Objective. To determine if recurrent community acquired pneumonia (RP) is a risk factor for developing childhood asthma (CA), compared with those children who only suffer one episode of pneumonia or non-recurrent pneumonia (NRP). To determine if patients with CA are more disposed to suffer RP.

Design. Historical cohort study.

Setting. Primary care.


Principal measurements. The relative risk (RR) and confidence interval (95% CI) of childhood asthma in the presence of recurrent pneumonia as compared to non-recurrent pneumonia, and the RR of recurrent pneumonia in the presence of childhood asthma.

Results. Of the 65 children included, 18 had RP (27.7%; 95% CI, 16.8-38.6). The prevalence of CA was 49.2% (32 children) (95% CI, 37.1-61.4). The diagnosis of CA at any time was higher in children with RP (RR=4.1; 95% CI, 1.9-8.9). There were no differences between the incidence of RP and NRP in children previously diagnosed with CA (RR=1.28; 95% CI, 0.5-3.0).

Conclusions. A special follow-up needs to be carried out on all children diagnosed with RP in primary care, since the possibility of presenting with CA is higher in these cases.

Key words: Pneumonia. Asthma. Primary health care. Child.
**Introduction**

Community-acquired pneumonia (CAP) is a common illness in children. Its incidence in primary care (PC) has been established at 4%-6% new cases/100 susceptible/year. The incidence of recurrent CAP (RP) has been estimated at 8% in hospital-based studies and its presence is associated with bronchial asthma, among other diseases. Clark et al. reported that children hospitalised due to CAP had a higher probability of subsequently developing asthma. After an exhaustive literature search, no studies in PC could be found which determined whether RP constituted a possible risk factor for the subsequent development of asthma, as compared to children who only have one episode of pneumonia (non-recurrent pneumonia, NRP). Children diagnosed with asthma or wheezing episodes could have a higher probability of presenting with CAP. These studies carried out in hospitals did not look at the association between asthma and the subsequent development of RP.

RP has been associated with different diseases besides asthma, the majority severe, and whose early diagnosis is essential. CAP can also have serious repercussions on the pulmonary parenchyma, particularly in RP, therefore it requires suitable treatment, as well as the identification and treatment of its predisposing factors. It is important to know the extent of RP in the community environment and establish whether it constitutes a possible risk factor for the subsequent development of childhood asthma (CA), the most prevalent chronic illness in childhood.

The present study was carried out to determine if RP is a risk factor for the subsequent development of CA as compared with the presence of only 1 episode of CAP (NRP) in PC, and if patients with CA are more predisposed to present with RP.

**Patients and Methods**

**Study Design**

Historical cohort study.

**Population**

All the episodes of CAP diagnosed in children <15 years old in the Girona Basic Health Area-4, between 1st January 1996 and 30th June 1999 were gathered (80 episodes in 65 children). The method for searching the CAP episodes has been published earlier.

All children <15 years old who had at least one episode of CAP diagnosed and controlled in PC were included. The diagnosis was carried out by 2 radiologists, independently and blindly.

**General Scheme of the Study**

Historic cohort study of the association between recurrent pneumonia and the subsequent development of previously undiagnosed childhood asthma.

CAP indicates community-acquired pneumonia; RP, recurrent pneumonia; NRP, non-recurrent pneumonia.

Episodes of CAP diagnosed, treated and monitored in the hospital environment and children with underlying chronic diseases (cystic fibrosis, heart disease, immunodeficiency) were excluded.

**Definitions**

Reviews of the computerised clinical histories were made to identify the cases according to the following definitions:

- RP: children diagnosed with more than one episode of pneumonia during the period of the study.
- NRP: children diagnosed with pneumonia on only one occasion during the period of the study.
- CA: children who comply with the criteria which defines asthma based on a medical diagnosis (clinical and/or functional), according to the criteria of the Asturia Regional Working Party on Childhood Asthma Consensus Group.

**Statistical Analysis**

Means, standard deviations (SD), ratios, and 95% confidence intervals (95% CI) were estimated. The χ² and the Student-Fisher t test were used, along with the estimation of the relative risk (RR) and its 95% CI.

**Results**

During the period of the study, 65 children presented with 80 episodes of CAP. The mean age±SD was 52.8±33.8 months. Of these, 38 were girls (58.5%). There were no significant differences between the age of those affected according to sex (53.1 vs 52.6 months; P=.9). Of the cases identified, 18 children (27.7%; 95% CI, 16.8-38.6) had more than 1 episode of CAP (RP). The prevalence of CA in the whole sample was 49.2% (32 children) (95% CI, 37.1-61.4).
RP was associated with the development of previously undiagnosed CA (Table 2). The risk of CA was greater in children with RP than in those who had NRP (RR=4.1; 95% CI, 1.9-8.9; \(P=0.002\)). The prevalence of CA among children with RP was 64.7% versus 15.4% in those who had NRP.

There were no significant differences between the percentages of RP and NRP in children previously diagnosed with CA who had not presented with any previous episode of CAP (Table 3); 26% had 1 episode of CAP and 33.3% more than 1 episode (RR=1.28; 95% CI, 0.5-3.0; \(P=0.6\)).

Of the 18 children with RP, 15 were previously diagnosed or were subsequently diagnosed with CA (\(P=0.007\)).

### Discussion

This study has some limitations. The definition of RP which has been used was less strict than that found in the literature (at least 2 episodes in 1 year or more than 3 episodes throughout life\(^\text{13}\)), whilst in the present study RP was considered when more than 1 episode was presented during the period of the study (approximately 3.5 years). Despite this fact, the definition of RP in this study has been sufficiently sensitive to be able to demonstrate significant and clinically relevant differences as regards the subsequent development of asthma after presenting with RP as compared to children diagnosed with NRP. Another important limitation of this work is its small sample size, a fact which prompts caution in the interpretation of the statistically non-significant associations, since this can happen in a beta type error. The 95% CI are too wide for the same reason. The sample size was not determined beforehand, but was arrived at by the number of patients who were detected with RP during the period of the study.

### Table 1

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Validity of the Condition</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to 24 months</td>
<td>Three episodes of wheezing</td>
<td>Criteria sufficient to accept as confirmed asthma</td>
</tr>
<tr>
<td>2 to 5 years</td>
<td>Three episodes of dyspnoea or wheezing or 2 in the last year, with a response to bronchodilator treatment</td>
<td>Criteria sufficient to accept as confirmed asthma</td>
</tr>
<tr>
<td>Over 5 years where pulmonary function might not be evaluated (due to lack of collaboration or non-availability of spirometer)</td>
<td>Three episodes of dyspnoea or wheezing or 2 in the last year, with a response to bronchodilator treatment</td>
<td>Criteria sufficient to accept as confirmed asthma</td>
</tr>
</tbody>
</table>

### Table 2

<table>
<thead>
<tr>
<th>Bronchial Asthma</th>
<th>P</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes n (%)</td>
<td>No, n (%)</td>
<td>.00019</td>
</tr>
<tr>
<td>RP 11 (61.1)</td>
<td>7 (38.9)</td>
<td></td>
</tr>
<tr>
<td>NRP 7 (14.9)</td>
<td>40 (85.1)</td>
<td></td>
</tr>
<tr>
<td>Total 18 (27.7)</td>
<td>47 (72.3)</td>
<td></td>
</tr>
</tbody>
</table>

*RP indicates recurrent pneumonia; NRP, non-recurrent pneumonia; RR, relative risk; CI, confidence interval.

### Table 3

<table>
<thead>
<tr>
<th>CAP</th>
<th>P</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Childhood asthma RP, n (%)</td>
<td>NRP, n (%)</td>
<td>.58</td>
</tr>
<tr>
<td>Yes 5 (33.3)</td>
<td>10 (66.7)</td>
<td></td>
</tr>
<tr>
<td>No 13 (26)</td>
<td>37 (74)</td>
<td></td>
</tr>
<tr>
<td>Total 18 (27.7)</td>
<td>47 (72.3)</td>
<td></td>
</tr>
</tbody>
</table>

*CAP indicates community acquired pneumonia; RP, recurrent pneumonia; NRP, non-recurrent pneumonia; RR, relative risk; CI, confidence interval.
Recurrent Community Acquired Pneumonia in Young Children: Risk Factor for the Development of Childhood Asthma?

What Is Known About the Subject

- In hospital based studies asthma is considered a predisposing factor for presenting with recurrent pneumonia in the paediatric population. The opposite hypothesis has hardly been studied.
- The incidence of recurrent childhood pneumonia in primary care is unknown.
- There are no community based studies to determine if there is an association between recurrent pneumonia and the subsequent development of asthma.

What This Study Contributes

- Recurrent childhood pneumonia seems to be a risk factor for the subsequent development of bronchial asthma.
- The percentage of recurrent pneumonia is not significantly higher than the percentage of non-recurrent pneumonia in children previously diagnosed with bronchial asthma.
- There is a strong association between bronchial asthma and recurrent childhood pneumonia in primary care: 15 out of 18 children (83.3%) with recurrent pneumonia developed asthma or suffered from it previously.

It is important that prospective studies are carried out in the future with sufficient statistical power to be able to provide more accurate data. This study suggests that RP can be a risk factor for the subsequent development of CA, as compared to the presence of only 1 episode. There are no PC studies carried out to be able to compare these results. In the hospital environment, it has been shown that children admitted due to CAP have a higher prevalence of CA (45%) in subsequent years. However, the repercussions of RP on the subsequent incidence of CA have not been studied separately. In our study, the prevalence of CA among patients with RP was unusually high. This fact should serve as a warning to the PC paediatrician: it is necessary to be alert and make a special follow-up on every child diagnosed with RP (at least 2 episodes of CAP), since the possibility of developing CA is multiplied by four; more studies in the community are needed to accurately determine the prevalence of CA in children previously diagnosed with CAP, to study whether the incidence of RP is higher than that of NRP in children previously diagnosed with CAP and to confirm if RP is a risk factor in PC for the subsequent development of asthma.

References

Recurrent Pneumonia. A Risk Factor for Developing Childhood Asthma?

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Pneumonia is defined as the presence of fever and respiratory symptoms together with radiological evidence of parenchymal infiltrate. It is a problem of great magnitude in paediatrics, as it preferentially affects children less than 5 years old. It causes more than 4 million deaths per year, particularly in developing countries. In Spain, community acquired pneumonia (CAP) has an incidence of 4%-6% per year in children.1 In other areas and incidence of CAP of 6.7%-7.4% has been reported in pre-school age children, of which 6.9%-8.2% had recurrent pneumonia (RP).2 According to other authors, up to 8% of children with pneumonia can present with RP.3 RP is defined as 2 or more episodes of pneumonia in 1 year or a total of 3 or more episodes throughout life, with normal radiology between episodes.4 An aetiological study should be started on any child who presents with acquired pneumonia in paediatrics is present in 1 out every 8 children with community acquired pneumonia.5

In 85% of cases an underlying cause can be identified.6 Asthma is the most common associated factor in children without a previously known disease.7 Children with 2 or more episodes of pneumonia are at risk of developing asthma.8

Key Points
- Recurrent pneumonia in paediatrics is present in 1 out every 8 children with community acquired pneumonia.
- In 85% of cases an underlying cause can be identified.
- Asthma is the most common associated factor in children without a previously known disease.
- Children with 2 or more episodes of pneumonia are at risk of developing asthma.
RP, to identify underlying causes which might not be known at the time of the diagnosis. Most of the studies which look at the causes of RP come from series of hospitalised children, and the diseases most frequently found differ, depending on the authors consulted. On many occasions, the underlying disease, previous to the pneumonia, is known (80.9%), in others it is discovered during the first episode (11.4%), and less frequently the causal diagnosis is made after the RP (7.7%). The disease processes which tend to be present before the first pneumonia are: bronchial aspiration, immunodeficiency, and congenital cardiac disease, while asthma, abnormalities of the respiratory tract and gastroesophageal reflux are those which are discovered after the first pneumonia or in RP.\(^3\) In another series of patients studied for RP, the most frequently found underlying disease processes were: asthma in 32%, gastro-oesophagus reflux in 15%, disease of the immunological system in 9%, lung and thoracic abnormalities in 6% and bronchopulmonary dysplasia in 4%, cystic fibrosis in 3%, tuberculosis in 3%, aspiration syndrome in 3%, and 15% with no identifiable cause. In children less than 1 year, gastroesophageal reflux is the most frequent underlying process and in those over 2 years old, asthma.\(^5\) As a conclusion it could be pointed out that after an appropriate investigation the causal diagnosis of RP can be arrived at in 85% of cases. When there is no previous diagnosis, asthma and gastroesophageal reflux should be actively investigated.

From the studies mentioned the great importance of asthma emerges as a background disease in the child with RP. However the role of recurrent pneumonia as a risk factor for the development of childhood asthma has not been sufficiently studied. The work of Picas et al\(^6\) makes an interesting contribution in this direction, since it tries to determine if acquired RP in the community is a risk factor for the development of childhood asthma (CA) as compared to the presence of only one episode of pneumonia, non-recurrent pneumonia (NRP), as well as determining if patients with CA are more predisposed to present with RP.

It must be emphasised that this study deals with children studied as out-patients of a health centre and that none of them required hospitalisation, while the majority of studies on RP come from hospital series. They recorded 80 episodes of CAP in 65 children <15 years old (mean age, 52.8 months) over a period of 3 and a half years.\(^1\) It excluded hospitalised children and those with previously known diseases. It should be pointed out that the definition criteria for RP has been less strict than that used by other authors,\(^4\) since it has considered that RP is present in all children diagnosed with more than one episode of pneumonia during the period of the study. The frequency of RP found among children who had a previous CAP is 27.7%, a figure higher than that reported by other authors (6.7%-7.4% and 8%)\(^2,3\); this fact can be explained by several factors; the diagnostic criteria to define RP is less strict than that used in other publications, the fact that they were out-patients, considering that only 10% of children with pneumonia require hospitalisation, as well as the sample size.

The present study has been able to detect that RP was associated with previously undiagnosed CA, as compared to the presence of NRP (RR=4.1; 95% CI, 1.9-8.9; \(P=0.002\)), while no significant differences were found between RP and NRP in children previously diagnosed with CA (RR=1.28; 95% CI, 0.5-3.0; \(P=6\)). This data is of special interest, since it demonstrates the strong association between RP and CA in children <15 years in primary care, while no association was found between previously diagnosed CA and RP.

Up until now, the factors associated with the prevalence of bronchial asthma in children and adolescents are: to be male, family history of asthma, rhinitis symptoms, respiratory infections, need to exclude any food from the diet, and wheezing or cough with exercise.\(^7\)

In primary care, the direct application of these findings is that children who present with RP, without previously known diseases, are a “high risk population” for the subsequent development of CA.

It is essential to concentrate diagnostic efforts, treatment and prevention directed at all children who present with acquired RP in the community, without previously known underlying diseases, due to the risk of subsequently developing CA.

It would be of great value to perform future prospective, multi-centred studies, carried out from primary care, to obtain more accurate data which could increase the value of the strength of association described.

References