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Management of wheezing in infant and children

Essay

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Dedication

To my lover husband , Ahmed Elkhateb who always inspire me , filling me with love , encouragement and did for me much more than I can ever do for myself.

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List of abbreviations

AMS:	Acute Mountain Sickness.
APCs:	Antigen-Presenting Cells.
ATP:	Adenosine Triphosphate .
ARDS:	Acute Respiratory Distress Syndrome.
BHR:	Bronchial Hyperresponsiveness .
BO:	Bronchiolitis Obliterans .
BPD:	Broncho Pulmonary Dysplasia .
CAM:	Cystic Adenomatoid Malformation .
CDC:	Centers for Disease Control and Prevention .
CF:	Cystic Fibrosis .
CLD:	Chronic Lung Disease .
CLE:	Congenital Lobar Emphysema .
CNOS:	Constitutive Nitric Oxide Synthase.
COPD:	chronic Obstructive Pulmonary Disease.
ED:	Emergency Department .
ELISA:	Enzyme Linked Immunosorbent Assay .
EPP:	Equal Pressure Point.
ERMI:	Environmental Relative Moldiness Index
ETS:	Environmental Tobaco Smoke .
FEV:	Forced Expiratory Volume.
FRC:	Functional Respiratory Capacity .
FVC:	Forced Vital Capacity .
GERD:	Gastroesophagal Reflux Disease .
GIT:	Gastrointestinal Tract .
HACE:	High-Altitude Cerebral Edema .
HAPE:	High-Altitude Pulmonary Edema.
HcoV:	Human Coronavirus .
HLA:	Human Leucocyte Antigen .
HMPV:	Human Metapneumovirus .
ICU:	Intensive Care Unite .
Ig:	Immunoglobulin .
IL:	Interleukine .
INF:	Interferon .
INOS:	Incudible Nitric Oxide Synthase.

IVIG:	Intravenous Immunoglobulin .
LES:	Lower Esophageal Sphincter .
LRI:	Lower Respiratory Illness .
LRTI:	Lower Respiratory Tract Infection.
LTEC:	Larengotracheoesophageal Cleft .
MAC:	Mycobacterium Avium Complex .
MAS:	Multicenter Allergy Study .
MEFV:	Maximum Expiratory Flow Rate .
NGF:	Neurotrophin Growth Factor .
NO:	Nitric Oxide .
PCD:	Primary Ciliary Dyskinesia .
PEF:	Peak Expiratory Flow .
PIVs:	Parainfluenza Virus .
RANTES:	Regulated on Activation , Normal T cell Expressed and Secreted
Raw:	Resistance airway .
RSV:	Respiratory Syncytial Virus .
RT-PCR:	Reverse Transcriptase Polymerase Chain Reaction .
RV:	residual Volume .
SNP:	Single Nucleotide Polymorphism .
SP:	Surfactant Protein .
TCT:	Thoracic Compression Technique .
TEF:	Tracheoesophageal Fistula .
TIV:	Trivalent Influenza Vaccine .
URTI:	Upper Respiratory Tract Infection .
WHO:	World Health Organization .

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Introduction

A wheeze can be defined as a breath sound that is heard during expiration .
It is often associated with prolongation of the expiratory phase of the breathing cycle. Wheeze indicates obstruction to airflow within the thorax
It can be high- or low-pitched , this differentiation indicates that the obstruction is likely to be in the smaller and larger airways ,respectively**(Robert et al,2008)**

A wheeze is historically considered a sign of intrapulmonary disease. It has been shown that wheezing can occur with extrapulmonary obstruction as in esophageal foreign body and mediastinal tumors (Newman et al.,1999).The most common cause of wheezing is asthma, but careful consideration of alternative diagnosis will reveal additional problems as bronchitis, bronchiolitis, tracheomalacia, bronchomalacia, foreign body inhalation and pulmonary edema **(Howard,2005)**.

Infants are prone to wheeze due to a differing set of lung mechanics in comparison to older children and adults. The obstruction to airflow is affected by the caliber and compliance of the infant lung. In children less than 5 years old , small caliber peripheral airways can contribute up to 50% of the total airway resistance . Marginal additional narrowing can cause further flow limitation and a subsequent wheeze . Other causes include viral infection, immunodeficiency states, molecular disorders and aspiration syndrome **(Richard et al.,2007)**

The resistance of the smallest peripheral airways falls with infancy which may be one explanation for the fact that infants are prone to small airway diseases (bronchitis) whereas in older children the small airways represent a clinically silent zone **(Helms .2008)**.

Most wheezing in infants is caused by inflammation (generally bronchitis) , but many other entities can present with wheezing . On the other hand

asthma is the most common cause of wheezing in children . Other causes include viral infection (e.g. Influenza and parainfluenza),anatomical abnormalities (central ,extrincic or intrincic airway anomalies), immunodeficiency state (e.g. IgA deficiency), mucocilliary clearance disorder (e.g. cystic fibrosis and brochiectasis) , bronchopulmonary dysplasia ,bronchiolitis obliterans , heart failure and aspiration syndromes **(Richard et al.,2007)**.

Treatment of an infant with wheezing depend on the underlying etiology. Most wheezing in infants is caused by bronchiolitis . For which a number of agents have been proposed as adjunctive therapy for bronchitis . Bronchodilators produce modest short term improvement in clinical features , but nebulized epinephrine may be more effective than B-agonist drugs .Corticosteroids and ribavirin have been also used for treatment of bronchiolitis . Palvizumab , Nebulized hypertonic saline (3%), intravenous immunoglobulins (IVIG) and prophylaxis with RSV monoclonal antibody are highly effective in treatment , prophylaxis and prevention of respiratory syncytial virus (RSV) bronchitis **(Helms and Henderson ,2008)**.

As regard asthma , New drugs are used to reduce symptoms, exacerbations and the use of steroids for treatment . An example of these drugs is omalizumab a recombiant humanized anti IGE antibody . This drug binds circulating free IGE and consequently reduces the level of free IGE in the bloodstream and prevents it from binding to mast cell membrane receptors thus curtailing the early and late asthmatic response . Leukotriene modifiers (e.g. monteleukast , zafirleukast and zileuton), cromolin , nedocromil and methylxanthine are also used for asthma treatment **(Vincent et al., 2007)**.

Aim of the work

The aim of the work is to provide a review of the currently available data regarding wheezing in children includes the following points :

1-Development , anatomy and physiology of respiratory system.

2-Definition , etiology and pathophysiology of wheezing.

3-Epidemiology of wheezing in children .

4- Clinical manifestation and diagnosis of common causes of wheezing .

5-Recent trends in the treatment of wheezing in infant and children .

DEVELOPMENT OF THE RESPIRATORY SYSTEM

I. FETAL AND PERINATAL DEVELOPMENT:

(A) Structural development:

Lung growth and development commences in early intrauterine life with the development of the trachea from the primitive esophagus at approximately 5 weeks of gestational age. The right and left lung buds develop at about 7 weeks and the formation of the main lobar structures is already evident by 9 weeks. This process of branching airway development continues through the first trimester of pregnancy and is largely complete by 16 weeks of gestational age By this time the lungs have a glandular appearance with alveoli emerging over the next 8-10 weeks, increasing in complexity and surface area up to and beyond term **(Hislop ,2004).**

Approximately 50% of alveoli are present at term with 85% complete by 2-3 years of age, a process accompanied by a reduction in interstitial tissue and the remodeling of capillaries into a single network, and with an enormous thinning of the blood-gas barrier **(Helms and Henderson ,2008).**

A network of elastin strands form the skeleton . between which the new alveoli are formed. Normal fetal breathing movements are important in promoting this growth **(Polgar, 2007).**

Many adverse intrauterine influences, e.g. congenital diaphragmatic hernia , renal agenesis and oligohydramnios can have devastating effects on subsequent lung growth and development. Insults during the early phase of airway development will reduce branching and will inevitably lead to reductions in the number of alveoli that can bud from a reduced number of terminal bronchioles (Fig.).Generally the earlier the insult the more profound the long term consequences **(Helms**

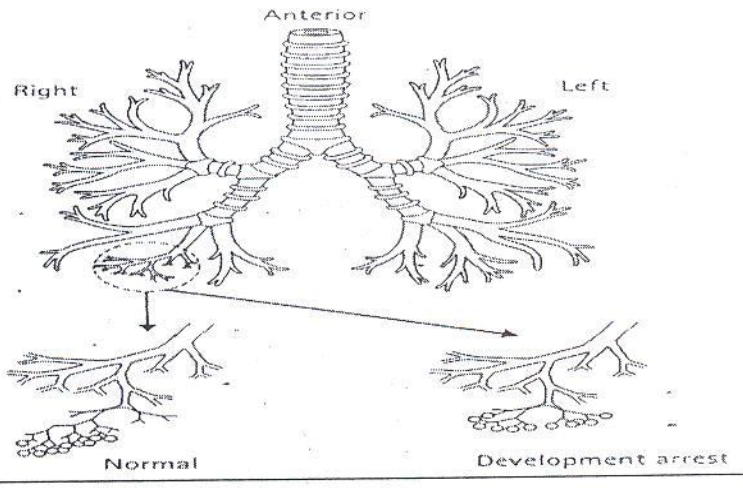

Fig.1 representation of the bronchial tree in a normal newborn infant and in an infant with intrauterine .pulmonary hypoplasia (Helms and Henderson ,2008).

fig .(1) presentation of the bronchial tree in normal newborn infant and in an infant with intrauterine pulmonary hypoplasia **(Helms and Henderson , 2008).**

The structures of the airways themselves also have important functional consequences. Generalized bronchomalacia or local disorders affecting the trachea and bronchi are associated with several important disorders, including tracheomalacia, stovepipe trachea and lobar emphysema **(Helms and Henderson ,2008).**

The most clearly identified adverse exposure at a whole population level is fetal tobacco smoke exposure associated with maternal smoking in pregnancy. Whereas postnatal or environmental tobacco smoke (ETS) exposure has a significant influence on respiratory morbidity in the young, the effects of prenatal exposure are likely to be more long lasting **(Abu-Shaweesh, 2004).**

The chest wall development:

The chest wall is defined as the structures which surround the lung and which have significant influences on lung growth and function. it includes the rib cage, the diaphragm and the abdominal contents together with the A paraspinal and accessory muscles of respiration **(Hislop , 2004)**

The chest wall has important influences on the function of the underlying lungs both in maintaining lung volume at rest (the lung tends to seek a lower volume whereas the chest wall recoils outwards) and in its role as the 'respiratory pump'. During growth and development important changes occur in the function of the chest wall, not only at rest but also during respiratory efforts that affect underlying lung function **(Polgar, , 2007).**

The diaphragm becomes a complete membrane by 8 weeks of gestation and the abdominal wall is complete at 9 weeks, allowing the establishment of effective fetal breathing **(Hislop , 2004).**

At birth, however, the proportion of fatigue resistant (Type 1) striated muscle fibers is approximately 10%, much less than the 50% found in adults. The proportion is even less in pre-term infants and along with the instability of the chest wall explains in part the tendency of preterm infants to develop respiratory failure and to suffer from apnea. The diaphragm is also inserted more directly into the chest wall with a reduced area of apposition (or alignment with the lower rib cage) than that found in mature subjects and this again results in a relative functional impairment in the infant and very young child **(Helms and Henderson, 2008).**

The thoracic configuration is also different in infants and young children in that the ribs are more horizontally placed with less potential for thoracic expansion than in older children and adults .As a consequence infants and very young children rely more on diaphragmatic activity and this, in combination with a more direct insertion into the ribcage and a reduced number of Type 1 muscle fibers (slow twitch high oxidative fibers), places the infant and young child at significant risk of developing respiratory failure when presented with an added respiratory load. Any additional impairment of the chest wall itself, e.g. in association with scoliosis or neuromuscular disorders, will only augment this relative inefficiency of the respiratory system in early life.(**Polgar, , 2007**)