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A REVIEW ON EFFECT OF ANTIBIOTIC USED FOR LOWER RESPIRATORY TRACT INFECTION

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ABSTRACT

One of the leading causes of disease and death worldwide is lower respiratory tract infections (LRTIs), especially in children and the elderly. LRTIs include bronchitis, pneumonia, and bronchiolitis and can be caused by bacteria, viruses, or other pathogens. While antibiotics are commonly used to treat LRTIs, their effectiveness is limited to bacterial infections, and overuse of antibiotics increases healthcare costs and leads to antibiotic resistance. Pharmacist treatments have been shown to improve patient health or reduce hospital readmissions; however, further study is needed to determine the optimal combination of interventions. Patients who had surgery, an organ transplant, or incidental exposure to hazardous metals were included in our study. Additionally included were patients who experienced any of the following pneumonia, CPAM, interstitial pneumonitis, infiltrating TB, or microbial invasions due to drug side effects. After receiving antibiotic treatment (cephalosporin, like cefuroxime or cefpodoxime), the patients symptoms went away. According to the results of all their tests, the body operates normally. The patient recovers more quickly and achieves better results as a result of the pharmacists interventions during therapy.

KEYWORDS: Prescription Patterns, Lrti, Antibiotics, Antibiotic Resistance, Bronchitis, Pneumonia.

1. INTRODUCTION

Around the world, lower respiratory tract infections (LRTIS) are one of the fatal lung diseases that have a major detrimental impact on public health and the economy. The lower parts of the respiratory tracts, such as the trachea and alveolar sacs, are particularly affected. Pseudomonas aeruginosa and Streptococcus pneumonia are two of the most common infectious gram-positive and gram-negative bacteria that cause LRTIs.

Chronic obstructive pulmonary disease (COPD) and cystic fibrosis (CF) are also commonly associated with this infectious disease. Oral and parenteral antibiotics come in big quantities that need to be administered often and have dosage-related side effects.[1]

Antibiotic resistance and antibiotic-related adverse effects, such as Clostridium difficile infections, may result from the frequent use of prolonged antibiotic courses in patients with lower respiratory tract infections (LRTIs). One Aliberti et al. showed that patients with community-acquired pneumonia (CAP) had an average treatment length of 11 days in a recent international audit involving 2000 patients. There was no discernible relationship between treatment time and sickness severity.

In patients with LRTIs, there is evidence that shorter antibiotic courses may be just as beneficial as longer ones. Three days of amoxicillin treatment was found to be similar to eight days of treatment in a randomized controlled trial of patients with mild to moderate pneumonia.4 Side effects associated with antibiotics were prevalent (21% in the 8-day group), although they tended to decline in the 3-day group (11%).[2]

Worldwide, respiratory tract infections are a leading source of illness and mortality, especially in underdeveloped nations. Respiratory tract infections, independent of location, are the second or third leading cause of death for children under five. Adenoviruses, influenza viruses A and B, parainfluenza viruses types 1-3, and human respiratory syncytial virus (RSV) have all been shown to be significant contributors to acute lower respiratory tract infections (ALRTI) in China. In 2001, the Netherlands isolated the human metapneumovirus (hMPV) for the first time from nasopharyngeal aspirates (NPAs) taken from children who had acute lower respiratory tract infections (ALRTI).[3]

It has been established that hMPV causes respiratory tract infections that resemble respiratory syncytial virus (RSV) symptoms. In newborns and young children, AMPV can cause a wide

range of clinical illnesses, including pneumonia, bronchiolitis, and upper respiratory tract infections.

Since hMPV replicates slowly in host cells, studies have shown, virus culture is rarely employed as a diagnostic test in epidemiological investigations. However, compared to other traditional techniques, real-time reverse transcription polymerase chain reaction for hMPV has numerous benefits. Therefore, this study first confirmed that real-time RTPCR assays targeting the hMPV F gene in serially diluted recombinant hMPV virus infected cell supernatants are reliable and reproducible.[3]

A significant and frequent cause of pediatric respiratory tract infections worldwide, particularly in colder climates, is the respiratory syncytial virus (RSV). Infants frequently contract RSV acute bronchiolitis, which can occasionally be fatal. Therefore, pediatricians benefit from an accurate and timely diagnosis of RSV infection. Additionally helpful is information on the epidemiology of RSV infection.

The enzyme immunoassay technique known as TESTPACK RAV has recently been developed as a convenient and reliable way to identify RSV antigen in nasopharyngeal specimens. The single biggest contributor to the worldwide burden of RSV disease in infants and young children as well as to viral death, primarily in rural regions, is India.[4]

Previous attempts at estimating this burden have relied primarily on hospital-based case fatality ratios (CFRS). There are several research on RSV-related in-hospital mortality, but there are few current prospective studies that calculate the burden of RSV disease in hospitals and the community, including mortality from it.[5]

The most frequent reason for individuals to visit their primary care physician is coughing, and in these cases, acute bronchitis is typically the diagnosis. Since pneumonia and asthma may require particular treatments not recommended for bronchitis, acute bronchitis should be distinguished from other frequent illnesses.

The average duration of bronchitis symptoms is three weeks. Lower respiratory tract infections caused by bacteria and viruses cannot be reliably distinguished by the presence or absence of colored (such as green) sputum. More than 90% of cases of acute bronchitis are caused by viruses. In order to prevent the spread of pertussis or if the patient is at a higher risk of contracting pneumonia, antibiotics should only be given in cases of bronchitis.[6]

2. ACUTE AND CHRONIC BRONCHITIS

2.1 *Acute Bronchitis*

The clinical illness known as acute bronchitis is characterized by a relatively short, self-limiting inflammatory process of the large and mid-sized airways that is not linked to chest radiography evidence of pneumonia. It is primarily brought on by viruses and is typified by a productive or dry cough that goes away in less than three weeks. In the winter, it is most prevalent.

Acute cough is one of the most common reasons people visit the doctor, regardless of age. One Due to significant overlap with symptoms of the common cold, pneumonia, and asthma, incidence figures may be imprecise. Estimates from the National Health Interview Survey of American households show that 5% of persons report receiving a medical diagnosis of acute bronchitis annually, with the highest prevalence occurring in the winter and in children under five. In UK investigations, comparable rates of 54 per 1000 individuals have been noted; these rates vary from 36 per 1000 for younger men to 225 per 1000 for those over 85.[7]

Acute bronchitis is one of the most common medical conditions observed in general care among otherwise healthy persons. Coughing and sputum production are hallmarks of this self-limiting, typically virally caused clinical condition, which also includes upper respiratory tract and systemic infection symptoms. The duration of this sickness varies; 25% of patients have a cough that lasts more than four weeks, and 50% of patients have a cough that lasts more than three weeks.

Acute bronchitis is substantially less common in the summer and peaks in the winter. Acute bronchitis has been associated with a number of viruses, including rhinovirus, respiratory syncytial virus, influenza virus, parainfluenza virus, adenovirus, and enterovirus. Chlamydia pneumoniae and Mycoplasma pneumoniae are responsible for between 10% and 15% of infections.[8]

In the UK, more than 40 out of every 1000 persons get acute bronchitis each year. Even though only around 50% of people have a recognized ailment, the causes are usually believed to be communicable. It is uncertain how smoking or consuming tobacco smoke from the environment can increase the risk of acute bronchitis. Recurrence or longer-lasting symptoms may occur in one- third of patients. Antibiotics only marginally reduce the length of coughing and may increase the risk of adverse effects when compared to a placebo. The

broad usage of antibiotics is still thought to increase the risk of resistance. Whether one antibiotic regimen is better than another cannot be determined. In patients with acute bronchitis, the use of broad-spectrum antibiotics, such as quinolones or amoxicillin–clavulanic acid (co-amoxiclav), in addition to amoxicillin alone is not yet supported by enough high-quality data. There is no evidence that smokers who do not have lung disease benefit more from antibiotics than nonsmokers do.[9]

Acute bronchitis and moderate upper respiratory infections have similar symptoms in the initial days of infection. Coughing after acute bronchitis typically lasts 10 to 20 days, but it can occasionally linger up to four weeks.

Many cases still have an unidentified cause. A community pandemic's existence or absence, influenza vaccination status, the time of year, and the population impacted are all important risk factors for certain illnesses. The incubation periods of the three atypical bacteria are longer than those of viruses, which typically last two to seven days.[10]

Coughing is the most typical and recognizable symptom of acute bronchitis. About one-third of patients with acute bronchitis develop a fever, and some people may seem a little sick. During lung auscultation, wheezes and rhonchi may be heard; these symptoms usually disappear upon coughing. It's important to rule out pneumonia. Concerning symptoms of pneumonia include high fever, moderate to severe illness, hypoxia, and evidence of lung consolidation, including crackles, egophony, increased tactile fremitus, bronchial breath sounds, and decreased breath sounds. Pneumonia is unlikely to strike nonfrail elderly people with normal vital signs and lung examination results.

Acute bronchitis can also include fever, headache, congestion in the nose, coughing, sputum production, and dyspnea. Infections with acute bronchitis may be confused with the common cold in the early stages. Coughing may cause pain in the chest wall or substernum. Fever is uncommon after the first few days, and if it rises above 100°F (37.8°C), influenza or pneumonia should be suspected. Sputum production, including purulent sputum, is normal and unrelated to bacterial infections.[11]

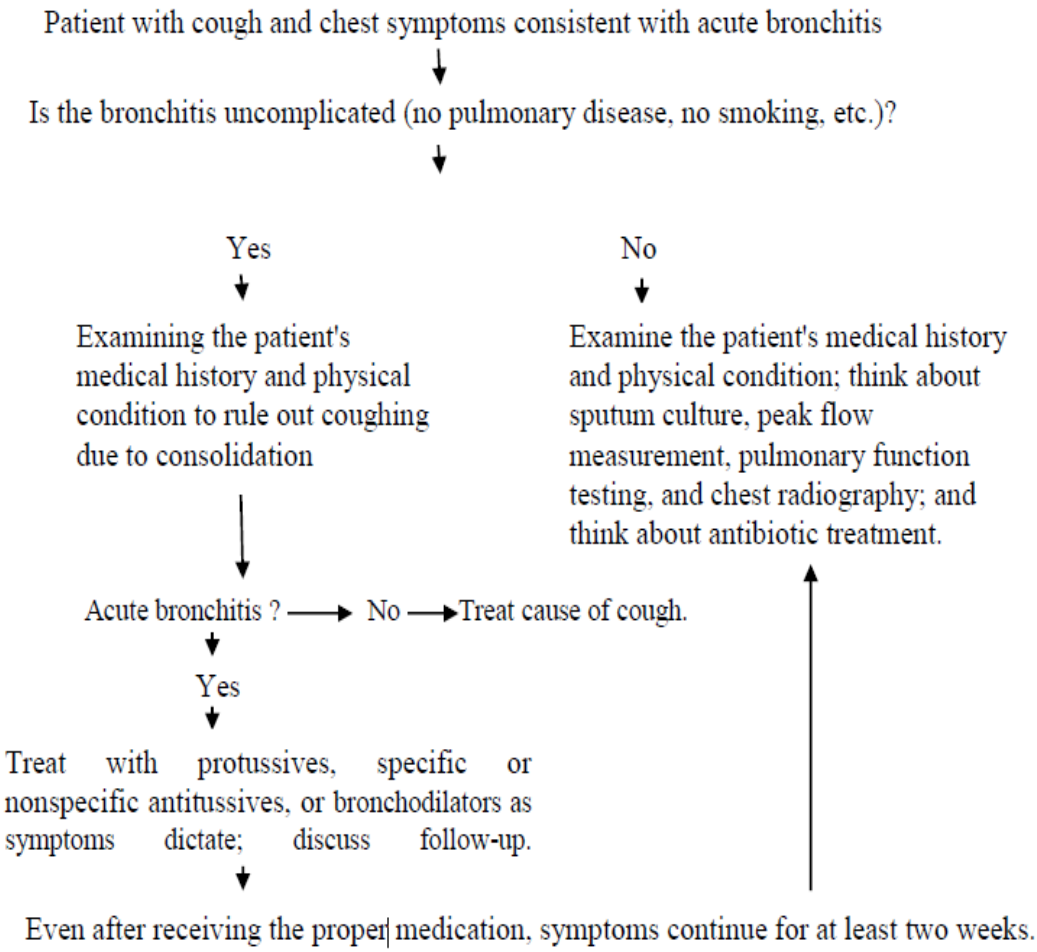

Figure 1: An algorithm for treating individuals suffering from acute bronchitis.[12]

2.2 *Chronic Bronchitis*

In chronic obstructive pulmonary disease (COPD), chronic bronchitis (CB) is a common but variable symptom. The cause of CB is goblet cells' overproduction and hypersecretion of mucus, which exacerbates airflow obstruction by obstructing small airways with luminal blockage, altering airway surface tension, and causing epithelial remodeling that makes the airway more prone to collapse. It has many clinical repercussions, such as a faster deterioration of lung function, an increased risk of airflow obstruction in smokers, a reduced risk of respiratory tract infections, a higher frequency of exacerbations, and a lower overall death rate. Goblet cells' overproduction and hypersecretion of mucus causes CB by causing luminal blockage of small airways, epithelial remodeling, and changes in airway surface tension that make the airways more prone to collapse.[13]

Chronic bronchitis, a type of chronic obstructive pulmonary disease (COPD) characterized by inflammation and irritation of the bronchial tubes, is one of the primary causes of the disease's global burden. This condition produces a persistent cough and the creation of

mucus. Patients with COPD may also experience dyspnea, wheezing, chest tightness, fatigue, activity limitation, coughing with or without sputum production, and acute respiratory events, which are characterized by a sudden worsening of respiratory symptoms known as exacerbations that require specific preventive and therapeutic measures.[14]

Chronic inflammation and remodeling of the airways are part of the pathophysiology of chronic bronchitis, which limits airflow and causes symptoms like coughing, sputum production, and dyspnea. This inflammation is often brought on by exposure to toxic chemicals, such as those found in cigarette smoke, air pollution, and industry. A major contributor to illness and death is chronic obstructive pulmonary disease (COPD). Studies on the global burden of sickness show that COPD ranks as the third most common cause of death in both the US and the world. In order to rule out other conditions that can cause similar symptoms and signs, chest radiography is typically done as part of the initial diagnostic evaluation when a patient has suspected COPD. COPD is associated with radiographic abnormalities such as hyperinflation of the lungs and hyperlucent areas with peripheral trimming of vascular patterns. For a stable patient with COPD, standard follow-up does not include chest radiography. Computed tomography (CT) can be used to determine the extent and distribution of emphysema and to identify thickening of the bronchial wall and gas trapping.[15]

The ongoing inflammation causes the airways to clog with too much mucus, making breathing challenging. Among the several factors that contribute to COPD are environmental risk factors and genetic predisposition. Cigarette smoking is a significant risk factor, which includes firsthand smoking, secondhand smoke exposure, and maternal smoking.

Other risk factors include genetics, air pollution, biomass exposure, occupational exposure, and past illnesses (e.g., childhood TB, childhood respiratory infections, and asthma). The risk of osteoporosis may be increased by a variety of characteristics that individuals with COPD may have.

For example, long-term corticosteroid usage by COPD patients can lead to bone loss, increasing the risk of osteoporosis; persistent lung and airway inflammation can promote bone resorption and prevent bone formation; and physical inactivity caused by breathing difficulties can diminish bone mineral density. Patients with COPD had a high prevalence of osteoporosis and a significant risk of fracture, according to a systematic literature review

(SLR), They also identified other prevalent risk factors, such as smoking cigarettes, not exercising, losing weight, and risk factors unique to a given disease.[16]

With an estimated 64 million cases of chronic bronchitis worldwide, COPD is a serious public health concernEven though disease is preventable and incurable once it has been established, effective self-management approaches can improve quality of life and lessen its burden. The prevalence, mortality, and disability adjusted life years (DALYs) of COPD, along with the risk factors that influence these outcomes, were reported for 204 countries and territories between 1990 and 2019 by the Global Burden of Disease 2019 research. Counts and rates per 100,000 population were given for each estimate, along with 95% CIs. The biggest risk factor for COPD-related mortality was smoking, and there was a negative correlation between the sociodemographic index and the burden of COPD.

COPD data has been provided by several major international consortia. For instance, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) initiative was established in 1998 and provides regular updates and evidence-based recommendations for the management of COPD. The European Community Respiratory Health Survey was established in 1990 in response to the increase in asthma incidence in the 1980s in order to determine the prevalence of asthma and the related healthcare burden on the continent.[17]

Due to increased exposure to both indoor and outdoor air pollution, the disease is more common in low- and middle-income nations. According to estimates, COPD costs the US economy more than $50 billion a year in lost productivity and medical expenses. The burden of COPD remains high for patients, their caregivers, and the healthcare system. In the United States, it ranks ninth in terms of disability-adjusted life years and fourth in terms of mortality. When the spirometer and timed measurement of forceful exhalation of expired air were developed, the diagnosis of this condition underwent a modification.

We propose adding exposure, spirometric data, image-based assessment of structural abnormalities, and the entire spectrum of symptoms to the criteria for diagnosing COPD. Participants were characterized by chest CT scans, spirometry (preceding and following inhalation of a bronchodilator), and patient-reported respiratory symptoms. The four characteristics of COPD that we examined were exposure, respiratory symptoms, spirometric evidence of impairment, and structural lung abnormalities as quantified by chest CT.[18]

A combination of imaging tests, spirometry, and clinical symptoms are usually used to diagnose chronic bronchitis. While computed tomography (CT) scans and chest radiography can assist in detecting emphysema and other lung problems, spirometry is utilized to evaluate airflow limitation.[14]

Chronic bronchitis is diagnosed when a patient has had a persistent cough and sputum production for at least three months during two years in a row. Among its many clinical repercussions are a faster deterioration of lung function, an increased risk of airflow obstruction in smokers, a tendency to lower respiratory tract infections, a higher frequency of exacerbations, and a lower overall death rate.

The pathophysiological basis for CB is mucous metaplasia, a process wherein mucus is overproduced in response to inflammatory signals. It has many clinical repercussions, such as a faster deterioration of lung function, an increased risk of airflow obstruction in smokers, a reduced risk of respiratory tract infections, a higher frequency of exacerbations, and a lower overall death rate .However, in the last few years, the importance of CB as a characteristic to identify patients who respond well to treatment has been better understood.[19]

The goals of treating chronic bronchitis are to lessen symptoms, enhance quality of life, and delay the course of the illness. This usually combines non-pharmacological treatments like quitting smoking and lung rehabilitation with pharmaceutical treatments like bronchodilators and inhaled corticosteroids. In individuals with chronic bronchitis, pulmonary rehabilitation has been demonstrated to increase exercise tolerance, lessen symptoms, and improve quality of life. The goal of pulmonary rehabilitation is to improve the physical and mental health of individuals with chronic respiratory diseases and to encourage long-term adherence to health-enhancing behaviors. It is a comprehensive intervention that begins with a thorough patient assessment and is followed by patient-tailored therapies, such as exercise training, education, and behavior modification.[20],[21]

Feature	Acute Bronchitis	Chronic Bronchitis
Duration	Days to weeks	≥3 months/year, ≥2 years
Cause	Usually viral infection	Smoking, pollution, fumes
Symptoms	Cough (± mucus), fever	Persistent cough with mucus
Prognosis	Self-limited	Progressive, no cure
Association	Often after cold/flu	COPD, long-term exposure

3. BACKGROUND

For two consecutive years, adults with chronic bronchitis have had a chronic cough that produces sputum for at least three months of the year. The hyperplasia of goblet cells causes an overabundance of mucus. This results in airway inflammation, structural alterations, and blockage when paired with decreased mucus clearance. Chronic bacterial infection of the airways causes persistent neutrophilic airway inflammation, which is the hallmark of chronic bronchitis in children.[22]

An isolated persistent wet cough that lasts more than four weeks, resolves after two weeks of proper antibiotic treatment, and has no evidence of an other etiology are the hallmarks of prolonged bacterial bronchitis (PBB). Childhood chronic bronchitis can last into adulthood, and as it can proceed to bronchiectasis, asthma, and lung function impairment, it is crucial to manage it properly. Furthermore, research shows that young adults aged 18 to 30 who have a persistent productive cough are more likely to experience cardiovascular events in the future and die young, most likely as a result of systemic inflammation.[23]

Airflow blockage, rapid lung function decrease, exacerbations of COPD, and higher lung disease- related and all-cause mortality are risk factors for individuals with isolated chronic bronchitis. Adults who smoke have a definite causal relationship with chronic bronchitis; however, smoking is not associated with many cases of chronic bronchitis, indicating alternative risk factors. For those who have never smoked, there are a number of well-known underlying causes of chronic bronchitis, such as exposure to burning biomass fuel, hard-rock mining, tunnel building, concrete manufacturing, non-mining industrial vocations, and livestock farming.[24]

Treating chronic bronchitis primarily aims to reduce inflammation, improve mucus clearance, reduce mucus production, and encourage effective coughing mechanisms. It is necessary to stop smoking and stay away from secondhand smoke in order to improve respiratory health and lessen airway damage. For at least two weeks, children with PBB require antibiotics; dosages are adjusted based on the specifics of the guidelines and the symptom's resolution.[25]

Overall mortality and long-term lung function are significantly impacted by PBB and chronic bronchitis. For proactive management of these illnesses, healthcare practitioners should employ a comprehensive combination of pharmacological and non-pharmacologic treatments. The primary cause of chronic bronchitis, which is caused by prolonged exposure

to lung-damaging irritants, is smoking. Current smokers have a cumulative incidence of 42% during the past 30 years. However, between 4 percent and 22 percent of individuals with chronic bronchitis have never smoked, indicating that there may be additional factors at work.[26]

A common reason of persistent coughing is chronic bronchitis. However, research on chronic cough only reveals a 5% or less prevalence of chronic bronchitis, and many smokers choose not to get treatment for their cough. On average, 27% to 35% of patients with COPD have chronic bronchitis, whereas 3% to 22% of people globally have it. In the United States, around 10 million people are impacted, with the majority falling between the ages of 44 and 65. Interestingly, 31% of those affected are between the ages of 18 and 44.[27]

Adults with asthma, obstructive sleep apnea, smoking, being older, having more severe COPD, being female, and not being Black or White are more likely to develop chronic bronchitis.[28]

PBB is the most common cause of wet cough in children under five and is responsible for about 40% of pediatric pulmonology referrals. With a median age of 1.8 to 4.8, PBB is most common in male toddlers ages 2 and under, while it can also afflict teenagers over the age of 12. Daycare attendance, a history of persistent coughing, wheezing reported by parents within the previous 12 months, crowded housing, and homelessness are risk factors for PBB.[29]

Adults who are exposed to cigarette smoke, repeated or chronic bacterial and viral infections, or hazardous environmental exposures can develop chronic bronchitis. Mucin is also released by humoral and inflammatory mediators to protect the airway from damaging stimuli. Moreover, inflammatory cells that activate the epidermal growth factor receptor (EGFR) cause the mucin gene to start transcription. A surplus of mucus is generated and secreted as a result of neutrophil- mediated elastase's increased activation and degranulation of neutrophils. EGFR receptor expression and activation are the main causes of mucus hypersecretion, with activated neutrophil involvement being a key factor.[30]

Early attacks like viral infections or bacterial pneumonia impair the lung's defenses in youngsters, leading to increased mucus production, reduced mucociliary clearance, and bacterial overgrowth, usually in the form of a biofilm. The extracellular polymeric matrix that covers the microbes on the surface of a biofilm increases bacterial persistence and protects

the germs from antibiotics, necessitating long-term antibiotic treatment. Environmental and genetic factors are significant, as are the impacts on the mother and the kid. For instance, smoking or being around air pollution exacerbates mucosal dysfunction and airway inflammation, which promotes the growth of bacteria.[31]

4. DIAGNOSIS AND TREATMENT

Supportive therapy and symptomatic treatment are the mainstays of care for acute bronchitis, which usually resolves on its own. Coughing can be cured using both nonpharmacological and pharmaceutical methods. Examples of nonpharmacological treatments include ginger, honey, hot tea, and throat lozenges. Interestingly, the effectiveness of these treatments has not been assessed by clinical trials. Due to their efficacy in treating the symptoms of chronic bronchitis and results from research on cough associated with the common cold, antitussive medications such as dextromethorphan (with or without codeine) are frequently used in clinical practice to suppress cough. The effectiveness of antitussive medications in treating acute bronchitis is not particularly evaluated by randomized studies. Because codeine can become addictive, it is not recommended to use it.[32]

The available research on the efficacy of mucolytic medications in treating acute bronchitis is conflicting, and there is not enough consensus on this topic. The utility of these medications to treat acute bronchitis is therefore still being studied and discussed. Beta-agonists are a frequent treatment for wheezing patients with acute bronchitis. However, there have been limited randomized control trials that have produced mixed results regarding the efficacy of beta-agonists for coughing in cases of acute bronchitis. Despite a slight impact in a subgroup of patients with wheezing and airflow obstruction at baseline, a Cochrane review comprising five studies found that beta-agonists did not significantly reduce daily cough. Similar results were found in a more recent Cochrane review.[33]

Fever, myalgia, and malaise are among the associated symptoms that analgesics and antipyretics can help manage. Steroids like prednisone can also be used to treat inflammation. Although their effectiveness in treating acute bronchitis is not well established, they may be helpful for patients who simultaneously have asthma or chronic obstructive pulmonary disease (COPD). As a short- term burst therapy, steroids are most frequently used. In some situations, a lengthy tapering course of steroids could be necessary, particularly for people who have underlying COPD or asthma.[34],[35]

ACCP recommendations recommend against the use of antibiotics for uncomplicated acute bronchitis in otherwise healthy adults. In a comprehensive Cochrane review of nine randomized, controlled trials of antibacterial medications, the average length of coughing was only slightly reduced (0.6 days); the overall duration of illness did not considerably decrease.[36]

Oseltamivir and zanamivir have been shown to have slight benefits in reducing the typical length of influenza symptoms in adults by half a day" As a preventative measure, these medications also effectively reduce the risk of experiencing influenza symptoms. The evidence supporting these medications' capacity to lower the risk of pneumonia or hospitalization is, however, scant. Furthermore, neuraminidase inhibitors are not sufficiently supported by evidence to prevent influenza from spreading from person to person, according to a Cochrane review.

Pneumonia and other influenza-related consequences cannot be reduced by therapeutic trials because of ambiguous diagnosis criteria. Adults who use oseltamivir are more likely to experience negative side effects, including nausea, vomiting, mental side effects, and renal problems. The benefits and drawbacks of using neuraminidase inhibitors for therapy or prevention must thus be carefully considered before making decisions.[37]

Reducing excessive mucus production, reducing inflammation to minimize mucus hypersecretion, improving ciliary transport for improved mucus clearance, lowering mucus viscosity, and supporting efficient cough mechanisms are the main goals of treating chronic bronchitis. Because chronic bronchitis, PBB, long-term respiratory health, and overall mortality are all linked, effective therapy is essential. Reducing exposure to dangerous environmental factors and quitting smoking are the cornerstones of treating chronic bronchitis. Goblet cell hyperplasia, airway damage, and mucociliary function are all greatly improved by quitting smoking and avoiding secondhand smoke.[38]

According to a 30-year longitudinal research, the cumulative incidence of chronic bronchitis is 26% among ex-smokers, 42% among current smokers, and 22% among non-smokers.[39]

Mucolytics that decrease mucus overproduction and improve its clearance, such as N-acetylcysteine, carbocysteine, and erdosteine, are the subject of conflicting guidelines and viewpoints. For the treatment of persistent cough in patients with stable chronic bronchitis,

the American Academy of Chest Physicians recommends against the use of mucolytics, bronchodilators, or antibiotics. Additionally, nonpharmacologic treatments like positive end-expiratory pressure are not advised by them.[40]

However, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) suggest that mucolytics may reduce the incidence of exacerbations by around one episode every three years.

For a little decrease in acute exacerbations and an enhancement in quality of life, GOLD recommends their regular use.[41]

Short-acting bronchodilators, such as albuterol, are the cornerstone of treatment for acute exacerbations. They are administered via a nebulizer or metered dosage inhaler (MDI) every 20 minutes for two to three doses, and then every two to four hours as required. Those with severe COPD or those who have difficulty utilizing MDI may find greater relief from the nebulized form, even though both are equally effective. If required, clinicians might mix albuterol with ipratropium bromide, an anticholinergic bronchodilator.

Because of its delayed start of effect, ipratropium, which is dosed every 4 to 6 hours, is rarely administered by itself during an acute exacerbation. Patients with moderate to severe symptoms should also receive systemic steroids equivalent to 40 mg of prednisone daily for five days.

If a patient has three of the following cardinal symptoms—increased dyspnea, sputum volume, and sputum purulence—an acute exacerbation calls for antibiotics.[42]

Antibiotic therapy

Antibiotic selection is influenced by patient risk factors, local resistance patterns, and the likelihood of a persistent Pseudomonas infection. For each of these elements, the following suggestions must to be taken into account:[43]

Patients at average risk: Doctors may recommend a macrolide or a second- or third-generation cephalosporin, like cefuroxime or cefpodoxime, for patients who do not have risk factors for poor outcomes or Pseudomonas colonization.

High-risk patients: Patients with the following characteristics should be treated with either

amoxicillin-clavulanic acid or a respiratory quinolone such as levofloxacin or moxifloxacin.

- At least 65 years of age
- Two or more exacerbations of COPD during the past 12 months
- One or more hospitalizations for COPD during the past 12 months
- FEV1 <50% anticipated
- Concomitant disorders such as ischemic heart disease or heart failure
- Ongoing additional oxygen.[44][45]

Other management considerations

For patients with severe COPD and chronic bronchitis who have previously had exacerbations, phosphodiesterase-4 (PDE-4) inhibitors, like roflumilast, can reduce exacerbations by reducing inflammation and promoting the relaxation of the smooth muscles in the airways. They stop cyclic adenosine monophosphate from hydrolyzing, which releases inflammatory mediators as it breaks down. According to GOLD guidelines, physicians should think about prescribing roflumilast to patients with chronic bronchitis and COPD who have experienced at least one hospitalization for an exacerbation in the last 12 months and whose forced expiratory volume is one second below 50% expected.[46]

An essential part of treating chronic bronchitis is pulmonary rehabilitation for at least six weeks. Successful pulmonary rehabilitation requires at least twice-weekly supervised exercise instruction, self-management education, and psychosocial support. In individuals who experience repeated exacerbations, pulmonary rehabilitation lowers hospitalization rates while improving exercise tolerance, dyspnea, and general health. Additionally, patients who receive pulmonary rehabilitation report feeling less anxious and depressed. For many patients, access and cost are obstacles to pulmonary rehabilitation participation.[47]

Vaccine Recommendations

Current recommendations prescribe the 21-valent pneumococcal conjugate (PCV21), 20-valent PCV20, or 15-valent PCV15 followed by 23-valent pneumococcal polysaccharide vaccine (PPSV23) for all persons with chronic lung disease who are 19 years of age or older. Patients should also receive an annual influenza vaccination. For adults, PCV21 is the recommended formulation, with the exception of those who are particularly vulnerable to serotype 4. PCV20 is the recommended vaccine for Navajo Nation members, those with substance use disorders, and homeless people in the Western United States and Canada. It provides serotype 4 coverage. At least a year after receiving PPSV23, those who previously

only received PPV10, PPV13, or PPSV23 should obtain PPV21 or PPV20. Healthcare professionals can access the most recent pneumococcal vaccination guidelines, including suggestions for revaccination, on the US Centers for Disease Control website.[48]

- The Covid-19 vaccination ought to be given.
- The recommended adult schedule should be followed for administering the tetanus, diphtheria, and pertussis vaccine (Tdap).
- The respiratory syncytial virus vaccination should be administered to people over 60 or those who have long-term heart or lung conditions.
- The herpes zoster vaccination should be administered to COPD patients 50 years of age and older.[49]

5. ANTIBIOTIC RESISTANCE

The most significant known contributing factor to the emergency of antibiotic resistance is a doctor's inappropriate prescription of antibiotics. Antibiotic resistance is defined as the resistance of microorganisms to antimicrobial agents that develops when bacteria adapt to protect themselves from antibiotics. When prescribing antibiotics, there are several critical aspects to take into account. The prescriber may be impacted by a number of factors, such as patient requests and self- prescriptions, overprescription of antibiotics, incorrect dosage or administration technique, anxiousness, and ignorance. But the most important known issue is that doctors are prescribing antibiotics incorrectly.[50]

Respiratory tract infections (RTIs) are being made worse by antibiotic resistance in both Gram- positive and grain-negative bacteria, and it is becoming increasingly difficult to treat emerging bacterial, viral, and fungal respiratory diseases. Increased international cooperation is desperately needed to fight multidrug-resistant bacteria and other new microbial dangers, as seen by the rising incidence of antibiotic resistance and the lack of effective therapies. Streptococcus pneumoniae that is resistant to three or more antibiotics was first identified in 1977 in South Africa93 and has since spread to many other nations. The United States and Spain have alarmingly high rates of 30–50% multidrug resistant S pneumoniae.[51]

An analysis of more than eight million patient data from 587 general practices in the UK revealed that about 19% of oral antibiotic prescriptions were for lower respiratory tract infections (LRTIs) and 31% were for URTIs.[52]

The first antibiotic, salvarsan, was created in 1910, and Alexander Fleming found

penicillin in 1928. Many antibiotics have since been developed, but after the "antibiotic era" of roughly a century, fewer new drugs are being developed, and serious antibiotic resistance has developed.[53] One of the biggest risks to human growth, food security, and world health today, according to the World Health Organization, is the overuse of antibiotics and the ensuing antimicrobial resistance (AMR).[54]

In clinical medicine, respiratory tract infections are among the most common and diverse forms of infections, and they have long been a major cause of morbidity. Pseudomonas aeruginosa, Streptococcus pneumoniae, Moraxella catarrhalis, and Hemophilus influenzae are some of the bacteria that cause respiratory tract infections. It has only recently been apparent how serious influenza virus infections may be for kids. At first, this acknowledgment was reliant on general results, including a rise in acute respiratory hospitalizations throughout the winter.[55]

For respiratory infections, especially acute bacterial sinusitis in adults and acute bacterial otitis in children, over 60% of all outpatient antibiotics are used. Antimicrobial resistance is a rising public health issue that is closely related to the use of antibiotics.[56]

It was found that LRTI patients had both gram-positive (like streptococcus pneumonia and staphylococcus aureus) and gram-negative (like Pseudomonas species, E. coli, and Klebsiella species) bacteria. The international medical and research community now views the threat of antibiotic resistance posed by bacteria against antibiotics as a significant one. Consequently, doctors and microbiologists worldwide are focusing on knowledge and strategies to stop antibiotic resistance from developing. Current knowledge of bacterial etiology and microbial susceptibility may enhance therapeutic results, reduce unnecessary antibiotic use, and slow the emergence of resistance.[57]

Acute bacterial sinusitis, the sixth most common diagnosis for which antibiotics are advised, is primarily caused by S. pneumoniae and H. influenzae. This condition is brought on by chronic obstructive pulmonary disease. The problem is made worse by rising antibiotic use, inadequate resistance, and a disregard for common safety measures in hospital environments. Patients receiving critical care may develop respiratory failure as a result of respiratory infections like pneumonia. Antibiotic awareness or resistance makes the use of local antibiograms as one technique to offer empirical antibiotic recommendations necessary.[58]

Haemophilus influenzae, Moraxella catarrhalis, and Streptococcus pneumoniae are the three main bacterial respiratory pathogens. Around the world, antibiotic resistance is spreading. Many national, regional, and international surveillance systems have been established in response to the necessity of keeping an eye on the growth of such resistance. But according to statistics from surveillance studies, susceptibility rates differ greatly over time and between geographical areas. Depending on the antibiotic pressure in a given area, the antibiotic resistance and frequent bacterial patterns may differ from one place to another. Therefore, it is crucial to have local resistance prevalence data to inform empirical prescribing and pinpoint regions with a higher medical need for novel medications.[59][60][61]

Antibiotic Class	**Resistance Mechanism**	**Reason for Resistance**
β-lactams (e.g., penicillin)	Enzymatic degradation (β-lactamases)	Bacteria produce enzymes that inactivate the drug
Macrolides (e.g., erythromycin)	Target modification	Mutation or gene acquisition
	(methylation of rRNA)	alters drug target
Tetracyclines	Efflux pumps, ribosome protection	Bacteria pump out drug or protect ribosome
Aminoglycosides	Enzymatic modification	Bacteria chemically modify the antibiotic Overuse in hospitals
Fluoroquinolones	Mutations in DNA gyrase/topoisomerase - Efflux pumps	Increased clinical use – Stepwise chromosomal mutations

6. DATA ANALYSIS

Summary of cases of LRTI along with risk factors, therapy given, intervention to ADRs and their outcomes.

S. No.	Ref. No.	Case of LRTI	condition	Risk factor	Gender		Age	Thearpy	ADRs	Interventions	Outcomes
					male	female	years				
1.	[62]	Congenital Pulmonary airway malformati-on (CPAM)	1)Right sided chest pain, fever and cough for around 12 days 2)Tach-ycardia 110-150 bpm, blood pressur- e 89/53, respira- tory rates 18 and oxygen saturat-	Smokin-g and drugs consum- ption	1	0	25	Admitted to the intensive care unit with the diagnosis of infected CPAM with suspected right lower lobe abscess and sepsis and was started on broad spectrum intravenous antibiotics, including vancomyci-n, piperacillin tazobactum	1) Com- plete blood count show- ed white cell count of 36.7k /mm3 2)Red man synd- rome as a side effect from vanco mycin	1)Antibi o-tics were deescal-ated to vanco-mycin alone . 2)Swit- ched the patient to IVclin-damyci- n with plans to dischar- ge him On oral clinda-mycin for 6 weeks	1)White cell count dropped to 26.7k/m m3 2)unfor-tunately the patient missed his next appoint-ment despite our attempt to contact him,so the follow-Up CT

2.	[63]	LRTI	ion >94% on room air 1)Patient was diagnos ed as SJS and later develop ed an acute ST-segmen -t elevate- on MI (STE- MI)		1	0	34	and levofloxac- in to cover and double cover and pseudomo- nas 1)He was prescribed tablet moxifloxa- cin	1)M- oxifl- oxac- in caus- es rash- es aggr- esiv- ely worse -nded to ooze, painf- ul reddis h eyes	1)Patie- nt was first given loading dose of oral aspirin and clopido- grel, anticoa- gulant and started on anti- ischem- ic medica- tions.	scan of the chest was not perfor- med 1)Later, transth- oracic echoca- rdiogra- m showed fair left ventric- ular systolic function with estimate -ed ejection fraction. 2) Postang ioplasty, patient remaine d

											stable and asympt omatic and mucocu taneous lesions improve
									and oral lesion, coug -h with sputu m, crack ed lips and lethargy.	2)He was immediately posted for coronary angiogram (CAG) For primary percuta neous coronary intervention (PP CI)	d signific antly .

7. FUTURE PROSPECTION

Clinical and Epidemiological Difficulties

Antimicrobial resistance is a developing problem, and lower respiratory tract infections (LRTIs) continue to be a major source of morbidity and mortality globally, especially in low- and middle- income countries (LMICs), where the burden is greatest.[64]

Future management techniques must address the dual challenges of identifying bacterial and viral LRTIs and minimizing the use of inappropriate antibiotics.[65]

New Methods of Diagnosis

Rapid Molecular Diagnostics: Improvements in multiplex PCR and other molecular techniques have significantly accelerated and improved the accuracy of LRTI diagnosis, making it possible to distinguish between bacterial and viral illnesses more clearly.[66]

Point-of-Care (POC) Testing: In settings with limited resources, the incorporation of POC pathogen and biomarker tests into clinical workflows promises quicker, more focused treatment decisions.[65]

eCDSTs, or electronic clinical decision support tools: In order to reduce the needless use of antibiotics and improve outcomes, future management may rely on eCDSTs, which integrate real- time surveillance data, machine learning algorithms, and patient-level predictors to guide diagnosis and therapy.[65]

Innovations in Therapeutics

Antibiotic Stewardship: To counteract resistance, judicious antibiotic usage is highly valued. For severe instances, this entails combining combination medicines and customizing treatment depending on local resistance patterns.[65]

Innovative Drug Delivery Systems: Antibiotic-loaded inhalable liposomal nanoparticles are being created to improve drug delivery straight to the lungs, possibly increasing effectiveness and lowering systemic side effects.[66]

Nebulized Antibiotics: Nebulized antibiotics are being researched for their potential to offer high local drug concentrations with fewer systemic effects, especially for gram-negative infections.[67]

Investigations and Preventive Measures

Mechanistic Research: In order to identify novel therapeutic targets and drugs, future studies will concentrate on comprehending the fundamental mechanics of severe LRTIs.

Pulmonary Rehabilitation: In the treatment of severe LRTIs, rehabilitation techniques meant to enhance lung function after infection are probably going to become increasingly common.[68] **Immunization and Public Health Measures:** Reducing the incidence and severity of LRTIs will require a sustained focus on vaccination (such as influenza and pneumococcal) and effective infection control.[64]

Figure 2: Key Future Directions in Lrti.

Area	Future Prospect
Diagnostics	POC testing, quick molecular testing, and AI/ML-powered eCDSTs
Treatment	Nebulized medicines, inhaled nanoparticles, and sensible antibiotic use
Research	Drug development, pulmonary rehabilitation, and mechanistic research
Public Health	Improved immunization, infection prevention, and monitoring

8. CONCLUSION

CPAM, formerly known as congenital cystic adenomatoid malformation (CCAM), is a rare congenital defect that appears in 0.004% of pregnancies and makes up around 25% of all congenital pulmonary malformations. We don't fully understand its genesis.

It is distinguished by localized glandular proliferation and a lack of bronchial development. There is no obvious genetic correlation, and its incidence seems to be the same for both genders and races. Although prenatal ultrasound is usually used to diagnose it, the literature also reports that it is rarely diagnosed in children and even less frequently in adults.

The radiological and histological appearance of adult-diagnosed CPAM may change as a result of persistent inflammation brought on by recurring infections. Malignant transformation is also believed to be triggered by this ongoing inflammatory process. This is a more prevalent sign of type I disease and is specifically linked to adenocarcinoma and bronchoalveolar carcinoma.

We introduced a type III CPAM in this instance, which is a rare kind of CPAM. Being asymptomatic till adulthood is quite rare in this type. When our patient first appeared at age 25, he had never received a lung infection diagnosis. Patients with solid organs are more likely to experience infection, cardiovascular issues, drug combinations, and toxicities, which can

make post-transplant care more difficult. Drugs that inhibit the immune system increase the risk of infection.

Lipid-lowering drugs, beta-blockers, amiodarone, cyclosporin, azathioprine, and other transplant- related drugs have also been linked to lung disease. Given that our second patient had been using amiodarone for a considerable amount of time, the fact that all of our patients had been exposed to at least one of the drugs described above rules out a causal link between sirolimus and interstitial pneumonia. However, there appears to be no alternative explanation given how quickly the symptoms of all three patients disappeared after ceasing sirolimus, especially but not only with steroid therapy.

The drug-interaction disease known as SJS causes epidermal detachment in less than 10% of the body's surface. TEN is the term for lesions that affect more than 30% of the skin's surface area, whereas 10% to 30% of lesions are thought to overlap the two disorders. Other than borderline hypocholesteremia, our patient had only one thrombotic lesion in his coronary arteries and no other cardiovascular risk factors or metabolic abnormalities, indicating that reactive thrombocytosis was the underlying pathophysiology of MI. According to estimates, SJS has a death risk of 1% to 3% since it results in long-term organ damage problems. Mild paralytic ileus to potentially fatal respiratory failure brought on by significant pulmonary oedema are among them. Furthermore, the illness is often associated with ocular abnormalities, while liver, renal, and pancreatic problems have been documented infrequently.

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