Assessment and 2-year follow-up of some factors associated with severity of respiratory infections in early childhood

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Objective. To assess the effect of some factors on the severity of acute respiratory infection (ARI) in children.

Design. In a case control study, children with pneumonia were matched with controls who had upper respiratory infection. They were compared in respect of nutrition, household crowding and smoke pollution, and the presence of current viral respiratory infection. Both cohorts were followed up for 18 - 24 months to determine if there was a difference in subsequent respiratory sequelae.

Setting. Primary health care-based cohorts of peri-urban township children.

Participants. Forty-eight children < 3 years of age with pneumonia (index cases) were matched by age and presentation time with controls who suffered only from upper respiratory infection. All came from underprivileged communities. Index cases were selected as they presented and the study was conducted between February 1988 and June 1991.

Main outcome measure. Any difference between index cases and controls in respect of the four factors listed under 'Design'. Follow-up home visits determined whether subsequent sequelae of the two grades of ARI were different.

Results. The presence of current viral infection at entry to the study was evident in 21 of those with pneumonia and 12 controls (difference between groups = 19.15%, 95% confidence intervals 0.25 - 38.05, $P = 0.052$). Overcrowding in the home was comparable. Index homes were occupied by a mean of 3.57 (SD 1.54) children and 5.26 (SD 4.84) adults, control homes by 3.51 (SD 1.80) children and 4.36 (SD 2.02) adults. Occupancy of the room in which the child slept was also not significantly different: index group mean 4.23 (SD 1.55) and controls 4.02 (SD 1.38) (mean difference 0.21, 95% CI 0.378 - 0.798, $P = 0.485$). Correlation of bedroom crowding with young age (< 1 year) or weight-for-age centiles was not significant in either cohort ($r < 0.3$ in all). The prevalence of viral infection was not increased by degree of crowding in either group ($P = 0.636$). Domestic smoke pollution was similar: cigarette smoking occurred in 75% of index homes and 69% of control homes. Wood or coal fires were used in 19% of index and 14% of control homes. The nutritional status of both groups proved to be similar. Fifteen per cent of index children and 12% of controls had weight-for-age centiles ≤ 10th centile (difference = 3.26%, 95% CI −10.72 - 17.24, $P = 0.649$). Two-year home follow-up visits were completed in 75% of the index and 69% of the control group. The balance were followed up for 18 months. There was no difference between index and control children in the recurrence of respiratory symptoms ($P = 0.664$) or need to visit a health facility ($P = 0.302$).

Conclusions. Factors shown elsewhere to contribute to the acquisition or severity of ARI could not be demonstrated as important in this study. The children with pneumonia and their matched controls with upper respiratory infections came from equally overcrowded and smoke-filled homes, had comparable nutritional status which was not markedly poor, and had an equal incidence of current viral infection. Subsequent ill-health was not found to be greater in the pneumonia group.

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Serious respiratory infections are more common in children of poor and developing populations than in those of developed communities[1,2] and carry a much higher mortality rate.[3] Along with malnutrition and diarrhoea, respiratory infections are the commonest cause of death in underprivileged children.

Some factors have been found that increase the likelihood and/or severity of lower respiratory infections. Young children suffer the most serious consequences of infection.[3,4] It is well known that measles depresses cellular immune response and increases susceptibility to infection. The incidence of pneumonia is far greater in malnourished children than in those of normal weight.[5] A heavy dose of an infecting agent can be expected from prolonged contact with an infectious household member, so large families increase this risk.[4,6] Environmental smoke pollution is accompanied by an increased incidence of respiratory infections and symptoms.[7,8]

In this prospective study we examined some factors that might increase the severity of acute respiratory infections (ARIs), and monitored subsequent respiratory symptoms during a 2-year follow-up.

Patients and methods

The study was carried out from February 1988 to June 1991. Forty-eight black children with pneumonia and 48 with upper respiratory infection, aged 3 months to 3 years and attending King Edward VIII Hospital, Durban, were recruited with parental consent. All lived in peri-urban townships where housing consists of 4-roomed brick dwellings and

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where the climate is mildly subtropical. Children less than 3 months of age or who weighed less than 2 500 g at birth were omitted to exclude those with lower respiratory disease consequent upon neonatal problems.

Overt protein energy malnutrition (oedema with or without skin or hair changes) was an exclusion criterion, lest it became a confounding factor.

Each pneumonia (index) case had radiologically proven pneumonia of recent onset (less than 3 days). A control case (with infection confined to the upper respiratory tract) was matched to within 1 month of presentation time and also for age (within 1 month if the index case was under 12 months of age, and within 3 months for those aged over 12 months). Lower respiratory infection was excluded in controls on clinical criteria of a respiratory rate of less than 50 breaths per minute and no wheezes or crackles on auscultation.[9] Chest radiographs were not considered an ethical way of proving the absence of pneumonia.

From each index case and control the following were obtained: (*i*) height and weight; (*ii*) pharyngeal epithelial cells, obtained by throat swab, which were cultured for common respiratory viruses and *Mycoplasma pneumoniae;* (*iii*) full blood counts, blood cultures and serum albumin samples.

In addition, the following were obtained from the index group: (*i*) paired sera for respiratory virus antibodies by complement fixation test (CFT). This was not done in control children as repeated venipuncture in a healthy child was considered to be unjustified; (*ii*) chest radiographs, which were scored for severity (1 - 4 points for pneumonic shadows, 1 point each for the outer one-third of lung field involvement by pneumonia or emphysema, 1 point for segmental collapse, 1 point for breakdown or effusion, maximum 8 points). This scoring system has previously proved successful in grading of the severity of pneumonia.[10,11]

An initial visit to the homes of all children in the study determined occupancy of the house and of the room in which the child slept. In addition, infectious contacts (a family member with recent respiratory infection and day-care centre attendance) were noted as well as parental smoking and indoor coal or wood fires for cooking or heating.

Subsequent home visits were made at 3-monthly intervals for 2 years. At these visits height, weight and respiratory symptoms were noted, and history of respiratory illness and the need to visit health facilities was taken for the previous 3 months.

Statistics

Spearman correlation coefficients were calculated for the associations between continuous variables of the index and control groups, as well as in the index group for associations between severity and other factors.

To compare the index and control groups with regard to haemoglobin, abnormal white blood cell (WBC) count, serum albumin, weight-for-age centiles and crowding, Wilcoxon 2-sample tests were used. A P-value < 0.05 was regarded as statistically significant.

For categorical data Pearson χ^2-tests were used. Where stratified analysis was undertaken, the Cochran-Mantel-Haenzel χ^2-test was applied; 95% confidence intervals were calculated for differences between the groups.

Results

Forty-eight pairs were studied: the index group consisted of 18 boys, 30 girls and the control group of 23 boys, 15 girls. Table I shows the ages of the children on entry to the study. There were two fatalities in the index group. One 8-month-old child recovered from her pneumonia. She was readmitted 5 days later with measles complicated by pneumonia, diarrhoea, herpes gingivostomatitis and *Escherichia coli* septicaemia; she subsequently died.

In the second child, aged 6 months, progress was complicated by meningitis with hemiplegia and communicating hydrocephalus. The blood culture on admission grew *Haemophilus influenza.*

Table I. Ages of index group and controls

	Index	Control
3 - 6 months	10	9
7 - 12 months	17	19
13 - 24 months	16	14
> 24 months	5	6

Evidence of current viral infection was found in 35% of the total: 21 index children (pharyngeal swab culture and/or 4-fold CFT titre rise) and 12 controls (pharyngeal swab culture): difference 19.15% (95% CI 0.25 - 38.05%, P = 0.052). Table II details the viral infections detected. Recognised respiratory pathogens (adenovirus, influenza, para-influenza, respiratory syncytial virus (RSV), *M. pneumoniae*) were present largely in the index group.

Table II. Virus isolation and/or serology

	Index		Controls
	Isolation ± serology	Serology only	Isolation
Adenovirus	4	3	0
Influenza B	1	2	0
Para-influenza	0	1	0
RSV	1	2	1
Mycoplasma	0	2	0
Enterovirus*	4	0	4
Herpes simplex	0	1	4
CMV	0	0	2
Paramyxovirus	0	0	1
Total	10	11	12

* Non-polio.
RSV = respiratory syncytial virus; CMV = cytomegalovirus.

The children of both groups came from equally overcrowded homes: the mean (SD) numbers of children (index 3.57 (1.54), controls 3.51 (1.80)) and adults (index 5.26 (4.84), controls 4.36 (2.08)) sharing the house were comparable. The occupancy of the index children's sleeping room (4.23, SD 1.55) was not greater than that of their controls (4.02, SD 1.38); mean difference 0.21, 95% CI –0.378 - 0.798, P = 0.485. Sleeping room occupancy was not related in either group to young age (< 1 year) (index r = –0.033, control r = 0.018) or weight centiles (index r = 0.264, control r = –0.022). The main incidence of viral infection was not affected by the degree of crowding of the sleeping room (P = 0.636).

Fig. 1 shows the weight-for-age centile distribution of both groups. The nutritional status of the index children and their controls was similar: 14,9% of index children and 11,6% of controls were ≤ 10th weight-for-age centile (difference 3.26%, 95% CI −10.72 - 17.24, $P = 0.649$). The mean (SD) serum albumin level was 34.92 g/l (9.15) in the index group and 37.25 g/l (6.31) in the controls. Only 1 index child and no controls had a level of ≤ 28 g/l. No correlations were found between weight-for-age centiles, abnormal WBC count ($< 5 \times 10^9$/l or $> 15 \times 10^9$/l) (index $r = 0.116$, control $r = 0.018$) haemoglobin (Hb) (index $r = -0.008$, control $r = -0.032$) or chest radiograph scores ($r = 0.111$).

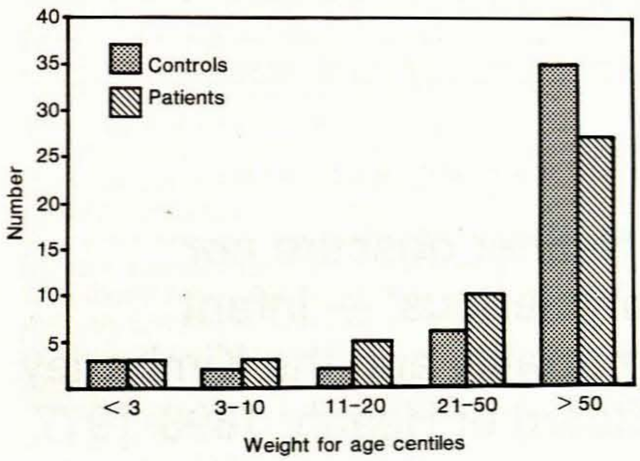

Fig. 1. Weight-for-age centiles — index cases and controls.

Home pollution risks were very similar in the two groups. The incidence of adults' smoking in the index homes was 75% and in control homes 69%. Wood or coal fires were used in 19% of index and 14% of control homes.

The mean (SD) Hb level was similar in both groups: index 9.6 (1.1), control 9.9 (1.3) g/dl ($P = 0.304$). WBC count was also similar: index 16.6 (6.31) 10^9/l, control 14.52 (4.53) 10^9/l ($P = 0.065$). Blood cultures were positive in 2 patients in the index group (*H. influenzae, Streptococcus pneumoniae*) and 1 control (*S. pneumoniae*).

The number of family contacts with respiratory infections at the time of admission of children to the study did not differ when index and control cases were compared ($P = 0.540$). Only 2 children in each group attended a day care centre.

Home visits were carried out for 2 years in 75% of index children and 69% of controls: the remainder completed 18 months of follow-up. There was no difference in the incidence of recurrence of respiratory symptoms among index children and controls ($P = 0.664$). Further, the necessity to seek treatment at health facilities during the follow-up period arose in 53% of index and 49% of control children. Most children in each group were thriving and gaining weight during the surveillance period.

The severity of pneumonia in index cases was also analysed. There was a moderate correlation between higher radiograph scores and both a longer length of stay in hospital ($r = 0.455$) and an abnormal WBC count ($r = 0,37$). Severity was not significantly affected by sleeping room crowding ($r = 0.056$), weight-for-age centiles ($r = -0.111$), anaemia ($r = 0.313$) or evidence of viral infection ($P = 0.94$).

Compared with those with milder disease, children with radiologically severe pneumonia did not experience increased recurrent respiratory symptoms or visits to health facilities during the follow-up period.

Discussion

The factors studied that are considered to be important determinants of the severity of ARI in young children were nutrition, domestic crowding and air pollution. The presence of respiratory viruses was also sought. Children under 3 years of age from a disadvantaged community were selected — patients with moderate or severe ARI (pneumonia) were matched for age and time of presentation with children who had mild ARI (coryza or pharyngitis).

Dissemination of respiratory infection at a young age is often the result of domestic crowding, and a heavy infecting load may result.[4-6] The study children lived in formal peri-urban housing where the typical dwelling was a 4-roomed brick house. The children of each group came from equally overcrowded homes, shared on average by 8 - 9 adults and children. When occupancy of the child's sleeping quarters was considered, there was also no difference between the two groups. There was no correlation between degree of crowding and age (< 1 year) or nutrition or evidence of viral infection either in index or control children.

In this study, the incidence of viral infection was not significantly different in the two groups, and the viral presence may have been underestimated in control patients since CFTs were not done. Of particular interest was the adenovirus, a frequent cause of upper respiratory symptoms, but also an important cause of pneumonia in the disadvantaged.[12] Enterovirus is a frequent finding in children of developing communities but may not always be associated with respiratory symptoms.[13] Herpes simplex may cause upper respiratory symptoms or subclinical infections.

If not responsible for pneumonia the viral infection may have enabled bacterial respiratory infection to occur. Pneumonia in children of poor communities is more commonly associated with bacterial than viral infection.[13,14] Apart from the obtaining of blood cultures on first arrival in the outpatient department, bacterial aetiology was not sought in this study. Prior administration of antibiotics by the referring general practitioner or clinic may explain the low blood culture yield.

Morbidity from respiratory infection is reported to be increased in children with malnutrition.[5] This could not be demonstrated in this study, possibly because the majority of the children proved to be relatively well-nourished. Anaemia or an abnormal total WBC count was not more common in those whc developed pneumonia.

Smoke is known to lead to an increase in respiratory symptoms.[7,8] Data obtained on home visits showed that cigarette smoking among adults was equally common and that open coal or wood fires were uncommon in the two groups. The similarity in the home pollution levels may lead to the failure to demonstrate smoke as a contributor to the development of pneumonia rather than mild ARI in this cohort.

The data were also analysed to detect whether any of the factors studied were associated with increased severity of pneumonia in the index group. There was a moderate correlation between chest radiograph score and length of stay in hospital, but these scores did not correlate with malnutrition, crowding of sleeping quarters, home pollution or current viral infection. The majority of the index patients could be classified on the basis of WHO clinical criteria[1] as having moderate ARI, with only 20% having severe ARI, and this finding may explain lack of correlation between severity and the factors studied.

An increased prevalence of recurrent symptoms and abnormal lung function tests has been noted on long-term follow-up of children who have had lower respiratory infections compared with normal controls.[15-17] In the present study all children were monitored by home visits for 18 - 24 months to detect any detrimental effect that could be ascribed to the respiratory infection, but ill-health was not found to be commoner in the index group. The frequency of subsequent respiratory symptoms and the need to consult a doctor or clinic for respiratory problems were the same in the two groups. A similar number of children in both groups was judged to be thriving. Even those with a high radiological pneumonia score did not have more prolonged respiratory symptoms or a greater need for health care facilities than those with milder pneumonia. In this study the finding of equally good health in both groups may be because of relatively moderate disease in index children, which was not severe enough to contrast with controls, and respiratory sequelae could therefore not be shown to differ.

Factors noted in other studies to affect the acquisition or severity of lower respiratory infection were not demonstrated in this study to be determinants of whether a child contracted lower rather than upper respiratory infections. Although the children came from a poor socio-economic community, their nutrition was relatively good and home pollution was very similar in both index and control groups. The small sample size might have prevented the demonstration of crowding as important; both groups lived in grossly overcrowded homes. The evidence of viral infection was comparable in patients and controls.

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HISTORY OF MEDICINE

'Neither obscure nor mysterious' — infant mortality and the Kimberley Board of Health, 1898-1977

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Annual reports of the Kimberley Board of Health, established in 1883, provide rich insight into public health discourse on infant mortality. Commentaries on the determinants of infant mortality, especially prior to 1950, largely focus on poverty and interracial disparities, issues relevant to current health policy.

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The debate on restructuring South African health care has been accompanied by renewed interest in the history of local public health initiatives and their relevance to current issues.[1,2] Most of the recent documentation has focused on exemplary individuals and institutions and there is a paucity of historical information on the routine public health activities of local authorities. Although some of the larger towns and cities have been collecting health information since the turn of the century, health service fragmentation and the lack of an integrated national health information system have led to an inevitable decline in the quality of South African health statistics.[3] The utility of local authority health data was demonstrated by Phillips, who used the Reports of the Medical Officer of Health of Cape Town to demonstrate

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