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# Acute bronchiolitis

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Acute bronchiolitis is a clinical diagnosis. A UK Delphic process reached a 90% consensus that bronchiolitis “is a seasonal viral illness, characterised by fever, nasal discharge and dry, wheezy cough. On examination, there are fine inspiratory crackles and/or high-pitched expiratory wheeze.”<sup>1</sup> Internationally, the definition is sometimes broadened to include a first episode of acute viral wheeze. It is an annual and major cause of morbidity in infancy. Acute bronchiolitis is a very common serious respiratory illness in children. Inappropriate treatment is often prescribed, and the relation between such treatment and subsequent asthma is unclear. This review focuses on management in the community and hospital ward.

## What causes acute bronchiolitis?

Respiratory syncytial virus (RSV) is responsible for about 80% of cases. Other causative agents include human metapneumovirus; rhinovirus; adenovirus (more likely to be followed by serious sequelae, such as obliterative bronchiolitis); influenza and parainfluenza viruses; and enteroviruses. Diagnosing RSV is important for preventing cross infection in hospital and for epidemiological information but does not affect acute management.

## Sources and selection criteria

We searched PubMed and the Cochrane database using the term “bronchiolitis” and hand selected what we deemed to be clinically relevant articles. We also used the evidence based, SIGN (Scottish Intercollegiate Guidelines Network) guidelines,<sup>2</sup> which we recommend to readers. We drew on our personal archives of references.

## Who gets acute bronchiolitis and how common is it?

Acute bronchiolitis is largely a disease of the first year of life; 2-3% of infants aged <1 year are admitted each year with bronchiolitis caused by RSV,<sup>3</sup> but many more will be managed in the community. The RSV “season” in the UK extends from November to March (fig 1). By age 3 years virtually all children have serological evidence of RSV infection. Unfortunately, infection does not produce protective immunity, so reinfection is common.

## Pathophysiology

Acute bronchiolitis is characterised by a neutrophilic inflammation,<sup>4</sup> and antenatal and early postnatal factors

“sow the seed” for acute bronchiolitis (box 1). Pre-existing anatomical<sup>5</sup> and immunological abnormalities<sup>6</sup> related to maternal smoking in pregnancy in particular may mean that an RSV infection presents as severe bronchiolitis, rather than a mild respiratory illness.

## Clinical presentation and diagnosis

The diagnosis is clinical. Typically, a 2-6 month old infant will present with worsening respiratory distress starting with a two to three day prodrome of coryzal symptoms. The infant is tachypnoeic with recession, and usually has showers of fine crackles all over the chest. Wheezing may be present, but this is not a prerequisite for the diagnosis. Most but not all infants are febrile, but a temperature of  $\geq 40$  degrees centigrade is rare<sup>9</sup> and should prompt a search for an alternative diagnosis. In severe cases cyanosis may occur. In young infants, particularly if born preterm, episodes of apnoea may be the first presentation of bronchiolitis.<sup>7</sup> The infant is rarely systemically toxic (drowsy, lethargic, irritable, pale, mottled, and tachycardic)—this feature should prompt a search for another diagnosis.

## Are investigations necessary?

Pulse oximetry should be performed if hypoxia is suspected. In hospital, the diagnosis of RSV bronchiolitis may be confirmed by a nasopharyngeal aspirate and viral immunofluorescence or polymerase chain reaction for infection control purposes. Otherwise, the infant with typical acute bronchiolitis requires no investigations. Specifically, chest radiography is not useful<sup>8</sup> and anecdotally may lead to the unnecessary

### Box 1 | Factors which predispose to acute bronchiolitis

Otherwise normal babies admitted to hospital for acute bronchiolitis have evidence of airflow obstruction before their bronchiolitic illness and this is still present at age 11 years<sup>7</sup>

Evidence exists of abnormality of immune function in umbilical cord blood in babies of mothers who smoke during pregnancy and these babies subsequently develop RSV infection<sup>8</sup>; the relation of these changes to RSV bronchiolitis has yet to be worked out in detail

In preterm babies who have airflow obstruction as a consequence of prematurity and of its treatment, a lesser degree of airway inflammation than usual can cause serious respiratory compromise<sup>5,6</sup>

prescription of antibiotics. C reactive protein is not a useful test to diagnose bacterial infection in this context,<sup>10</sup> and urea and electrolytes need only be measured if the infant is clinically dehydrated.<sup>7</sup>

**How should bronchiolitis be treated?**

**In the community**

The first decision is whether to admit the infant to hospital. As there is no specific treatment, the indication for admission would be the need for oxygen or tube feeding or impending or likely requirement for non-invasive or invasive respiratory support. Therefore, an absolute indication for hospital referral would be severe disease (box 2). Use a lower threshold for referral in very young infants and in infants of any age with an important comorbidity (box 3).

Clinical scoring systems have been proposed, but no evidence exists that they are better than clinical judgment.<sup>2</sup> In making the decision on whether to admit, remember that the infant may deteriorate for two to three days after the onset of respiratory distress, before starting to improve.<sup>9</sup> For those not admitted, maintain fluid intake and arrange review if there is no improvement. If the infant deteriorates at home, then arrange admission.

**In the hospital**

*Investigations*

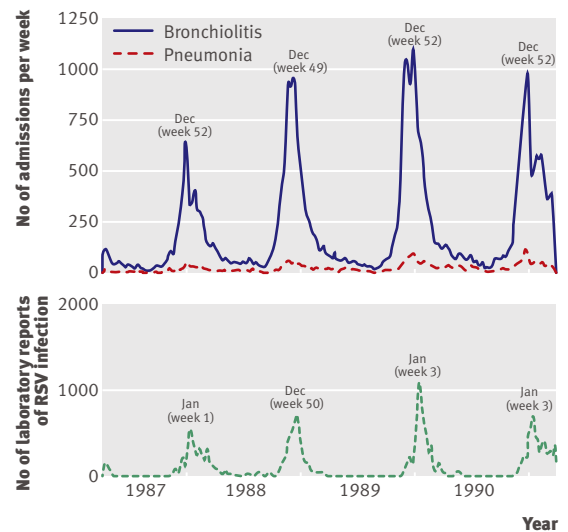
Oxygen saturation should be measured (box 4). The infant should receive barrier nursing—or, if this is not possible, at least be nursed only with other babies known to be RSV positive—to avoid nosocomial spread of infection. Capillary blood gas measurement to detect hypercapnia is indicated only if the infant is thought to be in imminent clinical need of respiratory support.<sup>2</sup> Blood and urine cultures are indicated only in infants who are toxic or febrile ( $\geq 40$  degrees centigrade).<sup>2</sup>

*Treatment*

Treatment is supportive. Appropriate supplemental oxygen is given. No study has shown worthwhile benefit for antibiotic treatment in uncomplicated bronchiolitis.<sup>2</sup> Tube feeding is started if the infant will not suck; only in really severely affected infants, in whom a nasogastric tube would compromise breathing, should intravenous fluids be given.

**RECENT ADVANCES**

- Our understanding of the mechanisms of the inflammatory cascades that lead to acute bronchiolitis is increasing. It is hoped that blocking specific chemokines, or more likely their receptors, may lead to new treatments
- A major player in the acute and chronic symptoms of bronchiolitis is perhaps the non-adrenergic, non-cholinergic airway nervous system, with involvement of neurokinins; this too may open up new avenues of treatment



**Fig 1 | Epidemiology of respiratory syncytial virus infection.** Note the close correlation between peaks of bronchiolitis (upper panel) and laboratory reports of RSV infection (lower panel). Adapted from information published by the Public Health Laboratory Service based on data from the Office of Population Censuses and Surveys and the Communicable Disease Surveillance Centre

- Bronchodilators may produce short term improvements in clinical scores but have never been shown to affect any important clinical outcome, such as obviating the need for ventilation or reducing inpatient stay.<sup>11</sup> Even these trivial benefits are probably overestimated as a result of the inclusion of participants with virus associated wheeze in some studies. Furthermore, even these minor improvements must be set against the cost of the medications, and the need to handle and thus distress the infant. The least ineffective bronchodilator is nebulised adrenaline (epinephrine).<sup>12</sup> Adrenaline, anticholinergics, and  $\beta_2$  agonists are not recommended as routine treatments.<sup>2</sup>
- Two randomised controlled trials showed no evidence of benefit for inhaled corticosteroids in acute bronchiolitis.<sup>13 14</sup> The Cochrane review showed no evidence of benefit for systemic steroids.<sup>15</sup> One trial found that a single injection of dexamethasone may help in acute bronchiolitis,<sup>16</sup> but another larger

**Box 2 | Absolute indications for hospital referral for acute bronchiolitis<sup>2</sup>**

- Cyanosis or really severe respiratory distress (respiratory rate  $>70$  breaths/min, nasal flaring and/or grunting, severe chest wall recession)
- Marked lethargy leading to poor feeding
- Respiratory distress preventing feeding ( $<50\%$  of usual intake in past 24 hours)
- Apnoeic episodes
- Diagnostic uncertainty (toxic infant, temperature  $\geq 40$  degrees centigrade)

**Box 3** | Relative indications for hospital referral for acute bronchiolitis<sup>2</sup>

Congenital heart disease  
 Any survivor of extreme prematurity  
 Any pre-existing lung disease or immunodeficiency  
 Down's syndrome: these babies have a degree of pulmonary hypoplasia and may also have potential or actual upper airway obstruction  
 Social factors: isolated family (concerns about the ability of the family to notice any deterioration)

one firmly shows that oral dexamethasone is not useful.<sup>17</sup> We therefore do not recommend the routine use of dexamethasone.

- The Cochrane review of nebulised ribavirin is a little confusing<sup>18</sup> because one study used a placebo that may have been harmful.<sup>19</sup> Even if this study is ignored, there is no evidence of benefit.<sup>2</sup> Ribavirin cannot be recommended, either nebulised or intravenously.
- A Cochrane review of RSV immunoglobulin found only four relevant studies and concluded that more work was necessary; it did not recommend this as useful in treatment.<sup>20</sup>
- A Cochrane review concluded that chest physiotherapy is a waste of time.<sup>21</sup> Gentle nasal suction to keep the air passages clear is recommended by expert consensus.

In summary, no treatment is effective in the acute phase, and no treatment in the acute phase has the least effect on the prevalence or severity of long term symptoms.

**Indications that intensive care is needed**

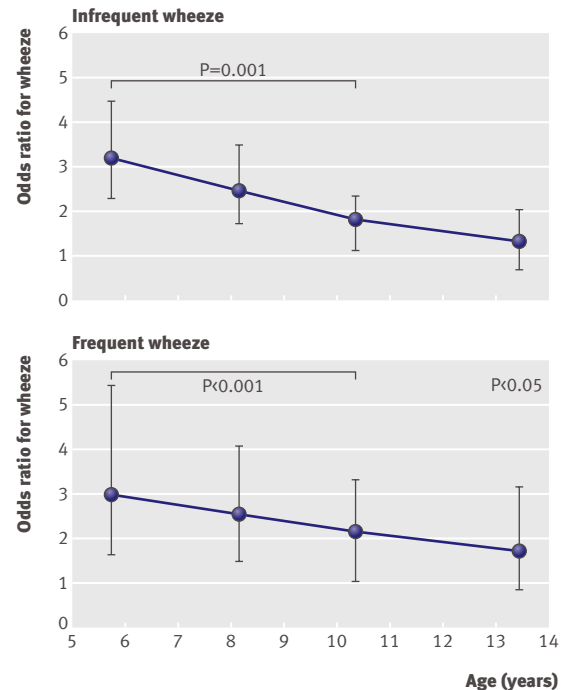
Rarely, a child may deteriorate in hospital, such that high dependency or intensive care is required. Indications for referral to higher level care include:

- Failure to maintain saturations  $>0.92$  with increasing oxygen requirement;
- Deteriorating respiratory status and impending exhaustion;
- Worsening episodes of apnoea.

In high dependency care a trial of continuous positive airway pressure ventilation using a nasal prong or mask may stabilise the child with impending respiratory failure and avoid intubation.<sup>22</sup>

**Box 4** | Action to be taken at first review in hospital, according to oxygen saturation at initial pulse oximetry reading

0.92—Admission to hospital mandatory  
 $\leq 0.94$  (but  $>0.92$ )—Consider risk factors; may be safe to discharge  
 $>0.94$ —Consider for discharge



**Fig 2** | Natural course of wheezing after respiratory syncytial virus infection, compared with a control, uninfected, group. Wheezing gradually declines over time until prevalence of wheeze returns to normal in the teenage years. Adapted from Stein et al<sup>25</sup>

**What next? When the baby goes home**

Many infants admitted to hospital with bronchiolitis have cough and wheeze lasting several weeks after bronchiolitis (post-bronchiolitic syndrome).<sup>2</sup> Most eventually recover completely, but intermittent symptoms may continue for several years, particularly with subsequent viral infections, and treatment is difficult.<sup>2</sup> No study has shown that inhaled steroids are effective<sup>2</sup>; one randomised controlled trial found that the leukotriene receptor antagonist montelukast may give short term, minor symptomatic benefit after acute bronchiolitis,<sup>23</sup> but widespread treatment with montelukast in this setting cannot be recommended.<sup>2</sup>

**RESEARCH QUESTIONS**

- When and how is continuous positive airway pressure best employed to support sick infants with bronchiolitis caused by respiratory syncytial virus?
- How do we stop mothers in particular, and all those coming into contact with infants, from smoking?
- Can we develop an effective vaccine against RSV?
- What are the detailed immunological responses to RSV bronchiolitis, and will modulating them be helpful?
- Can we find a specific treatment for established bronchiolitis?
- How do we prevent post-bronchiolitic symptoms?

**ADDITIONAL EDUCATIONAL RESOURCES****For parents**

British Lung Foundation ([www.lunguk.org](http://www.lunguk.org))—Provides a parent information leaflet *Bronchiolitis and Your Baby*  
 PatientUK ([www.patient.co.uk](http://www.patient.co.uk))—Provides information as given out by general practitioners during consultations

Scottish Intercollegiate Guidelines Network ([www.sign.ac.uk](http://www.sign.ac.uk))—Provides information leaflet on bronchiolitis for parents and carers (see [www.sign.ac.uk/patients/network/html](http://www.sign.ac.uk/patients/network/html))

**For health professionals**

Scottish Intercollegiate Guidelines Network (SIGN). Bronchiolitis in children. (A national clinical guideline.) 2006. [www.sign.ac.uk](http://www.sign.ac.uk)

Wheezing exacerbations may respond to standard bronchodilator therapy.

Infants with acute adenovirus bronchiolitis in particular may go on to an obliterative bronchiolitis, in which there is widespread disease of the small and large airways, including bronchiectasis. This complication is more rarely seen with other viral infections, including RSV, and may be more common in areas of social deprivation. The infant remains tachypnoeic, with a chronic cough and wheeze, and may produce chronic sputum (although this is usually swallowed). There may be prolonged oxygen dependency. No effective specific treatment can be recommended. Bronchiectasis is treated conventionally with chest physiotherapy and antibiotics. Symptoms may improve over the years.

**Can bronchiolitis be prevented?****Routine measures**

Breast feeding may be partially protective; parental smoking is deleterious (with antenatal and postnatal effects) and should be discouraged.<sup>2</sup> Simple measures such as promoting hand washing in nursery and day care facilities and washing of shared toys (preferably discouraging toy sharing) may help to decrease community spread.

**SUMMARY POINTS**

Bronchiolitis caused by respiratory syncytial virus is an important and seasonal cause of respiratory morbidity in the first year of life

No effective preventive or therapeutic strategies exist, and supportive management is offered

Unnecessary investigations and ineffective treatment must be avoided

Many infants have medium to long term post-bronchiolitic symptoms, which should not be confused with true asthma and which do not respond to any current treatments

**RSV immunoglobulin**

Hyperimmune RSV immunoglobulin is not licensed for treatment in the UK. The monoclonal RSV immunoglobulin palivizumab may be given as prophylaxis to high risk infants. It requires a monthly intramuscular injection. It offers partial protection and is expensive. It may be considered in infants aged less than 12 months in the following categories<sup>24</sup>:

- Survivors of extreme prematurity;
- Acyanotic congenital heart disease (palivizumab was not effective in cyanotic congenital heart disease);
- Congenital or acquired disease, significant orphan lung disease (that is, not uncomplicated wheezing syndromes; usually babies with an orphan lung disease being considered for palivizumab will be dependent on oxygen and/or non-invasive ventilation);
- Marked congenital or acquired immunodeficiency.

A systematic review concluded that the costs of the widespread use of palivizumab outweighed benefits.<sup>24</sup> Since most admissions are among term, low risk babies (because there are so many more of them than high risk babies) palivizumab is unlikely ever to affect substantially the prevalence of bronchiolitis in the community.

**RSV immunisation**

Research continues, but as yet no vaccine is available. Several problems need to be overcome:

- Even natural infection does not produce immunity to reinfection;
- An early vaccine caused worse bronchiolitis than occurred in a control, non-vaccinated group, and in the vaccinated group the bronchiolitis was accompanied by a damaging hyperimmune response;
- The optimal time to immunise, very early in life, may be a problem because of maternal antibody. Possibly immunising pregnant women may be helpful in the future.

**"Is it asthma, doctor?"**

The relation between RSV infection and subsequent asthma is hotly debated.<sup>25,26</sup> The best evidence is that RSV does not "cause" asthma—that is, an infant who has had RSV infection and goes on to develop asthma has not become asthmatic as a consequence of RSV infection. Indeed, post-bronchiolitic symptoms gradually improve (fig 2). However, pre-existing atopy may be a marker for more severe bronchiolitis,<sup>27</sup> and atopy itself predisposes to asthma. The separation of different phenotypes for preschool wheeze can be very difficult.

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## MTAS—Indian style

He was a callow young doctor who had been posted to a 100 bed, government district hospital in a small town in central India. In the hospital he came across a young woman doctor who had recently graduated from medical college. They decided to get married before their postings to remote corners of the country according to the prevailing government service rules. Their parents were vehemently opposed to the marriage, feeling that both were inexperienced and immature, and refused to attend their marriage ceremony.

The young couple brought their dilemma to the notice of the hospital's medical superintendent, a kind and jovial senior doctor. He arranged their marriage ceremony in the hospital temple. Their marriage rituals were performed by the hospital Hindu religious teacher.

Their flower bedecked vehicle was driven into the hospital premises, and they were greeted by the patients with floral bouquets. An impromptu party was arranged in the hospital courtyard by the staff and patients.

However, a busybody colleague in the hospital objected to the marriage as the couple had flouted an ancient government service rule—enacted in the pre-independence, British era—that forbade government servants from marrying before 25 years of age. He threatened to complain to the district commissioner.

The medical superintendent asked the young newlyweds to meet him at the golf course the next day. There, he introduced the couple to the district commissioner, an avid golfer, saying that they had come to seek his blessing. The district commissioner promptly blessed them and overruled the complaint.

Their next hurdle was the Damocles' sword of postings to separate locations hanging over their heads. The medical superintendent drafted an application to the health minister for their posting together on compassionate grounds, explaining their difficulties. This was followed by telephone calls to a concerned senior officer in the Health Ministry to circumvent the bureaucratic red tape.

The officer in charge of postings was persuaded and issued orders for their posting together to a small hospital at a beautiful hill station in the Himalayas on "extreme passionate grounds."

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