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Increasing respiratory dead space improves sleep disordered breathing and hypoxemia in patients with chronic mountain sickness

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Background: Chronic mountain sickness (CMS), which is characterised by hypoxemia, erythrocytosis and pulmonary hypertension, is a major public health problem in high-altitude dwellers. The only existing treatment is descent to low altitude, an option that for social reasons almost never exists. Sleep disordered breathing may represent an underlying mechanism. We recently found that in mountaineers increasing the respiratory dead space markedly improves sleep disordered breathing. The aim of the present study was to assess the effects of this procedure on sleep disordered breathing in patients with CMS.
Methods: In 10 male Bolivian high-altitude dwellers (mean ± SD age, 59 ± 9 y) suffering from CMS (haemoglobin >20 g/L) full night sleep recordings (Embletta, RespMed) were obtained in La Paz (3600 m). In random order, one night was spent with a 500 ml increase in dead space through a custom designed full face mask and the other night without it. Exclusion criteria were: secondary erythrocytosis, smoking, drug intake, acute infection, cardio- pulmonary or neurologic disease and travelling to low altitude in the preceding 6 months.
Results: The major new finding was that added dead space dramatically improved sleep disordered breathing in patients suffering from CMS. The apnea/hypopnea index decreased by >50% (from 34.5 ± 25.0 to 16.8 ± 14.9, P = 0.003), the oxygen desaturation index decreased from 46.2 ± 23.0 to 27.2 ± 20.0 (P = 0.0004) and hypopnea index from 28.8 ± 20.9 to 16.3 ± 14.0 (P = 0.01), whereas nocturnal oxygen saturation increased from 79.8 ± 3.6 to 80.9 ± 3.0% (P = 0.009). The procedure was easily accepted and well tolerated.
Conclusion: Here, we show for the very first time that an increase in respiratory dead space through a fitted mask dramatically improves nocturnal breathing in high-altitude dwellers suffering from CMS. We speculate that when used in the long-term, this procedure will improve erythrocytosis and pulmonary hypertension and offer an inexpensive and easily implementable treatment for this major public health problem.

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Do obstructive sleep apnea patients develop subclinical high altitude pulmonary edema even at moderate altitude?

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Background: In otherwise healthy susceptible subjects high altitude pulmonary edema (HAPE) occurs after rapid ascent to >3500 m. We reasoned that patients with a pre-existing breathing disorder associated with hypoxemia such as the obstructive sleep apnea syndrome (OSA) might develop HAPE at even lower altitude.
Purpose and hypothesis: To evaluate whether low altitude resident OSA patients treated with CPAP: 1) develop subclinical HAPE after rapid ascent to 2590 m; 2) acetazolamide in addition to nasal CPAP prevents HAPE.
Methods: 50 OSA patients living at <600 m (mean age ± SD 61 ± 8 yrs; 3 females, apnea/hypopnea index 53 ± 20/h) on long-term CPAP underwent 2 altitude sojourns of 3 days each at Davos (2 days at 1630 m, 1 day at 2590 m), separated by a 2 week washout period at <600 m. During the two altitude sojourns patients received either acetazolamide (750 mg/d) or placebo according to a double-blinded, randomized cross-over trial. Assessments of symptoms, blood pressure, weight and pulmonary function were performed in Zurich and at altitude.
Results: At altitude while on placebo, patients perceived mild symptoms of acute mountain sickness. They had reduced oxygen saturation, increased weight and blood pressure and FVC, FEV_1 and diffusion capacity were reduced. Acetazolamide prevented these changes with exception of oxygen saturation and diffusing capacity which were slightly reduced below baseline values.
Conclusion: The data suggest that OSA patients developed subclinical HAPE even at the moderate altitude of 2590 m. Alternatively, the findings may be explained by pulmonary congestion due to left ventricular heart failure. Acetazolamide prophylaxis prevented symptoms of acute mountain sickness, fluid retention and blood pressure elevation but did not influence the disturbance in pulmonary gas exchange at altitude.
Support: Swiss National Science Foundation, Lungenliga Zurich and Schaffhausen, Clinical Research Centre, University Hospital of Zurich, Philips/Respironics Switzerland.

	490m	2590m	
		Placebo	Acetazolamide
Acute mountain sickness score (Environmental symptoms cerebral score)	0.10 ±0.26	0.13 ±0.27*	0.09 ±0.22†
Complaint of cough (number of patients)	0/50	3/50	0/50
SpO2, %, awake, resting	95 ±1	91 ±2*	93 ±2*†
Weight, kg	100.8 ±18.4	101.2 ±18.6*	100.2 ±18.1*†
Mean blood pressure, mmHg	99±9	105±10*	97±9†
FVC, % predicted	113 ±15	106 ±14*	108 ±15*†
FEV1, % predicted	107 ±16	103 ±16*	106 ±16†
FEV1/FVC	74 ±5	76 ±6*	76 ±6*
DLCO, ml/min/mmHg	9.32±1.49	9.98±1.77*	9.83±1.87*
DLCO adjusted for PiO2, ml/min/mmHg	9.01 ±1.44	8.73 ±1.55*	8.61 ±1.64*
DLCO adjusted for PiO2, %predicted	85 ±13	82 ±11*	81 ±12*

Means ± SD. * P<0.05 vs. Zurich; † P<0.05 vs. Placebo.

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Effect of dexamethasone prophylaxis on sleep and breathing disturbances in high altitude pulmonary edema susceptible subjects after rapid ascent up 4559 meters

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Background: Dexamethasone has been shown to reduce pulmonary artery pressure and prevent clinical and radiological high altitude pulmonary edema (HAPE) in susceptible subjects after rapid ascent to high altitude. Little is known on the effects of dexamethasone prophylaxis on sleep and breathing disturbances in this setting.
Purpose and hypothesis: To investigate sleep and breathing discurbances in HAPE susceptible subjects at low and high altitude and to evaluate the effect of dexamethasone prophylaxis on sleep and breathing disturbances.
Methods: Twenty-two HAPE susceptible subjects (mean age 44.4 ± 9 years, 7 females) ascended from 490 m to Capanna Regina Margherita, Mt. Rosa, 4559 m, within <24 h. Nine subjects received prophylactic dexamethasone (2x4 mg/d) on the day before and during ascent. Symptoms and polysomnography were performed before ascent and in the first night at 4559 m.
Results: The table shows the polysomnographic data.
Conclusion: In HAPE susceptible subjects, rapid ascent to high altitude results in pronounced nocturnal hypoxemia, high altitude periodic breathing and a reduced sleep quality. Dexamethasone prophylaxis improves oxygen saturation in part by increasing ventilation. In addition, dexamethasone improves sleep quality.
Support: Swiss National Science Foundation, Lungenliga Zurich and Schaffhausen, Clinical Research Center, University Hospital of Zurich.

	Zurich 490 m	Capanna R. Margherita 1st night, 4559 m	
		no Dx prophylaxis n=13	Dx prophylaxis n=9
TST (min)	438 (400;465)	345 (190;434)*	459 (439;469)#
SE (%)	94 (88;96)	72 (65;89)*	93 (90;95)#
NREM stages 3&4 (%)	12 (9;16)	6 (3;12)*	5 (2;7)
REM (%)	7 (4;11)	0 (0;1)*	0 (0;0)*
AHI (1/h)	4.2 (1.4;7.5)	93.7 (11.8;141.7)*	69.2 (47.7;86.4)*
SpO2 (%)	96 (95;96)	70 (68;74)*	77.5 (74;78)* #
PetCO2 (mmHg)	38 (35;41)	29 (27;30)*	26 (25;27)*#
breath rate (1/h)	16 (14.1;18.9)	19 (17;21.5)*	19.5 (19;22)*
Tidal volume (L)	0.27 (0.24;0.36)	0.38 (0.27;0.46)*	0.27 (0.25;0.30)*
VE (l/min)	4.5 (3.8;6.0)	7.3 (5.2;9.0)	7.8 (6.9;8.7)
Heart rate (1/min)	62 (56;67)	89 (83;99)*	71 (66;77)*#

n=22, medians (quartiles) of polysomnographic data. Dx=Dexamethasone. TIB=time in bed. TST=total sleep time, NREM/REM=(non)rapid eye movement sleep, SE=sleep efficiency. AHI=apnea/hypopnea index, SpO2=oxygen saturation, PetCO2=ent-tidal carbon dioxide tension, VE=minute ventilation. *p<0.05 vs 490 m. #p<0.05 vs no Dx prophylaxis at 4559 m.

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Combined autoCPAP and acetazolamide treatment controls breathing disturbances in patients with obstructive sleep apnea syndrome at altitude

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Background: We have previously shown that patients with obstructive sleep apnea syndrome (OSA) have pronounced nocturnal hypoxemia, frequent central and obstructive apnea, elevated blood pressure and arrhythmia during overnight stay at moderate altitude. The optimal treatment modality in this setting has not been established.
Purpose and hypothesis: To evaluate whether autoCPAP alone or combined with acetazolamide provides optimal control of breathing

disturbances in OSA patients at altitude. We tested the hypothesis that autoCPAP does not control central apnea at altitude and that acetazolamide in addition to autoCPAP is superior to autoCPAP alone.
Methods: 50 OSA patients on long-term CPAP therapy and living at <600 m underwent 2 altitude sojourns of 3 days each at Davos (2 days at 1630 m, 1 day at 2590 m), separated by a 2 week washout period at <600 m. During the two altitude sojourns patients continued to use autoCPAP (pressure 5–15 cmH_2O). In addition, they received either acetazolamide (750 mg/d) or placebo according to a double-blinded, randomized cross-over trial. Polysomnographies and blood pressure measurements were performed in Zurich and at altitude. In this interim analysis we report the data of 35 of the 50 patients. Their mean age ± SD was 60 ± 9 yrs.
Results: (See table)
Conclusion: OSA patients require both AutoCPAP and acetazolamide for optimal control of symptoms of acute mountain sickness, sleep related breathing disturbances and blood pressure at altitude. Although AutoCPAP alone effectively prevents obstructive apnea even at altitude it does not eliminate central apnea.
Support: Swiss National Science Foundation, Lungenliga Zurich and Schaffhausen, Clinical Research Centre, University Hospital of Zurich, Philips/Respironics Switzerland.

	490m	1631m, autoCPAP		2590m, autoCPAP	
	autoCPAP	+Placebo	+Acetazolamide	+Placebo	+Acetazolamide
Oxygen saturation, %	95 (94;95)	93 (91;94)*	94 (93;95)*#	88 (87;90)*	91 (90;92)*#
Acute mountain sickness score	0.00 (0.00;0.10)	0.00 (0.00;0.09)	0.00 (0.00;0.00)*#	0.00 (0.00;0.18)	0.00 (0.00;0.00)#
AHI total, 1/h	6.9 (4.4;12.8)	10.1 (5.9;15.8)*	4.9 (3.1;7.3)*#	17.3 (11.3; 24.8)*	7.0 (4.0;11.7)#
AHI obstructive, 1/h	4.2 (2.4;8.3)	3.2 (1.7;7.4)	2.1 (1.0;4.3)*#	5.8 (2.6;8.6)	2.4 (1.2;5.8)*#
AHI central, 1/h	2.2 (0.8;4.6)	3.8 (1.9;10.4)*	1.4 (0.7;3.5)#	11.3 (4.6;20.6)*	3.5 (1.1;7.2)#
Systolic BP, mmHg	132 (126;144)	137 (125;142)	129 (123;141)#	140 (131;150)*	131 (121;144)#

Medians (quartiles). * P<0.05 vs. 490m; # P<0.05 vs. Placebo.

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Effects of added dead space on sleep disordered breathing at high altitude

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Introduction: Sleep disordered breathing with central apnea or hypopnea frequently occurs during sleep at high altitude. The aim of this study was to assess the effects of added dead space (DS) on sleep disordered breathing and transcutaneous CO_2 ($PtcCO_2$) level during sleep at high altitude.
Methods: Full night sleep recordings were obtained on 12 unacclimatized mountaineers (11 males, 1 female, mean age 39 ± 12 y.o.) during one of the first 4 nights after arrival in Leh, Ladakh (3500 m). In random order, half of the night was spent with a 500 ml increase in dead space through a custom designed full face mask and the other half without it. $PtcCO_2$ was measured in 3 participants.
Results: Baseline recordings reveled two clearly distinct groups: one with severe sleep disordered breathing (n = 5) and the other with mild or no disordered breathing (n = 7). Added dead space markedly improved breathing in the first group (baseline vs DS): apnea hypopnea index (AHI) 70.3 ± 25.8 vs 29.4 ± 6.9 (p = 0.013), oxygen desaturation index (ODI): 72.9 ± 24.1/h vs 42.5 ± 14.4 (p = 0.031), whereas it had no significant effect in the second group. Added dead space did not have a significant effect on mean oxygen saturation level. Respiratory events were almost exclusively central apnea or hypopnea except for one subject. Only a minor increase in mean $PtcCO_2$ (n = 3) was observed: 33.6 ± 1.8 mm Hg at baseline and 35.0 ± 2.62 mm Hg with DS. Sleep quality was preserved under dead space condition, since the microarousal rate remained unchanged (16.8 ± 8.7/h vs 19.4 ± 18.6/h (p = 0.51).
Conclusion: In mountaineers with severe sleep disordered breathing at high altitude, a 500 ml increase in dead space through a fitted mask significantly improves nocturnal breathing.

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Endothelial dependant coronary vasoreactivity measured by 82Rb cardiac PET in obstructive sleep apnea patients before and after CPAP treatment

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Introduction: Obstructive sleep apnea (OSA) is associated with an increased risk of cardiovascular diseases. Endothelial dysfunction is believed to be one of the pathophysiological mechanism underlying this association. Our aim was to compare endothelial dependent coronary vasoreactivity in obstructive sleep apnea (OSA) patients and controls by quantifying myocardial blood flow (MBF) response to cold pressure testing (CPT) with 82Rb cardiac PET/CT.
Methods: Twenty-four OSA patients (2W/22M, mean age 58 yo, mean BMI 28.6 kg/m^2) with an apnea-hypopnea index (AHI) >30/h and 9 healthy volunteers (AHI <10/h) underwent a full night sleep recording (PSG) and a dynamic 82 Rb cardiac PET/CT scan at rest, during CPT and adenosine stress. In OSA patients the same measurements (PSG and PET/CT) were respeated 6 weeks after initiating continuous positive airway pressure (autoCPAP) treatment. To reflect differences in baseline cardiac work, values were normalized according to ratepressure product (RPP).
Results: At baseline, untreated OSA patients had a mean AHI of 48.8/h and showed a lower MBF response to CPT than controls (1.1 ± 0.2 mL/min/g vs. 1.3 ± 0.4 mL/min/g, P = 0.048). When treated with CPAP, CPT-MBF was not different between controls and well-treated OSA patients (1.2 ± 0.3 mL/min/g vs 1.3 ± 0.4 mL/min/g, P = 0.68), but it was significantly lower for insufficiently treated patients (n = 10) with a residual AHI >10/h (0.9 ± 0.2 mL/min/g vs 1.3 ± 0.4 mL/min/g, P = 0.03). There was also a trend toward a difference in CPT-MBF between insufficiently and well-treated OSA patients (1.2 ± 0.3 mL/min/g vs 0.9 ± 0.2 mL/min/g, P = 0.15).
Conclusion: Untreated OSA patients have an impaired coronary endothelial function as measured by MBF response to CPT compared to control subjects. This difference disappears after 6 weeks of autoCPAP therapy but only in OSA patients showing a good response to CPAP (AHI <10/h). Further studies are needed to determine by which mechanism OSA and CPAP treatment influence coronary vasoreactivity.

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Surfactant protein A expression and gene deletion as prognostic markers in non-small cell lung cancer

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Background: Molecular markers are becoming increasingly important in non-small cell lung cancer (NSCLC) patients for personalized therapy decisions. Recent data suggest that Surfactant Protein A (SP-A) deletion is common in NSCLC. The aim of the present study was to investigate the prognostic value of SP-A protein expression and SP-A gene deletion in a large series of NSCLC patients.
Methods: Tissue micro arrays with a total of 1413 NSCLC were analyzed. SP-A expression was detected by immunohistochemistry (IHC) and SP-A gene copy number aberrations by fluorescence in situ hybridization (FISH). IHC and FISH data were correlated with clinicopathological features and overall survival.
Results: In multivariable analysis both SP-A expression (HR = 0.48, 95% CI: 0.3–0.8; p = 0.001) and SP-A deletion (HR = 1.54, 95% CI: 1.1–2.1; p = 0.006) were independent prognostic factors in NSCLC patients. The combined IHC/ FISH results stratify patients into four prognostic groups with SP-A IHC+/ FISH- NSCLC having the best (5-year survival rate: 69.3%, 95% CI: 54–80%) and SP-A IHC-/ FISH+ NSCLC having the worst prognosis (5-year survival rate: 32.3%, 95% CI: 21–44%) (p <0.001). These prognostic groups differ in histological cancer types. SP-A expression is prognostic in both adeno- and large cell carcinomas (p = 0.007 and p = 0.018, respectively), but SP-A deletion only in large cell carcinomas (p = 0.018). Neither SP-A expression nor SP-A deletion have a prognostic value in squamous cell carcinomas. SP-A expression remains prognostically significant in early stage IA and SP-A deletions in IB NSCLC patients (p = 0.017 and p = 0.045, respectively).
Conclusions: SP-A expression and SP-A deletion are prognostic in NSCLC and could become especially valuable in stage I NSCLC to stratify patients who might benefit from adjuvant treatment. Assessing the histological cancer type is important to select the appropriate molecular test.

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Modified mesenchymal stem cells attenuate bleomycin induced lung injury in the rat

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Background: Pulmonary fibrosis is a devastating disease of unknown etiology. Recently, hepatocyte growth factor (HGF) gene transfer to the bleomycin rat lung has shown to attenuate fibrosis. Bone marrow derived mesenchymal stem cells (BMSCs) were shown to localize in the fibrotic areas in the injured lung after intratracheal instillation and may therefore be utilized as carriers for novel therapies. In the present study we hypothesize that HGF modified BMSCs exhibit potent antifibrotic and regenerative effects in the bleomycin induced lung injury model.
Material and methods: BMSCs were isolated from adult male rats, culture-expanded and transfected by invitro electroporation using the AMAXA nucleofection system. Transfection efficiency was measured by determination of HGF levels in the conditioned medium. Adult male rats were instilled with 1.28 u bleomycin intratracheally at day 0; at day 7 post bleomycin instillation HGF transfected BMSCs were instilled intratraceally, and animals were sacrificed at day 7 and day 14 post BMSCs instillation and organs collected for analysis. Two other groups were cell culture media or BMSC only were instilled after bleomycin served as controls.
Results: The instillation of the HGF transfected BMSCs markedly attenuated bleomycin induced fibrosis in the rat lung; the hydroxyl proline content of the rat lung was 2446 ± 277.5 ug/gm vs 3066 ± 251.4 ug/gm at day 7 ($p < 0.05$) and 1487 ± 110.1 ug/mg at day 14 post HGF-BMSCs instillation. The Ashcroft score in the HGF modified BMSCs was 3.9 ± 0.2 vs 4.42 ± 0.36 in the control group at day 7, at day 14 further improvement was seen in the HGF-BMSCs group (3.17 ± 0.172). Stereological analysis showed decreased septal thickness (11.89 ± 0.91 µm vs 8.82 ± 9.485 µm), and increased alveolar surface area (2.29 ± 0.71 m^2 vs 1.40 ± 0,18 m^2) after 2 weeks in the treated group. The volume fraction (9.32 ± 1.02% vs 4.13 ± 2.81%) and total volume per lung of destructed/ fibrotic lung tissue was reduced more pronounced 2 weeks after therapy (0.20 ± 0.10 cm^3 vs 0.40 ± 0.10 cm^3).
Conclusion: HGF-modified BMSCs markedly attenuate bleomycin induced lung injury, as shown by histological, biochemical and stereological methods, further studies are needed to elucidate the antifibrotic mechanisms. Modified BMSCs may serve as a promising, novel therapeutic strategy to improve lung fibrosis.

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Deficient innate immune antiviral response to infection with rhinoviruses in cystic fibrosis airway epithelial cells

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Background: Rhinoviruses (RVs) are a major cause of exacerbations in asthma and cystic fibrosis (CF). However, the mechanisms of RV-induced pulmonary exacerbations are largely unknown. Recently, an impaired resistance to RV infection due to a deficient production of interferons (IFNs) by airway epithelial cells has been reported in asthma. We hypothesized that the deficiency in IFN production is not limited to asthma but also found in CF.
Methods: To study the IFN expression in response to RVs, we used bronchial epithelial CF and non-CF cell lines and primary nasal epithelial cells from patients with CF and from healthy controls. Cells were infected with two strains of RVs (RV16 and RV1B). Viral replication was analyzed by real time PCR and HeLa titration. IFN (IFN-beta and IFN-lambda) mRNA expression and production were analyzed by real time PCR and ELISA respectively. Cell viability was assessed by flow cytometry and LDH assay.
Results: RV replication was increased in airway epithelial CF compared to non-CF cells at 24h and 48h after infection (11 ± 2.2 vs 0.4 ± 0.1 x 10^5 TCID50/ml at 24 h after RV16 infection). Cell viability was decreased in CF cells when compared with normal cells. Examination of innate immune responses revealed profound impairment of virus-induced IFN production in airway CF cells. The addition of exogenous IFNs reduced virus replication in infected CF cells.
Conclusion: Cystic fibrosis airway epithelial cells have a deficient innate immune response to infection with rhinovirus, characterized by an impaired interferon production and resulting in increased viral replication. This suggests that in the inflammatory lung diseases asthma and cystic fibrosis, similar mechanisms lead to disturbances in innate immune responses to viral infection.

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Exposure of dendritic cells to biomedical nanoparticles decreases antigen processing capacity specific CD4+ T cell stimulation

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Rationale: Currently there is intense clinical research into the development of biomedical nanoparticles (NP) for therapeutic and diagnostic applications. Through its enormous surface area, straightforward accessibility, and thin alveolo-capillary barrier, the respiratory tract is potentially an attractive target organ for therapies with NP. Immune reactions and inflammatory responses to such NP in the respiratory tract with a high density of immune cells (e.g. dendritic cells, DC), remain insufficiently characterised to date. Through their unique localisation and function, respiratory tract DC interact with and may be functionally affected by inhaled nanoparticles. The aim of this study is to characterise effects of poly(vinylalcohol)-coated super-paramagnetic iron oxide nanoparticles (PVA-SPIONS) on DC phenotype and function.
Methods: Human blood monocyte-derived DC were exposed during 12 h to fluorochrome-labelled PVA-SPIONS and imaged by confocal (CM) or electron microscopy (EM). Expression of markers of differentiation and activation upon particle exposure and the capacity of DCs for antigen-uptake, -processing, and -presentation were studied using flow cytometry (FACS) and an autologous CD4+ T cell stimulation assay.
Results: Uptake of PVA-SPIONS by DC was dose-dependent and decreased by concomitant LPS exposure through a maturational effect. Intracellular PVA-SPIONS were identified by CM / EM, and did not affect expression of surface markers (CD80, CD83, CD86, myeloid DC, or plasmocytoid DC markers) as measured by FACS. While PVA-SPIONS did not affect antigen uptake by DC, antigen-processing, as well as specific CD4+ T cell proliferation and cytokine (IL-5, IL-6, IFN-gamma, TNF-alpha) production was reduced.
Discussion: Exposure to PVA-SPIONS did not alter the DC state of activation, but reduced antigen-specific CD4+ T cell proliferation and cytokine production, which may be attributed to reduced antigen-processing capacity by NP-exposed DC. Though DC surface phenotype was not altered, the functional changes suggest that DC may revert to a more immature state (high capacity for antigen uptake, low capacity for T cell stimulation) when exposed to PVA-SPIONS. These data highlight the necessity to meticulously characterise immunological and inflammatory effects of nanomaterials developed for novel therapeutic and diagnostic applications in the respiratory tract.

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Gene profiling of patients with acute exacerbation of COPD treated by systemic corticosteroids

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Introduction: The administration of a 2-week course of systemic corticosteroid to treat patients with acute exacerbation of COPD (AECOPD) is a current practice. The aim of this study was to investigate the impact of a cortiscosteroid treatment on AECOPD patients at the gene expression level with a particular focus on the function of the hypothalamic-pituitary-adrenal (HPA) axis.
Methods: Ten patients with AECOPD were treated by systemic corticosteroids (Figure 1A). Blood samples were taken at baseline, after 14 days of treatment and 7 days after the end of the treatment. Gene expression measurements were obtained using Affymetrix GeneChip HGU133a2 microarrays. Basal as well as ACTH-stimulated cortisol levels were measured on 6 occasions (baseline, days 2 and 14 during treatment, and days 2, 7 and 21 after corticosteroid withdrawal). Data were analyzed using the R statistical software.
Results: The time-course effect of corticosteroid was explored using correspondence analysis. As shown in Figure 1B, the treatment induced a dysregulation of a series of genes involved in cytokine-cytokine interactions, interferon-induced pathways, tumor suppression, kinase cascade and immunoglobulin response. Another set of genes strongly correlated with the cortisol level after ACTH stimulation, among which DEFA4 showed a particularly prominent correlation ($r = 0.88$, $p < 0.001$; Figure 1C). Furthermore, we identified genes whose baseline expression significantly predicted the profile of stimulated cortisol level during and after treatment (Figure 1D). Some of these genes were involved in pathways regulating the glycan structure and glycosphingolipid biosynthesis.

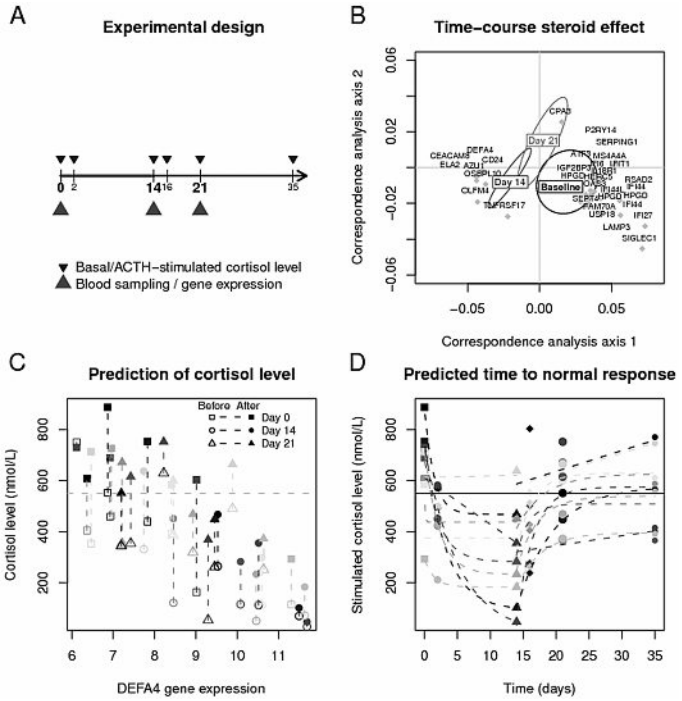

Figure 1
Corticosteroid effect at the gene expression level and stimulated cortisol. Panel A describes the study design. Panel B depicts the genes mostly associated with the corticosteroid effect (correspondence analysis). Panel C shows the correlation between the DEFA4 level and the stimulated cortisol level. Panel D illustrates the stimulated cortisol profile at the different study time points (1 color per patient).

Conclusion: Corticosteroid treatment in patients with AECOPD induced a strong gene dysregulation which was reversible after the end of the treatment, however highly variable among patients. DEFA4 gene expression correlated with the level of stimulated cortisol and might predict HPA function. Moreover, we could identify genes at baseline which could predict the severity of HPA suppression.

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Functional consequence of TLR2 and TLR4 induced activation of HIF-1a on maturation of human dendritic cells

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Dendritic cells (DC) are professional antigen presenting cells that represent an important link between innate and adaptive immunity. Danger signals such as toll-like receptor (TLR) agonists induce maturation of DC leading to a T-cell mediated adaptive immune response. In this study, we show that exogenous as well as endogenous inflammatory stimuli for TLR4 and TLR2 induce the expression of HIF-1a in human monocyte-derived DC, suggesting a functional TLR-HIF pathway under normoxic conditions. Inhibition of HIF-1a prevented phenotypic maturation of human DC mediated by pro-inflammatory stimuli as shown by a reduced up-regulation of CD40, CD80, CD86 and ICAM-1. On the functional level, inhibition of HIF-1a was associated with a reduced secretion of IL-6 and IL-10, whereas TNF-a and IL-1b were not significantly affected. Induction of HIF-1a by hypoxia or CoCl2 did not result in maturation of human DC. However, phenotypic maturation of DC induced by LPS was amplified under hypoxic conditions. In addition, we could show that TLR stimulation resulted in an increase of HIF-1a controlled VEGF secretion. These results suggest that the transcription factor HIF-1a plays a crucial role in TLR-mediated activation of human DC. These results demonstrate for the first time that HIF-1a can be induced in human DC under normoxic conditions in a time-dependent manner by both endogenous and exogenous TLR2- and TLR4 agonists.

Free communications III

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Follow-up of lung function in infants and children with cystic fibrosis

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Rationale: Early assessment of pulmonary function, its association with life events and its relation to genetics could provide an important insight into the initiation of the disease process in cystic fibrosis (CF).
Objectives: We aimed to evaluate the onset of functional characteristics during infancy with follow-up during childhood, as well as to determine the physiological factors of lung function predominantly influencing these mechanisms in relation to genotypes.
Methods: Lung function was assessed by serial infant whole-body plethysmography in 66 infants (30 males, 36 females) with CF at ages 6 to 21 months pertaining to functional residual capacity (FRCpleth) and effective airway resistance (sReff), as well as by whole-body plethysmography and multibreath nitrogen washout during childhood (5 to 14 years of age), featuring FRCpleth, lung clearance index (LCI), trapped gas (VTG), sReff, and forced expiratory indices (FEV_1, FEF50). Moreover, blood gases taken from the arterialized ear lobe (PaO_2, $PaCO_2$) were measured. Follow-up data expressed as standard deviation scores (SDS), equal to z-scores were evaluated by linear mixed effects model (LMM) analysis.
Results: At first assessment in infancy already 53% of CF patients presented with bronchial obstruction (sReff >2SDS), 3% with pulmonary hyperinflation (FRCpleth <2SDS), and 15.2% with a combination of both. Only 28.8% of CF infants showed normal lung function. CF infants, who presented with bronchial obstruction only demonstrated later in 72.7% ventilation inhomogeneities (LCI> 4SDS), whereas CF infants presenting with pulmonary hyperinflation and bronchial obstruction were prone to develop progressively a part from ventilation inhomogeneities ($p < 0.001$), also trapped gases ($p < 0.001$) and gas exchange disturbances (PaO_2: $p < 0.0001$; $PaCO_2$: $p < 0.001$) later in childhood. In regard to genotypes, F508del(2) and F508del/3905insT presented with the highest progression in pulmonary hyperinflation. Moreover sReff differentiated significantly between all genotypes ($p < 0.001$), showing the highest progression in patents with F508del/3905insT.
Conclusions: Functional abnormalities in CF patients assessed by infant whole-body plethysmography are detectable already in early infancy, and seem to be predictive for subsequent functional deficits in later childhood.

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A 2-year experience with long-term indwelling pleural catheter (Pleurx® Catheter) in patients with malignant pleural effusion

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Background: Malignant pleural effusion is a common problem in patients with metastatic cancer. Pleurodesis, preferentially with talc slurry or poudrage, is the therapy of choice in recurrent symptomatic effusions not responding to systemic treatment. If pleurodesis fails or patients present with trapped lung, the implantation of a long-term indwelling pleural catheter (Pleurx® Catheter, Surgimedics, Denver Biomaterials) enables repeated drainage of pleural effusion by relatives or nursing staff. In some patients, pleural fusion may be achieved. Catheter placement can be done in an outpatient setting. The catheter is inserted under local anesthesia in the endoscopy room.
Methods: We present retrospective data from 16 patients (10 men, 6 women) receiving a Pleurx® Catheter at our hospital since October 2007.
Results: 8 patients had lung cancer, 2 melanoma, 2 pleural mesothelioma, 1 non-Hodgkin lymphoma, 1 breast cancer, 1 pancreatic cancer and 1 primary peritoneal carcinoma. One patient received bilateral catheters. Indication for catheter placement was failure of pleurodesis in 9 patients, trapped lung in 7 patients, low chance of a successful pleurodesis in 1 patient. The median age was 67 (range 46–88) years. Drainage was performed in 9 cases by relatives, in 5 cases by nursing staff in a nursing home or hospital and in 2 cases by specialist nursing care in the community (Spitex). 13 patients died until 31.12.2009, median survival after catheter implantation was 84 (range 7–247) days, median catheter use was 34 (range 7–247) days.

Complications: One patient had implantation metastasis with secondary dislocation of the catheter and resultant infection (*S. aureus*). After removal a second Pleurx® catheter was placed without complication and radiation therapy performed. Another patient suffered a pleural infection (*S. aureus*) under chemotherapy-induced neutropenia. Both patients were treated successfully with antibiotics. Pleurodesis occured in three cases, catheters were removed. No skin infections were noted. Patients and there relatives were highly satisfied with Pleurx® Catheter (Visual Analogue Scale 9.2 ± 1.1). Handling of the catheters was described as easy; all patients would recommend an indwelling pleural catheter to others in a similar situation.
Conclusion: An indwelling pleural catheter appears to be a safe and easy to handle alternative in patients with malignant pleural effusion. The risk of complications is low.

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Accuracy of endobronchial ultrasound with guided transbronchial needle aspiration compared with PET/CT for evaluation of patients with suspected lung carcinoma

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Background: We have previously shown, that EBUS-TBNA can routinely and safely be performed in an ambulatory setting with good time performance requesting reasonable manpower (Hofer et al, ERJ 22: Suppl 45: 590s).
Aim: To investigate the accuracy of endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) and to compare it with PET/CT in patients with suspected or known lung carcinoma (NCSLC).
Methods: The following patients were evaluated: a) patients having been operated following the EBUS-TBNA (patients with neoadjuvant chemotherapy were excluded), b) patients with diagnosis of N2/3 disease according to EBUS-TBNA (cytological positive and not primarily operated) and c) patients with initial suspicion of lung carcinoma and negative EBUS-TBNA and negative evaluation of the primary tumor (T0, N0) . Patients of group c) had a strict follow-up with no sign of carcinoma afterwards. Sensitivity and specificity were calculated for EBUS-TBNA and PET/CT.
Results: 105 patients were evaluated. Mean age of patients was 65 ± 11 years. 103 out of 105 (98%) investigations were performed in an ambulatory setting with conscious sedation. In 45 (43%) patients a N2/3 could be diagnosed (true positive). Three of these had a negative PET/CT. 47 patients with a N0/N1-disease on EBUS-TBNA were operated. In four of these a N2 disease was found during operation (false negative). Two of the four had a negative PET/CT too. All 13 patients of group C) had a negative follow-up (true negative). 65 patients had a PET/CT. 27 (41.5%) patients had a true positive PET/CT and 6 (9.2%) a false negative PET/CT (positive EBUS and/or surgical, three with a N2 disease), 29 (44.6%) had a true negative PET/CT and 3 (4.6%) a false positive PET/CT (negative EBUS and/or surgical). Sensitivity and specificity of EBUS was 92% and 100%, respectively. Sensitivity and specificity of PET/CT was 82% and 91%, respectively. The negative predictive value of negative EBUS in combination with negative PET/CT was 97%.
Conclusions: EBUS for nodal staging in patients with NSCLC can easily performed in an ambulatory setting under conscious sedation. There is a high accuracy of EBUS for the nodal stage in lung carcinoma (higher than for PET/CT). In combination with PET/CT the negative predictive value is comparable to mediastinoscopy (gold standard).

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Electromagnetic navigation bronchoscopy: systematic review and prospective assessment of respective yield of different sampling modalities

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Background: Electromagnetic navigation bronchoscopy (ENB) is an emerging bronchoscopic approach using 3D-reconstructions of thoracic scanners to steer endoscopic tools to targeted peripheral lung lesions. ENB accuracy and safety have not been systematically assessed so far. Moreover, the respective yield of different sampling modalities in ENB setting is not known.
Methods: Step 1: we performed a systematic review to assess the diagnostic yield of ENB (defined as the rate of definitive diagnosis obtained obviating further testing), the sensibility/specificity to detect cancer and the complication's rate. Step 2: we describe our first case-series of 10 peripheral lung nodules sampled by ENB from 9 consecutive patients referred to Geneva University Hospital. Primary endpoints were respective diagnostic yields of cytobrushing, forceps biopsies, transbronchial needle aspiration (TBNA) and localised lavage. Secondary endpoints were diagnostic yield, successful target sampling, and complication's rate.
Results: 11 published trials report on diagnostic yield and safety, including 671 nodules. 661 (98.5%) were successfully accessed by electromagnetic navigation. By pooling the individual patient's data, we obtained an overall ENB diagnostic yield of 63.2% (424/671, figure 1). After exclusion of unsuitable data, the sensibility of ENB to detect cancer was 63% [CI 57–69%], with a specificity of 100% [CI 94–100%]. 15 pneumothorax were reported (2.2%) and 3 cases of moderate bleeding (0.4%). Our 9 patients (median age 67.5 years) presented 10 peripheral lung lesions with a median minimal diameter of 20.5 mm (range 12–34) and a median distance to pleura of 11.5 mm (range 0–43). No endobronchial lesion was detected during bronchoscopy. A conclusive diagnose was obtained in 7 cases (70%), all of them being neoplasia. Chronic inflammation was observed in 2 additional cases, meaning an overall successful target sampling of 90%. The yield of each sampling modality is described in table 1.
No bleeding and no pneumothorax were observed on systematic post interventional X-ray.
Conclusion: The diagnostic yield of 70% in our first series of ENB is comparable with the 63% diagnostic yield of published series, attesting a short learning curve. Histological proof of target sampling was obtained in 90% of cases, without any complication. Pooled risk of pneumothorax in literature (2.2%) is significantly lower than the risk from CT-guided transthoracic needle aspiration (23 to 38%).

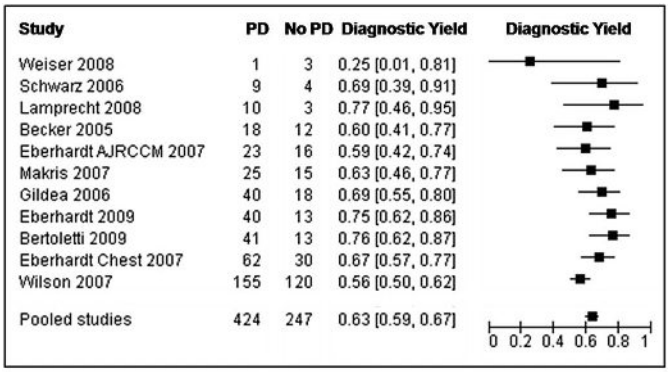

Figure 1: Systematic review of ENB diagnostic yield, with 95% confidence intervals
PD : positive diagnose

	Number of cases	Positive diagnostic	Diagnostic yield [95% CI]
cytobrushing	10	5	50% [19-81%]
forceps biopsies	9	2	22% [3-60%]
TBNA	6	2	33% [4-78%]
localised lavage	4	1	20% [1-72%]

Table 1 : Respective yield of different sampling modalities in ENB setting.
TBNA : transbronchial needle aspiration

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Second-hand tobacco smoke exposure in Switzerland

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A passive sampling device called Monitor of NICotine or "MoNIC", was constructed and evaluated by IST laboratory for determining nicotine in Second Hand Tobacco Smoke (SHTS). Vapour nicotine was passively collected on a potassium bisulfate treated glass fibre filter as collection medium. Analysis of collected nicotine on the treated filter by gas chromatography equipped with Thermoionic-Specific Detector (GC-TSD) after liquid-liquid extraction of 1 mL of 5N NaOH: 1 mL of n-heptane saturated with NH3 using quinoline as internal standard. Based on nicotine amount of 0.2 mg/cigarette as the reference, the inhaled Cigarette Equivalents (CE) by non-smokers can be calculated. Using the detected CE on the badge for non-smokers, and comparing with amount of nicotine and cotinine level in saliva of both smokers and exposed non-smokers, we can confirm the use of the CE concept for estimating exposure to SHTS. The regional CIPRET (Center of information and prevention of the addiction to smoking) of different cantons (Valais (VS), Vaud (VD), Neuchâtel (NE) and Fribourg (FR)) are going to organize a big campaign on the subject of the passive addiction to smoking. This campaign took place in 2007–2009 and has for objective to inform clearly the Swiss population of the dangerousness of the passive smoke. More than 3900 MoNIC badges were gracefully distributed to Swiss population to perform a self-monitoring of population exposure level to SHTS, expressed in term of CE. Non-stimulated saliva was also collected to determine SHTS biomarkers nicotine/cotinine levels of participating volunteers.
Results of different levels of CE in occupational and non-occupational situations in relation with SHTS were presented in this study. This study, unique in Switzerland, has established a base map on the population's exposure to SHTS. It underscored the fact that all the Swiss people involved in this campaign (N = 1241) is exposed to passive smoke, from <0.2 cig/d (10.8%), 1–2 to more than 10 cig/d (89.2%). In the area of high exposure (15–38 cig/d), are the most workers in public restaurant, cafe, bar, disco. By monitoring SHTS tracer nicotine and its biomarkers, salivary nicotine and cotinine, it is demonstrated that the MoNIC badge can serve as indicator of CE passive smoking. It is also demonstrated that the salivary nicotine (without stimulation) is a better biomarker of SHTS exposure than cotinine.

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COPD management in general practice – one year follow-up of the Swiss COPD cohort study

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Study aim: COPD is an increasing cause of morbidity and mortality worldwide. Based on our data of the Swiss COPD cohort, we assessed factors such as implementation of GOLD guidelines on exacerbation rate after 12 months of follow-up.
Methods: 565 COPD patients were recruited by 139 general practitioners in Switzerland. The general practitioners were asked to perform spirometries and fill in questionnaires about symptoms, comorbidities and treatment at a 3-months intervall.
Results: 111 patients dropped out of the study mainly due to comorbidities or nursing home admissions. 454 patients (66% male, mean age 67 years) were followed-up over 12 months. 111 patients (24%) did not have COPD according to spirometric criteria (FEV_1/FVC <70%). COPD GOLD I was found in 36 (8%) patients, GOLD II in 151 (33%) patients, GOLD III in 118 (26%) and GOLD IV in 38 (8%).
30 out of 187 patients (16%) had stopped smoking since Baseline visit. Guideline adherence did not change significantly after 12 months (53% vs. 56%). 15 patients (3%) died and 66 patients (15%) experienced an exacerbation/pneumonia which was 8% less than at baseline visit. 73 patients (16%) suffered from asthma. Predicting factors for an exacerbation/pneumonia adjusted for FEV_1 % predicted were male sex, ICS, ICS/LABA, LABA, systemic steroids, asthma and CVI as a comorbidity (table 1).
Conclusion: There is no change in guideline adherence after a one-year follow-up. Systemic steroids were given to 6% of all patients and were significantly associated with a higher risk for exacerbations. This supports the thesis that systemic steroids are not beneficial in stable COPD. The observed influence of ICS and ICS/LABA on exacerbation rate might be due to an over-prescription of ICS and ICS/LABA in patients without or with mild to moderate COPD. These patients might have developed pneumonia as a side effect of inhaled steroids. This finding needs further investigation.
Funding: Boehringer Ingelheim GmbH, Switzerland; Pfizer AG, Switzerland.

	OR(Risk)	95% C.I.	p-value
Sex	1.87	1.22 - 2.86	**0.00396**
Smoking	0.92	0.61 - 1.39	0.70292
ICS	1.82	1.14 - 2.91	**0.01287**
ICS/LABA	1.78	1.22 - 2.59	**0.00284**
LACH	1.05	0.72 - 1.53	0.81384
LABA	2.16	1.41 - 3.32	**0.00049**
Asthma	2.09	1.24 - 3.51	**0.00564**
CVI	3.66	1.60 - 8.34	**0.00223**
Guidelines	1.00	0.66 - 1.52	0.99533
CHD	1.16	0.70 - 1.92	0.56825
Heart failure	1.46	0.84 - 2.52	0.18141
Hypertension	1.28	0.81 - 2.02	0.28213
Systemic steroids	2.75	1.38 – 5.47	**0.00414**

ICS = inhaled corticosteroids; LABA = long acting bronchodilator; LACH = long acting anticholinergics; ICS/LABA = combination ICS and LABA; CVI = cerebro-vascular insult; Guidelines = adherence to GOLD guidelines; CHD = coronary heart disease

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Exhaled nitric oxide measured at different flow rates to detect early bronchiolitis obliterans syndrome after lung transplantation

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Background: In a preliminary study we have shown that extended FeNo (exhaled nitric oxide) measurements with different flow rates are feasible after lung transplantation (LTx) (ERJ 2008, 26: Suppl 49: 705s).
Aim: To prospectively investigate FeNO measured with different exhalation flows in patients under maintenance immunosuppression (at least one year after LTx) without bronchiolitis obliterans syndrome (BOS) and with early BOS (BOS 0-p = FEV_1 between 80% and 90% baseline or FEV_1 >90% baseline and FEF25-75 lower than 75% baseline).
Methods: FeNo was measured with Eco Medics(TM) (CLC 88 sp) with three different exhalation flows of 50 (FeNO50), 100 (FeNO100) and 200ml/sec (FeNO200). According to Tsoukias and George, and Hoegmann et al., bronchial NO-flux (JNO,Br) and alveolar NO-concentration (CAlv) were calculated.
Results: Between 5/09 and 9/09 57 LTx patients were evaluated (24 stable patients without BOS and 20 with BOS 0-p). Mean age was 46 ± 15 years and mean time after LTx was 5.4 ± 3.5 years. We found no significant differences between FeNO50, FeNO100 and FeNO200 in the two groups (15 ± 7 ppb, 8 ± 4 ppb and 5 ± 2 ppb in stable patients and 13 ± 6 ppb, 8 ± 6 ppb and 5 ± 2 ppb in early BOS). CAlv and JNO,Br was similar in the two groups (2.3 ± 1.6ppb and 2.1 ± 1.3 ppb; 0.610 ± 0.336 nl/sec and 0.543 ± 0.268 nl/sec). In contrast, the ratio of FeNO50 and FeNO200 was significantly lower in early BOS compared to patients without BOS (2.5 ± 0.6 and 3.1 ± 0.9, p = 0.01).
Conclusions: 1) FeNO50 does not differentiate between patients without BOS and patients with early BOS.
2) No difference between alveolar NO concentration and bronchial NO-flux in both groups was found.
3) The ratio of FeNO50 and FeNO200 seems to be a strong marker for early BOS.

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Screening for possible beryllium exposure among patients with sarcoidosis using a self-administered questionnaire

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Chronic beryllium disease (CBD) is a rare granulomatous disorder caused by exposure and sensitization to beryllium (Be). CBD may be misdiagnosed as sarcoidosis if Be exposure is not looked for. Since pulmonary physicians are not familiar with the multiple and diverse occupations associated with Be exposure, the latter is not well search in the work-up of patients with sarcoidosis. To determine how many patients diagnosed as sarcoidosis have potential Be exposure, we developed a self-administered questionnaire containing a list of relevant jobs and activities. The questionnaire was intended to be highly sensitive, aiming at excluding patients with unlikely Be exposure. Questionnaire was developed in German and French using standardized occupation descriptors, and tested for clarity on a non-pulmonary outpatient population (n = 50). Questionnaires were sent to 159 patients recorded in the SIOLD Registries as having sarcoidosis. The response rate was 31% (n = 49). 42 patients provided a filled questionnaire. 19/159 patients (12%) reported a current or previous occupation with potential Be exposure in the following activities: mecanic manufacturing (n = 15); metallurgy (n = 6); electricity and electronics (n = 4); shipbuilding, aeronautics, military, and nuclear (n = 2); watchmaking and jewelry (n = 1), medical and optic material manufacturing (n = 1); dentistry (n = 1); and recycling (n = 1). 9/159 (6%) reported >1 exposures. 23 had no occupation at risk. 10 reported possible exposure in leisure activities (5 with and 5 without occupational exposure). The questionnaire currently undergoes validation against a detailed face-to-face occupational interview.
Conclusion: the minimal rate of possible occupational Be exposure in an unselected population of sarcoidosis was 12%. A standardized questionnaire may help to detect Be exposure in patients diagnosed with sarcoidosis, and prompt further investigations to search for CBD.
This study is supported by the SUVA. The SIOLD Registries are supported by the Swiss Pulmonary League.

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Randomized, controlled multicentre trial evaluating long-term effectiveness of autoCPAP for sleep apnea 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 multicentre trial has been initiated comparing autoCPAP and fixed CPAP therapy during 2 years.
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.
Results: To date, 155 patients have been included in the ongoing study. Data from the first 105 patients (mean age ± SD 57 ± 11 yrs) followed for at least 12 months are summarized 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), SF-36 vitality (<10 points), sleep resistance time (OSLER <3 min), apnea/hypopnea index (<5/h), and for nocturnal oxygen saturation (<2%).
Conclusion: Our data show that autoCPAP and fixedCPAP therapy were both effective treatment modalities for OSA during at least one year. Symptoms, quality of life, breathing disturbances, blood pressure and vigilance were improved significantly and to a similar degree with auto and fixed CPAP.
Grant support: Swiss National Science Foundation.

Baseline and 12 months results in 105 Patients

	Baseline		12 months	
	Auto n=54	Fixed n=51	Auto n=54	Fixed n=51
Epworth sleepiness score	13.8±3.6	13.5 ±3.3	7.1 ±3.5***	7.7 ±3.7***
SF-6D utility	0.76 ±0.12	0.79 ±0.12	0.80±0.10**	0.78±0.13**
SF-36 vitality domain score	47 ±22	44±20	67 ±16***	63±19***
Functional outcome of sleep questionnaire	16.0 ±2.9	16.0±2.8	18.9±1.4***	18.3 ±1.9***
Mean nocturnal oxygen saturation (%)	90 ±5	92 ±4	95±2**	95±2***
Apnea/hypopnea index(1/h)	61.1±24.6	54.6 ±22.4	7.0 ±11.1***	7.7 ±10.6***
OSLER sleep resistance time (min)	28.8 ±10.8	32.3±11.2	37.5±5.4***	38.1±4.0**
OSLER missed stimuli (1/h)	1.28 ±1.03	0.94±1.32	0.46±1.28**	0.25 ±0.39***
Blood pressure 24h systolic (mmHg)	133 ±11	129 ±12	129 ±11**	132 ±39
Blood pressure 24h diastolic (mmHg)	80 ±8	78 ±8.0	76 ±9*	75 ±8**
Blood pressure night systolic (mmHg)	124 ±15	118 ±14	118 ±14**	114 ±11
Blood pressure night diastolic (mmHg)	72 ±9	70 ±9	69 ±9**	67 ±9
BMI (kg/m2)	33.8±5.0	34.5 ±6.8	34.0 ±5.0	39.4 ±33.4
CPAP (cm H2O)	NA	NA	8.4 ±2.4	10.6±2.0#
CPAP use (h/night)	NA	NA	5.9±0.9	6.3±1.2

*** $P<10^{-4}$, ** $\leq 10^{-1}$; *<0.05 comparisons within groups for changes vs. baseline within groups; P=NS between groups for all comparisons at corresponding time. OSLER=Oxford sleep resistance test; #P<0.05 autoCPAP vs. FixCPAP

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Brain tissue oxygenation during sleep in patients with the obstructive sleep apnea syndrome during an altitude sojourn

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Background: Near infrared spectroscopy (NIRS) of the brain is a novel non-invasive technique for monitoring brain tissue oxygenation (BTO) and cerebral blood flow. We employed NIRS to study physiologic effects of an altitude sojourn in patients with the obstructive sleep apnea syndrome (OSA). We hypothesised that nocturnal apnea would be associated with pronounced BTO, in particular during exposure to hypoxia at altitude and that acetazolamide would improve arterial oxygen saturation and BTO.
Methods: 15 OSA patients (median age 62 y) living at <600 m discontinued longterm CPAP therapy and underwent 2 altitude sojourns of 3 days each at Davos (2 days at 1630 m, 1 day at 2590 m), separated by a 2 week washout period at <600 m. At altitude patients received either acetazolamide (500 mg/d) or placebo according to a double-blinded, randomized cross-over trial. NIRS was continuously monitored during nocturnal polysomnography in Zurich and at altitude.
Results: Data are summarized in the table.
Conclusion: At altitude untreated OSA patients reveal a major increase of breathing disturbances due to central events, a significant reduction of arterial oxygen saturation and, to a similar degree, in BTO. Apparently, cerebrovascular autoregulation does not defend BTO during exposure to hypoxia in OSA patients. Acetazolamide improves arterial oxygen saturation but its effects on BTO were not significant, possibly due to the small sample size.

Table: Nocturnal Polysomnography incorporating NIRS

	Zürich, 490m	Davos Jakobshorn, 2590m	
		Placebo	Acetazolamide
Time in bed (hours)			
SpO2, %	93 (92;94)	86 (84;87)*	89 (86;90)*#
NIRS BTO, %	65 (63;69)	60 (57;63)*	63 (59;65)*
Difference BTO-SpO2, %	27 (25;29)	26 (21;31)	26 (23;30)
SpO2 drop from Zurich baseline, %		-7 (-5;-10)*	-5 (-7;-3)*#
NIRS BTO drop from Zurich baseline, %		-6 (-8;-3)*	-5 (-7;0)*
Apnea/hypopnea index	60.7 (32.0;73.1)	88.1 (57.9;121.2)*	67.5 (50.2;92.6)*#
central events, 1/h	21.1 (0.0;1.9)	50.8 (19.0;96.1)*	20.0 (10.0;30.5)*#

Values are medians (quartiles). SpO2=arterial oxygen saturation by finger pulse oximetry; * P<0.05 vs. Zurich; # P<0.05 vs. placebo

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Co-morbidity of obstructive sleep apnea in psychosomatic patients hospitalized in the Luzerner Höhenklinik Montana

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Introduction: Diagnosis of psychosomatic patients can be difficult. Once family doctors are convinced of the psychosomatic nature of their patients' ailment, they often hesitate to undertake further somatic investigations, fearing unnecessary cost production.
Methods: In a retrospective survey of all psychosomatic patients entering our rehabilitation clinic from January 2008 to December 2009, we assessed the co-morbidity of patients with psychosomatic diagnosis and obstructive sleep apnea (OSA). Screening was done according to clinical suspicion with nocturnal oxymetry and diagnostic assessment either with respiratory polygraphy or polysomnography. After diagnosis of OSA, CPAP treatment was initiated and continued when tolerated by the patient. A further group of patients with known OSA were also identified.
Results: Out of a total of 383 patients, 102 patients were screened with nocturnal oxymetry, Further diagnostic evaluation was made by respiratory polygraphy (28) or polysomnography (38). Despite high suspicion of OSA in oxymetry, 6 patients refused further diagnostic evaluation due to their psychosomatic symptoms.
A total of 35 patients were identified to have OSA: 14 (40%) had light, 7 (20%) moderate and 14 (40%) severe OSA. 19 were male and 16 female patients with an average BMI of 30.7 kg/m^2 and a mean age of 59. 18 had depressive disorders, 6 burn-out, 4 somatisation disorders and 7 suffered from various other disorders. Of those diagnosed with OSA, CPAP was initiated in 16 patients. 3 received other treatment (1 mandibular advancement therapy, 2 forced side sleeping position), and 16 refused CPAP treatment. A further group of 13 patients were identified, in whom OSA was already diagnosed before admission.
Conclusions: In 383 psychosomatic patients, 35 (9.1%) had newly diagnosed OSA, and 13 (3.4%) had already known OSA. Thus, a total of 48 (12.5%) were found to suffer from OSA. The association between depression and OSA has already been well established in the literature. Our data support this association, and suggest that OSA should be actively sought in psychosomatic patients, especially in those suffering from depression.

P68

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

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Background: Recent home ventilators provide the clinician with built-in softwares which record a multitude of items such as compliance, estimated tidal volume (VT) and minute ventilation (VE), leaks, respiratory rate (RR), percentage of inspiratory cycles triggered by the patient, and apnea-hypopnea index (IAH). The aim of this study was to analyze, in patients on long-term home mechanical ventilation (HMV) in a stable clinical condition, data downloaded from home ventilators during elective home visits performed by specialized nurses.
Methods: Among 179 patients on HMV regularly followed by our centre, 150 were treated with bi-level ventilators equipped with built-in software (Synchrony I and II, Philips Respironics®; VPAP III and IV, ResMed®). Ventilator settings had been adjusted in order to obtain optimal nocturnal $PtcCO_2$, SaO_2, and patient comfort.
Results: 150 patients aged 65 ± 14 yrs, 46% female, with diagnoses of: COPD: n = 30, Overlap syndrome: n = 31, Obesity hypoventilation: n = 38, other restrictive disorders: n = 39, Central or mixed sleep apnea: n = 12, ventilated either by facial (73%) or nasal masks (27%), for a total of 44 ± 31 months, were included. Ventilator settings are detailed in table 1. Compliance was on average: 408 ± 150 min/day (15% low compliance rate: <3:30 hrs/day); average VT was: 6.2 ± 2.3 ml/kg, and decreased significantly with BMI. Average respiratory rate was: 17 ± 3, i.e.: 2.5 ± 3.6 cycles above back-up RR. Patients triggered 50 ± 32% of respiratory cycles: 25% triggered more than 80% of respiratory cycles, and 29%, less than 20%. There was a trend for less triggered cycles in restrictive disorders (mainly neuromuscular disorders). Patients using Synchrony ventilators triggered significantly less cycles than those under VPAP (41 vs. 55%, p = .014). Estimated residual AHI was 5.9 ± 8.4/hr. Leaks (10.6 ± 11 L/min) were significantly lower with facial vs. nasal masks (p = .01 for average value, p = .0002 for upper 95th centile), but not influenced by IPAP or EPAP values.
Conclusions: Compliance to HMV is quite satisfactory. Use of facial masks decreases leaks. Most patients have a spontaneous RR close to the back-up rate; 29% are "captured" by their ventilator, and 25% are virtually on a spontaneous mode. Further studies are warranted to determine which among these options is optimal in terms of patient-ventilator synchronisation and comfort. Indeed, a low percentage of triggered inspiratory cycles may in fact reflect inspiratory efforts undetected by the ventilator.

Diagnosis	IPAP (Mean (SD); cm H_2O)	EPAP (Mean (SD); cm H_2O)	Set RR	Leaks Mean (SD) L/min	Spontaneous inspiratory cycles %, Mean (SD)	VT/kg Mean (SD)	AHI (Mean (SD); N/hr)
COPD and Overlap syndrome (n=61)	20 (4)	6 (2)	14 (2)	10 (11)	51 (31)	7 (3)	5 (5)
Obesity-hypoventilation (n=38)	20 (4)	9 (3)	14 (2)	10 (6)	54 (3)	5 (2)	6 (7)
Other restrictive disorders (n=39)	16 (4)	5 (2)	15 (3)	13 (14)	46 (34)	7 (3)	5 (7)
Central or mixed sleep apnea (n=12)	16 (4)	6 (2)	14 (2)	7 (10)	47 (3)	7 (2)	16 (21)

P69

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

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Rationale: Abdominal aortic aneurysms (AAA) are associated with life-threatening complications such as rupture. The likelihood that an AAA will rupture is particularly influenced by the diameter of the aneurysm and the expansion rate; the reasons for rapid expansion are largely unknown.
Objectives: To determine the prevalence of obstructive sleep apnea (OSA) in patients with AAA and to investigate the possible association between OSA and AAA expansion.
Methods: 127 patients (11 females) included in the AAA surveillance program agreed to participate and underwent a sleep study. Annual AAA expansion was determined by ultrasound. OSA was defined using an oxygen desaturation index (ODI) or apnea-hypopnea index (AHI) of >10/h. Univariate and multivariate analysis was performed to assess the effect of OSA severity on AAA expansion.
Measurements and main results: Mean ± SD age was 67.9 ± 6.0 years. Mean time following inclusion into the surveillance program until the final AAA measurement was 21.2 ± 15.7 months. An ODI or AHI of >10 was found in 40.5% and 41.5% of the patients, respectively. Patients with an ODI >30 had a significantly faster mean yearly AAA expansion (4.3 ± 3.7 mm) than patients with an ODI between 0-5 (1.7 ± 2.6 mm) or >5-15 (1.5 ± 2.4 mm) (p <0.05). In multivariate regression analysis controlling for cardiovascular risk factors and medications ODI >30 remained an independent risk factor for AAA expansion.
Conclusions: In patients with AAA OSA is highly prevalent and associated with more rapid expansion. Severe OSA may be a factor for faster AAA expansion but this needs to be proven in a randomized controlled intervention trial.

P70

Hypersensitivity pneumonitis induced by a CPAP ventilator?

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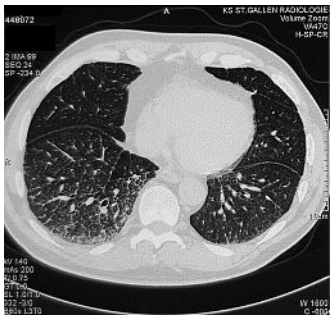
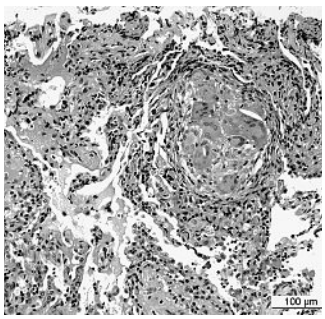
Introduction: Continuous positive airway pressure (CPAP) ventilation is the gold standard treatment for obstructive sleep apnea (OSA) and has so far not been associated with treatment-related inflammatory or allergic adverse reactions including hypersensitivity pneumonitis.
Case presentation: A 69-year-old man with severe OSA presented with progressive dry cough and exertional dyspnea. On presentation the patient was alert and in no respiratory distress. Auscultation revealed right basal inspiratory velcro-type crackles. Computed tomography of the chest showed reticulo-nodular opacities and interstitial thickening in both lower lung fields with a right-sided predominance. Ground glass opacities were present in the right lower lobe (fig. 1). Pulmonary function tests were normal apart from a reduced diffusion capacity for carbon monoxide (68% predicted). Arterial blood gas analysis showed hypoxemia and an elevated alveolar-arterial oxygen gradient. Bronchoalveolar lavage showed an increased total cell count with a lymphocytosis of 84%. Transbronchial biopsies revealed chronic inflammation, with presence of macrophages, histiocytic granuloma and interstitial fibrosis (fig. 2). The diagnosis of hypersensitivity pneumonitis (HP) was retained. Identification of an inciting agent at the patient's home failed. A treatment with systemic corticosteroids was started, but the patient relapsed after withdrawal. Symptoms, radiological and functional findings did not improve until CPAP therapy – which included a humidifier – was stopped. CPAP therapy was resumed later with new equipment without humidification. Since, the patient remained free of symptoms without medication.
Discussion: In case of HP the identification of the correct source of the pathogenic antigen is very important. After elimination of the CPAP device & humidifier as the potential source, our patient's symptoms resolved within a few weeks without further steroid treatment. Authors argued that the conditions in the water bath of a heated humidifier are bactericidal and humidifiers produce molecules of water too small to carry pathogens. Therefore, the use of sterilized water is not generally recommended. Interestingly, our patient handled his humidifier very carefully by changing the water daily and using only pre-boiled water. Nevertheless, given the clinical course, an association to a bacterial or fungal antigen in the CPAP device or humidifier seems to be the most likely cause of our patient's HP.





P71

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

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Background: Hepatocyte growth factor (HGF) gene transfer attenuates bleomycin induced lung fibrosis in the bleomycin model. HGF is multifunctional pleiotropic factor; it is a potent mitogen for alveolar epithelial cells and has antiapoptotic properties. Long term effect of HGF gene transfer on the alveolar epithelium is still not known; in the present study we investigated the long term effect of HGF gene transfer on the alveolar epithelial cells in the normal lung.
Material and methods: Adult male Fischer rats F344, were instilled

with 350 µl of pSpChHGF plasmid (Human HGF under control of surfactant protein C promoter), and extracorporal electroporation was performed 8 pulses of 200v/cm, at 10 ms interval. One month after HGF gene transfer, animals were sacrificed and the tissues were collected. Stereological assessment was performed to study the structural changes in the normal right lung after long term HGF gene transfer. Untreated normal adult male rat lungs served as controls.
Results: Stereology revealed that HGF transfer increased the total lung volume (4.51 ± 0.52 vs 3.41 ± 0.33, p <0.01). This could be attributed to an increase of both volume fraction (58.2 ± 0.7% vs 52.3 ± 3.0%, p <0.01) and total volume of alveoli per lung (2.43 ± 0.30 cm^3 vs 1.63 ± 0.22 cm^3, p <0.01), accompanied by an increase of total alveolar surface area (2.36 ± 0.07 cm^2 vs 2.07 ± 0.17 cm^2, p = 0.01). The mean septal thickness was slightly decreased after HGF transfer (5.12 ± 0.78 µm vs 6.57 ± 1.45 µm, p = 0.08).
Conclusion: Stereological analysis reveals that there is increased remodeling as evident by septal thickness changes and increase in the surface area of the alveoli and their total volume per lung, indicating that HGF is important in the alveolar development. These changes might be explained by an increased proliferation of alveolar epithelial cells.

P72

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

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

Poster session II

P73

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

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Setting: Mandatory initial screening of asylum seekers for tuberculosis in Switzerland 2004-05 and 2007-08.
Objective: To compare the yield of screening by chest radiography with an individual assessment based on geographical origin, personal history, and symptoms.
Method: Cross-sectional retrospective comparison of two periods of two years.
Results: The yield of screening was assessed as the proportion of screenees starting antituberculosis treatment for culture-confirmed pulmonary tuberculosis within 90 days. It was 14.3 per 10,000 asylum seekers screened (31/21,727) for chest radiography and 12.4 per 10,000 (29/23,402) for the individual assessment. Sensitivity of radiography was 100% vs. 55% for the individual assessment, but its specificity was lower (89.9% vs. 96.0%, respectively). The higher sensitivity of radiography meant shorter delays between screening and start of treatment (median of 6 vs. 25 days). Its lower specificity led to a larger proportion of screenees needing further investigations for suspicion of tuberculosis (12% vs. 4%).
Conclusion: The yield was equivalent in both systems. The interview-based system missed more cases. This led to delays until start of treatment with a potential to increase transmission and secondary cases. The radiographic system had a higher burden as more suspects require further investigations.

P74

Features of tuberculosis incidence and clinical forms for sarcoidosis patients

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Introduction: The problem of high tuberculosis(TB)incidence is very burning in Latvia during several number of years (incidence2006.-49,7/100000). At the same time,there was high level of TB resistant forms for patients(pts) with first time detected TB-22.7% in 2006. For the same time period, sarcoidosis incidence was 5,22/100000 in 2006. Though the ethiology of sarcoidosis is unknown we noted certain tendencies in the development of pathological processes in cases of added tuberculosis for sarcoidosis pts.
Methods: 3423 sarcoidosis pts were registered in Latvia during the period of observations 1958–2006. Added TB was detected only for 28 (~1%)of pts from this population. Among these pts we detected 16 pts with pulmonary TB,12-extrapulmonary TB pts. The duration of sarcoidosis was not less than 3 years for these pts before the incidence of tuberculosis. Various TB affections of bones and joints were detected for 8 of 12 extrapulmonaty Tb pts. We also have noted high level of drug resistant TB-13/31 pts (41,9%).
Conclusions: Our observations indicate low risk of TB incidence among the population of sarcoidosis in Latvia (0.94%). At the same time the risk of additional TB infection increases when sarcoidosis is in chronic process. These patients develop specific heavy forms of TB such as drug resistant TB, extrapulmonary TB.

P75

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

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

P76

Occupational chemical pneumopathy: an atypical case report

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

P77

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

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Background: Liquid oxygen (LOX) is widely used in Switzerland since portable devices enable patients to maintain mobility and regular physical activity outside their homes. A limitation however is the range of only 4–8 hours autonomy depending on the flow rate. To minimise this disadvantage the Genossenschaft LOX set up with LOX suppliers a network of refilling stations for LOX (Basle, Berne, Lausanne, Lucerne, Neuchâtel, St. Gallen, Winterthur, Zug, Zurich). Usually the refilling station is located in a pharmacy inside or near the railway station and it is accessible 24 h/7 days a week.
Aim: We wished to determine the rate of use, how the network corresponds to the needs of patients and how to expand the network.
Method: Questionnaires were sent to all patients using LOX in Switzerland. The answers were analysed and compared with the objective use of the refilling stations, as assessed by the record filled in by the users during their visits to the stations.
Results: The questionnaire was sent to the 2100 patients with LOX. 250(12%) were returned. 60 (23%) patients make day trips in their local area, 51 (19%) up to 20 km, 61 (23%) up to 50 km and 89 (34%) over 50 km. 65% of the patients knew about the LOX refilling stations but only 28% had ever used them. Despite two different adapter systems, the refilling at the stations was problem-free for 96% of the patients. The refilling was done between 6am and 12 pm with two peaks in the late morning and afternoon. During the first 2 years 435 patients made a total of 1156 refillings. The average number of refillings per patient was 2.65 with a huge range between 1 and 68. 50% used it more than once. 37% of the patients requested further refilling stations especially in the tourist regions of Switzerland (Valais, Bernese Alps, Grison and Ticino)
Conclusions: Although patients with LOX usually suffer from end stage pulmonary disease, there is still a big need for mobility. The refilling of the portable LOX devices at the stations is, despite the two adapter systems, for the patients without further assistance feasible and accepted. To standardise the adapter system would reduce the logistic costs and simplify use for the patient. LOX patients must receive better information from their health care providers about the existence and the use of the LOX refilling stations. Further refilling stations, especially in tourist regions, are required and could further improve the mobility and quality of life of the LOX patients.

P78

Incidence and prevalence of pulmonary lymphangioleiomyomatosis in Switzerland

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

P79

A complicated course of a spontaneous pneumothorax

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We report the case of a 38-year old non-smoking female with a history of spontaneous right-sided pneumothorax.
The first episode in June 2006 was treated with a chest tube. After two weeks the first relapse occurred and the patient was treated surgically with a right sided thoracoscopic pleurectomy. After an unproblematic early postoperative course the patient had a second relapse 4 weeks later. She was treated with a thoracoscopic talcpleurodesis with an unclear, but propably high amount of talc. Shortly after the surgical intervention, an air fluid level was seen on a chest x-ray, which was slowly progressive over weeks and compressed the right lung. In the follow up 6 months after the procedure the spirometry was compatible with a restrictive ventilation defect (FEV_1 56% predicted) and the CT scan showed two big calcified pseudocysts (10 x 17.5 cm and 5 x 9 cm). After an airway infection with hemoptysis, 2 years after the first pneumothorax, the patient presented to our facility because of a "fluid-clapping in the right hemithorax" and progressive dyspnea. We found a more severe restrictive ventilation defect (FEV_1 47%, TLC 66% predicted) and the CT scan showed very big, now nearly allconsuming, calcified pseudocysts, with significant compression of the right lung and an new mediastinal shift toward the left side with tracheal compression. An anterolateral thoracotomy with nearly total pleurectomy and resection of the cysts was performend, which lead to prolonged lung deflation, but an immediate decrease of the dyspnoe. Short term follow up of 6 weeks radiologically did not show development of new cysts. Since not published so far, the development of calcified pseudocysts after (recurrent) pneumothoraces seem to be a rare complication likely related to talcpleurodesis.

Poster session III

P81

Specific therapy for pulmonary hypertension in patients with interstitial lung disease

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Background: There is no evidence whether pulmonary hypertension (PH) in patients with interstitial lung disease should be treated with PH specific medications or not.
Methods: Retrospective analyses of data from patients with interstitial lung disease and PH confirmed by right heart catheterization (RHC) receiving treatment for PH.
Results: Between 1/2006 and 6/2008 we identified 7 patients (6 males, mean age 72±4 y) with emphysema/fibrosis (2), idiopathic pulmonary fibrosis (2), non-specific interstitial pneumopathy (2) and pneumoconiosis (1) with PH in RHC. Baseline hemodynamic data were the following (mean ± SD, (range)): mean pulmonary artery pressure 39 ± 9 mm Hg (27-50), pulmonary vascular resistance (PVR) 730 ± 421 dyn.s.cm^{-5} (312–1344), cardiac index 1.7 ± 0.3 l/min/m^2 (1.3–2.2), Wedge pressure 12 ± 5 mm Hg (2-17). Mean total lung capacity was 74 ± 15% of predicted normal (range 55–98). All patients had decreased diffusion capacity for carbon monoxide (DLCO mean 30 ± 7% predicted, range 21–46) and resting hypoxemia (mean pO_2 60 ± 5 mm Hg, range 53–66). Four patients had a baseline 6 minute walking test done (walking distance (WD) 310 ± 144 m (range 130–475) and showed severe desaturation (minimal oxygen saturation 69 ± 1% (range 67–70)). Five patients received bosentan and 2 sildenafil for first line PH treatment. Bosentan was replaced by sildenafil in one patient because of elevation of liver enzymes. Two patients received combination treatment after 1 (bosentan, sildenafil) and 8 (bosentan, ilomedin) months of treatment. At first follow-up visit after 3 (range 1–4) months of therapy WD remained stable or improved in 3 patients (+2%, +1%, +58%) and decreased in 1 patient (–18%). At second follow-up visit after 7 (range 5–13) months of therapy WD improved or remained stable in 3 patients (–5%, +5%, +16%) and decreased in 2 patients (–31%, –36%). After 13.5 (8-20) months of therapy WD remained stable or improved in (+2%, –7%, +27%, –5%) and decreased in 1 patient (–58%). Lung function remained stable. Two patients died: one with emphysema/fibrosis after 11 months of therapy, one with NSIP due to former bleomycin exposure after 2 months of therapy. These were the patients with the highest PVR, and both died of right heart failure.
Conclusion: We assume that PH contributes substantially to prognosis in patients with interstitial lung disease. Specific PH therapy might help to stabilize functional capacity and to improve outcome of these patients.

P82

Bosentan and/or Sildenafil for non-operable chronic thromboembolic pulmonary hypertension

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Objectives: To evaluate outcome of patients treated "off-label" by bosentan and/or sildenafil for chronic thromboembolic pulmonary hypertension (CTEPH).
Patients and methods: Since 2003, 18 patients (mean age 69 ± 11 years) have been treated with bosentan and/or sildenafil for CTEPH (mean pulmonary arterial resistance 8.1 ± 3.7 U Wood) in Lausanne University Hospital, with a follow-up of at least 12 months. Sixteen of them were inoperable because of distal disease and/or age or significant co-morbidities and 2 had persistent or recurrent pulmonary hypertension despite surgery. Efficacy of treatment was evaluated by comparison of New York Heart Association functional class (NYHA), six-minute walk test (6-MWT) and serum levels of N-terminal-pro brain natriuretic peptide (NT pro-BNP) at baseline (T0) and at 12 months (T12). Wilcoxon rank test was used for statistics.
Results: At T0, median NYHA class was III (range II-IV), 6-MWT was 348 meters (5 and 95 centiles:0, 539) and NT pro-BNP was 387 mmol/l (58, 3508). At T12, 11 patients were treated with bosentan, 5 with sildenafil, 1 with inhaled Iloprost (because of failure of the two other treatments) and 1 with a combination of sildenafil and Iloprost. NYHA had improved in 10 patients, remained stable in 7 and worsened in 1 (median decrease 0.5 (–2; 0.2) p = 0.013). Six-MWT improved by a median of 15 meters (–142, +270) (p = 0.047) and NT pro-BNP decreased by a median of 65 mmol/l (–2988, +187) (p = n.s.). Among the 10 patients with a follow-up of 2 years or longer, two thirds remained stable and one third had worsened at 24 month. Treatments were well tolerated and only one patient had significant side effects (cutaneous reaction to bosentan) necessitating a switch to another treatment.
Conclusion: In agreement with published data, bosentan and sildenafil improved functional status (NYHA, 6-MWT) and haemodynamics (NT pro BNP) in our patients with inoperable CTEPH. However these medications should not be used as substitute for surgery when the latter is applicable.

P83

High dose of Fluticasone admistered by controlled inhalation: a new possible tool for the treatment of uncontrolled asthma

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Introduction: In spite of guideline compatible therapy the management of severe uncontrolled asthma remains a challenge, often requiring higher doses of systemic corticosteroids, which may cause severe side effects. We introduced to treat these patients with high doses of inhaled corticosteroids using a special inhalation device,

the AKITA (Fa. Activaero). The principle of controlled inhalation has a proved pulmonal delivery of 80% of the nebulized substance. The inhalation steering can be adapted on the Inspiratory Capacity of the Patients. We have shown, that this is easily and effective possible in the in house setting (Data presented on the Annual Meeting of the DGP 2007 in Lübeck). As a next step, we did a retrospective analysis of data get a first confirmation of the efficiency of the therapy.
Methods: We analyzed all patients receiving the therapy in 2007 in our hospital by records. We were able to collect data of 112 patients. The indications for the therapy were uncontrolled asthma, acute exacerbation of a former controlled asthma and weaning of systemic steroids. All patients were treated with 2 mg Fluticason by controlled inhalation. The therapy was admistered about two to eight weeks, with a mean duration of 3 weeks.
Results: Under the therapy there was a significant decrease of exhaled NO (–44.5%), and a significant rise of FEV_1 (+ 17.2% / 340 ml) and FEV_1/VC (68.9% to 73.6%). The therapeutic dose of the patients receiving oral corticosteroids could be significantly tapered (33.2% / 7.6 mg prednisolone equivalent). We saw no worse side effects.
Conclusion: We assess these data as a first sign for the effectiveness of this therapeutical approach. It is a safe and well tolerated therapy. A prospective Study with a non-treatment control group is on the way.

P84

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

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Rationale: Previous studies suggest the phosphodiesterase 4 (PDE4) inhibitor roflumilast may improve lung function and prevent exacerbations in patients with chronic obstructive pulmonary disease (COPD) with moderate-to-severe airflow obstruction and exacerbations.
Methods: Two replicate, randomised, placebo-controlled, double-blind, multicentre trials were performed in patients with COPD, severe-to-very severe airflow obstruction, a history of exacerbations and chronic bronchitis. Patients were randomised and received either roflumilast, 500 µg once daily (n = 1537), or placebo (n = 1554) for 52 weeks. Co-primary endpoints were mean change in pre-bronchodilator forced expiratory volume in 1 second (FEV_1) from baseline to each post-randomisation visit, and the rate of moderate or severe exacerbations. Secondary endpoints included post-bronchodilator FEV1 and time to death from any cause.
Results: Both studies met their pre-specified primary endpoints. In a pre-specified pooled analysis, mean difference in pre-bronchodilator FEV1 between roflumilast- and placebo-treated patients was 48 mL ($p < 0.0001$), and the mean rate of moderate or severe exacerbations (pt/year) was 1.14 vs 1.37, respectively (reduction: 16.9%, $p = 0.0003$). Pooled post-bronchodilator FEV_1 also improved significantly with a mean between-treatment difference of 55 mL ($p < 0.0001$). Similar significant improvements were seen in pre- and post-bronchodilator forced vital capacity and pre-bronchodilator mid-expiratory flow. There was no difference in mortality between treatments.
Conclusions: Roflumilast significantly improved lung function and decreased exacerbations in COPD patients with chronic bronchitis and severe-to-very severe airflow limitation.
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P85

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

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Rationale: Morbidity and mortality due to COPD are increasing, despite various treatment options. The oral, selective phosphodiesterase 4 (PDE4) inhibitor roflumilast can improve lung function in COPD patients. Roflumilast, co-administered with long-acting bronchodilators, may have additional effects.
Methods: This double-blind, randomised, parallel-group study recruited patients with moderate-to-severe COPD. After a single-blind, 4-week baseline period with salmeterol (SAL) 50 µg twice daily (bid) and placebo once daily (od), patients were randomised to receive roflumilast 500 µg od (n = 466) or placebo od (n = 467) for 24 weeks concomitant with SAL 50 µg bid. The primary outcome was mean change in pre-bronchodilator FEV1 from baseline to each post-randomisation visit. Other outcomes included post-bronchodilator FEV_1 and exacerbation frequency.
Results: Compared with SAL alone, roflumilast concomitant with SAL significantly improved mean pre-bronchodilator FEV_1 by 49 mL ($p < 0.0001$) and mean post-bronchodilator FEV_1 by 60 mL ($p < 0.0001$). The concomitant regimen also reduced the mean annual rate of exacerbations (moderate or severe) by 36.8% ($p = 0.0315$; post-hoc) and increased the median time to first moderate or severe exacerbation (hazard ratio 0.6, $p = 0.0067$) compared with SAL alone. The safety profile of the concomitant treatment was consistent with that previously reported for roflumilast. Adverse events occurred in 63.1% of patients receiving roflumilast concomitant with SAL compared with 59.1% receiving SAL alone.
Conclusions: Roflumilast provides additional clinical benefits to COPD patients receiving SAL by statistically significantly improvement in lung function and reduction in exacerbations.
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P86

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

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Rationale: The phosphodiesterase 4 (PDE4) inhibitor roflumilast provides a novel approach to the treatment of chronic obstructive pulmonary disease (COPD).
Methods: Two replicate, randomised, placebo-controlled, double-blind, multicentre trials were performed in patients with COPD, severe-to-very severe airflow obstruction, a history of exacerbations and chronic bronchitis. Patients were randomised to receive either roflumilast, 500 µg once daily, or placebo for 52 weeks. Adverse events (AEs) and responses to enquiries about recent weight change were recorded at each visit. In one study, 24-hour Holter monitoring was undertaken at 19 sites.
Results: Both studies met their pre-specified primary efficacy endpoints. In the pooled study population, AEs were reported by 67% of patients in the roflumilast group (n = 1547) and 62% in the placebo group (n = 1545); serious AEs were reported by 20% and 22%, respectively. Discontinuations associated with AEs (14.2% vs 11.5%, respectively) were initially more common with roflumilast than with placebo, but after 8 weeks they were similar between treatment groups. Mean weight change was –2.09 kg with roflumilast and +0.08 kg with placebo, and not progressive beyond 6 months. Atrial fibrillation was reported in 1.1% of roflumilast- and 0.5% of placebo-treated patients. There were no differences between treatments in overall reported cardiovascular AEs, in the occurrence of rhythm disturbances in Holter-monitored recordings, and no increase in the incidence of pneumonia during roflumilast treatment.
Conclusions: Roflumilast was generally well tolerated with no excess neurological or cardiac events or cases of pneumonia. The weight change is the subject of further study.
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P87

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

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Rationale: The once-daily oral phosphodiesterase 4 (PDE4) inhibitor roflumilast (ROF) provides a novel approach to the treatment of chronic obstructive pulmonary disease (COPD). The pharmacokinetic (PK) profiles of ROF and its similarly pharmacologically active metabolite, roflumilast-N-oxide (ROF-NO), were investigated.
Methods: Plasma concentrations of ROF and ROF-NO were measured in 77 healthy volunteers (age: 18–45 years) in 5 phase I studies after application of oral once-daily doses of 250–1000 µg ROF or intravenously (150 µg).
Results: After oral application ROF was absorbed quickly and almost completely. Cmax was reached about 1 h (ROF) and 4–13 h (ROF-NO) after administration. The absolute bioavailability of ROF was 79%. Terminal plasma half-life (t1/2) was found to be in the range of 15–17 h (ROF) and 25–30 h (ROF-NO). PK Steady State conditions were reached after 4 days (ROF) and 6 days (ROF-NO) of oral once daily administration. The total exposure (AUC) of ROF-NO was about 10 times higher than that of ROF, indicating that ROF-NO could be the main carrier of the pharmacological activity. Plasma-Clearance was 0.14 L/h*kg after i.v.-application of 150 µg ROF. Volume of distribution (Vd area) was 2.9 L/kg. ROF and ROF-NO were almost completely cleared by metabolism and eliminated renally as inactive metabolites. Amounts of ROF and ROF-NO in urine are less than 1%. PK data

revealed no differences after day or nighttime application. Furthermore, food intake did not affect the PK of ROF-NO. Dose proportionality of PK parameters was found in the range of 250–1000 µg.
Conclusions: The observed PK characteristics of ROF – high absolute bioavailability, long half-life, dose linearity as well as a high volume of distribution – are fullfilling the PK-requirements for a once daily oral systemic treatment of chronic inflammatory diseases such as COPD.
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P88

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

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Rationale: Morbidity and mortality due to chronic obstructive pulmonary disease (COPD) are increasing, despite various treatment options. Roflumilast, an oral, selective phosphodiesterase 4 (PDE4) inhibitor, improves lung function and clinical outcomes in patients with COPD. Roflumilast, co-administered with long-acting bronchodilators, may have additional effects.
Methods: This double-blind, randomised, parallel-group study recruited patients with moderate-to-severe COPD associated with chronic bronchitis. After a single-blind, 4-week baseline period with tiotropium 18 µg once daily (od) and placebo (od), patients were randomised to receive concomitant treatment with roflumilast 500 µg od (n = 371) or placebo od (n = 372) for 24 weeks. The primary outcome was mean change in pre-bronchodilator forced expiratory volume in 1 second (FEV_1) from baseline to each post-randomisation visit. Other outcomes included post-bronchodilator FEV_1 and COPD exacerbations.
Results: Baseline characteristics were similar in the two groups. Compared with tiotropium alone, roflumilast concomitant with tiotropium significantly improved mean pre-bronchodilator FEV_1 by 80 mL ($p < 0.0001$) and mean post-bronchodilator FEV1 by 81 mL ($p < 0.0001$). A hazard ratio of 0.7 ($p = 0.0264$) indicated that exacerbations (mild, moderate or severe) were likely to occur later in patients taking the concomitant regimen. The safety profile of the concomitant regimen was consistent with that previously reported for roflumilast. Adverse events occurred in 46.0% of patients receiving the concomitant regimen and in 40.7% receiving tiotropium alone.
Conclusions: Roflumilast provides additional clinical benefits to COPD patients receiving tiotropium by significantly improvement in lung function and reduction in exacerbations.
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Poster session IV

P89

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

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Rationale: Recombinant human deoxyribonuclease (rhDNase) applied to patients with cystic fibrosis (CF) has been shown to improve lung function in short-term trials, and there is some evidence that the number of pulmonary exacerbations may be reduced. However, its long-term effect has not yet been clearly assessed.
Objectives: To assess the long-term efficacy of rhDNase on lung function parameters, taking in consideration potential confounder effects.
Methods: In this retrospective observational study, we analyzed data from our CF database including 170 children (85 males; 85 females) with CF followed over an age range of 5 to 18 years between 1978 and 2008. Linear mixed model (LMM) analyses were used to assess efficacy of rhDNase (2.5 mg/day) on lung function parameters, including residual capacity (FRCpleth), lung clearance index (LCI), trapped gas (VTG), effective airway resistance (sReff), and forced expiratory indices (FEV_1, FEF50), as well as on blood gases taken from the arterialized ear lobe (PaO_2, $PaCO_2$) and body mass index (BMI). Moreover, confounder effects including time point events (age at initiation and duration of rhDNase treatment), microbial colonization (*P. aeruginosa* and *S. aureus*) and development of allergic broncho-pulmonary Aspergillosis (ABPA) were studied.
Results: Comparing the slope of lung function parameter as index of progression obtained during a time period of 10 years before versus 10 years after initiation of rhDNase treatment, significant improvement in the degree of ventilation inhomogeneities (LCI; $p = 0.004$) was observed. There was no effect on flow limitation (FEV_1, FEF50), bronchial obstruction (sReff), pulmonary hyperinflation (FRCpleth), trapped gas (VTG), blood gases, or on BMI. Subgroup analysis showed that the beneficial effect of rhDNase on LCI was restricted to younger patients (age <12 years) and to those with mild lung involvement. In these patients, use of rhDNAse was also associated with increased trapped gases. The onset of *S. aureus* infection and to a lesser extent of *P. aeruginosa* infection influenced efficacy of rhDNase treatment
Conclusions: In our cohort, use of rhDNAse was associated with only modest long-term beneficial effect on lung function parameters in CF children, raising concerns about cost effectiveness.

P90

Allergic rhinitis as predictor for school age wheezing

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Background: Rhinitis in older children and adults has been shown to be a risk factor for adolescent and adult onset asthma. These findings suggest an interaction between the upper and lower airways. Whether rhinitis is associated with childhood onset asthma is unknown. The objective of the study was, therefore, to investigate whether rhinitis in early childhood is an independent risk factor for childhood onset wheezing in the German Multicentre Allergy Study (MAS) birth cohort.
Methods: The MAS followed 1314 healthy children from birth to 13 years of age. The children were followed and specific immunoglobulin E levels were measured at yearly intervals. Airway hyperresponsiveness was assessed at 7 years.
Results: Allergic rhinitis until the age of 5 years was a risk factor for subsequent wheezing onset with an adjusted RR of 3.79 ($p = <0.001$). This association was not attributable to the type of sensitization, the severity of sensitization or atopic dermatitis during the first 2 years of life. The population attributable risk fraction for allergic rhinitis on the incidence of wheezing was 41.5% (95% CI: 20.0–61.3). Non-allergic rhinitis until the age of 5 years was not significantly associated with wheezing onset in childhood (adjusted RR 0.77, $p = 0.678$). Neither allergic (adjusted RR = 1.37, $p = 0.503$) nor non-allergic rhinitis (adjusted RR = 1.16, $p = 0.656$) until the age of 2 years was associated with wheezing onset thereafter.
Conclusions: The first manifestation of allergic rhinitis occurs in preschool children where it is a risk factor for subsequent wheezing onset. Rhinitis until the age of two, however, does not influence the development of wheezing in childhood. Preschool children with rhinitis might thus benefit from early assessment of allergic sensitization to identify the children at high risk of developing wheezing.

P91

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

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Aim: We compared characteristics of medically versus surgically treated pleural empyema patients treated at Kantonsspital St. Gallen, a 900 bed hospital in Switzerland.
Methods: Electronic patient charts from 1/2001 to 12/2008 were searched for empyema and pleura. Retrieved charts were reviewed manually. Included for analysis were hospitalised patients, >16 years, with acute empyema based on the clinicians diagnosis (symptoms, fever, sonography, CT, Laboratory). Excluded were patients with malignant effusions, tuberculosis, iatrogenic empyema, transsudative effusion and previous pleurodesis. Demographic characteristics, deaths, concurrent diseases, duration of symptoms, treatment

(antibiotics, drainage with or without urokinase, surgery), duration of hospital stay and follow-up pain 3 and 12 months after discharge were collected.
Results: 78 of 215 retrieved charts fulfilled inclusion criteria. 4 died (1 surgery, 3 medical).
Conclusion: Medical treatment was successful in 62% of our empyema patients (48 of 78). If drainage and urokinase were applied, the success rate was 82% (28 of 34), significantly higher than for patients treated without urokinase (15 of 24, 64%) and for patients treated without drainage (5 of 20, 25%). No other predictors of success with medical treatment could be identified. Surgically treated patients were more likely to suffer chest pain 3 and 12 months after discharge.

		Total (n)	Medical treatment (n)	Medical treatment (%)	Surgical treatment (n)	Surgical treatment (%)	Odd's Ratio	95% Confidence Interval
All empyema patients treated		**78**	**48**	**61.5%**	**30**	**38.5%**		
Age groups [years]	<47	17	10	58.8%	7	41.2%	1	
	47 - 60	18	11	61.1%	7	38.9%	1.1	0.28 - 4.26
	61 - 73	22	12	54.5%	10	45.5%	0.84	0.23 - 3.02
	> 73	21	15	71.4%	6	28.6%	1.75	0.45 - 6.77
Gender	male	52	33	63.5%	19	36.5%	1	
	female	26	15	57.7%	11	42.3%	0.78	0.3 - 2.05
Treatment	**Antibiotics alone**	**20**	**5**	**25.0%**	**15**	**75.0%**	**1**	
	Drainage	**24**	**15**	**62.5%**	**9**	**37.5%**	**5**	**1.4 - 18.5**
	Drainage and Urokinase	**34**	**28**	**82.4%**	**6**	**17.6%**	**14**	**3.6 - 53.6**

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

P92

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

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Objective: Bronchial airways after lung resections are usually closed either by manual or mechanical suture. To prevent bronchopleural fistula (BPF) additional reinforcement of the bronchial stump by a pedunculated muscle flap (PMF) is often recommended. In very central tumours sleeve resection with anastomosis is generally preferred to direct closure with the aim of minimizing airway stenosis or avoiding incomplete resection. As a further alternative we describe a technique where only a PMF is used to cover an open and unsutured central airway defect by means of three high-risk patients.
Methods and results:
CASE 1: A 40-year-old man underwent extended right pneumonectomy because of central non small cell lung cancer (NSCLC) with severe poststenotic pneumonia. The tracheal defect at the bifurcation was covered by a PMF without preceding bronchial suture closure. There was no evidence of air leakage in intraoperative testing and repetitive bronchoscopy. No complications were seen in the postoperative course.
CASE 2: A 45-year-old woman underwent extended right pneumonectomy. After impressive tumour regression due to neoadjuvant chemotherapy the resection margin of the right bronchus was close to the carina. A PMF was used for coverage of the airway defect. Intraoperative testing including bronchoscopy showed no evidence of air leakage or contralateral prolapse of the muscle flap. The postoperative course was complicated by ARDS of the remaining left lung necessitating continuous positive airway pressure (CPAP). Delayed re-thoracotomy with muscle flap refixation had to be performed because of secondary air leakage.
CASE 3: A 72-year-old man with NSCLC and neoadjuvant chemotherapy underwent right bilobectomy with extended resection of the right intermediate bronchus up to the main bronchus. The defect of the main bronchus was covered using a PMF. Intraoperative bronchoscopy and air leakage testing were normal. The postoperative course was uneventfull.
Conclusion: Primary coverage of a central bronchial or tracheal defect using only a PMF is feasible. Predominantly in high risk patients direct suture at risk or extensive sleeve resection may be avoided.

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Preoperative endobronchial ultrasound for mediastinal staging in patients with lung carcinoma

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Background: Traditionally mediastinoscopy was been the gold standard for the mediastinal staging in patients with lung carcinoma. Nevertheless, endobronchial ultrasound (EBUS) can replace mediastinoscopy and can easily performed in an ambulatory setting (Hofer et al, ERJ 22: Suppl 45: 590s). EBUS has been routinely performed for preoperative mediastinal staging in our institution since March 2007.
Aim: To investigate the usefulness of EBUS for preoperative mediastinal staging in surgical patients with lung carcinoma (NSCLC).
Methods: Prospective evaluation of all surgical patients with NSCLS with perioperative EBUS since March 2007. The following parameters were evaluated: nodal stage of CT and PET/CT, results of EBUS and the surgical nodal stage. All patients had an extensive surgical nodal staging.
Results: 54 patients were evaluated of which five patients after neoadjuvant chemotherapy. Mean age was 64 ± 13 years. In the preoperative CT 12 patients had enlargement of N3-lymph nodes, 20 of N2-lymph nodes. Only 8 patients had a positive PET/CT for N2-disease. Out of these 8 N2-PET-positive patients, 3 (38%) had a negative EBUS of the PET-positive lymph nodes and the negative N2-disease was surgicaly confirmed. Four patients with a negative EBUS of N2-lymph nodes finally had a positive N2 disease (two of which with negative PET/CT). All of these four patients had an indication for surgical operation (contraindication for neo-adjuvant chemotherapy). EBUS-TBNA of N3-lymph nodes was performed in 17 (31.5%) patients, in 37 (68.5%) and 31 (54.4%) patients paratracheal and subcarinal N2-lymph nodes were evaluated, respectively. Interestingly in the four patients with false negative EBUS-TBNA the subcarinal lymph node were false negative. One out of the 5 patients with neoadjuvant treatment has a false negative EBUS (one micrometastasis in subcarinal lymph node and non-representative puncture in a paratracheal lymph node).
Conclusion: EBUS has a high clinical utility for preoperative mediastinal staging in patients with NSCLS. Interestingly in our population only subcarinal lymph nodes were false negative in EBUS and two of the four had a negative PET/CT too. Probably the combination with endoesophageal ultrasound (EUS) helps to evaluate these patients. In one patient out of five with neoadjuvant treatment EBUS was false negative. The combination of PET/CT and EBUS avoids in a major part of patients the use of mediastinoscopy.

P94

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

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Introduction: The diagnosis of centrally located pulmonary masses or nodules not visible on conventional bronchoscopy is a challenging issue. Convex probe endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a well established technique in the investigation of mediastinal and hilar lymph nodes.
Objectives: The purpose of our study is to address the feasibility and accuracy of convex probe EBUS-TBNA for the diagnosis of intra-pulmonary tumors located close to central airways (not assessable by conventional biopsy).
Methods: From June 2007 to December 2009, EBUS-TBNA was performed in 8 patients with endobronchially not visible pulmonary lesions adjacent to central airways. Conventional biopsies (transbronchial forceps and/or needle, and/or brush and transthoracic needle in 1 case) were performed in 7 of the 8 cases (87.5%). All of them were non-diagnostic.
Results: The size of the pulmonary lesions on CT varied from 12 to 62 mm (mean 36 mm). Transtracheal (n = 3) or transbronchial (n = 5) EBUS TBNA were performed. Cytological and/or histological (cell block) samples were diagnostic in all 8 cases. The final diagnoses were lung cancer in 6 cases (6 non-small cell lung carcinoma) and metastatic tumors in 2 cases (1 melanoma, 1 malignant nerve sheath tumor).
Conclusion: EBUS-TBNA is a useful diagnostic approach in intrapulmonary lesions not assessable by conventional bronchoscopic biopsy. In our serie, this minimal invasive outpatient procedure had a very high diagnostic yield (100%).

P95

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

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Background: Excessive mediastinal shift into the vacated thoracic cavity after pneumonectomy can result in dyspnea without hypoxemia by compression of the tracheobronchial tree, a phenomenon called postpneumonectomy syndrome. More rarely hypoxemia in upright position (platypnea-orthodeoxia syndrome, POS) after pneumonectomy can result from re-opening of an atrial right-to-left shunt through a patent foramen ovale (PFO) due to mediastinal distorsion. Review of literature also shows a unique report of pulmonary veins stenosis resulting in POS without intracardiac shunt after pneumonectomy.
Methods: We report the case of a 32-year-old woman who presented POS 6 months after right pneumonectomy for destroyed lung post tuberculosis.
Results: The patient described severe dyspnea disappearing when lying. SpO_2 decreased from 94% when lying to 60% sitting. Transthoracic echocardiography (TTE) suspected a possible PFO. We first tried to highlight clinical repercussions of PFO by noninvasive exams. Hyperoxia shunt quantification was not tolerated because of increased dyspnea in sitting position. Contrast bubbles TTE was difficult because of the important mediastinal shift but identified only rare left heart bubbles with/without Valsalva both in lying and sitting position, excluding a significant right-to-left shunt. A lung perfusion scintigraphy (injection while sitting) confirmed the absence of systemic isotope uptake. Computed tomographic pulmonary angiography (angio-CT) revealed a stretched but not stenosed left main bronchus, while the shift of the heart into the right cavity was major. Pulmonary angiography did not show embolism but revealed compression of the inferior vena cava (IVC) with impaired venous return to the right heart, as well as compression of the left pulmonary veins. There was no arteriovenous shunt. Cardiac MRI showed torsion of IVC at the level of the diaphragm, and strong atrial contraction contributing to a passive filling of the RV, while the right ventricle was normal. Right catheterism showed major hemodynamic disturbances with negative diastolic pressure in right heart cavities (atrium –12 mm Hg ventricle pressure –7 mm Hg). SaO_2 measured in the pulmonary artery decreased from 58% when lying to 45% sitting.
Conclusion: We described here an exceedingly rare and complex mechanism explaining POS after right pneumonectomy. Mediastinal repositioning with a silicone breast implant of appropriate size has been scheduled.

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A fastidious cough after pregnancy

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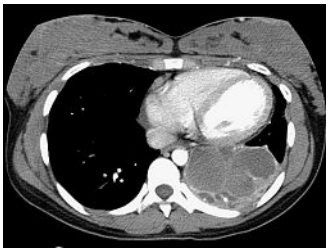
A 28-year-old woman presented to her physician because of cough lasting four months, halitosis and since a couple of weeks purulent and smelly sputum. She came from Santo Domingo but lived in Switzerland since five years. She was a healthy non smoking women known only for asthma with an exacerbation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



Poster session V

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

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Background: Smoking is a well known risk factor for cardiovascular, lung and many other diseases. Smoking can induce pulmonary arterial hypertension (PAH) in animal models and PAH is common in smokers with chronic obstructive pulmonary disease (COPD) and thereby not correlated to the degree of airway obstruction. The impact of tobacco smoke exposure on the development of PAH in human is not known.
Methods: In a case control study we assessed smoking and secondhand smoke exposure in all patients with PAH and chronic thromboembolic pulmonary hypertension (CTEPH) seen at our PH clinic from 2002 until July 2008. Data from PAH-patients were compared with CTEPH and healthy controls from the Swiss health survey 2007 (SHS).
Results: 91 PAH-patients were compared with 64 CTEPH-patients and 18747 controls (women 58, 36, 10331 respectively). Tobacco smoking was significantly more common in PAH compared to CTEPH and controls. This difference could be attributed to men. PAH-patients also smoked longer and heavier compared to CTEPH. In addition, secondhand smoke exposure was significantly more common in PAH-non-smokers compared to controls.
Conclusion: Our data indicate that tobacco smoke exposure may be a risk factor for men with PAH. Considering smoking as a risk factor for PAH will have implication in counseling patients and especially their hitherto unaffected relatives. Further research on the pathogenetic role of smoking in PAH is warranted.

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Factors influencing the success rates of smoking cessation intervention

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Background: At the cantonal hospital of St. Gallen (KSSG) smoking cessation counselling, as in other hospital settings, is under-utilized. One reason could be the absent or non-obvious association between smoking and the actual patient's diagnosis. We speculated whether patients from different departments react with different quit rates. Our aim was to evaluate which factors influence the success of smoking cessation.
Methods: We retrospectively analyzed the short-time success rate of 645 patients registered to the smoking cessation consultation at the KSSG between 2006 and 2009. The medical attendance provided by a trained physician consisted of counselling and optional pharmacological treatment. Using logistic regression, we tested the

influence of various factors (including referring department, diagnosis, malignancy and motivation assessed with the Prochaska-staging) on the quit rate 1 month after first consultation.
Results: More than half of 232 patients with a 1-month follow-up quit smoking (overall estimate quit rates between 2006 and 2009: 31–47%). We did not find any relationship between quit rate and the department referring the patient (χ^2-square test: p = 0.827). In addition, there was no significant difference between quit rates and different diagnoses. The presence of malignancy had no effect on the quit success (p = 0.54, OR = 0.8 [0.4–1.8]). On the other hand, motivation was significantly associated with the success rate. Patients in the active Prochaska stage have much higher success rates as compared to the low-motivated patients (p = 0.004, OR: 12.3 [2.6–89.9]).
Conclusion: Success rates after smoking cessation counselling and treatment seem to be independent of the department referring the patient and current diagnosis (incl. malignancy) leading to hospital admission. Motivation is a key factor in the smoking cessation process. Therefore, medical care givers of all departments should be encouraged to provide support in smoking cessation to every smoker; i.e. all patients should systematically get a short intervention at the time of admission, and motivated patients should be sent for additional intervention.

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Efforts of industry to influence tobacco control policy in Switzerland

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Background: Starting in parliament in 2004,the federal law on protection from passive smoke was voted in 2008.It allows smoking establishments and "fumoirs", where food may be served. Thus it does not meet international standards of the Framework Convention of Tobacco Control(FCTC), suggesting heavy lobbying during its elaboration despite low profile of the Tobacco industry(TI).
Aim: To find proofs for influencing policy by TI and proxys.
Method: Analysis of media reports, archives and parliamentary debates.
Results: 1990: The law on no smoking tables is rejected by the cantonal parliament of Lucerne. Philip Morris (PM) attributes this (intern.note PM2024195742) to briefing of its "allied" members of Parliament, the director of the restaurant owners association and the cantonal head of USAM (Schweiz.Gewerbeverband). 1992: The later rejected "twin initiative" to ban tobacco and alcohol advertising was diverted by the publicity industry to a debate about "abusive" restrictions on advertising. 1994: PM infiltrates HOtelREstaurant CAféInternat.and Gastrosuisse(GS). 1995: Internat.HoReCa congress is sponsored by PM: members of GS and its later director Fl.Hew participate. The congress resolution(rejection of "trends to ban eating, drinking and smoking", of governement interference and free choice of owners to decide about smoking) is re-edited 1996 by GS. 2005: Law professor Auer, paid by Reynolds Tobacco, refutes the constitutionality of the Geneva popular initiative for smoking ban. 2004-08: attempts to dilute the law proposal for a federal smoking ban come all from GS and USAM. Fl.Hew is at parliamentary hearing. 2008: USAM, GS, Hotelerie-suisse, Swiss publicity, Swiss Zigarren-fabrikanten, Swiss Tabakwarenhandel and others create the alliance on economy for a moderate prevention policy (AWMP). The USAM journal denigrates the head of the federal public health authority as "health taliban", the term is repeated in popular newspapers and TV emissions.
Conclusion: The TI allies GS, USAM and Swiss publicity undermine tobacco control policy since the ninenties.Because all media are heavily dependent on advertising money, the covering of public health and prevention issues is likely to be strongly influenced by Tobacco interests.

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

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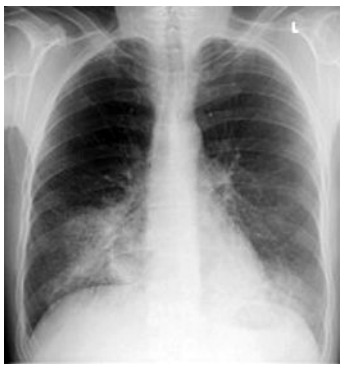
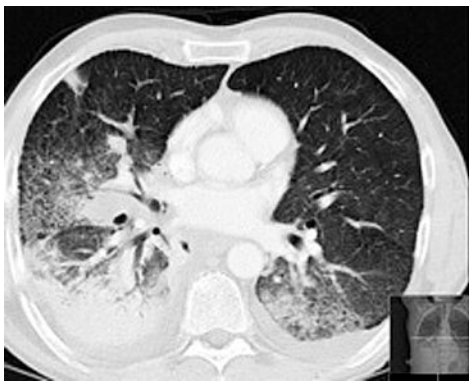
Background: Fire-eater's pneumonitis, also known as fire-eater's lung, is an acute imflammatory response of the lungs to the accidental aspiration of petroleum.
Case presentation: A 55-year-old, previously healthy, smoking, fire-eating male presented himself to the emergency department complaining of pleuritic pain, dyspnea, cough and hemopthysis. Two days before, during a pyrofluid performance, he accidentally aspirated a small amount of petroleum blowing out a mouthful petroleum against a burning stick. Physical examination revealed a cachectic, febrile and tachypneic patient with dullness on percussion and bilateral crackles. Blood tests showed elevated leukocytosis without left shift and a high serum level of CRP (100 mg/l). Chest radiogram and chest-CT revealed patchy bilateral alveolar infiltrates in the middle and lower parts of both lungs and pleural effusions (picture B and C). Within a week the patient's symptoms became worse with intermittend fever, hypoxemia requiring oxygen and a progession of the bilateral infiltrates and pleural effusions. Percutaneous catheter drainage was necessary. The bronchoscopy and cytobacteriologic findings were unremarkable. However, a treatment with antibiotics was started. The clinical and radiological course improved only slowly. After another four weeks of hospitalisation, the patient was ready for pulmonary rehabilitation. The intermittend fever attacks disappeared in the course of his rehabilitation. The clinical und radiological findings improved further, the arterial blood gases corrected and the lung function tests normalised. The patient reached a distance of 600 meters in his six-minute walk test.
Conclusion: 1. Fire-eater's pneumonitis is an infrequent clinical occurence caused by the accidental aspiration of petroleum products during a show of a fire-eater.
2. There is no good evidence, that systemic corticosteroids and antibiotics were effective in treating hydrocarbon aspiration.
3. The patient prepared his individual mixture of different petroleum distillates. This might also alter the clinical evolution.
4. This condition is a medical emergency and a potential cause of severe pleuropulmonary complications. Despite the severe initial clinical symptoms and radiological presentation, fire-eater's pneumonitis has usually a favourable evolution with "restitutio ad integrum".





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Severe acute respiratory distress syndrome after smoke bomb explosion

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A 23-year-old Swiss soldier was exposed to artificial smoke containing zinc chloride (ZnCl2) during a military exercise. He developed progressing respiratory distress, which led to respiratory failure and ARDS. Respiratory failure after $ZnCl_2$ exposure is a known toxic reaction and is usually prevented by wearing gas masks or by avoiding the use of zinc chloride-producing grenades at all. Only limited data are available regarding pathogenesis, clinical course or effective therapeutic strategies. Outcome in most reported cases was fatal. We present a case of acute alveolar injury after inhalation of $ZnCl_2$ to discuss its implication on lung structure and function over the course of acute illness and final recovery. We further summarize current knowledge and concepts in the management of patients exposed to smoke containing $ZnCl_2$. Zinc chloride is a major byproduct of chemical reactions occurring during the blast of explosives used as smoke bombs primarily in military settings. Due to their small size of 1 micrometer and their dense concentration, $ZnCl_2$ particles easily enter into the bronchial tree and eventually into the alveoli, thereby provoking a severe inflammatory response. As in our case, dramatic

structural changes have been documented in computer tomography series. Diffuse ground glass opacities in early phase are progressing to structural changes like interstitial infiltrates and parenchymal destruction with development of pneumatoceles and pneumothoraces. Therapeutically, apart from mechanical ventilation, no intervention is established nor does an antidote to $ZnCl_2$ exist. N-Acetylcystein, as a chelating agent, or steroids have not shown to improve outcomes. Treatment is thus limited to strict adherence to lung protective strategies during mechanical ventilation. Despite the generally grim prognosis, the mentioned radiological changes are potentially reversible as is the loss of lung function. Repeated lung function testing in our patient over several months showed impressive improvement in all markers of respiratory functions, particularly DLCO and ergospirometries. We conclude that despite of the deleterious effects of $ZnCl_2$ inhalation, outcome may be positively influenced by applying advanced respiratory ventilation concepts and by early rehabilitation. Further we suggest that use of smoke bombs containing $ZnCl_2$ should be banned from any exercise setting, military or other, because of the extremely destructive pulmonary effects described above.

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

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Background: A smoking cessation service (scs) exists at the Bürgerspital Solothurn since 1999 (1). With a one-off financial incentive by the Hospital Quit Support project of the Swiss Federal Office of Public Health (2) a smoking cessation counsellor could be recruited. We report on our data over 19 months 2008/09.
Methods: Behavioural and pharmacologic counselling for in- and outpatients as well as for employees by a MD and a counsellor specially trained in smoking cessation. Follow-up visits 1 and 3 months after first counselling and a phone call on Nov 30 2009 in pts with >= 3 interventions.
Results: 286 patients (pts) were admitted (176 men, 110 women): mean age 52 years (SD 13.5), 21.9 (SD 11.3) cigarettes/day, 41.2 (SD 28.2) pack years, Fagerström Test for Nicotine Dependence (0 low – 10 high): 4.4 (SD 2.4); 577 interventions overall. Interventions consisted of councelling alone (51% of pts), NRT (31%), Varenicline (16%), bupropion and bupropion/NRT (2%). At follow-up visits after 1 and 3 months 51/94 pts (54%) and 27/65 pts (42%) were quitters respectively. After 1 month 15/19 (79%) inpts and 36/75 (48%) outpts were quitters (p = 0.016) whereas no difference was found after 3 months. At the phone call Nov 2009 12/63 pts (19%) were smoke-free for more than 6 months (mean 396 [SD 127] days). 15/42 persistent smokers (36%) stopped smoking temporarily for <= 3 months (n = 8) and 3-6 months (n = 7). 14/42 persistent smokers (33%) reported a transient reduction of smoked cigarettes to <50%. Pts' ratings of our scs and the recommended medication were "not helpful" (8%/49%), "little helpful" (17%/14%), "helpful" (32%/16%) and "very helpful" (43%/21%) respectively.
Conclusion: Our scs had an important impact on smoking pts and prompted a substantial number of them to stop smoking either definitively or temporarily or to reduce the number of cigarettes smoked. A follow-up after discharge from hospital is crucial. The scs was very much appreciated, 75% of pts rated it as helpful or very helpful. The reserved ratings of the medications' helpfulness may be due to the fact that pts still have to pay for it and therefore tend to use it scarce. Scs should be made standard practice in hospitals and health insurance companies should accept the costs of medications for smoking cessation.
1) Eur Respir J 2005;26(Suppl.49):245s. 2) Swiss Med Wkly 2008;138(29–30):427.
Funding: This study was supported by the Swiss FOPH and by Pfizer.

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

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Background: Initiated 2004 by MP Gutzwiller, MD, the federal law on protection from passive smoke exposure was passed 2008.It comprises exceptions: smoking establishments and "fumoirs" with food service. Thus it fails to meet international standards of the WHO Framework Convention of Tobacco Control, signed by Switzerland in 2004, suggesting heavy lobbying by proxys of the Tobacco industry(TI).
Aim: To determine the political support/opposition of/to efficent Tobacco control measures by the federal parliament during elaboration of the new law.
Method: Analysis of parliamentary records, news reports and the smartvote database (pre-election answers of MP's).
Results: The original proposal of smoking ban in workplaces was expanded by the multiparty commission of the National council (lower chamber)to include public places, nonserviced "fumoirs" only tolerated. But the commission's minority proposal (smoking establishments and served "fumoirs" tolerated) by a SVP (right wing) party MP, on behalf of Gastrosuisse, was adopted by the lower chamber by 95 yes/77 no, in 2007. Four MP's of the CVP party and 2 of RL party voted for the adopoted proposal, while they were for a smoking ban according to smartvote. In fall 2007 elections took place. A newspaper reported that 56 of 62 newly elected MP's from french speaking Switzerland were for smoking bans in public places. For the debate of the upper chamber Swiss thoracic society's members wrote to MP's of the upper chamber: passive smoke is toxic, health professinals are not extremists, compromise only serves TI. MP's of both chambers received the book on the Philip Morris/Rylander case. By a vote of 25 yes/9 no and 2 abstentions the upper chamber adopted a smoking ban with the only exception of "fumoirs", where food would be served, provided written consent by the waiters; Cantons can enact stricter laws. In contrast, the lower chamber kept its proposal allowing smoking establishment and served "fumoirs" by 94 yes/86 no. Five CVP, 2 SVP, 2 RL and 2 SVP MP's did not vote as stated to smartvote and 15 out of the 56 MP who were for a strict smoking ban voted yes. Finally the actual law passed by a minimal majority.
Conclusion: Support of an efficent smoking ban is strongest on the left wing of the political spectrum and nearly none on the right. Voting discipline is strong (but not absolute)at both extremes, while discrepancies between declared opinion and actual vote are found in the center, more so in CVP than in RL.

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