

Recurrent Pneumonia (Recurrent lower respiratory tract infections)

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Key Points

- A single episode of uncomplicated pneumonia in an otherwise healthy child does not require investigation.
- Recurrent pneumonia is not an uncommon presenting symptom in general pediatric practice and one of the most common reasons for referral to pediatric pulmonologists.
- Recurrent pneumonia is usually defined as ≥ 2 episodes of pneumonia in a year or ≥ 3 in life.¹
- Many children with recurrent pneumonia do not need a full diagnostic work up, either because pneumonia episodes are not frequent or severe enough or because eventually children become asymptomatic.
- Evaluation of children with recurrent pneumonias begins by taking a careful history, an examination while the child is sick, and confirmation that the child is truly experiencing recurrent pneumonia.
- The majority of recurrent pneumonia causes in children have predictable risk factors (e.g., psychomotor retardation with feeding problems).
- Extensive investigations may not identify an underlying cause in up to 30% of children with recurrent pneumonia.¹
- The initial step in evaluating a child with recurrent respiratory symptoms includes distinguishing between recurrent wheezing versus recurrent infections.
- Studies show that asthma is being over diagnosed in children with recurrent respiratory symptoms.
- Patients with atypical asthma that does not respond to therapy should be investigated further.
- The evaluation of children with recurrent pneumonia should not be focused only on the respiratory tract.

- Investigation for other organ system involvement may help for ultimate diagnosis (e.g., cystic fibrosis).
- The presence of serious infection in other organs may suggest immunodeficiency.
- Persistent bacterial bronchitis (PBB) is a recently acknowledged condition that occurs from bacterial colonization of conducting airways associated with biofilm formation.
 - PBB was found to be the most common cause (40%) of children with chronic cough.
 - Recurrent lower respiratory tract infections usually occur with intercurrent viral infections, mimicking asthma.
 - Two (2) weeks of treatment with high dose antibiotics is required for the treatment of PBB.
 - Appropriate antibiotic therapy includes amoxicillin-clavulanate and most second and third generation cephalosporins to cover beta-lactamase producing organisms and *S. pneumoniae* in the community.³

Definition, Pathophysiology, Etiology, Assessment, and Diagnosis

Definition

- Infants and children vary considerably as to the number of respiratory tract infections experienced. The average child has 4 to 8 respiratory infections per year. Some infants and young children who do not attend daycares and schools may have only 1 or 2 infections per year, while others who reside in crowded environments may have 10 to 12 infections per year, particularly if they have older siblings or if they attend daycare or preschool.⁴
- A single episode of uncomplicated pneumonia in an otherwise healthy child does not require investigation. However, further investigation is mandated if the child has had a previous history of unusual infections, the pneumonia has an atypical course, there is a family history of an unexplained death from infection, etc.⁵
- Prematurity, atopy, passive smoking, indoor pollution, outdoor pollution, congenital abnormalities of the respiratory tract, cardiovascular diseases and neurological diseases are factors associated with increased frequency of lower respiratory tract infection (LRTI). The recommendation in such cases is to eliminate avoidable risk factors and adopt a wait and see approach.⁹
- Underlying serious structural or systemic diseases can predispose children to recurrent LRTI. Children with these conditions warrant further investigations.
- When evaluating a child with recurrent LRTI, the first step is to distinguish between otherwise healthy children from those with an underlying chronic disease that require further investigations.
 - Children with underlying chronic disease have the following characteristics⁹:
 - Severe recurrent lower respiratory tract infections in the first months of life that requires hospitalization
 - Slowed growth
 - Systemic involvement
 - Infection with uncommon pathogens
 - Absent or short periods of being well in between episodes
 - Family history of primary immunodeficiency or early death
- There are no evidence-based recommendations regarding when to investigate and the sequence of investigations; however, clinical judgment, depending on the history and existence

of other features suggestive of another condition, helps clinicians with decision-making.

- Recurrent pneumonia is usually defined as ≥ 2 episodes of pneumonia in a year or ≥ 3 throughout the life.¹
- Since respiratory tract infections are common in children, the challenge is to decide if more investigation should be done and/or referral to a specialist is required.
- Before proceeding to further investigation the primary care provider should make certain that the child has recurrent lower respiratory tract infections, not recurrent wheezing.
 - In a study in primary pediatrics care in Canada, as many as 64% of young children with recurrent wheeze had been treated with antibiotics.⁶
 - Repeated courses of antibiotics for such episodes can then lead to an incorrect diagnosis of recurrent pneumonia.
 - Contrarily, numerous children with persistent bacterial bronchitis (PBB) are being diagnosed with asthma.⁷

Pathophysiology

- Disruption of one of the defense mechanism of the respiratory system can cause recurrent pneumonias.
- Anatomical problems of airway and lung parenchyma such as airway narrowing, fistula, compression, pulmonary sequestration, etc.
- Functional problems
 - During swallowing, food and secretions are directed to the esophagus to prevent aspiration. Any anatomical and functional disruption of this phenomenon results in primary or secondary aspiration (dysphagia).
 - Primary aspiration and secondary aspiration
- Absence/weak cough reflex interferes with the removal of substances/airway clearance; patients with hypotonia, muscular dystrophy
- Abnormal airway clearance: Mucociliary system produces mucus that traps foreign, infectious particles then cleared by the upsweep motion of the ciliary epithelium lining the airways. Certain conditions are associated with abnormal airway clearance that causes recurrent respiratory symptoms and pneumonias.
 - Primary ciliary dyskinesia (PCD)
 - Cystic fibrosis (CF)
- Immunodeficiency
 - Patients with neutropenia and neutrophil function abnormalities as children with chronic granulomatous disease (CGD) present with recurrent staphylococcal and aspergillus-related pneumonia.
 - Primary immunodeficiency is a common cause of non-CF bronchiectasis.
- Persistent bacterial bronchitis (PBB) is a real and important cause of chronic/recurrent lower respiratory tract infections and has been recently adequately characterized by bronchoalveolar lavage fluid sampling.
 - Defined as the presence of isolated chronic (>4 weeks) wet cough, resolution of cough with prolonged (2 weeks) antibiotic treatment, and absence of pointers suggestive of a specific cause of cough⁸
 - It is a diagnosis of exclusion; conditions such as gastroesophageal reflux disease (GERD), immunodeficiency, CF, etc. should be eliminated.
 - Chest X-ray may be normal.
 - Many children with ultimate diagnosis of PBB were referred with a diagnosis of difficult asthma.⁷
 - Bronchoalveolar lavage shows neutrophilic inflammation with positive bacterial cultures.
 - Most children are young (<5 yr.).

- Asthma and PBB may co-exist.⁸
- Persistent bacterial bronchitis is associated with significant morbidity and antibiotic use.

Etiology

- Although it is logical to approach recurrent pneumonias that occur in the same anatomic location differently, as opposed to occurring in different lung fields, there are some exceptions.
- Eighty percent (80%) of children with humoral immunodeficiency had pneumonias recurring in the same lobe.
- Twenty percent (20%) of patients with confirmed structural lung abnormalities (airway stenosis) had recurrent pneumonias in different lung lobes.

Table 1: Conditions Associated with Recurrent Pneumonia Based on Anatomical Location

Recurrent localized pneumonia

- Intraluminal pathology/obstruction
 - Foreign body, tumor, right middle lobe syndrome, mucus plug
- Extraluminal compression
 - Lymph node (Most common)
 - Vascular ring/sling
 - Achalasia/ esophageal foreign body
- Structural abnormalities
 - Tracheal bronchus impairs drainage of right upper lobe, often leading to recurrent infections
 - Tracheobronchomalacia (TBM)
 - Bronchiectasis
 - Focal: Following severe bacterial or viral infection causing bronchial wall damage, persistent obstruction (e.g., retained foreign body) with recurrent pneumonia
 - Generalized: cystic fibrosis (CF), non-CF bronchiectasis, primary ciliary dyskinesia (PCD), early-on CF bronchiectasis may appear focal, especially right upper lobe
 - Congenital cystic adenoid malformation (CCAM): Diagnosed prenatally or shortly after birth
 - Pulmonary arterio-venous malformation (AVM)
 - Congenital lobar emphysema (CLE): Usually diagnosed during the newborn period. Some cases present later with recurrent pneumonia.
 - Pulmonary sequestration: Non-functioning pulmonary tissue separates from the tracheobronchial tissue and receives blood supply from the aorta; usually left lower lobe is involved.
 - Bronchogenic cyst: Infection may rarely occur in the cyst itself or in the surrounding tissue compressed by the cystic lesion.
 - Congenital heart disease may cause extrinsic compression of the airway by enlarged heart.

Recurrent generalized pneumonia

- Aspiration due to impaired swallowing
 - Central Nervous System (CNS) disease/muscular dystrophy/hypotonia, severe reflux
 - Anatomical abnormalities
 - Laryngomalacia/ laryngeal cleft, vascular ring/sling

- Tracheoesophageal fistula (TEF), esophageal obstruction and motility problems
- Tracheobronchomalacia (TBM)
- Persistent bacterial bronchitis (PBB)
- Bronchiectasis
 - Cystic Fibrosis
 - Primary Ciliary Dyskinesia (PCD): Ultrastructural defect in the cilia or abnormal organization of microtubules within each cilium; associated with recurrent pneumonia, chronic otitis media (OM), sinusitis ± Kartagener syndrome
- Asthma is the most common cause of recurrent/persistent infiltrate, usually in the right middle lobe. Simple viral infection with atelectasis is often misdiagnosed as pneumonia.
- Immunodeficiency
 - Primary: Includes humoral (recurrent sinopulmonary infections due to encapsulated bacteria and enteroviruses), cell-mediated (recurrent pneumonia due to pyogenic bacteria, *Pneumocystis jiroveci*, viruses), and complement deficiency (Bacteremia, septic arthritis, meningitis)
 - Secondary: Including Immunosuppressive drugs, HIV, Sickle cell disease, diabetes, malnutrition, etc.
- Increased pulmonary blood flow including ventricular septal defect (VSD), patent ductus arteriosus (PDA) causing large volume of left-to-right shunt. Congested lung may facilitate bacterial infections.
- Neurologic diseases associated with muscle weakness, hypoventilation
- Collagen vascular disease with pulmonary hemorrhage
- Granulomatous diseases such as sarcoid

Assessment

- The initial step should be deciding on whether the child has respiratory tract infections or if the issue is recurrent respiratory symptoms caused by other respiratory conditions (e.g., asthma).
- Distinguishing upper respiratory from lower respiratory tract infections may be difficult especially in young children who present with general symptoms (fever, not feeling well) during upper respiratory tract infections.
- Evaluation of children with recurrent pneumonias begins by taking a careful history, an examination while the child is sick, and confirmation that the child is truly experiencing recurrent pneumonia.
 - Birth history - Pregnancy history should be explored for maternal illness (e.g., HIV, cytomegalovirus), risky behaviors, and exposure to toxins, prescription medications, illicit drugs, tobacco, and alcohol. Birth history should include length of gestation, birth weight, and neonatal problems such as jaundice, respiratory distress, or need for intensive care.
 - Feeding history, including food intolerance and duration of breast feeding, choking during feeding, or symptoms suggestive of reflux should be investigated.
 - Growth and development - Weight, height, and head circumference should be plotted and followed over time.
 - Children with chronic disease or immunodeficiency often have poor weight gain/weight loss.
 - Children with chronic lung, heart, or gastrointestinal disease are often small because of anorexia, high-energy expenditure, or malabsorption.
 - Chronic disease and syndromic immunodeficiencies, such as ataxia-telangiectasia

- and DiGeorge syndrome, can lead to delay in attaining developmental milestones.
 - Progressive neurologic dysfunction is seen in young adults with Chediak-Higashi syndrome.
 - Delayed speech can occur with recurrent and chronic otitis media.
- Immunization history – Immunization history should be reviewed; a person who develops infections despite immunization may be immunodeficient or may be underimmunized and should be evaluated.
- Medications – Current and past medications should be recorded, including duration, effectiveness, and adverse reactions; use of any immunosuppressive medications, such as glucocorticoids, should be noted.
- Family history – The presence of family members with similar diseases, recurrent infections, unexplained death, or autoimmune disease suggests the possibility of a genetic illness.
- Social history
 - The home, parents' work environment, and daycare, school, or wherever the child spends a lot of time (after school activities, church, etc.) should be explored for exposures, such as allergens, tobacco smoke, contaminated water supply.
 - Prior residences and travel history may be important in exposure to infectious agents or allergens.
 - Daycare and school attendance increase the risk of exposure to respiratory pathogens.
 - Bottle propping is a common practice that can cause not only tooth decay but also aspiration.

Clinical Symptoms

- Wheezing may indicate asthma or airway malacia or foreign body aspiration; the nature of the wheezing may help identify the cause.
 - Monophonic wheeze (a single pitch and tonal quality heard over an isolated area) seen when there is a localized narrowing of a single airway (e.g., foreign body)
 - Polyphonic wheeze (multiple pitches and tones heard over a variable area) seen in asthma
- The nature of cough is important.
 - Loud, barking cough may indicate tracheobronchomalacia.
 - Chronic wet cough ± sputum production may indicate bronchiectasis, PBB, etc.
 - A cough associated with asthma is dry and usually responds to bronchodilator and inhaled steroids though patients with asthma do have mucus and a wet cough does not rule out asthma.
- Existence of other conditions should be investigated.
 - Congenital heart disease may increase pulmonary blood flow that may cause recurrent respiratory infections.
 - Patients with hypertonia (most notably children with cerebral palsy) may present with recurrent pneumonia.
 - Swallowing dysfunction and aspiration
 - Scoliosis causing restrictive lung disease and hypoventilation
 - Impaired airway clearance due to increased secretions
 - Neuromuscular diseases may affect lungs.
 - Hypoventilation due to muscle hypotonia of chest wall and diaphragm can cause atelectasis.
 - Chest wall abnormalities (scoliosis is a common finding) can cause restrictive lung disease.
 - Weak cough interferes with airway clearance.
 - Hypotonia may cause abnormal swallowing and aspiration.

- GERD can cause respiratory disease by aspiration or by esophagobronchial reflex.⁵
- Other clinical features
 - Clubbing may indicate a suppurative lung disease; asthma is not associated with clubbing.
 - Nasal polyps can be a symptom of CF or allergy, but if seen in children <10 years of age a sweat test is needed.
 - Dextrocardia is suggestive of PCD.
 - Chronic suppurative otitis media, sinus infection, candidiasis suggest immunodeficiency; recurrent sinusitis can be hard to ascertain objectively.
- Despite negative CF newborn screening, clinicians should keep a high index of suspicion in children with chronic respiratory symptoms since the screening can miss a small percentage of children with CF.

Further Evaluation Warranted

Children who should undergo further investigations in the presence of at least one of these features; further investigations are necessary because it is important to recognize the underlying disease early.⁹

- History of serious recurrent infections involving multiple sites or caused by opportunistic organisms
- History of recurrent pneumonia affecting the same lobe
- History of prolonged interstitial pneumonia with no infective cause
- History of chronic upper respiratory tract infection (rhinosinusitis, otitis media) from the first months of age
- Presence of chronic productive cough (lasting >4 weeks) with purulent sputum
- Persistence of abnormal thoracic examination findings with lung crackles on auscultation or the persistence of radiological abnormalities for more than 8 weeks
- Physical signs of malabsorption or digital clubbing
- Family history of severe infections or early death

Diagnosis

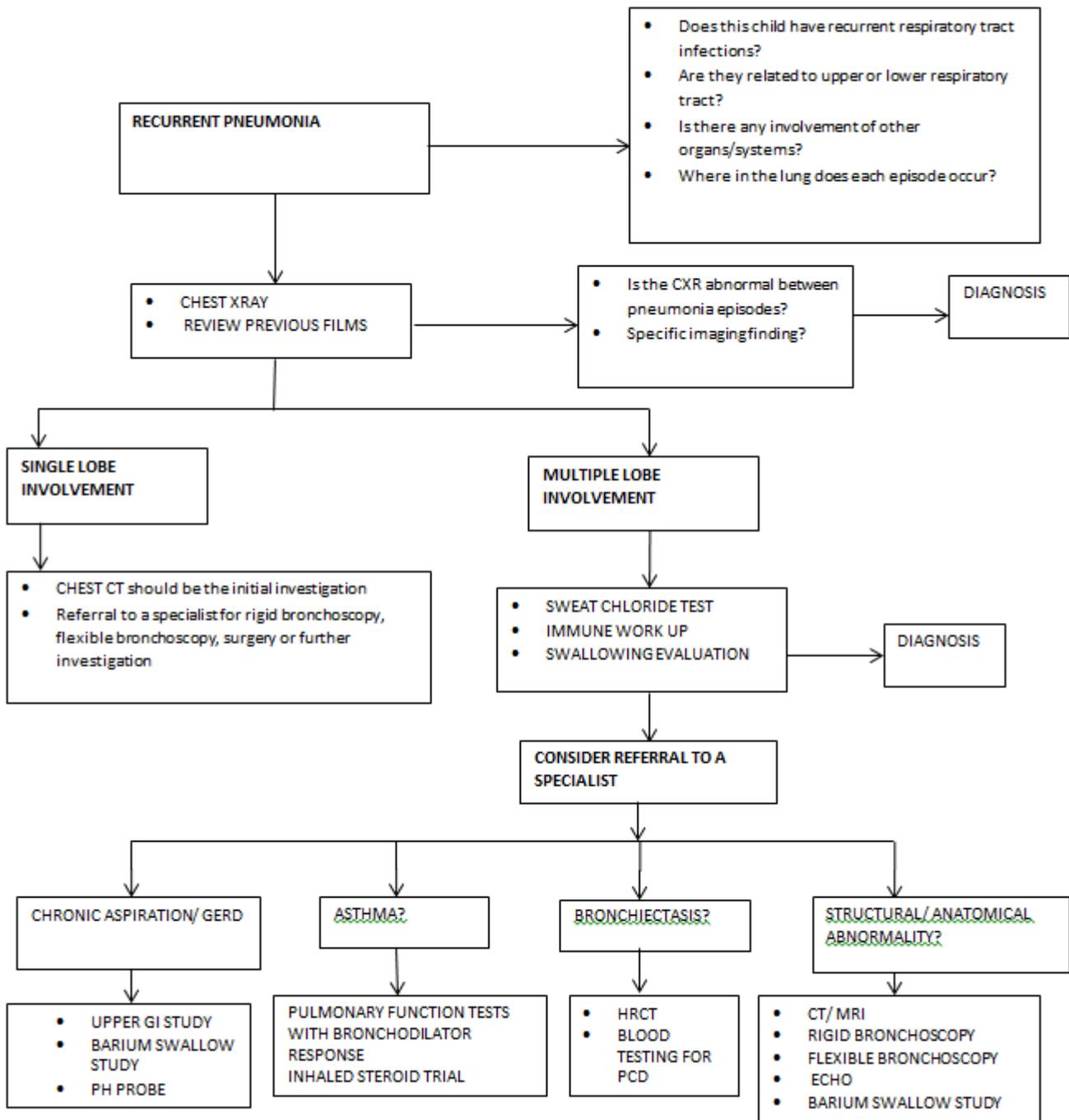
- Chest X-ray (CXR) is the initial imaging tool and is the gold standard for the diagnosis of pneumonia.
 - The radiologic changes of acute pneumonia may take 6-12 weeks or longer to resolve, depending on the organism; therefore, clinicians should be cautious with the diagnosis of recurrent pneumonia.⁵
 - A child with ≥ 2 CXR documented episodes of pneumonia, an incomplete clearing between pneumonia episodes, or a single episode that does not clear should be investigated further.
 - Repeat the CXRs when the child is well to identify persistent abnormalities
- Chest computed tomography (CT) is a viable alternative in the evaluation of vascular anomalies of the mediastinum.
 - It shows parenchymal abnormalities.
 - CT can be used in the evaluation of vascular rings, slings, and masses and can show early airway issues like bronchiectasis.
 - IV contrast also helps to differentiate vessel from hilar lymph nodes, which can be helpful in assessment of granulomatous diseases like sarcoid, fungal infections, TB, malignancy, etc.

- Ideally, CT should be performed when the child is not acutely infected because acute changes may complicate the interpretation.
- Young children may need sedation for the CT imaging.
- Sedation-related hypoventilation can cause dependent atelectasis that may mimic pulmonary infiltrates.
- IV contrast is helpful to delineate vascular anatomy.
- Chest MRI is the standard means for imaging airway compression due to vascular anomalies; although it is not associated with radiation exposure, children will need sedation for the procedure.
- Upper GI study is easy to perform and not associated with risk in experienced hands; it may detect a compressed esophagus, tracheoesophageal fistula (with a special technique), reflux, and delayed gastric emptying as well as other anatomical abnormalities like malrotation.
- Swallow evaluation, the second choice following CXR in most young children, with the help of a speech therapist is helpful for assessing the esophagus and the swallowing function.
- pH probe for the investigation of acid GERD; if serious GERD is present, investigate for food allergy.
- Sweat chloride test is the gold standard for the diagnosis of CF and should be performed at a Cystic Fibrosis Foundation-accredited center.
- Evaluation of immune system
 - A minimum screen involves CBC, measurement of immunoglobulins and complement levels, mannose-binding lectin level and IgG antibody responses to protein and polysaccharide vaccines,¹⁰ and can be ordered by the primary care providers.
 - If the initial screening is negative and further investigation is needed, a specialty referral is indicated.
- Echocardiography (ECHO) is performed to investigate major airway, substantial significant right-to-left shunt, and enlarged heart compressing the airways.
- Tuberculous skin test (TBST) should be performed in endemic areas or in children with risk factors.
- Erythrocyte Sedimentation Rate/C-Reactive Protein (ESR/CRP) may be useful to identify children with connective tissue disorders (Wegener's, systemic lupus erythematosus [SLE]) presenting with pulmonary infiltrates.
- Spirometry with a positive bronchodilator response is the gold standard for diagnosing asthma.
 - A majority of asthma patients will have a normal spirometry and may need a challenge test with methacholine, cold, exercise, etc.
 - When the history is suggestive of asthma, a treatment trial with inhaled corticosteroids that shows improvement in symptoms may confirm the diagnosis of asthma.
 - Occasionally, 2 different conditions can coexist. For example, a great portion of patients with CF may have a positive bronchodilator response and PBB may be associated with asthma.
 - Young children cannot perform a spirometry maneuver until age 5-7 years; in that case, close follow-up of symptoms and application of modified asthma predictive index¹¹ may be helpful.
- Mucociliary function (PCD) evaluation - Should be completed a few weeks after the patient has recovered from a respiratory tract infection to avoid confusion with temporarily acquired ciliary defects that are a consequence of recent injury.
- Bronchoscopy in experienced hands does not carry a major risk. Besides patients with significant pulmonary arterial hypertension and the ones with hemodynamic instability, there is no contraindication for a bronchoscopy procedure.
 - Besides patients with significant pulmonary arterial hypertension and the ones with

- hemodynamic instability, there is no contraindication for a bronchoscopy procedure.
- Some children may benefit from esophagogastroduodenoscopy (EGD) at the same time, especially in the setting of serious GERD with a concern for aspiration.
 - Rigid bronchoscopy is performed by ear-nose-throat (ENT) physicians and is the best way for the evaluation of the upper airway (fistula, cleft, etc.) and the only way to retrieve foreign bodies in children.
 - Flexible bronchoscopy in children is usually performed by pediatric pulmonologists allowing them to evaluate upper and lower airways.
 - Anatomical evaluation of the airway (stenosis, abnormal branching, compression, right middle lobe syndrome, etc.)
 - Functional evaluation of the airway (tracheobronchomalacia)
 - To obtain bronchoalveolar lavage sample.
 - Identify the type of the inflammatory cells.
 - Culture the lavage fluid
 - Show lipid-laden macrophages for aspiration syndromes

Figure 1. Diagnostic Algorithm for Children with Recurrent Pneumonia

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Management and Treatment

- Patients with CF should be followed by CF Foundation-accredited care centers.
 - Like others, these children can have other medical problems that need to be addressed by the primary care providers.
 - Good communication between the primary care providers and the CF center is essential for the optimal care of these patients.
- Asthma: Diagnosis is based on the history and spirometry response to bronchodilator treatment.
 - The majority of children with asthma can be treated and followed by primary care providers.
 - Inhaled steroids are the main chronic treatment in most cases while environmental

- exposure is avoided.
 - The most common treatment failure is suboptimal delivery of inhaled medication.
- PBB is a curable condition and recurrent PBB may occur.
 - Treatment involves eradication of the bacteria with prolonged appropriate antibiotic treatment (2-6 weeks).
 - If empirical antibiotic treatment is unsuccessful, the child should be referred to a specialist.
- When children with neuromuscular disorders are diagnosed, they should be followed by multidisciplinary tertiary care centers.
- Structural lung anomalies are mostly treated with surgical intervention.
- Dysphagia/GERD
 - Videofluoroscopic swallow study (VFSS), is the procedure of choice and is generally performed after a clinical evaluation of swallowing by a speech-language pathologist, and the radiographic findings are interpreted in conjunction with the clinical findings.
 - Patients with mild swallowing impairment can often be managed with changes in feeding position and posture, modification of bolus size, and the alterations of consistency, shape, and texture of food.
 - In a patient with neurologic impairment, documentation of clear aspiration during a swallow study, and chronic pulmonary symptoms attributable to recurrent aspiration, placement of a gastrostomy tube or skin-level gastrostomy device (button) and cessation of oral feeding is recommended.
 - For patients who are not fed orally because of aspiration risk, and with well-documented severe gastroesophageal reflux or a clear history of recurrent reflux-induced aspiration, evaluation for either fundoplication or jejunal feeding is recommended.

Prevention

- Besides routine immunization schedule, immunizations including yearly influenza, pneumococcal vaccine polyvalent 23 (Pneumo 23), and respiratory syncytial virus (RSV) are recommended for most patients except live vaccines for patients with immunodeficiency.
- Infection control practices may be required for children with immunodeficiency, CF, and other conditions that make them susceptible to infections.
- Airway clearance techniques (positive end expiratory pressure devices, vest, cough assist devices, manual chest physical therapy) to prevent airway occlusion, atelectasis, and infection
 - Children with CF are mostly treated with manual chest physical therapy during the first years of life and then VEST[®] therapy afterward. Positive Expiratory Pressure (PEP) devices (Flutter[™], Acapella[™]) are as effective as VEST[®] therapy.
 - Children with muscular dystrophy need mostly cough assist devices to improve airway clearance with or without other techniques such as VEST[®], manual chest physical therapy, or intrapulmonary percussive ventilation (IPV) device.
 - Patients with non-CF bronchiectasis will need airway clearance techniques like PEP devices or VEST[®].
 - Patients with tracheobronchomalacia (TBM), aspiration, etc. may require chest physical therapy when they are sick with pneumonia.
- Prolonged/chronic antibiotic use (systemic, inhaled, antibiotics in cycles) may be required for children with immunodeficiency, CF, and non-CF bronchiectasis, etc.
- Prevention of primary and secondary aspiration is essential to prevent further pulmonary damage and bronchiectasis.
- Children with chronic respiratory symptoms should be followed closely with a high index of suspicion and should be maintained for early diagnosis of conditions mentioned above to prevent permanent pulmonary damage.

Follow-Up

- Patients with chronic conditions should be followed by specialty clinics (immune deficiency, CF, non-CF bronchiectasis, TBM, etc.)
- Partnership between the primary care providers and the specialty care center is essential for the care of individuals with chronic respiratory conditions.

This guideline was developed to improve health care access in Arkansas and to aid health care providers in making decisions about appropriate patient care. The needs of the individual patient, resources available, and limitations unique to the institution or type of practice may warrant variations.

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