

# COMMUNITY ACQUIRED PNEUMONIA IN CHILDREN: A CLINICAL UPDATE

BEST PRACTICE

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**P**aediatric respiratory disease remains an important cause of morbidity in both the developing and the developed world. In the UK respiratory illness is the most common reason parents cite for taking their children to see the general practitioner, and for attendance to the emergency department with a paediatric medical problem.<sup>1</sup>

Community acquired pneumonia (CAP) refers to an infection of the lung by a variety of microorganisms acquired outside the hospital setting, resulting in inflammation of the lung tissue. It is typically associated with fever and respiratory symptoms such as cough and tachypnoea, but symptoms may be non-specific in young children. Radiographic changes *may* be useful to confirm the diagnosis. It remains an important cause of death in children throughout the world, especially in developing countries. Fortunately in the UK death in previously well children is an extremely rare consequence of CAP and most children do not need to be admitted to hospital for treatment. The groups at highest risk of long term morbidity and mortality include infants (especially low birth weight or premature), those who are immunocompromised, and those who have other underlying conditions such as cystic fibrosis or congenital heart disease. This article does not aim to address the management of children with such conditions.

Despite pneumonia being a condition commonly encountered by clinicians, uncertainty remains over the diagnosis, investigation, and treatment of the condition. The British Thoracic Society (BTS) has published clinical guidelines which provide an evidence base for the management of CAP.<sup>2</sup> The guidelines recognise, however, that there are still some recommendations based on consensus opinion due to the lack of available evidence. The aim of this article is to update the clinician on the management of CAP based on a combination of recommendations from the BTS guidelines,<sup>2</sup> and current literature.

## EPIDEMIOLOGY AND AETIOLOGY

Pneumonia is most common in children younger than 5 years of age.<sup>3</sup> In the developing world, there is not only a high morbidity but also mortality associated with the condition<sup>4</sup>; data from the World Health Organization confirm that acute respiratory illness remains a leading cause of childhood mortality, causing an estimated 1.6–2.2 million deaths globally in children < 5 years.<sup>4</sup> In North America the annual incidence in children younger than 5 years of age is 34–40 cases per 1000.<sup>5</sup> European figures taken from a study conducted in Finland are similar at 36/1000/year for children < 5 years of age and 16.2/1000/year > 5 years (hospital and community combined).<sup>6</sup> The only UK figures come from a hospital based audit from the northern region<sup>7</sup> reporting an incidence of 1.44/1000/year for children > 1 year. The audit excluded children < 1 year and no information was collected on the number of children treated in the community. This may account for the lower prevalence seen in this study.

CAP can be caused by a variety of organisms (table 1). Identification of the causative organism would direct treatment but accurate, fast, affordable, and widely available diagnostic tools are still awaited.

There is a current widely held belief that the causative organisms vary according to the age of the child, viruses being most common in children under 5 years old. Respiratory syncytial virus (RSV, most common in the very young), adenovirus, parainfluenza virus, influenza virus, and more recently metapneumovirus virus<sup>8</sup> have all been identified in this age group.

Bacterial causes are reported as being more common in older children. Most aetiology studies in the developed world from the last 15 years suggest that *Streptococcus pneumoniae* and mycoplasma account for most cases of bacterial pneumonia<sup>9–14</sup>; however, the number of cases attributable to these two organisms varies greatly between studies. The incidence of *S pneumoniae* varies from 4%<sup>15</sup> to 8%<sup>9</sup> to 21%.<sup>16</sup> Similar differences are seen for mycoplasma.

There are studies that support a preponderance of particular organisms in different age groups. For example, a Finnish study<sup>6</sup> found that in children younger than 5 years of age, the incidence of *S pneumoniae* infection was 8.6/1000 per year and mycoplasma 1.7/1000 per year. In children aged

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**Table 1** Causal organisms of community acquired pneumonia (CAP)

- ▶ Common viruses in children
  - respiratory syncytial virus (RSV)
  - adenovirus
  - parainfluenza virus
  - influenza virus
  - metapneumovirus virus
- ▶ Common bacterial causes
  - *Streptococcus pneumoniae*
  - *Mycoplasma*
- ▶ Mixed aetiology: common viruses plus bacteria
- ▶ Other organisms
  - *Chlamydia trachomatis*
  - *Bordetella pertussis*
  - *Staphylococcus aureus*
  - *Mycobacterium tuberculosis* (TB)

from 5–15 years, the incidence of *S pneumoniae* fell to 5.4/1000, while that of mycoplasma rose to 6.6/1000.

However, the audit by Clark *et al*<sup>7</sup> did not support this finding; in their study the mean age of children with mycoplasma infection was 3.5 years. Block *et al*<sup>17</sup> identified mycoplasma in 23% of 3–4 year old children, thereby disagreeing with the suggestion that aetiology relates to the age of the child.

#### OTHER ORGANISMS TO CONSIDER

Apart from *S pneumoniae* and mycoplasma, other organisms that need to be considered include *Chlamydia trachomatis*, *Bordetella pertussis*, *Staphylococcus aureus*, and *Mycobacterium tuberculosis* (the causal organism of tuberculosis). Table 2 highlights some of the important features of these organisms.

#### PREVENTION

The pneumococcal polysaccharide vaccine protects against 23 serotypes of pneumococcal bacteria. It is not effective in young children. A new conjugate vaccine has been developed for children under 2 years of age but is currently not offered routinely in the UK to children in this age range. The vaccine has been used more extensively in the USA and has been shown to be safe and effective at reducing the burden of pneumococcal disease.<sup>18</sup> The introduction of the vaccine in the UK may alter the aetiology and epidemiology of the disease in future years.

**Table 2** Features of other causal organisms of CAP

<i>Chlamydia trachomatis</i>	Most common in infants and young children. History of sticky eye in neonatal period is common finding
<i>Bordetella pertussis</i>	Despite primary pertussis vaccination, this disease has been affecting an increasing number of very young children, probably due to older children and young adults who have not been immunised
Staphylococcal infection	Rare in developed countries, most commonly found in infants
Tuberculosis (TB)	A resurgence of TB has been noted. More common in ethnic minorities and people infected with HIV. Increasingly common in the UK indigenous population

## DIAGNOSIS

### Clinical presentation

Children and infants may present with a number of different clinical symptoms and signs such as fever, cough, and tachypnoea. A minority of children will present with pyrexia of unknown origin and may have no respiratory symptoms or signs.

The WHO has developed an algorithm<sup>3</sup> to aid medical and non-medical health care workers in diagnosing lower respiratory tract infection without radiological confirmation. This algorithm was designed for use in the developing countries but is still useful as a clinical tool in the UK. The WHO algorithm stresses the importance of tachypnoea (table 3) as an indicator of pneumonia. Studies from the developed world support this finding.<sup>19–20</sup> Palafox<sup>19</sup> found that tachypnoea (as defined by WHO) had a 74% sensitivity and 67% specificity for radiologically defined pneumonia. However, clinicians must be cautious in children who present early in the disease. In children who had the disease for less than three days,<sup>19</sup> tachypnoea had a lower sensitivity and specificity of illness. Clinicians must be aware that the absence of tachypnoea does not necessarily mean the absence of pneumonia.<sup>20</sup>

Tachypnoea as a sign of pneumonia must also be used with caution in children with co-morbid conditions such as asthma where tachypnoea is a sign of deterioration of the underlying condition; even when combined with a fever and cough it would not necessarily require the addition of an antibiotic.

Grunting and nasal flaring increase the chance of pneumonia, but their absence cannot be relied upon to rule out pneumonia.<sup>19</sup> Other signs that relate to the severity of the pneumonia are chest in-drawing, nasal flaring, and cyanosis. Other noises such as rales, rhonchi, or crackles alone are not sensitive or specific for the diagnosis of pneumonia.

High fever in young children (aged up to 3 years) is also found to be a sign of pneumonia.<sup>21–22</sup> A temperature > 38.5°C is a feature of bacterial pneumonia.<sup>2</sup> The BTS guidelines have suggested that in children under 3 years old a combination of fever > 38.5°C, chest recession, and respiratory rate of more than 50 indicates pneumonia. Breathing difficulty itself is a more reliable sign in older children.

The absence of clinical signs is more helpful to a clinician than their presence. If *all* clinical signs are negative, pneumonia is unlikely. However, if signs are present, they can be used in combination to guide the clinician to consider a diagnosis of pneumonia but do not secure a definitive diagnosis.

### Alternative ways of presenting

A child with mycoplasma infection may present with symptoms such as wheeze and cough, therefore mycoplasma infection should be considered in a patient with suspected asthma not responding to treatment. Mycoplasma may also present with abdominal pain or chest pain.

**Table 3** WHO defined tachypnoea

▶ <2 months of age	>60 breaths/min
▶ 2–12 months	>50 breaths/min
▶ >12 months	>40 breaths/min

Abdominal pain may also be caused by bacterial pneumonia owing to diaphragm irritation. It is one of the differential diagnoses in a child who presents with fever and abdominal pain, and can present to the surgeons as well as to paediatricians.

Pneumonia needs to be excluded in infants presenting with pyrexia of unknown origin or a picture of generalised sepsis.

### Admission to hospital

A child may be admitted to hospital if:

- ▶ they are not tolerating oral medication due to vomiting, or
- ▶ there are social concerns—for example, family unable to provide appropriate support, or
- ▶ they have signs or symptoms of severe breathing difficulty.

Table 4 is a summary of recommendations from the BTS, WHO, and Paediatric Accident and Emergency Research Group<sup>2 3 25</sup> guidelines to help clinicians to identify which children may need to be admitted to hospital.

### Serological diagnosis and other laboratory tests

A variety of different laboratory tests are currently used in combination with clinical assessment to diagnose pneumonia. Indications for their use are discussed below.

The white blood cell count, C reactive protein (CRP), and erythrocyte sedimentation rate (ESR) have been used as markers of infection, but none of them have been shown to be helpful in distinguishing between bacterial, viral, or a mixed pneumonia.<sup>23</sup> The routine measurement of acute phase reactants in the child with pneumonia is therefore not recommended.<sup>2</sup>

Blood cultures are routinely taken in many hospitals, but they have a low yield for identification of the causal organism(s).<sup>9 16</sup> In addition they take 2–3 days for a positive result and so are not helpful in informing initial antibiotic prescribing. It is not recommended that blood cultures are taken in the community setting, although within the hospital setting the BTS guidelines<sup>2</sup> still recommend that they are performed.

Polymerase chain reaction (PCR) enhances the identification of the pneumococcal organism<sup>9</sup> and mycoplasma. PCR testing is expensive, not widely available, and not rapid enough to affect initial management. The routine use of PCR is currently not recommended, but in the future may provide important evidence of specific aetiology and guide treatment.

Mycoplasma pneumonia remains difficult to diagnose clinically and serologically, therefore treatment is often started empirically. Cold agglutinins seen in mycoplasma infection have been used during the acute phase but have limited value since the positive predictive value is only 70%.<sup>24</sup> The gold standard remains paired serology 14 days apart. The BTS guidelines do not give clear recommendations of when serological tests for mycoplasma should be performed since most children are treated for the disease empirically based on

**Table 4** Indications for admissions to hospital<sup>2 3 25</sup>

- ▶ Oxygen saturation <92% in air
- ▶ RR >70/min in infants, >50/min in older children
- ▶ Signs of severe breathing difficulty; chest wall in-drawings, nasal flaring, grunting, apnoea
- ▶ Feeding less than half normal intake
- ▶ Signs of dehydration

RR, respiratory rate.

**Table 5** Useful investigations in hospital<sup>2 25</sup>

- ▶ Blood cultures if suspected to have bacterial pneumonia
- ▶ Acute serum, and convalescent serum if no diagnosis made during acute illness
- ▶ Nasopharyngeal aspirate in children <18 months
- ▶ If significant pleural fluid present, pleural aspiration

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the clinician's suspicion of the organism being present. Until more evidence is available it is useful for paired samples to be taken in children who are not responding to treatment.

Nasopharyngeal aspirate for viral immunofluorescence and viral antigen detection may be useful in identifying a virus but has little effect on the immediate management of a patient. These tests are highly sensitive and help to identify RSV positive children so that they can be isolated, thereby avoiding infection of other children on the ward. The results of this test are also useful for epidemiological purposes, but it is important to be aware that pneumonia may have a mixed aetiology and may still require antibiotic treatment.

Table 5 provides a summary from the BTS and the Paediatric Accident and Emergency Research Group guidelines<sup>2 25</sup> of investigations useful for children admitted to hospital with suspected pneumonia based on current evidence.

### Radiological diagnosis

The chest x ray (CXR) is still considered to be the gold standard for diagnosing pneumonia in the developed world. However, there is poor concordance between radiologists about what radiological changes constitute pneumonia. An additional problem is the variation in reporting CXRs between radiologists. Davies *et al*<sup>26</sup> studied the CXRs of 40 infants under the age of 6 months admitted with lower respiratory tract infection and showed that there is variation in intra-observer and inter-observer agreement among radiologists. Others have confirmed this.<sup>27</sup> Consolidation on the CXR was most commonly identified by the radiologists and generally agreed to represent pneumonic change.<sup>26</sup>

WHO has recognised the difficulties with CXR interpretation and developed a tool to standardise the reporting of CXR for use in epidemiological studies of pneumonia. This system classifies CXR as normal appearance, infiltrates or end stage consolidation defined as a "significant amount of alveolar type consolidation". So does a normal CXR rule out pneumonia? There is anecdotal evidence for having pneumonia with a normal CXR. Fever and tachypnoea may present before CXR changes are seen. How this is managed will depend on the individual case taking into account factors such as age and length of illness.

Can CXR be used to assess aetiology? In an earlier section, the difficulty with serological diagnosis was highlighted. A similar difficulty arises in trying to use CXR to distinguish aetiology. Swischuk<sup>28</sup> found a 90% accuracy rate overall when trying to differentiate bacterial from viral pneumonia. However, in this study cases were classed as being viral or bacterial on clinical grounds, a system which is known to be flawed. Bettenay<sup>29</sup> found that there was only a 30% chance of isolating a bacteria when the CXR suggested a bacterial cause using the system designed by Swischuk.<sup>28</sup> Thus, although consolidation is reliable for diagnosing pneumonia, it should not be used to assume a bacterial infection. This was

further demonstrated in an aetiology study by Virkki *et al.*<sup>30</sup> In this study, aetiology and radiological changes were assessed in 254 children; only 72% of those with alveolar infiltrates had a bacterial infection. In children with solely viral pneumonia 50% had alveolar changes. Looking at the group with interstitial changes, half had evidence of viral infection and the other half had bacterial infection. This has been confirmed in a systematic review looking at the differentiation between viral and bacterial lower respiratory chest infection.<sup>31</sup>

### When should CXR be performed?

A systematic Cochrane review<sup>31</sup> indicates that there is no evidence to show that performing a CXR in ambulatory children (that is, children not admitted to hospital) aged over 2 months with an acute lower respiratory infection affects outcome and therefore it is not routinely necessary to perform CXR before treatment. In these children the clinician can use clinical signs and symptoms to direct management.

It is unclear which clinical signs should indicate the need for CXR. The available studies which examine the relation between clinical signs and radiological changes give different results, but with the evidence available<sup>32–35</sup> the BTS<sup>2</sup> has concluded that “it is advisable to consider a CXR in a child <5 years with a fever of 39°C of unknown origin unless classical features of bronchiolitis are present”.

The contribution of CXR to management of children admitted to hospital with more severe symptoms is also not clear. CXRs have not been shown to alter management decisions or the time taken to recovery. CXRs are helpful when a complication such as pleural effusion is suspected, or pneumonia is prolonged or unresponsive to antimicrobials.

In summary, CXR is not helpful in determining aetiology and does not contribute to the management of ambulatory children with mild uncomplicated lower respiratory tract illness. CXR to diagnose pneumonia may be helpful in some scenarios as detailed above. Table 6 provides some guidance<sup>2</sup> for clinicians as to which children would benefit from CXR. The guidance is not very specific because of the lack of research in this area.

### TREATMENT

The clinician faces four problems:

- ▶ Whether to treat with antibiotics or not
- ▶ If the decision is to treat, whether to use a narrow or broad spectrum antibiotic
- ▶ Whether to administer the antibiotics via the oral or the intravenous route
- ▶ Whether admission to hospital is required.

There has been only one study addressing the question of whether to treat or withhold antibiotics. Friis *et al.*<sup>36</sup> conducted a prospective randomised controlled trial allocating children with pneumonia to receiving either antibiotics or placebo. No difference was seen between the two groups in

the course of the acute disease or with the development of pulmonary complications. However, 15 of the 64 children in the placebo group went on to receive antibiotics. On the basis of this study the BTS guidelines<sup>2</sup> suggest that young children (no age range given in the guidelines) presenting with mild symptoms of lower respiratory tract infection need not be treated with antibiotics. For all other children antibiotic treatment is warranted, but which antibiotic and by which route is by no means clear. Unfortunately, there exists a paucity of well conducted adequately powered randomised controlled trials comparing the effectiveness of different classes of antimicrobial agents in paediatric pneumonia.

Most children will be able to be treated using oral antibiotics in the community.

Inpatient treatment is required if:

- ▶ there are social concerns about the care of the child or concerns that the child will be given the antibiotics at home
- ▶ the child is vomiting and either requires a trial of oral antibiotics in hospital or intravenous antibiotics if oral preparations are not tolerated
- ▶ the child has signs of severe disease and requires supportive therapy—for example, oxygen
- ▶ the child has severe disease and requires intravenous antibiotics
- ▶ the child needs to be admitted to intensive care or high dependency.

### Which antibiotic?

The choice of antibiotic is largely empirical, based on the most likely organism from aetiology studies while also considering the age of the child. The most common cause of bacterial pneumonia is *S pneumoniae*. Resistance of *S pneumoniae* to penicillin is increasing but overall remains low in the UK (7% according to the Communicable Disease Report UK 2000). The BTS guidelines<sup>2</sup> therefore suggest oral amoxicillin as first line treatment in children < 5 years, with co-amoxiclav, cefaclor, erythromycin, clarithromycin, and azithromycin as alternatives. Recommendations for the treatment of children > 5 years are less clear. The true incidence of mycoplasma, even in the younger age group, is not known and varies widely in aetiology studies, from 2%<sup>17</sup> to 39%.<sup>37</sup> Therefore the use of macrolides either as first line treatment alone or in addition to a penicillin poses a much more difficult question for the clinician. Studies comparing the use of macrolides with other groups of antibiotics as first line treatment have not been able to provide clear recommendations.<sup>38–40</sup> A clinical trial comparing antibiotic treatment options is required.

### Route of administration

There have been no randomised controlled trials to investigate whether children admitted to hospital should be treated with oral or intravenous (iv) antibiotics. The BTS guidelines<sup>2</sup> suggest that iv antibiotics should be reserved for children with severe symptoms or signs or those who are unable to tolerate oral antibiotics. In practice, however, many children deemed unwell enough to be admitted to hospital (for example, who are vomiting or requiring some oxygen) are treated with iv antibiotics irrespective of the severity of their signs or symptoms. The BTS guidelines<sup>2</sup> initially stated that antibiotics administered orally are safe and effective for children presenting with CAP. Following appraisal by the quality of practice committee at the Royal College of

**Table 6** Indications for CXR in either primary care or hospital<sup>2</sup>

- ▶ For diagnosis of child <5 years with fever of 39°C of unknown origin
- ▶ If complication (for example, pleural effusion) suspected
- ▶ Atypical symptoms or unresponsive to treatment
- ▶ For follow up of children with lobar collapse or ongoing symptoms

Paediatrics and Child Health, this statement was amended to “amoxicillin administered orally is effective for children > 6 months who are well enough to be treated without hospital admission”. This is based on a trial comparing the efficacy of one dose of intramuscular penicillin to oral amoxicillin given to children in accident and emergency who were well enough to be discharged home.<sup>41</sup> Results of a multicentre randomised controlled trial comparing oral and iv treatment for children who require admission to hospital should be available later this year.

### Length of treatment

There is currently little research to indicate the most appropriate length of time that a child with CAP should be treated with antibiotics. Oral antibiotics are routinely prescribed for 5–7 days, but treatment duration is increased to 10 days for severe infections (depending on which antibiotic is used). This practice is not based on clinical research and depends on the individual clinician. A multicentre randomised controlled trial has been completed in India,<sup>42</sup> but this study only compared children with “non-severe” pneumonia in the paediatric outpatient department and cases of pneumonia were based on a clinical diagnosis and not confirmed by CXR.

There are no randomised controlled trials in children addressing the issue about when to switch from intravenous antibiotics to oral antibiotics. If the child is clearly improving the clinician makes a judgment that it is safe to transfer to oral antibiotics.<sup>2</sup> Most often this is after 24 hours of intravenous treatment, when the temperature falls and symptoms of breathing difficulty are resolving.

### Complications

Most children with CAP improve without any sequelae. However, a small proportion develop complications which need treating. Table 7 provides a list of complications that may be encountered in children presenting with CAP.

### Follow up

Once the patient has been discharged from hospital, some clinicians arrange follow up x rays at 6–8 weeks. The value of this has been questioned and unless the child continues to be symptomatic or has lobar collapse or “round pneumonia”, it is not recommended.<sup>43 44</sup>

### GUIDELINES

The BTS has published a guideline on the “Management of community acquired pneumonia in childhood”,<sup>2</sup> and the Paediatric Accident and Emergency Research Group by Lakhanpaul *et al*<sup>25</sup> have developed a problem based guideline for “The management of children with breathing difficulty presenting acutely to hospital”. Both are based on a systematic literature review, but emphasise the difficulty with the current investigations available for assessing

**Table 7** Complications of CAP<sup>2</sup>

- ▶ Treatment failure caused by antibiotic resistance
- ▶ Pleural effusion and empyema
- ▶ Lung abscess
- ▶ Septicaemia
- ▶ Metastatic infection—for example, osteomyelitis or septic arthritis

**Table 8** Key recommendations of guidelines<sup>2 25</sup>

- ▶ A child over 2 months old presenting in the community with clinical signs consistent with pneumonia does not require any microbiological or radiological investigation before initiating treatment
- ▶ Despite blood cultures having a low sensitivity it is still recommended that they should be performed on all children admitted to hospital with pneumonia
- ▶ Acute phase reactants do not help distinguish between viral and bacterial pneumonia and should not be measured routinely
- ▶ A child <5 years old presenting to hospital with pyrexia (>39°C) of unknown origin should be considered for a chest radiograph
- ▶ Consolidation is the only reliable sign for the diagnosis of pneumonia
- ▶ There is currently no consensus as to whether all children admitted to hospital with clinically diagnosed pneumonia should have a chest radiograph. In fact, both guidelines highlight the difficulty with clinicians basing their diagnosis on the radiograph
- ▶ Further research is required to develop affordable, specific, and sensitive investigations for the diagnosis of bacterial and viral pneumonia
- ▶ Amoxicillin is the first choice for oral antibiotic treatment in children <5 years old; alternatives are co-amoxiclav, cefaclor, erythromycin, clarithromycin, and azithromycin
- ▶ Because mycoplasma pneumonia is more prevalent in older children, macrolide antibiotics may be used as first line empirical treatment in children aged ≥5 years
- ▶ Amoxicillin administered orally is effective for children >6 months who are well enough to be treated without hospital admission
- ▶ Intravenous antibiotics should be used in the treatment of pneumonia in children when the child is unable to absorb oral antibiotics or presents with severe symptoms and signs

children with pneumonia and highlight the need for further research. The key recommendations of these guidelines are listed in table 8.

### CONTINUING UNCERTAINTY

Reviews of the literature and current clinical guidelines<sup>2 3 25</sup> have identified areas of uncertainty in the management and investigation of children with CAP (table 9). Further research is required to answer the unresolved clinical questions so that clinicians can move further towards practising evidence based medicine.

### CONCLUSIONS

CAP is still a common disease in the developed world. Research is ongoing to identify the most sensitive and specific tools by which to identify the causative organism so that more directed treatment can be used. International travel, the

**Table 9** Areas of continuing uncertainty

- ▶ The most useful clinical signs and symptoms that help to predict a diagnosis of pneumonia
- ▶ Which children require a chest x ray before treatment
- ▶ Which test to detect the causative organism will be sensitive, specific, affordable, and quick and easy to use
- ▶ Which antibiotic should be prescribed
- ▶ Which route should be used for administering the antibiotic prescribed
- ▶ If the intravenous route is used when should a switch to oral antibiotics occur
- ▶ Which children should continue to take low dose prophylactic antibiotics following a diagnosis of pneumonia
- ▶ Whether all children under 2 years should be given the new conjugate pneumococcal vaccine
- ▶ Variation in individual host response to the disease

introduction of new vaccines, and the development of new treatments will all have an impact on the way this disease is managed in years to come.

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