

Therapeutic Advances in Respiratory Disease

<http://tar.sagepub.com/>

Long-term respiratory outcome of babies born prematurely

Kamal Ali and Anne Greenough

Ther Adv Respir Dis published online 9 February 2012

DOI: 10.1177/1753465812436803

The online version of this article can be found at:

<http://tar.sagepub.com/content/early/2012/02/09/1753465812436803>

Published by:



<http://www.sagepublications.com>

Additional services and information for *Therapeutic Advances in Respiratory Disease* can be found at:

Email Alerts: <http://tar.sagepub.com/cgi/alerts>

Subscriptions: <http://tar.sagepub.com/subscriptions>

Reprints: <http://www.sagepub.com/journalsReprints.nav>

Permissions: <http://www.sagepub.com/journalsPermissions.nav>

>> [OnlineFirst Version of Record](#) - Feb 9, 2012

[What is This?](#)

Long-term respiratory outcome of babies born prematurely

Kamal Ali and Anne Greenough

Abstract: Chronic respiratory morbidity is a common adverse outcome of premature birth, particularly in infants who develop bronchopulmonary dysplasia (BPD). Prematurely born infants who had BPD may require supplementary oxygen at home for many months, but few remain oxygen dependent beyond 2 years of age. Readmission to hospital is common, particularly for those who had BPD, but only in the first 2 years after birth. The readmissions are usually for respiratory problems, particularly respiratory syncytial virus lower respiratory infections. Recurrent respiratory symptoms requiring treatment are common, particularly in those who had BPD, even at school age and in adolescence. Affected children have evidence of airways obstruction. Pulmonary function does improve with age, but children with BPD may have ongoing airflow limitation. Computed tomography of the chest gives helpful information at follow up of patients with ongoing respiratory problems who had BPD.

Keywords: bronchopulmonary dysplasia, prematurity, respiratory syncytial virus

Introduction

Chronic respiratory morbidity is a common adverse outcome of premature birth, particularly in infants who developed bronchopulmonary dysplasia (BPD).

BPD occurs most frequently in infants born very immaturely and of very low birthweight. Forty-one per cent of infants born before 29 weeks of gestation from the UK Oscillation Study (UKOS) developed BPD defined as oxygen dependency beyond 36 weeks postmenstrual age (PMA) irrespective of the mode of ventilation used in the newborn period [Johnson *et al.* 2002] and in another series 22% of infants with birth weights of between 501 and 1500 g were affected using the same definition [Fanaroff *et al.* 2007]. The differences in BPD incidence between the two populations likely reflect the inclusion of larger birth weights and, therefore, less at risk infants, in the second series [Fanaroff *et al.* 2007]. The diagnosis of BPD is based on the need for supplementary oxygen beyond 28 days after birth [Jobe and Bancalari, 2001] and, for infants born at gestational ages of less than 32 weeks, the severity of BPD is graded according to the level of respiratory support required at 36 weeks PMA [Jobe and Bancalari, 2001].

Northway first described 'classical' BPD in 1967 in a group of relatively mature infants following severe respiratory failure in the neonatal period and, at postmortem, fibrosis and airway smooth muscle hypertrophy were prominent [Northway *et al.* 1967]. Nowadays, BPD occurs commonly in very prematurely born infants who may have had minimal or even no initial respiratory distress, the airways are spared and inflammation is less prominent [Coalson, 2006]; this has been called 'new' BPD. It has been suggested that new BPD is mainly a developmental disorder in which the lungs fail to reach full structural complexity and there is reduction of the surface area for gas exchange [Jobe, 1999]. This review describes the long-term respiratory outcomes of prematurely born infants, particularly those who developed BPD.

Supplementary oxygen at home

Prematurely born infants who had BPD may require supplementary oxygen at home (home oxygen) for many months. However, there is usually progressive improvement in pulmonary function such that few infants remain oxygen dependent beyond 2 years of age [Greenough *et al.* 2006]. Although use of home oxygen allows

Ther Adv Respir Dis

[2012] 0(0) 1–6

DOI: 10.1177/

1753465812436803

© The Author(s), 2012.

Reprints and permissions:

[http://www.sagepub.co.uk/](http://www.sagepub.co.uk/journalsPermissions.nav)

[journalsPermissions.nav](http://www.sagepub.co.uk/journalsPermissions.nav)

Correspondence to:

Anne Greenough, MD

Neonatal Intensive Care
Centre, 4th Floor Golden
Jubilee Wing, King's
College Hospital, Denmark
Hill, London SE5 9RS, UK
anne.greenough@kcl.ac.uk

Kamal Ali, MBBS

Division of Asthma, Allergy
and Lung Biology, The
MRC & Asthma UK Centre
in Allergic Mechanisms
of Asthma, King's College
London, UK

infants to be discharged earlier from the neonatal unit, it can adversely impact on the quality of life of their families [McLean *et al.* 2000]. Infants can be discharged even earlier on home oxygen if there is support in the community for them to also be nasogastrically fed. Such a policy has not been associated with an increase in re-hospitalization, but rather with a reduced total health-related cost of care due, on average, to 2 weeks less neonatal unit stay [Greenough *et al.* 2004b]. Nevertheless, overall, infants who require home oxygen compared with other infants who had BPD require twice the number of hospital readmissions in the first 2 years [Greenough *et al.* 2002] and at preschool age they have more outpatient attendances, are more likely to wheeze and require an inhaler [Greenough *et al.* 2006]. Even at school age, those who required home oxygen only during the first 2 years have greater respiratory-related outpatient attendances than infants who did not require home oxygen [Greenough *et al.* 2011]. The greater healthcare utilization of infants who had BPD and require home oxygen is likely due to the greater severity of their respiratory illness, but it is important that appropriate planning is made for the follow-up of such patients, even when they no longer require home oxygen.

Rehospitalization

Readmission to hospital in the first 2 years is common in prematurely born infants, particularly for those with BPD. In one series, 73% of infants with BPD required at least one readmission and 27% had three or more readmissions [Greenough *et al.* 2001]. The majority of admissions are for respiratory disorders and rehospitalization is particularly increased in infants who have a respiratory syncytial virus (RSV) lower respiratory tract infection [Broughton *et al.* 2005]. Amongst 159 prematurely born infants who were prospectively followed in the first year after birth, BPD, younger gestation and lower birth weight significantly increased the risk of hospitalization with RSV infection [Drysdale *et al.* 2011]. Hospitalization rates decline after the second year [Greenough *et al.* 2004a] and were found to be infrequent in 14-year-old children born prematurely, regardless of their BPD status [Doyle *et al.* 2001]. In a population-based case-control study, however, adults aged between 18 and 27, with a history of very low birth weight or moderately low birth weight, were at increased risk of hospitalization

for respiratory illness. The odds ratio for hospitalization for respiratory illness was 1.83 for very low birth weight [95% confidence interval (CI) 1.28–2.62; $p = 0.001$] and 1.34 for moderately low birth weight (95% CI 1.17–1.53; $p < 0.0005$) [Walter *et al.* 2009].

Respiratory symptoms

Recurrent respiratory symptoms are common in prematurely born children, particularly those who had BPD. Follow up of 492 of infants born before 29 weeks of gestation from the UKOS highlighted that 27% were coughing and 20% wheezing at 6 and 12 months [Greenough *et al.* 2005b]. Risk factors for increased respiratory morbidity were BPD, male gender, having older siblings aged less than 5 years and living in rented accommodation [Greenough *et al.* 2005b]. In another series, 47 of 224 infants born prematurely wheezed in the first year after birth compared with 18 of 224 infants born at term [Koivisto *et al.* 2005]. It is not just very prematurely born infants or those who developed BPD who are at increased risk of respiratory morbidity in infancy. In a study which monitored infants born between 34 and 42 weeks of gestation from birth to 18 months, those born between 34 and 36 weeks of gestation had significant increases in a persistent asthma diagnosis [adjusted odds ratio (aOR) 1.66] and numbers of acute respiratory visits (aOR 1.44) [Goyal *et al.* 2011].

Respiratory symptoms remain common at pre-school age. In a cohort of 190 patients with BPD, 28% coughed more than once a week and 7% wheezed more than once a week [Greenough *et al.* 2006]. A greater proportion of those who required home oxygen wheezed, wheezed more than once a week and used inhaler medications [Greenough *et al.* 2006]. At school age, prematurely born children, particularly if they had BPD, are more likely to be symptomatic than their classroom colleagues born at term. Twenty-five per cent of 11 year olds born at or less than 25 completed weeks of gestation had a diagnosis of asthma which was twice that reported in classmate controls [Fawke *et al.* 2010]. Northway and colleagues reported more wheezing, episodes of pneumonia and long-term medication use in young adults who survived BPD than in controls [Northway *et al.* 1990]. However, it is not only those who had BPD who are more likely to be symptomatic as adults. In another series, 27% of prematurely born young adults with a median age of 21.7 years had cough or wheeze

compared with only 8% of controls [Narang *et al.* 2008].

Lung function at follow up

Significantly lower lung volumes at 36 weeks PMA have been reported in chronically oxygen-dependent infants compared with similarly aged prematurely born infants without BPD and term born infants [Greenough *et al.* 2005a]. It is possible that those results were due to poor gas mixing resulting in an underestimation of the lung volumes because a helium gas dilution technique was used. However, the results could also be explained by abnormal antenatal lung growth. Prematurely born infants, particularly those who were symptomatic, have been demonstrated to have evidence of airways obstruction (high airways resistance and gas trapping) in the first 2 years after birth [Yuksel and Greenough, 1991]. In the present population of very prematurely born infants similar abnormalities have been reported and the number of days of wheeze significantly correlated with the degree of gas trapping [Broughton *et al.* 2007]. Lung function abnormalities, however, are not restricted to infants born very prematurely, as a group of healthy infants born at 32–34 weeks of gestation and without respiratory complications were shown to have decreased forced expiratory flows at 2 months of age [Friedrich *et al.* 2006]. Worryingly, longitudinal measurements of forced expiratory flows by the raised volume rapid thoracic compression technique obtained in the first and second year after birth in infants born between 30 and 34 weeks of gestation demonstrated persistently reduced flows in the presence of normal forced vital capacity and the absence of catch up growth in airway function [Friedrich *et al.* 2007].

Small airway function in infants who had BPD with a mean birthweight of 850 g was reported to deteriorate between 6 and 12 months of age, but only in those who had been supported by conventional ventilation in the neonatal period [Hofhuis *et al.* 2002]. Use of high-frequency oscillation ventilation (HFOV) compared with conventional ventilation was associated with a smaller decline in lung function over the time period. The allocation of ventilation mode, however, was not randomized, but the infants who received HFOV had more severe lung disease and might have been expected to have the worse outcome. Follow up at school age of infants entered in to the UKOS

study [Johnson *et al.* 2002] is currently underway to determine whether HFOV might protect small airway function. Inhaled nitric oxide given in a randomized trial to prematurely born infants with severe respiratory failure, however, was not associated with better lung function at follow up [Hoo *et al.* 2009].

Pulmonary function does improve with age but at 2 years of age BPD survivors were reported to still have airway function impairment, lower forced expiratory flows [maximal flow at functional respiratory capacity ($V_{\max}$ FRC)] with individual values below 40% of predicted values in 70% of the children [Baraldi *et al.* 1997]. A significant correlation between $V_{\max}$ FRC at 2 years of age and the forced expiratory volume in 1 s at school age (mean age 8.8 years) was reported and suggests children with BPD may suffer ongoing airflow limitation [Filippone *et al.* 2003]. Other follow-up studies indicate air flow obstruction may persist [Lum *et al.* 2011; Baraldi and Filippone, 2007]. Follow up from the EPICURE study demonstrated that, at 11 years of age, 56% of children born at or less than 25 completed weeks of gestation had abnormal baseline spirometry and 27% had a positive bronchodilator response, the abnormalities being most marked in those with prior BPD [Fawke *et al.* 2010]. A study of young adolescents reported that those of very low birth weight had reduced forced expiratory flow at 25–75 of the forced vital capacity (FEF_{25-75}), suggesting distal airflow obstruction compared with controls [Anand *et al.* 2003]; the association was with premature birth rather than low birthweight, the level of respiratory support or BPD. Doyle and colleagues reported that those who had had BPD had airflow limitation in late adolescence, and worryingly, the airflow limitation had worsened between 8 and 18 years [Doyle *et al.* 2006]. Even in young adulthood, evidence of airways obstruction has been found in those who suffered severe BPD, 52% had reactive airway disease as evidenced by a positive response to bronchodilator or metacholine and 24% had fixed airway obstruction [Northway *et al.* 1990]. Prematurely born school children [Hakulinen *et al.* 1996] and young adults [Vrijlandt *et al.* 2006] have also been shown to have reduced diffusing capacities compared with term born controls. A recent study highlighted that infants and toddlers with chronic lung disease in infancy have decreased pulmonary diffusing capacity, but normal alveolar volume, suggesting an impairment of alveolar development after very premature birth [Balinotti *et al.* 2010].

Pulmonary abnormalities on imaging

The severe chest radiograph abnormalities described in infants with classical BPD are now uncommon. Nevertheless, a review of chest radiographs taken at 28 days and 36 weeks PMA from 60 infants born prior to 29 weeks of gestation revealed that only three were without abnormalities [Greenough *et al.* 2000]. Interstitial changes and hyperinflation but not cystic abnormalities were common [Greenough *et al.* 2000]. The presence of interstitial abnormalities at 28 days and 36 weeks PMA was predictive of wheeze in the first 6 months after birth [Thomas *et al.* 2003].

Computed tomography (CT) of the chest may give useful information at follow up of patients who had BPD with ongoing respiratory problems. The CT scans of the chest at follow up of children and young adults who had BPD demonstrate the majority have abnormalities. In one series, all 23 children with a mean age of 4 years had an abnormal CT scan appearance with multifocal areas of hyperaeration, linear opacities and triangular subpleural opacities [Oppenheim *et al.* 1994]. Eighty-six percent of patients born prior to 28 weeks of age or with a birth weight equal to or less than 1000 g studied at 10 or 18 years had lung parenchymal abnormalities on CT scan [Aukland *et al.* 2009]. A prolonged neonatal requirement for oxygen treatment predicted poor outcome and there was a positive association of the severity of pulmonary function test abnormalities and the extent of the CT abnormalities [Aukland *et al.* 2009]. Abnormalities on CT scan in young adults who had had BPD were reduced lung attenuation, bronchial wall thickening and decreased bronchus to pulmonary artery diameter ratio [Howling *et al.* 2000]. Emphysematous changes in young adults who had severe BPD have been reported [Wong *et al.* 2008]. Interestingly, however, some of the some individuals with markedly abnormal CT scan appearances had normal lung function test results and minimal respiratory symptoms. CT changes in 41 infants with BPD aged between 10 and 20 months born in the era of the new BPD were found to be similar to those described in older children born in the presurfactant era [Mahut *et al.* 2007]. New advances in magnetic resonance imaging techniques, including the use of arterial spin labelling and hyperpolarized gas [Hopkins *et al.* 2007], may help to provide useful functional information about lung ventilation and perfusion [Wilson, 2010].

Acknowledgement

We thank Mrs Deirdre Gibbons for secretarial assistance.

Funding

Dr Kamal Ali was supported by the King's College Hospital Research Initiative Grant.

Conflict of interest statement

The authors declare no conflicts of interest in preparing this article.

References

- Anand, D., Stevenson, C.J., West, C.R. and Pharoah, P.O. (2003) Lung function and respiratory health in adolescents of very low birth weight. *Arch Dis Child* 88: 135–138.
- Aukland, S.M., Rosedahl, K., Owens, C.M., Fosse, K.R., Eide, G.E. and Halvorsen, T. (2009) Neonatal bronchopulmonary dysplasia predicts abnormal pulmonary HRCT scans in long-term survivors of extreme preterm birth. *Thorax* 64: 405–410.
- Balinotti, J.E., Chakr, V.C., Tiller, C., Kimmel, R., Coates, C., Kisling, J. *et al.* (2010) Growth of lung parenchyma in infants and toddlers with chronic lung disease of infancy. *Am J Respir Crit Care Med* 181: 1093–1097.
- Baraldi, E. and Filippone, M. (2007) Chronic lung disease after premature birth. *N Engl J Med* 357: 1946–1955.
- Baraldi, E., Filippone, M., Trevisanuto, D., Zanardo, V., and Zacchello, F. (1997) Pulmonary function until two years of life in infants with bronchopulmonary dysplasia. *Am J Respir Crit Care Med* 155: 149–155.
- Broughton, S., Roberts, A., Fox, G., Pollina, E., Zuckerman, M., Chaudhry, S. *et al.* (2005) Prospective study of healthcare utilisation and respiratory morbidity due to RSV infection in prematurely born infants. *Thorax* 60: 1039–1044.
- Broughton, S., Thomas, M.R., Marston, L., Calvert, S.A., Marlow, N., Peacock, J.L. *et al.* (2007) Very prematurely born infants wheezing at follow-up: lung function and risk factors. *Arch Dis Child* 92: 776–780.
- Coalson, J.J. (2006) Pathology of bronchopulmonary dysplasia. *Semin Perinatol* 30: 179–184.
- Doyle, L.W., Cheung, M.M., Ford, G.W., Olinsky, A., Davis, N.M. and Callanan, C. (2001) Birth weight <1501 g and respiratory health at age 14. *Arch Dis Child* 84: 40–44.
- Doyle, L.W., Faber, B., Callanan, C., Freezer, N., Ford, G.W. and Davis, N.M. (2006)

- Bronchopulmonary dysplasia in very low birth weight subjects and lung function in late adolescence. *Pediatrics* 118: 108–113.
- Drysdale, S.B., Wilson, T., Alcazar, M., Broughton, S., Zuckerman, M., Smith, M. *et al.* (2011) Lung function prior to viral lower respiratory tract infections in prematurely born infants. *Thorax* 66: 468–473.
- Fanaroff, A.A., Stoll, B.J., Wright, L.L., Carlo, W.A., Ehrenkranz, R.A., Stark, A.R. *et al.* (2007) Trends in neonatal morbidity and mortality for very low birthweight infants. *Am J Obstet Gynecol* 196: 147.e1–8.
- Fawke, J., Lum, S., Kirkby, J., Hennessy, E., Marlow, N., Rowell, V. *et al.* (2010) Lung function and respiratory symptoms at 11 years in children born extremely preterm: the Epicure Study. *Am J Respir Crit Care Med* 182: 237–245.
- Filippone, M., Sartor, M., Zacchello, F. and Baraldi, E. (2003) Flow limitation in infants with bronchopulmonary dysplasia and respiratory function at school age. *Lancet* 361: 753–754.
- Friedrich, L., Pitrez, P.M.C., Stein, R.T., Goldani, M., Tepper, R. and Jones, M.H. (2007) Growth rate of lung function in healthy preterm infants. *Am J Respir Crit Care Med* 176: 1269–1273.
- Friedrich, L., Stein, R.T., Pitrez, P.M., Corso, A.L. and Jones, M.H. (2006) Reduced lung function in healthy preterm infants in the first months of life. *Am J Respir Crit Care Med* 173: 442–447.
- Goyal, N.K., Fiks, A.G. and Lorch, S.A. (2011) Association of late preterm birth with asthma in young children: practise based study. *Pediatrics* 128: e830–e838.
- Greenough, A., Alexander, J., Boorman, J., Chetcuti, P.A., Cliff, I., Lenney, W. *et al.* (2011) Respiratory morbidity, healthcare utilisation and cost of care at school age related to home oxygen status. *Eur J Pediatr* 170: 969–975.
- Greenough, A., Alexander, J., Burgess, S., Bytham, J., Chetcuti, P.A., Hagan, J. *et al.* (2006) Preschool healthcare utilisation related to home oxygen status. *Arch Dis Child Fetal Neonatal Ed* 91: F337–F341.
- Greenough, A., Alexander, J., Burgess, S., Bytham, J., Chetcuti, P. A., Hagan, J. *et al.* (2004a) Health care utilisation of prematurely born, preschool children related to hospitalisation for RSV infection. *Arch Dis Child* 89: 673–678.
- Greenough, A., Alexander, J., Burgess, S., Chetcuti, P.A., Cox, S., Lenney, W. *et al.* (2002) Home oxygen status and rehospitalisation and primary care requirements of infants with chronic lung disease. *Arch Dis Child* 86: 40–43.
- Greenough, A., Alexander, J., Burgess, S., Chetcuti, P.A., Cox, S., Lenney, W. *et al.* (2004b) High versus restricted use of home oxygen therapy, health care utilisation and the cost of care in chronic lung disease infants. *Eur J Pediatr* 163: 292–296.
- Greenough, A., Cox, S., Alexander, J., Lenney, W., Turnbull, F., Burgess, S. *et al.* (2001) Health care utilisation of infants with chronic lung disease, related to hospitalisation for RSV infection. *Arch Dis Child* 85: 463–468.
- Greenough, A., Dimitriou, G., Bhat, R.Y., Broughton, S., Hannam, S., Rafferty, G.F. *et al.* (2005a) Lung volumes in infants who had mild to moderate bronchopulmonary dysplasia. *Eur J Pediatr* 164: 583–586.
- Greenough, A., Dimitriou, G., Johnson, A.H., Calvert, S., Peacock, J. and Karani, J. (2000) The chest radiograph appearances of very premature infants at 36 weeks post-conceptional age. *Br J Radiol* 73: 366–369.
- Greenough, A., Limb, E., Marston, L., Marlow, N., Calvert, S. and Peacock, J. (2005b) Risk factors for respiratory morbidity in infancy after very premature birth. *Arch Dis Child Fetal Neonatal Ed* 90: F320–F323.
- Hakulinen, A.L., Jarvenpaa, A.L., Turpeinen, M. and Sovijarvi, A. (1996) Diffusing capacity of the lung in school-aged children born very preterm, with and without bronchopulmonary dysplasia. *Pediatr Pulmonol* 21: 353–360.
- Hofhuis, W., Huysman, M.W., Van Der Wiel, E.C., Holland, W.P., Hop, W.C., Brinkhorst, G. *et al.* (2002) Worsening of V_{max} FRC in infants with chronic lung disease in the first year of life: a more favourable outcome after high-frequency oscillation ventilation. *Am J Respir Crit Care Med* 166: 1539–1543.
- Hoo, A.F., Beardsmore, C.S., Castle, R.A., Ranganathan, S.C., Tomlin, K., Field, D. *et al.* (2009) Respiratory function during infancy in survivors of the INNOVO trial. *Pediatr Pulmonol* 44: 155–161.
- Hopkins, S.R., Levin, D.L., Emami, K., Kadlecsek, S., Yu, J., Ishii, M. *et al.* (2007) Advances in magnetic resonance imaging of lung physiology. *J App Physiol* 102: 1244–1254.
- Howling, S.J., Northway, W.H., Jr., Hansell, D.M., Moss, R.B., Ward, S. and Muller, N.L. (2000) Pulmonary sequelae of bronchopulmonary dysplasia survivors: high-resolution ct findings. *AJR Am J Roentgenol* 174: 1323–1326.
- Jobe, A.J. (1999) The new BPD: an arrest of lung development. *Ped Res* 46: 641–643.
- Jobe, A.H. and Bancalari, E. (2001) Bronchopulmonary dysplasia. *Am J Respir Crit Care Med* 163: 1723–1729.

- Johnson, A.H., Peacock, J.L., Greenough, A., Marlow, N., Limb, E.S., Marston, L. *et al.* for the United Kingdom Oscillation Study Group (2002) High frequency oscillatory ventilation for the prevention of chronic lung disease of prematurity. *New Engl J Med* 347: 633–642.
- Koivisto, M., Marttila, R., Saarela, T., Pokela, M.L., Valkama, A.M. and Hallman, M. (2005) Wheezing illness and re-hospitalization in the first two years of life after neonatal respiratory distress syndrome. *J Pediatr* 147: 486–492.
- Lum, S., Kirkby, J., Welsh, L., Marlow, N., Hennessy, E. and Stockes, J. (2011) Nature and severity of lung function abnormalities in extremely preterm children at 11 years of age. *Eur Respir J* 37: 1199–1207.
- Mahut, B., De Blic, J., Emond, S., Benoist, M.R., Jarreau, P.H., Lacaze-Masmonet, T. *et al.* (2007) Chest computed tomography findings in bronchopulmonary dysplasia and correlation with lung function. *Arch Dis Child Fetal Neonatal Ed* 92: F459–F464.
- McLean, A., Townsend, A., Clark, J., Sawyer, M.G., Baghurst, P., Haslam, R. *et al.* (2000) Quality of life of mothers and families caring for preterm infants requiring home oxygen therapy: a brief report. *J Pediatr Child Health* 36: 440–444.
- Narang, I., Rosenthal, M., Cremonesi, D., Silverman, M. and Bush, A. (2008) Longitudinal evaluation of airway function 21 years after preterm birth. *Am J Respir Crit Care Med* 178: 74–80.
- Northway, W.H., Jr, Moss, R.B., Carlisle, K.B., Parker, B.R., Popp, R.L., Pitlick, P.T. *et al.* (1990) Late pulmonary sequelae of bronchopulmonary dysplasia. *New Engl J Med* 323: 1793–1799.
- Northway, W.H., Jr, Rosan, R.C. and Porter, D.Y. (1967) Pulmonary disease following respiratory therapy of hyaline-membrane disease: bronchopulmonary dysplasia. *N Engl J Med* 276: 357–368.
- Oppenheim, C., Mamou-Mani, T., Sayegh, N., De Blic, J., Scheinmann, P. and Lallemand, D. (1994) Bronchopulmonary dysplasia: value of CT in identifying pulmonary sequelae. *AJR Am J Roentgenol* 163: 169–172.
- Thomas, M., Greenough, A., Johnson, A., Limb, E., Marlow, N., Peacock, J.L. *et al.* (2003) Frequent wheeze at follow up of very preterm infants: which factors are predictive? *Arch Dis Child Fetal Neonatal Ed* 88: F329–F332.
- Vrijlandt, E.J., Gerritsen, J., Boezen, H.M., Grevink, R.G. and Duiverman, E.J. (2006) Lung function and exercise capacity in young adults born prematurely. *Am J Respir Crit Care Med* 173: 890–896.
- Walter, E.C., Ehlenbach, W.J., Hotchkiss, D.L., Chien, J.W. and Koepsell, T.D. (2009) Low birth weight and respiratory disease in adulthood: a population-based case-control study. *Am J Respir Crit Care Med* 180: 176–180.
- Wilson, A.C. (2010) What does imaging the chest tell us about bronchopulmonary dysplasia? *Paediatr Respir Rev* 11: 158–161.
- Wong, P.M., Lees, A.N., Louw, J., Lee, F.Y., French, N., Gain, K. *et al.* (2008) Emphysema in young adult survivors of moderate-to-severe bronchopulmonary dysplasia. *Eur Respir J* 32: 321–328.
- Yuksel, B. and Greenough, A. (1991) Relationship of symptoms to lung function abnormalities in preterm infants at follow-up. *Pediatr Pulmonol* 11: 202–206.

Visit SAGE journals online
http://tar.sagepub.com

SAGE JOURNALS
Online