Correspondence

TRANSIENT CLINICAL DETERIORATION IN HIV PATIENTS WITH *PNEUMOCYSTIS CARINII* PNEUMONIA AFTER STARTING HIGHLY ACTIVE ANTIRETROVIRAL THERAPY: ANOTHER CASE OF IMMUNE RESTORATION INFLAMMATORY SYNDROME

To the Editor:

We read with interest the article by Wislez and colleagues (1) describing the clinical deterioration of three patients who had initiated highly active antiretroviral therapy (HAART) early, after the diagnosis of *Pneumocystis carinii* pneumonia (PCP).

We also observed a transient clinical deterioration in three patients with confirmed PCP soon after the introduction of HAART. These cases were diagnosed between May 1999 and October 2000, during which time there were 16 confirmed cases of PCP in total. All three presented with advanced HIV disease (median CD4 26 cells/mm^3, mean $\log_{10}$ viral load 5.5). Despite severe disease, significant clinical and radiological improvement was observed by day 12–15 after administration of parenteral cotrimoxazole and high dose oral steroids. HAART was introduced within 15–18 days of PCP diagnosis. A median of 5 days later (range 3–17), all patients experienced acute respiratory failure accompanied by swinging fever and deterioration of the chest radiograph. Bronchoalveolar lavage revealed *P. carinii* cysts only. Further investigations did not reveal additional pathogens. Clinical recovery was observed on reintroducing high dose steroids and alternative PCP therapy. Two weeks after initiating HAART, the median CD4 count was 62 cells/mm^3 (range 14–82). The $\log_{10}$ viral load had fallen to 2.87. All patients made a full recovery by 29–40 days after PCP diagnosis.

These cases bear close similarity to those described by Wislez and coworkers. After initiation of HAART, rapid improvement in host immune responses result in inflammatory reactions at established infection sites. Such paradoxical inflammatory responses are well described in HIV-related tuberculosis (2, 3), cytomegalovirus infection (4), and cryptococcosis (5); however, these have rarely been described in PCP, a common HIV-related opportunistic infection. In patients coinfected with HIV/TB cases experiencing paradoxical responses had larger drops in viral load compared with patients who remained well (3). All three patients in this report demonstrated significant decreases in viral load at 2 weeks (median viral load drop 2.6 logs).

All three patients in this series improved after the reintroduction of steroids and a change of anti-PCP therapy. Alternative management strategies may include delaying the introduction of HAART in the early stages of PCP or prolonging steroid use if HAART is commenced. Given that we observed this phenomenon in approximately one-fifth (18.8%) of PCP patients presenting to our unit, the possibility of immune restoration inflammatory syndrome, particularly in patients with severe PCP and advanced HIV disease in whom HAART is started early, should be considered.

Gillian L. Dean

Deborah I. Williams

Duncan R. Churchill

Martin J. Fisher

Royal Sussex County Hospital
Brighton, United Kingdom

1. Wislez M, Bergot E, Antoine M, Parrot A, Carette M-F, Mayaud C, Cadranel J. Acute respiratory failure following HAART introduction in patients treated for *Pneumocystis carinii* pneumonia. *Am J Respir Crit Care Med* 2001;164:847–851.
2. Chien JW, Johnson JL. Paradoxical reactions in HIV and pulmonary TB. *Chest* 1998;114:933–936.
3. Narita M, Ashkin D, Hollender ES, Pitchenik AE. Paradoxical worsening of tuberculosis following antiretroviral therapy in patients with AIDS. *Am J Respir Crit Care Med* 1998;158:157–161.
4. Karavellas MP, Azen SP, MacDonald JC, Shufelt CL, Lowder CY, Plummer DJ, Glasgow B, Torriani FJ, Freeman WR. Immune recovery vitritis and uveitis in AIDS: clinical predictors, sequelae, and treatment outcomes. *Retina* 2001;21:1–9.
5. Woods ML 2nd, MacGinley R, Eisen DP, Allworth AM. HIV combination therapy: partial immune restitution unmasking latent cryptococcal infection. *AIDS* 1998;12:1491–1494.

From the Authors:

Dean and colleagues are confirming our previous observation on the risk of paradoxical worsening after introduction of HAART in patients with *Pneumocystis carinii* pneumonia (PCP) (1). Since the publication of our paper, we observed three new cases. The 18% prevalence of paradoxical worsening of PCP reported by Dean and colleagues is higher than that we have previously shown. In our experience, paradoxical worsening of PCP represents 4.6% of the patients referred for PCP to our instititution, and 7% of those receiving steroids because of acute respiratory failure. This discrepancy probably reflects variation of the incidence of severe PCP between institutions, and the diversity of schedules of adjunctive steroid therapy and of HAART introduction used in severe PCP (2, 3).

All the patients reported with paradoxical worsening of PCP had a very similar presentation. All had severe PCP ($Pa_{O_2} < 70$ mm Hg) requiring adjunctive steroids. Moreover, HAART was introduced early after PCP diagnosis (1 to 16 days) and steroid therapy was stopped too early (< 15 days). Lastly, this phenomenon occurs in severely immunocompromised patients in whom a dramatic decrease of plasma viral load was observed after HAART introduction. The peripheral blood CD4 cell counts did not increase in parallel, suggesting CD4 cell pulmonary sequestration as shown in lung tissue specimen (1). However, it is also important to emphasize that the diagnosis of paradoxical PCP worsening implies that cotrimoxazole-resistant PCP, pulmonary superinfection, and drug-induced pulmonary toxicity have been previously ruled out.

Finally, the fact that patients with paradoxical PCP worsening improved after HAART discontinuation or steroid introduction suggests either the need for an overlap period between HAART introduction and steroid cessation in the case of early HAART introduction, or to delay HAART introduction until after the end of PCP steroid adjunctive therapy. Whatever the measure adopted to prevent paradoxical PCP worsening after HAART introduction, steroid adjunctive therapy might probably not be shorter than 3 weeks, as recommended by consensus statement (4).

Marie Wislez

Jacques Cadranel

Hôpital Tenon and Université Paris VI, UFR Saint-Antoine
Paris, France

1. Wislez M, Bergot E, Antoine M, Parrot A, Carette M-F, Mayaud C, Cadranel J. Acute respiratory failure following HAART introduction in patients treated for *Pneumocystis carinii* pneumonia. *Am J Respir Crit Care Med* 2001;164:847–851.
2. Gagnon S, Boota AM, Fischl MA, Baier H, Kirksey OW, La Voie L. Corticosteroids as adjunctive therapy for severe *Pneumocystis carinii* pneumonia in the acquired immunodeficiency syndrome. A double-blind, placebo-controlled trial. *N Engl J Med* 1990;323:1444–1450.
3. Bozzette SA, Sattler FR, Chiu J, Wu AW, Gluckstein D, Kemper C, Bartok A, Niosi J, Abramson I, Coffman J, *et al.* A controlled trial of early adjunctive treatment with corticosteroids for *Pneumocystis carinii* pneumonia in the acquired immunodeficiency syndrome. California Collaborative Treatment Group. *N Engl J Med* 1990;323:1451–1457.
4. The National Institutes of Health-University of California Expert Panel for Corticosteroids as Adjunctive Therapy for Pneumocystis Pneumonia. Consensus statement on the use of corticosteroids as adjunctive therapy for pneumocystis pneumonia in the acquired immunodeficiency syndrome. *N Engl J Med* 1990;323:1500–1504.

MONITORING REACTIVE NITROGEN SPECIES IN BIOLOGICAL MILIEU: A DIFFICULT JOURNEY

To the Editor:

Corradi and colleagues report that the concentration of S-nitrosothiols (RSNO), nitrite, and exhaled nitric oxide (eNO) are increased in some inflammatory airway diseases. The chemistry of reactive nitrogen species (RNS) in biological systems is complex (2) and it is still unclear whether point estimates of concentration of RNS in blood and urine provide information on endogenous NO metabolism (3). Although collection of exhaled breath condensate (EBC) and eNO measurements may offer attractive alternative methods for measuring RNS, great care in sample handling and interpretation of results is mandatory.

EBC was collected using a glass condensing device, by cooling of the exhalate during tidal breathing for 15 minutes while wearing a nose clip. Contamination by trace transition metals, leaching from any glass containers, and exposure to light may have accelerated RSNO decomposition. Total RSNO content in EBC was measured by spectrophotometry, using a method adapted from Saville and Griess that involves cleavage of the NO group with mercuric chloride followed by quantitative detection of nitrite in the diazotation assay (the Griess assay). Artifactual loss of nitrite due to its disproportionation to NO or nitrosation of the remaining thiol-containing compounds in the EBC during the necessary sample acidification step in the Griess assay, would also be a possibility. Exhaled breath measurements in inflammatory disorders are prone to additional confounding factors. For example, we have recently confirmed that nitrite releases free NO even at physiological pH (4). Moreover, recent advances by Hunt and Gaston (5) suggest that endogenous airway acidification is a pathological feature of asthma. This would accelerate decomposition of nitrite to NO producing eNO (4, 5).

The cellular origin of exhaled RNS varies according to the disease. The elevated concentrations of eNO in asthma could be from epithelial NOS II (inducible NOS) or of neural origin (6). Identification of the isoform of NOS responsible for RNS production in inflammatory disorders will have to await the introduction of selective inhibitors of the different isoforms of the enzyme. Monitoring RNS in biological milieu is a challenging endeavour, and selective methods to measure endogenous NO production *in vivo* will certainly help unravel the complex interactions between nitrogen oxides and their derivatives.

Eric Demoncheaux

David Crowther

Alan C. Spivey

Tim W. Higenbottam

University of Sheffield and Sheffield Hallam University Sheffield, United Kingdom

1. Corradi M, Montuschi P, Donnelly LE, Pesci A, Kharitonov SA, Barnes PJ. Increased nitrosothiols in exhaled breath condensate in inflammatory airway diseases. *Am J Respir Crit Care Med* 2001;163:854–858.
2. Gaston B, Drazen JM, Loscalzo J, Stamler JS. The biology of nitrogen oxides in the airways. *Am J Respir Crit Care Med* 1994;149:538–551.
3. Baylis C, Vallance P. Measurement of nitrite and nitrate levels in plasma and urine - what does this measure tell us about the activity of the endogenous nitric oxide system? *Curr Opin Nephrol Hypertens* 1998;7:59–62.
4. Demoncheaux E, Higenbottam T, Foster P, Borland C, Smith A, Marriott H, Akamine S, Bee D, Davies M. Circulating nitrite anions are a directly acting vasodilator and are donors for nitric oxide. *Clin Sci (Lond)* 2002;102:77–83.
5. Hunt J, Gaston BM. Endogenous airway acidification. Implications for asthma pathology. *Am J Respir Crit Care Med* 2001;163:293–294.
6. Berlyne G, Barnes N. No role for NO in asthma? *Lancet* 2000;355:1029–1030.

From the Authors:

We thank Dr. Demoncheaux and coworkers for their insightful comments on our article raising concerns about the measurement of reactive nitrogen species in exhaled breath condensate (1).

Demoncheaux and colleagues suggest that exhaled breath condensate samples may be contaminated by trace transition metals from any glass containers or tubing, and that exposure to light may accelerate the decomposition of S-nitrosothiols. There is currently no evidence that either of these factors have any influence on the concentrations of S-nitrosothiols in exhaled breath condensate, but systematic studies are needed. We have shown that the concentrations of S-nitrosothiols are identical to those reported in our manuscript when using a condenser system that does not contain any glass component and is protected from light, suggesting that these factors are unlikely to have any significant effect on measurements. Furthermore, we looked at concentrations of S-nitrosothiols in different groups of subjects, and are more interested in the differences between these groups than the absolute concentrations in the samples.

Demoncheaux and colleagues are concerned that airway acidification may reduce the concentrations of S-nitrosothiols in patients with asthma. In fact, the pH of exhaled breath condensate is no different than normal in stable asthma and is lower only during acute exacerbations (2, 3).

We agree that selective NOS inhibitors will help us to identify the isoforms of NOS responsible for the production of reactive nitrogen species in inflammatory diseases of the lungs. We have previously demonstrated that inhaled aminoguanidine, which has some selectivity in inhibiting inducible NOS, causes a greater reduction in exhaled NO in patients with asthma compared with normal control subjects (4). Our recent unpublished observations have demonstrated that a more potent and specific iNOS inhibitor was capable of reducing exhaled NO by over 90% in patients with asthma, confirming that iNOS accounts for the majority of exhaled NO in asthma.

Monitoring of markers in exhaled breath condensate in patients with pulmonary disease has enormous potential as a noninvasive means of monitoring airway inflammation and oxidative stress (5), and represents a clear way forward rather than a difficult journey.

Peter J. Barnes

Sergei A. Kharitonov

National Heart and Lung Institute, Imperial College London, United Kingdom

1. Corradi M, Montuschi P, Donnelly LE, Pesci A, Kharitonov SA, Barnes PJ. Increased nitrosothiols in exhaled breath condensate in inflammatory airway diseases. *Am J Respir Crit Care Med* 2001;163:854–858.
2. Hunt JF, Fang K, Malik R, Snyder A, Malhotra N, Platts-Mills TA, Gaston B. Endogenous airway acidification: Implications for asthma pathophysiology. *Am J Respir Crit Care Med* 2000;161:694–699.
3. Palaiologou A, Loukides S, Papatheodorou G, Panagou P, Xronas G, Kalogeropoulos N. pH in expired breath condensate of patients with asthma. *Eur Respir J* 2000;16:40S.
4. Yates DH, Kharitonov SA, Thomas PS, Barnes PJ. Endogenous nitric oxide is decreased in asthmatic patients by an inhibitor of inducible nitric oxide synthase. *Am J Respir Crit Care Med* 1996;154:247–250.
5. Kharitonov SA, Barnes PJ. Exhaled markers of pulmonary disease. *Am J Respir Crit Care Med* 2001;163:1693–1722.

RAPID TRANSLOCATION OF NANOPARTICLES FROM THE LUNG TO THE BLOODSTREAM?

To the Editor:

In their brief communication, Nemmar and colleagues (1) report rapid clearance of instilled albumin nanoparticles from the lungs to the bloodstream of hamsters (25–30% in 5 minutes), suggesting an explanation for observed cardiovascular effects of urban, airborne particulate matter reported in epidemiological studies (2). Although this hypothesis is attractive, the results of this particular study (1) are in conflict with decades of studies on respiratory clearance of aerosolized solutes (3–6). In particular, Peterson and colleagues (3) found that aerosolized Tc99m-aggregated albumin (mol wt = 383,000 daltons; approx mol size = 20 nm) similar to the tracer used by Nemmar and colleagues (1), delivered to the lungs of sheep cleared exponentially at a rate of 0.04% per minute over an 80-minute period (less than 5% lung clearance during that time). Even the rate constant for the smallest tracer (DTPA) used in their study (3) was only 0.4% per minute with less than 10% clearance in 30 minutes. These data are inconsistent with the observations of Nemmar and colleagues (1), i.e., a rapid rate of 5–6% per minute.

Huchon and colleagues (4) also studied the clearance of a variety of aerosolized, radioactive solutes from the lungs of dogs. They found that solute clearance was inversely related to molecular weight, with negligible clearance of the largest molecular weight solute, labeled transferrin (mol wt = 76,000 daltons), over a 30-minute period of observation. At the other extreme, free pertechnetate (TcO_4^-) (mol wt = 163 daltons) had a clearance rate of 6% per minute. Clearance rates in humans (5, 6) for aerosolized solutes that are smaller in molecular size than that employed by Nemmar and colleagues (1) are also considerably slower than that seen during the first 5 minutes of observation in their study.

The above cited studies are only a few of many that are incompatible with the study by Nemmar and colleagues. The reasons for these differences are not clear, but one clear difference in protocol is that particles were instilled in their study rather than inhaled. Nevertheless, it is important that the authors fully address the discrepancies between their results and previous findings and possible reasons for those differences. Careful study of inhaled particle dosimetry is needed to lead toxicologists towards a better understanding of the biological effects of exposure to ambient particulate matter (2).

William D. Bennett

University of North Carolina at Chapel Hill Chapel Hill, North Carolina

1. Nemmar A, Vanbilloen H, Hoylaerts MP, Hoet PHM, Verbruggen A, Nemery B. Passage of intratracheally instilled ultrafine particles from the lung into the systemic circulation in hamster. *Am J Respir Crit Care Med* 2001;164:1665–1668.

2. Peters A, Liu E, Verrier RL, Schwartz J, Gold DR, Mittleman M, Baliff J, Oh JA, Allen G, Monahan K, Dockery DW. Air pollution and incidence of cardiac arrhythmia. *Epidemiology* 2000;11:11–17.
3. Peterson BT, Dickerson KD, James HL, Miller EJ, McLarty JW, Holiday DB. Comparison of three tracers for detecting lung epithelial injury in anesthetized sheep. *J Appl Physiol* 1989;66:2374–2383.
4. Huchon GJ, Montgomery AB, Lipavsky A, Hoeffel JM, Murray JF. Respiratory clearance of aerosolized radioactive solutes of varying molecular weight. *J Nucl Med* 1987;28:894–902.
5. Bennett WD, Ilowite JS. Dual pathway clearance of Tc99m-DTPA from the bronchial mucosa. *Am Rev Respir Dis* 1989;139:1132–1138.
6. Morrison D, Skwarski K, Millar AM, Adams W, MacNee W. A comparison of three methods of measuring Tc99m-DTPA lung clearance and their repeatability. *Eur Respir J* 1998;11:1141–1146.

From the Authors:

Dr. Bennett states that our data (1) are in conflict with decades of studies on respiratory clearance of aerosolized solutes. We would contend that those who attempted to evaluate pulmonary permeability in a noninvasive way by measuring the decrease of radioactivity over the chest after inhaling a radiolabeled tracer failed to measure radioactivity in blood soon after inhaling the tracer.

Our question was "Do ultrafine pollutant particles have the potential to translocate from the lungs into the blood?" Using surrogate particles (namely ^{99m}Tc-labeled nanoparticles of denatured albumin) we showed this to be the case in hamsters (1), and we have since obtained similar evidence in humans using more relevant particles, namely ^{99m}Tc-labeled carbon particles (2). Aerosolised insulin also gives a rapid therapeutic effect (3).

Whole body scans after the inhalation of ^{99m}Tc-labeled tracers readily show that substantial radioactivity rapidly appears outside the lungs. This is not solely due to free ^{99m}Tc (i.e., ^{99m}Tc in the form of pertechnetate) as shown by Peterson and colleagues (4) and ourselves (1, 2). A striking fact in the studies cited by Dr. Bennett is that radioactivity was rarely measured in blood. Peterson and colleagues (4) mention in their methods section that in control sheep, only 8% of plasma ^{99m}Tc was unbound 1 hour after the administration of ^{99m}Tc-albumin, but unfortunately, the total radioactivity in plasma is not reported. However, this observation does imply that there had been passage of the tracer into the blood, although admittedly this could have occurred through lymphatic drainage.

We accept that intratracheal administration may have affected the quantity of particles that passed into the blood. However, the discrepancies between reported lung clearance rates and our estimated amount of particles that passed into the blood could be explained by the fact that to measure clearance, various assumptions must be made about the starting values of radioactivity. In other words, the method may well miss a brief first phase of rapid translocation. In fact, as Figure 3 of our article shows (1), if we had assessed the passage of label on the basis of the change in radioactivity in the lungs between 5 and 60 minutes, we would also have concluded that there was hardly any translocation. However, measurements in blood showed particle-bound radioactivity within minutes of pulmonary deposition. It remains to be established why the passage then seems to slow down. However, the fact appears incontrovertible that ultrafine particles may pass rapidly from the lungs into the blood circulation, not only in hamsters (1) but also in humans who inhaled an aerosol of particles (2).

We believe that this is relevant to investigate, and perhaps even to explain, at least some of the extrapulmonary effects of exposure to pollutant particles (5).

ABDERRAHIM NEMMAR
HUBERT VANBILLOEN
MARC F. HOYLAERTS
PETER H. M. HOET
ALFONS VERBRUGGEN
BENOIT NEMERY
Katholieke Universiteit Leuven
Leuven, Belgium

1. Nemmar A, Vanbilloen H, Hoylaerts MF, Hoet PHM, Verbruggen A, Nemery B. Passage of intratracheally instilled ultrafine particles from the lung into the systemic circulation in hamster. *Am J Respir Crit Care Med* 2001;164:1665–1668.
2. Nemmar A, Hoet PH, Vanquickenborne B, Dinsdale D, Thomeer M, Hoylaerts MF, Vanbilloen H, Mortelmans L, Nemery B. Passage of inhaled particles into the blood circulation in humans. *Circulation* 2002; 105:411–414.
3. Steiner S, Pfutzner A, Wilson BR, Harzer O, Heinemann L, Rave K. Technosphere/Insulin–proof of concept study with a new insulin formulation for pulmonary delivery. *Exp Clin Endocrinol Diabetes* 2002; 110:17–21.
4. Peterson BT, Dickerson KD, James HL, Miller EJ, McLarty JW, Holiday DB. Comparison of three tracers for detecting lung epithelial injury in anesthetized sheep. *J Appl Physiol* 1989;66:2374–2383.
5. Peters A, Dockery DW, Muller JE, Mittleman MA. Increased particulate air pollution and the triggering of myocardial infarction. *Circulation* 2001;103:2810–2815.

ERRATUM

There was an error in the 2002 American Journal of Respiratory and Critical Care Medicine International Conference Abstracts book (Volume 165, Number 8). Because of a printer's error, two abstracts on page A499 were printed with their top portion missing. Below we reproduce the abstracts by Gutierrez and colleagues and by Ishibashi and colleagues in their entirety.

REPRODUCIBILITY OF INSPIRATORY CAPACITY DURING BASELINE RESTING CONDITIONS AND HYPERVENTILATION IN NORMAL SUBJECTS.

Gutierrez C, Chakravorty S, Latty P, McCLean P, Zamel N.
Department of Medicine, University of Toronto, Toronto, Ontario, Canada.

Rationale: FEV_1 is the more widely used pulmonary function test. It has been of great usefulness in the study and management of asthma in particular. By the same token its utility was extrapolated to other obstructive diseases such as COPD. Recently, it was suggested that measurement of inspiratory capacity (IC) in these patients might be a better approach in their evaluation as the severity of the dyspnea during standard exercise testing correlated with decreases in IC. There is not much published on IC either in health or disease. We therefore decided to study the characteristics of IC among normal subjects comparing baseline breathing and mild hyperventilation.
Methods: We studied 21 normal volunteers, 8 males and 13 females with mean age of 37±12.5 years of age. We measured baseline IC while breathing normally at rest conditions and then hyperventilating to a metronome set at two times the baseline frequency.
Results: Mean baseline IC was 2.98 ± 0.71L and 2.9 ± 0.68L during hyperventilation. The mean change from baseline was -2.7% ± 6.3%, paired t-test p=0.035. An intraclass correlation coefficient was 0.96..
Conclusions: We have shown that hyperventilating at 2 times the baseline frequency does not change the IC. Hence, IC change may be a useful parameter in the assessment of obstructive diseases.

This abstract is funded by:

LUNG VOLUME REDUCTION SURGERY (LVRS) IMPROVES CO_2 RESPONSIVENESS AND BREATHING EFFICIENCY IN THE PATIENTS WITH PULMONARY EMPHYSEMA.

M.Ishibashi, T.Kuraki, H.Toyoshima, M.Shiraishi, A.Iwasaki*, M.Yoshida. Respiratory Med., Dept. of Surgery*, School of Med., Fukuoka Univ., Fukuoka, Japan

Purpose We investigated the effects of LVRS on CO_2 responsiveness and breathing efficiency ($\Delta \dot{V}E/\Delta P0.1$) in 19 patients with pulmonary emphysema. **Methods** Pulmonary functions including lung volumes were measured by body plethysmography and helium dilution method and trapped gas volume estimated as FRCbox -FRCHe. Responses of mouth occlusion pressure (P0.1) and ventilation to hypercapnia ($\Delta P0.1/\Delta PACO2$, $\Delta \dot{V}E/\Delta PACO2$) were measured by rebreathing, and the ratio of the two($\Delta \dot{V}E/\Delta P0.1$) was estimated as breathing efficiency that indicated the increase in ventilation obtained by a given increase in neuromuscular output to hypercapnia

Results The results before and after LVRS are shown as following (*p<0.05) ;

	FEV1.0 ml	trapped gas volume ml	$\Delta P0.1/\Delta PACO2$ cmH2O/mmHg	$\Delta \dot{V}E/\Delta PACO2$ L/min /mmHg	$\Delta \dot{V}E/\Delta P0.1$ L/min/cmH2O
Before	860 ±420	1480 ±590	0.58±.41	1.40±1.20	1.50 ±1.00
After	1080±560*	940 ±610*	0.41 ±.25	2.10±1.70*	3.30±1.20*

There was a signifficant correlation between changes in $\Delta VE/\Delta P0.1$ and FEV1.0 ($r=0.72$, $p<0.01$) or trapped gas volume ($r=0.56$, $p<0.05$) after LVRS.

Conclusion These results suggest that increase in CO_2 responsiveness and breathing efficiency may reflect improvement of mechanical efficiency of breathing due to decrease in air flow limitation and hyperinflation by LVRS, and mainly represent the mechanism to reduce dyspnea on exertion in the patients with pulomnary emphysema.

This abstract is funded by: