INTRODUCTION

The health effects of air pollution exposure have become an area of increasing focus in the past 30 years. A growing body of evidence has demonstrated that there are serious health consequences to community air pollution and that these consequences are not spread equally among the population ***(Schwartz, 2004)***.

Outdoor air pollution at levels occurring in many urban areas around the world has substantial adverse effects on health. Children in general and children with asthma in particular, are sensitive to the adverse effects of outdoor air pollutants. A growing number of studies also show that children living in environments near traffic have increased risks of new-onset asthma, asthma symptoms, exacerbations, school absences, and asthma-related hospitalizations ***(Frank, 2009).***

Children are vulnerable to the effects of air pollution because their lungs and immune systems are developing, they are more active in environments with high levels of pollutants (eg, while participating in sports in the afternoon), and they receive higher doses, relative to adults, because of differences in breathing rates and patterns. The inflamed and hyperreactive airways of children with asthma create a new level of vulnerability ***(Meng et al., 2006).***

Consistent with the increased vulnerability of children, a large and growing number of studies show that children living near traffic or high levels of ozone, nitrogen dioxide, or PM have increased risks of adverse respiratory effects ***(Brauer et al., 2007).***

Lung function of children, as the main indicator of ambient air pollution's effect on children's health, is widely used in relevant researches ***(Ling Liu and Jinliang, 2008)***.

Exhaled markers of inflammation allow completely noninvasive monitoring of inflammation and oxidative stress in the respiratory tract in inflammatory lung diseases ***(Khariotonv and Barnes, 2001).***

Exhaled CO (**eCO**) originates from the inspiration of ambient CO and from endogenous metabolic sources that include heme metabolism catalyzed by heme oxygenase (**HO**) enzymes. HO occurs in both constitutive ($\mathbf{HO_{-2}}$) and inducible ($\mathbf{HO_{-1}}$) forms; the latter responds to pro-inflammatory or pro-oxidative stimuli ***(Ryter and Sethi, 2007).***

AIM OF THE WORK

The aim of this work was to study dynamic lung volume via spirometry and exhaled carbon monoxide as noninvasive biomarkers of oxidative stress in the lungs in healthy school children in Suez Governorate.

RESPIRATORY SYSTEM

Introduction:

1) Lung growth and development:

Human lung growth starts as a primitive lung bud in early embryonic life and undergoes several morphological stages which continue into postnatal life. Each stage of lung growth is a result of complex and tightly regulated events governed by physical, environmental, hormonal and genetic factors ***(Joshi and Kotecha, 2007)*.**

The events of antenatal growth and development of human lung have traditionally been divided into 5 stages ***(Burri, 2006)*.**

Table (1): Stages of lung growth.

Stage	Time	Events
Embryonic	0–7 weeks	Formation of trachea, right and left main bronchi, segmental bronchi, and vasculogenesis around airway buds
Canalicular	7–17 weeks	Differentiation of epithelial cells, formation of conduction airway and terminal bronchioles, formation of pulmonary arteries and veins
Pseudoglandular	17–27 weeks	Formation of respiratory bronchioles, alveolar ducts and primitive alveoli, differentiation of type I and type II pneumocytes and formation of alveolar capillary barrier
Saccular	28–36 weeks	Increment in gas exchange areas, further differentiation of type I and type II cells
Alveolar	36 weeks–2 years	Septation and multiplication of alveoli
	Until 18–22 years	Enlargement of terminal bronchioles and alveoli
Microvascular maturation	Birth to 2–3 years	Fusion of double alveolar capillary network into a single layer

(Burris, 2006)

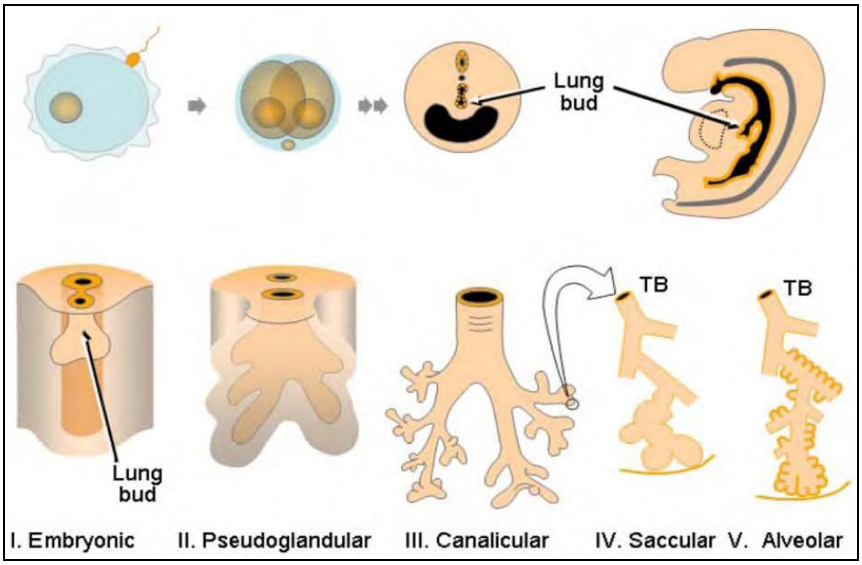

Fig. (1): Embryonic origin of the lung ***(Jeffrey et al., 2004)***.

1. Embryonic stage (0–7 weeks in utero):

At around 3–4 weeks of embryonic life, the lung develops as an outgrowth of the ventral wall of the primitive foregut, the laryngotracheal groove. The epithelial cells from the foregut endoderm invade the surrounding mesenchyme to form the trachea. During the embryonic stage, the trachea branches into the right and left main bronchi and subsequently into lobar and segmental bronchi. Lobar and segmental bronchi appear at about the 5th week ***(Jeffery, 1998)*** and by the end of this stage, 18 major lobules are recognizable ***(Kotecha, 2000)***.

2. Pseudoglandular stage (7–17 weeks in utero):

Pseudoglandular stage is marked by further branching of airway and vascular network and progressive differentiation of

epithelial cells to form adult structures of cartilage, submucosal gland, bronchial smooth muscle and epithelial cell types ***(Kotecha, 2000)***.

3. Canalicular stage (17–27 weeks in utero):

Canalicular stage is marked by two important steps in the development of the lung: differentiation of type I and type II pneumocytes and formation of the alveolar capillary barrier ***(Hislop, 2002)***.

4. Saccular stage (28–36 weeks in utero):

Enlargement of the peripheral airways with dilatation of acinar tubules forming 'saccules' and thinning of the airway walls. This ensures increased surface area for gas exchange ***(Kotecha, 2000)***.

5. Alveolar stage (36 weeks in utero—2 years):

Recognition of secondary septa in the terminal airway and formation of definitive cup shaped alveoli marks the alveolar stage ***(Burri, 2006)***.

6. Postnatal lung growth:

It has been estimated that the number of alveoli at birth ranges from 20–50 million ***(Kotecha, 2000)***. Alveolar multiplication

continues in the postnatal period at least up to the age of 2–3 years and alveolar size and surface increases until after Adolescence ***(Hislop, 2002)***. Final number of alveoli in a fully developed adult lung reach 300–800 million with approximately 170 alveoli per cubic millimeter ***(Ochs et al., 2004)***.

In recent years, it was noted that both the small bronchioles and alveoli expanded significantly in size with increasing age and height up to the age of 22 years ***(Zeman and Bennet, 2006)***.

7. Stage of microvascular maturation (several months to 2–3 years):

Essentially, during this period, the double capillary network gradually merges as a single capillary layer. This is an extremely important event in the postnatal lung growth as angiogenesis and alveolarization go hand in hand and once the capillary network fuses into a single layer; new alveolar septa cannot be formed. This has now been postulated as the major cause of premature arrest of lung growth following postnatal dexamethasone treatment in premature infants with chronic lung disease ***(Joshi and Kotecha, 2007)***.

2) Basics of Respiration:

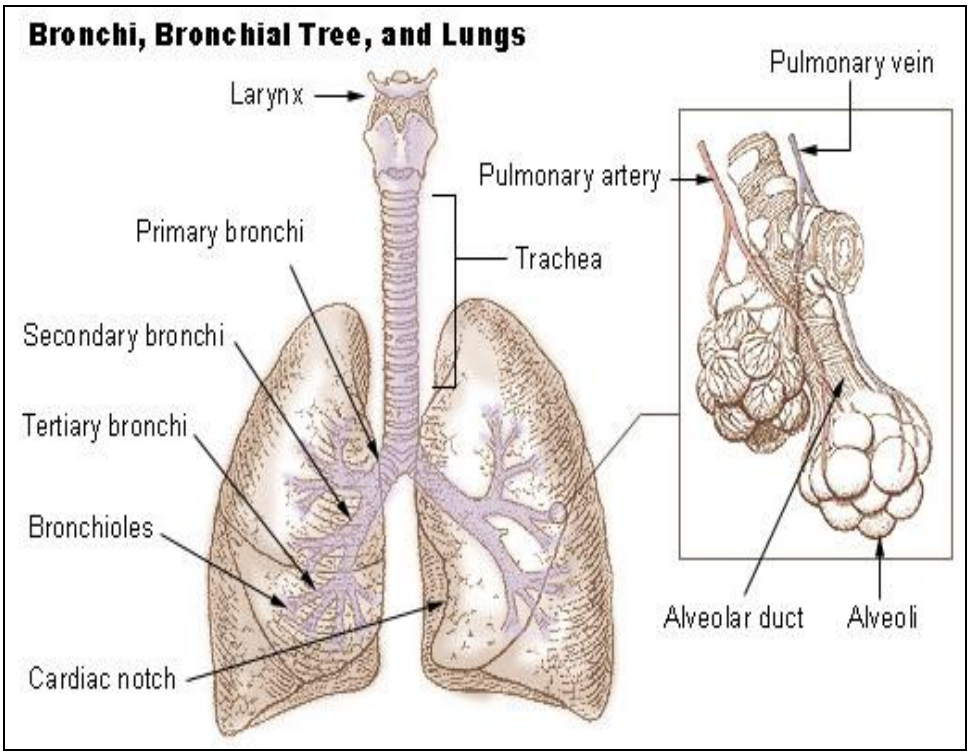

Fig. (2): The respiratory tract ***(CDC, 2008)***

The exchange of oxygen from the outside environment for carbon dioxide from venous blood defines the fundamental process of respiration. This exchange occurs at the surface of each of the approximately 300 million alveoli contained in the lungs. The alveoli have a combined total surface area for gas exchange that is equivalent to the size of a tennis court ***(CDC, 2008)***.

Table (2): Physiological reasons for the increased susceptibility of infants for respiratory compromise in comparison to adults:

Cause	Physiological or anatomical basis
Metabolism ↑	O_2 consumption ↑
Risk of apnoea ↑	Immaturity of control of breathing
Airway resistance ↑	
Upper airway resistance ↑	Nose breathing
	Large tongue
	Airway size ↓
	Collapsibility ↑
	Pharyngeal muscle tone ↓
	Compliance of upper airway structures ↑
Lower airway resistance ↑	Airway size ↓
	Collapsibility ↑
	Airway wall compliance ↑
	Elastic recoil ↓
Lung volume ↓	Numbers of alveoli ↓
	Lack of collateral ventilation
Efficiency of respiratory muscles ↓	Efficiency of diaphragm ↓
	Rib cage compliance ↑
	Horizontal insertion at the rib cage
	Efficiency of intercostal muscles ↓
	Horizontal ribs
Endurance of respiratory muscles ↓	Respiratory rate ↑
	Fatigue-resistant type I muscle fibres ↓

(Hammer and Eber, 2005)

AIR POLLUTION

Definition of air pollution:

Defining "air pollution" is not simple. One could claim that air pollution started when humans began burning fuels. In other words, all man-made (anthropogenic) emissions into the air can be called air pollution, because they alter the chemical composition of the natural atmosphere. The increase in the global concentrations of greenhouse gases CO_2, CH_4 and N_2O (shown in Table3), can be called air pollution using this approach, even though the concentrations have not found to be toxic for humans and the ecosystem ***(Daly and Zannetti, 2007).***

"Air pollutant" is any substance emitted into the air from an anthropogenic, biogenic, or geogenic source, that is either not part of the natural atmosphere or is present in higher concentrations than the natural atmosphere, and may cause a short-term or long-term adverse effect ***(Daly and Zannetti., 2007).***

Table (3): National Ambient Air Quality Standards for Criteria Air Pollutants, 1997

Pollutant Primary Standards*	
Ozone	
1-h average	0.12 ppm (235 _g/m3)
8-h average	0.08 ppm (157 _g/m3)
PM10	
Annual arithmetic mean	50 _g/m3
24-h average	150 _g/m3
PM2.5	
Annual arithmetic mean	15 _g/m3
Sulfur dioxide	
Annual arithmetic mean	0.03 ppm (80 _g/m3)
24-h average	0.14 ppm (365 _g/m3)
Nitrogen dioxide	
Annual arithmetic mean	0.053 ppm (100 _g/m3)
Carbon monoxide	
8-h average	9 ppm (10 mg/m3)
1-h average	35 ppm (40 mg/m3)
Lead	
Quarterly average	1.5 _g/m3

Additional information on air quality standards are available at:www.epa.gov/air/criteria.html

(Jonathan et al., 2008)

Epidemiology of air pollution:

1) Age:

A given dose of a pollutant will have a greater impact on a child than on an adult not only due to their smaller size, but because of the nature of their growing bodies and minds. At sensitive points in child development, environmental exposures can have especially harmful effects ***(Jerome, 2011)***.

The special vulnerability of children to exposure to air pollution is related to several differences between children and adults. The ongoing process of lung growth and development, incomplete metabolic systems, immature host defences, high rates of infection by respiratory pathogens and activity patterns specific to children can lead to higher exposure to air pollution and higher doses of pollutants reaching the lungs. The efficiency of detoxification systems exhibit a time-dependent pattern during prenatal and postnatal lung development that in part accounts for the increased susceptibility of young children to pollutants at critical points in time ***(Krzyzanowski et al., 2005)***.

Children are particularly sensitive to the effects of air pollution. Their smaller diameter airways are more likely to be affected by inflammation produced by air pollution. Children breathe more air per unit of body weight than adults, and thus receive proportionately higher doses of pollutants ***(Leech et al., 2002).***

Children take in more air per unit body weight at a given level of exertion than do adults. When a child is exercising at maximum levels, such as during a soccer game or other sports event, they may take in 20 percent to 50 percent more air -- and more air pollution -- than would an adult in comparable activity. There are several good studies that show children to have losses in lung functions even when they don't cough or feel discomfort. This

is important because symptoms are often warning signals and can be used to trigger protective behavior. Children may not perceive these warning signals and might not reduce their activities on smoggy days ***(Michael, 2000).***

Table (4): Categories of factors determining susceptibility of children to inhaled pollutants

Factors category	Application
Related to lung growth and development	• Vulnerability of developing and growing airways and alveoli • Immature host defence mechanisms
Related to time-activity patterns	• Time spent outdoors • Increased ventilation with play and exercise
Related to chronic disease	• High prevalence of asthma • Rising prevalence of cystic fibrosis
Related to acute disease	• High rates of acute respiratory infection

(WHO Regional Office for Europe, Air quality guidelines for Europe, 2nd ed. Copenhage; 2000)

2) Sex:

Ambient compound air pollution was associated with respiratory symptoms and diseases in young children. Among children without an allergic predisposition, males might be more susceptible to ambient air pollution than females; whereas among children with an allergic predisposition, more associations were detected in females ***(Guang-Hui Dong et al., 2010).***

3) Genes:

Exposure of the developing lung to air pollution reduces the maximal functional capacity achieved as the child enters adulthood, and thus reduces the functional reserve. Polymorphic variation in genes involved in protecting against tissue injury or regulating tissue repair may explain some of the variation in individual susceptibility to the adverse effects of pollutants on health ***(Samet and Krewski, 2007).***

Also susceptibility to health effects of air pollution on lung function growth is associated with genetic variation in the *GSS* gene, a gene involved in glutathione production and oxidative injury. Glutathione plays an important role in antioxidant and inflammatory processes in the lung. Alterations in glutathione metabolism are a central feature of several chronic lung diseases ***(Breton et al., 2011)***.

Differences in genetic make-up may increase the likelihood that some individuals will respond biologically to a particular environmental insult. This enhanced susceptibility might be caused by the presence of one or more genetic alleles that "protection" (e.g, resistance) from environmentally induced disease, it is not clear whether of how these genetic factors are associated with specific ethnic /racial subgroups ***(Rios et al., 1993)***.

Among the genetic differences that may give rise to differential vulnerability to air pollution exposures are : deficiency of the enzyme glucose-6-phosphate dehydrogenase (G-6-PD) in people from Africa, Asia, and the Mediterranean (e.g., possible increased proneness to effects of ozone and nitrogen dioxide); sickle cell anemia in African-Americans (e.g., may increase risks from carbon monoxide exposures); and slow rate of acetylation in the liver (e.g., risk factor for bladder cancer associated with exposure to aromatic amines) ***(Calabrese 1986; Brain et al., 1988; Polednak, 1989; Frampton et al., 1989; Grandiean et al., 1991).***

4) Race:

The nonwhite person appears to be more adversely affected by the effects of air pollution. This is because the nonwhite persons have a larger baseline rate of being admitted to the hospital for respiratory causes than the white persons. This may be due partly to the lack of access to adequate preventive healthcare experienced by nonwhites ***(Gwynn and George, 2001).***

5) Social status:

There are many possible reasons why one might expect lower socioeconomic position to increase susceptibility to the deleterious effects of air pollution including: increased exposure to the air pollutants of interest, increased exposure to co-pollutants from occupational dusts and fumes and cigarette smoke, fewer