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Paediatric respiratory diseases

Introduction



Key points

- About one-quarter of primary care consultations among children relate to respiratory complaints.
- There is no effective vaccination programme for respiratory syncytial virus, the most common cause of bronchiolitis and lower respiratory tract infections in the first year of life.
- Community-acquired pneumonia is not a serious threat to most children in western Europe but mortality rates are more than 10 times higher in some eastern European countries.
- There are clear differences in infant and childhood mortality from respiratory disease between western, central and eastern Europe.
- Vaccination has markedly decreased the rate of respiratory infections such as pertussis, measles, *Haemophilus influenzae*, and pneumococcus in all European countries.

This chapter covers various respiratory diseases in children, with particular focus on acute infections, perinatal lung disease and bronchopulmonary dysplasia, tuberculosis (TB) and congenital respiratory disorders, and immunisation against the common infections of childhood. Asthma (chapter 12) and cystic fibrosis (chapter 14) in children are covered elsewhere.

In cross-sectional surveys in 1987 and 2001 in the Netherlands, the most frequent reason for children consulting a general practitioner was respiratory morbidity, accounting for about 25% of all consultations by children (figure 1). About 10% of consultations are for asthma, with the other main respiratory diseases being bronchiolitis, acute bronchitis and respiratory infections. Furthermore, a recent US report showed that pneumonia, asthma and acute bronchitis are consistently the three leading diagnoses in children (excluding the newborn) admitted to hospital for any cause. Recent comparable European data are not available but it can be assumed that similar conclusions apply, at least to western European countries. It is also likely that the burden of respiratory disease is even higher in eastern European countries. The Dutch survey also demonstrates that the burden of respiratory morbidity in a western European country fluctuates with time: it depends, for example, on unpredicted epidemics such as Mexican influenza, changes in vaccination programmes, development of antibiotic resistance and variations in climate. It also implies that in children, the cost of first-line care for

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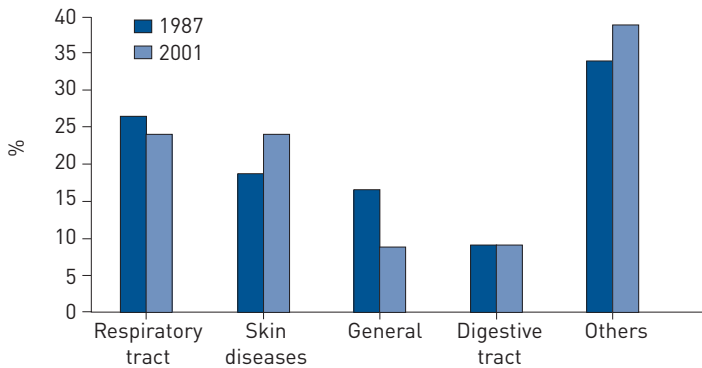


Figure 1 – Consultations for respiratory tract problems, skin diseases, digestive tract diseases, general complaints and other diseases at general practitioners for children in 1987 and 2001. Reproduced and modified from OTTERS *et al.*, 2005, with permission from the publisher.

respiratory tract problems, together with skin conditions, represents about half of the total costs of first-line healthcare.

Acute bronchiolitis

Bronchiolitis is usually the result of viral inflammation of the very small airways (bronchioles). In affected children of less than 2 years of age it is characterised by rapid breathing, chest retraction and wheezing.

Respiratory syncytial virus (RSV) infection is the most important cause of bronchiolitis and other lower respiratory tract infections during the first year of life, and is also one of the major causes of hospital admissions in infants under 1 year of age. Affected children characteristically present with symptoms of a viral infection with mild rhinorrhoea, cough, and, on occasion, a low-grade fever. Within 1 or 2 days, these symptoms are followed by rapid respiration, chest retraction and wheezing. The infant may be irritable, feeding poorly and vomiting. Other causative viruses for bronchiolitis are human meta-pneumovirus, rhinovirus, adenovirus and influenza virus. Prevalence studies have shown that up to 50% of infants are infected by RSV by their first birthday and almost 100% by 2 years of age, with the highest prevalence during the winter. In the first year of life, the hospitalisation rate for RSV infection, *i.e.* bronchiolitis, has been reported to be 1–2% of all infants and 10–15% in high-risk infants. Intensive care admissions for bronchiolitis are high, as recently reported in a retrospective study in

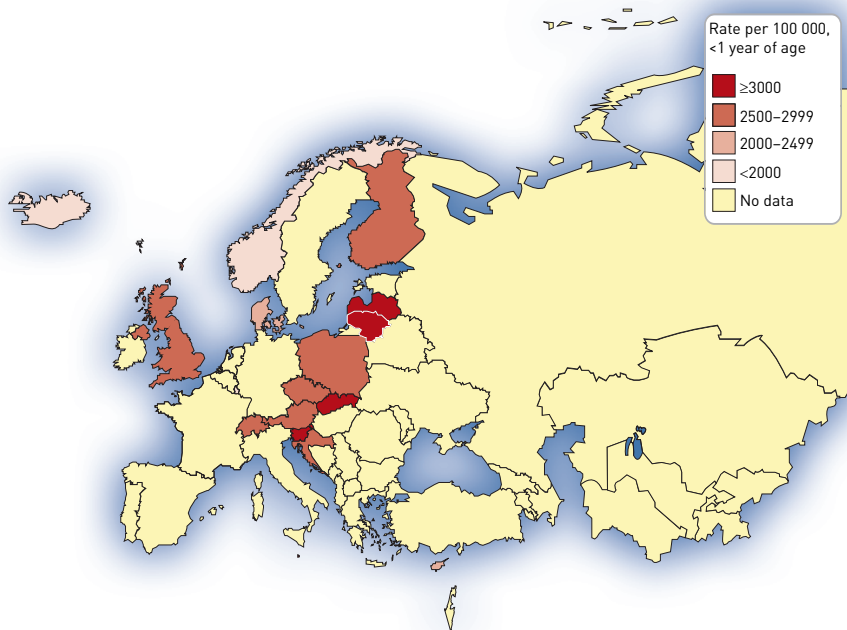


Figure 2 – Hospital admission rates for acute bronchitis and bronchiolitis in infants. Data from the World Health Organization Hospital Morbidity Database, October 2011 update.

France of 467 children admitted to 24 paediatric intensive care units (PICUs); 75% were aged less than 2 months, 76% had positive RSV tests and about one-third required noninvasive and/or mechanical ventilation. Six of the infants died. More than 50% of the neonates had a predisposing condition such as prematurity, respiratory disease including bronchopulmonary dysplasia (BPD) and congenital heart disease.

Hospital admission rates for acute bronchitis and bronchiolitis combined in children less than 1 year of age vary between countries and are particularly high in the Baltic states (Lithuania and Latvia), Finland, and the UK. For most European countries, however, this information is not available (figure 2).

Mortality from bronchitis and bronchiolitis in western Europe is generally low, but in many countries in eastern Europe, mortality rates for these diseases are unexpectedly and alarmingly high, as shown in figure 3.

The development of a vaccine to prevent RSV bronchiolitis has thus far not been successful. Furthermore, it is unclear how early in life such a vaccine should be administered. It is reasonable to assume that an RSV vaccination programme would have to start before the conventional vaccination programme against common childhood infections, *i.e.* before the age of 2 months.

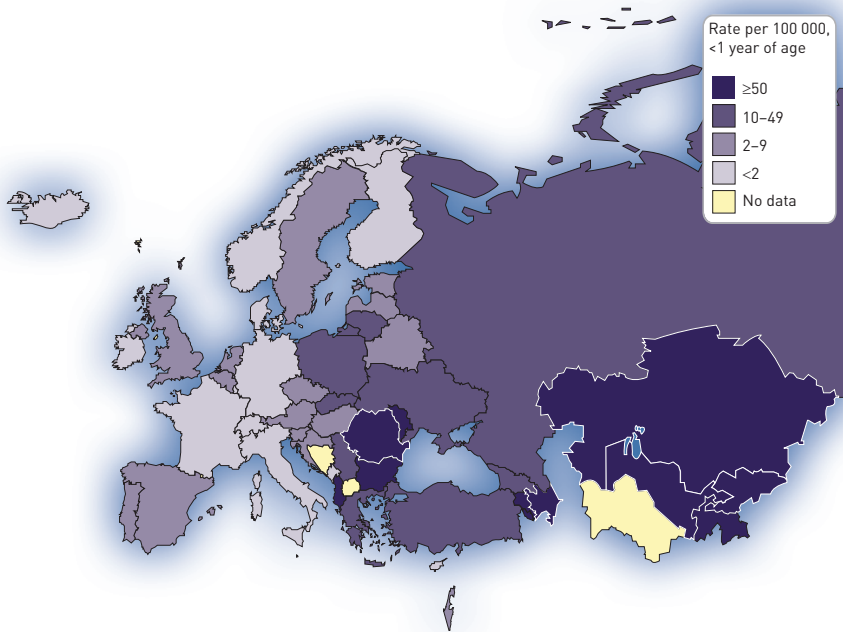


Figure 3 – Mortality rate for acute bronchitis, bronchiolitis and pneumonia combined in infants. Data from the World Health Organization World and Europe Mortality Databases, November 2011 update.

The monoclonal antibody palivizumab has been proven to reduce severe RSV infections in high-risk infants and protection appears to extend beyond the current monthly dosing. However, studies indicate that its cost-effectiveness is low. The high costs of prophylaxis with palivizumab mean it is not available in many European and low-income countries.

It is important that a reliable and highly effective vaccine and a prevention programme becomes available in the future, especially for high-risk infants. A reduction of the number of deaths due to failure of therapy in bronchiolitis, especially in eastern European countries, should be the aim of future European health programmes.

Perinatal respiratory diseases and BPD

The perinatal period, *i.e.* the period from birth (and especially premature birth) to the 28th day of life, is the period of greatest mortality. Pre-term birth is the major determinant of neonatal mortality and morbidity. In the modern era, with survival of extremely premature infants (gestational age of ≤ 26 weeks) and low-birthweight infants, post-neonatal mortality contributes significantly to the infant mortality rate.

In a US survey in 2002, the neonatal mortality rate was 6.9 per 1000 babies born at 35–36 weeks, 18.5% in babies born at 30–34 weeks, and 28.5% among babies born at < 30 weeks. In a recent follow-up of 100 infants born at 23 weeks, 60 died prior to hospital discharge, most from respiratory failure. There is an increasing trend to initiate resuscitation and treatment at an earlier gestational age; however, it is concerning that this results in an increasing proportion of children with long-term respiratory and/or neurological impairment.

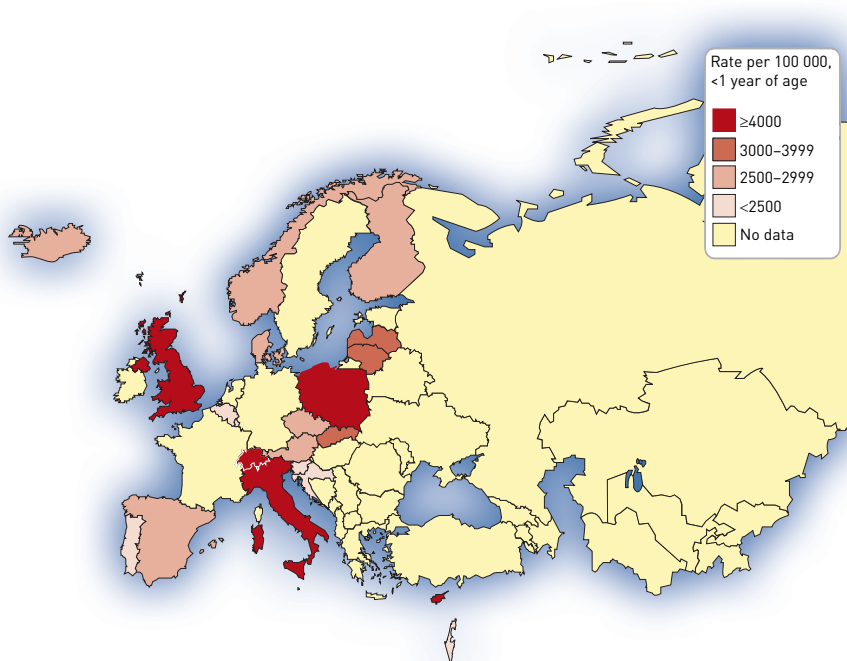


Figure 4 – Hospital admission rate for perinatal respiratory disorders in infants. Data from the World Health Organization Hospital Morbidity Database, October 2011 update.

Hospital admission rates for perinatal respiratory disorders are presented in figure 4. It is unfortunate that data are not available from all countries, but it can be expected that, as in Switzerland, the UK, Italy, Poland and Cyprus, rates will increase across Europe and worldwide owing to the trend to start treatment at an earlier gestational age.

Another concern is the number of perinatal deaths in Europe (figure 5). Differences between western, central and eastern Europe are clearly apparent and may reflect variation in the quality of care available for these children. Also, more advanced equipment and expensive medication, such as surfactant, may not be available in some countries, whose health and budgetary priorities differ from those of western Europe.

One important long-term consequence of prematurity is BPD, or chronic lung disease of prematurity (CLD). This can be defined as oxygen dependency at 36 post-menstrual weeks. It is one of the most important complications of prematurity, with a reported incidence of 23% of infants born at 28 weeks, increasing to 73% of infants born at 23 weeks. It is characterised by prolonged respiratory support, compromised lung function and recurrent respiratory infections during the first year of life. Furthermore, BPD is considered an independent risk for and is associated with neurodevelopmental impairment.

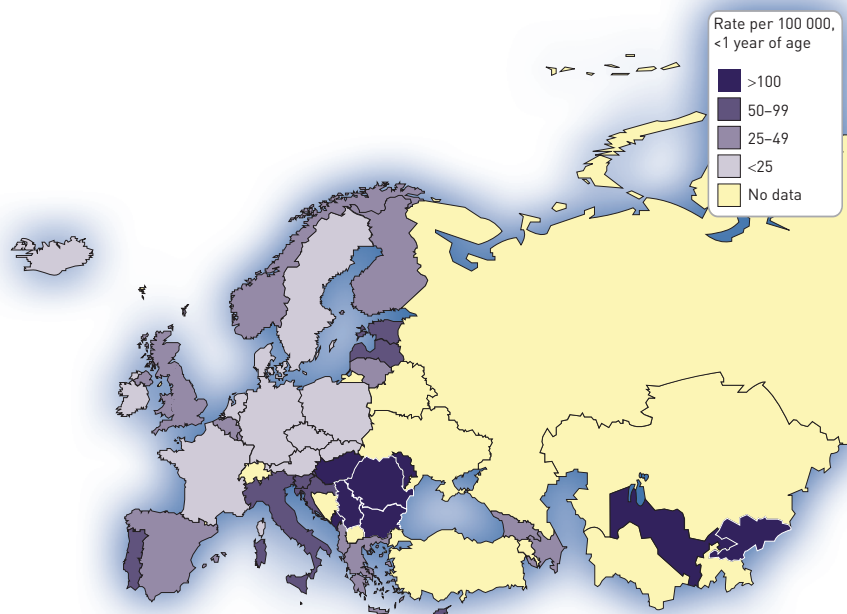


Figure 5 – Mortality rate for perinatal respiratory disorders in infants. Data from the World Health Organization World and Europe Detailed Mortality Databases, November 2011 update.

Overall, therefore, there is concern about both the short- and long-term respiratory, but also developmental, consequences of treatment of very premature children. Attention needs to be paid to developing new and effective medication for children born with immature lungs. Until now, treatment for BPD has not been effective. There is a particular need to focus on the improvement of care for premature infants with these conditions in central and eastern Europe. Although lung function in children with BPD improves with age, impairment of lung function persists into adulthood, with impaired exercise capacity, airflow limitation and airway hyperreactivity. One has to take into account that these measurements are only available in children who are able to perform lung function tests. Since only limited data about the burden and the long-term effects of prematurity and BPD are available, the development of a European databank to study the costs, the cost-effectiveness and the long-term effects of treatment of these infants should be a priority so that information is available about the number of infants with BPD in each country and the long-term effects of extreme prematurity. In addition, guidelines for the treatment of these infants are needed, perhaps developed in conjunction with health organisations in other continents.

Severe community-acquired pneumonia in children

Community-acquired pneumonia (CAP) is common among children all over the world, but its incidence and mortality rate are significantly higher in developing countries than in the industrialised world. It is estimated that about 151 million new episodes a year occur among children < 5 years of age in the developing world, with an incidence of 0.29 episodes per child-year and a mortality rate of 1.3–2.6%, or a mortality rate of > 2 million per year. In industrialised countries, the total number of new episodes

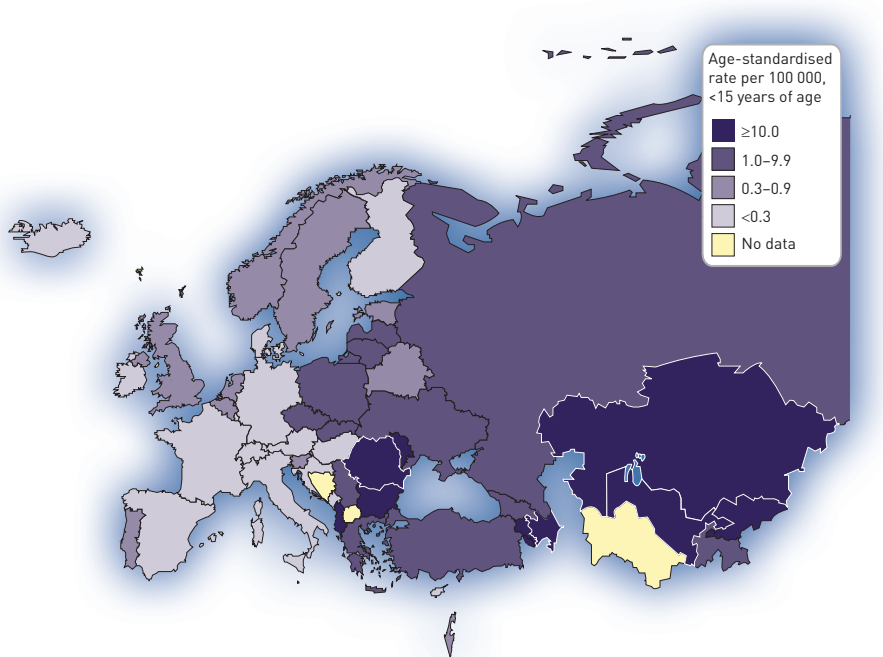


Figure 6 – Mortality rate for pneumonia in children. Data from the World Health Organization World and Europe Mortality Databases, November 2011 update.

in the same age group is about 4 million (an incidence of 0.05 episodes per child-year), with an extremely low risk of mortality in otherwise healthy children. In the industrialised world, CAP mortality is a relatively important risk only in subjects with severe chronic underlying diseases.

Global variation in CAP prevalence and mortality results from a number of factors, including malnutrition, crowding, low birthweight, pre-existing HIV infection, the effectiveness of immunisation programmes (especially pneumococcal and *Haemophilus influenzae* immunisation) and variation in the incidence of measles.

Mortality rates vary considerably within Europe, and are highest in eastern European countries (figure 6).

The reasons for these differences within Europe are not clear, but they may include variations in the number of HIV-infected children and other underlying disease such as TB, as well as the presence of multidrug-resistant bacteria, poor immunisation rates and/or admission to hospital at a late stage of the disease.

In the future, it is important to identify and register the causes of the differences in mortality rates between European countries, and to set up an intervention programme.

Tuberculosis in children

Childhood TB has been neglected for decades and has long been an overlooked area within global TB control. Poor ascertainment and reporting of cases of TB prevent accurate estimation of the European burden of disease in children.

TB in children most commonly results from household contact with someone with active TB, and represents ongoing transmission of *Mycobacterium tuberculosis* in the community. Infants and young children have an increased risk of infection following exposure and progress more readily from infection to active TB. In the absence of intervention, infants have a 50–60% risk of disease in the first year following infection. Young children more commonly present with disseminated disease and miliary TB and have an increased risk of death. Even low bacillary loads in children can lead to acute and severe illness, be it respiratory or disseminated; this is particularly the case in children less than 2 years of age. The generally accepted assumption is that qualitative and quantitative differences in the immune responses to mycobacterial infection between adults and children determine the outcome.

The total number of childhood TB cases in Europe in 2010 was about 11 000, with 3365 reported cases in children aged 0–4 years and 7549 reported cases in children from 5–15 years. The proportion of TB cases differs greatly between western and eastern European countries. The proportions of children with TB in eastern Europe aged 0–4 years and 5–15 years are expected to be two and four times higher, respectively, than those in western Europe.

The geographical distribution of TB in children is presented in figure 7.

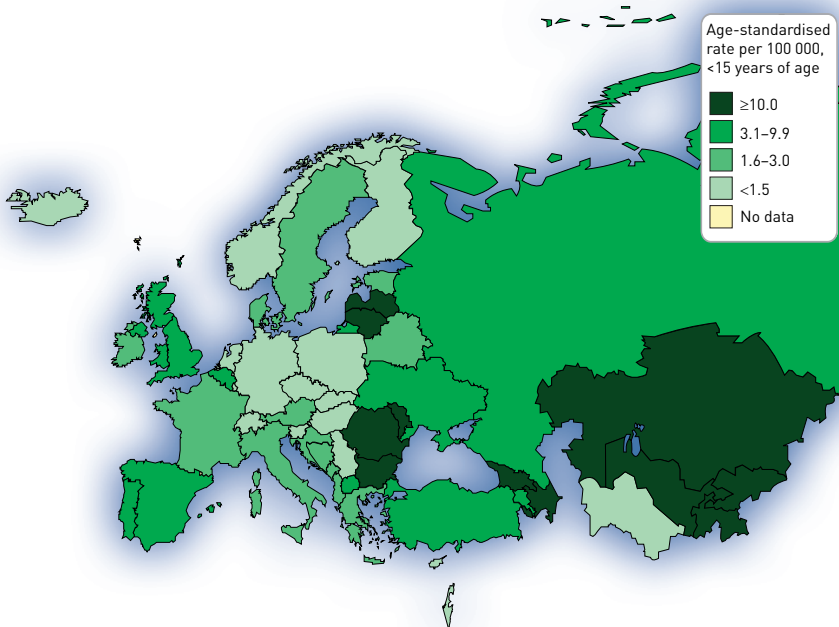


Figure 7 – Tuberculosis cases in children, notified in 2010. Data from European Centre for Disease Prevention and Control, 2012.



The exact number of children with TB in eastern European countries is not known, but of greater concern is the lack of information regarding multidrug-resistant (MDR) and extensively drug-resistant (XDR) cases in children in Europe. Outside Europe, the highest rates of paediatric MDR-TB are reported in low-income countries and in some regions the incidence of MDR-TB has risen sharply in the past two decades. For instance, in Western Cape, South Africa, the proportion of culture-confirmed cases of MDR-TB has tripled in the past 15 years from 2.3% to 7.3% of all TB cases.

Given the overwhelming burden of TB and the vulnerability of young children to active TB disease, it is surprising that TB does not feature among the leading causes of death in children. The explanation might be the protection afforded by the bacille Calmette–Guérin (BCG) vaccination, although the protective efficacy of BCG is suboptimal.

Confirmation of the diagnosis of TB in children may be difficult, since collecting specimens of spontaneously produced sputum is problematic, although gastric aspiration and sputum induction (with or without laryngopharyngeal suction) are feasible alternative methods of collection. The tuberculin test and the interferon- γ release assay fail to differentiate *M. tuberculosis* infection from active disease, especially in vaccinated children. When a combination of clinical, radiological, laboratory and histopathological findings are consistent with a diagnosis of TB and there is epidemiological evidence of exposure to TB, an accurate diagnosis is possible in most cases.

In the future, better and more simple diagnostic tests must be developed to enable a rapid and 100% reliable diagnosis of TB. Furthermore, information on the prevalence and incidence of TB, MDR-TB and XDR-TB in children is urgently required for the whole European continent.

More information on TB can be found in chapter 17.

Immunisation

Immunisation programmes are very effective in preventing childhood respiratory infections and, depending on the country in question, usually have a coverage of about 90%. The number of cases of infections included in the immunisation schedule, such as pertussis, measles, *H. influenzae*, and pneumococcus, has decreased considerably over the past 20 years in all European countries.

Pertussis, or whooping cough, is an acute respiratory infection caused by the bacterium *Bordetella pertussis*. It is

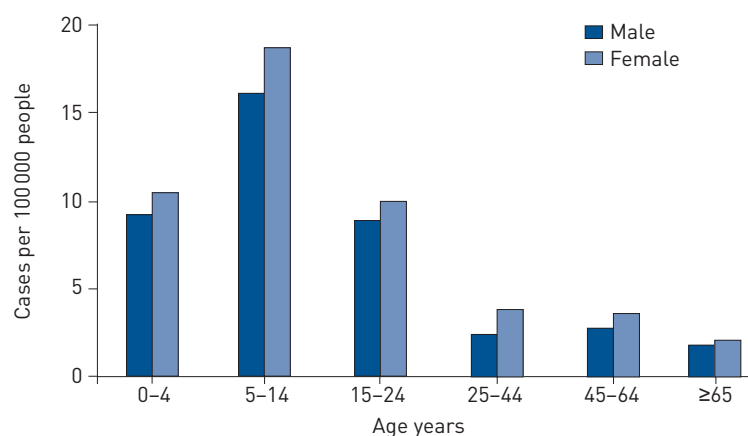


Figure 8 – Rates of reported confirmed pertussis cases, by age and sex in European Economic Area countries, 2009. Reproduced and modified from European Centre for Disease Prevention and Control, 2011.

an endemic infection common to children everywhere and is included in the primary immunisation schedule of all European Union countries. It is often unrecognised, and increasingly may occur in adults. After immunisation, the symptoms of pertussis are mostly mild and result in a prolonged period of coughing (weeks to months). However, in neonates, pertussis can be life-threatening and can result in prolonged periods of intensive care.

Despite the high immunisation coverage, cycles of outbreaks of pertussis have continued to occur, because neither infection nor immunisation produces lifelong immunity to pertussis, in the same way that they do for diseases such as measles. *B. pertussis* continues to circulate in a manner similar to that of the pre-vaccine era. Outbreaks have been reported in all European countries, especially in infants and children (figure 8). Urgent requirements are: the development of vaccines resulting in lifelong immunity; a focus on public awareness of the symptoms of the disease and the danger of contagion, especially in relation to contact with newborns.

Measles is an acute illness caused by the measles virus of the genus *Morbillivirus*. It is one of the most contagious diseases, and clusters and outbreaks of the disease are common. Infection can cause significant disability and death. One of the most common and serious complications is measles pneumonia, which develops in 5–10% of children with measles. It is caused by direct invasion of the lungs by the measles virus (primary measles pneumonia) or may occur due to a secondary infection by other viral or bacterial pathogens.

More information on immunisation can be found in chapter 26.

Congenital respiratory disorders

The incidence of congenital disorders of the respiratory tract is low and their effects are particularly seen during the first year of life. Congenital disorders can be subdivided into abnormalities of the thorax, specifically the diaphragm (hernia of the diaphragm), the lung (lung sequestration, cystic adenomatoid malformation, bronchogenic cyst, foregut cyst), the blood supply (aberrant vascularisation, double arch of the aorta), the airways (tracheal rings, tracheomalacia, tracheal atresia) and the larynx and oral cavity. Investigation and management of these diseases is usually organised in specialised centres.

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Primary ciliary dyskinesia is an inherited disorder characterised by specific ultrastructural defects of cilia that are associated with impaired ciliary motion and mucociliary clearance. It results in ineffective clearance of mucous secretions and inhaled particles, including bacteria. The disease is characterised by recurrent or persistent rhinitis, sinusitis, otitis media and bronchitis. The predominant pulmonary complication is bronchiectasis (see chapter 15). The incidence of the disease is low and often the diagnosis is difficult to assess. Therefore, both diagnosis and treatment should be organised in experienced centres.

In general, children with congenital respiratory disorders should be admitted to a specialised centre at an early stage as prompt assessment and, if necessary, treatment, are often important in determining survival.

General remarks

Most childhood respiratory diseases have a high morbidity and/or mortality and healthcare needs to become more focused on these diseases. It is concerning that there are huge differences between European countries. The European Union should move to address these differences and should also pay attention to the increasing burden of respiratory disease caused by prematurity across all countries.

Further reading



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