15	6-37	NS
Pulmonary function							
FVC (% p.v.)	103	96-122	103	75-123	101	82-114	NS
FEV1 (% p.v.)	103	97-135	103	78-121	98	83-120	NS
TLC (% p.v.)	99	93-118	100.5	78-116	98.5	79-110	NS
RV (% p.v.)	86	78-106	82.5	66-134	87	74-140	NS
DLCO (% p.v.)	92	77-111	100	60-130	96	67-113	NS

8-isoprostane in exhaled breath condensate



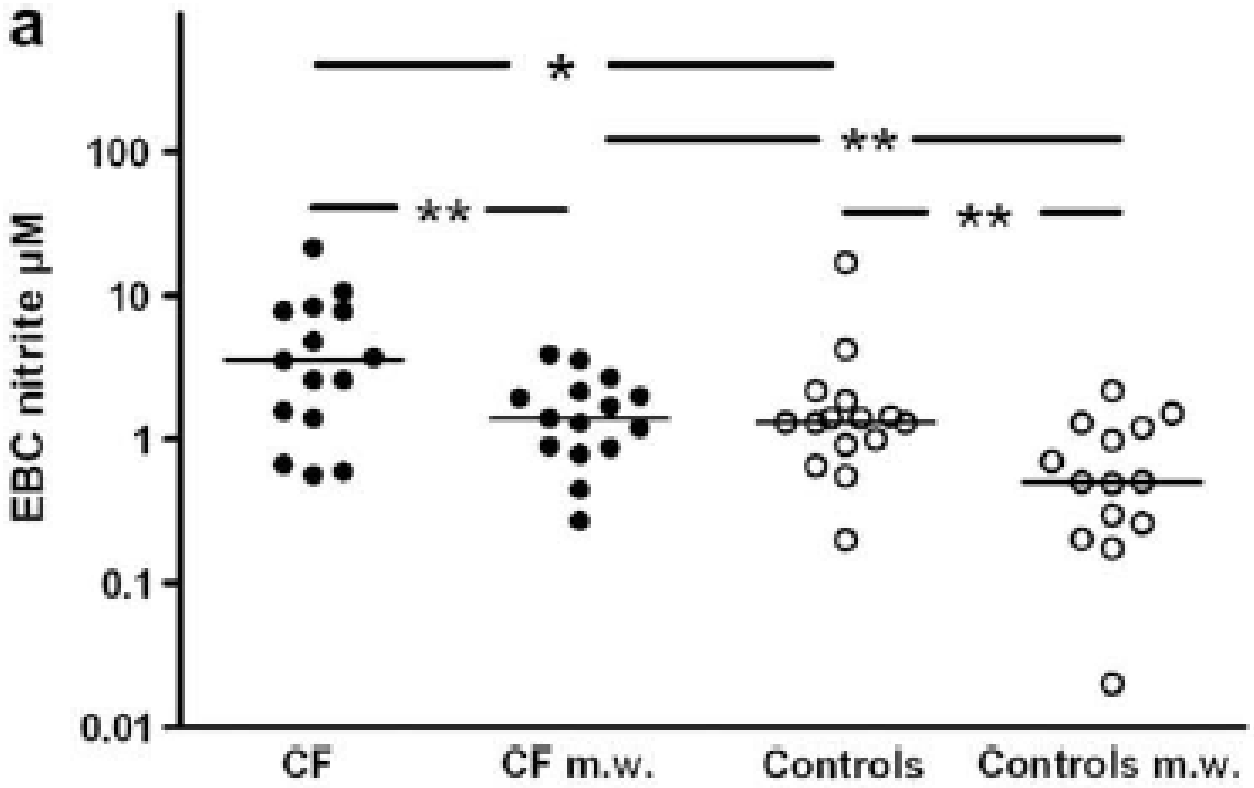
Murgia et BAS 2011

Induced sputum, exhaled breath condensate and nasal lavage fluid in electroplating workers exposed to chromium.

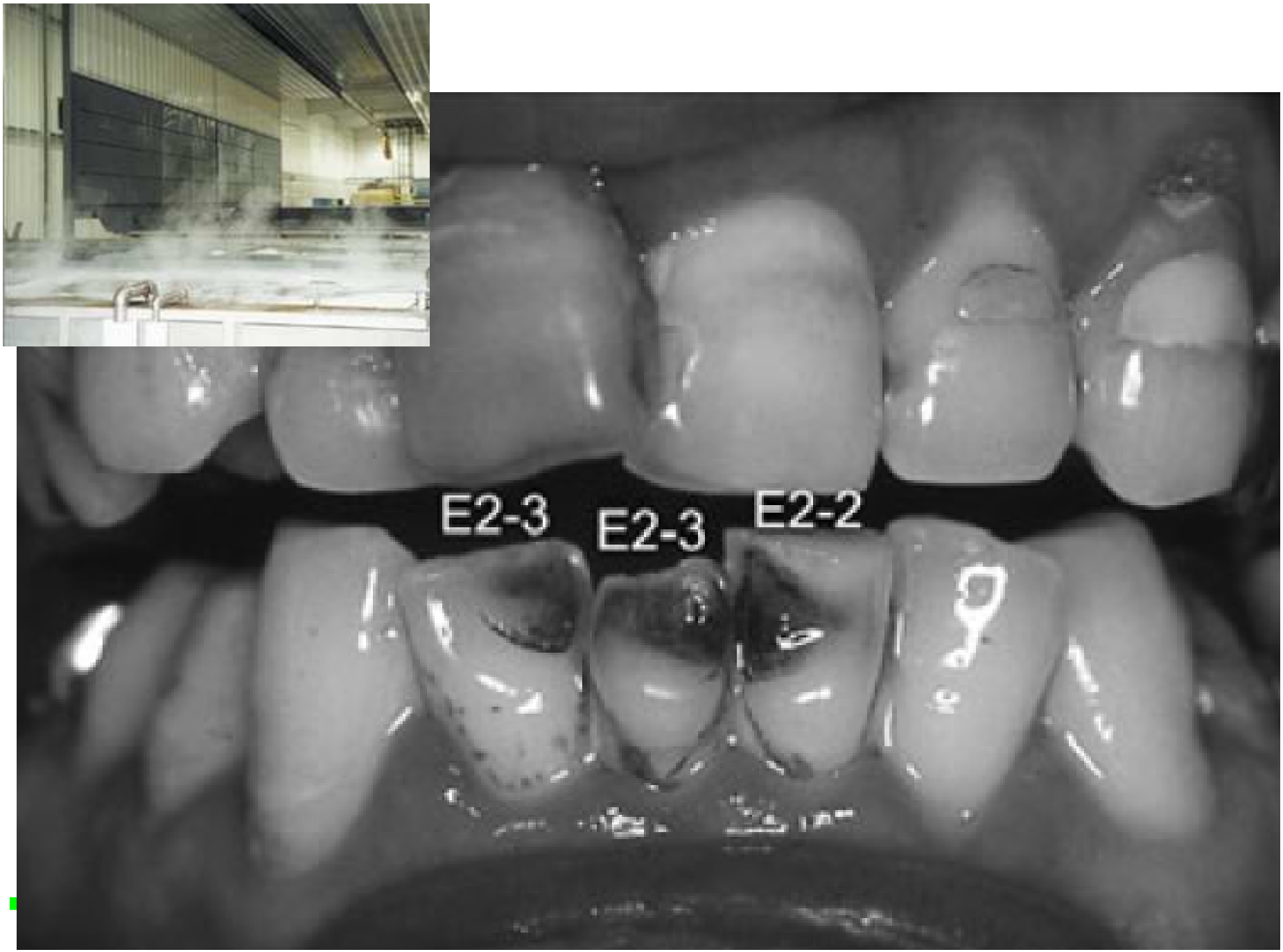


Murgia et al Int J Immunophatol Pharmacol 200

Nitrite and oral hygiene



Zetterquist W et al Res Med 2009


E2-3
E2-3
E2-2

doi: 10.1111/cea.12373

Clinical & Experimental Allergy, **44**, 1100–1118

REVIEW

The role of non-invasive biomarkers in detecting acute respiratory effects of traffic-related air pollution

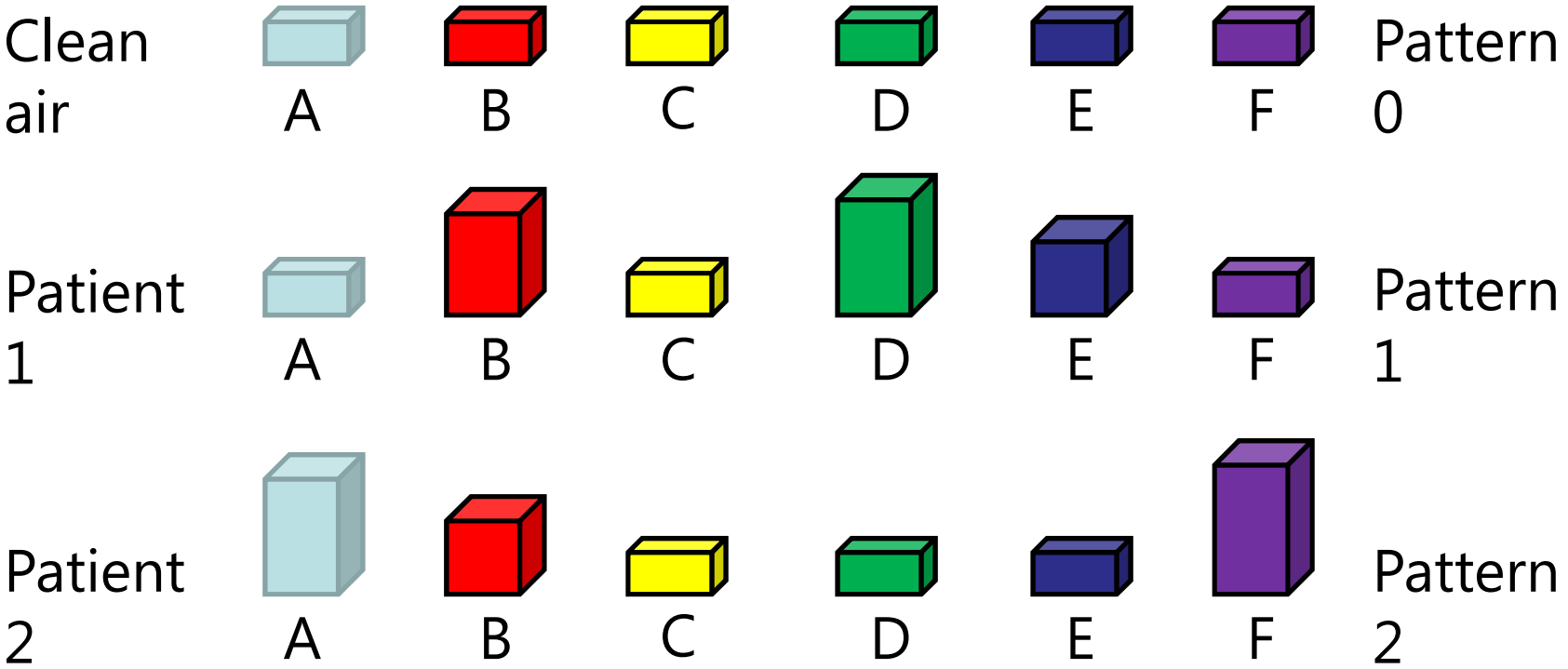
M. C. Scarpa[1], N. Kulkarni[2] and P. Maestrelli[1]

[1]Department of Cardiologic, Thoracic and Vascular Sciences, University of Padova, Padova, Italy and [2]Institute for Lung Health, Glenfield Hospital, Leicester, UK

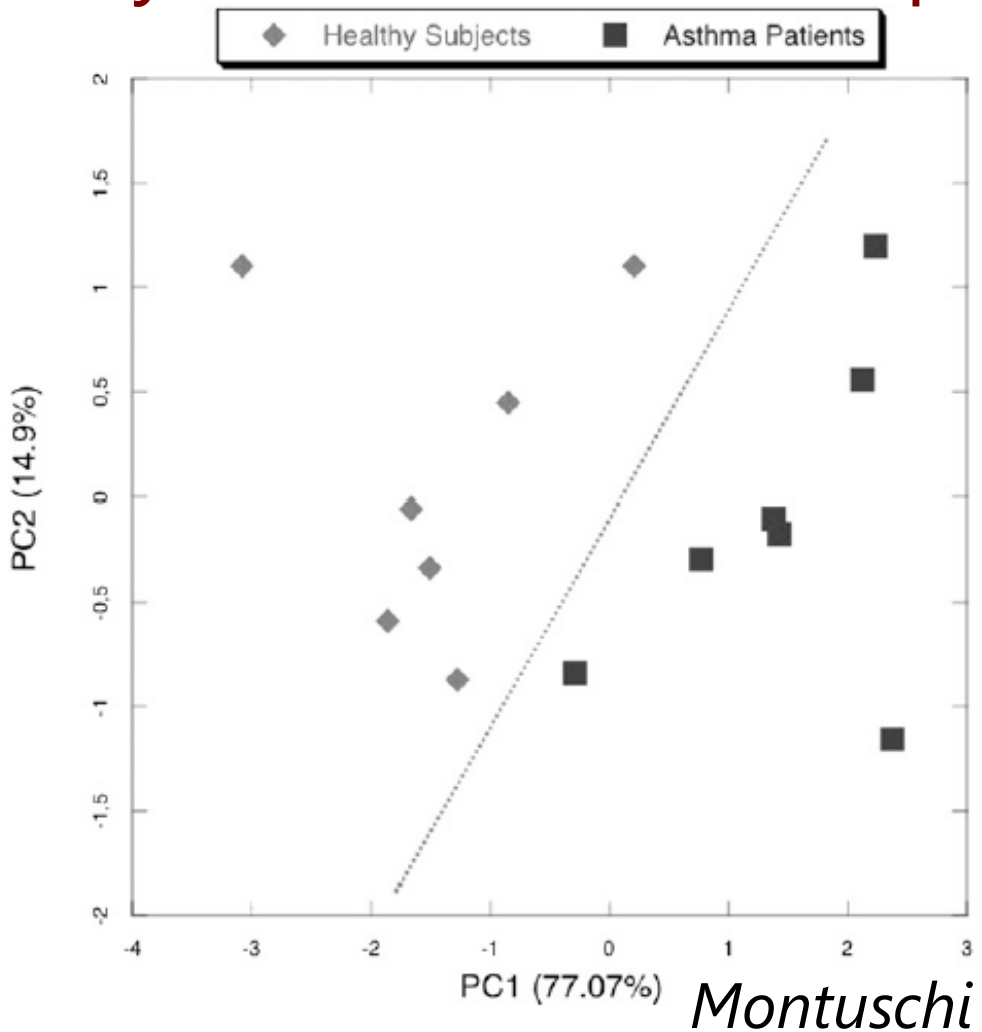
This survey of the current literature displays the complexity of this research field, highlights the significance of short-term studies on traffic-related air pollution and gives important tips when planning studies to detect acute respiratory effects of pollution in a non-invasive way.

Nuovi metodi di valutazione degli effetti precoci e reversibili sull'apparato respiratorio

- **Naso elettronico (eNose)**
- **Particelle esalate (PexA)**


Clean air
A
B
C
D
E
F
Pattern 0
Patient 1
A
B
C
D
E
F
Pattern 1
Patient 2
A
B
C
D
E
F
Pattern 2
Sensors

Airway disease and breathprints

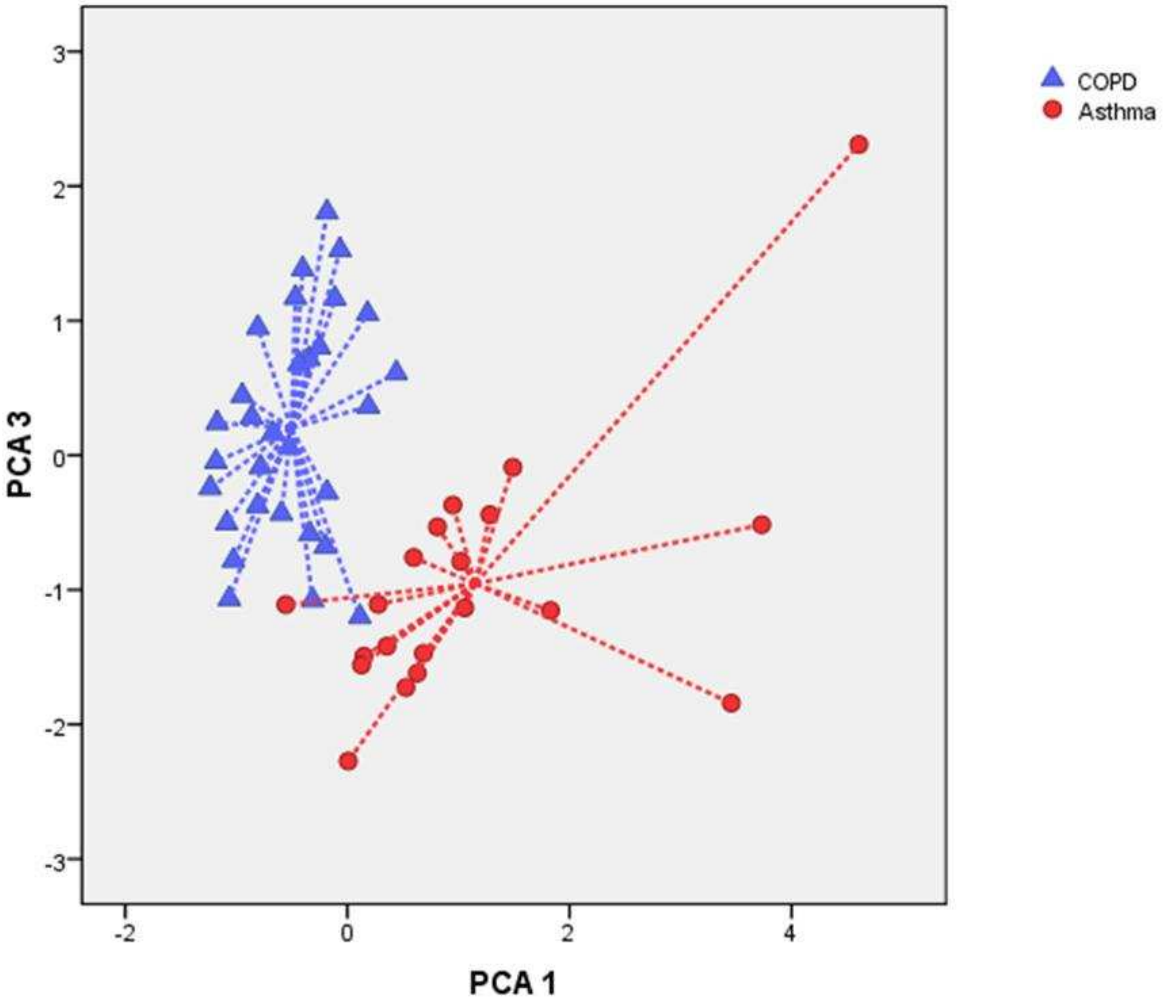


Montuschi P et al Chest 2010

Airway disease and breathprints

Asthma : red

COPD : blue

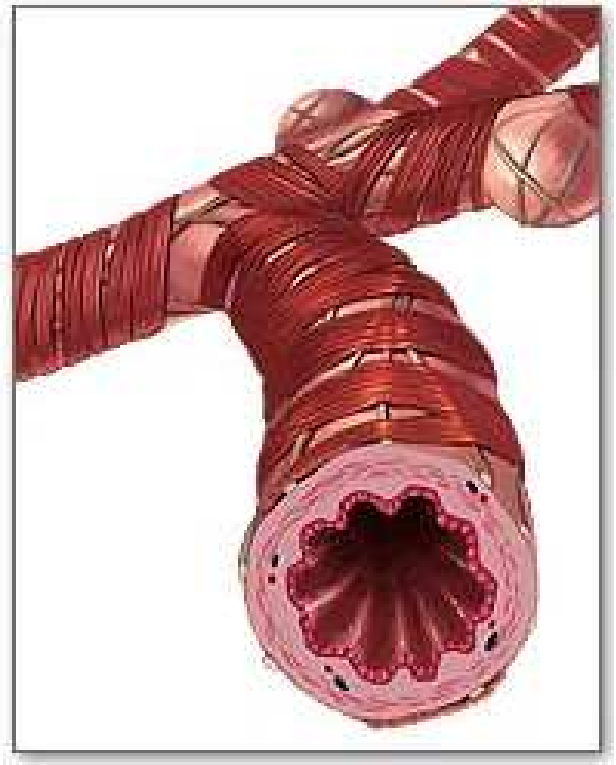


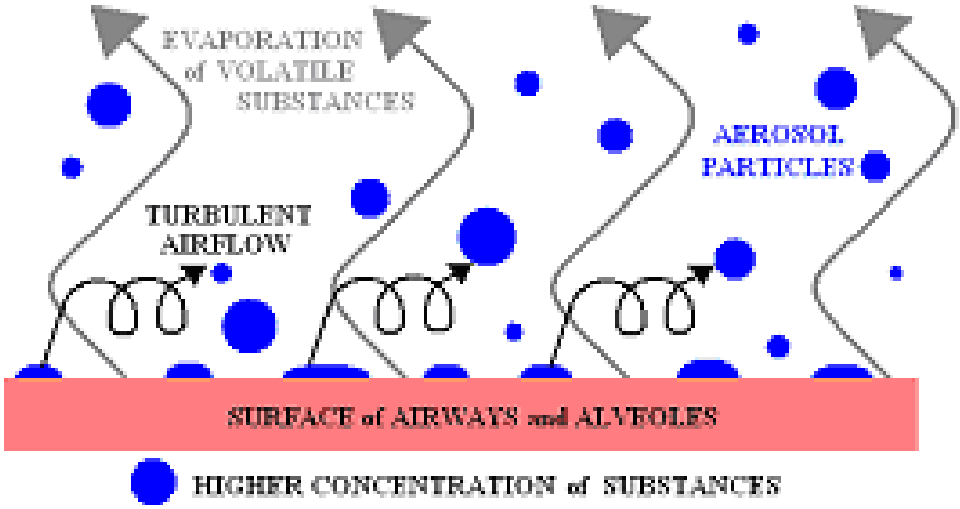
Fens N et al AJRCCM 2009

Nuovi metodi di valutazione degli effetti precoci e reversibili sull'apparato respiratorio

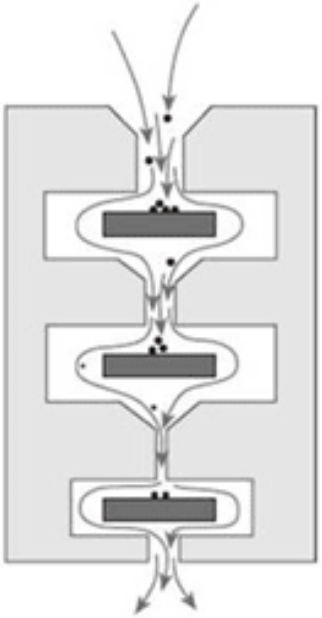
- **Naso elettronico (eNose)**
- **Particelle esalate (PexA)**

Cytokines and Chemokines.





Exhaled particle collection



Almstrand AC et al. Anal Chem 2009

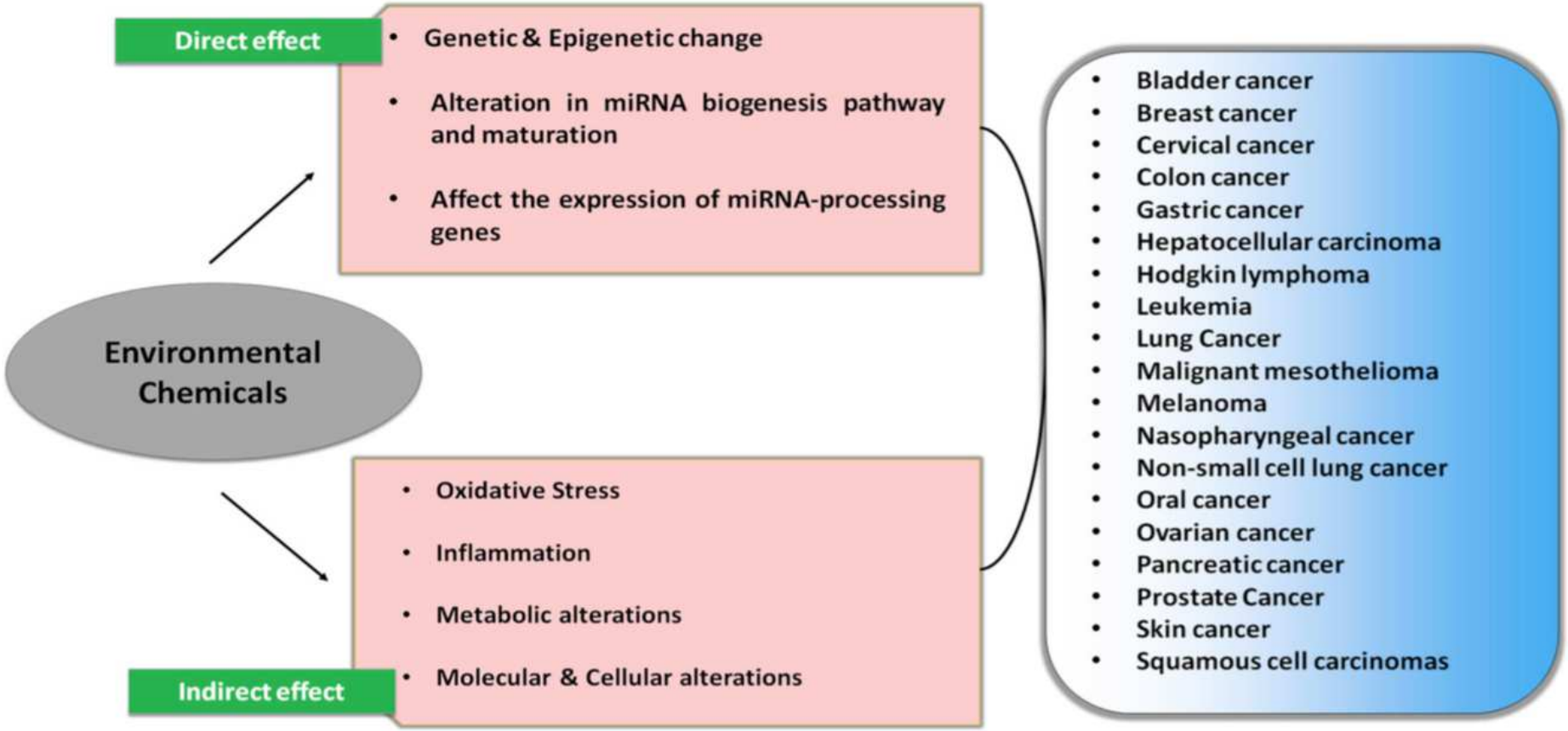
Exhaled particle analysis

Subject	PEx-SP-A (au)		EBC-SP-A (au)	
	Session 1	Session 2	Session 1	Session 2
1	1.4	1.5	<LoD	<LoD
2	4.0	3.3	<LoD	0.76
3	3.5	2.7	<LoD	<LoD
4	3.4	2.8	<LoD	<LoD
5	2.2	1.9	1.65	<LoD
6	2.5	3.0	0.57	<LoD
7	2.1	2.8	<LoD	0.48
8	2.2	3.0	<LoD	<LoD
9	2.4	2.2	<LoD	<LoD
Median (Q1–Q3)	2.6 (2.2–3.0)		–	

Larsson P et al Res Med 2012

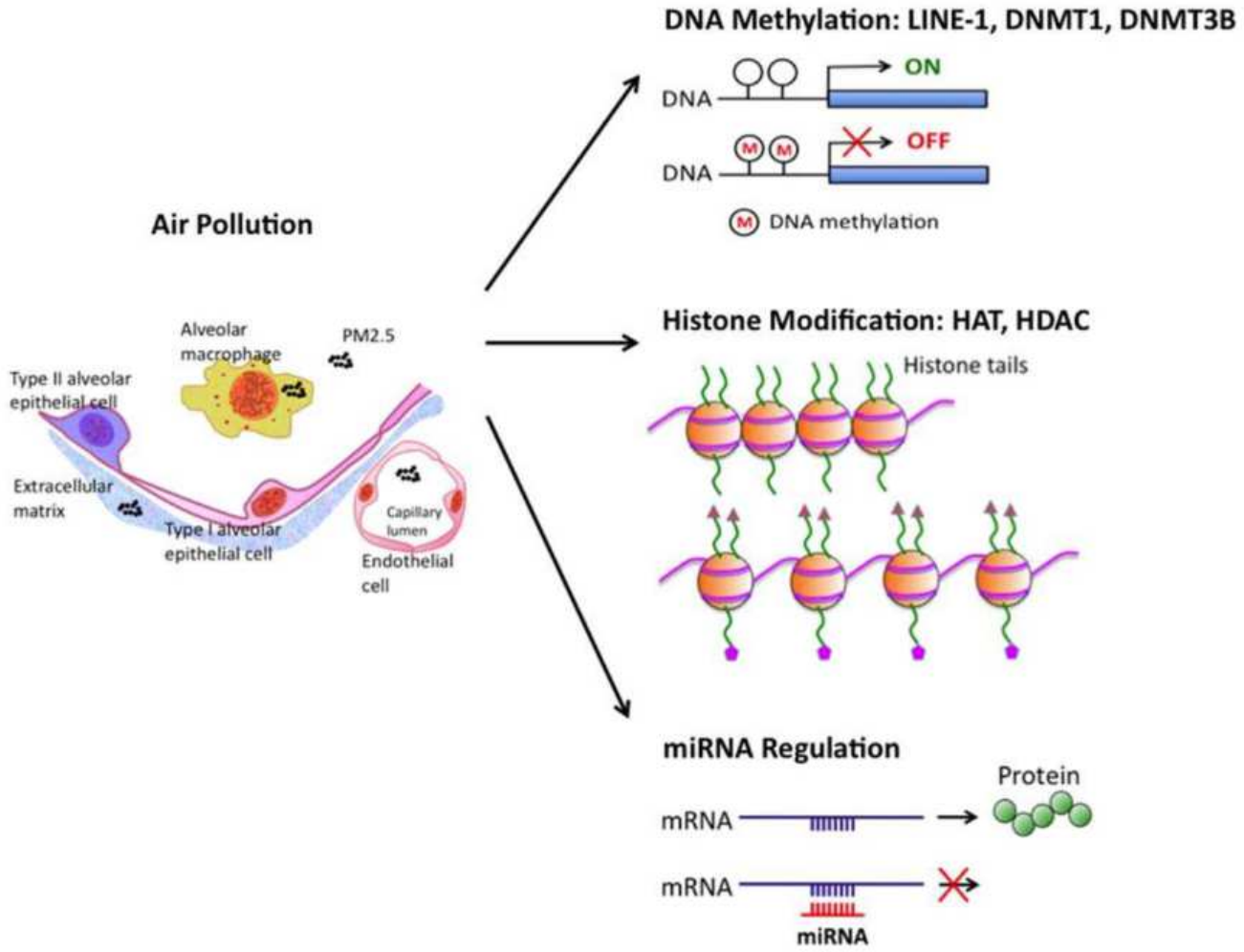
Valutazione degli effetti precoci e reversibili sull'apparato respiratorio

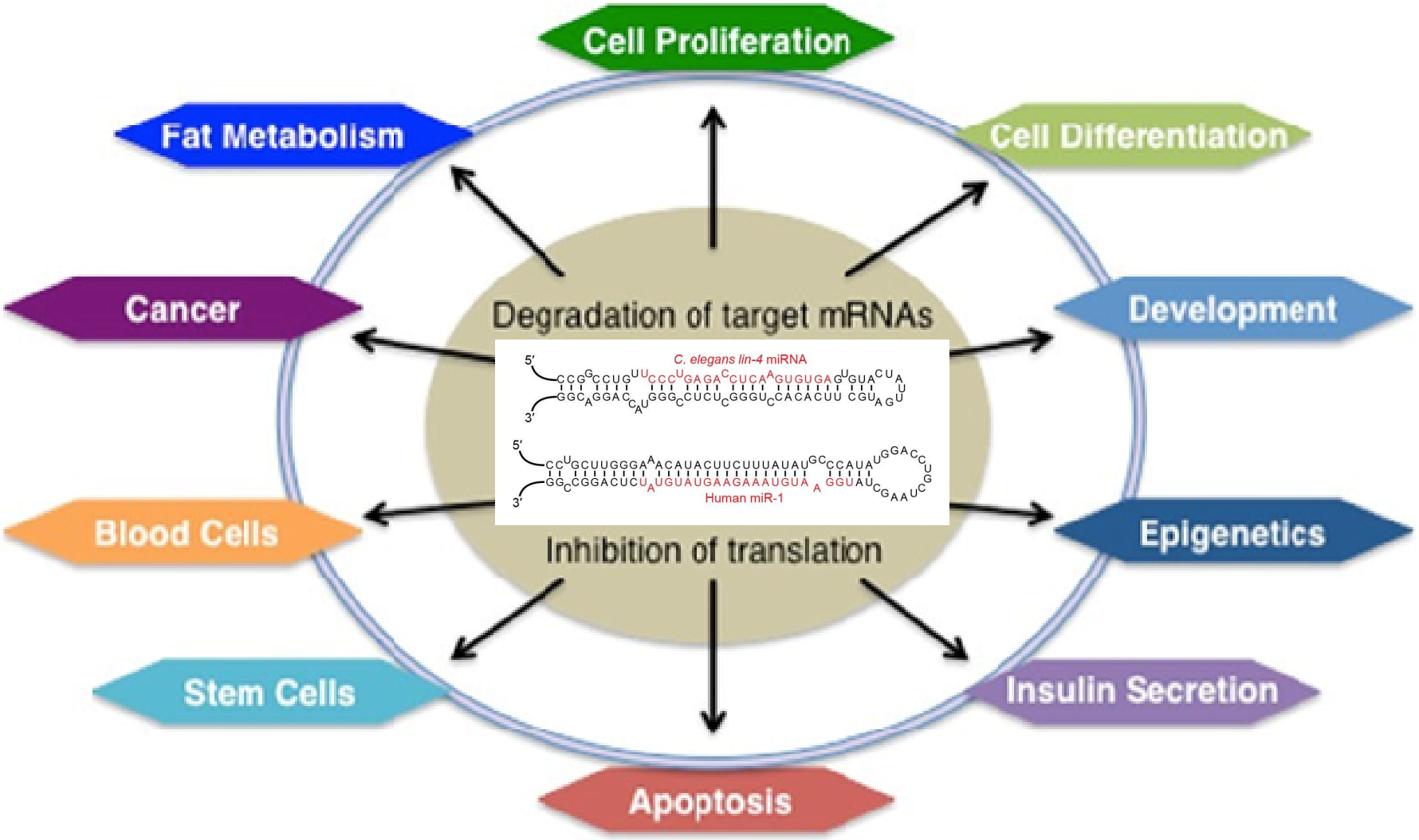
- Espettorato indotto
- Ossido nitrico esalato
- Condensato dell'aria espirata
- **Ricerca mutazioni in sangue e urine**
- **Citologia nasale e buccale**


Direct effect
Genetic & Epigenetic change
Alteration in miRNA biogenesis pathway and maturation
Affect the expression of miRNA-processing genes
Environmental Chemicals
Oxidative Stress
Inflammation
Metabolic alterations
Molecular & Cellular alterations
Indirect effect
Bladder cancer
Breast cancer
Cervical cancer
Colon cancer
Gastric cancer
Hepatocellular carcinoma
Hodgkin lymphoma
Leukemia
Lung Cancer
Malignant mesothelioma
Melanoma
Nasopharyngeal cancer
Non-small cell lung cancer
Oral cancer
Ovarian cancer
Pancreatic cancer
Prostate Cancer
Skin cancer
Squamous cell carcinomas

Nuovi metodi di valutazione degli effetti precoci e reversibili sull'apparato respiratorio

- **Modificazioni epigenetiche**
  - **miRNA**
  - **Metilazione del DNA**
  - **Modificazione degli istoni**


DNA Methylation: LINE-1, DNMT1, DNMT3B
DNA
ON
DNA
OFF
DNA methylation
Air Pollution
Alveolar macrophage
PM2.5
Type II alveolar epithelial cell
Extracellular matrix
Type I alveolar epithelial cell
Capillary lumen
Endothelial cell
Histone Modification: HAT, HDAC
Histone tails
miRNA Regulation
Protein
mRNA
mRNA
miRNA


Cell Proliferation
Fat Metabolism
Cell Differentiation
Cancer
Development
Degradation of target mRNAs
C. elegans lin-4 miRNA
Human miR-1
Blood Cells
Epigenetics
Inhibition of translation
Stem Cells
Insulin Secretion
Apoptosis

A Section 508–conformant HTML version of this article is available at http://dx.doi.org/10.1289/ehp.1408459.

Environmental Health Perspectives • VOLUME 123 | NUMBER 5 | May 2015

Review

MicroRNAs as Potential Signatures of Environmental Exposure or Effect: A Systematic Review

Karen Vrijens,[1] Valentina Bollati,[2] and Tim S. Nawrot[1,3]

[1]Centre for Environmental Sciences, Hasselt University, Diepenbeek, Belgium; [2]Center of Molecular and Genetic Epidemiology, Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Milan, Italy; [3]Department of Public Health and Primary Care, Environment and Health Unit, Leuven Univeristy, Leuven, Belgium

Table 1. miRNAs that are responsive to personal or environmental exposure and their roles in human disease.

miRNA	Regulated	Exposure	Diseases	Sources
Let-7e	Down	TCDD	HCC, lung, pituitary, and breast cancer, GEP tumors	Feitelson and Lee 2007; Qian et al. 2009; Rahman et al. 2009; Sakurai et al. 2012; Takamizawa et al. 2004
	Up	RDX	Heart failure, asthma	Polikepahad et al. 2010; Thum et al. 2007
Let-7g	Down	BPA, PM	Lung carcinoma, GEP tumors, breast cancer	Rahman et al. 2009; Sakurai et al. 2012
miR-9	Down	PM	Brain cancer, Huntingon's disease	Ferretti et al. 2009; Lau and de Strooper 2010
	Up	Aluminum	Hodgkin lymphoma, breast cancer	Leucci et al. 2012; Ma et al. 2010
miR-10b	Down	Formaldehyde, PM	Gastric cancer	Kim K et al. 2011
miR-21	Down	Smoking	Diabetes type 2	Zampetaki et al. 2010
	Up	DEP, metal-rich PM	Breast cancer, glioblastoma, neo-intimal lesions, cardiac hypertrophy, atherosclerosis	Ji et al 2007; Raitoharju et al. 2011; van Rooij et al. 2007; Volinia et al. 2006
miR-26b	Down	DEP, BPA, PFOA	Schizophrenia, CRC, breast cancer	Earle et al. 2010; Liu et al. 2011; Perkins et al. 2007
miR-31	Down	DEP, TCDD	Medulloblastoma, T-cell leukemia	Ferretti et al. 2009; Yamagishi et al. 2012
miR-34b	Down	Smoking (2×)	CRC, pancreatic, mammary, ovarian, and renal cell carcinoma	Vogt et al. 2011
miR-92b	Down	Smoking, DDT	Medulloblastoma	Genovesi et al. 2011
miR-122	Down	Smoking	HCC	Bai et al. 2009
	Up	TCDD	Hepatitis C, renal cell carcinoma, male infertility, sepsis, hyperlipidemia	Gao et al. 2012; Henke et al. 2008; Wang C et al. 2011; Wang H et al. 2012; White et al. 2011
miR-125b	Down	Smoking (2×)	Breast cancer, head and neck cancer	Nakanishi et al. 2014; Zhang et al. 2011
	Up	Aluminum sulfate (2×)	Endometriosis, cardiac hypertrophy, Alzheimer's disease	Busk and Cirera 2010; Lukiw and Alexandrov 2012; Ohlsson Teague et al. 2009

..continua

Conclusioni

- **Metodi validati ancora attuali ma non sufficienti a valutare i danni precoci**
- **Vecchi metodi non invasivi per studiare l'infiammazione possono essere utili (FeNO)**
- **Nuovi metodi per studiare l'infiammazione ancora da validare**
- **Valutazione dei danni genetici (……)**
- **Epigenetica promettente ma ancora costosa e in espansione**