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Prevalence of airway obstructions in smokers and non-smokers in Switzerland

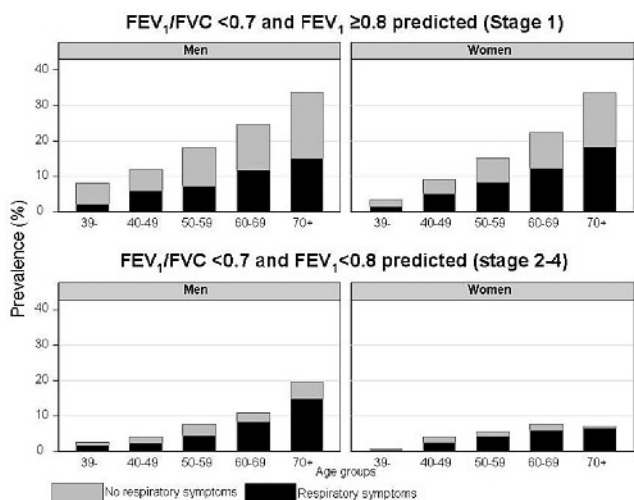
P.-O. Bridevaux, N. W. Probst-Hensch, C. Schindler, O. Braendli, M. Brutsche, L. Burdet, M. Frey, M. W. Gerbase, B. Knöpfli, M. Pons, J.-M. Tschopp, T. Rochat, E. W. Russi for the SAPALDIA

Background: Accurate estimates of prevalence of airways obstruction (AO) help to predict future public healthcare need and to provide probability of AO for patients seeking medical attention. AO prevalence is unknown in Switzerland. We aimed to measure prevalence of AO in smokers and never smokers using pulmonary function tests (PFTs) and respiratory symptoms.

Methods: The SAPALDIA study (Swiss Cohort Study on Air Pollution and Lung Diseases in Adults) provided PFTs on 6127 adults in 2002 (mean age 52 [range 28–73]; men 48%, smoking status: never 43%; former 32%; current 25%). Obstruction was defined and graded according to The Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommendations. Separate analyses were performed on smokers and never-smokers.

Results: Overall, prevalence of AO stage 2–4 was 5.9%. It ranged from 1.7% in subjects aged 30–39 to 12.5% in those aged 70 or more (see figure). In multivariate analysis, age (OR aged 70+ vs aged 30–39 7.3), ever smoking (OR 1.7), atopy (OR 1.4), asthma, (OR 5.8), obesity (OR body mass index 30+ vs <21 1.9) and being a foreigner (OR 1.4) were associated with obstruction stage 2–4. Environmental tobacco smoke represented an additional risk only in smokers. Never smokers constituted 30.5% of subjects with stage 2–4 obstruction. Never smokers with AO were younger, had more frequently asthma, atopy and positive methacholine challenge than obstructive smokers. Symptoms were equally present and quality of life scores equally impaired in smokers and never smokers with AO.

Conclusions: Prevalence of AO in Switzerland is similar in magnitude compared to other western countries. Never smokers account for a third of the prevalence which is higher than elsewhere. Detection of AO in never smokers should be considered.



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Safety of large-particle talc pleurodesis after talc poudrage under thoracoscopy for primary spontaneous pneumothorax. A European multicentre prospective study

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Background: Safety of talc pleurodesis is disputed after reports of acute respiratory distress syndrome (ARDS) and death. Small particle size talc use may have caused these adverse events. The safety of larger particles is however still debated. We report the safety results of the largest prospective study on the use of large-particle talc for talc poudrage pleurodesis to prevent recurrence of primary spontaneous pneumothorax (PSP).

Method: Patients with recurrent or primary spontaneous pneumothorax (n = 390) from 9 centres in Europe and South Africa participated in a prospective study between 2002 and 2007 with records of minor and major complications. Main exclusion criteria were infection, heart disease, coagulation disorders. Serious adverse events (ARDS, death, other) were recorded up to 30 days after procedure.

Results: Patients mean age was 30.3 (SD 12.4; range 15–84), male sex (n = 277, 71%). All had thoracoscopy with pleurodesis by talc poudrage. Pleural drains were removed after day 4 for 80% of patients. During the 30 day observation period after the talc poudrage, no ARDS, intensive care unit admission or death were recorded. One patient presented hazy infiltrate 2 hours after poudrage. After pleurodesis, mean body temperature increased by 0.41 °C (CI95% 0.33–0.48; p < 0.001) at day 1 and by 0.37 °C (CI95% 0.29–0.44; p < 0.001) at day 2. No significant temperature differences were present at day 3.

Conclusion: Serious adverse events, including ARDS or death were absent in this large, multicentric cohort. This supports the safety of pleurodesis by talc poudrage under thoracoscopy using large-particle talc to prevent recurrence of primary spontaneous pneumothorax.

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Evaluation of fitness to use self containing breathing apparatus in the Swiss Armed Forces

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Background: Breathing dry cold air may cause bronchoconstriction in asthmatics working with self containing breathing apparatus (SCBA). Recruits who are assigned to work with SCBA are evaluated during conscription to rule out active asthma. It is unclear if a bronchial challenge test with mannitol (BCTM) can predict fall in FEV₁ during exercise with SCBA, healthcare resource use and days off work due to sick leave during military basic training (MBT).

Methods: Prospective study of recruits assigned to work with SCBA at the Rttg RS 75 in Wangen aA. Self administered questionnaire on respiratory symptoms, BCTM (Aridol, Pharmaxis, French Forest, Australia) and measurement of exhaled nitric oxide (eNO; NioxMINO, Aerocrine, Solna, Sweden). Subjects with a positive BCTM (BCTM+) and a group of subjects with negative BCTM underwent exercise test on bicycle ergometer (ET) while using SCBA (PA 94plus and mask Panorama Nova (Dräger, Luebeck, Germany)). Mannitol test was considered as positive if FEV₁ dropped more than 10% between two measurements or a drop of FEV₁ of 15% from baseline. Asthma was defined as having a positive BCTM and symptoms. Exercise test was counted as positive if FEV₁ dropped >10% from baseline or exercise challenge was terminated because of dyspnoea.

Results: 106 recruits participated in this study. 102 underwent BCTM and 28 ET. 19/97 had a positive BCTM and 6/27 a positive ET. 17 out of 19 with a positive BCTM had current respiratory symptoms like wheeze, cough, chest tightness or dyspnoea. Sensitivity, specificity, positive predictive value and negative predictive value for a positive ET under SCBA were 100%, 64%, 43% and 100% for the BCTM. The negative predictive value of eNO levels lower than 22.5 ppb for asthma were 81% overall and 93% in non-smokers. Lack of a history of hayfever and eNO <22.5 ppb excluded asthma in 96% (Specificity). BCTM positive subjects had a mean of 3.2 doctors visits during MBT compared to 1.9 visits in BCTM negatives (p = 0.156). BCTM positive subjects had a mean of 1.6 days of hospitalization during MBT compared to 0.6 visits in BCTM negatives (p = 0.003).

Conclusion: Despite medical evaluation and exclusion of asthmatics by a physician during conscription, a high proportion of recruits assigned to work with SCBA do have respiratory symptoms and a positive BCTM suggesting current asthma. BCTM has a high sensitivity to predict significant fall in FEV₁ after exercise with SCBA and subjects with a positive BCTM tend to use more healthcare resources during MBT.

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Outpatient hospital-based pulmonary rehabilitation in Solothurn 2000–2008

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Background: Data of the outpatient hospital-based pulmonary rehabilitation program (OPR) 2000–2008 in the city of Solothurn are presented.

Methods: 253 patients (pts) (65 ± 10 years; FEV₁: 1.45 L (± 0.63) = 58%; 61% men) with a clinically relevant pulmonary problem (COPD 74%, asthma 14%, others 12%) were evaluated. The OPR-program following the guidelines of the Swiss society of pulmonary physicians consisted in physical training (predominantly cycling), gymnastics and information three times a week two hours for three months. Lung function (spirometry), exercise capacity (incremental cycle-ergometer test, 6-min walk distance), dyspnea and quality of life (chronic respiratory disease questionnaire (CRQ), SF-36) were assessed at baseline and after the program.

Results: While lung volumes and cycle-ergometer tests did not change, 6-min walk distance improved significantly from 366 m (± 97) to 406 m (± 103) (p < 0.001) after OPR. All domains of the CRQ improved significantly (p < 0.001). All domains of the SF-36 improved,

50% of them significantly ($p < .05$). 32/253 pts (13%) dropped out due to a lack of motivation (9), medical (9) or unknown reasons (14). 91/253 pts (36%) participated in an individual open end follow-up program (FUP) once a week. Pts participating in the FUP had better results concerning lung function, exercise capacity, CRQ and SF-36 before and after OPR compared to pts who did not attend the FUP.

Conclusions: Overall attendance rate of the OPR was good despite an intensive program with three sessions per week. As in other OPR COPD was the most frequent diagnosis, whereas postoperative pts were relatively underrepresented indicating a possible need for sensitizing our surgeons and GPs for OPR. Exercise capacity (endurance performance more than maximum workload), quality of life and overall performance in daily life improved after OPR. Drop out rate was low indicating a good patient selection, a good job of our physiotherapists and an adequate support from the pts GPs. Participation in the FUP was relatively low and represented a selection of the anyway better pts. Offering additional locations for FUP nearer to the pts home may ameliorate its attendance rate.

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Adverse health effects of altitude on untreated patients with obstructive sleep apnoea. A randomised, controlled study

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Background: Many patients with obstructive sleep apnea syndrome (OSA) travel to the mountains for recreational and professional activities while temporarily discontinuing CPAP. Since the physiologic consequences of altitude exposure in OSA patients are not known, we evaluated the hypothesis that sleep related breathing disturbances are aggravated and cardiovascular stress is enhanced by hypoxia in these patients.

Methods: 34 OSA patients, median age 62y, residing at <600 m discontinued long-term CPAP therapy for 8 nights. They spent days 1 to 4 at low altitude and days 5 to 9 at high altitude in 2 mountain resorts (Davos Schatzalp, 1850 m, and Davos Jakobshorn, 2590 m), 2 days and nights each. They were randomized to undergo clinical evaluation and polysomnographies either during the last day in Zurich (490 m) before ascent to altitude and during 4 days in Davos, or during 4 days in Davos and on the first day after their return to Zurich, respectively.

Effect of altitude exposure in untreated OSA patients		
	Zurich, 490m	Davos, 2'590m, 1 st night
SpO ₂ (%)	94 (93;95)	88 (84;89)*
PtcCO ₂ (mmHg)	47 (44;50)	37 (34;42)*
AHI total (1/h total sleep time)	51 (32;74)	90 (62;103)*
AHI obstructive (1/h, NREM)	42 (21;82)	31.1 (3;52)
AHI central (1/h, NREM)	3 (1;10)	54 (31;78)*
AHI obstructive (1/h, REM)	36 (21;63)	34 (0;65)
AHI central (1/h, REM)	3 (0;2)	10 (1;38)*
NREM stage 3+4 (%)	14 (8;23)	6 (0;12)*
REM (%)	13 (9;18)	10 (4;16)*
Sleep efficiency (%)	86 (80;89)	78 (61;84)*
Arousal index (1/h)	36 (25;43)	51 (38;66)*
Heart rate (1/min TIB)	57 (55;62)	66 (58;72)*
Premature beats (1/h TIB)	3 (1;11)	7 (2;30)*
BP systolic (mmHg)#	130 (120;140)	144 (132;160)*
BP diastolic (mmHg)#	85 (80;90)	85 (81;90)
Weight (kg)#	99 (83;111)	100 (85;112)*

n=34, medians (quartiles) of polysomnographic data. Variables marked with # were measured in the following morning. AHI=apnea/hypopnea index, SpO₂=oxygen saturation, PtcCO₂=transcutaneous carbon dioxide tension, NREM/REM=(non)rapid eye movement sleep, TIB=time in bed, BP=blood pressure. * $p < 0.05$ vs. 490m.

Results: The table summarizes the results. Compared to Zurich, in the 1st night at Jakobshorn (2590 m), oxygen saturation and carbon dioxide tension were reduced while the apnea/hypopnea index was nearly doubled due to frequent central apnea in NREM sleep. Slow wave sleep was reduced and arousals were more prevalent. Heart rate and prevalence of premature beats were increased, blood pressure was elevated and patients had gained weight at altitude.

Conclusions: These findings indicate that untreated OSA patients at altitude experience a further destabilization of their ventilation by hypoxic ventilatory stimulation causing hypocapnia and a reduced CO₂ reserve. Consistent with ventilatory control theory, central apnea at altitude prevails mostly in NREM sleep. Hypoxia, pronounced oscillatory breathing, disturbed sleep and enhanced cardiovascular stress with water retention are all potentially serious adverse effects that occur even during a short-term sojourn at moderate altitude in untreated OSA patients. Therefore, effectiveness of CPAP and other treatment modalities should be evaluated in this setting.

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Ultrathin bronchoscope versus standard-size bronchoscope in the assessment of solitary pulmonary nodules: a randomised pilot trial

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Background: Bronchoscopic evaluation of solitary pulmonary nodules (SPN) is challenging when the lesion is not visible during endoscopy. The aim of this study is to compare the diagnostic yield of flexible bronchoscopy using an ultrathin bronchoscope (UB, Olympus XP 40, outer diameter 2.8 mm, working channel 1.2 mm) with that of a standard-size bronchoscope (SB) in SPN.

Methods: Consecutive patients (pts) with SPN (diameter <6 cm) on CXR and negative sputum cytology and microbiology were evaluated with contrasted computed tomography (CT) scan and bronchoscopy. Written informed consent for study inclusion was obtained. Pts with endoscopically non-visible lesions on SB were randomised during the procedure to continued bronchoscopy with SB or to UB (= immediate change to UB). All biopsy methods (brush, needle, forceps, wash) were used guided by fluoroscopy, and sent for cytological, histological and microbiological examination. All bronchoscopists were familiar with the UB.

Results: Of the 40 evaluable patients (22 females) the mean age was 55 years for UB (N = 20) and 52 years for SB (N = 20). The mean diameter of the lesion was 2.2 cm for both groups. The nodule was reached on fluoroscopy in 60% and 65% for UB and SB groups, respectively. Lesions were clearly moved during biopsy in 4/20 in UB and 7/20 in SB. Two lesions (1 malignant) were visualised endoscopically by UB. Mean procedure time was 31 min for (SB+UB) and 26 min for SB. The following final diagnoses were made (by surgery 16 pts, serial chest X-rays or CT scans with clinical follow-up for >2 years 19, and transthoracic biopsies 5): Carcinomas 16/40, active tuberculosis 4/40, and benign lesions 20/40. Bronchoscopic evaluation (using all available results) was considered diagnostic for 11/20 in UB and for 16/20 in SB. Malignancy was documented in 4/8 in UB and in 5/8 in SB groups. Complications during bronchoscopy occurred in 6/20 with UB: severe blockage of working channel or insufficient suction (3pts), unusually restless patients (2), hypertensive crisis (1) and 1/20 with SB: strong bleeding after biopsy prolonging procedure.

Conclusion: Only 10% of lesions were visualised endoscopically by the ultrathin bronchoscope. More complications and prolonged procedure time were drawbacks of ultrathin bronchoscopy. These results indicate no advantage of ultrathin bronchoscopy over standard-size bronchoscopy alone in the evaluation of solitary pulmonary nodules.

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Stem cells reduce pulmonary fibrosis in an animal model

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Background: Abnormal alveolar wound repair leads to pulmonary fibrosis. Bone marrow derived mesenchymal stem cells (BMSC) are multipotential stem cells and capable of differentiation to various cell types. We showed that BMSCs increase alveolar epithelial repair in vitro and therefore investigated the in vivo effect of BMSC in an animal model of bleomycin induced lung injury and fibrosis.

Method: Seven days after bleomycin induced lung injury the rats were intratracheally instilled with 3x10⁶ of BMSC that were isolated from bone marrow of rats, whereas the control animals were instilled with culture media only. 7 days after BMSC instillation the animals were sacrificed and tissues collected for analysis.

Results: Bleomycin induced lung fibrosis was reduced 7 days after BMSC instillation as assessed by histology (Ashcroft Score) and the hydroxyproline assay compared to the control animals (3066 ± 377 vs 4421 ± 469 ug/mg of lung tissue). BMSC homed to a higher extent at the site of injury compared to relatively normal lung tissue, as shown by confocal microscopy. High expression of metalloproteinase-2 (MMP2), as detected by zymography suggests a possible MMP-dependent mechanism that may be at least in part responsible for the reduced fibrosis in presence of BMSC.

Conclusion: BMSC reduce bleomycin induced pulmonary fibrosis in the rat model. The BMSC home to a higher extent at injured sites. Furthermore, there is possible involvement of MMP2 in reduction of fibrosis. BMSC may represent a promising therapeutic option for the treatment of pulmonary fibrosis and need further investigation.

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Decreased intrathrombocytic serotonin levels and transpulmonary gradient in patients with pulmonary hypertension

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Background: The serotonin system may be pathogenetically involved in pulmonary hypertension (PH). We measured plasmatic and intrathrombocytic serotonin levels of arterial and mixed venous blood in patients with pulmonary hypertension and in controls.

Methods: Catheters were placed in the radial and pulmonary artery in patients with PH (n = 13) for diagnosis and in controls (n = 6) before percutaneous closure of patent foramen ovale. Arterial and mixed venous blood was obtained and each sample immediately centrifuged to obtain plasma and platelets and thereafter frozen at -80 °C. After careful thawing, plasmatic and intrathrombocytic serotonin levels were determined by ELISA.

Results: PH was classified as arterial in 3 and chronic thromboembolic in 10 patients with a mean pulmonary artery pressure of 38 ± 9 mm Hg. Intrathrombocytic serotonin content was significantly lower in PH vs. controls (48 vs. 149 ng/ml, p < .001 in arterial and 59 vs. 120 ng/ml, p = .02 in mixed venous blood). The mean transpulmonary gradient (arterial-mixed venous) was negative in PH and positive in controls (-11 ± 21 vs. 30 ± 38 ng/ml, p = .03). Plasmatic serotonin levels were much lower and did not differ between PH and controls (5.1 ± 2 vs. 6.1 ± 1 and 5.3 ± 3 vs. 6.2 ± 1 ng/ml for arterial and mixed venous).

Conclusion: We herein demonstrate for the first time lower intrathrombocytic serotonin levels in PH vs controls. The negative transpulmonary serotonin gradient in PH might point towards a serotonin consumption in the PH-lung. In contrast to others (Herve P, Am J Med 1995), we did not find higher plasmatic serotonin levels in PH compared with controls.

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Development of Elispot and CFSE flow cytometric assays for detecting beryllium sensitivity

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Background: Beryllium sensitization (BeS) is caused by exposure to beryllium in the workplace and may progress to chronic beryllium disease (CBD). This granulomatous lung disorder mimics sarcoidosis clinically, but is characterized by beryllium specific CD4+ T-cells immune response. BeS is classically detected by beryllium lymphocyte proliferation test (BeLPT), but this assay requires radioactivity and is not very sensitive. In the context of a study aiming to evaluate if CBD patients are misdiagnosed as sarcoidosis patients in Switzerland, we developed EliSpot and CFSE beryllium flow cytometric test.

Methods: 23 patients considered as having sarcoidosis (n = 21), CBD (n = 1) and possible CBD (n = 1) were enrolled. Elispot was performed using plate covered with gamma-IFN mAb. Cells were added to wells and incubated overnight at 37 °C with medium (neg ctrl), SEB (pos ctrl) or BeSO₄ at 1, 10 and 100 microM. Anti-IFN-gamma biotinylated mAb were added and spots were visualized using streptavidin-horseradish peroxidase and AEC substrate reagent. Results were reported as spot forming unit (SFU). For Beryllium specific CFSE flow cytometry analysis, CFSE labelled cells were cultured in the presence of SEB and 1, 10 or 100 microM BeSO₄. Unstimulated CFSE labeled cells were defined as controls. The cells were incubated for 6 days at 37 °C and 5% CO₂. Surface labelling of T-lymphocytes and vivid as control of cells viability was performed at the time of harvest.

Results: Using EliSpot technology, we were able to detect a BeS in 1/23 enrolled patients with a mean of 780 SFU (cut off value at 50 SFU). This positive result was confirmed using different concentration of BeSO₄. Among the 23 patients tested, 22 showed negative results with EliSpot. Using CFSE flow cytometry, 1/7 tested patients showed a positive result with a beryllium specific CD4+ count around 30% versus 45% for SEB stimulation as positive control and 0.6 % for negative control. This patient was the one with a positive EliSpot assay.

Conclusions: The preliminary data demonstrated the feasibility of Elispot and CFSE flow cytometry to detect BeS. The patient with a beryllium specific positive EliSpot and CFSE flow cytometry result had been exposed to beryllium at her workplace 20 years ago and is still regularly controlled for her pulmonary status. A positive BeLPT had already been described in 2001 in France for this patient. Further validation of these techniques are in progress.

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Exposure to super-paramagnetic iron oxide nanoparticles reduces dendritic cell-dependent antigen-specific T-cell proliferation

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Background: Despite intense research efforts for the development of biomedical nanomaterials, there is growing concern about their clinical applicability for therapeutic and diagnostic purposes, especially in the vulnerable respiratory tract environment. The vast potential for future clinical applications stands in sharp contrast with toxicological data that stems from epidemiological and experimental research on ambient nanoparticles (NP). To date, very few general trends have emerged that enable prediction of inflammatory and immune responses to a specific type and size of biomedical NP. Dendritic cells (DC) are key antigen-presenting cells that induce innate immunity and regulate T cell responses in the respiratory tract.

Methods: Monocyte-derived human DC (MDDC) were exposed for 12 h to fluorescent poly(vinylalcohol)-coated super-paramagnetic iron oxide NP (PVA-SPIONS), uptake was quantified by FACS and imaged by confocal (CM) or electron microscopy (EM).

Results: Uptake of PVA-SPION by MDDC was detected by a dose-dependent fluorescence increase by FACS that was decreased by concomitant LPS exposure. Intracellular PVA-SPIONS were readily imaged by CM / EM, and did not induce surface phenotypic changes (CD80, CD83, CD86, myeloid DC, or plasmacytoid DC markers) as measured by FACS. PVA-SPION exposure altered DC function by decreasing antigen specific (tetanus toxoid) CD4+ T cell proliferation.

Conclusion: Though PVA-SPIONS did not induce DC activation, exposure modulated antigen-specific CD4+ T cell proliferation. To further delineate immune effects of NP, forthcoming studies will investigate NP-cell interactions and alterations in antigen uptake, processing, and presentation. The development of novel therapeutic and diagnostic applications for nanomaterials in the respiratory tract will require meticulous clarification of exposure-related immunological and inflammatory effects.

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Performance anxiety: cardiorespiratory activity in high- and low-anxious professional music students in a performance situation

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Questionnaire studies indicate that high-anxious musicians may suffer from hyperventilation symptoms before and/or during performance. Reported symptoms include amongst others shortness of breath, fast or deep breathing, dizziness and thumping heart. A self-report study by Widmer, Conway, Cohen and Davies (1997) shows that up to seventy percent of the tested highly anxious musicians are hyperventilators during performance. However, no study has yet tested if these self-reported symptoms reflect actual cardiorespiratory changes just before and during performance. Disturbances in breathing patterns and hyperventilation may negatively affect the performance quality in stressful performance situations.

The main goal of this study is to determine if music performance anxiety is manifest physiologically in specific correlates of cardiorespiratory activity. We studied 74 professional music students of Swiss Music Universities divided into two groups (high- and low-anxious) based on their self-reported performance anxiety (State-Trait Anxiety Inventory by Spielberger). The students were tested in three distinct situations: baseline, performance without audience, performance with audience. We measured a) breathing patterns, end-tidal carbon dioxide, which is a good non-invasive estimator for hyperventilation, and cardiac activation and b) self-perceived emotions and self-perceived physiological activation.

Analyses of heart rate, respiratory rate, self-perceived palpitations, self-perceived shortness of breath and self-perceived anxiety for the 15 most and the 15 least anxious musicians show that high-anxious and low-anxious music students have a comparable physiological activation during the different measurement periods. However, high-anxious music students feel significantly more anxious and perceive significantly stronger palpitations and significantly stronger shortness of breath just before and during a public performance.

The results indicate that low- and high-anxious music students a) do not differ in the considered physiological responses and b) differ in the considered self-perceived physiological symptoms and the self-reported anxiety before and/or during a public performance.

Asthma in Swiss Armed Forces conscripts

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Background: The military environment contains numerous asthma exacerbating factors that can influence the fitness for military service of an asthmatic subject. Active asthma may lead to a failure and drop out during basic military training with significant financial burden for the Swiss Armed Forces (SAF). At conscription conscripts are evaluated by a team of military physicians (MP) regarding diseases which can influence the fitness for military service such as asthma.

Methods: We identified all subjects with a diagnosis of asthma in the SAF conscription database who underwent medical evaluation in 2005 and in whom the status fitness for service was defined. For each subject we reviewed the medical letters that were available to the MP at conscription and determined on what basis (eg. referral to specialist, symptoms, asthma tests done) the diagnosis was based.

Results: We could identify 1741 (5.9%) out of 29610 conscripts with a diagnosis of asthma. Asthmatic subjects had lower FEV₁/FVC ratios, FEV₁, predicted values, more positive auscultation findings and a lower distance covered in the 12 minute running test when compared to non-

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asthmatic subjects. In 928 (53.4%) subjects with a diagnosis of asthma, no pre-conscription medical certificate was available. 31% presented with a letter issued by a general practitioner, in 8.9% of medical letters was mentioned that the subject had been evaluated by a respiratory physician and in 7.8% a letter issued by a respiratory physician was available. 551 (31.6%) of the asthmatic conscripts were declared fit for service, 1141 (65.5%) were declared unfit for military service, in 13 subjects the decision was postponed and in 35 subjects no decision was recorded.

Conclusion: Asthma is a common diagnosis among young male conscripts and these subjects are often declared unfit for military service. However, in less than half of these conscripts, asthma was documented by a physician prior to conscription and/or results of objective testing were available. This raises the possibility that a significant proportion of these subjects might not have been classified as asthmatics, if accurate testing would have been performed. As asthma is a chronic disease causing significant costs to the health care system as well as it can be stigmatizing, correct diagnosis is very important. Subjects with a possible diagnosis of asthma should be accurately evaluated with objective tests and these results must be available for conscription.

Free communications III – SGARM/SSMT

Contribution of occupational medicine to reduce Baker's asthma

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Background: Allergies to flour are one of the most common reasons for occupationally induced asthma, leading annually to 20–30 occupational bans for bakers due to baker's asthma in Switzerland. In connection with the occupational health program «Branchenlösung Arbeitssicherheit und Gesundheitsschutz» the Swiss bakers association has therefore set the goal to reduce the number of cases of occupationally induced baker's asthma. Measures of occupational health are being employed to achieve this goal in addition to measures of occupational hygiene.

Methods: To assess the risk of developing baker's asthma, candidate apprentices were asked to fill in a specific questionnaire.

Questionnaires containing positive answers were transmitted to the consulting occupational health practitioner, who decided – if applicable in consultation with the family doctor – whether an expanded assessment of occupational aptitude by a regionally assigned pneumologist or allergologist was warranted. The occupational health practitioner made a decision with respect to professional aptitude (suitable / conditionally suitable / serious concerns), which was communicated to the candidate apprentice. In the case of conditional suitability or serious concerns, the state of health was assessed by telephone interview 8 months after the start of the apprenticeship. Two thirds (66) of the affected persons could be reached.

Results: During the period from 2003–2007, 187 questionnaires out of a total of 405 returned to the competence center were further evaluated by the occupational practitioner with respect to specific occupational risk. In 67 (36%) cases out of 187 the decision was “suitable”, in 72 (38%) “conditionally suitable” and in 48 (26%) there were “serious concerns”. The later evaluation by telephone interview showed that out of 25 apprentices who had started the training despite serious concerns, 16 (64%) had been forced to terminate their apprenticeship due to health problems connected to exposure to flour. In the group of those with conditional suitability 17% (7 out of 41) were affected.

Conclusion: Risk assessment for occupations associated with an increased risk of allergies, e.g. with bakers, by means of a dedicated questionnaire and followed by evaluation by an occupational health practitioner familiar with the specific work environment in collaboration with a pneumologist/allergologist, is able to reliably identify candidate apprentices with a high risk of developing baker's asthma.

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Results: Men showed a higher frequency with 62%. The greatest risk was found among employees in the “chemical products” sector with 18% and in the “public administration” branch including public hospital staff (9%). The professional groups most affected were the “laboratory workers” with a figure of 7%, followed by painters with 5% and those employed in the chemicals industry with 4%. The most frequent age category at the onset of occupation-related urticaria was that of 21–25 years. In 15% the disease began within one month in a new job. 41% suffered from a chronic urticaria and 95% from a contact urticaria. Latex was the most common material causing contact urticaria with 12% of all cases followed by epoxy resins and plants/plant parts with a figure of 5%. Only in 30% a clearly allergic mechanism was found. Just over half of the patients with contact urticaria suffered from generalized urticaria or extracutaneous symptoms, and in 6% anaphylactic shock occurred. In most cases (68%), the occupational disease was diagnosed fairly quickly after its onset within less than one month. The majority (95%) of the Suva cases were acknowledged as an occupational disease within one year of the urticaria diagnosis. In almost half of the investigated cases healing or improvement of the urticaria was noted with the introduction of protective measures at the workplace. Nevertheless in more than one third a change of workplace or profession was necessary with the result that the urticaria healed or improved in almost 90%.

Conclusions: In comparison to contact dermatitis urticaria is a rare form of occupational disease, caused by a wide range of occupational substances. It was observed mainly in young men, and lasted often more than 6 weeks. Heavy extracutaneous reactions were noted in almost one quarter of cases. Protective measures in the workplace are apparently of particular importance and other measures such as internal transfer or change of profession have shown good results and can be considered effective.

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Occupational exposure to beryllium in Switzerland: exposed workers and occupations at risk

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Introduction: Beryllium (Be) is increasingly used in various industrial applications. Occupational exposure to Be may lead to chronic beryllium disease (CBD), a pulmonary granulomatous disorder closely similar to sarcoidosis, which develop in 1 to 15% of exposed workers. Although Switzerland is one of the major Be importers worldwide, little information is available about occurrence of exposure and the number of workers exposed in this country.

Objectives: 1) evaluate the number of workers potentially exposed to Be in Switzerland; 2) construct a screening tool to allow potential Be exposure detection in a clinical setting.

Methods: After identification of industrial sectors involving beryllium exposure based on expert reports and scientific literature, an estimation of the number of workers employed in these relevant industries was made using data from the Swiss federal population census and registries of economic activities. A second analysis was performed to estimate the fraction of workers really exposed to Be in each industrial sector. This adjustment was made according to the

Occupational urticaria in Switzerland 1984–2005

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Background: To investigate all cases of urticaria acknowledged as occupational disease between 1984 and 2005.

Methods: 237 cases could be evaluated. Using Suva's patient dossiers (202 cases) and additional statistical data, investigations were made for gender, age, causes, time in job before onset, activity, type and course of the disease, diagnostic investigations, treatment as well as measures taken after diagnosis.

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results of a French survey (INRS, Institut National de Recherche et de Sécurité) conducted by questionnaire addressed to 4500 companies in relevant industries on their use of beryllium and other issues such as percentage of employees really exposed. These realistic data were used to develop a self-administrated screening questionnaire allowed to identify patients with possible Be exposure.

Results: In Switzerland, the number of workers employed in industries using Be was nearly 150 000. The estimated number of workers exposed to beryllium in these industries ranged from 2000 to 4000. Relevant sectors were: microengineering, precision turning, watchmaking and metal waste treatment and recycling. The validation of the self-administrated questionnaire containing a list of jobs and leisure activities associated with potential Be exposure is in progress within the framework of a national study.

Conclusions: The number of workers potentially exposed to Be in Switzerland is rather high compared to estimations for other industrialized countries and might constitute an underestimated occupational health problem. Undetected Be exposure in patients with sarcoidosis may occur and result in misdiagnosis. Once validated, the self-administrated questionnaire could be used by clinicians to screen for Be exposure in patients with granulomatous lung disorders.

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Socioeconomic consequences of isocyanate-induced occupational asthma: results of a 12-year follow-up study

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Introduction: Isocyanates belong to the most important industrial sensitizers which can cause occupational asthma. Therefore it is of interest to study not only the medical but also the socioeconomic consequences of this disease.

Aim: To study the occupational as well as the economic situation of those patients suffering from isocyanate induced asthma who were registered by Suva from 1993 to 1995 between their date of registration and approximately 12 years thereafter.

Methods and material: The information was gathered by directly interviewing patients when they were medically examined and by collecting data provided after informed consent from the administrations of both Suva and the Swiss Federal Invalidity Insurance (IV).

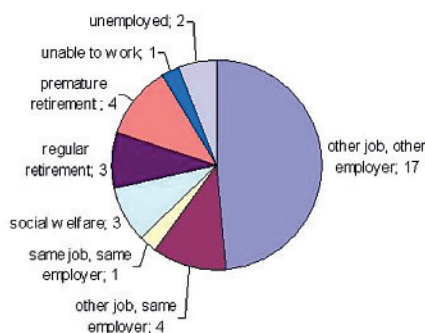
Results: 49 patients (47 males, 2 females, mean age 38.0 ± 12.7 years) were included. 35 of them could be followed-up during 12.0 ± 1

years until the end of the study in 2006. In the beginning of the study, the participants held the following jobs: car spray painter (9), polyurethane casting operator (9), industrial spray painter (5), polyurethane cellular plastic machine operator (4), interior fitting specialist (3), others (5). All but one of the patients were excluded from further occupational contacts with isocyanates and consequently had to change their workplaces or their jobs (fig. 1). In 2006, 22 of the 35 patients were still employed while 13 weren't economically active any more (fig. 1). 10 of those still employed had been offered occupational retraining by IV whereas 12 had had to look for another job on their own. When looking at those who were still economically active in 2006, their gross annual income in the 12 year observation period rose from CHF 58'368 (38'350–105'300) to CHF 63'879 (11'700–108'329). According to the federal index of salaries, the increase should have amounted to CHF 67'974 (44'177–121'301), resulting in a slight loss of income of CHF 4095. Those who had been offered an occupational retraining programme realised a net increase of income of CHF 9'333 p.a.; on the other hand, those who couldn't profit of such a programme had to bear a loss of CHF 13'047 (–77'920 to + 22'658). The total cost per case for Suva and IV (only 9 cases with complete IV database) amounted to CHF 119'047 (5'350–479'671) for Suva and CHF 97'646 (25'372–233'602) for IV, i.e. to a total of CHF 216'693 per case.

Conclusions: 1. Even in the presence of a developed social security system, the majority of patients suffering from isocyanate induced occupational asthma are confronted with a net loss of income.

2. Those who are offered and who finish an occupational retraining programme benefit financially, and those who don't or who are rejected from such programmes lose income.

3. Nevertheless each case has to be carefully investigated before removing the patient from any further isocyanate exposure in order to offer him an occupational retraining programme. 4. Further preventive measures are still needed.



Free communications IV– Surgical/paediatrics

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Identification of CD9+ MSC-like cells in human lung parenchyma capable of differentiating into airway epithelial cells

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The lack of effective therapies for end-stage lung disease validates the need for stem cell based-therapeutic approaches as alternative treatment options. Recent studies have demonstrated the presence of multipotent "mesenchymal stem cells" (MSCs) in the adult lung. The majority of these, however, are limited to animal models, and to date there has been no report of an analogous cell population in adult human lung parenchyma. Here we demonstrate the identification of a population of CD9+ MSC-like human parenchyma cells (pHLPs) derived from intra-operative normal lung parenchyma biopsies. Surface and intracellular immunophenotyping revealed a similar expression pattern of surface antigens characteristic with MSCs including CD73, CD166, CD105, CD90 and STRO-1. In addition, flow cytometry analysis illustrates that cultures do not contain alveolar type I epithelial cells or Clara cells and are devoid of the following hematopoietic markers: CD34, CD45 and CXCR4. Our CD9+ MSC-like pHLPs have the ability to differentiate along the adipogenic and osteogenic mesenchymal pathways when cultured in the respective differentiation conditions. More importantly, when placed in small airway growth media, pHLP cell cultures show the expression of aquaporin 5 and Clara cell secretory protein identified with alveolar type I epithelial cells and Clara cells respectively. Further characterization of cultures, depicted the presence of a side population phenotype, which could potentially be identified as the source of the MSC-like population. To the best of our knowledge, this is the first report to illustrate endogenous human lung parenchyma MSC-like cells capable of differentiating into cell types of the lung. Further investigation of these resident cells may elucidate a therapeutic cell population capable of lung repair and/or regeneration.

Pneumonectomy after chemo- or chemoradiotherapy for advanced non-small cell lung cancer

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Objective: Pneumonectomy after chemo- or chemoradiotherapy is reported to be associated with a mortality of up to 20%. We retrospectively reviewed medical records of patients who underwent standard or extended pneumonectomy after induction therapy for advanced NSCLC.

Method: 827 patients underwent induction therapy for NSCLC after staging with CT, PET-CT and/or mediastinoscopy in two different centers from 1998–2007. Induction chemotherapy consisted mainly of 3 cycles of a platin-based regimen. Chemoradiotherapy consisted of an additional radiation of 45 Gy. Re-staging was performed with CT, PET-CT and/or re-mediastinoscopy prior to surgical resection. Patients who underwent a pneumonectomy were further analyzed.

Results: 176 pneumonectomies were performed. 117 (66%) were extended resections including pericardium in 108 (60%), left atrium in 31 (18%), diaphragm in 10 (6%), chest wall in 8 (5%), superior vena cava in 7 (4%), aorta in 7 (4%) and oesophageal muscle in 5 (3%) patients. R0-resection was achieved in 165 (94%). Pre-induction clinical stage was IIB in 8 (5%), IIIA in 96 (54%), IIIB in 71 (40%) and IV in 1 (1%) patient. Post-induction pathological stage was a complete response in 36 (20%), stage I in 31 (18%), II in 39 (22%), III in 58 (33%) and IV in 12 (7%). There were 6 perioperative deaths (3% mortality) due to pulmonary embolism in 3, respiratory failure (pneumonia/ARDS) in 2 and cardiac failure in 1 patient. Within 90 post-operative days, 22 major complications occurred in 19 patients (11%): 6 (27%) broncho-pleural fistulas (BPF), 6 (27%) pneumonias/ARDS, 5 (23%) empyemas without BPF, 4 (18%) pulmonary embolism and 1 (5%) gastric herniation due to displacement of the diaphragmatic repair. 3- and 5-year survivals for the overall population were 55% and 38%, respectively.

Conclusion: Pneumonectomy after chemo- or chemoradiotherapy as induction for advanced NSCLC can be performed with a perioperative mortality rate of 3% and should not exclude patients from surgical resection. The achieved 5-year survival rate of 38% justifies aggressive surgery within a multimodality concept for selected cases.

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Higher burden of mesothelioma morbidity in a chemical industrialised area in Valais

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Background: Malignant pleural mesothelioma (MPM) has a poor outcome with a long latency between exposure and disease. Many risk factors have been identified, the greater one being occupational exposure to asbestos fibres. Since many years, local pulmonologists had a feeling of higher incidence of MPM in the industrialized area of Monthey where there are important chemical industries as well as a big power station burning oil residues. On the other hand were not aware of local differences in smoking prevalence in Valais (VS). Therefore one should discover there, a higher incidence of MPM and not of lung cancer confirming the major role of occupational risk in MPM development. There should be no statistically relevant differences in small cell and non small cell lung cancers (LC) incidence between both areas, allowing us to indirectly control the quality of the registered data by the health observatory of VS.

Material and methods: Between 1989 and 2006, all cases of MPM and LC have been registered. We then compared the Monthey area with the rest of the canton of VS.

Results:

Table 1:				Cumulative incidence [10 ⁻³]	Chi-Test	
		MPM	no MPM		X ²	p
MPM	Monthey	23	37'482	61	21.918	< 0.0001
	Rest of VS	51	254'019	20		
	Total	74	291'501	25		
LC	Monthey	240	37'265	640	2.463	0.117
	Rest of VS	1'458	252'612	574		
	Total	1'698	289'877	582		

Conclusion: There is a 3 times higher incidence of mesothelioma in an exposed industrialized area as compared to the rest of the canton of Valais without any significant change in incidence of lung cancer confirming the major role of occupational exposure in MPM incidence. This finding confirms the utility of health observatories even in small Swiss cantons and should make the authorities well aware of closed monitoring of occupational risk factors to decrease the future burden of mesothelioma in exposed working populations.

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Determinants of ILT3 and ILT4 gene expression in cord blood

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Background: In recent years a number of studies have suggested that tolerogenic dendritic cells, characterized by up-regulated immunoglobulin-like transcript (ILT)-3 and ILT4, play a role in regulating allergic diseases. Specific environmental factors have been shown to protect from the development of allergic diseases particularly when exposure occurs prenatally. The prenatal effect of such environmental factors on tolerogenic dendritic cells is unknown. The objective of the study was to determine the environmental factors that influence the gene expression of ILT3 and ILT4 in cord blood of a prospective birth cohort.

Methods: A birth cohort was established in rural areas of five European countries (Austria, Germany, Finland, France and Switzerland). Information on maternal exposures was collected by questionnaires during pregnancy. The expression of the genes of ILT3 and ILT4 was analysed by real time polymerase chain reaction in the cord blood of 927 children.

Results: Girls had an increased gene expression of ILT4 ($p = 0.034$) and ILT3 ($p = 0.072$). The gene expression of ILT3 and ILT4 was positively associated with prenatal exposure to a farming environment (ILT3: $p = 0.019$, ILT4: $p = 0.007$) and maternal vitamin D supplementation during pregnancy (ILT4: $p = 0.003$, ILT3: $p = 0.068$).

Conclusions: Vitamin D supplementation during pregnancy, gender and exposure to a farming environment increased the mRNA levels of ILT3 and ILT4 in cord blood. These findings may point towards an early induction of tolerogenic immune responses.

Poster session I – Cell biology, PH, occupational

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Intravenous line complications during continuous iloprost therapy using directly inserted subclavian catheters

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Objective: Continuous intravenous prostaglandin therapy still is the most effective treatment for pulmonary hypertension. Because of the potential occurrence of line infection and sepsis, most centres use tunnelled catheters. Since in our program we always use directly inserted conventional subclavian catheters, we wondered, whether the infection rate might be higher in our cohort.

Methods: We analysed 14 patients (8 females, median age 46 yrs, range 22–70) with PH (7 IPAH, 5 associated PAH, 2 CTEPH) receiving continuous iv iloprost for a median of 174 days (range 56–888).

Results: There were 2 line-related sepsis episodes (1 SKN, 1 Brevibacterium) during 9.06 patient-years resulting in an incidence of 0.22 per patient-year. This figure is comparable to those of the two largest centres treating altogether 340 patients, namely 0.14 [1] and 0.19 [2]. In additional 4 instances the lines were extracted inadvertently by the patient, and in the case with the Brevibacterium sepsis, the catheter was changed once previously because of a continuous bacteremia [3]. Hence, the overall necessity for line replacement in 7 instances resulting in an incidence of 0.77 per patient-year compared with 0.55 in a large cohort [1] was somewhat higher, however, in all but 1 case not directly caused by the line itself.

Conclusions: The use of directly inserted conventional subclavian catheters for continuous iv prostaglandin therapy has a comparable incidence of sepsis like the tunnelled catheters. Since inadvertent removal by the patient is obviously easier with the non-tunnelled lines, our overall replacement necessity was somewhat higher.

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2. Sitbon O, et al. J Am Coll Cardiol. 2002;40:780–8.
3. Ulrich S, et al. Infection. 2006;34:103–6.

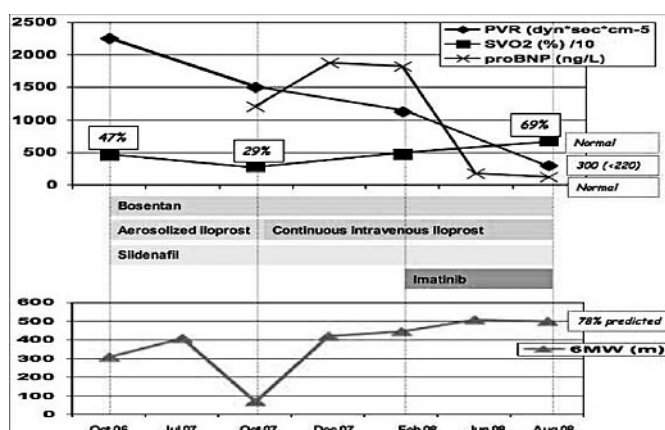
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Imatinib – Is there a hope for the cure of pulmonary arterial hypertension?

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Objective: Proliferative changes are the main factor for progression of pulmonary arterial hypertension (PAH). One of the important players is Platelet-derived Growth Factor (PDGF), which is dominantly expressed in lung tissue of these patients. In a rat monocrotaline model, the PDGF inhibitor Imatinib (Glivec®), induced regression of the vascular changes. Single case reports and a phase II study have also shown promising results in humans with PAH.



Methods: A 38 y women with severe idiopathic PAH was treated with Imatinib 400 mg/d as first case in our compassionate use program.

Results: Despite a triple therapy, the patient worsened again becoming almost moribund in October 07. She improved with intravenous Iloprost, but her PVR still was $>1000 \text{ dyn}\cdot\text{s}\cdot\text{m}^{-5}$. A six-month trial of Imatinib led to an almost complete normalization of hemodynamics. Most impressive, BNP decreased and normalized only after the start of Imatinib.

Conclusion: Imatinib added to a combination therapy can cause an almost complete regression of PAH. Especially, it may have the potential to normalize right heart function.

This study was partly founded by Novartis Pharma Schweiz AG

P70

Absolute values of the 6 minute walk distance are equally good to predict disease severity in pulmonary hypertension as percent predicted formulas

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Objective: The 6-minute walking distance (6MWD) is an important treatment goal and endpoint in trials Pulmonary Arterial Hypertension (PAH). There is an ongoing debate if absolute values of 6MWD or percentages of predicted calculated by reference equations perform better in comparing the severity of disease. In addition, there is also a controversy, which equation performs best.

Methods: We analysed 93 patients (55 females, mean age 54, b17) with PAH (51 idiopathic) using the 3 reference equations for the 6MWD by Enright (E), Gibbons (G) and Troosters (T) with respect to other outcome parameters in PAH.

Results: Absolute values of 6MWD and all three equations performed equally well when compared with pulmonary vascular resistance ($r_2 -0.36$ to -0.49 ; $P(\text{max}) = 0.003$), mixed venous saturation ($r_2 0.37$ to 0.38 ; all $P = 0.002$), NYHA/WHO functional class ($r_2 -0.47$ to -0.58 ; all $P < 0.001$), brain natriuretic peptide ($r_2 -0.34$ to -0.39 ; $P(\text{max}) = 0.026$), and quality of life assessed by the Minnesota Living with Heart Failure Questionnaire Quality of Life resistance ($r_2 -0.38$ to -0.44 ; $P(\text{max}) = 0.002$). However, with respect to the NYHA/WHO functional classes, the %predicted calculated by the equations of Gibbons and Troosters were 10–13% lower compared with the Enright formula.

Conclusion: The 3 reference equations did not perform better than the absolute values of the 6MWD with respect to the most relevant outcome parameters in PAH. However, the most used Enright formula might overestimate the percentage of predicted values.

P71

Surfactant alters dendritic cell phenotype and function

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Dendritic cells (DC) are potent antigen presenting cells that act as immunological sentinels in the lung, where they form a network in close contact with epithelial cells in the airways and alveoli. Surfactant, a lipid, phospholipid, and protein monolayer, constitutes the initial biophysical and immunological barrier that covers the mucus film secreted by lung epithelial cells. Due to close proximity, and in particular in the situation of lung epithelial injury or surfactant-coated particle uptake, DC get in direct contact to surfactant. We therefore tested the hypothesis if surfactant modulates DC maturation in vitro. Monocyte-derived human DC (MDDC) were matured in the presence of different concentrations of surfactant (Curosurf®) in combination with LPS or control media. No significant phenotypic changes occurred in the presence of surfactant compared to control media, as measured by FACS (CD80, CD83, CD86, myeloid DC, or plasmacytoid DC markers). Surfactant-treated DC displayed a reduced non-antigen-specific (LPS), but unaffected antigen-specific (tetanus toxoid) CD4+ T cell proliferation. In conclusion, although surfactant does not affect DC phenotype and function, it may alter innate immune responses by reducing non-specific T cell activation. Forthcoming studies will investigate the effect of different surfactant components and cytokine patterns generated during DC and T cell co-culture and activation in order to understand mechanisms that are involved in DC modulation by surfactant.

P72

The impact of human Met11Thr single nucleotide polymorphism on morphology of SP-D deficient mice

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Surfactant protein D (SP-D) deficient mice develop emphysema, type II cell hypertrophy and hyperplasia and a disturbed surfactant

homeostasis, characterized by an alveolar lipoproteinosis and an increase of the intracellular surfactant pool. These changes are associated with a chronic inflammation. SP-D has important functions concerning the innate immune system. The single nucleotide polymorphism (SNP) Met11Thr of the SP-D-gene has been recognized as a factor that influences susceptibility to pulmonary infections suggesting different activities of the gene products. Thus, the proteins might have different impact on the phenotype of SP-D knock-out mice. SP-D knock-out mice expressing either human Met- or Thr-SP-D were analyzed by stereology at the light and electron microscopic level and compared to a wild type und SP-D knock-out group. Emphysema, type II cell changes and the intracellular surfactant pool (assessed as the volume of lamellar bodies) were quantified. Both Met-SP-D and Thr-SP-D were able to normalize the alveolar number per lung, without any statistical differences among these groups. The number of type II cells per lung was significantly reduced in the Met-SP-D group compared to the SP-D knock-out group, whereas in the Thr-SP-D group no change was found. Furthermore, the amount of intracellular surfactant per type II cell and lung was significantly lower in the Met-SP-D group compared to both the Thr-SP-D and SP-D knock-out group. Although both gene products were able to influence emphysema equally, morphological changes related to type II cells and intracellular surfactant stayed more pronounced in the Thr-SP-D group, indicating different biological activities with impact on lung structure.

P73

The impact of human hepatocyte growth factor in bleomycin-induced pulmonary fibrosis: a morphometric analysis

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Idiopathic pulmonary fibrosis (IPF) is a progressive and fatal lung disease with no effective therapy available. An abnormal wound repair of the alveolar epithelium has been recognized to play a key role in the pathogenesis of IPF. Human hepatocyte growth factor (hHGF) has been shown to contribute to wound repair in diverse organs. In IPF patients an impaired activation of hHGF has been observed. The bleomycin-induced pulmonary fibrosis is an established animal model for IPF with proven therapeutic effects of hHGF on biochemical indices of pulmonary fibrosis. The aim of our study was to quantify the impact of type II cell specific hHGF-expression on structural abnormalities in bleomycin-induced pulmonary fibrosis in rats by means of design-based stereology, focussing on parameters related to gas-exchange and fibrosis. Two groups were compared, both receiving bleomycin intratracheally. In one group hHGF was expressed by alveolar type II cells under control of the SP-C promoter. Gene transfer was achieved by electroporation 7 days after bleomycin instillation. The other group did not receive therapy. Stereological data showed a reduction of the total volume of destructed lung parenchyma due to expression of hHGF. This was accompanied by a significant reduction of the mean thickness of alveolar septa as well as the blood-gas barrier. The amount of collagen fibres in alveolar septa could be reduced. The number of type II cells did not differ between the groups, although hHGF-expression reduced type II cell hyperplasia. In conclusion, our data show a beneficial impact of hHGF on morphometric indices of pulmonary fibrosis by a reduction of the septal thickness and collagen fibres in this animal-model.

P74

Indoor air quality in a public building following smoking bans

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Introduction: Exposure to environmental tobacco smoke (ETS) is a major environmental risk factor. Indoor contaminants come from a variety of sources, which can include inadequate ventilation, volatile organic compounds (VOCs), biological agents, combustion products, and ETS. Because ETS is one of the most frequent causes of IAQ complaints as well as the high mortality of passive smoking, in June 2004 the University of Geneva made the decision to ban smoking inside the so called "Uni-Mail" building, the biggest Swiss University human science building of recent construction, and the ordinance was applied beginning in October 2004. This report presents the finding related to the IAQ of the "Uni-Mail" building before and after smoking bans using nicotine, suspended dust, condensate and PAHs level in air as tracers to perform an assessment of passive tobacco exposure for non-smokers inside the building.

Methods:

Respirable particles (RSP)

A real time aerosol monitor (model DataRAM) was placed at sampling post 1, level ground floor.

Condensate

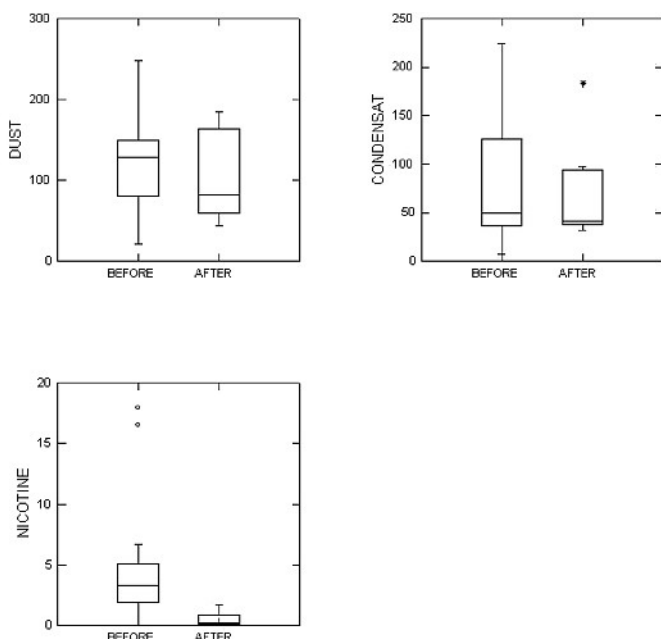
It consists in extracting any organic matter taken on the glass fibre filters by MeOH, and then measuring the total absorbent of the MeOH extract to the UV wavelength of 447 nm.

Nicotine

Nicotine was taken by means of cartridges containing of XAD-4 to the fixed flow of 0.5 L/min. The analytical method used for the determination of nicotine is based on gas chromatography with Nitrogen selective detector GC-NPD.

Results: Figure 1 shows the box plot density display of 3 parameters before and after smoking bans for all 7 sampling posts: dust, condensate and nicotine in air in $\mu\text{g}/\text{m}^3$.

Conclusion: Before the smoking ban, the level of the concentrations of respirable particles (RSP) is raised more, average of the day $320 \mu\text{g}/\text{m}^3$, with peaks of more than $1000 \mu\text{g}/\text{m}^3$, compared with the values of the surrounding air between 22 and $30 \mu\text{g}/\text{m}^3$. The nicotine level is definitely more important (average $5.53 \mu\text{g}/\text{m}^3$, field 1.5 to $17.9 \mu\text{g}/\text{m}^3$). Once the smoking bans inside the building were applied, one notes a clear improvement in terms of concentrations of pollutants. For dust, the concentration fell by 3 times (average: $130 \mu\text{g}/\text{m}^3$, range: 40 to $160 \mu\text{g}/\text{m}^3$) and that of nicotine by 10 times (average: $0.53 \mu\text{g}/\text{m}^3$, range: 0 to $1.69 \mu\text{g}/\text{m}^3$) compared to that found before smoking bans. The outdoor air RSP concentration was $22 \mu\text{g}/\text{m}^3$ or 10 times lower. Nicotine seems to be the best tracer for ETS free of interference, independent of location or season.

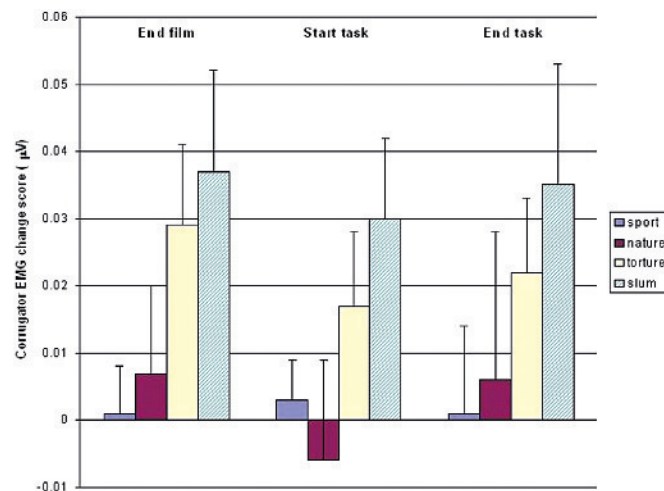


Valence lasts longer than arousal: persistence of induced moods as assessed by psychophysiological measures

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How long induced moods last is a critical question for mood research but has been only poorly addressed. In particular, physiological parameters have been rarely included to assess the effectiveness of mood induction procedures. Adopting a dimensional model of mood, we investigated the persistence of four different moods (positive high-arousal, positive low-arousal, negative high-arousal, negative low-arousal) induced by four film clips ("sport", "nature", "torture", "slum") during a 9-minute computer task. We measured subjective mood state (valence and arousal), respiration, skin conductance level (SCL), heart rate, and corrugator activity in 76 subjects. Viewing of the selected film clips induced the expected effects both subjectively and physiologically. Corrugator activity was higher at the end of the negative clips than the positive clips, and ventilation and SCL were higher for the arousing clips than for the less arousing clips. People who watched the negative clips still reported more negative valence after the computer task and also showed more facial frowning (cf. figure) and lower SCL during the task than people who watched the positive clips. No arousal effects persisted throughout the task. The results suggest that induced changes in the valence dimension of moods are maintained throughout an intervening task and are physiologically best reflected by corrugator activity and SCL, whereas induced changes in the arousal dimension dissipate quickly. The findings of this study enrich, first, our knowledge concerning the relationships between subjective feelings and their physiological substrate. Second, they inform us about the effectiveness of film clips as a mood induction instrument. Third and most important, they suggest that induced changes in valence last longer than induced changes in arousal. High-arousal moods can last for an extended

period of time in daily life, but they seem to be short-lived when induced in the lab. An important methodological consequence is that investigating the effect of the arousal dimension of a person's mood induced in the lab may be only possible when the subsequent task is relatively short. Finally, the findings show which physiological measures may be useful in tracking mood states.

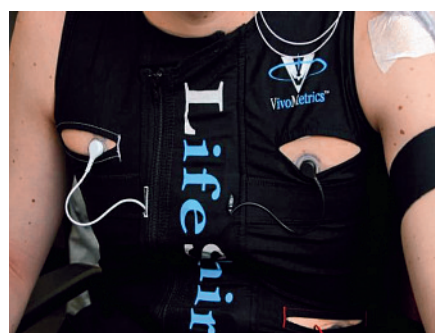


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Respiration, metabolic balance, and attention in affective picture processing

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The jointly voluntary and involuntary control of respiration, unique among essential physiological processes, the interconnection of breathing with and its influence on the autonomic nervous system, and disease states associated with the interface between psychology and respiration (e.g., anxiety disorders, hyperventilation syndrome, asthma) make the study of the relationship between respiration and emotion both theoretically and clinically of great relevance. However, the respiratory behavior during affective states is not yet completely understood. We studied breathing pattern responses to 13 picture series varying widely in their affective tone in 37 adults (18 men, 19 women, mean age 26). Time and volume parameters were recorded with the LifeShirt system (VivoMetrics Inc., Ventura, California, USA, see image). We also measured end-tidal pCO_2 (EtCO_2) with a Microcap Handheld Capnograph (Oridion Medical 1987 Ltd., Jerusalem, Israel) to determine if ventilation is in balance with metabolic demands and spontaneous eye-blinking to investigate the link between respiration and attention. At the end of each picture series, the participants reported their subjective feeling in the affective dimensions of pleasantness and arousal. Increasing self-rated arousal was associated with increasing minute ventilation but not with decreases in EtCO_2 , suggesting that ventilatory changes during picture viewing paralleled variations in metabolic activity. EtCO_2 correlated with pleasantness, and eye-blink rate decreased with increasing unpleasantness in line with a negativity bias in attention. Like MV, inspiratory drive (i.e., mean inspiratory flow) increased with arousal. This relationship reflected increases in inspiratory volume rather than shortening of the time parameters. This study confirms that respiratory responses to affective stimuli are organized to a certain degree along the dimensions of pleasantness and arousal. It shows, for the first time, that during picture viewing, ventilatory increases with increasing arousal are in balance with metabolic activity and that inspiratory volume is modulated by arousal. MV emerges as the most reliable respiratory index of self-perceived arousal. Finally, end-tidal pCO_2 is slightly lower during processing of negative as compared to positive picture contents, which is proposed to enhance sensory perception and reflect a negativity bias in attention.

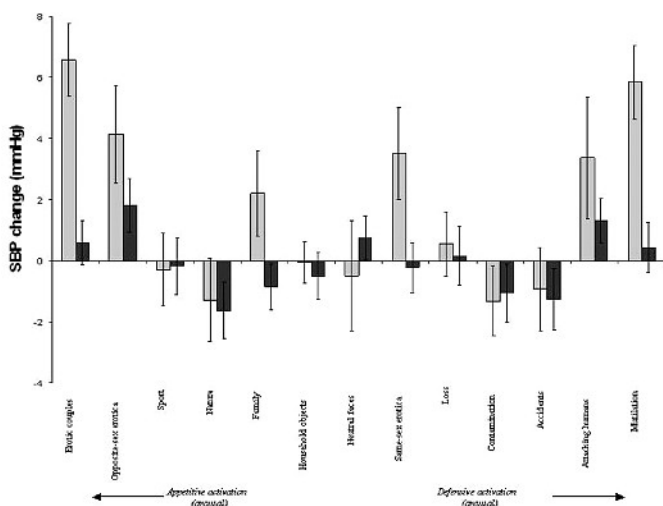


Men and women differ in their cardiovascular responses to affective pictures

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Empirical evidence supports the hypothesis that emotional states might contribute to cardiovascular disease and health through multiple pathways. To the extent that the acute cardiovascular response to emotional events plays a role in cardiovascular health and disease, an essential step in order to understand this possible link is to define the hemodynamic response to affective challenges. This was the aim of the present study. We assessed blood pressure (BP), heart rate (HR), stroke volume (SV), cardiac output, and total peripheral resistance (TPR) in response to 13 picture series in 18 men and 19 women (mean age 26) in order to investigate their hemodynamic responses associated with activation of the appetitive and defensive motivational systems underlying emotional experience. The hemodynamic parameters were recorded by finger-cuff photoplethysmography with Finometer™ (FMS Finapres Medical Systems, Amsterdam) and electrocardiography with the Lifeshirt system (VivoMetrics Inc., Ventura, California). Participants rated self-perceived pleasantness and arousal for each series. In men, BP and SV, but not TPR, increased with increasing self-rated arousal both for appetitive and defensive activation, whereas in women these relationships were almost absent, especially, for defensive activation. HR decelerated more in response to negative than positive and neutral pictures, and more so in men than women. These findings indicate striking sex differences. In particular, it is suggested that the sympathetic inotropic effect to the heart increases with increasing self-rated arousal strongly in men but only weakly in women. Regardless of sex differences, the modulation of the cardiovascular response to affective pictures along the dimensions of pleasantness and arousal is primarily myocardial, and the pattern of cardiovascular response is consistent with a configuration of cardiac sympathetic-parasympathetic coactivation. One possible implication of the observed sex differences concerns the link between affective states and cardiovascular health and disease. Men have a higher incidence of cardiovascular diseases than premenopausal women, and exaggerated sympathetic reactivity to emotional events is a potential pathophysiological mechanism. These findings extend current knowledge showing that under several acute behavioral challenges men demonstrate stronger cardiovascular reactivity than women.



The Swiss Federal Law for the protection of the population against passive smoking of Oct 3, 2008: difficulties of application in respect of the existing laws on protection of workers, the federal constitution, and cantonal laws

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Background: The newly enacted law took its origin from an initiative by member of parliament (national council) Felix Gutzwiller MD. The aim was to improve the existing law on protection of workers by an article stating, that exposure to passive smoking should not be allowed

in closed workplaces. In the parliamentary process the law was separated from the protection of workers and became a law text on its own. Article 1 and 2 state, that in all closed spaces with public access smoking should be banned, but the following paragraphs and Art.3 introduce exceptions: special smoking rooms are allowed, provided they are designated as such and efficiently ventilated. Exceptionally and with their written consent, employees are allowed to work in such rooms. Moreover, restaurants may be authorized to be run as "smoking establishments," provided their total surface is less than 80 square meters, they are adequately ventilated, clearly designated as such and they employ only persons having given written consent. However for workers other than in restaurants the new law means efficient protection, since smoking is banned in all closed workplaces, where more than two people are concerned.

Methods: We compared the new law with the existing law on protection of workers and checked its compatibility with the federal constitution and the rulings of the federal court on smoking bans. Cantonal smoking bans were also compared.

Results: We found several possible application difficulties of the new law, that also enters into conflict with stricter smoking bans already enacted in some cantons by popular vote. Although the present law specifically states, that the cantons may apply stricter rulings, this discrepancy may initiate litigation and interpretation of the "derogatory clause" of federal law (federal law generally breaks cantonal laws).

Conclusion: The present law on passive smoking presents difficulties of application because it creates inequalities among workers, public establishments between themselves and compared with other workplaces, and smoking bans in different cantons. Therefore it may become source of litigation. These problems arise from the exceptions of the smoking ban that should concern everybody in closed spaces to be efficient for health protection.

Chronic beryllium disease as a re-emerging occupational disorder possibly misdiagnosed as sarcoidosis: a Swiss study project

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Background: Beryllium (Be) is increasingly used worldwide for numerous industrial applications. Occupational exposure to Be may lead to Be sensitization (BeS), a CD4-mediated immune response. BeS may progress to chronic beryllium disease (CBD), a granulomatous lung disorder closely resembling sarcoidosis. The recognition of CBD requires detection of Be exposure at occupational history, and detection of BeS on blood or BAL lymphocytes. Since methods for CBD detection are not routinely available in Switzerland, we hypothesized that CBD cases are not recognized but misdiagnosis as sarcoidosis.

Objective: To present an ongoing Swiss study screening patients with sarcoidosis in search of Be exposure, BeS, and CBD.

Methods: Both a prospective and a retrospective cohort are being studied. In the prospective cohort, the main steps include: 1) recruitment of 100 consecutive patients with newly diagnosed pulmonary sarcoidosis at 2 centers (Lausanne, Bern). 2) screening for possible occupational Be exposure by self-administered patient questionnaire. 3) standardized detailed occupational interview and clinical visit by occupational health specialist. If step 3 is positive, then 4) blood and BAL sampling for detection of BeS by specifically developed Elispot assay and CFSE flow cytometry, with subsequent comparison to the classical Be lymphocyte proliferation test. If step 4 is positive, then 5) review of medical records and diagnostic revision from sarcoidosis to CBD. 6) appropriate measures for exposure cessation and case reporting to SUVA as occupational disease. The retrospective cohort will include 400 patients with previously diagnosed pulmonary sarcoidosis, either treated or untreated, recruited through the SIOLD Registries. Steps 2 to 5 will be performed as above, except for a) end of study after step 2 if screening questionnaire does not reveal Be exposure, and b) step 4 done on blood sample only (BAL not needed).

Current status: Self-administered screening questionnaire and tools for standardized occupational interview have been developed. BeS testing has been implemented and undergoes validation. Inclusions in the prospective phase have started at both study sites. The retrospective phase is in preparation.

Conclusion: The current study status allows to conclude to technical feasibility of the project.

The prospective phase if this study is funded by the SUVA. The SIOLD Registries are supported by the Swiss Pulmonary League.

Surgical treatment of recurrent catamenial pneumothorax

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Catamenial pneumothorax is a rare cause of recurring spontaneous pneumothorax due to thoracic endometriosis or endometriosis of the diaphragm. We report the surgical treatment of three women suffering from catamenial pneumothorax, who were treated at our department during the last two years. All three women had recurrent mens-associated, right-sided pneumothoraces. Two of them had a previous thoracoscopic wedge-resection of the apex of the lung followed by a pleural abrasio. Initially thoracoscopy was performed on the patients to confirm the tentative diagnosis of catamenial pneumothorax, and disseminated endometriosis of the diaphragm was found in all three cases. In one case a macroscopic perforation of the diaphragm could be documented by the combination of thoracoscopy and laparoscopy. In all cases the pathologic endometriotic area of the diaphragm was resected by a right-sided thoracotomy. In two cases a diaphragm excision followed by suturing the diaphragm was performed, in one case the resected area was covered by a mesh implant. The histological examination confirmed the intraoperative diagnosis of endometriosis of the diaphragm. The postoperative recovery was uneventful in all cases. Postoperatively, treatment with oral contraceptives was continued, respectively started. During the follow-up of two years one woman had a recurrent spontaneous pneumothorax after stopping the oral contraceptive. The two other women had no recurrent pneumothorax and are free of any complaints. If necessary, the successful treatment of catamenial pneumothorax requires a resection of the pathologic diaphragm. Oral contraceptives should be continued according to consensus guidelines.

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Pulmonary thrombendarterectomy for chronic thromboembolic pulmonary hypertension

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Pulmonary thrombendarterectomy is the definitive treatment for chronic pulmonary hypertension resulting from idiopathic thromboembolic disease. This surgery has been performed on 5 such patients between 1998 and 2007 in Lausanne University Hospital. Preoperatively, 4 patients (among which 1 received Bosentan) had class III NYHA disease whereas 1 had class II disease under Iloprost. Median preoperative pulmonary vascular resistance was 697 dynes/sec.cm⁵ (range 312–1485). The patient with the highest preoperative resistance (1485 dynes/sec.cm⁵) died in the postoperative period. His intolerance to Iloprost made a lowering of his preoperative systolic pulmonary pressure (sPAP) impossible and his severe right dysfunction worsened in the postoperative period. In the 4 survivors, median immediate postoperative pulmonary vascular resistance was 275 dynes/sec.cm⁵ (range 193–367), representing a mean decline of 48%. As complications of surgery, 3 had reperfusion pulmonary oedema and 1 had cardiac tamponade requiring surgical revision. Mean hospital stay was 17.5 days. After 1 year follow-up, 3 patients had >50% reduction in sPAP as measured by echocardiography, all with near normal right ventricular function, whereas the fourth patient had only 22% reduction of sPAP, which further improved with Bosentan. Mean reduction in NYHA class disease was 1.25 at 1 year. In conclusion, thrombendarterectomy is beneficial in most patients; high pulmonary vascular resistance (>1200 dynes/sec.cm⁵) is correlated with worse outcome and should be a relative contraindication to surgical treatment. The new vasodilators need to be considered pre and/or postoperatively to optimize outcomes.

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Oncological resection and lymphadenectomy for ACTH-producing neuroendocrine tumour of the lung

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Introduction: We report a case of surgical removal of an ACTH-secreting, malignant neuroendocrine tumour by oncological surgery including mediastinal lymphadenectomy.

Method and results: The patient was a 29-year old male with the typical clinical symptoms of Cushing disease. Cerebral magnetic resonance tomography was without pathological findings. The thoraco-abdominopelvic computer tomography revealed a solitary pulmonary nodule within the upper lobe of the left lung. This nodule was positive in octreotide-scintigraphy. Therefore the nodule was removed by thoracoscopic wedge-resection. The histological examination confirmed the diagnosis of a neuroendocrine tumour of low malignancy (1.5 x 1.4 x 0.6 cm) with carcinomatous lymphangiosis

near a small bronchus. ACTH receptor expression was positive. After 3 months only a partial regression of the clinical symptoms occurred. An oncologic resection of the upper lobe of the left lung as well as mediastinal lymphadenectomy was performed. Metastases could be found 2 of 12 peribronchial lymph nodes. After surgery the endocrine functions normalised. Two years after surgery the patient has no complaints and the radiological and endocrinological follow-up shows no pathological results.

Conclusions: Metastatic disease in two lymph nodes confirms the oncological resection including mediastinal lymphadenectomy for small malignant neuroendocrine tumours.

Pulmonary blastoma in a young female patient with extension into the left atrium

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Background: Pulmonary blastoma is a very rare tumor in adults consisting of malignant epithelial and mesenchymal cells (biphasic). Only few case reports have been published. Therapy of biphasic pulmonary blastoma includes surgery as well as adjuvant radiotherapy and chemotherapy. No guidelines for treatment exist. We report a case of biphasic pulmonary blastoma with extension into the left atrium.

Case: A 28 year old female presented with dyspnea and pain in the left hemithorax 2 weeks after a Cesarean section. A CT scan showed a tumor in the left lower lobe with compression of the left lower pulmonary vein. Staging showed no other tumor manifestations. After an unsuccessful CT-guided biopsy, a thoracotomy with lobectomy of the lower lobe and mediastinal lymphadenectomy was performed. Postoperatively, the patient developed a left sided hemiplegia of arm and leg. A CT scan of the brain showed ischemic areas, likely due to tumor emboli. Meanwhile, a new CT-Scan revealed tumor progression along the left lung vein into the left atrium. The patient was transferred to a tertiary center for subsequent surgery with extirpation of the residuary tumor. The patient recovered very well and went on to receive additive chemotherapy for 6 months. Currently there is no evidence of disease recurrence and the patient continues regular follow-up.

Discussion: The patient has recovered completely from the cerebral embolism, the surgery and the chemotherapy. The further outcome remains uncertain. According to the literature, outcome is poor in patients with metastatic disease. However, in cases of successful local resection, longterm survival has been reported.

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Bochdalek hernia: a very rare cause of dyspnoea and long lasting abdominal pain in adults

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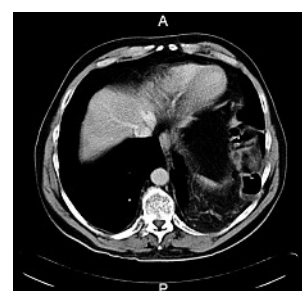
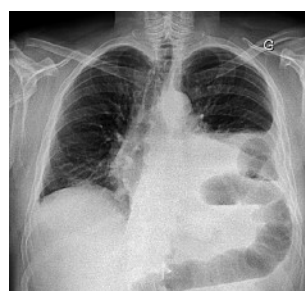
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Introduction: Bochdalek hernia (BH) is a posterolateral congenital defect of the diaphragm which usually affects only neonates. In adults, it is very rare that BH is responsible for clinical symptoms. Less than 100 cases of adults have been reported till now in literature. We present here a case with long lasting abdominal pain and dyspnea due to BH.

Case: A 61year old man present with a 2 day history of epigastric pain irradiating in the left upper abdominal quadrant. Clinical examination showed pain on palpation in the in the epigastric region and left upper abdominal quadrant without defense. Laboratory analysis revealed elevated white blood count of 12.4 G/L with normal C-reactive protein. Abdominal radiography showed no signs of ileus and the patient was discharged. He complained thereafter of continuous nausea, vomiting and progressive dyspnea. Clinical examination disclosed severe pain on with peritoneal irritation. Analysis revealed an elevated C-reactive protein 341 mg/l (<5 mg/l) and white cell blood count of 22.4 G/L. Chest radiography (figure A) suggested the presence of a ruptured left diaphragm with herniation of small bowel into the left pleural cavity. An computed tomography of the chest and abdomen

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(figure B) revealed multiple small bowel loops and peritoneal fat through a posterolateral diaphragmatic hernia in the left chest. The patient was operated by laparotomy: herniated small bowel loops were reduced into the abdominal cavity with tight closure of the diaphragmatic defect. The post-operative follow-up was uneventful and 14 day later he leaves the hospital.

Discussion: Bochdalek hernia in adulthood presents with non-specific symptoms may also occur even in a sixty year old patient and become a surgical emergency because of the high risk of strangulation.

P85

Inflammatory pseudotumour of the trachea – A case report

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Background: Primary tracheal tumors are rare and the majority of them are malignant. Inflammatory pseudotumor is an uncommon benign lesion in this region. In 2008 we observed a case with tracheal inflammatory pseudotumor treated by surgical resection followed by a complicated course postoperatively.

Case report: A 59-year-old non-smoking woman underwent a medical checkup for a 4-month history of hemoptysis. Computed tomography (CT) demonstrated a soft-tissue mass narrowing the tracheal lumen and showing no evidence of invasion of the cartilage or adjacent structures. Bronchoscopy revealed a tumor of the ventral tracheal wall with a diameter of 2 cm and lying 6 cm over the carina. Diagnostic biopsy taken by bronchoscopic laser resection showed an inflammatory pseudotumor. To rule out definitively a malignant tumor and to prevent local recurrence the mass was removed through a right thoracotomy with partial resection of the tracheal wall (length: 2.5 cm; 50% of the circumference) followed by myoplasty enforced by a small segment of the 4th rib. Further bronchoscopic inspections postoperatively showed an endoluminal prolapse of the muscle flap with a 60% stenosis of the tracheal lumen. To splint the prolapse for securing the airway an implantation of an Y-stent was performed. 2 months after this procedure and followed several bronchoscopic inspections the stent could be removed. Further bronchoscopies showed a regular and stable situation of the tracheal lumen.

Conclusion: Inflammatory pseudotumor is a benign lesion that most commonly involves the lung and the orbit, but it has been reported to occur in nearly every site in the body. The trachea is an uncommon location for this tumor. As reported in previous studies, patients with tentative diagnosis of inflammatory pseudotumor should undergo surgical resection to obtain a definitive histologic diagnosis and to prevent recurrence disease.

P86

Transphrenic budding of the liver

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Introduction: Peritoneopleural transphrenic passage of gases, solids or liquids by way of a common anatomic feature – a diaphragmatic defect – was first introduced as “porous diaphragm syndrome” in 1998. In the 1930s to 1950s, diaphragmatic defects were most commonly of iatrogenic origin. They were usually revealed by pneumothorax caused by repetitive artificial pneumoperitoneum used as an adjunctive form of collapse therapy for pulmonary tuberculosis. Nowadays, diaphragmatic endometriosis counts for the most common origin of these lesions. In this condition, the latter are revealed by catamenial pneumothorax or pneumothorax following intraperitoneal insufflation of air during laparoscopy. We report here for the first time transphrenic passage of liver tissue in this rare “porous diaphragm syndrome” context.

Method: A 56 year old post-menopausal woman with a history of 3 right sided spontaneous pneumothorax 14 years ago was treated by chest tube drainage followed by thoracoscopic pleurectomy and finally talc pleurodesis. No emphysema-like lesion of the lung was present. Recently, ten days following laparoscopic appendectomy, she reported acute right hemithoracic discomfort with moderate dyspnea. While the X-ray confirmed a right pneumothorax, the computed tomography of the chest showed a transphrenic budding of the liver. Thoracotomy revealed defects in the tendinous portion of the diaphragm through which intrathoracic liver buds were identified. After detaching the liver from the diaphragm, the tendinous portion including the multiple defects were resected and closed by a running suture.

Result: The postoperative course was uneventful. The etiology of the diaphragmatic defects in the case we present remains unclear since no history of endometriosis was ever present and no endometrial tissue was found after histopathological examination of the edges of the defects.

Conclusion: Transphrenic passage of liver tissue by way of a diaphragmatic defect can illustrate the rare “porous diaphragm syndrome”.

Primary malignant achromic melanoma of the lung: a case report and review of the literature

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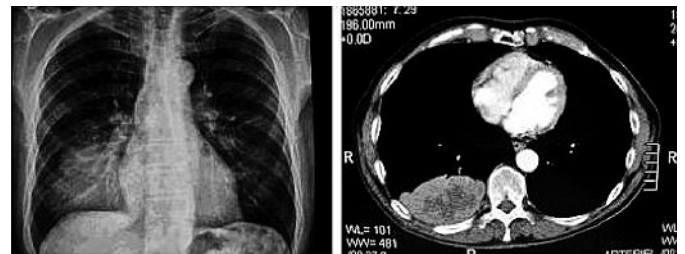
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Background: About 25 cases of primary malignant melanoma of the lung have been reported in the literature till now, sometimes with incomplete diagnostic criteria. More than 90% of melanomas are cutaneous in origin and the majority of the noncutaneous melanomas are localized in the lung. Thus, strict criteria for primary malignant achromic melanoma of the lung (PML) diagnosis have been published and include; malignant melanoma associated with bronchial epithelial changes; a solitary lung tumour; no prior history of a cutaneous, mucous membrane, intestinal or ocular melanoma and absence of any other detectable tumour at the time of diagnosis.

Methods: case report

Results: A 82-year-old male nonsmoker presented with a 5-month history of upper gastrointestinal tract symptoms and generalized weakness. There were no respiratory symptoms or history of lung disease or skin tumor. He was known for an adenocarcinoma of the prostate under hormonal treatment and post-radiotherapy 3 years before with a normal PSA at admission of 0.2 µg/l. The chest radiography showed a right lower lobe mass (fig. 1). A bronchoscopy was negative for an endoluminal mass. Computed tomography (CT) of the brain, chest and superior abdomen failed to reveal mediastinal adenopathy, adrenal mass or other metastatic lesions. The patient underwent a right pneumonectomy. Histopathological examination of the mass confirmed the diagnosis of achromic malignant melanoma. Clinical examination (gastroscopy, colonoscopy, dermatoscopy and fundoscopy of the eyes) and postoperative positron emission tomography (PET-CT) did not reveal an other primary localisation of the melanoma but multiple mediastinal lymphnodes and left adrenal metastasis.

Conclusion: Less than 30 cases of primary malignant melanoma of the lung have been published since 1886 with many of the early cases failing to meet the criteria mentioned previously. The possibility of occult or antecedent primary skin or mucosal lesion cannot be excluded especially if the lesion has regressed. The mechanism of primary lung melanoma arousal is not understood. Theories involve migration of melanocytes along the primordial tubular respiratory tract during fetal development. Another theory refers to a melanogenic metaplasia of respiratory epithelial cells. The prognosis is poor and surgical resection with or without adjuvant chemotherapy and/or radiotherapy remains the mainstay of treatment for PML.



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Oximetry alone versus portable polygraphy for sleep apnoea screening before bariatric surgery

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Background: Bariatric surgery is now recognized as the only effective treatment for the morbidly obese patients. Obstructive sleep apnea (OSA) is a commonly encountered comorbidity in morbidly obese patients undergoing bariatric surgery. Screening for OSA is thus recommended as part of the preoperative assessment of these patients. The objective of this study was to compare the sensitivity of oximetry alone versus portable polygraphy in the preoperative screening for obstructive sleep apnea.

Methods: We retrospectively reviewed polygraphic data recorded as part of the preoperative assessment before bariatric surgery from 68 consecutive morbidly obese patients between November 2006 and June 2008. Sleep apnea screening was performed with an Embletta system. The pulse oximeter (Nonin, Plymouth, MN, USA) had a sampling rate of 10 Hz. For each patient we compared the sensitivity of 3% or 4% desaturation index (oximetry alone) with apnea hypopnea index (polygraphy) to diagnose OSA and classify the patients as normal (< 5 events/h), mild (5–15 events/h) moderate (16–30 events/h) or severe (>30 events/h).

Results: Using apnea hypopnea index, 17.6% of the patients were classified as severe, 17.6% as moderate, 36.8% as mild and 28% as normal. Using 3% desaturation index, 22.1% of the patients were classified as severe, 29.4% as moderate, 38.2% as mild and 10.3% as

normal. With 4% desaturation index, 20.6% were classified as severe, 10.3% as moderate, 39.7% as mild and 29.4 as normal. Overall, 4% desaturation index as compared to AHI yielded a 95% negative predictive value to rule out obstructive sleep apnea (AHI <5/h) and a 100% sensitivity (0.85 positive predictive value) to detect severe OSA (AHI >30).

Conclusion: Using oximetry with 4% desaturation index as a screening tool for OSA could allow us to rule out significant OSA in almost a third of morbidly obese patients during preoperative work up for bariatric surgery. This widely available technique could accelerate preoperative work up of these patients. We hypothesize that this high sensitivity of oximetry is specific to morbidly obese patients due to a reduction of their lung volume, especially when they lay supine. Patients with a positive oximetry should however undergo further sleep investigations to confirm the diagnosis and patients complaining of daytime sleepiness should be referred to a sleep specialist when oximetry is negative.

COPD management in general practice: preliminary data of the Swiss COPD cohort study

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Study aim: COPD is a leading cause of morbidity and mortality. Based on our Swiss COPD cohort, we wanted to assess the implementation of the GOLD guidelines in general practice.

Methods: 139 general practitioners in Switzerland were invited to recruit COPD patients (smokers or ex-smokers older than 40 years). They were asked to perform spirometries and fill in questionnaires about symptoms, comorbidities and treatment.

Results: 615 patients (64% male, mean age 69 years) were recruited by 139 general practitioners. Based on the GOLD criteria, no COPD (FEV₁/FVC >70%) was seen in 269 patients (44%), COPD GOLD Stage I in 29 patients (4.7%), GOLD Stage II in 155 patients (25%), GOLD Stage III in 130 patients (21%) and GOLD Stage IV in 32

patients (5.2%). 339 patients (55%) were current smokers. Concomitant coronary heart disease was reported in 124 patients (20%), chronic heart failure in 93 patients (15%), hypertension in 312 patients (51%), and lung cancer in 14 patients (2.2%). Medication is displayed in table 1.

Conclusion: In a general practitioners based cohort, 44% of the included patients do not have airway obstruction in the spirometry. 5.7% of all COPD patients in our cohort were treated with systemic steroids and 75.5% of COPD GOLD Stage I and II patients were treated with inhaled corticosteroids.

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Table 1:

	N	LABA	LACH	ICS	ICS/LABA	Syst. Steroids
No COPD	269	55	63	43	102	15
COPD I	29	9	10	8	11	0
COPD II	155	37	54	32	88	7
COPD III	130	38	64	33	79	11
COPD IV	32	12	17	12	23	2

LABA = long acting bronchodilator
LACH = long acting anticholinergics
ICS = inhaled corticosteroids
ICS/LABA = combination ICS and LABA
Syst. Steroids = systemic steroids

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Posters session III – CF, asthma, smoking

Multiple brain abscesses – A rare complication of cystic fibrosis

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We report the history of a 14-year-old girl presenting with fatal multiple intracerebral abscesses which is an uncommon complication of cystic fibrosis (CF). The girl had advanced CF lung disease (FEV₁ 30%) with persistent colonization by *Pseudomonas aeruginosa*. Her previous history was remarkable for several admissions for antibiotic therapy of pulmonary exacerbations, gastrostomy tube placement at 11 years of age, and a work-up and antibiotic treatment for purulent gonarthrit six months before presentation. Bacterial cultures of the synovial fluid remained negative. The girl presented to our out-patient clinics with a one-week history of frontal headaches and low-grade fever. Apart from the known respiratory disease, physical examination including a thorough neurologic and fundoscopic exam was normal. Laboratory examinations revealed a normal CRP and respiratory alkalosis in the blood gas analysis. The girl was started on oral ciprofloxacin for suspected sinusitis and pulmonary exacerbation of CF lung disease. Fever ceased on the next day at home, but headaches persisted. Three days later, the girl started to vomit and developed generalized seizures. On arrival in the emergency room, the girl was comatose with dilated pupils and posturing. An immediate CT scan revealed multiple bilateral brain abscesses partly rupturing into the ventricular system and cerebral edema. The patient died despite instant neurosurgical intervention and decompressive craniectomy. *Streptococcus viridans* was isolated from the brain abscesses. Autopsy was refused by the parents which precluded the search for further septic foci. Brain abscesses have been rarely reported in CF patients. Other case reports have pointed at the paucity of clinical signs and the difficulty in making an early diagnosis. Infectious agents often originate from the oral flora and not from respiratory pathogens; although brain abscesses are almost exclusively reported in older patients with advanced disease. Whether haematogenous spread through right-to-left shunts bypassing the filter effect of the pulmonary capillary tree is facilitated in advanced CF lung disease remains a matter of speculation. Early consideration of a head CT in patients with advanced CF complaining of headache seems the safest approach for timely detection of this rare and fatal complication.

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Diagnosis of idiopathic pulmonary fibrosis: from guidelines to clinical practice

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Background: In 2000, an ATS/ERS expert panel published the first guidelines on diagnosis and management of idiopathic pulmonary fibrosis (IPF, Am J Respir Crit Care Med 2000; 161:646). To what extent are these recommendations applied in clinical practice is unknown.

Objective: To determine the difference between recommendations and clinical practice for the diagnosis and initial management of IPF in Switzerland.

Methods: Retrospective analysis of consecutive cases with presumed IPF diagnosed after 2000, and reported to a web-based IPF registry.

Results: 36 cases were included (men 72%). Population characteristics were (mean ± SD): age 68 ± 11 yr, total lung capacity 72 ± 18% pred, TLCO 48 ± 16% pred, resting PaO₂ 66 ± 15 mm Hg, 6-min walking distance 341 ± 118 m with SaO₂ drop 10 ± 7%. The diagnostic work-up was made at tertiary care hospitals (52%), pulmonary private practice (30%), or regional hospitals (18%). High-resolution computed tomography (HRCT) was performed in 86%, bronchoalveolar lavage (BAL) in 58% and transbronchial biopsy (TBB) in 14%. Surgical lung biopsy (SLB) was done in 15 cases (42%), and showed usual interstitial pneumonia (UIP) pattern in all. In cases without SLB (n = 21), the 4 major ATS/ERS diagnostic criteria were met with the following frequency: 1) exclusion of other causes of interstitial lung disease: 100%, 2) restrictive ventilatory defect or impaired gas exchange: 90%, 3) bibasilar reticular opacities with minimal ground glass on HRCT: 71%, and TBB or BAL showing no features of alternative diagnosis: 38%. Minor diagnostic criteria were met in all patients. Requested criteria for IPF diagnosis without SLB (4 major + 3 minor) were fulfilled in 5/21 cases (24%). One or more criteria were missing in the remaining 16 cases (76% of those without SLB, and 44% of whole population). The frequency of multidisciplinary assessment was: formal 25%, informal 25%, none 50%. HRCT were evaluated by a general radiologist (76%) or a lung radiologist (24%). Biopsies and BAL were evaluated by a general pathologist (70%) or a lung pathologist (30%). Treatment was given in 64%, and included corticosteroids (83%), azathioprin (17%), N-acetylcystein (13%), and enrolment in randomized trial (11%).

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Conclusion: ATS/ERS diagnostic criteria were fulfilled in half of cases. The most common missing criterion was BAL. Multidisciplinary assessment was performed in a minority of patients and should be developed. Enrolment in trials should be encouraged. This study is funded by Actelion

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Delivery of smoking cessation care: experience and results from the University Hospital Zurich

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Background: Smoking cessation care is less than optimal in hospitals. The University Hospital of Zurich started an interprofessional smoking cessation programme in 2006. We therefore report on our data in 2008.

Methods: Intensive counselling with both behavioural and pharmacologic approaches for hospitalized and out-patient clients as well as employees by MD, psychologist and nurse with a special training in smoking cessation. Data assessment 1, 3 and 6 months after first counselling.

Results: In 2008 165 new clients were admitted (male 102, female 63); 104 outpatients, 43 hospitalized patients, 18 employees. The number of counselling was 290. According to the transtheoretical model clients showed different levels of motivation: precontemplation $n = 8$ (5%), contemplation $n = 27$ (16%), preparation $n = 85$ (52%), action $n = 22$ (13%), missing data $n = 23$ (14%). Outpatient clients (employees included, $n = 122$) had a mean age of 48 years ($SD = 14.2$, $n = 118$), smoked 21.2 cigarettes a day ($SD = 10.9$, $n = 116$) and had 30.3 pack years ($SD = 20.3$, $n = 115$). Addiction by Fagerström questionnaire (FTND-Score, range from 0, very low, to 10, very high) was 5.4 ($SD = 2.3$, $n = 114$). The major pharmacologic approaches ($n = 97$) included nicotine replacement therapy ($n = 57$), bupropion and NRT ($n = 16$), bupropion alone ($n = 1$), and varenicline ($n = 23$). At follow-up after 1, 3 and 6 months, 40 (38%), 26 (35%) and 14 (29%) respectively of the 122 outpatient clients were "quitters". A significant reduction of less than 50% of the number of cigarettes was reported in 33%, 27% and 14% of the clients after 1, 3 and 6 months, a reduction between 50–80% or no change in 10%, 14%, 20% of the clients, and unknown in 19%, 24% and 37%. Follow-up after 1, 3 and 6 months was still open in 18, 48 and 73 clients. On a scale from 1 (not helpful) to 4 (very helpful) clients assessed personal communication as most helpful ($m = 3.81$, $SD = .4$), followed by repeated counselling ($m = 3.6$, $SD = .6$), improved knowledge ($m = 3.5$, $SD = .6$) and pharmacological support ($m = 3.4$, $SD = 1.0$).

Conclusion: Hospitals are key settings for the provision of smoking cessation care. Hospitals should implement system wide procedures to ensure that smokers are identified and trained staff is available to provide smoking cessation consults. The challenge will be to incorporate smoking behaviour monitoring and smoking cessation interventions as part of standard practice. Future research should identify effective methods for increasing smoking care provision in this setting. In addition, standardized measures of smoking care should be developed.

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Are exhaled and nasal NO measurements useful in cystic fibrosis adult patients

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Introduction: Exhaled NO (FeNO) is elevated in inflammatory lung diseases such as asthma, but it has been found low to normal in cystic fibrosis (CF) patients compared to healthy controls. In addition nasal NO (nNO) is also usually thought to be lower in CF patients compared to controls. However, studies have provided controversial data, and the effect of lung capacity decrease, the role of infectious exacerbations and of colonization with *Pseudomonas aeruginosa* (Pa) on FeNO and nNO values are not clear.

Methods: we prospectively measured FeNO ($n = 316$) and nNO ($n = 225$) in 32 adults CF patients followed at the CF clinic at the CHUV (Lausanne) over a 2.5 years period. Measurements were performed with a NIOX[®] chemiluminescence analyzer. Mean age of the patients was 29.4 ± 8 years and mean FEV₁ was $66.5 \pm 3.7\%$ of predicted. Twenty-three of the 32 patients were colonized with Pa. **Results:** median FeNO value was 7.5 ppb in CF patients colonized with Pa vs. 9.2 ppb in patients not colonized with Pa (not significant). Normal FeNO values are from 5 to 25 ppb. Median nNO was 417 ppb in CF patients colonized with Pa vs. 306 ppb in patients not colonized with Pa ($p < 0.001$). Normal nNO values have not been clearly determined and we used those from Kharitonov (2005), which are 827 ± 320 ppb. Thus, we found that 219/316 FeNO values (69%) but only 59/225 nNO values (26%) were in the normal range. No correlation was found between FeNO and nNO and FEV₁, but a significant correlation was present between FeNO and nNO levels ($p < 0.0001$).

Three patients had FeNO values mostly over 30 ppb (up to 82 ppb) and presented mainly with a pancreatic form of the disease. Finally, 1 patient had a FeNO increase from 8 to 35 ppb that could be attributed to asthma.

Conclusions: A low value of FeNO can suggest the diagnosis of CF but a normal value is common in adult CF patients. FeNO is not associated with Pa colonization or FEV₁ decrease. In contrast, colonization with Pa is correlated with higher nNO levels. Moreover, a high FeNO value in adult CF subjects may be suggestive of concomitant asthma or of a predominantly pancreatic form of the disease. The significant correlation between FeNO and nNO levels suggests that a common mechanism may affect the upper and lower airways when abnormal NO values are found. Although, FeNO and nNO measurements might be useful in CF, more data are needed to clarify their role in clinical practice.

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Exhaled nitric oxide and asthma in paralympic athletes with spinal cord injury

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Background: Fraction of exhaled nitric oxide (FeNO) is related to airway responsiveness, sputum eosinophilia and total IgE in patients with asthma. FeNO has been studied as a screening tool for asthma in adults and as a predictor of exercise-induced bronchoconstriction in children. In literature there exist no FeNO data in a population with spinal cord injury. The objective of this study was to compare the values for FeNO with the diagnosis of asthma in athletes with spinal cord injury, all members of the Swiss Paralympic Team Beijing 2008.

Methods: In the course of the medical checkup for the Paralympic Games in Beijing 2008 FeNO was measured in 30 wheelchair athletes (18 male/12 female). The subject's characteristics were: age 35.6 ± 12.1 years, height 169.6 ± 12.9 cm, weight 63.7 ± 15.1 kg. FeNO was measured by a portable device (NIOX mino). FeNO values beyond 25 ppb were considered as increased. FeNO was measured at the beginning of the medical checkup. Athletes with established asthma were advised to stop the treatment for at least 1 week prior to the examination. A prick test for allergic reaction was performed at the same day, whereas a skin reaction of >3 mm was seen as positive. Asthma was defined as having symptoms (dysnea or cough) and signs of airway hyperresponsiveness (either reversibility of FEV₁ after inhaling salbutamol or positive challenge test e.g. eucapnic hyperventilation or mannitol test).

Results: 11 out of the 30 athletes were diagnosed as asthmatic ($= 36.7\%$). The mean FeNO values were not different between asthmatics (27 ± 14 ppb) and non-asthmatics (38 ± 33 ppb; $p = 0.28$). 10 of 19 non-asthmatic athletes (53%) showed FeNO values of more than 25ppb compared to 6 of 11 (55%) in the group of asthmatics. In the group of asthmatics 64% (7 of 11) had a positive prick-test, but only 26% (5 of 19) of the non-asthmatics. From the athletes with a positive prick test 75% (9 of 12) showed a FeNO value of >25 ppb. **Conclusion:** There were no differences in FeNO values between asthmatic and non-asthmatic spinal cord injured paralympic athletes.

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Treatment of allergic bronchopulmonary aspergillosis with anti-IgE antibody (omalizumab) in an asthmatic adult – A case report

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Allergic bronchopulmonary aspergillosis (ABPA) originates from an IgE mediated pulmonary response to *Aspergillus* spp. and a close relationship between ABPA and allergic asthma has been described. Prevalence of ABPA in asthmatic patients is approx. 1–2% and standard treatment of ABPA comprises systemic steroids and supplementary use of antifungal agents. Since ABPA is associated with elevated levels of IgE, treatment with monoclonal anti-IgE antibody (omalizumab) might be a therapeutic approach. Previous reports have demonstrated successful use of omalizumab in children with ABPA and underlying cystic fibrosis. We report a 25-year old female with allergic asthma and relapsing ABPA, who was treated with monoclonal anti-IgE antibody; standard treatment was primarily initiated with good clinical success, but during course of treatment IgE levels remained elevated. Since the patient had experienced adverse side effects with prior steroid therapy, we started additional omalizumab treatment to spare steroids. This therapy resulted in sustained relief of symptoms, despite notable reduction of steroid dosage. The long term outcome has to be awaited. Omalizumab appears to be a promising alternative in the treatment of ABPA as steroid sparing drug, but it has yet to be evaluated in further prospective trials.

Desensitisation with ASS in patients with morbus Widal: a retrospective analysis of data

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Chronic sinusitis with nasal polyps often complicates asthma and may be associated with intolerance to ASS and NSAID (Morbus Widal/Samter trias). Desensitisation to ASS is a promising approach to reduce nasal symptoms by preventing growth of polyps and improving sense of smell. In a retrospective analysis in December 2008 we tried to contact by phone all 35 patients having been desensitised between July 2007 and September 2008 with ASS in our clinic. 29 could be interrogated allowing us to fill in a specially designed questionnaire including length of ASS-treatment, dosage, nasal symptoms, and reasons of an eventual discontinuation of therapy. The mean duration of ASS treatment at that very moment was 7.9 months (4 to 15). 23 patients (79%) acknowledged an improvement of nasal symptoms. 17 had less symptoms of the upper airways and 15 reported an improvement of their sense of smell. 18 patients were still on ASS therapy. The main side effects were hematoma (5) and gastric symptoms (4). 11 patients stopped ASS desensitisation in between: 2 due to gastric symptoms, 4 due to scheduled operations (in 2 cases sinus surgery), 3 due to subjective ineffectiveness, and 1 due to asthmatic exacerbation. In one case the pulmonary physician had advocated to stop ASS treatment assuming a potential worsening of osteoporosis. Severe side effects did not occur. Discontinuation of therapy occurred always within the first 6 months of treatment, at a meantime of 4 to 15 months. We therefore conclude that after 6 months of treatment with ASS the success rate can be judged already. ASS desensitisation is a secure and effective approach to cure nasal polyps in combination with ASS intolerance. Thorough instruction of patients and their practitioners at home about this specialised therapeutic option may help to improve the potential benefit. We are going to conduct a prospective study on patients with nasal polyps and ASS intolerance using the SNOT-20 symptom score to better evaluate nasal symptoms.

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Methods: Patients ≥ 18 yrs ($n = 1681$) with mild to moderate asthma insufficiently controlled on ICS or ICS+LABA were treated daily with add-on oral montelukast 10 mg by 290 office-based respiratory physicians in Germany for 6 months. The primary endpoint was a change in the Asthma Control Test (ACT) score.

Results: At baseline visit, 23% and 69% of patients were on ICS or ICS+LABA alone, respectively. Most patients reported daytime symptoms (72%) or rescue medication use (57%) >2 times/week at baseline. The results showed that at baseline 57% had uncontrolled asthma, but after 6 months 58% had controlled asthma on added montelukast. The ACT score, Mini-AQLQ score, FEV₁, and PEF were significantly improved at 6 months (table).

Conclusion: The addition of montelukast significantly improved both asthma control and quality of life in patients suboptimally controlled with ICS or ICS+LABA in this study under real-life conditions. Support: Funded by a research grant from MSD Germany.

	Baseline visit	6-month visit ¹
PERCENTAGE OF PATIENTS IN EACH ACT CATEGORY		
Uncontrolled asthma (≤ 16 score)	57.2	17.4
Badly-controlled asthma (16-19 score)	25.0	21.6
Well-controlled asthma (20-24 score)	13.9	46.7
Completely controlled asthma (≥ 25 score)	1.2	11.7
ACT COMBINED SCORE ²	14.6 \pm 4.6	19.5 \pm 4.4
MINI-AQLQ OVERALL SCORE ²	4.0 \pm 1.1	5.3 \pm 1.1
FEV ₁ (L) ²	2.47 \pm 0.90	2.61 \pm 0.92
PEF (L/s) ²	5.76 \pm 2.39	6.15 \pm 2.41
ASTHMA STATUS		
Percentage of physicians or patients rating as "better" or "very much better"		82.8-83.1

¹After 6 months of add-on montelukast
²Values in mean \pm SD
³P<0.001 for difference between 6-month and baseline visit for all mean values

Asthma tests in the assessment of military conscripts

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Background: Exercise induced bronchoconstriction is often present in asthmatic subjects and may affect individuals fitness for military service. To equally treat and diagnose subjects with symptoms of asthma at conscription regarding their fitness for military service, objective and reliable tests are needed.

Methods: 18–20 year old male swiss conscripts. Questionnaire, spirometry, bronchial challenge test (BCT) with methacholine and mannitol, exhaled nitric oxide, skin prick testing. Asthma was defined as having symptoms of dyspnoea or wheeze during exercise and airway hyperresponsiveness.

Results: 284 conscripts voluntarily participated in this study. Test results for all the BCT were available for 235 conscripts (83%). 60 (26%) were current smoker, 175 (74%) were non- or former smoker. Asthma was present in 16 (7%) of conscripts. The utility of tests in the diagnosis of asthma can be seen in table 1. Limiting the analysis to non-smokers only increased the sensitivity of FeNo >20 ppb to 83%.

Conclusion: BCT with mannitol has a high sensitivity and specificity to diagnose subjects with exercise dyspnoea and wheezing. Due to a low prevalence of exercise dyspnoea and wheezing in our population positive predictive value is low. BCT with mannitol might be a useful tool to diagnose exercise induced asthma in young males presenting for conscription in the Swiss Armed Forces.

Utility of test in diagnosing Asthma (n=235)				
Test	Sensitivity	Specificity	Positive predictive Value	Negative predictive Value
Methacholine PD 20 (n=33)	75 %	90 %	36 %	98 %
Mannitol PD 15 (n=31)	81 %	92 %	42 %	99 %
FeNO >20 ppb (n=97)	67 %	61 %	11 %	96 %
FeNO >25 ppb (n=79)	63 %	68 %	12 %	96 %
FeNO >30 ppb \pm FeNO >40 ppb I (n=52)	56 %	80 %	17 %	96 %
Skin prick test positive (n=98)	81 %	61 %	13 %	98 %
FEV ₁ /FVC <0.7 (n=8)	0	96 %	1 %	93 %

Non smoker, Smoker

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Implementation of a standardised smoking cessation programme in a respiratory rehabilitation clinic – First results

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Background: Respiratory rehabilitation clinics should have skilled and continuously updated staff for smoking cessation counselling and pharmacological support.

Objective: Implementation and documentation of a standardised, interdisciplinary smoking cessation program in a respiratory rehabilitation clinic largely based on the guidelines provided for Hospital QuitSupport smoking cessation clinics.

Methods: All patients from two respiratory / internal medicine wards were questioned about their smoking status at admission during a six months period starting first of July 2008. Various baseline information was obtained including age, gender, previous smoking habits, motivation, barriers and facilitators concerning smoking cessation. The assessments were done by the ward physician in collaboration with a specialised nurse. All smokers were encouraged to benefit from the opportunity of cost-free smoking cessation counselling during the hospitalisation. Participants had the right to refuse participation. The results of the assessment and the treatment plan (pharmacological, counselling aspects) became an integral part of the final report to the general practitioner after discharge.

Results: During the first 6 months 161 patients were assessed on the two wards: 24,2% (39) of patients were smokers and 75.8% (122) patients were non- or ex-smokers. Among the smokers 7 (18%) refused individual smoking cessation counselling. The number of patients refusing to participate decreased over time. Of the 32 patients who received individual counselling only one person had a relapse during the rehabilitation (usual duration 3 weeks). 13 (33%) received a nicotine replacement therapy (NRT), 2 smokers continued previously started NRT and one person was treated with varenicline.

Conclusions: The introduction of a standardised smoking cessation program raised the awareness and the importance of this topic among all health professional categories in the clinic. It further improved the professional approach and motivation to provide this service routinely. It was interesting to note that in this population with predominantly severe COPD patients roughly one quarter of the patients are still active smokers. Only 2 patients arrived with smoking cessation treatment and very few patients had received counselling from the referring hospitals. Future efforts will address the lack of follow-up visits to obtain outcome data.

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Efficacy of montelukast in asthma patients inadequately controlled on inhaled steroids and long-acting beta-agonists: a real-life open-label study

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Background: Asthma often remains uncontrolled in patients despite treatment with inhaled corticosteroids (ICS) or ICS + long-acting beta-agonists (LABA), thus necessitating additional therapy.

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Acute hypersensitivity pneumonitis in a paint quality controller: a case report

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Introduction: Isocyanates are sensitizing chemicals used in various industries such as polyurethane foam production or paint-related purposes. Acting as haptens recognized by T-lymphocytes, they can cause allergic asthma and rarely hypersensitivity pneumonitis (HP). We aim to present a case report of acute HP due to hexamethylene diisocyanate (HDI) in a paint quality controller, a profession not generally considered at a high risk for work-related Isocyanates exposure.

Case report: A 30-yr-old otherwise healthy female, light smoker working as a paint quality controller developed shortness of breath, malaise, sweating and chills at workplace six hours after handling a HDI-based hardener. Upon admission to emergency department, symptoms had progressed to severe respiratory failure. HR computer tomography (HRCT) showed bilateral ground-glass attenuation without pleural effusion. Rapid clinical and radiological improvement occurred under facial oxygen supply and systemic steroid therapy. Occupational medicine investigations revealed regular handling of HDI using latex gloves without respiratory protection. Assessment at workplace showed insufficient air renewal (1.5 times per hour), inadequate local aspiration and HDI exposure at levels of 1–4.25 ppb/m³ (Swiss Occupation Exposure Limit 5 ppb/m³). Biological monitoring after identical work procedure executed by a co-worker showed HDI exposure (5.1 micrograms hexamethylene diamine/g creatinine). Resumption of work was disadvised because of the life-threatening event.

Discussion: The diagnosis of occupational HP is highly supported by classical findings on imagery and typical symptoms occurring within approved latency interval, associated with rapid clinical improvement. Although neither broncho-alveolar lavage nor specific IgG diagnosis (en route) were performed during the acute episode, various blood tests managed to rule out evidence of an infection or autoimmune disease. Other causes of HP seem unlikely as the patient did not have any recurrence of symptoms since absence from work. Workplace evaluation provided significant information on HDI exposure and allowed substantial recommendations to diminish Isocyanate exposure for the 20 still healthy laboratory co-workers. Although the entryways (air or skin) and precise mechanism of toxicity remain unclear, the present case clearly shows that Isocyanates may trigger acute HP in susceptible workers in a profession not generally considered at a high risk.

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results and recommendations, the company undertook some measures to reduce the exposure to Mesalazine. A new health evaluation of the employees in the Mesalazine production is hence planned in 2009. As each year new causes of occupational asthma are described, the possible work relation of new asthma onset has to be carefully investigated as the consequences for the patient e.g. removal from exposure and for the exposed co-workers are of substantial importance.

Prospective monitoring of exposure and lung function among cement workers

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Background: Several published cross-sectional studies support a causal relationship between cement dust exposure and reduced measures of lung function, but there are to our knowledge no published prospective studies to support this. The hypothesis of the present study is that inhalation of cement dust may possibly induce reduced lung function in excess of the expected loss of function due to increasing age. Twenty-four cement plants in eight European countries participate with a total of approximately 4200 employees. In Switzerland the cement plant Jura Cement Wildeggen participates. The study is conducted by the National Institute of Occupational Health (NIOH) in Oslo. The study is financially supported by CEMBUREAU, Brussels, Belgium.

Aims of the study: Exposure studies: To characterize exposure to cement dust among cement production workers during 2007–2011. Lung function studies: To study prospectively the association between cement dust exposure and lung function in 4000 cement workers during 2007–2011.

Study design: The study is carried out as a prospective study for at least 4 years from 2007–2011 in a cohort recruited among the employed workers at selected Portland cement plants in eight European countries. All employees of the participating plants were invited to take part in the study. Job titles were categorized as: Production, cleaning, maintenance, foreman, management, laboratory, other and unknown. Exposure information is obtained using individual measurements. About 1/3 of the participants carry monitoring equipment for one or two days and they fill in an Exposure Sampling Log of the tasks performed during each of these days. The cement content in the samples will be estimated by gravimetry, and selected samples will be characterized by chemical analysis. Outcome information is obtained from all participants of the study, using repeated spirometry to measure lung function parameters and filling in a health questionnaire at the time of spirometry. The health questionnaire provides information on potential confounding factors. Lung function measurements are carried out at each plant site by occupational health personnel using a Vitalograph 2160 bellow spirometer. The FEV₁ is the main parameter of interest in the study. The validity criteria for spirometry have been defined according to ATS and ERS requirements. All data are anonymized and transmitted to the NIOH for statistical analysis. Results of the main study are expected to be published in 2012.

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Occupational asthma in workers exposed to Mesalazine powder inhalation

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Background: Due to complaints of respiratory symptoms of some employees a pharmaceutical company asked in 2008 the occupational medical department of the Institute for Work and Health in Lausanne to evaluate the health status of their workers exposed to Mesalazine powder, which is the active agent of a drug used for the treatment of bowels inflammation. Therefore we examined the 21 workers exposed to Mesalazine powder.

Method: After a visit of the pharmaceutical company in order to investigate the Mesalazine powder production, we performed an individual medical evaluation of the 21 workers. Our medical protocol was based on the safety data sheet of Mesalazine, the data found in the scientific literature and the «Compendium Suisse des Médicaments» and covered upper and lower respiratory tract as well as skin and eyes.

Results: Sixty two percent (62%) of the exposed employees had symptoms of skin, eyes and throat irritation. Three employees reported respiratory symptoms such as dyspnoea, cough and expiratory wheezing, which appeared during the working hours. The Peak Flow series performed at the workplace was lowered in the three employees with lower respiratory tract symptoms. None of the three had consulted a physician, even though the symptoms had been present since some months. The pneumological evaluation confirmed for all three cases the asthma diagnoses.

Conclusion: It is known that patients who are treated with drugs including Mesalazine can develop adverse health effect such as asthma. However occupational asthma in workers exposed to Mesalazine powder inhalation is until now not described in the literature. Immunologic investigations in order to know if the occupational asthma caused by Mesalazine is of allergic or mechanical irritation nature are still ongoing. Concerning the three workers with asthma, inability to work with Mesalazine was pronounced. Furthermore, the SUVA recognized the three patients with asthma as occupational respiratory diseases. Following our

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Case report on the effect of tobacco dust on work-related asthma

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Background: We report the case of a man of African origin, born in 1971. He is a non smoker, known for his atopic status, who has worked in Switzerland since 2004 as a cleaner of industrial plants in a factory which produces cigarettes. In 2006, he suffered from repeated colds and persistent fits of coughing with an exacerbation of these symptoms in spring 2007. In June 2007, after having carried out cleaning work which involved a strong exposure to tobacco dust, he exhibited a more intense reaction, with a cutaneous eruption and an intense crisis of dyspnea. He exhibited these symptoms, despite being under a course of treatment comprising corticosteroid inhaled therapy, antihistamines and inhaled beta 2-agonist.

Methods: The case has undergone pneumologic and allergologic investigations, including a visit to the work site.

Results: The physical examination (177 cm for 69 kg) was found to be within the norms, including cardiopulmonary status. The spirometries, carried out between the exacerbations, were found to be normal in relation to values for black Africans. The laboratory tests did not show an eosinophilia, but the level of total Ig E was increased to 307 kU/l (N <100 kU/l). The prick-tests were positive for grass pollen, the alder, the ash and were found to be uncertain to positive for birch and hazel trees. A prick-test made with sheets of tobacco and two various combinations of tobacco dust, appeared positive (there was a negative result with a non-allergic control). Analyses of specific Ig E (UniCAP® System) were also carried out. Seasonal mixture RX1 (pollens of birch,

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phlegm, mugwort and parietaria) showed a high level: (class 4) to 42.30 kUa/l. The perannuel mixture RX2 (house dust mites, dander of cat, dog, horse and alternaria) showed a moderate value: (class 2) with 0.94 kUa/l. Specific Ig E for tobacco remained negative (<0.35 kU/l). A visit to the work site made it possible to observe the nature of the work carried out and the level of dust contamination. On this occasion, the patient felt respiratory discomfort.

Conclusion: The symptoms were alleviated when the patient was on sick-leave. The prick-test carried out with dust taken from the work site confirmed the allergenic nature of tobacco as documented in literature. The worker was subsequently declared unfit to work with tobacco.

Allergic asthma to thaumatin: case report

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Background: Thaumatin is a protein originally isolated from an African fruit (the "katemfe"), but various thaumatin-like proteins have been found in apples, grapes, kiwis and olives, etc. Thaumatin has natural sweetening properties and is about 2000 to 3000 times more potent than sucrose. It is therefore used in the food industry, particularly in the processing of low-calories sweeteners. Recently, thaumatin-like proteins have been described as a new family of allergens.

Methods: We report the case of a 44-year-old woman occupationally exposed to thaumatin, who developed an allergy to it. The first symptom was an urticaria, which she presented two years after the factory she was working in (a sweeteners manufacturer), started to use thaumatin. Later on, she perceived an acute episode of a sensation of lump in the throat, persisting mild dyspnea, dysphonia and cough. Despite normal peak flow values and a normal chest examination, her general practitioner treated her with local corticoids and systemic antihistaminic drugs, which improved the symptoms. As occupational physicians, we were asked about the likelihood of an occupational disease. We visited her working place, and assessed the exposure to thaumatin. We concluded that the probability for a delayed asthma related to a thaumatin exposure was high, despite the lack of an exposure test.

Results: The case was submitted to the insurance company as an occupational disease, and was accepted as such. It was therefore decided not to perform the exposure test, given the absence of true benefit for the patient, who was advised to switch job, and to avoid any exposure to thaumatin in the future. A few months later, the symptoms had completely disappeared.

Conclusion: Some molecules only used in specific industry sectors, can cause health problems, such as allergy, but also toxic impairments, etc. The occupational physician, trained to find out which products and identify which molecules are involved, can contribute to the diagnosis, and help make possible a safe return to work for the patient.

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Rhinitis due to acrylates: case report

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Background: Acrylates and methacrylates (salts and esters of acrylic and metacrylic acid respectively), are monomers commonly found in polymer plastics, resins and glues, and are widely used in many industry sectors. The first adverse health effects described were skin reactions and asthma. Exposure to acrylates, for instance when using multicomponent glues, is now a well known cause of occupational asthma.

Methods: We report the case of a rhinitis – and possible asthma – to acrylates, in a 38-year-old woman, working in a nail beauty salon. She was currently treated for hypertension, and otherwise known for obesity and seasonal rhinoconjunctivitis, but did not have any respiratory problem. Two years after starting this activity, she progressively started to complain of anosmia, rhinitis, and intermittent dyspnea. Her job consisted in decorating nails with a mixture of a polymer powder and a liquid monomer, after removing the previous artificial nail with a small sander. We assessed exposure to acrylates at her working place, both as dust (from sanded nails) and volatile compound (from the mixture described above), and she was asked to measure her peak flow values twice a day for ten days, in order to detect a possible relationship between her occupational activities, the symptoms and the peak flow values.

Results: Measures made during the visit of the patient's place of work showed that the existing aspiration system was efficient for eliminating the dust produced by nail sanding, but not for eliminating the volatile components. Thus, occupational exposure to acrylates was demonstrated. Moreover, the peak flow measures showed an average decrease of almost 10 percent when the patient was at work, compared to when she stayed home. We concluded that she actually suffered from professional rhinitis and, possibly, professional asthma (not certain because of the limited number of peak flow measures per day).

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Conclusion: Although exposure to acrylates is a well known cause of occupational asthma, it should be emphasized that the exact mechanisms of action remain unknown, despite the abundant literature about it. Some professions, which tend to be more frequent nowadays (such as working in a nail beauty salon), can expose the worker to particular risks. This highlights the need of always inquiring not only about the profession, but also the related activities, when facing a case of suspected asthma.

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Duration of exposure with symptoms and socioeconomic status in workers with occupational asthma

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Background: Occupational asthma (OA) is a type of asthma caused by the workplace. Workers with a longer exposure with symptoms are more at risk of remaining with permanent asthma after exposure ends. Socioeconomic factors may influence this interval.

Methods: Subjects with OA compensated by the Quebec Commission de la santé et sécurité du travail (CSST) from 2002 onwards were contacted to obtain information on their current socioeconomic status. The duration of exposure with symptoms before application was made to the CSST was obtained from their medicolegal file. This preliminary report includes data in the first 44 workers studied.

Results: 32 male and 12 female workers aged 41 ± 11 years at diagnosis of OA were included. The duration of symptomatic exposure was 5.0 ± 6.7 yrs. This interval was significantly longer in men (mean ± SD: 5.6 ± 7.5 yrs) than in women (mean ± SD: 1.0 ± 1.1 yrs) (p = 0.002) and tended (p = 0.1) to be longer in patients with annual incomes 40 000 \$ CAN (6.6 ± 7.3 yrs vs 3.4 ± 6.3 yrs). This interval was not significantly related to education level or marital status. At the follow-up, FEV₁ was significantly (p = 0.05) lower (78% ± 17% vs 91 ± 20%) as well as PC20 (3.8 vs 12.7 mg/ml) in those with incomes 40 000 \$ CAN at the time of diagnosis.

Conclusion: These preliminary data in workers compensated for OA in Quebec suggest that: 1) male vs female workers and 2) workers with higher incomes remain symptomatic for a longer period before they apply to the CSST. This delay in seeking care may increase their risk of developing more severe asthma.

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The farmer's lung disease: occupational medicine input

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Background: Although there has been an abundant literature in recent years about farmer's lung disease, few addressed occupational measures able to maintain the farmer in his work. Nevertheless we know now that most of the farmers can be kept at the workplace by the way of occupational preventive measures.

Methods: This matter is discussed from a case report. A farmer affected by the farmer's lung disease was sent to us by his pneumologist, in order to estimate the possibility of maintaining him in his job and to determine relevant changes at his workplace to minimize risk of exposure to dust antigen. This approach required a visit to the workplace by occupational physician and hygienist.

Results: The visit of the workplace pointed out different habits and architectural particularities which were potential sources of exposure. The two main proposed measures to reduce the risk, were to wear respiratory masks while working inside the barn, such as preparing hay, feeding the cattle or sweeping the floor, and to build a direct access from the bathroom (shower and toilet) to the outside, allowing to go out of the barn after taking a shower and changing, without risk of being contaminated again. Although upgrading the shower-toilet is not yet completed to date, the already performed modifications led currently to significant clinical improvements, despite the risk of exposure was high since the animals were in the barn for more than two months.

Conclusion: The treatment of the farmer's lung disease must be multidisciplinary involving general practitioner, pneumologist, occupational hygienist and occupational physician.

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Malt as a cause of occupational asthma and extrinsic alveolitis

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Background: Malting is a process in which grains are made to germinate by soaking in water, this process being stopped by heating and drying the cereal. Malting grains develop the enzymes that are required to modify the grain's starches into sugars. Due to his high enzyme content, barley is the most common malted grain.

History: We report two cases of workers with hypersensitivity to malt. A 40-year old machine operator working in a malt company complained of increasing dyspnoea, cough and sputum production. Lung function showed moderate obstruction and hyperresponsiveness to methacholine (PC20 = 0.06 mg/ml). Skin prick test for common allergens were negative and for malt slightly positive. On inhaled budesonide his asthma was uncontrolled and had to be stabilized with montelukast and formoterol before specific inhalation challenge (SIC) could be performed. Occupational asthma was confirmed by a significant fall of FEV₁ after SIC. A 40-year old longshoreman with a past history of hay fever noted rhino-sinusitis, dyspnoea, wheezing and cough when unloading malt from ships. After a severe exposure he needed emergency treatment for asthma. When evaluated in our hospital, his lung function was normal and he did not have bronchial hyperresponsiveness (PC20 >128 mg/ml). Skin prick test to common allergens as well as to malt were negative. There was no decrease of FEV₁ during SIC but he developed nasal congestion, cough, chest tightness, shivering, hyperthermia and leucocytosis with neutrophilia. Total lung capacity, functional residual capacity and carbon monoxide diffusion capacity were significantly lower when compared to pre-SIC values. A diagnosis of extrinsic alveolitis was made.

Conclusion: In workers exposed to malt and with respiratory symptoms, it is relevant to consider the possibility of two diagnoses: asthma and extrinsic alveolitis. Skin prick tests can be falsely negative because of the poor quality of commercial extracts.

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Sensitisation to common allergens and rhinoconjunctivitis symptoms among policemen and firefighters

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Background: Policemen and especially firefighters are exposed to different irritative substances such as diesel exhaust particles and different chemical products during work that may cause symptoms of rhinoconjunctivitis. Despite being considered a healthy worker population and screened for asthma at recruitment, we could demonstrate in the past, that the rate of asthma among firefighters is the same as in the general population.

Methods: The findings of 66 policemen, 101 firefighters ("healthy workers") and 735 males of the Swiss study on Air Pollution And Lung Disease in Adults (SAPALDIA) 1 population sample investigated in Basel ("general population") were compared. We used the European Respiratory Health Survey and National Institute for Occupational Safety and Health questionnaire. Skin prick tests to common allergens were performed by the same method used in the SAPALDIA study. Atopy was defined as having at least one positive skin prick test to common allergens.

Results: The rate of current smokers was 34.1% in the "healthy workers" group compared to 40% in the "general population" (p = 0.149). The group of "healthy workers" indicated that they were more often exposed to dust, gases, damp, smoke, aerosols, odours at work (all p < 0.001). The rate of atopy was higher among "healthy workers" compared to the "general population" (47.3% vs. 32.4%, p < 0.001). "Healthy workers" more often complained of eye itching, running nose, pharyngitis symptoms, cough and dyspnoea at work than the "general population" (all p < 0.001). However the rate of self-reported allergic rhinitis was the same in both groups. The rate of rhinitis and conjunctivitis symptoms in the last 12 months was the same between firefighters and policemen. Aggravation of rhinitis symptoms during work occurred in 6% of firefighters and 9% of policemen (p = 0.679) whereas aggravation of conjunctivitis symptoms occurred in 12% of firefighters and 28% of policemen (p = 0.229).

Conclusion: Sensitization to common allergens is common among policemen and firefighters and might be due to exposure to airway irritants encountered during work. The implication of this finding is currently unclear, as the rate of self reported allergic rhinitis symptoms is the same as in the general population. However some "healthy workers" do have aggravation of symptoms during work. It is possible that sensitized symptomatic policemen or firefighters more often change to a less physically demanding profession with less irritant exposure.

Model of risk assessment of passive intramural exposure related to asbestosis: the place for occupational medicine

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Background: In September 2007 two cases of diseases related to asbestos, a malignant pleural mesothelioma and a case of bilateral calcified pleural thickening, were diagnosed among the employees of a college in Geneva. The causal relation between these pathologies and the multiple renovation work carried out in the contaminated buildings has been established. This events highlighted an aspect till now underestimated which is the passive intramural exposure for professional categories generally considered as not being at risk. This unusual situation led to the realization of medical consultations of screening in occupational medicine, to the development of a model assessment of the passive intramural exposure itself and to the definition of the place of occupational medicine in this model.

Methods: From January to July 2008 the occupational medicine service of the public administration of Geneva (SPE) carried out 123 medical consultations with risk assessment, X-ray and CT-scan if necessary, for the employees having worked in the establishment for 10 years and more since its opening in 1973. In this context of research-action a model of risk assessment of the passive intramural exposure related to asbestos has been developed and the place of the occupational medicine in this model has been defined.

Results: No new case of pathology due to asbestos was found. The cumulative exposure related to the emergence of possible pathology, used for example by the SUVA, is confirmed one more. The place of occupational medicine is at the end of a process where risk assessment is predominant.

Conclusion:

- 1) Using the list of professions at risk for asbestos is insufficient to exclude a possible causal relation in the presence of a pathology possibly related to asbestos
- 2) The classic measures realized by industrial hygienists for quantitative assessment of asbestos fibers do not take into account the possibility of a cumulative exposure
- 3) The cumulative exposure related to the emergence of a possible pathology due to asbestos is again confirmed
- 4) The positive predictive values of X-ray and CT-scan related to the low prevalence of asbestosis pathologies in the specific context of passive intramural exposure demonstrate that systematic medical screening is useless
- 5) The medical screening concerns people at risk according to the conclusions of risk assessment

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A low number of Swiss companies uses nanoparticles

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Nanoparticles <100 nanometres are being introduced into industrial processes, but they are suspected to cause similar negative health effects to ambient particles. Poor knowledge about the scale of introduction has not allowed global risk analysis until now. In 2006 a targeted telephone survey among Swiss companies (1) showed the usage of nanoparticles in a few selected companies but did not provide data to extrapolate to the full Swiss workforce. The purpose of the study presented here was to provide a quantitative estimate of the potential occupational exposure to nanoparticles in Swiss industry.

Method: A layered representative questionnaire survey among 1626 Swiss companies of the production sector was conducted in 2007. The survey was a written questionnaire, collecting data about the used nanoparticles, the number of potentially exposed persons in the companies and their protection strategy.

Results: The response rate of the study was 58.3%. The number of companies estimated to be using nanoparticles in Switzerland was 586 (95% Confidence Interval 145 to 1027). It is estimated that 1309 workers (95% CI 1073 to 1545) do their job in the same room as a nanoparticle application. Personal protection was shown to be the predominant protection means. Such information is valuable for risk evaluation. The low number of companies dealing with nanoparticles in Switzerland suggests that policy makers as well as health, safety and environmental officers within companies can focus their efforts on a relatively small number of companies or workers. The collected data about types of particles and applications may be used for research on prevention strategies and adapted protection means. However, to reflect the most recent trends, the information presented here has to be continuously updated, and a large-scale inventory of the usage should be considered.

Funding: Swiss Federal Offices for Health (FOPH), the Environment (FOEN) and the Economy (SECO), the Swiss National Accident Insurance Fund (SUVA) and the French Agency for Environmental and Occupational Health and Safety (AFSSET)

1 Schmid, Riediker, Environ. Sci. Technol. 2008;42(7):2253–60.

P112
Swimming-induced pulmonary oedema during the Swiss gigathlonW. Kistler¹, E.W. Russi²¹Spital (Davos); ²Universitätsspital Zürich (Zürich)

Background: Pulmonary edema (PE) in healthy scuba divers, swimmers (SIPE), aqua-joggers and in ultra-marathon runners is a rarely observed and poorly understood event and information on its prevalence is lacking. The one week lasting Swiss gigathlon 2007, consisting of race cycling, mountain biking, inline skating, running and swimming, gave the opportunity to study respiratory problems of the participants.

Patients and methods: The hospital charts of patients, who were admitted to various local hospitals were retrieved and analyzed retrospectively. The criteria of "proven" PE consisted of: shortness of breath, cough occurring during exercise, hypoxemia, bilateral rales and radiological infiltrates in both lungs on admission, remission within 24 to 48 hours and no evidence of heart disease nor a history or clinical features suggestive of asthma. "Possible" PE was defined as: shortness of breath, cough occurring during swimming, no history and no clinical features suggestive of asthma, no rales on auscultation, no CXR performed or unilateral infiltrates without evidence for aspiration of water and/or consecutive aspiration pneumonia. All patients with evidence of aspiration, pneumonia or exacerbated bronchial asthma were excluded from further analysis.

Results: Out of 6210 athletes 41 (0.66%) had to be cared for respiratory problems. 16 (0.26%) athletes were admitted to a local hospital. 7 persons (0.11%) fulfilled the criteria of definitive and 5 (0.08%) of possible PE (7 men, 5 women; median age: 35.5 years; range: 23–52 years). 2 persons were treated as inpatients, one with non-invasive ventilation, and 10 as outpatients. All PEs occurred exclusively while the athletes were swimming (SIPE). We found no relationship between the occurrence of SIPE and the water temperature. SIPE occurred more frequently in athletes with a high cumulative activity and happened earlier during the competition in athletes performing the whole competition on their own or as a pair of two as compared to teams of five athletes.

Conclusions: SIPE may occur in well trained healthy hobby athletes and the prevalence seems higher than previously assumed.

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Propofol sedation for thoracoscopy or bronchoscopy: a prospective study in a non-university hospitalJ.-M. Schnyder, L. Purek, G. Clark, J.-G. Frey, J.-M. Tschopp
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Background: During thoracoscopy (TS) and fiberoptic bronchoscopy (FB), we decided to use Propofol (P), an intravenous sedative agent, after having shown in a randomized controlled trial its better tolerance and sedative quality as assessed by the patient and the operator when compared with midazolam (M). The aim of this study was therefore to prospectively collect all the complications in a normal clinical setting of a community hospital.

Material and method: P sedation was performed using a predefined sedative protocol with systematic data collection for routine TS and FB cases requiring a more extensive procedure (transbronchial or EBUS biopsies) and/or in patients who previously had a FB and reported to have badly tolerated the procedure under M. All patients were closely monitored for blood pressure and SaO₂. Minor complications were defined as follows: Hypotension systolic blood pressure <100 mm Hg and/or diastolic pressure <60 mm Hg, tachycardia heart rate (HR) >100 bpm, bradycardia HR <50 bpm, hypoxemia SaO₂ <90% for more than 30 sec. Major complications were defined as mortality, procedure related morbidity requiring some closed monitoring for more than 15 minutes after end of the procedure or any procedure interruption because of complications.

Results: Fifty four interventions have been performed, 32 TS (12 malignant pleural effusion with talc pleurodesis, 8 diagnoses of pleural effusion and 12 pleurodesis for spontaneous pneumothorax) and 22 FB (4 cases requiring transbronchial or lymph node biopsies, 18 cases who already had had a previous FB with M and had badly tolerated it).

Table 1:

	Major complications		Minor complications		
	Hypotension	Tachycardia	Bradycardia	Hypoxemia	
FB N = 22 m/f = 12/10 age = 60.7 (37-78)	0	2 (9%)	3 (14%)	0 (0%)	6 (27%)
TS N = 32 m/f = 21/11 age = 53 (15-84)	1	20 (63%)	9 (28%)	3 (9%)	4 (13%)

We recorded only 1 MC, i.e., a bleeding episode requiring thoracotomy following pleural biopsy in a patient under aspirin and clopidogrel. This complication is not related to the sedative procedure. All other complications were well controlled by intravenous crystalloids or nasal oxygen. There was no interruption of procedure.

Conclusion: P sedation is a safe procedure in normal clinical setting of a non university hospital. This confirms previous results obtained on a large scale in other endoscopic procedures. However this sedative agent requires a well predefined protocol and more staff which may increase the cost of the procedure.

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Metastatic angiosarcoma arising from the right atrium: unusual presentation and excellent response to treatment in a 36-year-old patientM. Fehr, M. Kuhn, K.A. Mayer, B. Padberg, R. Cathomas
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Introduction: Angiosarcomas arising from the heart are very rare. In the case of metastatic disease they often respond poorly to treatment and median survival is very short.

Case report: A 36-year-old patient experienced impaired exercise tolerance, which deteriorated rapidly to dyspnoea at rest (NYHA IV) within 5 weeks. Computed tomography (CT) showed multiple lung nodules and ground glass infiltrates, a right pleural effusion and a tumour mass in the right atrium. Echocardiography and magnet resonance imaging (MRI) demonstrated a thrombus-formation within the right atrium adjacent to the tumour. Tissue samples from a CT guided biopsy, pleural effusion and bronchoalveolar lavage fluid were not diagnostic. Wedge resection of a lung nodule was necessary, which revealed the diagnosis of a high-grade angiosarcoma. In view of the rapidly progressive extensive disease, systemic chemotherapy with doxorubicin (75 mg/m²) and ifosfamid (7500 mg/m²) was commenced only 7 days after surgery. Moreover anticoagulation with low-molecular-weight heparin was started. Within the first days after starting the chemotherapy, the dyspnoea improved considerably. Five weeks later, the patient's general condition had considerably improved and dyspnoea had subsided to NYHA grade I. A CT scan after 2 cycles of chemotherapy showed marked regression of lung metastases, reduction of the atrial tumour by 30% and complete resolution of the ground glass infiltrates. The atrial thrombus had disappeared in an echocardiographic control. Chemotherapy was continued for a total of 6 cycles. Repeated CT scan showed further improvement resulting in a good partial remission after 4.5 months of treatment.

Discussion: Our case illustrates the diagnostic challenges of cardiac angiosarcoma and underlines the importance of gaining adequate tissue samples. The impressive improvement of both clinical symptoms and measurable disease in our case is likely due to the combination of rapid onset of aggressive chemotherapy as well as the initiation of anticoagulation. Although the prognosis of the patient was dismal at start of the treatment, it was important not to postpone the start of the chemotherapy, as the patient's bad general condition was a direct consequence of the rapidly progressive metastatic sarcoma. Moreover anticoagulation is warranted in patients with cardiac tumours and clinically evident recurrent embolic disease and represents a very important part of the treatment.

P115
Severe suppurative tracheobronchitis in a case of asymptomatic ulcerative colitisG.M. Tini, T. Schneider, N. Nierhoff
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Case report: In 1991 a 19-year-old female non-smoker presented with a 3-month history of severe productive cough. There was no evidence of asthma, chronic rhino-sinusitis or gastro-oesophageal reflux disease. After unsuccessful oral treatment with cefuroxime, the cough resolved with inhaled steroids over 1 month. Six months later, the same patient developed intermittent intestinal symptoms such as nausea, watery and bloody diarrhoea. In 1994 ulcerative colitis was found. In September 2007 the 35-year-old patient developed a disabling productive cough. No improvement with either antibiotic treatment (doxycycline, ceftriaxone), symptomatic therapy with codeine nor a 1 month course of esomeprazole 80 mg/die. CT-scan revealed mildly ectatic central airways and no signs for chronic rhino-sinusitis. Pulmonary function tests and diffusion capacity were normal, no signs of bronchial hyperreagibility were found. Bronchoscopy showed severe bronchial inflammation and suppuration. Bronchoalveolar lavage (BAL) fluid showed a normal cell-count with an unremarkable cellular pattern. Bronchial biopsy showed a moderate to severe chronic lymphocytic inflammation and a moderate infiltration with neutrophils. Cultures of BAL fluid identified copious growth of Haemophilus influenzae. We assumed a correlation between suppurative tracheobronchitis and the known ulcerative colitis. Inhaled steroids (Budenosid 1600 mcg/die) and appropriate antibiotic treatment over 14 days (amoxicillin/clavulanic acid, 2 g/die) led to a lasting relief of symptoms after 1–2 weeks.

Discussion: (Suppurative) tracheobronchitis is a rare extraintestinal manifestation of ulcerative colitis and can be effectively treated with inhaled or oral steroids. The endoscopic pattern is remarkable: diffuse erythema with swelling and sometimes irregular pseudotumoral

bulbing of the mucosa. Histology shows squamous metaplasia of the mucosa, marked lymphocytic and plasmacellular infiltration of the submucosa and infiltration by neutrophils. Other causes of bronchitis have to be excluded. The severity of bronchial involvement does not correlate with the activity of the inflammatory bowel disease: our patient had few intestinal symptoms during the preceding 15-month period, infrequently using mesalazine as her only treatment.

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Acute life threatening lipid pneumonia after accidental intravenous injection of an anabolic steroid

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Lipid pneumonia rarely occurs after inhalation or aspiration of oily compounds; only few cases have been described after intravenous injection in suicidal intention or rarely for radiological procedures. A 29 year old body builder chronically using various anabolic steroids presented in the emergency room in respiratory distress. Few minutes after an intramuscular injection of trenbolon acetate (an oily anabolic steroid suspension) he felt a metallic taste and a kind of dizziness. 2 hours later he woke up with shortness of breath and dry cough. 9 hours later he was admitted to the ICU with severe respiratory insufficiency (PaCO₂ 3.9 kPa, PaO₂ 6.9 kPa) and hemodynamic instability. Blood analysis showed marked elevation of inflammatory markers (CRP and ProCT) and chest x-ray revealed patchy alveolar opacities. He was stabilized with NIV and intravenous catecholamines. HD CT of the lung confirmed diffuse alveolar opacities. Bronchoalveolar lavage (BAL) showed many foamy vacuolated macrophages and elevation of neutrophils, transbronchial lung biopsies revealed acute diffuse alveolar damage with fibrinous exudate and septal edema. Under supportive therapy we observed a complete clinical, functional and radiological resolution after ten days. The clinical and radiological picture with the temporal association between the injection and the beginning of the symptoms are very suggestive for an acute severe lipid pneumonia due to an accidentally intravenous administration of anabolic steroids with an ARDS-like picture. The results of the BAL examination are consistent with this diagnosis. Complications after accidentally intravenous injection of anabolic steroids are not reported in the medical literature but are discussed in the bodybuilding blogs and forums: the "tren cough" or "fina cough" is a well known "side effect" of such self administered injections. It appears suddenly and is often self limited and only seldomly causes prolonged symptoms. The picture of an acute diffuse alveolar damage suggests a severe chemical induced inflammatory reaction, which takes place in the lungs, the first capillary filter encountered by the intravenously injected oily suspension.

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Pulmonary involvement in neurofibromatosis (von Recklinghausen's disease): an uncommon manifestation

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Background: Neurofibromatosis (NF) is one of the diseases of the phacomatosis family. The incidence of the common subtype NF1 ranges between 1:2300–1:3000. About half of the cases are familial with an autosomal dominant inheritance, the rest are due to spontaneous mutations. Consequences are dysplasia of ecto- and mesoderm. Diagnostic criteria are café-au-lait maculas, neurofibromas, etc. Although thoracic manifestations are diverse and quite common, the involvement of lung parenchyma in NF1 appears to be rare. Studies report a prevalence of interstitial lung disease in 1.9–20% of NF1.

Methods: Two cases are reported and compared with the literature.

Results: Case 1: 56-yr. old man, never-smoker, with shortness of breath at rest. NF1 first diagnosed 1990 on appearance of café-au-lait maculas and cutaneous and subcutaneous neurofibromas. In 2005 parenchymal lung involvement was diagnosed with fibrocystic and interstitial lung manifestations in chest-CT. Severe pulmonary hypertension (PH) with systolic pressure of 80 mm Hg was also found. Congenital-resistance against activated protein C was detected, which can cause recurrent thromboembolism, also leading to PH.

Case 2: 69-yr. old man, ex-smoker, 20 packyears, with crackles over the lungs. The patient suffered from pulmonary tuberculosis in 1977. Diagnosis of NF1 based on café-au-lait maculas and subcutaneous neurofibromas. Chest x-ray showed diffuse parenchymal abnormalities, mostly in both upper lobes. Further tests showed a moderate obstructive lung disorder and moderate hypoxemia.

Conclusions: A search of the literature implies that lung involvement is an uncommon manifestation of NF1. Our assumption is, that the actual frequency of pulmonary manifestations is probably overestimated, since parenchymal abnormalities in NF1 are difficult to differentiate from other lung disorders. The diagnosis of lung

involvement in NF1 is often based on CT-morphology combined with extra-pulmonary stigmata. Specific histological or characteristic bronchoalveolar patterns are unknown. Our second case illustrates these difficulties: the described parenchymal abnormalities could also be smoking-related and/or due to tuberculosis. For prognostic reasons, differentiation from other lung disorders is important, especially from idiopathic interstitial pneumonias and in particular from the prognostically worse idiopathic pulmonary fibrosis.

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Appropriateness of respiratory care: development of evidence-based guidelines in an acute care hospital

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Background: Respiratory care is universally recognised as useful, but its indications and practice vary markedly. In order to improve appropriateness of respiratory care in our hospital, we developed evidence-based local guidelines in a collaborative effort involving physiotherapists, physicians, and health services researchers.

Methods: Recommendations were developed using the standardised RAND appropriateness method. A literature search was performed for the period between 1995 and 2008 based on terms associated with guidelines and with respiratory care. Publications were assessed according to the Oxford classification of quality of evidence. A working group prepared proposals for recommendations which were then independently rated by a multidisciplinary expert panel. All recommendations were then discussed in common and indications for procedures were rated confidentially a second time by the experts. Each indication for respiratory care was classified as appropriate, uncertain, or inappropriate, based on the panel median rating and the degree of intra-panel agreement.

Results: Recommendations were formulated for the following procedures: non-invasive ventilation, continuous positive airway pressure, intermittent positive pressure breathing, intrapulmonary percussive ventilation, mechanical insufflation-exsufflation, incentive spirometry, positive expiratory pressure, nasotracheal suctioning, non-instrumental airway clearance techniques. Each recommendation referred to a particular medical condition, and was assigned to a hierarchical category based on the quality of evidence from literature supporting the recommendation and on the consensus of experts.

Conclusion: Despite a marked heterogeneity of scientific evidence, the method used allowed us to develop commonly agreed local guidelines for respiratory care. In addition, this work fostered a closer relationship between physiotherapists and physicians in our institution.

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Olfaction improvement: an overlooked benefit of diaphragm pacing in tetraplegia

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Introduction: Cervical spinal cord injuries responsible for quadriplegia and ventilator-dependency induce extreme handicap, tactile isolation and communication difficulties. Tracheotomized quadriplegic patients are also bound to be deprived of the sense of smell. We hypothesized that diaphragm pacing, driving inspiration through negative intrathoracic pressure, would improve olfaction.

Patients and methods: We studied 10 consecutive quadriplegic patients during positive pressure mechanical ventilation and during diaphragm pacing. Their olfactory performances were quantified using the French version of the University of Pennsylvania Smell Identification Test (UPSIT). Quality of life was assessed using the Satisfaction With Life Scale (SWLS) and a diaphragm pacing oriented questionnaire developed specifically for the study.

Results: Olfaction was very poor during positive pressure mechanical ventilation (UPSIT 17.1 ± 6.4, "anosmia" or "severe microsmia" in all cases). It improved significantly during diaphragm pacing (UPSIT 35.2 ± 1.9, "normosmia" or "mild microsmia"; P < 0.0001, t = 9.167, df = 9). This corresponded to unanimous reporting of a diaphragm pacing-related improvement in olfaction. The SWLS score was 18.3 ± 5, which corresponds to a state of slight dissatisfaction with life. Nine patients out of 10 considered that diaphragm pacing had improved their quality of life. They all considered that improved olfaction had contributed to this improvement, among other factors.

Conclusion: Improved olfaction is among the benefits of diaphragm pacing and should be mentioned to patients considered for this therapy. More generally, attention to olfaction is warranted in tracheotomized ventilator-dependent patients, as a putative path towards improvement of quality of life.

Phrenic stimulation to prevent ventilator induced diaphragmatic dysfunction: a feasibility pilot study

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Introduction: The mechanical unloading and respiratory muscle inactivity incurred by critically ill patients with controlled mechanical ventilation induces diaphragmatic dysfunction, which could theoretically contribute to difficult ventilator weaning. It has been hypothesized that phrenic stimulation might prevent ventilator induced diaphragmatic dysfunction (VIDD). The aim of this study was to assess the feasibility and tolerance of repetitive cervical magnetic stimulation of the phrenic nerves (rCMS), a safe and relatively simple non-invasive technique, in healthy subjects.

Methods: rCMS was applied for 800 ms trains in 7 healthy subjects, during spontaneous breathing and non-invasive ventilation (NIV). Frequency was increased from 1 to 30 Hz and intensity from 50 to 100% maximum output. Transdiaphragmatic pressure (Pdi) was measured. Tolerance was rated on a 10 cm visual analogue scale (VAS).

Results: rCMS produced an involuntary and sustained contraction of the diaphragm. Pdi increased with stimulation frequency and intensity. Discomfort was important at 100% intensity and high frequency (VAS 6.4 ± 2.2 at 25 Hz), but decreased at lower frequencies and lower intensities. A stimulation intensity of 65% at 15 Hz proved the best compromise between Pdi (18.5 ± 2.0 cmH₂O) and discomfort (VAS 2.0 ± 0.5). rCMS increased tidal volume during NIV (from 635 ± 50 to 880 ± 59 ml) without increasing discomfort.

Conclusion: rCMS at low frequency and intensity produces a sustained involuntary diaphragmatic contraction with limited discomfort, supporting the potential clinical feasibility of this technique. Future work is needed to determine the rCMS paradigm that might be most effective in preventing or reversing VIDD.

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Use of International Classification of Functioning, Disability and Health to describe patient-reported functioning in sleep apnoea and identification of relevant environmental factors

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Background: The International Classification of Functioning, Disability and Health (ICF) aims to classify functioning and health by a number of categories divided over 4 components: body functions and body structures, participation and activities, and environmental factors.

Methods: We report preliminary results from a cross-sectional survey of 13 Sleep Apnea patients conducted in three sleep centers in Switzerland. Their Sleep Apnea-related problems were linked to ICF categories (second level) using the ICF checklist, which was extended based on a preceding linking process of 80 sleep questionnaires.

Results: One hundred and thirty-two (83%) out of 159 categories of the extended ICF checklist were identified to be at least mildly impaired or restricted. The categories include 52 (33%) for body function, 9 (6%) body structure, 45 (28%) activities and participation and 26 (16%) for environmental factors. "Sleep" (18%) and respectively "respiratory functions" (14%) were the most severely impaired categories of body functions followed by "blood pressure functions" (4%) and "other functions of the skin" (4%)[cooling, sweat secretion]. With regard to the component activities and participation patients felt most restricted in the categories of "watching" [e.g. TV](7%), "using transportation" (7%) and "handling stress" (6%). Within the component environmental factors the categories "support of immediate/extended family", "health professionals" and "medication" were the most important facilitators, "climate", "light" and "sound" were the most important barriers.

Conclusion: This study is a first step in the use of the ICF applied to persons with Sleep Apnea and towards the development of the ICF Core Set for Sleep for persons with any kind of sleep disorder from a comprehensive, bio-psycho-social perspective.

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Impact of NIV on REM sleep

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REM sleep represents a complex cerebral task, that may be impaired in patients in respiratory failure with acidosis, hypoxia and hypercapnia. Assisted ventilation aims at improving blood gases, but may have an impact on sleep.

Patients: We reviewed polysomnographic and blood gas data obtained between 1987 and 2008 in 42 patients with neuro-musculo-skeletal diseases (mean ± SD: age: 46 ± 20 years, 59% male) in respiratory failure put on non-invasive positive pressure assisted ventilation (NIV, volumetric and barometric ventilators in roughly

similar proportions). All had a restrictive ventilatory defect (total lung capacity 55.3 ± 15% of predicted values).

Results: Awake arterial blood gases improved on NIV (p <0.01 by paired t-test with Bonferroni correction for pH, PaCO₂ and PaO₂). There was no change in total sleep time (TST), whereas REM sleep increased non significantly in minutes but significantly in % of TST (from 11.8 ± 9.6 to 17.9 ± 9.1% of TST). Asleep saturation increased and desaturation index decreased, both significantly (p <0.001).

Conclusion: Assisted ventilation can not only improve blood gases, but can also allow for an improvement in REM sleep.

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Positional therapy for obstructive sleep apnoea: an objective assessment of its efficacy and usage at home

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Introduction: Positional therapy preventing patients from sleeping supine has been used for many years to treat positional obstructive sleep apnea (OSA). However, the actual usage and efficacy of this therapy have never been objectively assessed.

Methods: Ten patients with positional OSA, who refused or could not tolerate CPAP were recruited for this study. Nine of these patients, in whom the efficacy of a positional therapy device was confirmed by an overnight study, were instructed to use it every night for 3 months. Objective usage of the device was assessed by an actigraph placed inside the positional device (patients were informed). A third night study was performed at the end of the 3 months period.

Results: During the diagnostic night study, mean apnea-hypopnea index (AHI) was 24.2 ± 10 events/h (49.7 ± 21.8 supine and 6.5 ± 6.6 non-supine), with an average of 48.6 ± 30% of the night spent supine. During the night study with the positional therapy, mean AHI was reduced to 5.7 ± 3.2 events/h (p = 0.0018) and the % of time spent supine dropped to 8.1 ± 8.4% (p = 0.011). Two of the nine patients stopped using the positional device, one because of a back pain and another because of a broken clavicle. Overall the positional device was worn 63 ± 34% of the night (range 9.1–96.6%) for an average of 8.2 ± 2.3 hours per night. Six of the seven patients who were still using the device at the end of the study had a third night study with the device: Mean AHI was 5.8 ± 4.1 events per hour with 4.5 ± 5.9% of the night spent supine.

Conclusion: Usage of a positional therapy for OSA over a 3 months period is comparable to the reported CPAP usage and its efficacy persists at the end of this period.

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Randomised, controlled multi-centre trial comparing effectiveness of autoCPAP and fixed CPAP for sleep apnoea therapy

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Introduction: Short-term trials suggest that autoCPAP is a convenient and effective treatment for the obstructive sleep apnea syndrome (OSA). Whether autoCPAP is equivalent to CPAP with fixed pressure in the long-term therapy of OSA is not known. To address this point, a multi-center trial has been initiated comparing autoCPAP and fixed CPAP therapy during 2 years.

Table. Baseline and 12 months results in 60 Patients

	Baseline		12 months	
	Auto n=32	Fixed n=28	Auto n=32	Fixed n=28
Epworth sleepiness score	13.1 ± 4.0	12.6 ± 3.0	6.7 ± 3.3*	7.9 ± 4.5*
SF-36 vitality domain score	53 ± 22	46 ± 22	70 ± 14**	66 ± 23*
Oxygen saturation (%)	90 ± 5	91 ± 4	95 ± 2*	96 ± 2*
AHI (1/h)	57.2 ± 23.0	60.2 ± 22.8	7.1 ± 12.2*	9.1 ± 12.3*
OSLER (min)	31.3 ± 9.6	31.0 ± 11.1	37.5 ± 5.7*	38.0 ± 3.8*
Systolic BP (mmHg)	128 ± 12	118 ± 12#	114 ± 12*	115 ± 10
Diastolic BP (mmHg)	75 ± 9	70 ± 8#	68 ± 10*	67 ± 8
CPAP (cmH ₂ O)	NA	NA	8.8 ± 2.6	10.1 ± 2.5#
CPAP use (h/night)	NA	NA	5.9 ± 0.9	6.3 ± 1.2
Cumulative costs (SFR)	0	0	1478 ± 1030	2185 ± 971#

* P<0.05 within groups; # P<0.05 between group. AHI=apnea/hypopnea index. OSLER=Oxford sleep resistance test. Costs do not include baseline diagnosis and CPAP rental from Lung Leagues which is identical for autoCPAP and fixed CPAP

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Methods: Consecutive patients with OSA (apnea/hypopnea index AHI > 10/h, Epworth score > 8) were randomized to autoCPAP or fixedCPAP therapy at the 90.-ile of mask pressure during a 2–4 weeks autoCPAP adaptation period. Assessments included sleepiness, quality of life, AHI, and blood pressure at baseline and at 1, 3, 12 and 24 months. Direct medical costs were also recorded.

Results: A total of 122 patients have been recruited so far. Preliminary data from the first 60 patients (7 females, age 56 ± 11 yrs) followed for at least 12 months are reported in the table. The 95% confidence interval of differences between treatment effects of the two modalities did not exceed predefined equivalence ranges for the Epworth score (< 2 points), for SF-36 vitality (< 10 points), and for systolic and diastolic nocturnal blood pressure (< 2 mm Hg).

Conclusion: Our data show that autoCPAP and fixedCPAP were both effective treatment modalities for OSA during at least one year. Symptoms, quality of life, breathing disturbances and vigilance were improved significantly and to a similar degree with auto and fixed CPAP. However, costs for auto CPAP were lower because fewer treatment adjustments were required.

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Mycobacterium avium complex infection with endobronchial lesions and pleuritis in a non-immunocompromised patient

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We report the case of a 73 year old male patient with recurrent episodes of productive cough. His past medical history was significant for a chronic pulmonary sarcoidosis, but he never underwent longterm treatment with glucocorticoids. The pulmonary function test showed a mild obstructive ventilatory defect (FEV₁ 73% predicted). In the CT scan of the chest there were changes compatible with the sarcoidosis (i.e. mediastinal and bilateral hilar adenopathy with calcification, subpleural nodules, mild fibrosis and traction bronchiectasis) and a moderate pleural effusion on the left. Analysis of this unilateral effusion revealed an exudate with a very high lymphocyte count (89%). The culture of the effusion remained negative, but sputum showed growth of *Mycobacterium avium* complex (MAC). A bronchoscopy was performed, where small polypoid lesions were seen in the trachea and right main bronchus. A focal, granulomatous and necrotizing inflammation was seen in the biopsies of these lesions and MAC grew in the biopsy specimen as well as in the culture of the bronchial

secretions. We started a treatment with Rifampicin, Ethambutol and Clarithromycin, which was tolerated without side effects. Within 3 months the productive cough disappeared, the pleural effusion resolved and pulmonary function improved significantly (FEV₁ 73 → 96% predicted). By bronchoscopy the endobronchial lesions were not visible anymore and the mycobacteria cultures of bronchial secretions and follow up sputums remained negative. Treatment was continued 12 months beyond the first negative *Mycobacteria* culture for a total of 16 months. Endobronchial lesions and pleuritis are known as infrequent MAC-associated manifestations in patients with HIV-infection, but are exceptionally rare in non-immunocompromised individuals.

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Autoantibodies frequently found in arterial and chronic thrombotic pulmonary hypertension at the time of diagnosis

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Background: It is well known that connective tissue diseases (CTD) are frequently associated with pulmonary arterial hypertension (PAH). We investigated the frequency of different autoantibodies in PAH not associated to CTD and chronic thromboembolic pulmonary hypertension (CTEPH) and looked for associations with marker of disease severity.

Methods: Antinuclear antibodies (ANA), antibodies to double-stranded DNA (anti-dsDNA), anti-SCL70, anti-centromer, antineutrophilic cytoplasmic antibodies (ANCA) and rheumatoid factor (RF) were measured at the time of diagnostic right heart catheterisation in patients with differently classified PH.

Results: A total of 74 patients (48 PAH, 26 CTEPH, mean \pm SD age 54 ± 17 y, 6 MWD 382 ± 123 m, mPAP 49 ± 16 mm Hg, cardiac index 2.2 ± 0.7 ml/min/m²) were investigated. ANA were positive in 63% (65% in PAH, 58% in CTEPH) and significantly increased ($\geq 1:160$) in 23% (21% in PAH, 27% in CTEPH). Patients with ANA were older, similarly limited but had less severe pulmonary hemodynamics. anti-dsDNA above 1:20 were present in 5% (2% in PAH, 12% in CTEPH), ANCA in 10% (9% PAH, 13% CTEPH) and RF in 11% (7% PAH, 17% CTEPH), all unrelated to disease severity. None of the patients had elevated Anti-SCL70 and/or anti-centromer.

Conclusion: We confirm that autoantibodies are frequently present in PAH not associated to CTD and extend these findings to patients with CTEPH. However, commonly measured autoantibodies are not related to disease severity.

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