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P68

**What do built-in softwares in home ventilators tell us? An observational study of 150 patients on home mechanical ventilation in Geneva**

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**Background:** Recent home ventilators provide the clinician with built-in softwares which record a multitude of items such as compliance, estimated tidal volume (VT) and minute ventilation (VE), leaks, respiratory rate (RR), percentage of inspiratory cycles triggered by the patient, and apnea-hypopnea index (IAH). The aim of this study was to analyze, in patients on long-term home mechanical ventilation (HMV) in a stable clinical condition, data downloaded from home ventilators during elective home visits performed by specialized nurses.

**Methods:** Among 179 patients on HMV regularly followed by our centre, 150 were treated with bi-level ventilators equipped with built-in software (Synchrony I and II, Philips Respironics®; VPAP III and IV, ResMed®). Ventilator settings had been adjusted in order to obtain optimal nocturnal PtcCO<sub>2</sub>, SaO<sub>2</sub>, and patient comfort.

**Results:** 150 patients aged 65 ± 14 yrs, 46% female, with diagnoses of: COPD: n = 30, Overlap syndrome: n = 31, Obesity hypoventilation: n = 38, other restrictive disorders: n = 39, Central or mixed sleep apnea: n = 12, ventilated either by facial (73%) or nasal masks (27%), for a total of 44 ± 31 months, were included. Ventilator settings are detailed in table 1. Compliance was on average: 408 ± 150 min/day (15% low compliance rate: <3:30 hrs/day); average VT was: 6.2 ± 2.3 ml/kg, and decreased significantly with BMI. Average respiratory rate was: 17 ± 3, i.e.: 2.5 ± 3.6 cycles above back-up RR. Patients triggered 50 ± 32% of respiratory cycles: 25% triggered more than 80% of respiratory cycles, and 29%, less than 20%. There was a trend for less triggered cycles in restrictive disorders (mainly neuromuscular disorders). Patients using Synchrony ventilators triggered significantly less cycles than those under VPAP (41 vs. 55%, p = .014). Estimated residual AHI was 5.9 ± 8.4/hr. Leaks (10.6 ± 11 L/min) were significantly lower with facial vs. nasal masks (p = .01 for average value, p = .0002 for upper 95th centile), but not influenced by IPAP or EPAP values.

**Conclusions:** Compliance to HMV is quite satisfactory. Use of facial masks decreases leaks. Most patients have a spontaneous RR close to the back-up rate; 29% are "captured" by their ventilator, and 25% are virtually on a spontaneous mode. Further studies are warranted to determine which among these options is optimal in terms of patient-ventilator synchronisation and comfort. Indeed, a low percentage of triggered inspiratory cycles may in fact reflect inspiratory efforts undetected by the ventilator.

Diagnosis	IPAP (Mean (SD); cm H <sub>2</sub> O)	EPAP (Mean (SD); cm H <sub>2</sub> O)	Set RR	Leaks Mean (SD) L/min	Spontaneous inspiratory cycles %; Mean (SD)	VT/kg Mean (SD)	AHI (Mean (SD); N/hr)
COPD and Overlap syndrome (n=61)	20 (4)	6 (2)	14 (2)	10 (11)	51 (31)	7 (3)	5 (5)
Obesity-hypoventilation (n=38)	20 (4)	9 (3)	14 (2)	10 (6)	54 (3)	5 (2)	6 (7)
Other restrictive disorders (n=39)	16 (4)	5 (2)	15 (3)	13 (14)	46 (34)	7 (3)	5 (7)
Central or mixed sleep apnea (n=12)	16 (4)	6 (2)	14 (2)	7 (10)	47 (3)	7 (2)	16 (21)

P69

**Obstructive sleep apnea in patients with abdominal aortic aneurysms: highly prevalent and associated with aneurysm expansion**

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**Rationale:** Abdominal aortic aneurysms (AAA) are associated with life-threatening complications such as rupture. The likelihood that an AAA will rupture is particularly influenced by the diameter of the aneurysm and the expansion rate; the reasons for rapid expansion are largely unknown.

**Objectives:** To determine the prevalence of obstructive sleep apnea (OSA) in patients with AAA and to investigate the possible association between OSA and AAA expansion.

**Methods:** 127 patients (11 females) included in the AAA surveillance program agreed to participate and underwent a sleep study. Annual AAA expansion was determined by ultrasound. OSA was defined using an oxygen desaturation index (ODI) or apnea-hypopnea index (AHI) of >10/h. Univariate and multivariate analysis was performed to assess the effect of OSA severity on AAA expansion. Measurements and main results: Mean ± SD age was 67.9 ± 6.0 years. Mean time following inclusion into the surveillance program until the

final AAA measurement was 21.2 ± 15.7 months. An ODI or AHI of >10 was found in 40.5% and 41.5% of the patients, respectively. Patients with an ODI >30 had a significantly faster mean yearly AAA expansion (4.3 ± 3.7 mm) than patients with an ODI between 0-5 (1.7 ± 2.6 mm) or >5-15 (1.5 ± 2.4 mm) (p <0.05). In multivariate regression analysis controlling for cardiovascular risk factors and medications ODI >30 remained an independent risk factor for AAA expansion. **Conclusions:** In patients with AAA OSA is highly prevalent and associated with more rapid expansion. Severe OSA may be a factor for faster AAA expansion but this needs to be proven in a randomized controlled intervention trial.

P70

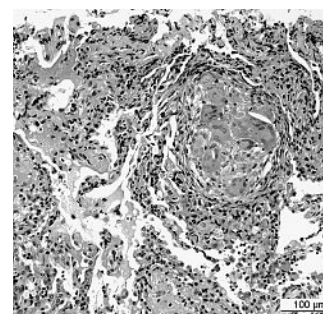
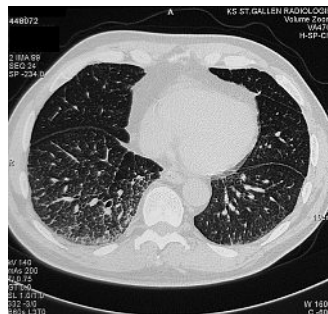
**Hypersensitivity pneumonitis induced by a CPAP ventilator?**

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**Introduction:** Continuous positive airway pressure (CPAP) ventilation is the gold standard treatment for obstructive sleep apnea (OSA) and has so far not been associated with treatment-related inflammatory or allergic adverse reactions including hypersensitivity pneumonitis.

**Case presentation:** A 69-year-old man with severe OSA presented with progressive dry cough and exertional dyspnea. On presentation the patient was alert and in no respiratory distress. Auscultation revealed right basal inspiratory velcro-type crackles. Computed tomography of the chest showed reticulo-nodular opacities and interstitial thickening in both lower lung fields with a right-sided predominance. Ground glass opacities were present in the right lower lobe (fig. 1). Pulmonary function tests were normal apart from a reduced diffusion capacity for carbon monoxide (68% predicted). Arterial blood gas analysis showed hypoxemia and an elevated alveolar-arterial oxygen gradient. Bronchoalveolar lavage showed an increased total cell count with a lymphocytosis of 84%. Transbronchial biopsies revealed chronic inflammation, with presence of macrophages, histiocytic granuloma and interstitial fibrosis (fig. 2). The diagnosis of hypersensitivity pneumonitis (HP) was retained. Identification of an inciting agent at the patient's home failed. A treatment with systemic corticosteroids was started, but the patient relapsed after withdrawal. Symptoms, radiological and functional findings did not improve until CPAP therapy – which included a humidifier – was stopped. CPAP therapy was resumed later with new equipment without humidification. Since, the patient remained free of symptoms without medication.

**Discussion:** In case of HP the identification of the correct source of the pathogenic antigen is very important. After elimination of the CPAP device & humidifier as the potential source, our patient's symptoms resolved within a few weeks without further steroid treatment. Authors argued that the conditions in the water bath of a heated humidifier are bactericidal and humidifiers produce molecules of water too small to carry pathogens. Therefore, the use of sterilized water is not generally recommended. Interestingly, our patient handled his humidifier very carefully by changing the water daily and using only pre-boiled water. Nevertheless, given the clinical course, an association to a bacterial or fungal antigen in the CPAP device or humidifier seems to be the most likely cause of our patient's HP.



P71

**Long-term effect of hepatocyte growth factor on the normal lung: a stereological assessment**

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**Background:** Hepatocyte growth factor (HGF) gene transfer attenuates bleomycin induced lung fibrosis in the bleomycin model. HGF is multifunctional pleiotropic factor; it is a potent mitogen for alveolar epithelial cells and has antiapoptotic properties. Long term effect of HGF gene transfer on the alveolar epithelium is still not known; in the present study we investigated the long term effect of HGF gene transfer on the alveolar epithelial cells in the normal lung.

**Material and methods:** Adult male Fischer rats F344, were instilled

with 350 µl of pSpChHGF plasmid (Human HGF under control of surfactant protein C promoter), and extracorporeal electroporation was performed 8 pulses of 200v/cm, at 10 ms interval. One month after HGF gene transfer, animals were sacrificed and the tissues were collected. Stereological assessment was performed to study the structural changes in the normal right lung after long term HGF gene transfer. Untreated normal adult male rat lungs served as controls.

**Results:** Stereology revealed that HGF transfer increased the total lung volume ( $4.51 \pm 0.52$  vs  $3.41 \pm 0.33$ ,  $p < 0.01$ ). This could be attributed to an increase of both volume fraction ( $58.2 \pm 0.7\%$  vs  $52.3 \pm 3.0\%$ ,  $p < 0.01$ ) and total volume of alveoli per lung ( $2.43 \pm 0.30$  cm<sup>3</sup> vs  $1.63 \pm 0.22$  cm<sup>3</sup>,  $p < 0.01$ ), accompanied by an increase of total alveolar surface area ( $2.36 \pm 0.07$  cm<sup>2</sup> vs  $2.07 \pm 0.17$  cm<sup>2</sup>,  $p = 0.01$ ). The mean septal thickness was slightly decreased after HGF transfer ( $5.12 \pm 0.78$  µm vs  $6.57 \pm 1.45$  µm,  $p = 0.08$ ).

**Conclusion:** Stereological analysis reveals that there is increased remodeling as evident by septal thickness changes and increase in the surface area of the alveoli and their total volume per lung, indicating that HGF is important in the alveolar development. These changes might be explained by an increased proliferation of alveolar epithelial cells.

### Bacterial-induced protection against allergy through a novel multi-component immunoregulatory mechanism

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Airborne microbial products have been reported to promote immune responses that suppress asthma, yet how these beneficial effects take place remains controversial and poorly understood. We have found that pulmonary exposure with the bacterium *Escherichia coli* leads to a suppression of allergic airway inflammation, characterized by reduced airway-hyperresponsiveness, eosinophilia and cytokine production by T cells in the lung. This immune modulation was neither mediated by the induction of a Th1 response nor regulatory T cells; was dependent on TLR-4 but did not involve TLR-desensitization. Dendritic cell migration to the draining lymph nodes and subsequent activation of T cells was unaffected by prior exposure to *E.coli* indicating that the immunomodulation was limited to the lung environment. In non-treated control mice ovalbumin was primarily presented by airway CD11b+ CD11c+ DCs expressing high levels of MHC class II molecules whilst the DCs in *E.coli*-treated mice displayed a less activated phenotype and had impaired antigen presentation capacity. Consequently, in situ Th2 cytokine production by ovalbumin-specific effector T cells recruited to the airways was significantly reduced. The suppression of airways hyper responsiveness was mediated through the recruitment of IL-17-producing  $\gamma\delta$ -T cells; however, the suppression of dendritic cells and T cells was mediated through a distinct mechanism that could not be overcome by the local administration of activated dendritic cells, or by the *in vivo* administration of TNF-alpha. Taken together, these data reveal a novel multi-component immunoregulatory pathway that acts to protect the airways from allergic inflammation.

P72

## Poster session II

P73

### Screening for tuberculosis in asylum seekers: comparison of chest radiography with an interview-based system

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**Setting:** Mandatory initial screening of asylum seekers for tuberculosis in Switzerland 2004-05 and 2007-08.

**Objective:** To compare the yield of screening by chest radiography with an individual assessment based on geographical origin, personal history, and symptoms.

**Method:** Cross-sectional retrospective comparison of two periods of two years.

**Results:** The yield of screening was assessed as the proportion of screenees starting antituberculosis treatment for culture-confirmed pulmonary tuberculosis within 90 days. It was 14.3 per 10,000 asylum seekers screened (31/21,727) for chest radiography and 12.4 per 10,000 (29/23,402) for the individual assessment. Sensitivity of radiography was 100% vs. 55% for the individual assessment, but its specificity was lower (89.9% vs. 96.0%, respectively). The higher sensitivity of radiography meant shorter delays between screening and start of treatment (median of 6 vs. 25 days). Its lower specificity led to a larger proportion of screenees needing further investigations for suspicion of tuberculosis (12% vs. 4%).

**Conclusion:** The yield was equivalent in both systems. The interview-based system missed more cases. This led to delays until start of treatment with a potential to increase transmission and secondary cases. The radiographic system had a higher burden as more suspects require further investigations.

P74

### Features of tuberculosis incidence and clinical forms for sarcoidosis patients

M. Bratkovskis for the LZI Working Party

**Introduction:** The problem of high tuberculosis (TB) incidence is very burning in Latvia during several number of years (incidence 2006.-49,7/100000). At the same time, there was high level of TB resistant forms for patients (pts) with first time detected TB-22.7% in 2006. For the same time period, sarcoidosis incidence was 5,22/100000 in 2006. Though the etiology of sarcoidosis is unknown we noted certain tendencies in the development of pathological processes in cases of added tuberculosis for sarcoidosis pts.

**Methods:** 3423 sarcoidosis pts were registered in Latvia during the period of observations 1958–2006. Added TB was detected only for 28 (~1%) of pts from this population. Among these pts we detected 16 pts with pulmonary TB, 12-extrapulmonary TB pts. The duration of sarcoidosis was not less than 3 years for these pts before the incidence of tuberculosis. Various TB affections of bones and joints were detected for 8 of 12 extrapulmonary TB pts. We also have noted high level of drug resistant TB-13/31 pts (41,9%).

**Conclusions:** Our observations indicate low risk of TB incidence among the population of sarcoidosis in Latvia (0.94%). At the same time the risk of additional TB infection increases when sarcoidosis is in chronic process. These patients develop specific heavy forms of TB such as drug resistant TB, extrapulmonary TB.

P75

### Occupational recurrent flu-like and breathing symptoms of an electronic engineer

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Working in a plastic industry can cause various respiratory health problems like occupational asthma, inhalation fever or hypersensitivity pneumonitis. In such activity, multiple processes are used and can expose the worker to dust or fume emissions containing multiple chemical substances. A 37-year old electronic engineer who works in a cable factory has to assemble some tetrafluoroethylene (Teflon) copper cables with connectors. For that, he uses a mixture of epoxy resins and hardener. Teflon isolated copper cables are placed in this mixture in a cast and then heated up to seventy degrees during twenty-four hours for hardening. The patient does not use any personal protective equipment to handle the chemical products. Regularly after performing this type of work, symptoms like myalgias, coldness, chills, fever and thoracic pain appear eight hours later at home and resolve three hours after beginning. In the last episode, residual symptoms such as intense fatigue, persistent thoracic pain and restless sleep disappeared only after two weeks. This symptomatology is suggestive for polymer fume fever (inhalation fever) or hypersensitivity pneumonitis. Inhalation fever could be triggered by Teflon fumes released during heating of the cables. Acute hypersensitivity pneumonitis could result from inhalation of phthalic anhydride contained in epoxy resins. Both diagnoses are described in such occupational activity. In order to clarify the diagnosis, the patient was sent to a pneumologist to perform additional pulmonary investigations. Nevertheless, as the temporal relation between this activity and the appearance of symptoms is strong, the diagnosis of occupational disease is retained. Additionally, a workplace visit will be performed in order to analyze and improve the working conditions. Anyway, depending on the frequency and duration of the exposed activity, it is very likely that this patient will need to be removed from this work, because he will realistically be unable to wear a protective mask for more than few hours per day.

P76

### Occupational chemical pneumopathy: an atypical case report

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A 39-year old woman, never smoker, presented breathing difficulties related to her new activity of cleaning lady in a fitness centre. Since she was assigned to the cleaning of the locker rooms and showers, work-related symptoms began with nose, throat and eyes irritation, frequent nose bleeding and occasional cough. As they became more frequent and dyspnea also appeared, she was treated for pneumonia. Antibiotics being without effect, she was sent to lung specialists in Geneva University Hospital (HUG). A restrictive syndrome with decreased diffusing capacity of the lungs for carbon monoxide was found. The computerized tomography showed bilateral infiltrates and the bronchoalveolar lavage showed lymphocytosis, which was compatible with hypersensitivity pneumonitis. "Hot tub lung" was suspected. The patient was withdrawn from work for two months and treated with corticosteroids for a month with partial remission. Besides, she was referred to the Institute for Work and Health (IST) for an occupational medicine evaluation. A visit of her working place was performed with an occupational hygienist, in order to assess biological and chemical exposure. No mold or mycobacterium avium complex, often involved with "hot tub lung", were found in the shower water, but contrarily multiple occupational chemical exposure in bad working conditions was confirmed. Among others, identified chemicals were chlorine vapors, produced by the mixing of bleach and acids, and limonene and quaternary ammonium, both sensitizers, as compounds of the cleaning products. Chemicals usually described with hypersensitivity pneumonitis, such as isocyanates, were not found. Our interpretation of these results was that the most likely origin of her symptoms would be chemical pneumonitis, caused by irritative and corrosive products inadequately used. Nevertheless, clinical findings were also compatible with hypersensitivity pneumonitis, developed shortly after a specific occupational activity. Thus, implication of new chemicals such as limonene or quaternary ammonium compounds as triggering event of a hypersensitivity pneumonitis might also be possible. However, to our knowledge, this has never been described in the literature.

P77

### Improvement of mobility in patients with long-term oxygen therapy through liquid oxygen refilling stations

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**Background:** Liquid oxygen (LOX) is widely used in Switzerland since portable devices enable patients to maintain mobility and regular physical activity outside their homes. A limitation however is the range of only 4–8 hours autonomy depending on the flow rate. To minimise this disadvantage the Genossenschaft LOX set up with LOX suppliers a network of refilling stations for LOX (Basle, Berne, Lausanne, Lucerne, Neuchâtel, St. Gallen, Winterthur, Zug, Zurich). Usually the refilling station is located in a pharmacy inside or near the railway station and it is accessible 24 h/7 days a week.

**Aim:** We wished to determine the rate of use, how the network corresponds to the needs of patients and how to expand the network.

**Method:** Questionnaires were sent to all patients using LOX in Switzerland. The answers were analysed and compared with the objective use of the refilling stations, as assessed by the record filled in by the users during their visits to the stations.

**Results:** The questionnaire was sent to the 2100 patients with LOX. 250 (12%) were returned. 60 (23%) patients make day trips in their local area, 51 (19%) up to 20 km, 61 (23%) up to 50 km and 89 (34%) over 50 km. 65% of the patients knew about the LOX refilling stations but only 28% had ever used them. Despite two different adapter systems, the refilling at the stations was problem-free for 96% of the patients. The refilling was done between 6am and 12 pm with two peaks in the late morning and afternoon. During the first 2 years 435 patients made a total of 1156 refillings. The average number of refillings per patient was 2.65 with a huge range between 1 and 68. 50% used it more than once. 37% of the patients requested further refilling stations especially in the tourist regions of Switzerland (Valais, Bernese Alps, Grison and Ticino)

**Conclusions:** Although patients with LOX usually suffer from end stage pulmonary disease, there is still a big need for mobility. The refilling of the portable LOX devices at the stations is, despite the two adapter systems, for the patients without further assistance feasible and accepted. To standardise the adapter system would reduce the logistic costs and simplify use for the patient. LOX patients must receive better information from their health care providers about the existence and the use of the LOX refilling stations. Further refilling stations, especially in tourist regions, are required and could further improve the mobility and quality of life of the LOX patients.

P78

### Incidence and prevalence of pulmonary lymphangioleiomyomatosis in Switzerland

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Pulmonary lymphangioleiomyomatosis (LAM) is a rare disorder affecting almost exclusively women, and characterized by mutations in TSC1/2 genes, constitutive activation of the kinase mammalian target of rapamycin (mTOR), proliferation of abnormal smooth muscle cells in the lungs, kidneys and axial lymphatics, and multiple pulmonary cysts leading to progressive lung destruction and respiratory insufficiency. LAM may be either sporadic (S-LAM) or associated with tuberous sclerosis complex (TSC-LAM). Due to rarity of the disorder, only few epidemiological data are available. To determine the minimal incidence and prevalence rates of S-LAM in Switzerland, we analysed cases of LAM reported to the SIOLD Registries by a nationwide network of 200 pulmonary physicians. 25 cases, all women, were reported between 2002 and 2009. Cases with TSC-LAM were excluded (n = 7). Diagnoses were made between 1993 and 2008. The mean age at diagnosis was 42 ± 10 years. The mean annual incidence was calculated over 3 periods of 4 years' duration i.e. 1997–2000, 2001–2004 and 2005–2008. Cases diagnosed before 1997 were excluded (n = 4). 3 patients underwent lung transplantation, 2 died and 1 was lost to follow-up. Population at risk were women aged 20–69 according to Swiss population census. The mean annual incidence was stable over the 3 periods with respectively 0.42, 0.41 and 0.49 cases/mio/yr (mean 0.44) similar to the only available comparison data (France 1991–1996 : 0.4/mio/yr). Prevalence on January 1st 2001, 2005 and 2009 was respectively: 3.3, 4.4 and 5.8 cases/mio, higher than the only 2 available comparison data (France 1997: 2.6/mio; UK 2000: 2.7/mio).

**Conclusions:** Although data may be biased by underreporting, minimal incidence and prevalence rates of S-LAM in Switzerland can be determined, and appear similar those of 2 other European countries.

The SIOLD Registries are supported by the Swiss Pulmonary League.

P79

**A complicated course of a spontaneous pneumothorax**A. Kunz, D. Schilter, C. Mordasini  
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We report the case of a 38-year old non-smoking female with a history of spontaneous right-sided pneumothorax. The first episode in June 2006 was treated with a chest tube. After two weeks the first relapse occurred and the patient was treated surgically with a right sided thoracoscopic pleurectomy. After an unproblematic early postoperative course the patient had a second relapse 4 weeks later. She was treated with a thoracoscopic talcpleurodesis with an unclear, but probably high amount of talc. Shortly after the surgical intervention, an air fluid level was seen on a chest x-ray, which was slowly progressive over weeks and compressed the right lung. In the follow up 6 months after the procedure the spirometry was compatible with a restrictive ventilation defect (FEV<sub>1</sub> 56% predicted) and the CT scan showed two big calcified pseudocysts (10 x 17.5 cm and 5 x 9 cm). After an airway infection with hemoptysis, 2 years after the first pneumothorax, the patient presented to our facility because of a

“fluid-clapping in the right hemithorax” and progressive dyspnea. We found a more severe restrictive ventilation defect (FEV<sub>1</sub> 47%, TLC 66% predicted) and the CT scan showed very big, now nearly allconsuming, calcified pseudocysts, with significant compression of the right lung and an new mediastinal shift toward the left side with tracheal compression. An anterolateral thoracotomy with nearly total pleurectomy and resection of the cysts was performed, which lead to prolonged lung deflation, but an immediate decrease of the dyspnoe. Short term follow up of 6 weeks radiologically did not show development of new cysts. Since not published so far, the development of calcified pseudocysts after (recurrent) pneumothoraces seem to be a rare complication likely related to talcpleurodesis.

## Poster session III

P81

**Specific therapy for pulmonary hypertension in patients with interstitial lung disease**C. Tueller, S. Krebsler, T. Geiser  
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**Background:** There is no evidence whether pulmonary hypertension (PH) in patients with interstitial lung disease should be treated with PH specific medications or not.

**Methods:** Retrospective analyses of data from patients with interstitial lung disease and PH confirmed by right heart catheterization (RHC) receiving treatment for PH.

**Results:** Between 1/2006 and 6/2008 we identified 7 patients (6 males, mean age 72±4 y) with emphysema/fibrosis (2), idiopathic pulmonary fibrosis (2), non-specific interstitial pneumopathy (2) and pneumoconiosis (1) with PH in RHC. Baseline hemodynamic data were the following (mean ± SD, (range)): mean pulmonary artery pressure 39 ± 9 mm Hg (27-50), pulmonary vascular resistance (PVR) 730 ± 421 dyn.s.cm<sup>-5</sup> (312-1344), cardiac index 1.7 ± 0.3 l/min/m<sup>2</sup> (1.3-2.2), Wedge pressure 12 ± 5 mm Hg (2-17). Mean total lung capacity was 74 ± 15% of predicted normal (range 55-98). All patients had decreased diffusion capacity for carbon monoxide (DLCO mean 30 ± 7% predicted, range 21-46) and resting hypoxemia (mean pO<sub>2</sub> 60 ± 5 mm Hg, range 53-66). Four patients had a baseline 6 minute walking test done (walking distance (WD) 310 ± 144 m (range 130-475) and showed severe desaturation (minimal oxygen saturation 69 ± 1% (range 67-70)). Five patients received bosentan and 2 sildenafil for first line PH treatment. Bosentan was replaced by sildenafil in one patient because of elevation of liver enzymes. Two patients received combination treatment after 1 (bosentan, sildenafil) and 8 (bosentan, ilomedin) months of treatment. At first follow-up visit after 3 (range 1-4) months of therapy WD remained stable or improved in 3 patients (+2%, +1%, +58%) and decreased in 1 patient (-18%). At second follow-up visit after 7 (range 5-13) months of therapy WD improved or remained stable in 3 patients (-5%, +5%, +16%) and decreased in 2 patients (-31%, -36%). After 13.5 (8-20) months of therapy WD remained stable or improved in (+2%, -7%, +27%, -5%) and decreased in 1 patient (-58%). Lung function remained stable. Two patients died: one with emphysema/fibrosis after 11 months of therapy, one with NSIP due to former bleomycin exposure after 2 months of therapy. These were the patients with the highest PVR, and both died of right heart failure.

**Conclusion:** We assume that PH contributes substantially to prognosis in patients with interstitial lung disease. Specific PH therapy might help to stabilize functional capacity and to improve outcome of these patients.

P82

**Bosentan and/or Sildenafil for non-operable chronic thromboembolic pulmonary hypertension**E. Langenskiöld, A. Bonetti, L. P. Nicod, J.-D. Aubert  
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**Objectives:** To evaluate outcome of patients treated “off-label” by bosentan and/or sildenafil for chronic thromboembolic pulmonary hypertension (CTEPH).

**Patients and methods:** Since 2003, 18 patients (mean age 69 ± 11 years) have been treated with bosentan and/or sildenafil for CTEPH (mean pulmonary arterial resistance 8.1 ± 3.7 U Wood) in Lausanne University Hospital, with a follow-up of at least 12 months. Sixteen of them were inoperable because of distal disease and/or age or significant co-morbidities and 2 had persistent or recurrent pulmonary hypertension despite surgery. Efficacy of treatment was evaluated by comparison of New York Heart Association functional class (NYHA), six-minute walk test (6-MWT) and serum levels of N-terminal-pro brain natriuretic peptide (NT pro-BNP) at baseline (T0) and at 12 months (T12). Wilcoxon rank test was used for statistics.

**Results:** At T0, median NYHA class was III (range II-IV), 6-MWT was 348 meters (5 and 95 centiles: 0, 539) and NT pro-BNP was 387 mmol/l (58, 3508). At T12, 11 patients were treated with bosentan, 5 with sildenafil, 1 with inhaled iloprost (because of failure of the two other treatments) and 1 with a combination of sildenafil and iloprost. NYHA had improved in 10 patients, remained stable in 7 and worsened in 1 (median decrease 0.5 (-2; 0.2) p = 0.013). Six-MWT improved by a median of 15 meters (-142, +270) (p = 0.047) and NT pro-BNP decreased by a median of 65 mmol/l (-2988, +187) (p = n.s.). Among the 10 patients with a follow-up of 2 years or longer, two thirds remained stable and one third had worsened at 24 month. Treatments were well tolerated and only one patient had significant side effects (cutaneous reaction to bosentan) necessitating a switch to another treatment.

**Conclusion:** In agreement with published data, bosentan and sildenafil improved functional status (NYHA, 6-MWT) and haemodynamics (NT pro BNP) in our patients with inoperable CTEPH. However these medications should not be used as substitute for surgery when the latter is applicable.

P83

**High dose of Fluticasone administered by controlled inhalation: a new possible tool for the treatment of uncontrolled asthma**H. Jung, G. Menz  
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**Introduction:** In spite of guideline compatible therapy the management of severe uncontrolled asthma remains a challenge, often requiring higher doses of systemic corticosteroids, which may cause severe side effects. We introduced to treat these patients with high doses of inhaled corticosteroids using a special inhalation device,

the AKITA (Fa. Activaero). The principle of controlled inhalation has a proved pulmonary delivery of 80% of the nebulized substance. The inhalation steering can be adapted on the Inspiratory Capacity of the Patients. We have shown, that this is easily and effective possible in the in house setting (Data presented on the Annual Meeting of the DGP 2007 in Lübeck). As a next step, we did a retrospective analysis of data get a first confirmation of the efficiency of the therapy.

**Methods:** We analyzed all patients receiving the therapy in 2007 in our hospital by records. We were able to collect data of 112 patients. The indications for the therapy were uncontrolled asthma, acute exacerbation of a former controlled asthma and weaning of systemic steroids. All patients were treated with 2 mg Fluticason by controlled inhalation. The therapy was administered about two to eight weeks, with a mean duration of 3 weeks.

**Results:** Under the therapy there was a significant decrease of exhaled NO (-44.5%), and a significant rise of FEV<sub>1</sub> (+ 17.2% / 340 ml) and FEV<sub>1</sub>/VC (68.9% to 73.6%). The therapeutic dose of the patients receiving oral corticosteroids could be significantly tapered (33.2% / 7.6 mg prednisolone equivalent). We saw no worse side effects.

**Conclusion:** We assess these data as a first sign for the effectiveness of this therapeutical approach. It is a safe and well tolerated therapy. A prospective Study with a non-treatment control group is on the way.

P84

#### Efficacy of the PDE4 inhibitor roflumilast in COPD patients with chronic bronchitis

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**Rationale:** Previous studies suggest the phosphodiesterase 4 (PDE4) inhibitor roflumilast may improve lung function and prevent exacerbations in patients with chronic obstructive pulmonary disease (COPD) with moderate-to-severe airflow obstruction and exacerbations.

**Methods:** Two replicate, randomised, placebo-controlled, double-blind, multicentre trials were performed in patients with COPD, severe-to-very severe airflow obstruction, a history of exacerbations and chronic bronchitis. Patients were randomised and received either roflumilast, 500 µg once daily (n = 1537), or placebo (n = 1554) for 52 weeks. Co-primary endpoints were mean change in pre-bronchodilator forced expiratory volume in 1 second (FEV<sub>1</sub>) from baseline to each post-randomisation visit, and the rate of moderate or severe exacerbations. Secondary endpoints included post-bronchodilator FEV<sub>1</sub> and time to death from any cause.

**Results:** Both studies met their pre-specified primary endpoints. In a pre-specified pooled analysis, mean difference in pre-bronchodilator FEV<sub>1</sub> between roflumilast- and placebo-treated patients was 48 mL (p < 0.0001), and the mean rate of moderate or severe exacerbations (pt/year) was 1.14 vs 1.37, respectively (reduction: 16.9%, p = 0.0003). Pooled post-bronchodilator FEV<sub>1</sub> also improved significantly with a mean between-treatment difference of 55 mL (p < 0.0001). Similar significant improvements were seen in pre- and post-bronchodilator forced vital capacity and pre-bronchodilator mid-expiratory flow. There was no difference in mortality between treatments.

**Conclusions:** Roflumilast significantly improved lung function and decreased exacerbations in COPD patients with chronic bronchitis and severe-to-very severe airflow limitation.

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P85

#### The PDE4 inhibitor roflumilast provides additional clinical benefit in COPD patients receiving salmeterol

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**Rationale:** Morbidity and mortality due to COPD are increasing, despite various treatment options. The oral, selective phosphodiesterase 4 (PDE4) inhibitor roflumilast can improve lung function in COPD patients. Roflumilast, co-administered with long-acting bronchodilators, may have additional effects.

**Methods:** This double-blind, randomised, parallel-group study recruited patients with moderate-to-severe COPD. After a single-blind, 4-week baseline period with salmeterol (SAL) 50 µg twice daily (bid) and placebo once daily (od), patients were randomised to receive roflumilast 500 µg od (n = 466) or placebo od (n = 467) for 24 weeks concomitant with SAL 50 µg bid. The primary outcome was mean change in pre-bronchodilator FEV<sub>1</sub> from baseline to each post-randomisation visit. Other outcomes included post-bronchodilator

FEV<sub>1</sub> and exacerbation frequency.

**Results:** Compared with SAL alone, roflumilast concomitant with SAL significantly improved mean pre-bronchodilator FEV<sub>1</sub> by 49 mL (p < 0.0001) and mean post-bronchodilator FEV<sub>1</sub> by 60 mL (p < 0.0001). The concomitant regimen also reduced the mean annual rate of exacerbations (moderate or severe) by 36.8% (p = 0.0315; post-hoc) and increased the median time to first moderate or severe exacerbation (hazard ratio 0.6, p = 0.0067) compared with SAL alone. The safety profile of the concomitant treatment was consistent with that previously reported for roflumilast. Adverse events occurred in 63.1% of patients receiving roflumilast concomitant with SAL compared with 59.1% receiving SAL alone.

**Conclusions:** Roflumilast provides additional clinical benefits to COPD patients receiving SAL by statistically significantly improvement in lung function and reduction in exacerbations.

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P86

#### Safety of the PDE4 inhibitor roflumilast in COPD patients with chronic bronchitis

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**Rationale:** The phosphodiesterase 4 (PDE4) inhibitor roflumilast provides a novel approach to the treatment of chronic obstructive pulmonary disease (COPD).

**Methods:** Two replicate, randomised, placebo-controlled, double-blind, multicentre trials were performed in patients with COPD, severe-to-very severe airflow obstruction, a history of exacerbations and chronic bronchitis. Patients were randomised to receive either roflumilast, 500 µg once daily, or placebo for 52 weeks. Adverse events (AEs) and responses to enquiries about recent weight change were recorded at each visit. In one study, 24-hour Holter monitoring was undertaken at 19 sites.

**Results:** Both studies met their pre-specified primary efficacy endpoints. In the pooled study population, AEs were reported by 67% of patients in the roflumilast group (n = 1547) and 62% in the placebo group (n = 1545); serious AEs were reported by 20% and 22%, respectively. Discontinuations associated with AEs (14.2% vs 11.5%, respectively) were initially more common with roflumilast than with placebo, but after 8 weeks they were similar between treatment groups. Mean weight change was -2.09 kg with roflumilast and +0.08 kg with placebo, and not progressive beyond 6 months. Atrial fibrillation was reported in 1.1% of roflumilast- and 0.5% of placebo-treated patients. There were no differences between treatments in overall reported cardiovascular AEs, in the occurrence of rhythm disturbances in Holter-monitored recordings, and no increase in the incidence of pneumonia during roflumilast treatment.

**Conclusions:** Roflumilast was generally well tolerated with no excess neurological or cardiac events or cases of pneumonia. The weight change is the subject of further study.

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P87

#### Pharmacokinetic characteristics of the selective phosphodiesterase 4 (PDE4)-inhibitor roflumilast

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**Rationale:** The once-daily oral phosphodiesterase 4 (PDE4) inhibitor roflumilast (ROF) provides a novel approach to the treatment of chronic obstructive pulmonary disease (COPD). The pharmacokinetic (PK) profiles of ROF and its similarly pharmacologically active metabolite, roflumilast-N-oxide (ROF-NO), were investigated.

**Methods:** Plasma concentrations of ROF and ROF-NO were measured in 77 healthy volunteers (age: 18–45 years) in 5 phase I studies after application of oral once-daily doses of 250–1000 µg ROF or intravenously (150 µg).

**Results:** After oral application ROF was absorbed quickly and almost completely. C<sub>max</sub> was reached about 1 h (ROF) and 4–13 h (ROF-NO) after administration. The absolute bioavailability of ROF was 79%. Terminal plasma half-life (t<sub>1/2</sub>) was found to be in the range of 15–17 h (ROF) and 25–30 h (ROF-NO). PK Steady State conditions were reached after 4 days (ROF) and 6 days (ROF-NO) of oral once daily administration. The total exposure (AUC) of ROF-NO was about 10 times higher than that of ROF, indicating that ROF-NO could be the main carrier of the pharmacological activity. Plasma-Clearance was 0.14 L/h\*kg after i.v.-application of 150 µg ROF. Volume of distribution (V<sub>d</sub> area) was 2.9 L/kg. ROF and ROF-NO were almost completely cleared by metabolism and eliminated renally as inactive metabolites. Amounts of ROF and ROF-NO in urine are less than 1%. PK data

revealed no differences after day or nighttime application. Furthermore, food intake did not affect the PK of ROF-NO. Dose proportionality of PK parameters was found in the range of 250–1000 µg.

**Conclusions:** The observed PK characteristics of ROF – high absolute bioavailability, long half-life, dose linearity as well as a high volume of distribution – are fulfilling the PK-requirements for a once daily oral systemic treatment of chronic inflammatory diseases such as COPD.

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P88

#### The PDE4 inhibitor roflumilast provides additional clinical benefit in COPD patients treated with tiotropium

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**Rationale:** Morbidity and mortality due to chronic obstructive pulmonary disease (COPD) are increasing, despite various treatment options. Roflumilast, an oral, selective phosphodiesterase 4 (PDE4) inhibitor, improves lung function and clinical outcomes in patients with COPD. Roflumilast, co-administered with long-acting bronchodilators, may have additional effects.

**Methods:** This double-blind, randomised, parallel-group study recruited patients with moderate-to-severe COPD associated with chronic bronchitis. After a single-blind, 4-week baseline period with tiotropium 18 µg once daily (od) and placebo (od), patients were randomised to receive concomitant treatment with roflumilast 500 µg od (n = 371) or placebo od (n = 372) for 24 weeks. The primary outcome was mean change in pre-bronchodilator forced expiratory volume in 1 second (FEV<sub>1</sub>) from baseline to each post-randomisation visit. Other outcomes included post-bronchodilator FEV<sub>1</sub> and COPD exacerbations.

**Results:** Baseline characteristics were similar in the two groups. Compared with tiotropium alone, roflumilast concomitant with tiotropium significantly improved mean pre-bronchodilator FEV<sub>1</sub> by 80 mL (p < 0.0001) and mean post-bronchodilator FEV<sub>1</sub> by 81 mL (p < 0.0001). A hazard ratio of 0.7 (p = 0.0264) indicated that exacerbations (mild, moderate or severe) were likely to occur later in patients taking the concomitant regimen. The safety profile of the concomitant regimen was consistent with that previously reported for roflumilast. Adverse events occurred in 46.0% of patients receiving the concomitant regimen and in 40.7% receiving tiotropium alone.

**Conclusions:** Roflumilast provides additional clinical benefits to COPD patients receiving tiotropium by significantly improvement in lung function and reduction in exacerbations.

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### Poster session IV

P89

#### Long-term efficacy of human deoxyribonuclease on lung function parameters in children with cystic fibrosis

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**Rationale:** Recombinant human deoxyribonuclease (rhDNase) applied to patients with cystic fibrosis (CF) has been shown to improve lung function in short-term trials, and there is some evidence that the number of pulmonary exacerbations may be reduced. However, its long-term effect has not yet been clearly assessed.

**Objectives:** To assess the long-term efficacy of rhDNase on lung function parameters, taking in consideration potential confounder effects.

**Methods:** In this retrospective observational study, we analyzed data from our CF database including 170 children (85 males; 85 females) with CF followed over an age range of 5 to 18 years between 1978 and 2008. Linear mixed model (LMM) analyses were used to assess efficacy of rhDNase (2.5 mg/day) on lung function parameters, including residual capacity (FRCpleth), lung clearance index (LCI), trapped gas (VTG), effective airway resistance (sReff), and forced expiratory indices (FEV<sub>1</sub>, FEF50), as well as on blood gases taken from the arterialized ear lobe (PaO<sub>2</sub>, PaCO<sub>2</sub>) and body mass index (BMI). Moreover, confounder effects including time point events (age at initiation and duration of rhDNase treatment), microbial colonization (*P. aeruginosa* and *S. aureus*) and development of allergic bronchopulmonary Aspergillosis (ABPA) were studied.

**Results:** Comparing the slope of lung function parameter as index of progression obtained during a time period of 10 years before versus 10 years after initiation of rhDNase treatment, significant improvement in the degree of ventilation inhomogeneities (LCI; p = 0.004) was observed. There was no effect on flow limitation (FEV<sub>1</sub>, FEF50), bronchial obstruction (sReff), pulmonary hyperinflation (FRCpleth), trapped gas (VTG), blood gases, or on BMI. Subgroup analysis showed that the beneficial effect of rhDNase on LCI was restricted to younger patients (age < 12 years) and to those with mild lung involvement. In these patients, use of rhDNase was also associated with increased trapped gases. The onset of *S. aureus* infection and to a lesser extent of *P. aeruginosa* infection influenced efficacy of rhDNase treatment.

**Conclusions:** In our cohort, use of rhDNase was associated with only modest long-term beneficial effect on lung function parameters in CF children, raising concerns about cost effectiveness.

P90

#### Allergic rhinitis as predictor for school age wheezing

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**Background:** Rhinitis in older children and adults has been shown to be a risk factor for adolescent and adult onset asthma. These findings suggest an interaction between the upper and lower airways. Whether rhinitis is associated with childhood onset asthma is unknown. The objective of the study was, therefore, to investigate whether rhinitis in early childhood is an independent risk factor for childhood onset wheezing in the German Multicentre Allergy Study (MAS) birth cohort.

**Methods:** The MAS followed 1314 healthy children from birth to 13 years of age. The children were followed and specific immunoglobulin E levels were measured at yearly intervals. Airway hyperresponsiveness was assessed at 7 years.

**Results:** Allergic rhinitis until the age of 5 years was a risk factor for subsequent wheezing onset with an adjusted RR of 3.79 (p = < 0.001). This association was not attributable to the type of sensitization, the severity of sensitization or atopic dermatitis during the first 2 years of life. The population attributable risk fraction for allergic rhinitis on the incidence of wheezing was 41.5% (95% CI: 20.0–61.3). Non-allergic rhinitis until the age of 5 years was not significantly associated with wheezing onset in childhood (adjusted RR 0.77, p = 0.678). Neither allergic (adjusted RR = 1.37, p = 0.503) nor non-allergic rhinitis (adjusted RR = 1.16, p = 0.656) until the age of 2 years was associated with wheezing onset thereafter.

**Conclusions:** The first manifestation of allergic rhinitis occurs in preschool children where it is a risk factor for subsequent wheezing onset. Rhinitis until the age of two, however, does not influence the development of wheezing in childhood. Preschool children with rhinitis might thus benefit from early assessment of allergic sensitization to identify the children at high risk of developing wheezing.

P91

#### Characteristics of medically and surgically treated empyema patients: a retrospective analysis

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**Aim:** We compared characteristics of medically versus surgically treated pleural empyema patients treated at Kantonsspital St. Gallen, a 900 bed hospital in Switzerland.

**Methods:** Electronic patient charts from 1/2001 to 12/2008 were searched for empyema and pleura. Retrieved charts were reviewed manually. Included for analysis were hospitalised patients, > 16 years, with acute empyema based on the clinicians diagnosis (symptoms, fever, sonography, CT, Laboratory). Excluded were patients with malignant effusions, tuberculosis, iatrogenic empyema, transudative effusion and previous pleurodesis. Demographic characteristics, deaths, concurrent diseases, duration of symptoms, treatment

(antibiotics, drainage with or without urokinase, surgery), duration of hospital stay and follow-up pain 3 and 12 months after discharge were collected.

**Results:** 78 of 215 retrieved charts fulfilled inclusion criteria. 4 died (1 surgery, 3 medical).

**Conclusion:** Medical treatment was successful in 62% of our empyema patients (48 of 78). If drainage and urokinase were applied, the success rate was 82% (28 of 34), significantly higher than for patients treated without urokinase (15 of 24, 64%) and for patients treated without drainage (5 of 20, 25%). No other predictors of success with medical treatment could be identified. Surgically treated patients were more likely to suffer chest pain 3 and 12 months after discharge.

All empyema patients treated	Total (n)	Medical treatment		Surgical treatment		Odd's Ratio	95% Confidence Interval
		(n)	(%)	(n)	(%)		
	78	48	61.5%	30	38.5%		
Age groups [years]							
<47	17	10	58.8%	7	41.2%	1	
47 - 60	18	11	61.1%	7	38.9%	1.1	0.28 - 4.26
61 - 73	22	12	54.5%	10	45.5%	0.84	0.23 - 3.02
> 73	21	15	71.4%	6	28.6%	1.75	0.45 - 6.77
Gender							
male	52	33	63.5%	19	36.5%	1	
female	26	15	57.7%	11	42.3%	0.78	0.3 - 2.05

Treatment	Antibiotics alone	Drainage	Drainage and Urokinase
	20	24	34
	5	15	28
	25.0%	62.5%	82.4%
	15	9	6
	75.0%	37.5%	17.6%
	1	5	14
		1.4 - 18.5	3.6 - 53.6



All empyema patients treated	Total (n)	Medical treatment		Surgical treatment		Odd's Ratio	95% Confidence Interval
		(n)	%	(n)	%		
	78	48	61.5%	30	38.5%		
Treatment							
no drainage	20	5	25.0%	15	75.0%	1	
Drainage alone	24	15	62.5%	9	37.5%	5	1.4 - 18.5
Drainage and Urokinase	34	28	82.4%	6	17.6%	14	3.6 - 53.6
Duration of symptoms [days]							
< 4	18	13	72.2%	5	27.8%	1	
4 - 6	14	11	78.6%	3	21.4%	1.41	0.27 - 7.28
7 - 14	28	16	57.1%	12	42.9%	0.51	0.14 - 1.83
> 14	18	8	44.4%	10	55.6%	0.3	0.08 - 1.23
Bacteriology							
Streptococcus milleri	25	16	64.0%	9	36.0%	1	
other positive culture	23	15	65.2%	8	34.8%	1.05	0.32 - 3.44
negative or unknown	30	17	56.7%	13	43.3%	0.73	0.24 - 2.19
Duration of hospital stay [days]							
<17	17	12	70.6%	5	29.4%	1	
17 - 22	21	15	71.4%	6	28.6%	1.04	0.25 - 4.26
23 - 31	20	11	55.0%	9	45.0%	0.51	0.13 - 2.00
> 31	20	10	50.0%	10	50.0%	0.42	0.11 - 1.62
C-reactive protein							
<245	19	10	52.6%	9	47.4%	1	
245 - 305	18	13	72.2%	5	27.8%	2.34	0.59 - 9.2
306 - 387	22	11	50.0%	11	50.0%	0.9	0.26 - 3.07
> 387	19	14	73.7%	5	26.3%	2.52	0.64 - 9.83

P92

### Primary pedunculated muscle flap coverage of bronchial and tracheal defects as an alternative to direct closure or bronchotracheal sleeve resection

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**Objective:** Bronchial airways after lung resections are usually closed either by manual or mechanical suture. To prevent bronchopleural fistula (BPF) additional reinforcement of the bronchial stump by a pedunculated muscle flap (PMF) is often recommended. In very central tumours sleeve resection with anastomosis is generally preferred to direct closure with the aim of minimizing airway stenosis or avoiding incomplete resection. As a further alternative we describe a technique where only a PMF is used to cover an open and unsutured central airway defect by means of three high-risk patients.

#### Methods and results:

**CASE 1:** A 40-year-old man underwent extended right pneumonectomy because of central non small cell lung cancer (NSCLC) with severe poststenotic pneumonia. The tracheal defect at the bifurcation was covered by a PMF without preceding bronchial suture closure. There was no evidence of air leakage in intraoperative testing and repetitive bronchoscopy. No complications were seen in the postoperative course.

**CASE 2:** A 45-year-old woman underwent extended right pneumonectomy. After impressive tumour regression due to neoadjuvant chemotherapy the resection margin of the right bronchus was close to the carina. A PMF was used for coverage of the airway defect. Intraoperative testing including bronchoscopy showed no evidence of air leakage or contralateral prolapse of the muscle flap. The postoperative course was complicated by ARDS of the remaining left lung necessitating continuous positive airway pressure (CPAP). Delayed re-thoracotomy with muscle flap re-fixation had to be performed because of secondary air leakage.

**CASE 3:** A 72-year-old man with NSCLC and neoadjuvant chemotherapy underwent right bilobectomy with extended resection of the right intermediate bronchus up to the main bronchus. The defect of

the main bronchus was covered using a PMF. Intraoperative bronchoscopy and air leakage testing were normal. The postoperative course was uneventful.

**Conclusion:** Primary coverage of a central bronchial or tracheal defect using only a PMF is feasible. Predominantly in high risk patients direct suture at risk or extensive sleeve resection may be avoided.

P93

### Preoperative endobronchial ultrasound for mediastinal staging in patients with lung carcinoma

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**Background:** Traditionally mediastinoscopy was been the gold standard for the mediastinal staging in patients with lung carcinoma. Nevertheless, endobronchial ultrasound (EBUS) can replace mediastinoscopy and can easily performed in an ambulatory setting (Hofer et al, ERJ 22: Suppl 45: 590s). EBUS has been routinely performed for preoperative mediastinal staging in our institution since March 2007.

**Aim:** To investigate the usefulness of EBUS for preoperative mediastinal staging in surgical patients with lung carcinoma (NSCLC). **Methods:** Prospective evaluation of all surgical patients with NSCLC with perioperative EBUS since March 2007. The following parameters were evaluated: nodal stage of CT and PET/CT, results of EBUS and the surgical nodal stage. All patients had an extensive surgical nodal staging.

**Results:** 54 patients were evaluated of which five patients after neoadjuvant chemotherapy. Mean age was  $64 \pm 13$  years. In the preoperative CT 12 patients had enlargement of N3-lymph nodes, 20 of N2-lymph nodes. Only 8 patients had a positive PET/CT for N2-disease. Out of these 8 N2-PET-positive patients, 3 (38%) had a negative EBUS of the PET-positive lymph nodes and the negative N2-disease was surgically confirmed. Four patients with a negative EBUS of N2-lymph nodes finally had a positive N2 disease (two of which with negative PET/CT). All of these four patients had an indication for surgical operation (contraindication for neo-adjuvant chemotherapy). EBUS-TBNA of N3-lymph nodes was performed in 17 (31.5%) patients, in 37 (68.5%) and 31 (54.4%) patients paratracheal and subcarinal N2-lymph nodes were evaluated, respectively. Interestingly in the four patients with false negative EBUS-TBNA the subcarinal lymph node were false negative. One out of the 5 patients with neoadjuvant treatment has a false negative EBUS (one micrometastasis in subcarinal lymph node and non-representative puncture in a paratracheal lymph node).

**Conclusion:** EBUS has a high clinical utility for preoperative mediastinal staging in patients with NSCLC. Interestingly in our population only subcarinal lymph nodes were false negative in EBUS and two of the four had a negative PET/CT too. Probably the combination with endoesophageal ultrasound (EUS) helps to evaluate these patients. In one patient out of five with neoadjuvant treatment EBUS was false negative. The combination of PET/CT and EBUS avoids in a major part of patients the use of mediastinoscopy.

P94

### High diagnostic yield of EBUS guided TBNA in the diagnosis of centrally located intrapulmonary lesions

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**Introduction:** The diagnosis of centrally located pulmonary masses or nodules not visible on conventional bronchoscopy is a challenging issue. Convex probe endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a well established technique in the investigation of mediastinal and hilar lymph nodes.

**Objectives:** The purpose of our study is to address the feasibility and accuracy of convex probe EBUS-TBNA for the diagnosis of intrapulmonary tumors located close to central airways (not assessable by conventional biopsy).

**Methods:** From June 2007 to December 2009, EBUS-TBNA was performed in 8 patients with endobronchially not visible pulmonary lesions adjacent to central airways. Conventional biopsies (transbronchial forceps and/or needle, and/or brush and transthoracic needle in 1 case) were performed in 7 of the 8 cases (87.5%). All of them were non-diagnostic.

**Results:** The size of the pulmonary lesions on CT varied from 12 to 62 mm (mean 36 mm). Transtracheal (n = 3) or transbronchial (n = 5) EBUS TBNA were performed. Cytological and/or histological (cell block) samples were diagnostic in all 8 cases. The final diagnoses were lung cancer in 6 cases (6 non-small cell lung carcinoma) and metastatic tumors in 2 cases (1 melanoma, 1 malignant nerve sheath tumor).

**Conclusion:** EBUS-TBNA is a useful diagnostic approach in intrapulmonary lesions not assessable by conventional bronchoscopic biopsy. In our serie, this minimal invasive outpatient procedure had a very high diagnostic yield (100%).

P95

### Vascular postpneumonectomy syndrome: inferior vena cava and pulmonary vein compression as unusual cause for platypnea-orthodeoxia following pneumonectomy

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**Background:** Excessive mediastinal shift into the vacated thoracic cavity after pneumonectomy can result in dyspnea without hypoxemia by compression of the tracheobronchial tree, a phenomenon called postpneumonectomy syndrome. More rarely hypoxemia in upright position (platypnea-orthodeoxia syndrome, POS) after pneumonectomy can result from re-opening of an atrial right-to-left shunt through a patent foramen ovale (PFO) due to mediastinal distortion. Review of literature also shows a unique report of pulmonary veins stenosis resulting in POS without intracardiac shunt after pneumonectomy.

**Methods:** We report the case of a 32-year-old woman who presented POS 6 months after right pneumonectomy for destroyed lung post tuberculosis.

**Results:** The patient described severe dyspnea disappearing when lying. SpO<sub>2</sub> decreased from 94% when lying to 60% sitting. Transthoracic echocardiography (TTE) suspected a possible PFO. We first tried to highlight clinical repercussions of PFO by noninvasive exams. Hyperoxia shunt quantification was not tolerated because of increased dyspnea in sitting position. Contrast bubbles TTE was difficult because of the important mediastinal shift but identified only rare left heart bubbles with/without Valsalva both in lying and sitting position, excluding a significant right-to-left shunt. A lung perfusion scintigraphy (injection while sitting) confirmed the absence of systemic isotope uptake. Computed tomographic pulmonary angiography (angio-CT) revealed a stretched but not stenosed left main bronchus, while the shift of the heart into the right cavity was major. Pulmonary angiography did not show embolism but revealed compression of the inferior vena cava (IVC) with impaired venous return to the right heart, as well as compression of the left pulmonary veins. There was no arteriovenous shunt. Cardiac MRI showed torsion of IVC at the level of the diaphragm, and strong atrial contraction contributing to a passive filling of the RV, while the right ventricle was normal. Right catheterism showed major hemodynamic disturbances with negative diastolic pressure in right heart cavities (atrium -12 mm Hg ventricle pressure -7 mm Hg). SaO<sub>2</sub> measured in the pulmonary artery decreased from 58% when lying to 45% sitting.

**Conclusion:** We described here an exceedingly rare and complex mechanism explaining POS after right pneumonectomy. Mediastinal repositioning with a silicone breast implant of appropriate size has been scheduled.

P96

### A fastidious cough after pregnancy

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A 28-year-old woman presented to her physician because of cough lasting four months, halitosis and since a couple of weeks purulent and smelly sputum. She came from Santo Domingo but lived in Switzerland since five years. She was a healthy non smoking woman known only for asthma with an exacerbation during her first pregnancy three years before. The cough started during her second pregnancy but lasted in spite of her antiobstructive therapy. She had subfebrile temperatures, marked tiredness and since four weeks pain on the left hemithorax. A chest X-ray was performed showing a left inferior infiltration. She had a CRP of 27 mg/l and a erythrocytation of 32 mm/h. She was hospitalized, a chest CT-scan was performed showing a large necrotic pneumonia in the left lower lobe. Bronchoscopy showed a very inflamed lower lobe bronchus disclosing *Streptococcus salivarius*. Acid fast stains were negative but PCR for TBC was positive while a Mantoux test and a T-spot test were negative, HIV was negative in 2006. Cefuroxim and Clyndamicin were started with some clinical improvement. A month later the radiological picture was unchanged as was sputum and cough. She was addressed to a thoracic surgeon who asked for a reevaluation before proceeding with a lobectomy. A second bronchoscopy was performed at our institution showing complete obstruction of the left lower lobe with a fibrous mass. 7 cm of material were extracted which turned out to be mucoid impaction with Charcot-Leyden crystals. Antibiotics were continued with intensification of antiobstructive therapy and three weeks later an endoscopic reevaluation was performed disclosing again complete obstruction of the lower lobe. To avoid lobectomy, rigid bronchoscopy was performed with the extraction of huge masses of hard mucous leaving free but very enlarged segmental bronchi. Despite of the antibiotics *S. salivarius* and *Peptostreptococcus* grew in culture. One month later in spite of a clear clinical improvement a CT-scan still showed the necrotic lesion. A difficult lobectomy with rethoracotomy because of recidive of the infection was performed. After four weeks the patient recovered completely and pulmonary function tests were only mildly impaired.

**Conclusions:** This case nicely illustrates how uncontrolled asthma during pregnancy led to severe mucoid impaction with development of a necrotic poststenotic pneumonia resulting in giant bronchiectasis only to be managed with surgery because of its chronification.



### Poster session V

P97

### Tobacco smoke: a risk factor for pulmonary arterial hypertension? A case control study

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**Background:** Smoking is a well known risk factor for cardiovascular, lung and many other diseases. Smoking can induce pulmonary arterial hypertension (PAH) in animal models and PAH is common in smokers with chronic obstructive pulmonary disease (COPD) and thereby not correlated to the degree of airway obstruction. The impact of tobacco smoke exposure on the development of PAH in human is not known.

**Methods:** In a case control study we assessed smoking and secondhand smoke exposure in all patients with PAH and chronic thromboembolic pulmonary hypertension (CTEPH) seen at our PH clinic from 2002 until July 2008. Data from PAH-patients were compared with CTEPH and healthy controls from the Swiss health survey 2007 (SHS).

**Results:** 91 PAH-patients were compared with 64 CTEPH-patients and 18747 controls (women 58, 36, 10331 respectively). Tobacco smoking was significantly more common in PAH compared to CTEPH and controls. This difference could be attributed to men. PAH-patients also smoked longer and heavier compared to CTEPH. In addition, secondhand smoke exposure was significantly more common in PAH-non-smokers compared to controls.

**Conclusion:** Our data indicate that tobacco smoke exposure may be a risk factor for men with PAH. Considering smoking as a risk factor for PAH will have implication in counseling patients and especially their hitherto unaffected relatives. Further research on the pathogenetic role of smoking in PAH is warranted.

P98

### Factors influencing the success rates of smoking cessation intervention

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**Background:** At the cantonal hospital of St. Gallen (KSSG) smoking cessation counselling, as in other hospital settings, is under-utilized. One reason could be the absent or non-obvious association between smoking and the actual patient's diagnosis. We speculated whether patients from different departments react with different quit rates. Our aim was to evaluate which factors influence the success of smoking cessation.

**Methods:** We retrospectively analyzed the short-time success rate of 645 patients registered to the smoking cessation consultation at the KSSG between 2006 and 2009. The medical attendance provided by a trained physician consisted of counselling and optional pharmacological treatment. Using logistic regression, we tested the

influence of various factors (including referring department, diagnosis, malignancy and motivation assessed with the Prochaska-staging) on the quit rate 1 month after first consultation.

**Results:** More than half of 232 patients with a 1-month follow-up quit smoking (overall estimate quit rates between 2006 and 2009: 31–47%). We did not find any relationship between quit rate and the department referring the patient ( $\chi^2$ -square test:  $p = 0.827$ ). In addition, there was no significant difference between quit rates and different diagnoses. The presence of malignancy had no effect on the quit success ( $p = 0.54$ , OR = 0.8 [0.4–1.8]). On the other hand, motivation was significantly associated with the success rate. Patients in the active Prochaska stage have much higher success rates as compared to the low-motivated patients ( $p = 0.004$ , OR: 12.3 [2.6–89.9]).

**Conclusion:** Success rates after smoking cessation counselling and treatment seem to be independent of the department referring the patient and current diagnosis (incl. malignancy) leading to hospital admission. Motivation is a key factor in the smoking cessation process. Therefore, medical care givers of all departments should be encouraged to provide support in smoking cessation to every smoker; i.e. all patients should systematically get a short intervention at the time of admission, and motivated patients should be sent for additional intervention.

P99

### Efforts of industry to influence tobacco control policy in Switzerland

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**Background:** Starting in parliament in 2004, the federal law on protection from passive smoke was voted in 2008. It allows smoking establishments and “fumeurs”, where food may be served. Thus it does not meet international standards of the Framework Convention of Tobacco Control (FCTC), suggesting heavy lobbying during its elaboration despite low profile of the Tobacco industry (TI).

**Aim:** To find proofs for influencing policy by TI and proxys.

**Method:** Analysis of media reports, archives and parliamentary debates.

**Results:** 1990: The law on no smoking tables is rejected by the cantonal parliament of Lucerne. Philip Morris (PM) attributes this (intern.note PM2024195742) to briefing of its “allied” members of Parliament, the director of the restaurant owners association and the cantonal head of USAM (Schweiz.Gewerbeverband). 1992: The later rejected “twin initiative” to ban tobacco and alcohol advertising was diverted by the publicity industry to a debate about “abusive” restrictions on advertising. 1994: PM infiltrates HÔtelREstaurant CAFéInternat.and GASTROSUISSE(GS). 1995: Internat.HoReCa congress is sponsored by PM: members of GS and its later director FI.Hew participate. The congress resolution(rejection of “trends to ban eating, drinking and smoking”, of government interference and free choice of owners to decide about smoking) is re-edited 1996 by GS. 2005: Law professor Auer, paid by Reynolds Tobacco, refutes the constitutionality of the Geneva popular initiative for smoking ban. 2004-08: attempts to dilute the law proposal for a federal smoking ban come all from GS and USAM. FI.Hew is at parliamentary hearing. 2008: USAM, GS, Hotellerie-suisse, Swiss publicity, Swiss Zigarren-fabrikanten, Swiss Tabakwarenhandel and others create the alliance on economy for a moderate prevention policy (AWMP). The USAM journal denigrates the head of the federal public health authority as “health taliban”, the term is repeated in popular newspapers and TV emissions.

**Conclusion:** The TI allies GS, USAM and Swiss publicity undermine tobacco control policy since the nineties. Because all media are heavily dependent on advertising money, the covering of public health and prevention issues is likely to be strongly influenced by Tobacco interests.

P100

### Case report of a 55-year-old man with fire-eater’s lung

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**Background:** Fire-eater’s pneumonitis, also known as fire-eater’s lung, is an acute inflammatory response of the lungs to the accidental aspiration of petroleum.

**Case presentation:** A 55-year-old, previously healthy, smoking, fire-eating male presented himself to the emergency department complaining of pleuritic pain, dyspnea, cough and hemoptysis. Two days before, during a pyrofluid performance, he accidentally aspirated a small amount of petroleum blowing out a mouthful of petroleum against a burning stick. Physical examination revealed a cachectic, febrile and tachypneic patient with dullness on percussion and bilateral crackles. Blood tests showed elevated leukocytosis without left shift and a high serum level of CRP (100 mg/l). Chest radiogram and chest-CT revealed patchy bilateral alveolar infiltrates in the middle and lower

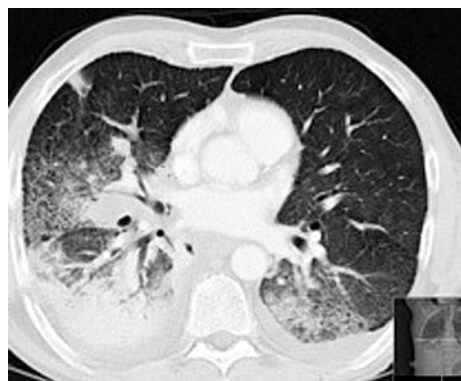
parts of both lungs and pleural effusions (picture B and C). Within a week the patient’s symptoms became worse with intermittent fever, hypoxemia requiring oxygen and a progression of the bilateral infiltrates and pleural effusions. Percutaneous catheter drainage was necessary. The bronchoscopy and cytbacteriologic findings were unremarkable. However, a treatment with antibiotics was started. The clinical and radiological course improved only slowly. After another four weeks of hospitalisation, the patient was ready for pulmonary rehabilitation. The intermittent fever attacks disappeared in the course of his rehabilitation. The clinical and radiological findings improved further, the arterial blood gases corrected and the lung function tests normalised. The patient reached a distance of 600 meters in his six-minute walk test.

**Conclusion:** 1. Fire-eater’s pneumonitis is an infrequent clinical occurrence caused by the accidental aspiration of petroleum products during a show of a fire-eater.

2. There is no good evidence, that systemic corticosteroids and antibiotics were effective in treating hydrocarbon aspiration.

3. The patient prepared his individual mixture of different petroleum distillates. This might also alter the clinical evolution.

4. This condition is a medical emergency and a potential cause of severe pleuropulmonary complications. Despite the severe initial clinical symptoms and radiological presentation, fire-eater’s pneumonitis has usually a favourable evolution with “restitutio ad integrum”.



P101

### Severe acute respiratory distress syndrome after smoke bomb explosion

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A 23-year-old Swiss soldier was exposed to artificial smoke containing zinc chloride (ZnCl<sub>2</sub>) during a military exercise. He developed progressing respiratory distress, which led to respiratory failure and ARDS. Respiratory failure after ZnCl<sub>2</sub> exposure is a known toxic reaction and is usually prevented by wearing gas masks or by avoiding the use of zinc chloride-producing grenades at all. Only limited data are available regarding pathogenesis, clinical course or effective therapeutic strategies. Outcome in most reported cases was fatal. We present a case of acute alveolar injury after inhalation of ZnCl<sub>2</sub> to discuss its implication on lung structure and function over the course of acute illness and final recovery. We further summarize current knowledge and concepts in the management of patients exposed to smoke containing ZnCl<sub>2</sub>. Zinc chloride is a major byproduct of chemical reactions occurring during the blast of explosives used as smoke bombs primarily in military settings. Due to their small size of 1 micrometer and their dense concentration, ZnCl<sub>2</sub> particles easily enter into the bronchial tree and eventually into the alveoli, thereby provoking a severe inflammatory response. As in our case, dramatic

structural changes have been documented in computer tomography series. Diffuse ground glass opacities in early phase are progressing to structural changes like interstitial infiltrates and parenchymal destruction with development of pneumatoceles and pneumothoraces. Therapeutically, apart from mechanical ventilation, no intervention is established nor does an antidote to ZnCl<sub>2</sub> exist. N-Acetylcystein, as a chelating agent, or steroids have not shown to improve outcomes. Treatment is thus limited to strict adherence to lung protective strategies during mechanical ventilation. Despite the generally grim prognosis, the mentioned radiological changes are potentially reversible as is the loss of lung function. Repeated lung function testing in our patient over several months showed impressive improvement in all markers of respiratory functions, particularly DLCO and ergospirometry. We conclude that despite of the deleterious effects of ZnCl<sub>2</sub> inhalation, outcome may be positively influenced by applying advanced respiratory ventilation concepts and by early rehabilitation. Further we suggest that use of smoke bombs containing ZnCl<sub>2</sub> should be banned from any exercise setting, military or other, because of the extremely destructive pulmonary effects described above.

P102

### Impact of a smoking cessation service in a non-university hospital

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**Background:** A smoking cessation service (scs) exists at the Bürgerspital Solothurn since 1999 (1). With a one-off financial incentive by the Hospital Quit Support project of the Swiss Federal Office of Public Health (2) a smoking cessation counsellor could be recruited. We report on our data over 19 months 2008/09.

**Methods:** Behavioural and pharmacologic counselling for in- and outpatients as well as for employees by a MD and a counsellor specially trained in smoking cessation. Follow-up visits 1 and 3 months after first counselling and a phone call on Nov 30 2009 in pts with >= 3 interventions.

**Results:** 286 patients (pts) were admitted (176 men, 110 women); mean age 52 years (SD 13.5), 21.9 (SD 11.3) cigarettes/day, 41.2 (SD 28.2) pack years, Fagerström Test for Nicotine Dependence (0 low – 10 high): 4.4 (SD 2.4); 577 interventions overall. Interventions consisted of counselling alone (51% of pts), NRT (31%), Varenicline (16%), bupropion and bupropion/NRT (2%). At follow-up visits after 1 and 3 months 51/94 pts (54%) and 27/65 pts (42%) were quitters respectively. After 1 month 15/19 (79%) inpts and 36/75 (48%) outpts were quitters (p = 0.016) whereas no difference was found after 3 months. At the phone call Nov 2009 12/63 pts (19%) were smoke-free for more than 6 months (mean 396 [SD 127] days). 15/42 persistent smokers (36%) stopped smoking temporarily for <= 3 months (n = 8) and 3-6 months (n = 7). 14/42 persistent smokers (33%) reported a transient reduction of smoked cigarettes to <50%. Pts' ratings of our scs and the recommended medication were "not helpful" (8%/49%), "little helpful" (17%/14%), "helpful" (32%/16%) and "very helpful" (43%/21%) respectively.

**Conclusion:** Our scs had an important impact on smoking pts and prompted a substantial number of them to stop smoking either definitively or temporarily or to reduce the number of cigarettes smoked. A follow-up after discharge from hospital is crucial. The scs

was very much appreciated, 75% of pts rated it as helpful or very helpful. The reserved ratings of the medications' helpfulness may be due to the fact that pts still have to pay for it and therefore tend to use it scarce. Scs should be made standard practice in hospitals and health insurance companies should accept the costs of medications for smoking cessation.

1) Eur Respir J 2005;26(Suppl.49):245s. 2) Swiss Med Wkly 2008;138(29–30):427.

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P103

### Support of an efficient passive smoke protection by parties and individual mp's in the Swiss Federal Parliament, 2004–2008

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**Background:** Initiated 2004 by MP Gutzwiller, MD, the federal law on protection from passive smoke exposure was passed 2008. It comprises exceptions: smoking establishments and "fumeurs" with food service. Thus it fails to meet international standards of the WHO Framework Convention of Tobacco Control, signed by Switzerland in 2004, suggesting heavy lobbying by proxies of the Tobacco industry (TI).

**Aim:** To determine the political support/opposition of/to efficient Tobacco control measures by the federal parliament during elaboration of the new law.

**Method:** Analysis of parliamentary records, news reports and the smartvote database (pre-election answers of MP's).

**Results:** The original proposal of smoking ban in workplaces was expanded by the multiparty commission of the National council (lower chamber) to include public places, nonserviced "fumeurs" only tolerated. But the commission's minority proposal (smoking establishments and served "fumeurs" tolerated) by a SVP (right wing) party MP, on behalf of Gastro Suisse, was adopted by the lower chamber by 95 yes/77 no, in 2007. Four MP's of the CVP party and 2 of RL party voted for the adopted proposal, while they were for a smoking ban according to smartvote. In fall 2007 elections took place. A newspaper reported that 56 of 62 newly elected MP's from french speaking Switzerland were for smoking bans in public places. For the debate of the upper chamber Swiss thoracic society's members wrote to MP's of the upper chamber: passive smoke is toxic, health professionals are not extremists, compromise only serves TI. MP's of both chambers received the book on the Philip Morris/Rylander case. By a vote of 25 yes/9 no and 2 abstentions the upper chamber adopted a smoking ban with the only exception of "fumeurs"; where food would be served, provided written consent by the waiters; Cantons can enact stricter laws. In contrast, the lower chamber kept its proposal allowing smoking establishment and served "fumeurs" by 94 yes/86 no. Five CVP, 2 SVP, 2 RL and 2 SVP MP's did not vote as stated to smartvote and 15 out of the 56 MP who were for a strict smoking ban voted yes. Finally the actual law passed by a minimal majority.

**Conclusion:** Support of an efficient smoking ban is strongest on the left wing of the political spectrum and nearly none on the right. Voting discipline is strong (but not absolute) at both extremes, while discrepancies between declared opinion and actual vote are found in the center, more so in CVP than in RL.

### Index of first authors

The numbers refer to the pages of this supplement.

Baty F 4 S	Heinzer R 3 S	Lazor R 7 S	Savic S 3 S
Beck E 13 S	Hillgärtner F 17 S	Lepper PM 5 S	Schertel A 8 S
Becker JC 13 S	Hofer M 6 S, 7 S	Leuenberger A 9 S	Schiess R 16 S
Bethke TD 13 S	Huynh CK 7 S	Lovis A 3 S	Schmid T 11 S
Blank F 4 S		Ludwig P 16 S	Schneeberger Geisler S 10 S
Borer H 18 S	Jochmann A 7 S		Studer A 5 S
Bratkovskis M 10 S	Jung H 12 S	Nembrini C 10 S	Studer D 17 S
Brun P 10 S		Noirez L 16 S	
	Kaelin M 17 S	Nussbaumer-Ochsner Y 2 S	Tueller C 12 S
Chiarini B 11 S	Kaelin R 18 S		
	Kern L 9 S	Pasquina P 9 S	Ulrich Somaini S 8 S
Dorn P 15 S	Köhler M 9 S	Prella M 11 S	
Dumont P 15 S	Kraemer R 5 S, 14 S		Vareille M 4 S
	Kroker A 14 S	Rexhaj E 2 S	Weber M 14 S
Gazdhar A 4 S	Kunz A 12 S	Rochat M 14 S	
Gelpke H 15 S		Rolke M 13 S	Yerly R 11 S
Gex G 6 S	Langenskiöld E 12 S		
Györök S 16 S	Latshang T 2 S, 8 S		