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Review

Recurrent Lower Respiratory Tract Infections in Children: A Practical Approach to Diagnosis

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SUMMARY

Many children are affected by recurrent lower respiratory tract infections (LRTIs), but the majority of them do not suffer from serious lung or extrapulmonary disease. The challenge for clinicians is to distinguish the recurrent RTIs with self-limiting or minor problems from those with underlying disease. The aim of this review is to describe a practical approach to children with recurrent LRTIs that limits unnecessary, expensive and time-consuming investigations. The children can be divided into three groups on the basis of their personal and family history and clinical findings: 1) otherwise healthy children who do not need further investigations; 2) those with risk factors for respiratory infections for whom a wait-and-see approach can be recommended; and 3) those in whom further investigations are mandatory. However, regardless of the origin of the recurrent LRTIs, it is important to remember that prevention by means of vaccines against respiratory pathogens (i.e. type b *Haemophilus influenzae*, pertussis, pneumococcal and influenza vaccines) can play a key role.

INTRODUCTION

Respiratory tract infections are common in young children. Most of them are viral upper respiratory tract infections (URTIs) that are self-limiting, and epidemiological studies indicate that up to seven episodes/year in the first three years of life and up to five episodes/year after the age of three years can be considered normal.[1] By the age of 6 years, approximately 60% of children have had at least one URTI and should not require in-depth investigation.[2] Lower respiratory tract infections (LRTIs), including bronchitis, bronchiolitis and pneumonia, are less common and affect approximately 6% of infants during the first two years of life.[3]However, there is no clear definition of what recurrent "LRTI" actually means. Wald defines recurrent pneumonia as two episodes of pneumonia in one year or three episodes during any time frame, with intercritical radiographic normality;[4] other authors use the same term when more than one LRTI occurs.[5] Which definition of recurrent LRTIs is used could obviously affect the incidence and this is in an area where the available published data are already limited. A recent population-based birth cohort of 900 Dutch children prospectively followed up from birth to the age of four years included 55 (6%) who experienced ≥3 respiratory tract infections (RTIs)/year (from otitis to bronchitis and pneumonia) and 715 (79%) who experienced ≥1/year.[6] The Isle of Wight birth cohort study (1989–1990) of 1,336 children followed up until they were 10 years old found that the prevalence of repeated (two or more) LRTIs in infancy was 7.4%,[7] and retrospective cohort studies (1999–2001) of children in Germany aged 5–7 years old (28,000–30,000 cases) found 6.7–8.2% of the children had a positive history of community-acquired pneumonia (CAP), 6.9–8.2% of whom had recurrent CAP.[8] Finally, data from Toronto's Hospital for Sick Children showed that 10% of more than 2,900 children admitted because of CAP had experienced two or more previous LRTIs.[9] Attending an Emergency Room (ER) because of acute respiratory tract infection has become quite common in Italy over recent years.[10] In 2010, 1,264 children with bronchitis, bronchiolitis or pneumonia were admitted to our pediatric ER and 232 (18%) had experienced at least one other episode of LRTI during their lives.[10]Given the number of children affected by recurrent LRTIs, it is clear that most of them do not suffer from serious lung or extra-pulmonary disease. The challenge for the clinician is to distinguish the children with self-limiting or minor problems and those with underlying disease. The aim of this review is to describe a practical approach to children with recurrent LRTIs with the aim of limiting unnecessary, expensive and time-consuming investigations. Three groups of children are considered on the basis of their personal and family history and clinical findings: 1) otherwise healthy children who do not need further investigations; 2) those with risk factors for respiratory infections for whom a wait-and-see approach can be recommended; and 3) those in whom further investigations are mandatory.

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OTHERWISE HEALTHY CHILDREN WHO DO NOT NEED FURTHER INVESTIGATIONS

Most healthy children are at risk of LRTIs: this is particularly true of those aged 2-4 years,[3,10,11] as the incidence physiologically decreases during school age. The infections are typically seasonal, with a higher incidence in autumn and winter when children, especially those belonging to large families,are exposed to a large number of viruses at home and in daycare centres or nursery schools. Moreover, when children first attend a daycare centre, there may be a substantial increase in the number of LRTIs, which may become recurrent. However, these children have relatively long periods of clinical well-being (at least in the summer), and most of the infections are viral and self-limiting.[12] They do not have a history of risk factors for recurrent RTIs and they experience normal growth and development, show normal physical examination results, respond quickly to appropriate treatment, recover completely, and are healthy between infections. They therefore do not require any specific investigation.

CHILDREN WITH RISK FACTORS FOR RESPIRATORY INFECTIONS FOR WHOM A WAIT-AND-SEE APPROACH CAN BE RECOMMENDED

Table 1 shows the clinical and enviromental factors associated with an increased frequency of LRTIs. The mechanisms underlying the occurrence of LRTIs vary with the risk factor, but in presence of these risk factors the infections may appear earlier and be more severe than those observed in children without risk factors, and they may require hospitalisation. LRTIs mainly originate from a viral infection or bacterial colonization involving the upper respiratory tract and occur during most of the year, although there is usually an improvement in the warmer seasons and, more generally, with growth.[5] The recommendation in such cases is to eliminate avoidable risk factors and adopt a wait-and-see approach.

Prematurity

During the first years of life, premature children (particularly those with bronchopulmonary dysplasia) experience greater respiratory morbidity and are hospitalised more frequently than children born at term.[13] The most common causes of re-hospitalisation in this population are LRTIs with respiratory distress,[14] which have been attributed to inadequate immunity due to lower levels of maternal antibodies and pre-existing poorer lung function. More recently, it has been reported that neonatal hyperoxia might affect the response to respiratory pathogens, thus altering the innate immunoregulatory response of the lungs and contributing to viral vulnerability.[15]

Respiratory morbidity improves over time, especially in the children whose neonatal course was less severe. However, a recent population-based case-control study found that adults aged 18–27 years who had had a lower weight at birth were 83% more likely to be hospitalised because of asthma, respiratory infections and respiratory failure than young adults with a normal birth weight.[16]

Table 1
Conditions associated with an increased risk of recurrent LRTIs.

Condition
Prematurity
Atopy
Passive smoking
Indoor pollution
Outdoor pollution
Congenital abnormalities of the respiratory tract
Cardiovascular diseases
Chronic neurological diseases

Atopy

Atopy is another risk factor for recurrent RTIs involving both the upper and lower airways. Various studies have shown that allergic children have more and longer-lasting RTIs than those without allergies.[17] Allergic mucosal inflammation may predispose to upper airway infections as it induces the expression of adhesion molecules such as intercellular adhesion molecule-1 (ICAM-1) on epithelial cells.[18] ICAM-1 is the most important receptor for rhinovirus and its up-regulation may be a risk factor for this type of viral infection.[19] Moreover, epithelial cells from asthmatic patients show a defective innate immune response that may partially explain the recurrence of LRTIs.[20] Finally, interleukin(IL)-13, which is a crucial cytokine in allergic inflammation, seems to reduce mucociliary clearance, thus facilitating viral adhesion to airway epithelial cells.[21] At the same time, viral RTIs may contribute to initiating an allergic response by increasing mucosal permeability or as a result of the virally-induced secretion of pro-inflammatory mediators.[22]

On the other hand, especially in non-English spoken communities as there is no synonym for ‘‘wheeze’’ many children with bronchiolitis or asthma exacerbation are diagnosed as ‘‘pneumonia’’. Bronchiolitis group may be a part of children with self-limiting disease and asthmatic children may constitute a part of ‘‘wait-and-see’’ group.

Passive smoking

It has been shown that prenatal exposure to maternal smoking is a major risk factor for lower lung volume, poor lung function, and increased susceptibility to LRTIs.[23] Tobacco smoke acts on developmental lung defects directly (fetal hypoxia and ischemia) and indirectly on the growing fetus, thus predisposing newborns to increased respiratory morbidity.[24] In the first two years of life, passive smoking has been associated with a higher dose-dependent incidence of LRTIs and hospitalisation.[25,26] This may be due to a direct effect of cigarette smoke on host defences because it has been shown that smoking reduces the production of oxygen radicals by neutrophils and monocytes/macrophage cells, and suppresses their phagocytic activity.[27] Furthermore, the children of smoking mothers have an impaired neonatal toll-like receptor-mediated immune response.[28] Finally, passive smoking increases bacterial adherence and the risk of inflammation as well as further respiratory infections.[29] It is very important to improve education with simple material showing to the general population risks associated with smoking, even when passive.

Indoor pollution

Air pollutants increase the frequency and the severity of LRTIs by causing inflammation of the lung airways and alveoli. In addition to tobacco smoke, the most important indoor pollutants are particulate matter, smoke from household solid fuels, nitrogen dioxide from cooking stoves, carbon monoxide, volatile organic compounds and biological allergens (i.e. mites, moulds and pet allergens).[30] Infants and young children are particularly susceptible to these pollutants because of the immaturity of their respiratory defence mechanisms and the anatomy of their airways.[31] Indoor exposure to mould and dampness is also frequently associated with asthma symptoms, with the highest risk being associated with mould and dampness in the living room or the child’s bedroom.[32] Moulds may induce recurrent respiratory