have recently became commercially available for noninvasive measurements [3]. These developments can be helpful to further explore the role of neonatal lung function in the development of respiratory diseases in later life.

@ERSpublications
Impaired neonatal lung function is associated with life respiratory symptoms; its measurement at birth is important http://ow.ly/rJjyd

Anne C. van der Gugten[1], Cornelis K. van der Ent[1] and Cuno S.P.M. Uiterwaal[2]
[1]Dept of Paediatric Pulmonology, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, and [2]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands.

Correspondence: A.C. van der Gugten, Dept of Paediatric Pulmonology, Wilhelmina Children's Hospital, University Medical Center Utrecht, Office KH.01.419.0, PO Box 85090, 3508 AB Utrecht, The Netherlands.
E-mail: a.c.vandergugten@umcutrecht.nl

Received: Oct 02 2013 | Accepted: Oct 03 2013

Conflict of interest: Disclosures can be found alongside the online version of this article at www.erj.ersjournals.com

References

1 van der Gugten AC, Uiterwaal CS, van Putte-Katier N, *et al.* Reduced neonatal lung function and wheezing illnesses during the first 5 years of life. *Eur Respir J* 2013; 42: 107–115.
2 Collins SA, Pike KC, Inskip HM, *et al.* Validation of novel wheeze phenotypes using longitudinal airway function and atopic sensitization data in the first 6 years of life: evidence from the Southampton women's survey. *Pediatr Pulmonol* 2013; 48: 683–692.
3 MediSpirit. www.medispirit.eu Date last accessed: November 18, 2013.

Eur Respir J 2014; 43: 921–922 | DOI: 10.1183/09031936.00172013 | Copyright ©ERS 2014

Bronchoalveolar lavage cytology resembles sarcoidosis in a subgroup of granulomatous CVID

To the Editor:

We read with great interest the article by Bouvry *et al.* [1] regarding similarities and differences between interstitial lung disease (ILD) in granulomatous common variable immunodeficiency (CVID) and sarcoidosis. In this retrospective study, differential bronchoalveolar lavage (BAL) cytology was analysed in 14 patients with granulomatous CVID and ILD. The authors found BAL lymphocytosis (>20%) in 11 out of 14 patients and a mean±SD proportion of BAL lymphocytes of 37.3±15.3%. Unlike the sarcoidosis group (5.3±4.0), the CD4/CD8 ratio was low in the analysed patients with granulomatous CVID and ILD (1.6±1.1, n=10) and even <1 in half of the patients (n=5). Bouvry *et al.* [1] concluded that there are significant differences in differential BAL cytology between sarcoidosis and granulomatous CVID.

We therefore retrospectively analysed a subgroup of 11 CVID patients (seven females and four males) with histologically proven granulomatous disease according to the inclusion criteria used by Bouvry *et al.* [1] and analysed BAL findings. Patients were 41.5±15.2 years of age and referred to the Centre of Chronic Immunodeficiency, University Medical Centre Freiburg (Freiburg, Germany) between 2003 and 2012. CVID was diagnosed based on the European Society for Immunodeficiencies/Pan-American Group for Immunodeficiency criteria [2]. In nine out of 11 patients, transbronchial biopsy was performed during bronchoscopy. In six (67%) of the biopsies, lymphocytic infiltrations could be detected, which did not fulfil the criteria for lymphocytic interstitial pneumonia. BAL lymphocytes (53.3±19.8%) exceeded 20% in all patients. CD4 cells accounted for 68.7±18.1% and CD8 cells for 16.6±8.2% of BAL cells. In contrast to the results reported by Bouvry *et al.* [1], we found a high CD4/CD8 ratio of 6.8±7.0 and no patient had a CD4/CD8 ratio <1.5. Moreover, the CD4/CD8 ratio (n=10; r=0.719, p=0.019) and the percentage of BAL CD4 lymphocytes (n=9; r=0.816, p=0.004) correlated negatively with BAL neutrophils (6.5±8.5%). The study by Bouvry *et al.* [1] showed significant differences in chest high-resolution computed tomography (HRCT) morphology between CVID and sarcoidosis patients. In particular nodules, air bronchograms, halo

TABLE 1 High-resolution computed tomography (CT) morphology and follow-up data

Patient	BAL CD4/CD8	CT findings at baseline									Follow-up		
		Macronodules			Random micronodules	Bronchiectasis	Consolidation	Ground glass	Lines		CT[#]	Lung function[#]	Steroid treatment
		Smooth margin	Halo	Air bronchogram					Subpleural	Reticular			
1	7.5	X			X		X			X	↑ (83)	ND	No
2	12.9	X	X	X							↓ (74)	↑ (49)	No
3	ND					X		X	X		↓ (97)	= (93)	Yes
4	2.2	X		X		X				X	= (14)	= (36)	Yes
5	3.8			X		X			X	X	= (53)	↓ (56)	Yes
6	24.0	X							X		= (6)	↑ (6)	No
7	5.1	X		X						X	↑ (16)	= (30)	No
8	1.5					X	X			X (coarse)	ND	= (40)	No
9	2.0	X	X	X							= (23)	↑ (24)	Yes
10	2.5	X			X	X	X	X		X	ND	ND	No
11	6.4							X			ND	↓ (10)	Yes

Stable lung function (=) was defined as a deviation of <10% predicted in forced vital capacity, total lung capacity or diffusing capacity for carbon monoxide. Also changes in high-resolution CT during follow-up were categorised as stable (=), improved (↑) or worsened (↓). BAL: bronchoalveolar lavage; ND: not determined; X: present. [#]: follow-up time in months is shown in parentheses.

signs and bronchiectasis predominated in CVID. In line with their findings, in our cohort with proven granulomatous disease, the majority of HRCTs demonstrated macronodular lung involvement (eight out of 11 patients). The two patients with micronodular involvement showed a randomly distributed pattern, which also differs to the characteristic perilymphatic distribution in sarcoidosis, as already shown by BOUVRY *et al.* [1]. Moreover, some patients presented with predominant coarse reticular lines or ground-glass lesions. It is intriguing to speculate whether the difference in CD4/CD8 ratio reflects different forms or stages of pulmonary inflammation in CVID, which may correlate to certain computed tomography morphology. This has been previously described in sarcoidosis, where lower CD4/CD8 ratios and increased neutrophils correlated with progressive, fibrotic disease and the need for steroid treatment [3–5]. In our small CVID cohort, lung function and computed tomography findings were mostly stable during follow-up, suggesting that a high CD4/CD8 ratio in granulomatous CVID is associated with a mild and nonprogressive ILD (table 1). Only two patients showed a deterioration of lung function parameters. Interestingly, both of these patients showed rather low CD4/CD8 ratios in comparison to the total study population (2.0 and 3.8).

In conclusion, in addition to the report by BOUVRY *et al.* [1], we found that in a subgroup of CVID patients with histologically confirmed granuloma formation, BAL cytology resembles sarcoidosis. All patients presented with high BAL lymphocytosis, high CD4/CD8 ratio and the majority with nodular lung disease on computed tomography. Thus, differences in BAL cytology and computed tomography morphology most likely reflect heterogeneity in CVID-associated granulomatous and interstitial lung disease. Our preliminary data suggest a rather favourable prognosis of ILD in this subgroup of CVID with high CD4/CD8 ratio in the BAL. Some of these findings may potentially guide management and predict outcome of these patients, but larger studies are needed to determine diagnostic and prognostic value of specific markers during detailed characterisation of interstitial lung disease in this heterogeneous disease.

@ERSpublications
Bronchoalveolar lavage cytology resembles sarcoidosis in a subgroup of granulomatous chronic variable immunodeficiency http://ow.ly/pU6Pl

Florian Kollert[1,2], Nils Venhoff[1,2], Sigune Goldacker[2], Claudia Wehr[2], Niklas Lützen[3], Reinhard E. Voll[1,2], Antje Prasse[4,5] and Klaus Warnatz[1,2,5]
[1]Centre of Chronic Immunodeficiency, University Medical Centre and University of Freiburg, Freiburg, [2]Dept of Rheumatology and Clinical Immunology, University Medical Centre Freiburg, Freiburg, [3]Dept of Radiology, University Medical Centre Freiburg, Freiburg, and [4]Dept of Pneumology, University Medical Centre Freiburg, Freiburg, Germany. [5]Both authors contributed equally.

Correspondence: F. Kollert, Dept of Rheumatology and Clinical Immunology, University Medical Centre Freiburg, Hugstetterstr. 55, Freiburg 79106, Germany. E-mail: florian.kollert@uniklinik-freiburg.de

Received: Feb 10 2013 | Accepted after revision: July 30 2013

Conflict of interest: Disclosures can be found alongside the online version of this article at www.erj.ersjournals.com

References

1 Bouvry D, Mouthon L, Brillet PY, *et al.* Granulomatosis-associated common variable immunodeficiency disorder: a case–control study *versus* sarcoidosis. *Eur Respir J* 2013; 41: 115–122.
2 Al-Herz W, Bousfiha A, Casanova JL, *et al.* Primary immunodeficiency diseases: an update on the classification from the international union of immunological societies expert committee for primary immunodeficiency. *Front Immunol* 2011; 8: 54.
3 Prasse A, Katic C, Germann M, *et al.* Phenotyping sarcoidosis from a pulmonary perspective. *Am J Respir Crit Care Med* 2007; 177: 330–336.
4 Ziegenhagen MW, Rothe ME, Schlaak M, *et al.* Bronchoalveolar and serological parameters reflecting the severity of sarcoidosis. *Eur Respir J* 2003; 21: 407–413.
5 Kollert F, Geck B, Suchy R, *et al.* The impact of gas exchange measurement during exercise in pulmonary sarcoidosis. *Respir Med* 2010; 105: 122–129.

From the authors:

We would like to thank F. Kollert and co-workers for their interest in our article [1] and their accurate analysis and comments.

Our study was designed to compare interstitial lung disease (ILD) in granulomatosis-associated common variable immunodeficiency disorder (CVID) (ILD/CVID/granulomatous disease) with pulmonary sarcoidosis.