



# **Inquinanti Ambientali e Patologie dell'Apparato Respiratorio: Asma**

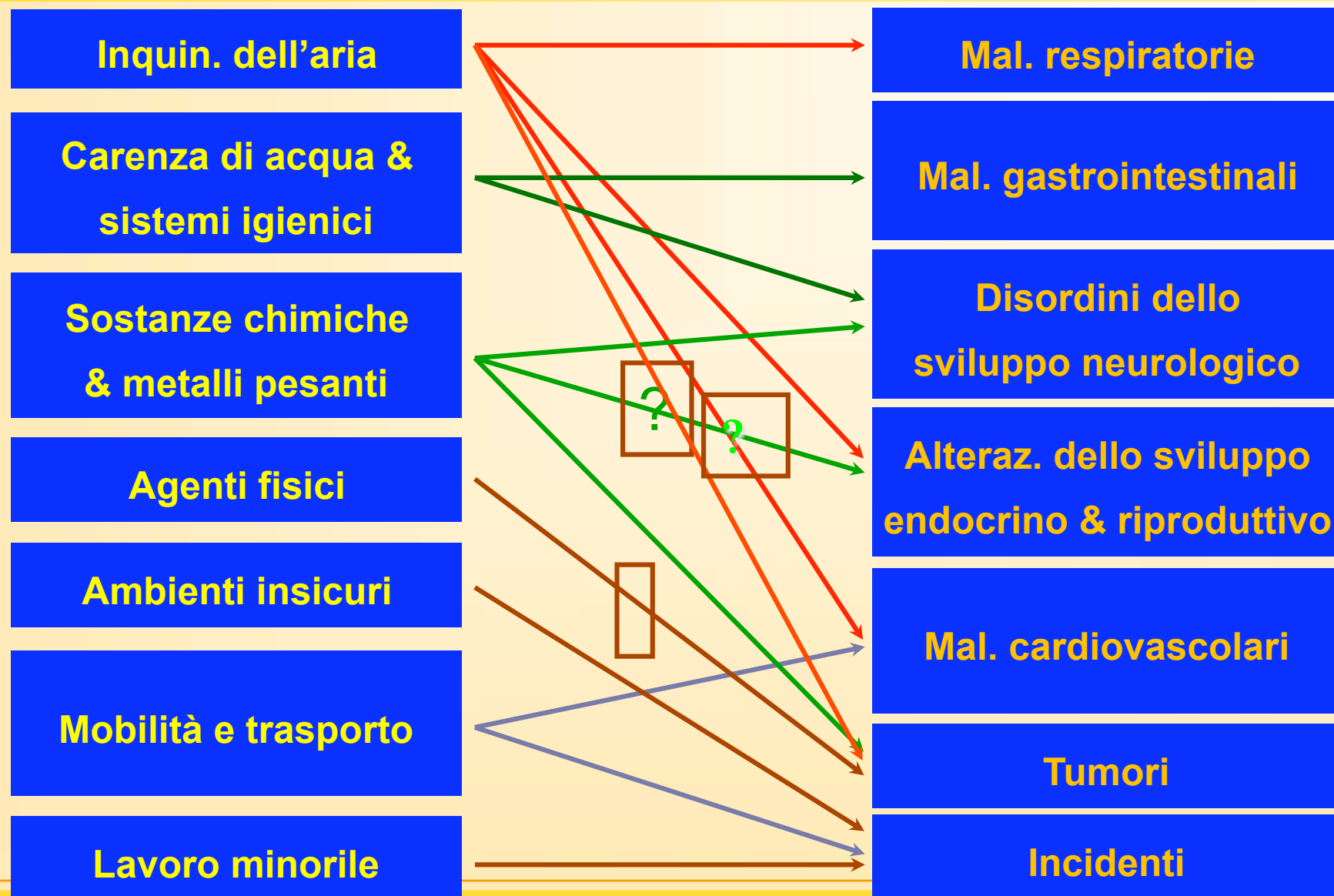
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Clinical Immunology**

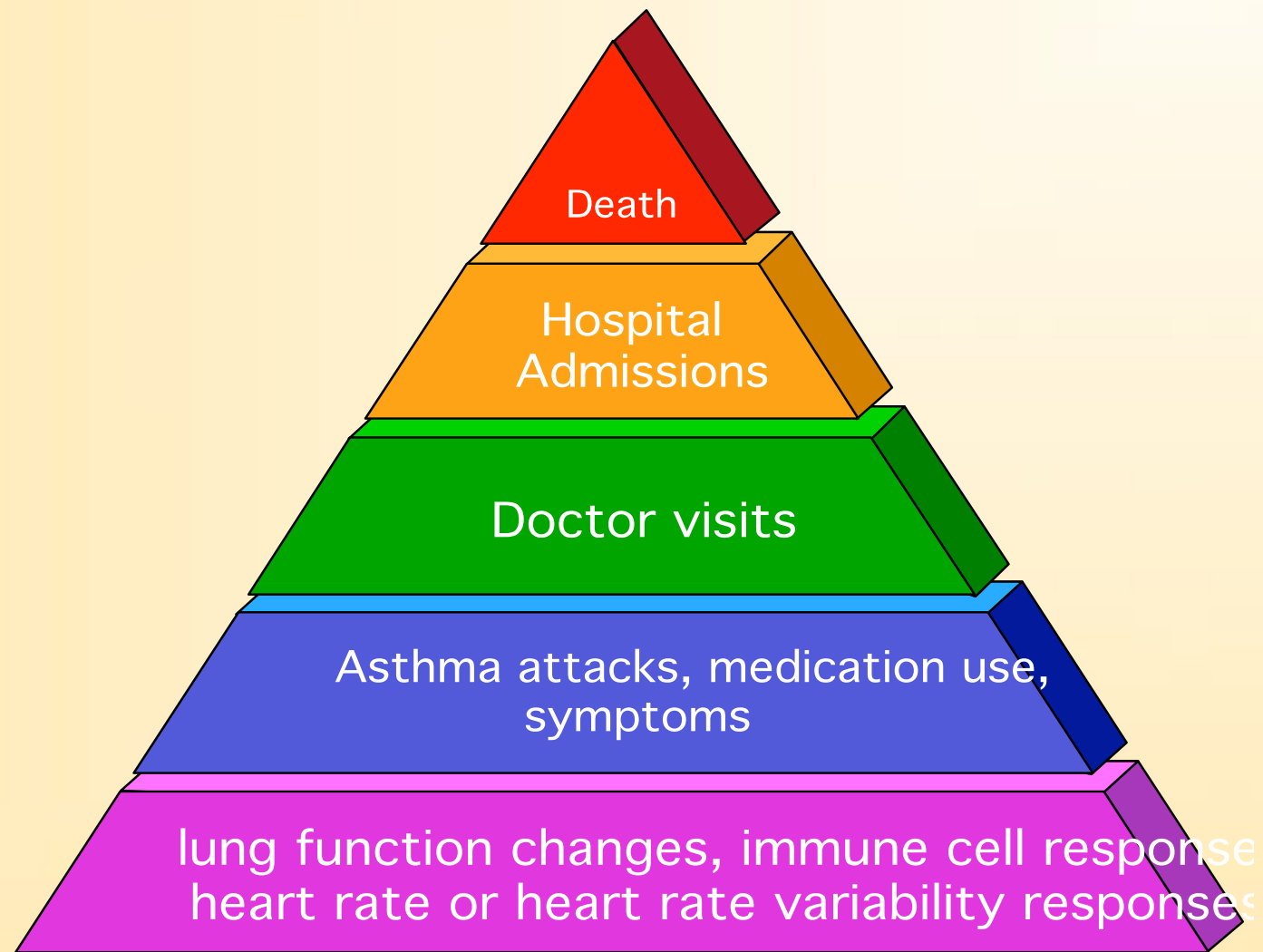
**CeSI  
Allergy Related Disease Unit**



# Relazioni tra fattori ambientali e salute



# “Pyramid of Effects”



# Morti per anno negli USA

■ Inquinamento	23,000
■ Ubriachezza al volante	17,000
■ Omicidi	20,000

<b>Health outcome</b>	<b>N.casi attribuibili Inquinamento totale (PM10)</b>			<b>N.casi attribuibili Inquinamento traffico-correlato</b>		
	<i>Austria</i>	<i>Francia</i>	<i>Svizzera</i>	<i>Austria</i>	<i>Francia</i>	<i>Svizzera</i>
<b>Mortalità totale (&gt;35a)</b>	<b>5600</b>	<b>31700</b>	<b>3300</b>	<b>2400</b>	<b>17600</b>	<b>1800</b>
<b>Ricoveri m.respiratorie</b>	<b>3400</b>	<b>13800</b>	<b>1308</b>	<b>1500</b>	<b>7700</b>	<b>700</b>
<b>Ricoveri m.cardiache</b>	<b>6700</b>	<b>19800</b>	<b>3000</b>	<b>2900</b>	<b>11000</b>	<b>1600</b>
<b>Incidenza bronchite cronica (adulti&gt;25a)</b>	<b>6200</b>	<b>36700</b>	<b>4200</b>	<b>2700</b>	<b>20400</b>	<b>2300</b>
<b>Episodi bronchite (bambini&lt;15a)</b>	<b>48000</b>	<b>450000</b>	<b>45000</b>	<b>21000</b>	<b>250000</b>	<b>24000</b>
<b>Attacchi asma (adulti &gt;15a)</b>	<b>94000</b>	<b>577000</b>	<b>63000</b>	<b>40000</b>	<b>321000</b>	<b>33000</b>
<b>Attacchi asma (bambini&lt;15a)</b>	<b>35000</b>	<b>243000</b>	<b>24000</b>	<b>15000</b>	<b>135000</b>	<b>13000</b>

Kunzli et al. *The Lancet* 2000; 356(2):795-801

Health outcome	Rischio relativo	N.casi attribuibili per 10mcg/m <sup>3</sup> PM10 e 1.000.000 abitanti		
		<i>Austria</i>	<i>Francia</i>	<i>Svizzera</i>
<b>Mortalità totale (&gt;35a)</b>	1.043	370	340	340
<b>Ricoveri m.respiratorie</b>	1.013	230	150	130
<b>Ricoveri m.cardiache</b>	1.013	450	210	300
<b>Incidenza bronchite cronica (adulti&gt;25a)</b>	1.098	410	390	430
<b>Episodi bronchite (bambini&lt;15a)</b>	1.306	3200	4830	4620
<b>Attacchi asma (adulti &gt;25a)</b>	1.039	6280	6190	6370
<b>Attacchi asma (bambini&lt;15a)</b>	1.044	2330	2600	2400

Kunzli et al. *The Lancet* 2000; 356(2):795-801



# COMMENTO

- Il rischio individuale per esposizione all'inquinamento atmosferico è relativamente basso.
- Essendo molto alto il numero di soggetti esposti, l'impatto sulla salute pubblica è elevato.
- L'inquinamento da polveri fini nell'ambiente urbano è responsabile ogni anno di 100.000 morti in Europa (*WHO, 2002*)
- L'inquinamento atmosferico rappresenta l'ottava causa di morte più importante in Europa (*Ezzati et al. Lancet 2002; 360:1347-60*)

# PRINCIPALI INQUINANTI ATMOSFERICI

Inquinante	Formula	Proprietà	Nocività
ossidi di zolfo	SO <sub>2</sub> ; SO <sub>3</sub>	gas, intenso odore, solubile in H <sub>2</sub> O dà acidi	danni a uomo, biota e materiali
ossidi di azoto	NO <sub>x</sub>	gas, intenso odore, solubile in H <sub>2</sub> O dà acidi	danni a uomo, biota, materiali + smog fot.
monossido di carbonio	CO	gas incolore ed inodore	molto tossico
diossido di carbonio	CO <sub>2</sub>	gas incolore ed inodore	effetto serra
Idrocarburi + benzene; IPA	C <sub>x</sub> H <sub>y</sub>	gas, liquidi o solidi	tossici, cancerogeni smog fotochimico.
Polveri totali PM10	-	aerosol	danni a uomo, biota e materiali



# Who is at Risk?

- Children
- People with pre-existing respiratory problems
- Healthy adults who are active outside (includes athletes)
- Some individuals are more susceptible to ozone exposure
- Senior citizens
- Pregnant women



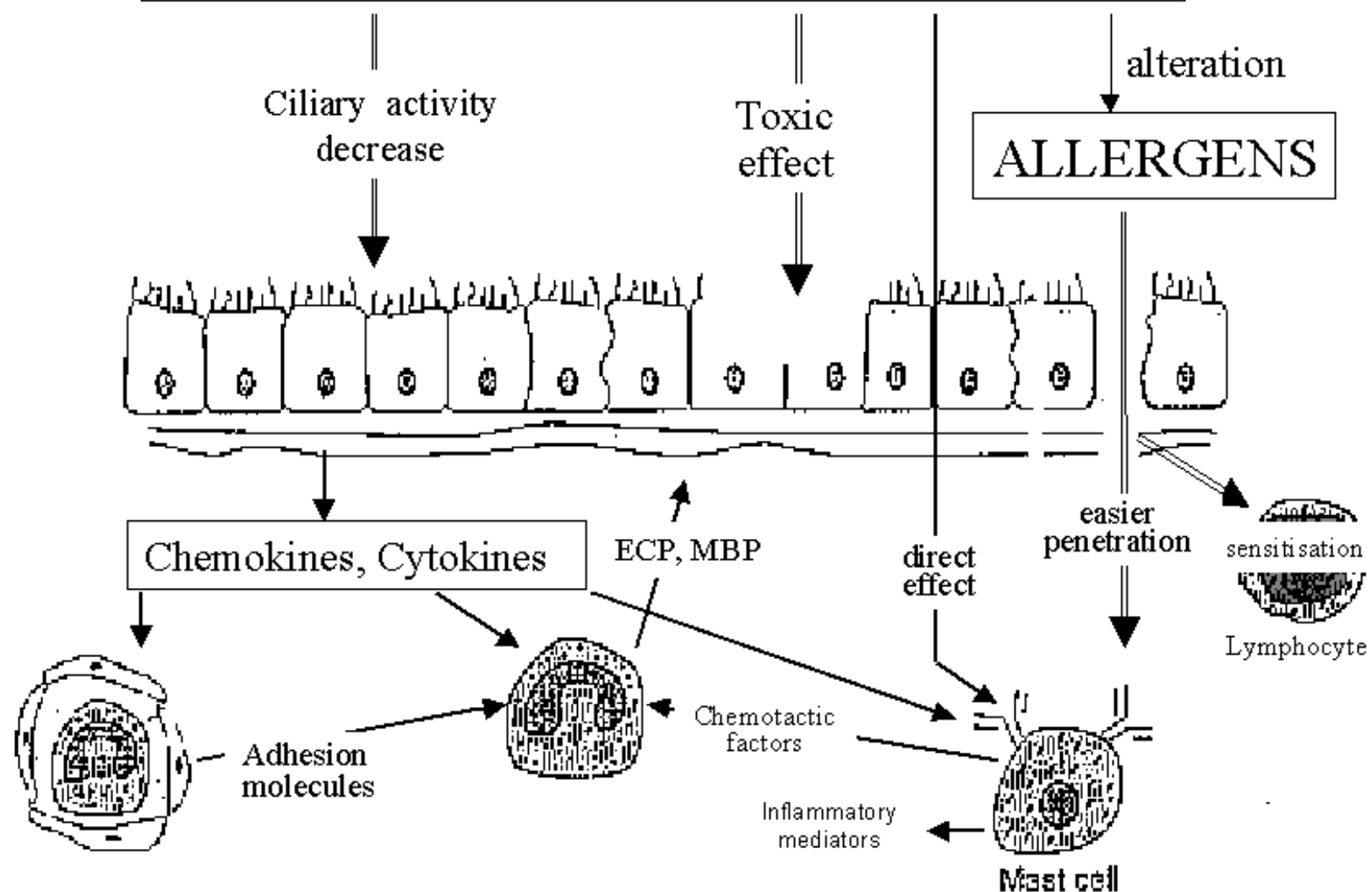
# Esposizione maggiore

## Rapporto tra bambini (1 anno) e adulti nell'introito di:

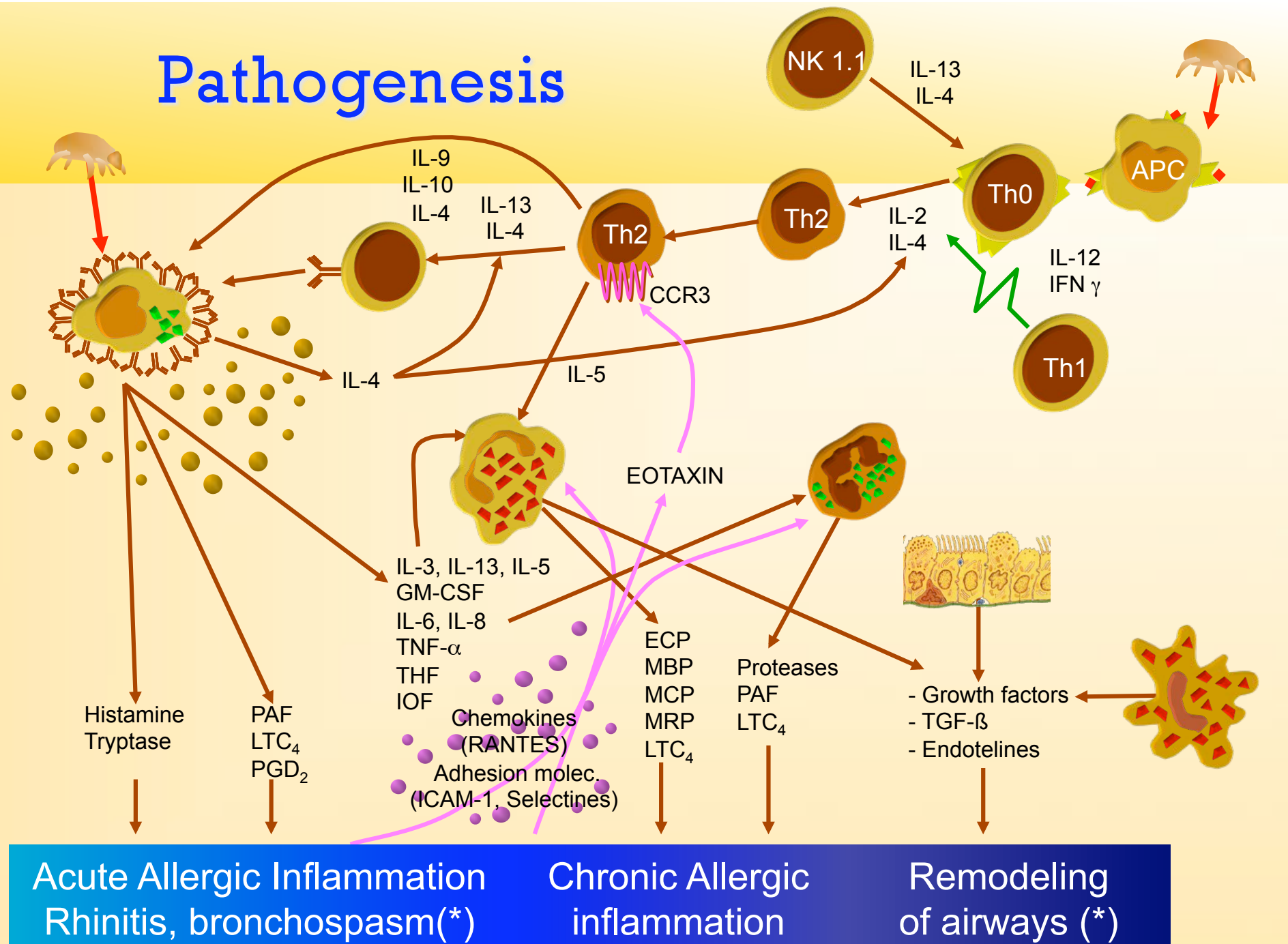
■ Aria	2.3 volte
■ Acqua/liquidi	4.8 volte
■ Cibo	6.3 volte

Derived from data in: US Environmental Protection Agency (1997), National Research Council (1993) and Gephart et al. (1994).

# NO<sub>2</sub>, SO<sub>2</sub>, O<sub>3</sub>, DEP, Other Toxic Pollutants

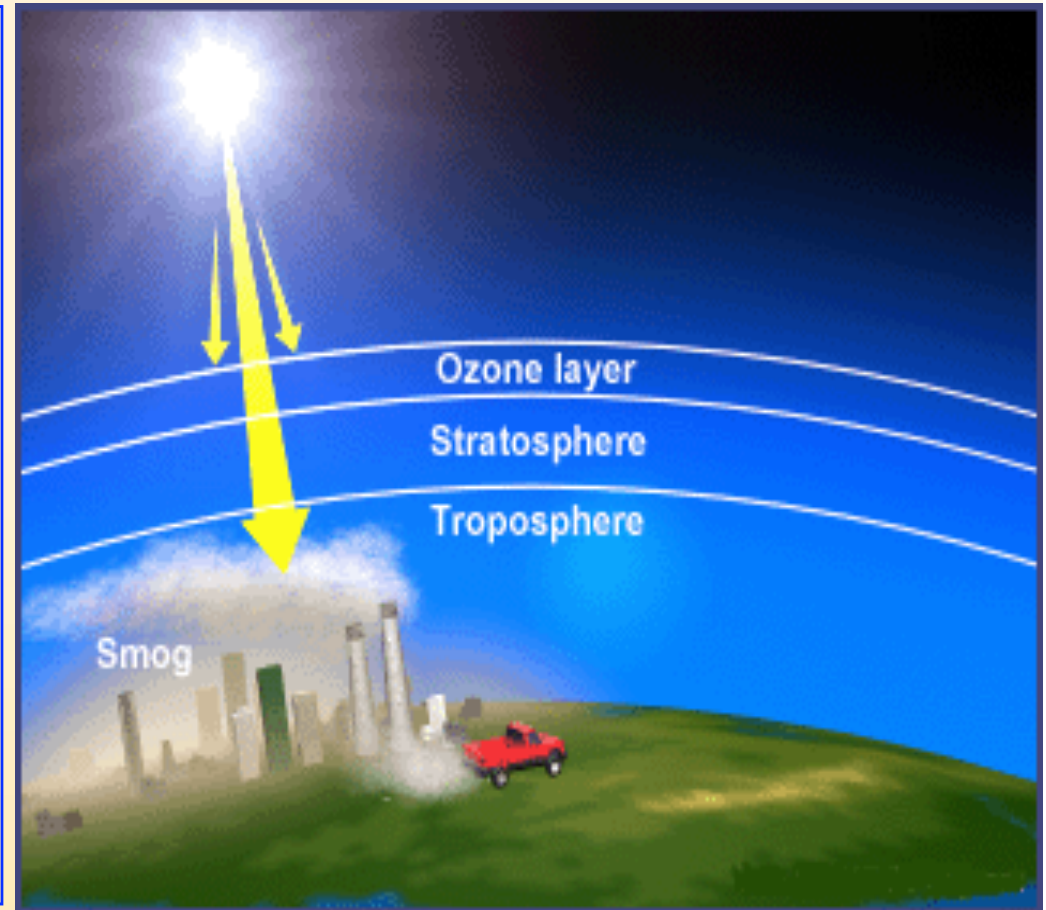


# Pathogenesis



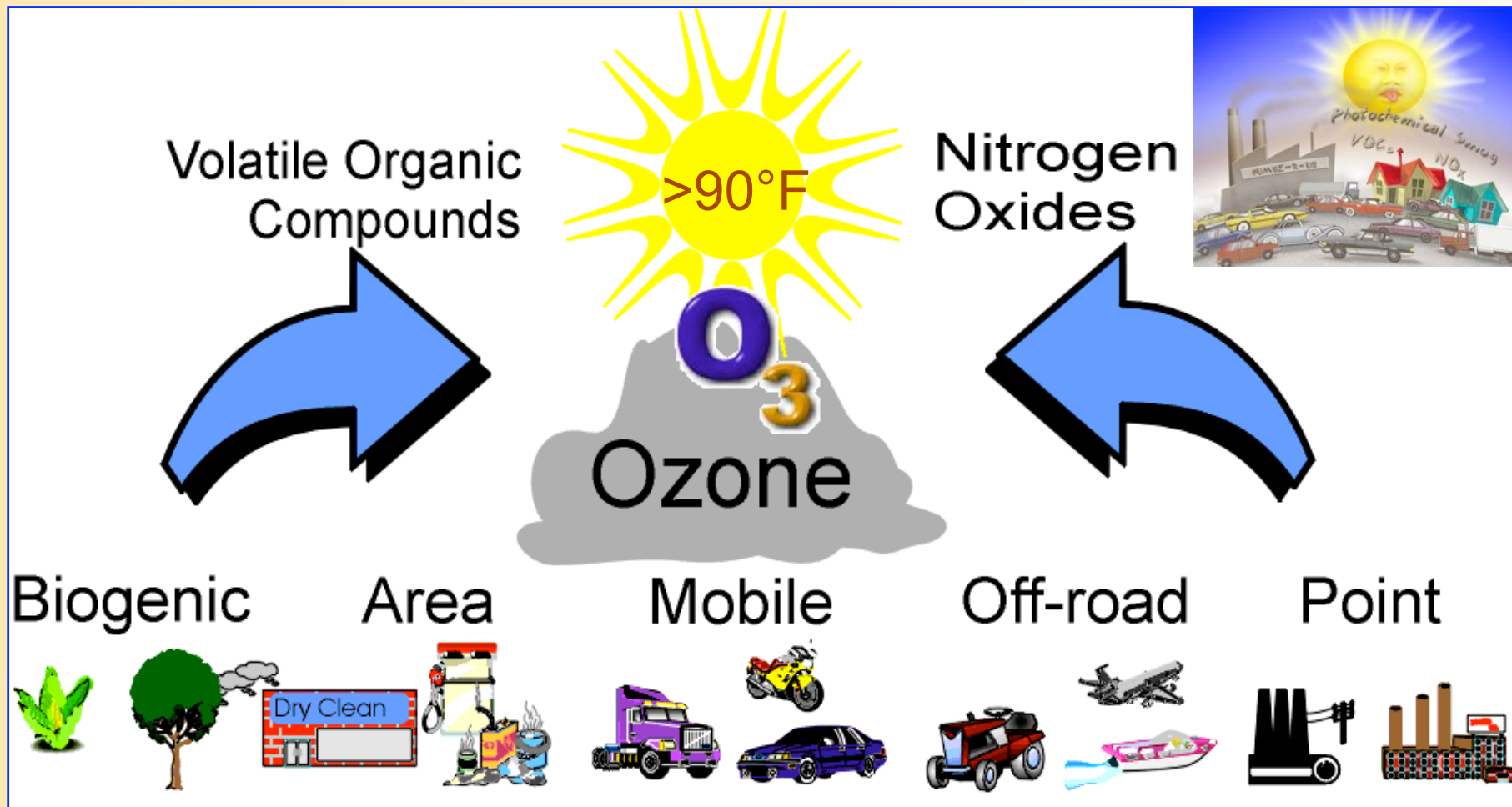
# Ozono

- Good Ozone: Ozone in the stratosphere high above the earth protects human health and the environment
- Bad Ozone: Ground Level ozone is a respiratory irritant to human health

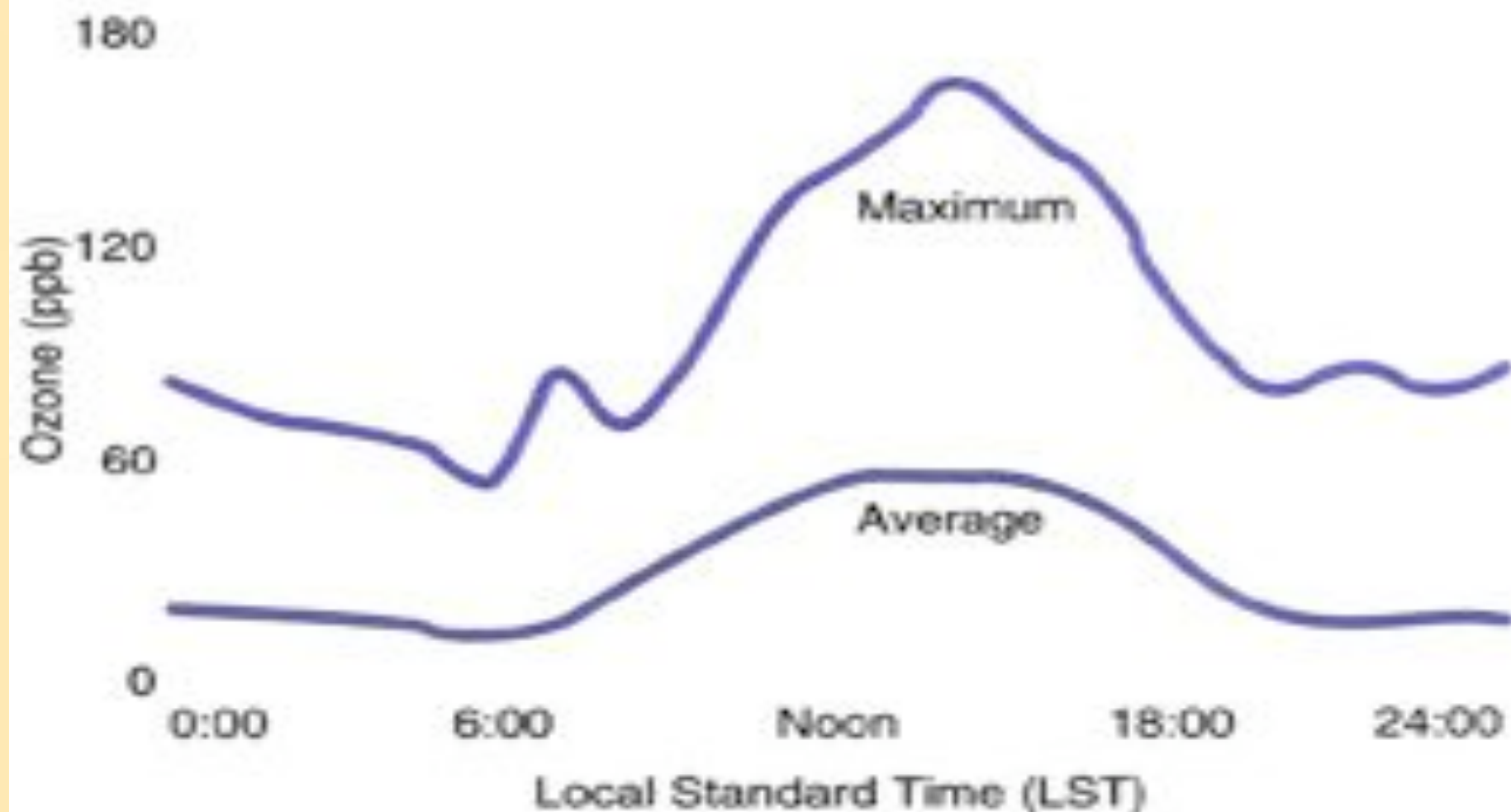




# How Ground Level Ozone is Formed



**Figure 12.10. Typical Ozone Concentrations by Time of Day**



Source: U.S. Environmental Protection Agency. Data reflect all observations recorded at the Plaza Rd. site in Charlotte, 1981-89.

# Health Effects- Short Term

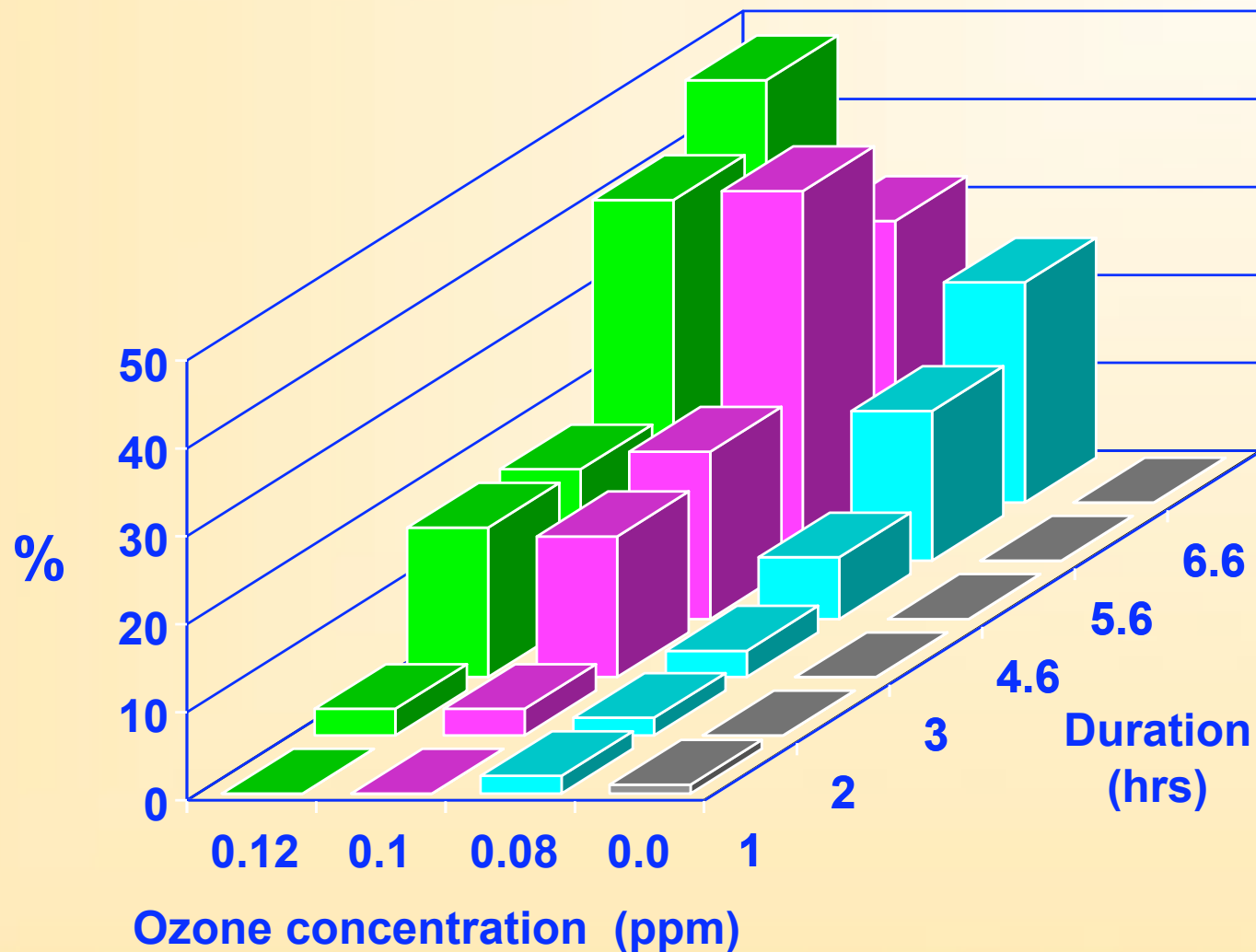
- Short Term Exposure: 1-6 hours/day
- Lung damage is typically reversible
- Symptoms include:
  - Reduced lung function (difficulty breathing)
  - Chest pain
  - Throat and eye irritation
  - Aggravated asthma
  - Increased asthma attacks
  - Increased sensitivity to allergens and pollutants



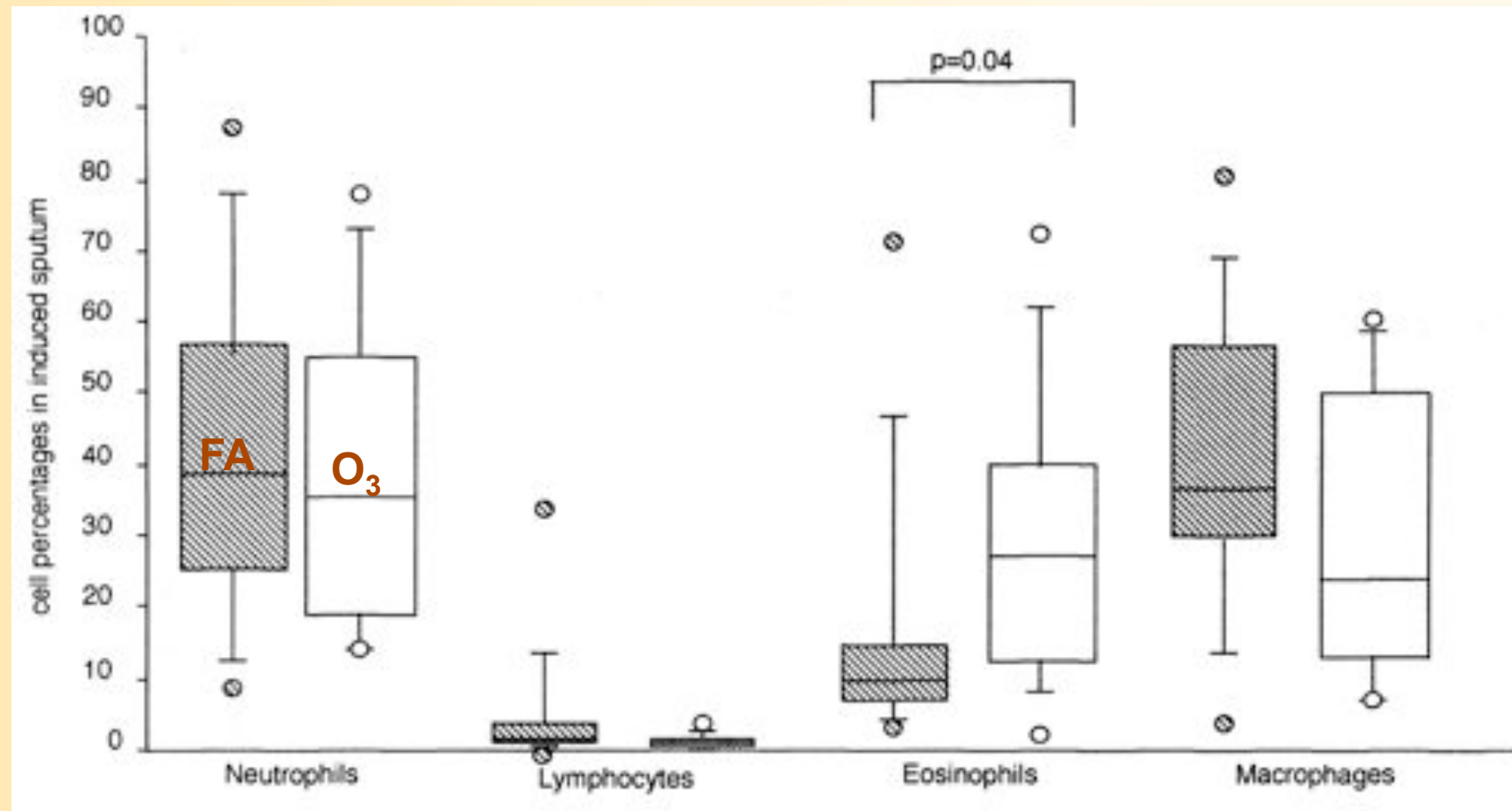


# Effect of ozone exposure

Proportion experiencing  $\geq 10\%$  decrease in  $FEV_1$



# Differential Cell Counts

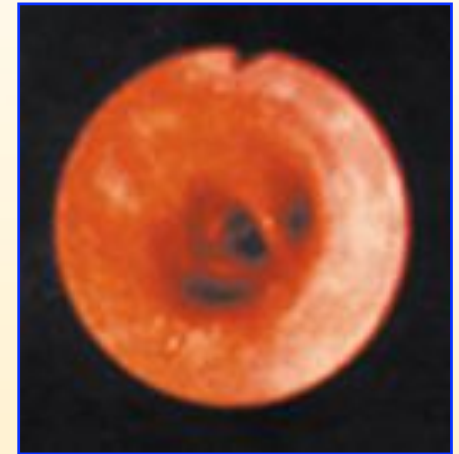
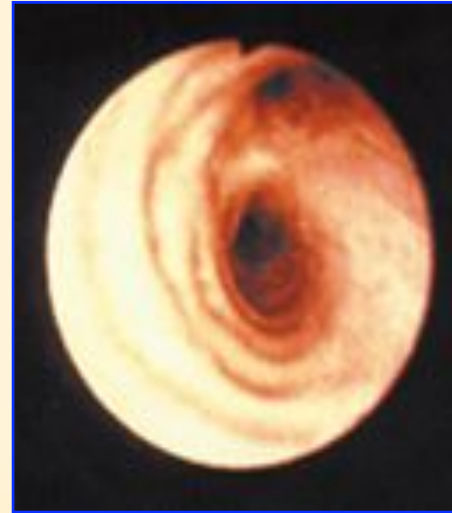


# Health Effects: Long Term

- Long Term Exposure: 6+ hours/day
- Cumulative exposure causes permanent lung damage
- Symptoms include:
  - Reduced lung function
  - Inflammation of lung lining
  - Higher rate of developing asthma
  - Increased lung cancer mortality rates

# Health Effects: Long Term

- Lung tissue damage
  - “sunburn” to the lungs
- Permanent lung damage
  - Children: decreased lung function
  - Adults: premature aging of lungs



Ozone can inflame the lung's lining.  
A healthy lung air way (left)  
and an inflamed air way (right)

# OZONE

- In studenti esposti da sempre ad ozono, è stata rilevata una riduzione dei flussi delle medie e piccole vie aeree (“small airways dysfunction”) (Kunzli et al.).
- Una riduzione dei flussi respiratori è stata anche individuata in soggetti che risiedevano per più di 4 anni in zone con alti livelli di ozono (Galizia and Kinney).

# **Meccanismi di tossicità dell' ozono**

- **Ossidazione diretta**
- **Formazione di radicali liberi**
- **Perossidazione lipidica**
- **Inflammazione/rimodellamento**



# **OZONE AND ASTHMA**

## **WHAT WE DON'T KNOW (I)**

- **What is the mechanism of ozone-associated asthma exacerbations?**
- **What is the mechanism of ozone enhancement of response to allergen?**
- **What is the relative importance of exposure to ambient ozone as a trigger for asthma exacerbations?**

# OZONE AND ASTHMA

## WHAT WE DON'T KNOW (II)

- What is the effect of childhood exposure to ozone on the subsequent course of asthma?
- Is there a subset of asthmatic persons at particular risk for ozone-induced asthma exacerbation? If so, are there specific genetic determinants of this risk?



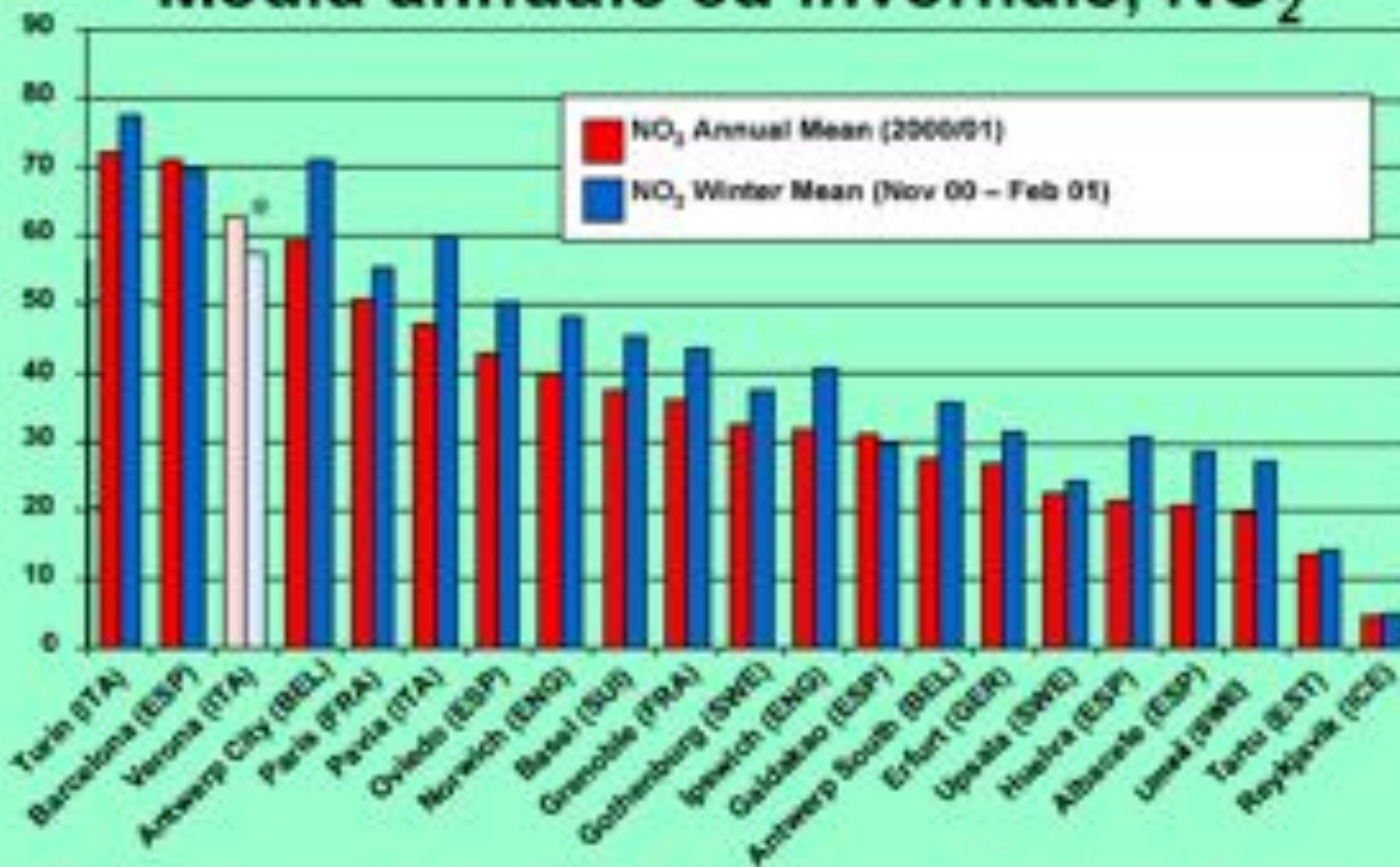
# Ossidi di azoto (NO<sub>x</sub>)

- Gas marrone chiaro composto da azoto e ossigeno
- Sorgenti : traffico veicolare, centrali elettriche a combustione di fossili, forni a legna



[ $\mu\text{g}/\text{m}^3$ ]

## Media annuale ed invernale, $\text{NO}_2$



$\text{NO}_2$  winter mean concentrations are generally higher than the annual mean.

\*Less than 50% of data available

# OXIDES OF NITROGEN

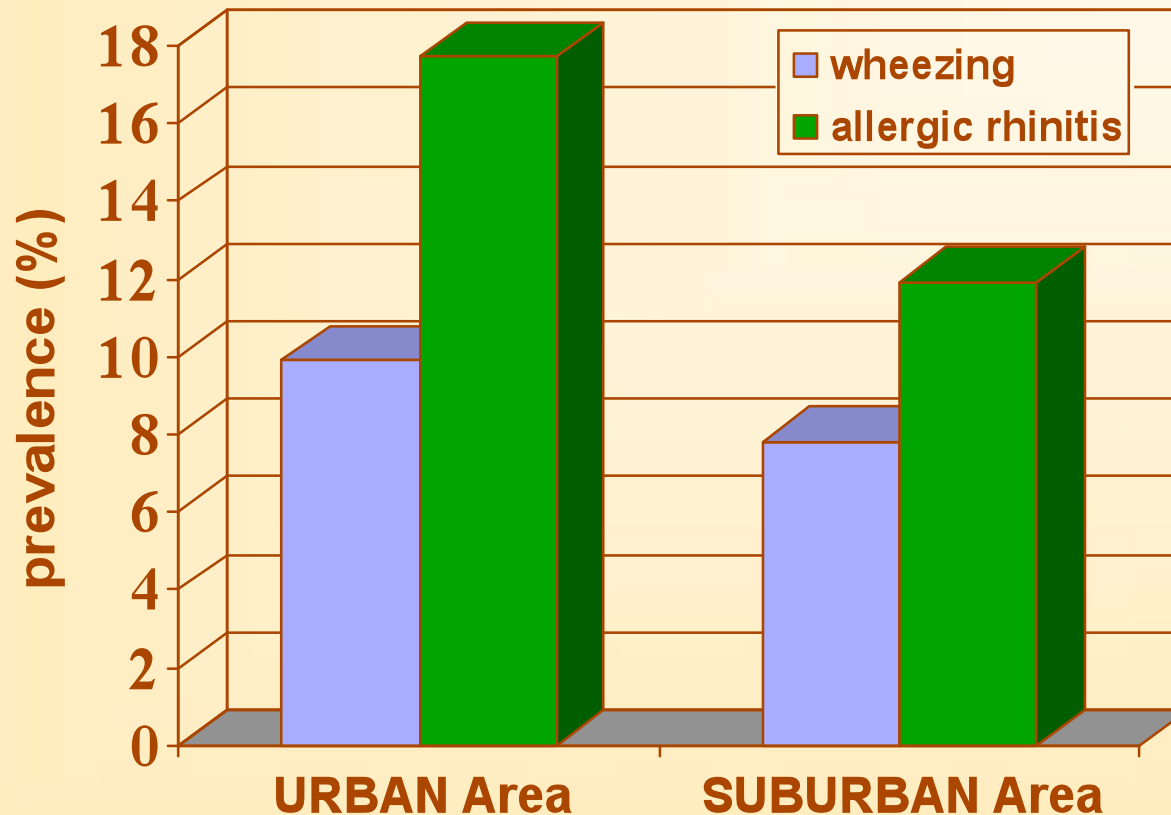
- $\text{NO}_2$  not as potent of an oxidant as ozone
- $\text{NO}_2$  reacts with  $\text{H}_2\text{O}$  to form  $\text{HNO}_3$
- ?  $\text{NO}_2$ -ozone interaction

# **NO<sub>2</sub> ED ASMA**

**Da studi di esposizione sull'uomo controllati**

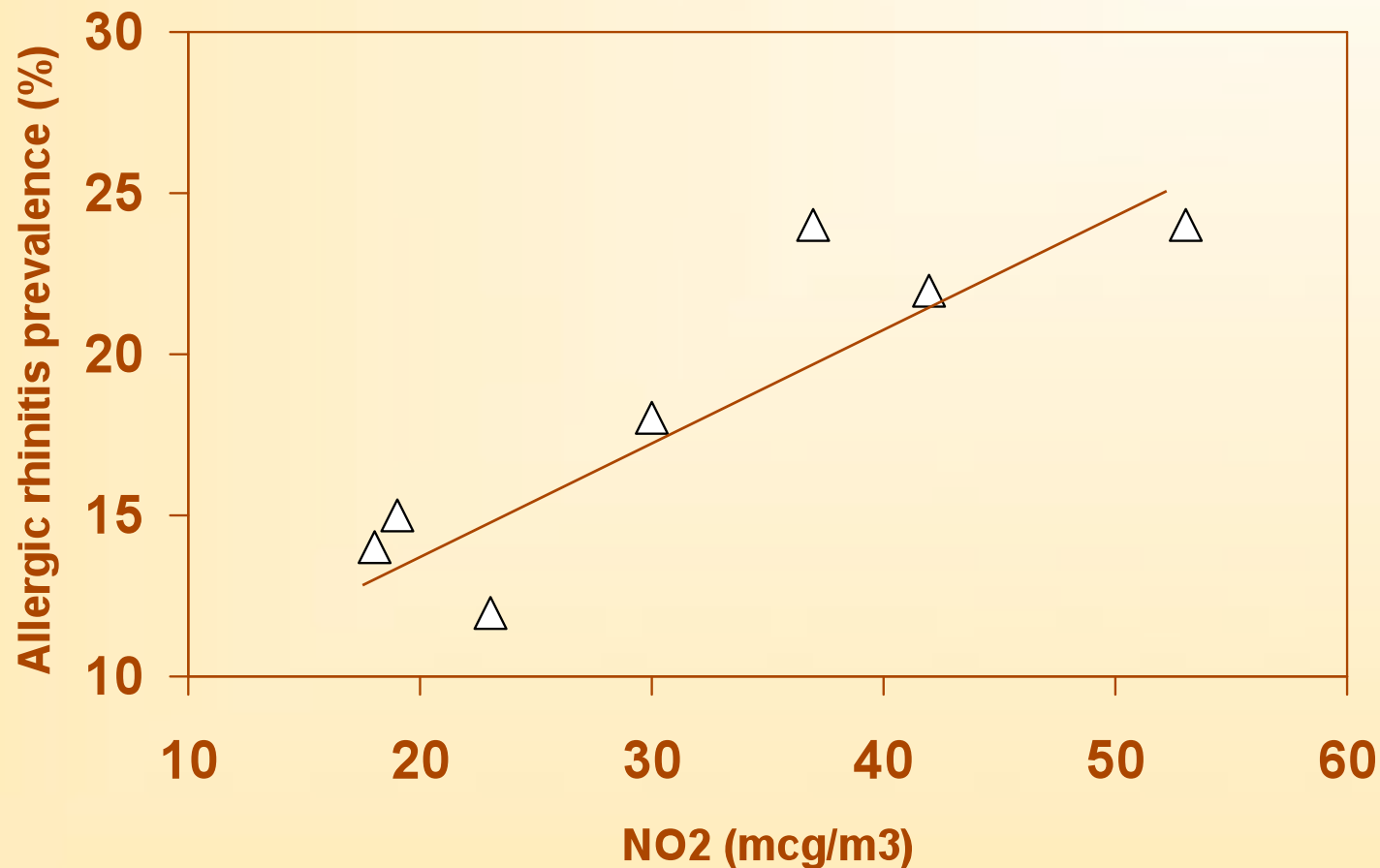
- **Aumento della reattività bronchiale**
- **Infiammazione delle piccole vie aeree anche in soggetti sani, come per l'ozono**
- **Aumentata risposta infiammatoria e broncocostrittiva agli allergeni**

## Prevalence of asthma and asthma-like symptoms in an adult population sample from Verona



C Campello, M Ferrari, A Poli et al. *Arch Chest Dis* 1998; 53:505-509

## The impact of climate and traffic-related NO<sub>2</sub> on the prevalence of asthma and allergic rhinitis in Italy

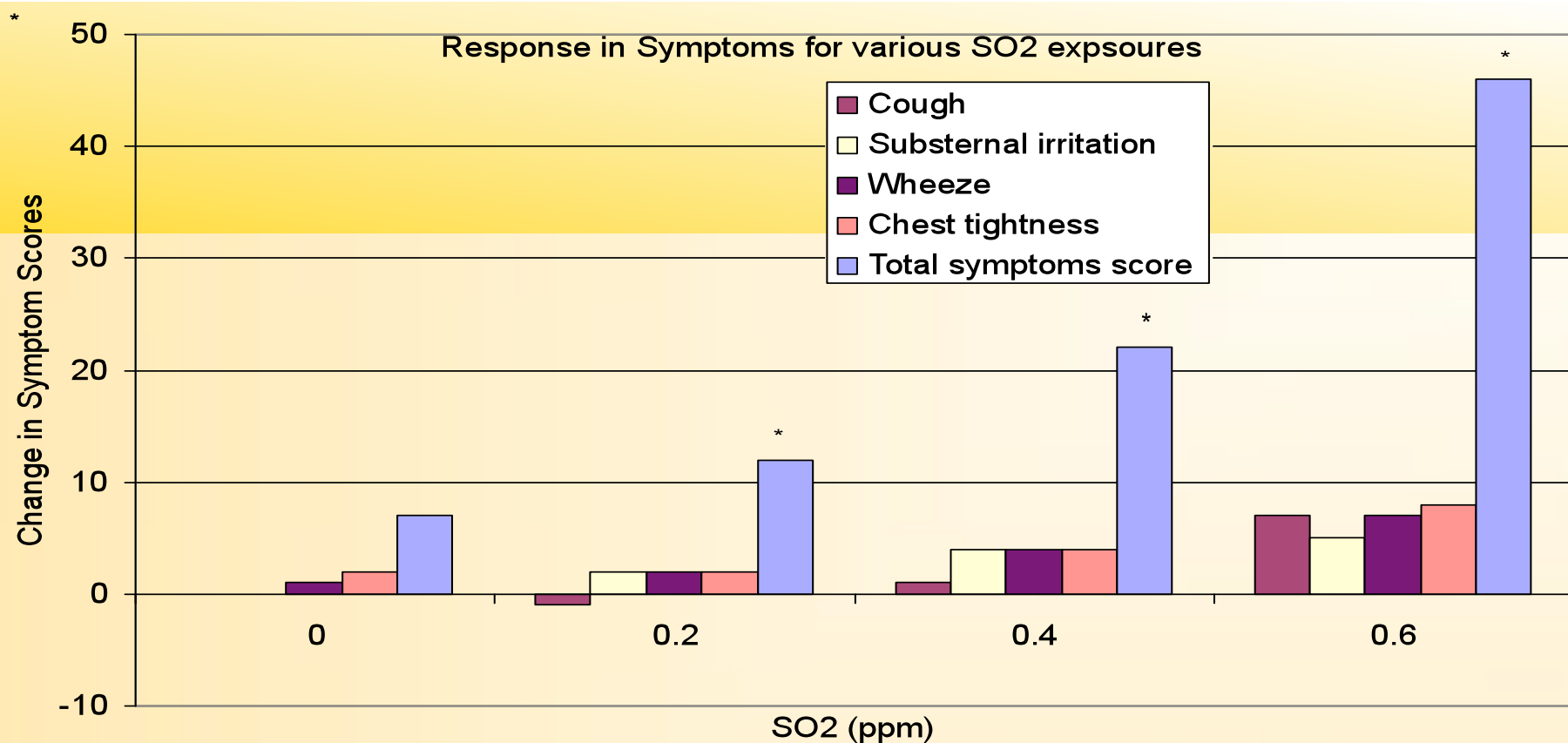


# Sulphur Dioxide

- Soluble, irritant gas
- Product of burning sulphurous fossil fuel

## EFFECTS

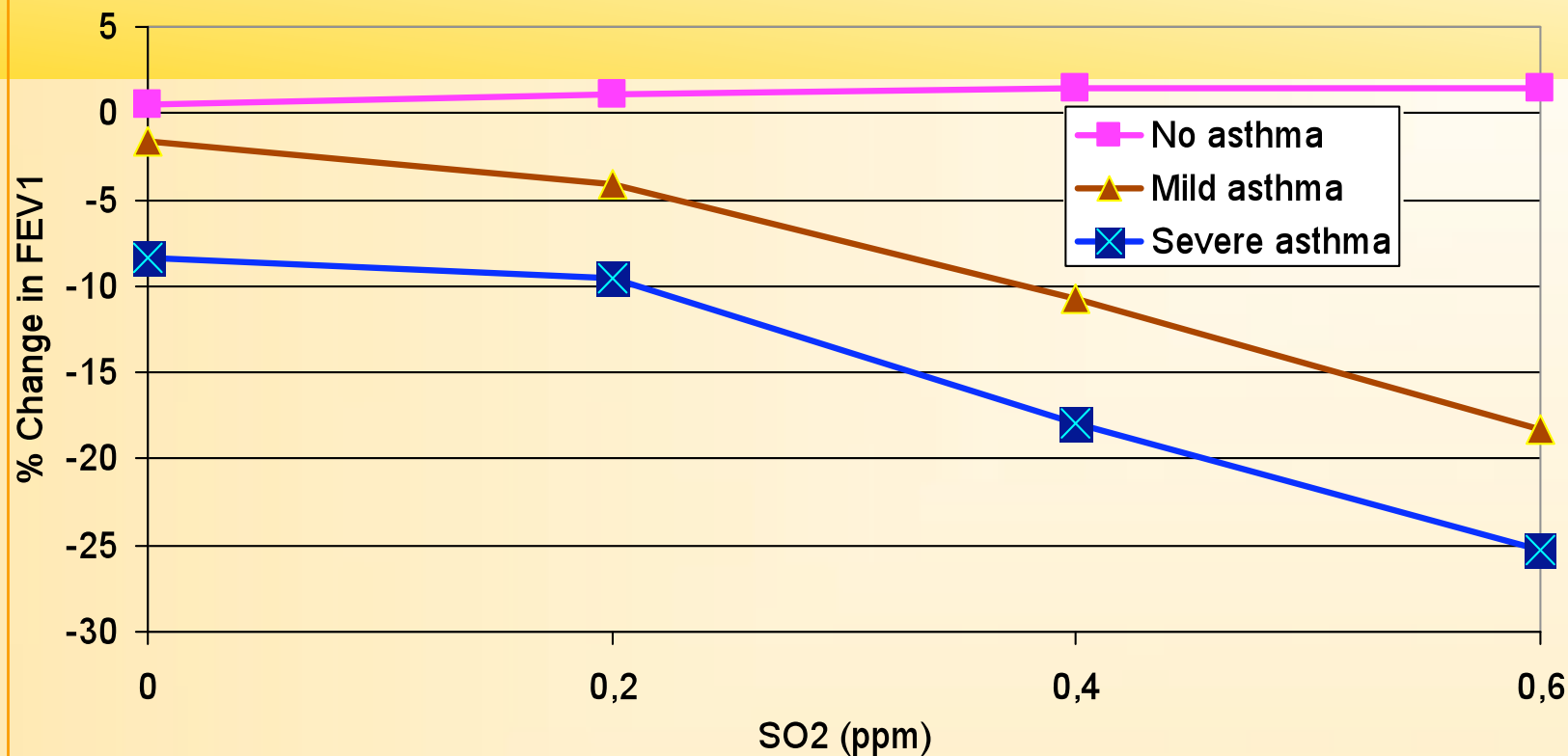
- Potent trigger for bronchoconstriction in people with asthma
  - Individual variability in susceptibility
  - Very brief exposure required
  - Partially blocked by ipratropium and indomethacin
- No effect in people without asthma up to 5ppm



SO<sub>2</sub> dose response relationship for symptoms in 23 people with mild asthma when exposed to a range of SO<sub>2</sub> concentrations for ~5 minutes. \* =  $P < 0.05$ . Total symptoms score is the aggregate of cough, sputum, substernal irritation, wheeze, chest tightness, dyspnea, throat irritation, nasal discharge/congestion, fatigue, headache, eye irritation and any other symptoms.



Change in FEV1 in Non- asthmatics, mild asthmatics and sever asthmatics with 15 minute expsoure to various SO2 concentrations.



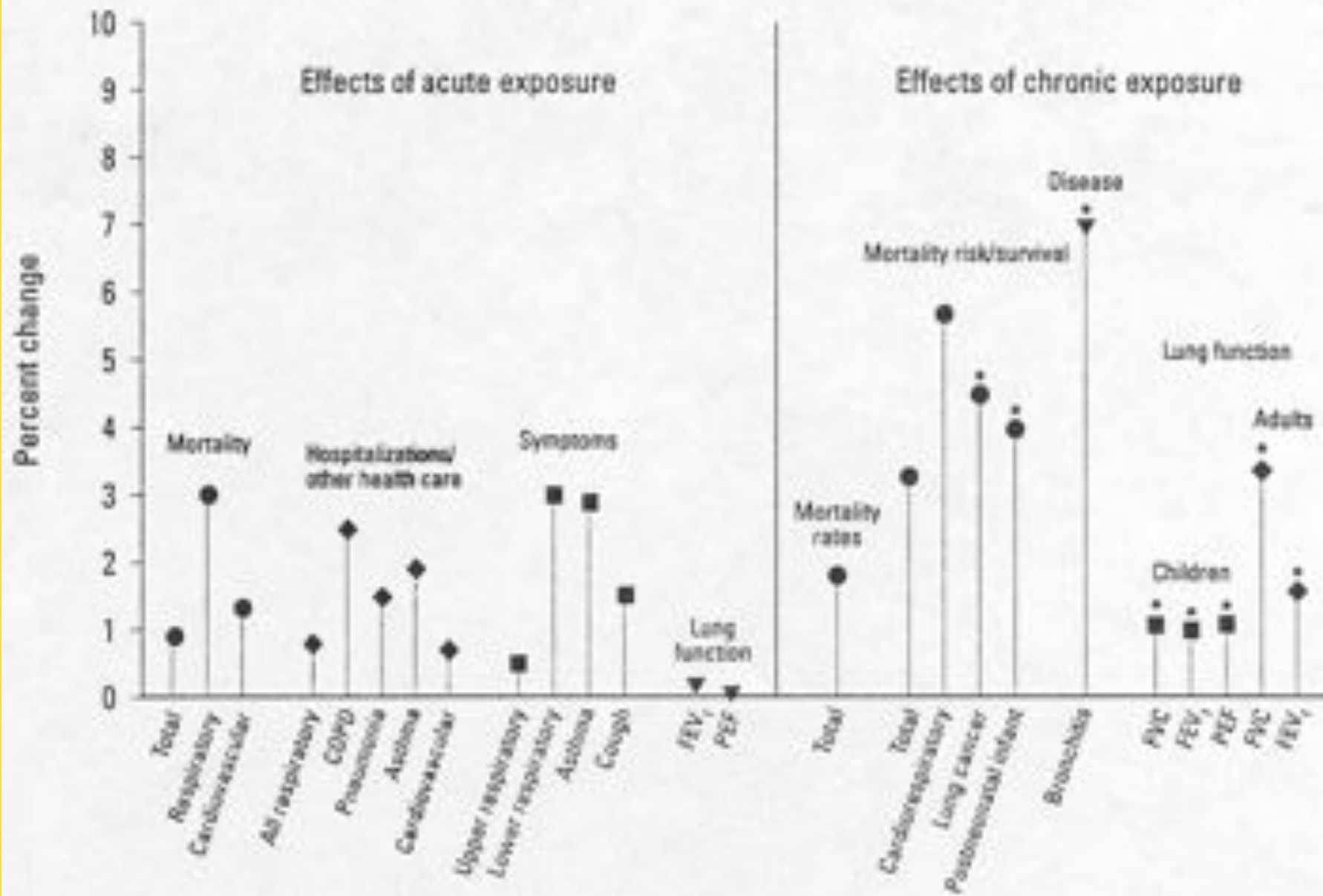
SO2 dose response relationship for FEV1 in non-asthmatics, mild and severe Asthmatics when exposed to arrange of SO2 concentrations for 15 minutes.

85 people including 24 non-atopic and non-asthmatics, 21 atopics, 16 minimal/mild asthmatics and 24 moderate/severe asthmatics.

# Particulates

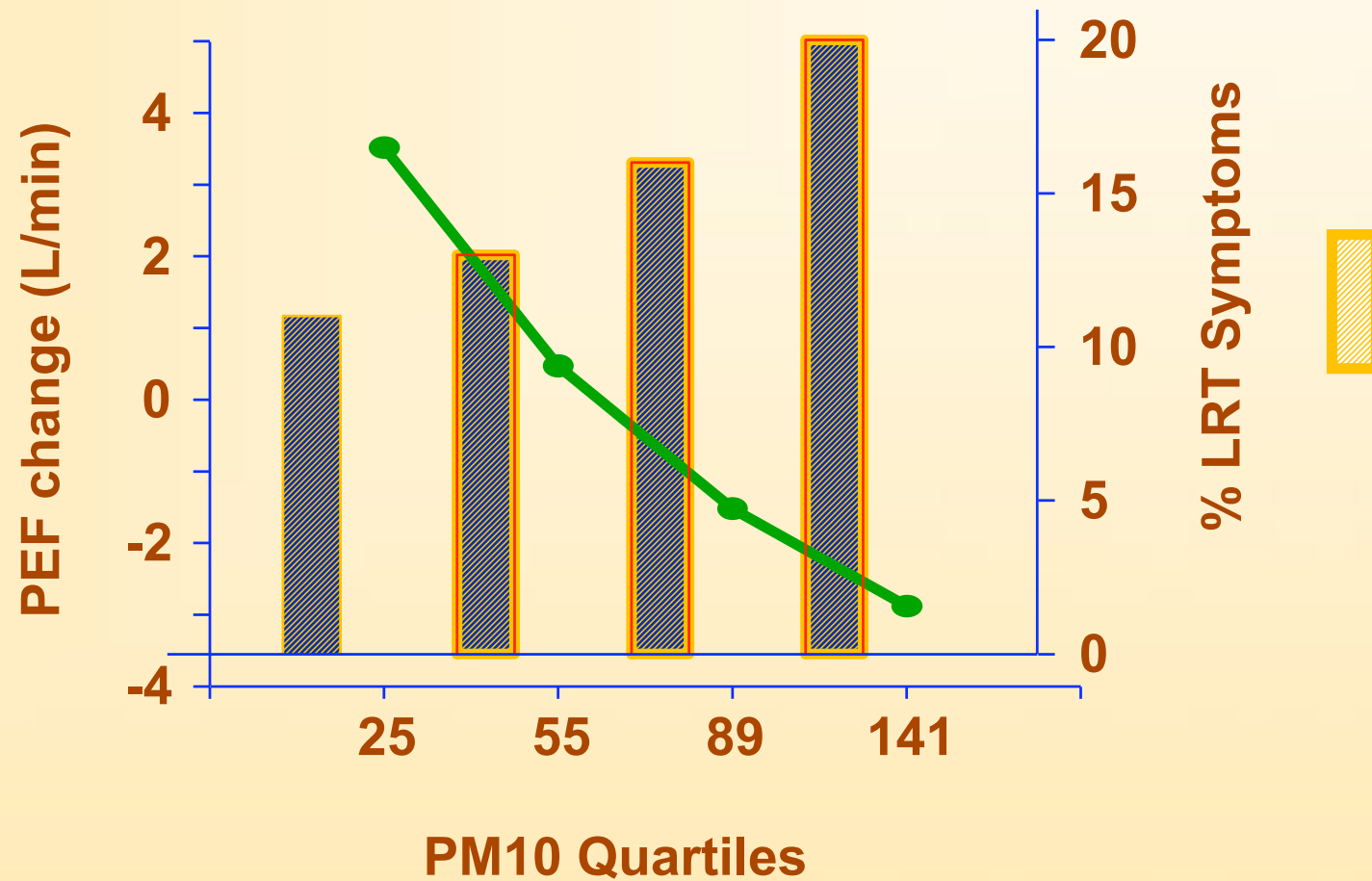
- Non-gaseous airborne pollutants
- Heterogeneous
  - Size matters
  - Composition
- Diesel exhaust particulates modulate immune response in the lung
  - ? Metals as catalysts
  - ? Carrier
  - ? Other toxic effect

## Aumento per 10 $\mu\text{g}/\text{m}^3$ PM<sub>10</sub>



# Particulates

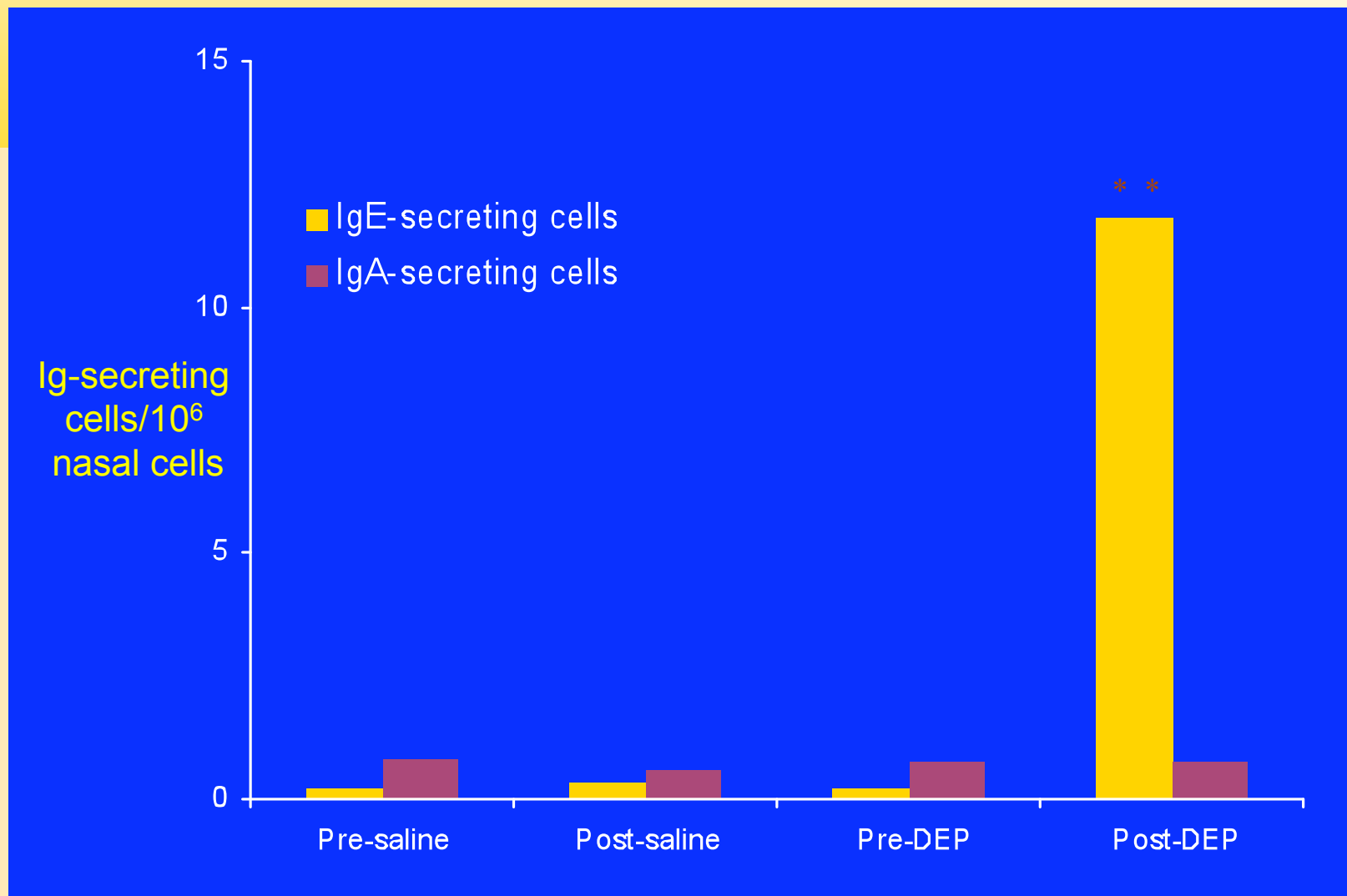
## Symptoms and lung function



# **PM ED ASMA**

## **PARTICOLATO DIESEL**

- **Induce infiammazione bronchiale in soggetti normali**
- **Aumenta la risposta agli allergeni.**
- **Nell'animale da esperimento induce una iperreattività bronchiale ed aumenta la risposta agli allergeni**



DEP enhances the production of IgE- but not IgA-secreting cells. Total cells recovered from nasal lavages before or 4 days after challenge with 0.3 mg DEP or saline were assayed for IgE or IgA cells by filter spot assay. All results are the mean obtained from 7 subjects. \*\*p<0,001 Compared to prechallenge levels.

## PM – Allergia al lattice popolaz. generale -cause

- Gli allergeni del lattice o i ***latex cross-reactive materials***
- presenti nella polvere sedimentata o aereodispersa,
- derivante dall'usura dei pneumatici, generalmente dal traffico pesante urbano
- sembrano essere il **principale responsabile** dell'aumento di questa allergia **nella popolazione generale** non prof. esposta.

# TRAFFICO VEICOLARE

- Molti studi hanno dimostrato un aumento della prevalenza di sintomi asmatici in soggetti che abitano vicino a strade ad alta densità di traffico.
- Studio Germania Est v/s Ovest alla riunificazione:
  - Est > di malattie allergiche e di asma, in relazione al traffico veicolare (correlazione con NO particolarmente significativa)
  - Ovest > di bronchiti croniche, BPCO e tumori in relazione all'attività industriale con emissioni poco controllate



# **PM AND ASTHMA**

## **WHAT WE DON'T KNOW**

- **What is the relative importance of exposure to ambient PM as a trigger for asthma exacerbations?**
- **What is the component(s) of PM that acts as a trigger for asthma exacerbations?**
- **What is the mechanism of DEP enhancement of response to allergen?**

# **PM AND ASTHMA**

## **WHAT WE DON'T KNOW**

- **What is the effect of childhood exposure to PM on the subsequent course of asthma?**
- **Is there a subset of asthmatic persons at particular risk for PM-induced asthma exacerbation? If so, are there specific genetic determinants of this risk?**

***L'uomo bianco non capisce. Per lui un pezzo di terra non si distingue da un altro pezzo di terra, dato che lui è un estraneo che arriva di notte e strappa la terra a chi ne ha bisogno. La Terra non è sua sorella ma sua nemica e, dopo averla assoggettata, egli se ne va alla ricerca di un altro luogo. Tratta sua madre, la Terra, e suo fratello, il Cielo, come cose da comprare e da rubare, come se fossero pelli di capretto o perline senza valore. La sua bramosia esaurirà la terra, lasciando dietro di sé solamente dei deserti (Capo Indiano Seattle , 1865)***