Introduction

Respiratory infections have always been considered a worldwide health problem and a major cause of morbidity and mortality, with infants and young children especially susceptible ***(Zar and Ferkol, 2014)***.

Among these infections, bronchiolitis is the commonest lower respiratory infection in infants. Over 60% of infants have been infected on the first year of life, and by 2 years old over 80%. The antibodies that develop following early childhood infection do not prevent further RSV infections throughout life ***(Cheung et al., 2012),*** RSV is most common cause of bronchiolities. More than half of all infants are exposed to this virus by their first birthday ***(Brieu et al., 2008).***

Pneumonia stays the predominant cause of childhood mortality, causing nearly 1.2 million deaths each year in children younger than 5 years. Most of these deaths occur in developing countries ***(Izadnegahdar et al., 2013)***. In Egypt, it was estimated that 10% of children deaths below the age of 5 years is likely caused by pneumonia and other acute respiratory infections ***(WHO, 2014).***

Community-acquired pneumonia (CAP) is one of the most common serious infections in children. Its incidence among children aged less than 5 years in developing countries reached 0.29 child per year, with a mortality rate of 1.3–2.6% ***(Cardinale et al., 2013)***.

Despite a long-held belief that physical examination findings and proper auscultation are sufficient to rule in or out the presence of bronchiolitis and pneumonia. Multiple pressures in clinical practice have driven increased use of chest radiography and occasionally CT ***(Blaivas, 2012).***

In ***1986 Weinberg et al.,*** described a new method of evaluating CAP by the use of lung ultrasonography (LUS). Numerous subsequent studies have shown that it is an accurate, reliable and radiation-free tool in the diagnosis of pneumonia ***(Copetti and Cattarossi, 2008; Parlamento et al., 2009; Iuri et al., 2009; Reissig et al., 2012; Caiulo et al., 2013).***

For many years, Transthoracic Ultrasound (TUS) was limited exclusively to the examination of pleural effusions. However, over the past few years ultrasonography of the pleural space and lung parenchyma is gaining a wide consensus in different conditions in clinical practice, particularly in emergency conditions ***(Smargiassi et al., 2013).***

Chest ultrasound allows prompt management based upon reproducible data and generates fewer computed tomography (CT) examinations, therefore decreasing irradiation, delays, cost and discomfort to the patient ***(Lichtenstein, 2009).***

Point-of-care ultrasound imaging, performed at the patient's bedside, decreases the delays of chest radiography in diagnosis of pulmonary diseases ***(Al-khayat and Alam-Eldeen, 2014).***

Aim of the Work

To study ultrasonography findings in infants with acute lower respiratory tract infection and to test its sensitivity and specificity in comparison to clinical and conventional x-ray for diagnosis of childhood acute lower respiratory tract infection.

Acute Lower Respiratory Tract Infection (ALRI)

Standard definition of childhood ALRI is inflammation of the airways/pulmonary tissue, due to viral or bacterial infection, below the level of the larynx.

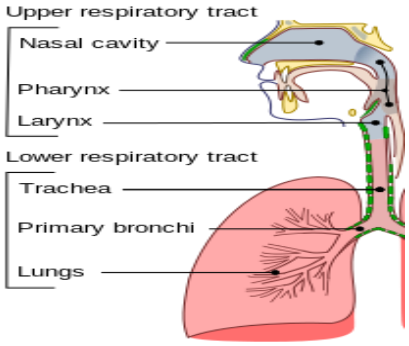

Figure (1): Respiratory conducting passage

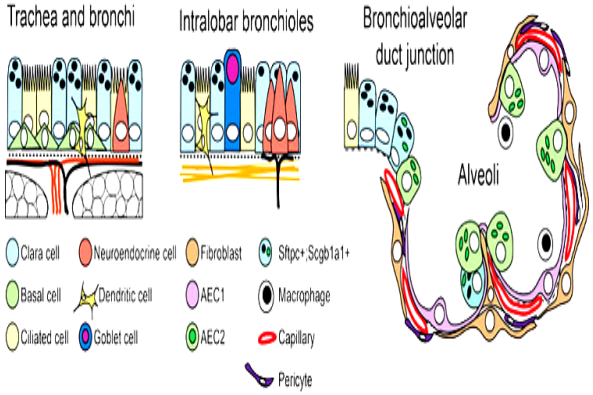

Figure (2): Normal histology of respiratory conducting passage

Acute lower respiratory infections (ALRI), such as pneumonia and bronchiolitis, are the leading cause of morbidity and mortality in children under five years of age ***(Walker et al., 2013).***

According to recent estimates, every year about 120–156 million cases of ALRI occur globally with approximately 1.4 million resulting in death. More than 95% of these deaths occur in low and middle income countries (LMIC) ***(Rudan et al., 2013).***

In 2015 there were about 291 million cases around the world. These resulted in 2.74 million deaths down from 3.4 million deaths in 1990. This was 4.8% of all deaths in 2013 ***(GBD, 2015).***

In Egypt, it was estimated that 10% of children deaths below the age of 5 years is likely caused by pneumonia and other acute respiratory infections ***(WHO, 2014).***

Risk factors: A large number of factors determine whether the contact with an etiologic agent will result in a severe episode of ALRI, and whether the episode will result in death. Some of these factors are related to the child (e.g. age, sex, and underlying diseases), others to the disease (e.g. type of infection), others may be related to the environment, the family and its socio-economic status, or to the health system and type of care ***(Mathews et al., 2013).***

❖ Lower respiratory tract infections include conditions, which may or may not involve the parenchyma:

- Infections not involving the parenchyma as acute bronchitis and bronchiolitis.
- Infections involving the parenchyma as pneumonia.

(Falconer et al., 2013)

Acute Lower Respiratory Tract Infection are caused by:

- Number of infective agents, with Streptococcus pneumonia being generally the most frequently identified bacterial agent.
- Respiratory Syncytial Virus being the most frequent viral agent and other viral infections like Adenovirus, Influenza and Human parainfluenza viruses.

(Jackson et al., 2013)

Chapter 1
Bronchiolitis

Introduction:

Bronchiolitis is a common acute viral lung infection in young children causing bronchiolar inflammation and congestion in the small airways bronchioles associated with groups of clinical manifestations in children below 2 years of age, start with an upper respiratory prodrome, followed by increasing respiratory effort and wheezing ***(Anantham and Ernst, 2010).***

Epidemiology:

Bronchiolitis is the commonest lower respiratory infection in infants. Over 60% of infants have been infected on the first year of life, and by 2 years old over 80%. The antibodies that develop following early childhood infection do not prevent further RSV infections throughout life ***(Cheung et al., 2012).***

One study used Hospital Episode Statistics to identify all children aged below 2 years who were discharged from hospital with a primary code of bronchiolitis in England, between 1 April 2007 and 31 March 2010. This reported a total of 75,318 admissions during the study period. Hospital admission rates have increased over a period of ten years. Admission rates are more among infants and young children with prematurity and

congenital anomalies, chronic pulmonary diseases, immunodeficiency, congenital heart disease, BPD ***(Smith et al., 2012).***

Approximately 80% of cases of bronchiolitis occur in the first year of life, with a peak age of incidence between 2-6 months. By two years of age, virtually all children have been infected by RSV at least once and about half of them, twice. Boys are more frequently affected by RSV bronchiolitis; the male-to-female ratio is approximately1.5:1 ***(Anderson et al., 2007).***

Bronchiolitis occurs world widely, except in the subtropical areas of the south eastern United States (eg, Florida) where RSV is endemic throughout the year. The highest RSV activity usually occurs in winter, with peaks from October to February and relative subsidence only from March to July ***(Panozzo et al., 2007).***

Risk factors for the development of severe bronchiolitis include prematurity, cardiopulmonary disease, immuno-deficiency, tobacco exposure, daycare attendance, lower socioeconomic status, overcrowding, lack of breast feeding, congenital heart diseases and BPD ***(Ricart et al., 2013)***.

Causative organisms:

The virus is spread to infants by:

- Direct contact with nose and throat fluids of house hold contacts who has the illness.
- Sneezes or coughs nearby and tiny droplets in the air are then breathed in by the infant
- Touches toys or other objects that are then touched by the infant

(Watts et al., 2011)

Viral etiology:

1. RSV is most common cause of bronchiolities. More than half of all infants are exposed to this virus by their first birthday.
2. Other causes include: Adenovirus, Influenza, Parainfluenza, Rhinovirus, Human bocavirus, Coxsackievirus, Herpes simplex virus, metapneumovirus.

(Brieu et al., 2008)

Pathophysiology:

Bronchioles are small airways (< 2 mm in diameter) and lack cartilage and sub mucosal glands. The terminal bronchiole, a 16th-generation airway, is the final conducting airway that terminates in the respiratory bronchioles.

The gas exchange unit of the lung consists of respiratory bronchioles, the alveolar duct, and alveoli. The bronchiolar lining

formed of surfactant-secreting cells and neuroendocrine cells, which are the source of bioactive products such as somatostatin, endothelin, and serotonin ***(Budhiraja et al., 2012).***

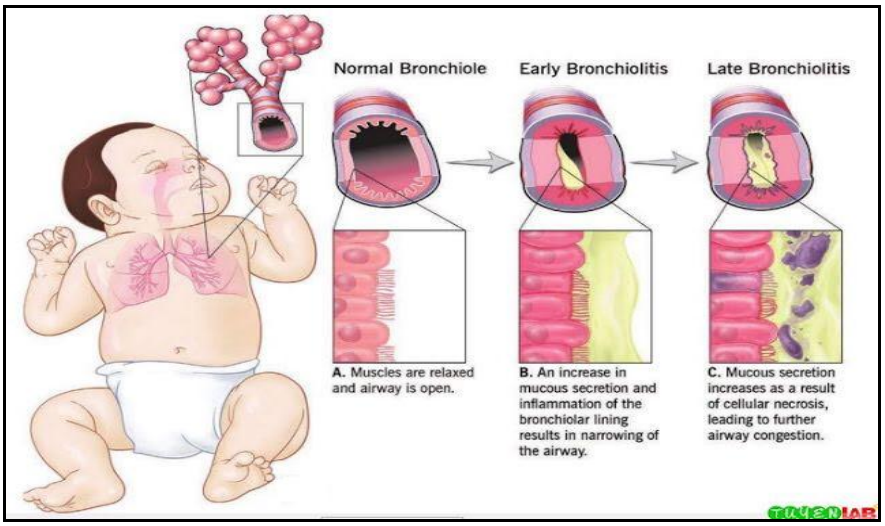

Figure (3): Bronchiolar changes during bronchiolities

The effects of bronchiolar injury include:

Increased mucus secretion, Bronchial obstruction and constriction, Alveolar cell death, mucus debris, viral invasion, Air trapping, Atelectasis, Reduced ventilation that leads to ventilation-perfusion mismatch and laboured breathing ***(Verma et al., 2012).***

Complex immunologic mechanisms play a role in pathogenesis of Bronchiolitis:

- Type 1 allergic reactions mediated by immunoglobulin E (IgE) may account for some clinically significant bronchiolitis. Infants

who are breastfed with colostrum rich in immunoglobulin A (IgA) appear to be protected from bronchiolitis.

- Necrosis of the respiratory epithelium is one of the earliest lesions in bronchiolitis and occurs within 24 hours of acquisition of infection.
- Proliferation of goblet cells results in excessive mucus production, so, epithelial regeneration with no ciliated cells impairs elimination of secretions.
- Lymphocytic infiltration may result in submucosal edema. The inflammation, edema and debris result in obstruction of bronchioles, leading to hyperinflation, increased airway resistance, atelectasis, and ventilation-perfusion mismatching. Infants are affected most often because of their small airways, high closing volumes, and insufficient collateral ventilation ***(Budhiraja et al., 2012).***
- Recovery begins with regeneration of bronchiolar epithelium after 3-4 days however; cilia do not appear for as long as 2 weeks. Mucus plugs are predominantly removed by macrophages ***(Dornelles et al., 2007).***

The immune response elicited by RSV may be both protective and pathogenic, there appear to be functional differences between initial infections in a seronegative infant and re-infection in an older child.

Despite the induction of both antibody and T-cell responses after a primary infection evidence suggests that both

the relative balance between type 1 and type 2 helper T cells determines the extent of RSV disease ***(Meissner et al., 2014)***.

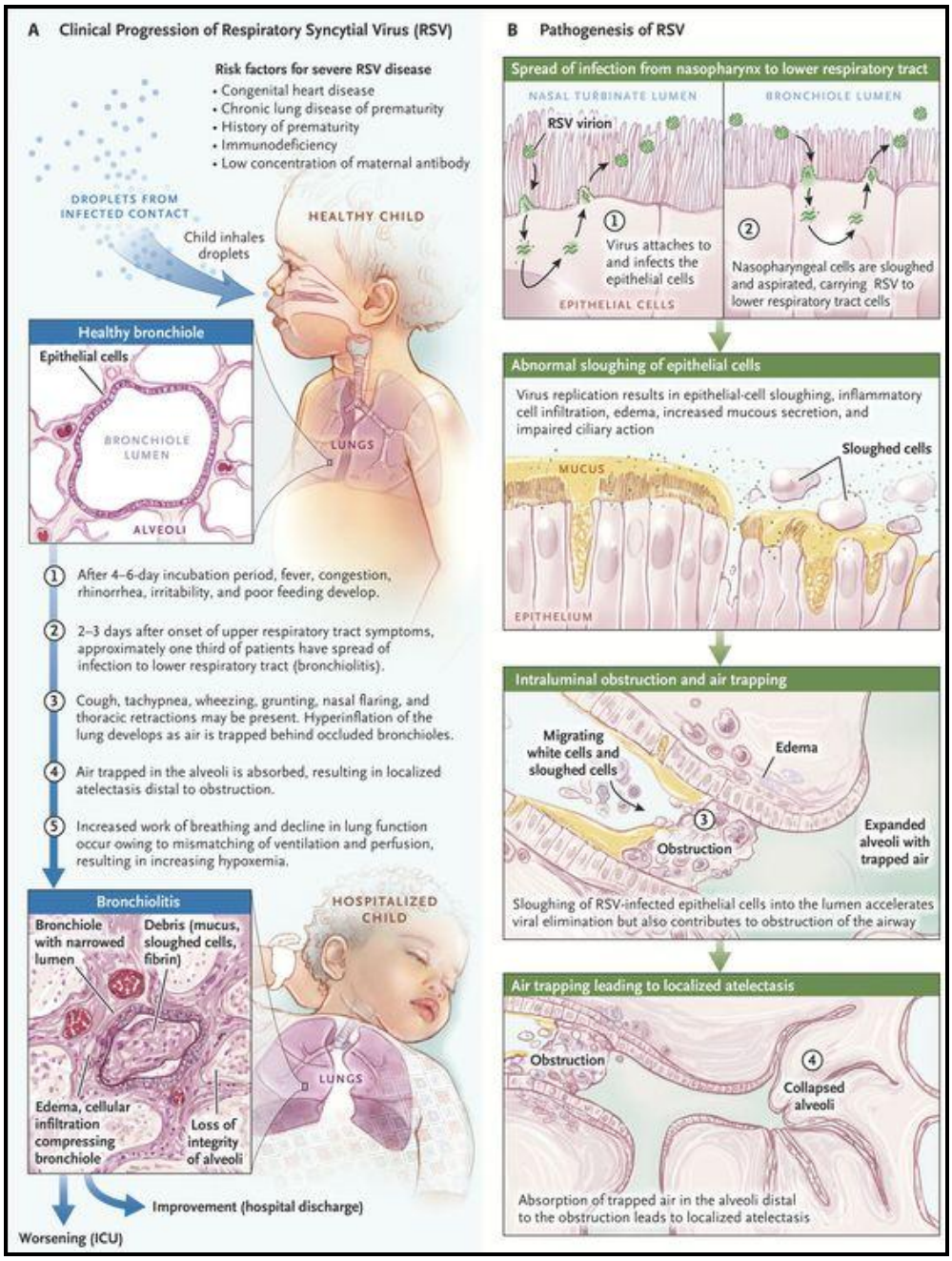

Figure (4): Clinical progression and pathogenesis of respiratory syncytial virus ***(Budhiraja et al., 2012).***

Clinical presentation:

Most clinicians recognize bronchiolitis as a group of clinical signs and symptoms occurring in children younger than 2 years, including a viral upper respiratory tract prodrome followed by increased respiratory effort and wheezing.

The main target in the history and physical examination of infants presenting with wheeze or other lower respiratory tract symptoms, particularly in the winter season is:

1. To differentiate infants with probable viral bronchiolitis from those with other disorders.
2. Detection of disease severity (increased respiratory rate, retractions, and decreased oxygen saturation).

(Alvarez et al., 2013)

Clinical signs and symptoms of bronchiolitis consist of rhinorrhoea, cough, tachypnea, wheezing, rales, and increased respiratory effort manifested as grunting, nasal flaring, and intercostal or subcostal retractions.

The course of bronchiolitis is variable and dynamic, ranging from temporary signs, such as apnea, to progressive respiratory distress from lower airway obstruction.

Important issues to assess in the history include the effects of respiratory symptoms on mental status, feeding, and hydration, ***(Ricart et al., 2013)***

Pulse oximetry has been used in clinical assessment of children with bronchiolitis. It reliably detects hypoxemia not suspected on physical examination. Reductions in pulse oximetry (<95% on room air) predict progression of disease or need for a return observational visit, Apnea has been reported to occur with great prevalence estimates and viral etiologies ***(Schroeder et al., 2013).***

❖ Clinical scoring of Bronchiolitis severity:

Table (1): Severity score of infant with respiratory distress (Score of RD in infant with acute lower respiratory infection) ***(Scalini et al., 2011)***

Clinical parameter	**0**	**1**	**2**	**3**
RR	<40	40-60	60-70	More than 70
Use of accessory muscle	none	1 muscle used	2muscle used	More than 3 muscle used
Color	Pink in room air	Cyanosed with crying	Cyanosed Pink with o2	Cyanosed with o2 or arrest
Auscultation	Normal	Decrease air entry, no Ronchi	Decrease air entry, heard Ronchi,wheezy	Silent chest

Healthy =0, **mild RD** =1-4
Moderate RD=5-8, **severe RD** =9-12

Investigation:

1. Imaging:

A. Chest X-rays: Children with a clear clinical diagnosis of bronchiolitis do not require a chest x-ray. CXR in bronchiolitis will show signs of hyperinflation, peribronchial thickening, and often patchy areas of consolidation and collapse. This may lead to some confusion with pneumonia, however if hyperinflation and wheeze are present the diagnosis should be regarded as bronchiolitis. CXR is indicated in severe cases or where the diagnosis uncertain ***(Perrotta et al., 2007).***

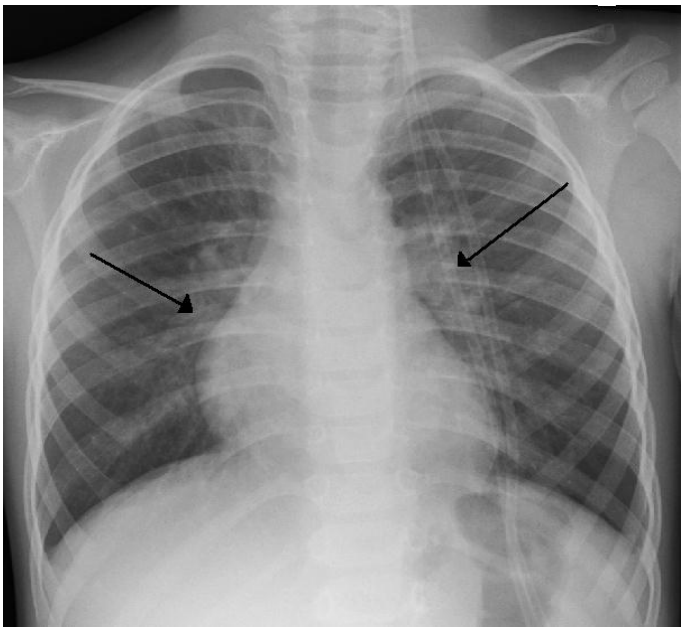

Figure (5): This X-ray shows:

1- Bilateral hyperinflation of the lungs

2- Peribronchial cuffing.

B. Ultrasound:

The diagnosis of bronchiolitis is mainly based on clinical signs and symptoms but lung ultrasound (LUS) may offer a non-invasive, rapid, reproducible, and relatively inexpensive diagnostic tool that could be of exceptional help in the clinical management of bronchiolitis. Thinner chest walls and smaller lung mass make infants and neonates ideal candidates for ultrasound scans, without exposing them to the greater cancer risk of ionizing radiation relative to adults.

In paediatric patients with bronchiolitis, LUS reflects the clinical respiratory inflammation of small air way in the form of significant B lines and can be used as a rapid and reproducible screening technique to help the physician in the unequivocal identification of infants in need of hospitalization and oxygen supplementation. Use of LUS for safely reducing hospitalization might have a great impact on socioeconomic aspect of this disease ***(Volpicelli et al., 2013).***

The role of lung US will be discussed on separate chapter.

2. Blood tests:

The most common tests are:

A. The WBC count has been decried for its poor test characteristics. Among infants with a febrile illness, WBC values are highly variable. No WBC count threshold has good discriminatory value for the presence