



ZDRUŽENJE PNEVMOLOGOV SLOVENIJE
SLOVENIAN RESPIRATORY SOCIETY

Zbornik povzetkov: Book of Abstracts

MEETING OF THREE RESPIRATORY SOCIETIES:

Slovenia, Croatia, Hungary

Portorož, Slovenia, May 8-9, 2009

Published by
Slovenian Respiratory Society

Editors
Nadja Triller
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Portorož, Slovenia, May 8-9, 2009

Number of copies: 200

Abstracts in this book have not been edited.

CIP - Kataložni zapis o publikaciji
Narodna in univerzitetna knjižnica,
Ljubljana

616.2(082)

MEETING of Three Respiratory Societies:
Slovenia, Croatia, Hungary
(2009 ; Portorož)
Zbornik povzetkov = Book of abstracts
/ Meeting of Three
Respiratory Societies: Slovenia,
Croatia, Hungary, Portorož,
Slovenia, May 8-9, 2009 ; [editors Nadja
Triller, Mitja Lainšček].
- Golnik : Slovenian Respiratory
Society, 2009

ISBN 978-961-91900-4-3
1. Triller, Nadja
245489664

This meeting has been kindly supported by:

Astra Zeneca
Boehringer Ingelheim
Glaxo SmithKline
Medis
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PROGRAM

Friday, May 8: 9.00–17.00

1. Pulmonary Medicine Emergencies

8.30–9.00	<i>Registration</i>	
9.00–10.30	<i>Chairpersons</i>	<i>Ema Mušič, Attila Somfay</i>
9.00–9.15	Franc Šifrer	Severe community-acquired pneumonia and nosocomial pneumonia
9.15–9.30	Ema Mušič	Acute exacerbation of COPD
9.30–9.45	Tjaša Šubic	Severe asthma
9.45–10.00	Darinka Leiler Trinkaus	Acute respiratory failure – role of noninvasive and invasive ventilation
10.00–10.15	Nadja Triller	Interventional bronchoscopy in malignant stenosis of large airways
10.15–10.30	Goran Popić	Near drowning: fresh water, seawater or cold water – is there any difference?
10.30–11.00	<i>Coffee break</i>	
11.00–13.00	<i>Chairpersons</i>	<i>Katarina Osolnik, Goran Popić</i>
11.00–11.15	Marjeta Terčelj	Hemoptoe
11.15–11.30	Katarina Osolnik	The diffuse alveolar haemorrhage syndromes
11.30–11.45	Matevž Srpčič	Acute mediastinal conditions
11.45–12.00	Aleš Rozman	Pleural disorders
12.00–12.15	Miha Mežnar	Anaphylaxis: rapid recognition and treatment
12.15–12.30	Mitja Lainščak	Acute right and left heart failure
12.30–13.00	Satellite symposium	Medis
13.00–14.00	<i>Lunch</i>	
13.00–13.30	Lunch session	Mitja Lainščak: How to write a good manuscript
13.30–14.00	Poster Discussion (1-7)	Ema Mušič, Károly Fónay
14.00–14.45	Stefan D. Anker	Cachexia in patients with COPD, CHF and cancer
14.45–15.30	<i>Chairpersons</i>	<i>Barbara Salobir, Franc Šifrer</i>
14.00–15.30	Case reports (4)	Interactive session
15.30–16.00	<i>Coffee break</i>	
16.00–17.30	<i>Chairpersons</i>	<i>Gabriella Galfy, Nadja Triller</i>
16.00–17.30	Oral presentations	
16.30–17.15	Satellite symposium	Boehringer Ingelheim, Pfizer
19.00	<i>Gala dinner</i>	

Saturday, May 9: 9.00–18.00

2. Obstructive Pulmonary Diseases

9.00–10.20	<i>Chairpersons</i>	<i>Sanja Popović Grle, Matjaž Fležar</i>
9.00–9.20	Sanja Popović Grle	Diagnostic methods in asthma
9.20–9.30	Matjaž Fležar	Asthma – how to choose and interpret lung function tests – a view of a referring physician
9.30–9.40	Matjaž Fležar	COPD – how to choose and interpret lung function tests – a view of a referring physician
9.40–10.00	Jelena Ostojčić	COPD and heart failure
10.00–10.15	Aleš Rozman	Clinical manifestations and diagnosis of bronchiectasis
10.15–10.35	Satellite symposium	Astra Zeneca
10.35–11.10	<i>Coffee break</i>	
10.35–13.00	<i>Chairpersons</i>	<i>Jelena Ostojčić, Mitja Košnik</i>
11.10–11.30	Attila Somfay	New interventions in the rehabilitation of patients with COPD
11.30–11.45	Jurij Šorli	Quality of life and functional capacity improved (walking tests, SGRQ questionnaire, BORG and MRC scales) in the group of patients with COPD, who participated pulmonary rehabilitation
11.45–12.00	Matjaž Fležar	Adult cystic fibrosis – multiple inhalation therapy
12.00–12.10	Luka Camlek	Patients with lung disease and air travel
12.10–12.30	Satellite symposium	Glaxo Smith Kline
12.30–13.30	<i>Lunch</i>	
12.00–13.00	Lunch session	Aleš Rozman, Jurij Regvat: Meeting of young pulmonologists from Slovenia, Croatia and Hungary
13.00–13.30	Poster Discussion (8-14)	Tamas Major Sr., Mitja Košnik
13.00–14.30	<i>Chairpersons</i>	<i>Tamás Major Jr., Matjaž Turel</i>
13.00–14.30	Case reports (4)	Interactive session
14.30–15.00	<i>Coffee break</i>	
15.00–16.30	<i>Chairpersons</i>	<i>Neven Miculinić, Ilonka Osrajnik</i>
15.00–17.00	Oral presentations	

Pulmonary Medicine Emergencies, Friday, May 8, 09:00-12:30

PL1-01

Severe pneumonia

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Community-acquired pneumonia (CAP) is considered as severe when admission to the intensive care unit is necessary. This may be indicated because of severe respiratory distress, sepsis or septic shock, and occurs in about 9-16 % of hospitalized CAP patients.

Criteria for severe pneumonia include having a respiratory rate above 30, multi-lobe involvement on chest x-ray and severe hypoxemia. Patients have a fatality rate up to 50% and most likely have pneumonia resulting from *S. pneumoniae*. Mortality remains high in spite of adequate antibiotic therapy and management of comorbidities. Because of differences in baseline characteristics, mortality, and pathogens there is a relatively new concept of health-care-associated pneumonia (HCAP) – it includes patients with any of the following: hospitalization for more than 2 days in the preceding 90 days, residence in nursing home or extended care facility, home infusion therapy (including antibiotics), long-term dialysis or home wound care. In case of HCAP we should routinely consider multi-drug-resistant pathogen in determining the empirical treatment. Early recognition of the severity of the illness, rapid and appropriate resuscitation, targeted antibiotic treatment, and the critical care support of multiple failing organ systems are all important aspects of care. Despite the fact that evidence for some recommendations are weak appropriate process of care should include assessment of oxygenation, performing blood cultures before initiating antibiotic therapy, administering first antibiotic dose within 4 hours of presentation and early goal-directed therapy of sepsis.

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Updated approach to acute exacerbation of COPD (AECOPD)

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Definition of AECOPD

AECOPD is clinically defined by Anthonisens criteria as: increased sputum volume, increased sputum purulence and increased dyspnea over baseline. The most severe, or type I, exacerbation includes the presence of all three of these symptoms. A type II exacerbation exhibits two symptoms. A type III exacerbation has one symptom plus at least one of the following: an upper respiratory tract infection in the previous five days, increased wheezing, increased cough, fever without an obvious source, or a 20% increase in respiratory rate or heart rate above baseline.

In pathogenetic sense, AECOPD means acute worsening of symptoms, increased airway inflammation and physiologic deterioration. The most common cause is infection and air pollution, but 1/3 of cases remain unidentified. *The frequency of AECOPD has an important influence on accelerating the decline in FEV1 that is on prognosis of COPD.*

Some clinicians propose the use of major and minor criteria to define an exacerbation. The major criteria are the three from Anthonisens group. The minor criteria include wheeze, sore throat, or symptoms of a common cold such as nasal discharge or congestion. The AECOPD must have the presence of at least two major symptoms or one major and one minor symptom for at least two consecutive days. The typical patient with COPD has averages two to three AECOPD episodes.

The new GOLD document defines AECOPD as » an event in the natural course of the disease characterized by a change in the patient dyspnoea, cough and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a **change in regular medication in a patient with COPD**. The airway inflammation is enhanced at exacerbation.

The causes AECOPD

The mainly causes of AECOPD are microorganisms and pollutants. The causes of exacerbations may be multiple, but we have no good way to identify them in individual cases. There is good evidence that both viruses and bacteria may cause exacerbations, but it is hard to tell these two etiologies. It is very likely that some exacerbations occur also without infections due to pollution, smoking, heart insufficiency. It has to be stressed also a chronic bacterial colonization or even a subclinical chronic bacterial airway infection in progressive forms of COPD, where the airway remodeling enables no efficient mucociliary clearance more. Even in non-infectious primary cause, the secondary infection is common occurring, so the AECOPD often indicates the antimicrobial therapy, while bacterial colonization in advanced stages of COPD progresses to clinical infection. Therefore, AECOPD is preventable and treatable phase of disease, in that pulmonary and extrapulmonary effects contribute to the severity in individual patient. Antimicrobial therapy is crucial in treatment to achieve the duration of

AECOPD. We must ensure extra hospital and hospital care of patients according to stage of COPD and severity of AECOPD. Next to antibiotics new statements are given also for long-acting β 2-agonists and inhaled glucocorticoids, both are favorising in severe AECOPD and in patients with 2 or more exacerbations yearly.

Severity assessment of AECOPD and antibiotic therapy.

The severity assessment is based on the patient medical history in stable phase, symptoms, physical examination, lung function tests, arterial blood gasses measurements, and other laboratory tests. According to the GOLD, classification of severity from 2003 four different classes should be differentiated based on the lung function measurements in the stable phase, the main criteria is FEV1 in that condition.

Anthonisen and co-workers developed classification-identifying patients that benefited from antimicrobial therapy. The patients with all three symptoms: increased dyspnoea, increased sputum volume, sputum purulence improved better with antibiotics compared with patients on placebo. Patients with only one symptom did not differ from those on placebo. In patients with slight diminished FEV1 in stable phase (Severity 1) the bacteria causing AECOPD are *Streptococcus pneumoniae*, *Haemophilus influenzae* and in elderly *Moraxella catarrhalis*, can be also some atypical. In moderate obstruction rate with FEV1 about 50% (Severity 2) of normal, the causing bacteria are like from severity group 1 and additionally *Klebsiella pneumoniae*, *Staphylococcus* species. In more severe chronic persistent obstruction with FEV1 lower than 50% (Severity 3) bacterial infection is mostly mixed with presence of *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Escherichia coli*, *Enterobacteriaceae*, *Pseudomonas aeruginosa*, also more invasive or resistant *Streptococcus pneumoniae*. In each severity group, 1, 2, 3 the empiric effective antibiotics are suggested. In Severity 1, the older amoxicillin and macrolides are the true choice, but in severity 2 or 3 the superiority of amoxicillin+clav (AMC) has been stressed in many studies. Second and third generation of cephalosporins represent the alternative in more severe AECOPD. They can be in initial days combined by macrolides like Clarithromycin or Azithromycin by adding next to anti-infective also their immunomodulatory effects. In last years, the new respiratory quinolons are combating in the efficacy for the first place, since they are effective against most community- acquired respiratory pathogens. In expecting Gram-negative infection Ciprofloxacin is the first choice, in Gram positive and atypical infection can be resistant to β -lactams, the Moxifloxacin is more and more suggested.

What is the mortality of AECOPD?

Hospitalization due to AECOPD carries a 4% short-term mortality rate for patients with mild-to-moderate disease. The mortality rate can be up-to 24% in those admitted to ICU with respiratory failure. Even in case of survival of such severe patients, the one-year mortality rates of up-to 46%. The readmissions are often needed. The antibiotic choice is very important and must be combined and isolation of pathogen and sensitivity oriented. Our analysis from 2008 showed the mortality in severest forms of hospitaly treated AECOPD in 4%.

The role of bacterial inflammation

Four possible bacterial mechanisms may result in changes in bronchial inflammation during exacerbation:

- New strain in colonization
- Antigenic production of bacteria
- An increase of bacterial load
- A relative increase of inflammatory potential of colonizing flora

In patients with secondary bronchiectases, the colonization with *H. Influenzae* has shown that some exacerbations are associated with changes in the outer membrane protein gene, while the phenotype is similar to the stable state isolate.

Evidence indicates that the presence of purulent sputum as opposed to mucoid sputum is one of the best and easiest methods of predicting a high bacterial load in respiratory tract secretions and the need for antibiotic therapy. The Gram stain of the sputum is the most usable method for assessing infective AECOPD. Errors in the microbiological sampling may cause problems in diagnosis, while intracellular *H. Influenzae* is present in advanced COPD, and not always in secretions and also bad sputum samples is the problem.

Recent advances in AECOPD

COPD patients have about 0,5-3,5 AECOPD/year and 0,09-2,4% hospitalizations/year. The mortality rate in GOLD stages 3 or 4 is to 42,9/1000 person. The airway bacterial and viral infection and colonization favorise enhancing of inflammation, therefore suppressing of them leads to less episodes of AECOPD. Also cold season predict the AECOPD. Current research deals by genetic guided upregulations of chemoattraction of neutrophils, activation and production of proinflammatory cytokines, the relationship of oxidant/antioxidant in bronchial mucosa. The simplest biomarkers of inflammation in serum are CRP, fibrinogen, procalcitonin; they should be followed during treatment showing in case of improvement the longer prediction of new exacerbation. Persistent high CRP, fibrinogen and IL-6 can predict longer term risk of decline in lung function, hospitalizations and higher mortality. Adrenomedullin is another member of calcitonin peptide superfamily and improve the prognostic assessment of AECOPD. Various hormones are biomarkers and inflammatory mediators. They combat against invading microbes. Fibronectin is a marker of repair and in relation to CRP shows the better outcome.

Update in AECOPD 2009

AECOPD have a marked effect on quality of life, morbidity and mortality in COPD. Reducing exacerbations is an important outcome measure in evaluation of COPD treatment. Older patients and those with milder stages of COPD have less episode of AE. In more severe stages in AECOPD the clinical signs and the biomarkers of inflammation must be used as objective measure to monitor the development and resolution of exacerbation. Australian study showed isolated serum amyloid A (SAA) as specific biomarker of AECOPD, especially in infective cause. It should be more sensitive than CRP. In prediction of mortality, the bad criteria are age > 70years, number of clinical signs of severity (cyanosis, impaired

neurological status, lower-limb edema, asterixis, use of accessory respiratory muscles), dyspnea grade at baseline.

Treatment of AECOPD

Medical therapy includes bronchodilators, steroids, antibiotics, Oxygen therapy, theophyllines. All from the world and our SLO societies is declared in Zdrav Vestn 20098:19-32. Diagnostic and therapeutic approaches are suggested and the indication for hospital admittance as well. The most important is the following of diseases symptoms, oxygenation and the dynamic of inflammatory parameters. The hospital admission is needed:

Impairment of respiratory insufficiency

- Marked impairment of dyspnea at rest
- Severe stage of COPD
- Respiratory acidosis
- Raising cyanosis, peripheral edema
- The comorbidities worsening
- Cardiac arrhythmias
- Not proven AECOPD
- Social factors

In hospital, the most important measure is the decision for noninvasive or invasive mechanical ventilation, controlled oxygen supply, surway of comorbidities and rational and microbiological suggested and evidenced antibiotic therapy. Other measures are pharmacotherapy, chest physiotherapy, new respiratory stimulants, supportive measures, palliative care for the terminally ill, the plan of discharge and suggestions for home regime and the insurance of future control.

Modifications of current therapy

Long-acting β_2 agonists may find increasing use as rescue therapy, so also long-acting antimuscarinics. Some anti-infective agents include antimicrobial peptides, new antiviral and toll-like receptor antagonists. Teophylline is returning in therapy of COPD through its activity on alveolar macrophages. Phosphodiesterase inhibitors have been shown to inhibit the formation of reactive oxygen species and leukotriene B₄ synthesis. Leukotriene B₄ and IL-8 antagonists may inhibit chemotaxis. Further work must be done on the interaction between viruses and bacteria. Does viral infection trigger the swift strain of colonizing bacteria or is it the effect mainly on bacterial load? The future therapy should specific inhibit the inflammatory pathway in the airways.

Fudostein is a novel mucoactive agent, which may inhibit the mucin production by reducing mucine hypersecretion-Gen expression.

Antibiotic use in AECOPD is established as effective in infection and appropriate choice reduces risk of subsequent AECOPD, especially if added to oral corticosteroids for shorter time. B-blockers are safe in AECOPD, but with caution if BHR or dynamic asthma is accompanied state. **Antibiotic prophylaxis is not general suggested for COPD** cases, except for diffuse panbronchiolitis and cystic fibrosis.

Anxiety and depression in COPD

Symptoms of anxiety and depression are common in COPD. Cognitive behavioral and antidepressive therapy like selective serotonin reuptake inhibitors, tricyclic antidepressants and low-dose benzodiazepines can be effective in treating some patients only in AECOPD or permanent.

From studies on etiology, diagnostics and therapy of AECOPD at Respiratory Clinic Golnik

1. In 169 patients admitted to pulmonary department due to AECOPD, the bacterial infection as primary or secondary cause was established in 2006 58% of cases. The causing bacteria were in Severity I group: *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis* and Atypicals. In Severity 2 group, we found *Klebsiella pneumoniae*, *Proteus* species, *Escherichia coli* and the pathogens like in Severity group 1. The severity group 3 was infected mostly by Enterobacteriaceae, *Pseudomonas aeruginosa*, resistant *Haemophilus influenzae* and in some cases was the infection combined. In 2006, we analyzed 112 hospital treated patients with stage I (Anthonissen), at least 3 exacerbations/year. We compared the effectivity of two antibiotics: Amoxicillin / Moxifloxacin. Clinically significant sooner was the improvement in cases on Moxifloxacin according to favorable and fast penetration into bronchial mucosa and bactericidal properties for respiratory pathogens. That is comparable with some prominent international studies on AECOPD. Such therapy enables also faster improvement of lung function deterioration, the airway resistance becomes sooner on stable level of the patient, so hypoxemia and also extrapulmonary symptoms are improving.

2. Similar analysis from year 2007 made by Polak D. Et al in 242 patient with severe or very severe COPD in 95,5% of them showed good quality lower respiratory tract specimens in 60,9%. The most frequently isolations were *Pseudomonas aeruginosa*, *Haemophilus influenzae* and *Stenotrophomonas maltophilia*, followed by *Moraxella catarrhalis*, *Staphylococcus aureus*, *Acinetobacter baumani*, *Str. Pneumoniae*, *Klebsiella oxytoca* and *E.coli*. *H. Influenzae* isolates were resistant to ampicillin and in 20% to cotrimoxazol, but not resistant to macrolides and fluorquinolones. None of *Pseudom. Aeruginosa* was R to Ceftasidim, Imipenem, Ciprofloxacin, but 50% were R to cefotaxim and ceftriaxon. Amoxicillin +clav.acid was most often prescribed (44%), followed by Moxifloxacin (28%), Ciprofloxacin alone (9%), and Cipro.+ Ceftazidim (6%). In together 25% of isolations, the resistance to empirical chosen antibiotic was found.

Again, in 2008 the analysis of severest AECOPD was done at Golnik By Music et al. In 127 patients, 43% of them were on home oxygen therapy in stable phase. Only in 40 % of cases, the sputum was qualitative for analysis of pathogens. The most frequent pathogen was *P. aeruginosa* alone or in combination with Enterobacteriaceae, followed by *H. Influenzae*. Rare isolations were *Str.pneumoniae* or MSSA. The treatment according to the guidelines improved the cases, except of 5 patients who died. So severe infective AECOPD require hospital admission and experienced, microbiological supported therapy and other

supporting measures for comorbidities. In out of 37 cases of this group only 2 patients had not elevated value of CRP, the others had moderate to severe elevation of CRP according to moderate or more intensive Anthonissens clinical signs of AECOPD with mean value 47+/- 56 mg/L and the highest value was 218 mg/L.

The new Slovenian guidelines for treatment of AECOPD

In April 2008 the Slovenian guidelines was published, being formulated by pulmonologists, infectologists and general practitioners with purpose to improve the quality insurance of aecopde diagnostics and treatment. The needed registration, follow up and mortality outcome according to frequency of AECOPB was suggested together with antibiotic therapy of AECOPD as follows:

1. For Severity group 1 with les then 2 AECOPD per year: Amoxycillin or one of the Macrolides.
2. For Severity group 2: Amoxicillin+clav or Cefuroxim or in cases with more then 3 AECOPD per year the Quinolons II (for Gram-) or Quinolons III- Moxifloxacin, Levofloxacin (for Gram+)
3. For severity group 3, that is the severest progressive and hypoxaemic stage of COPD: The Quinolons II/III or Cephalosporin III/IV or Amoxicillin+ clav are suggested according to general condition and comorbidities of the patient, also to known praevius aetiologies of AECOPD.

The classification of COPD in stable phase according to chronic obstruction and the severity assesment of infective AECOPD helps us in clinical approach to the patient, especially to antibiotic treatment. Other general measures for sustain the ventilation and oxygeanation together with support the heart sufficiency are also of great importance. Not only infection but also inflammatory activity and its consequences in systemic sense and in prognosis must be considered in each case of AECOPD, where therapy should include antibiotics, antiinflammatory agents and antisecretory approach. Biomarkers of inflammation in the blood, also CRP, PCT, fibrinogen can be helpful in management. And comorbidities should treated as well. The number of AECOPD episodes pro year is of great prognostic importance, therefore the therapy of each episode must be very intensive and under control.

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PL1-3

Severe asthma exacerbation

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Severity of asthma exacerbation is classified as mild, moderate, severe and near-fatal (respiratory arrest imminent) regarding particularly PEF, pulse rate, respiratory rate and pulse oximetry. The most prominent symptoms include severe breathlessness, important impairment of talk and changes in alertness. Severe exacerbations are potentially life threatening. Patients with severe asthma exacerbation are usually treated in hospital and near-fatal asthma exacerbation needs admission to intensive care unit and often mechanical ventilation. Last years less and less patients in our community present with severe asthma exacerbation thanks to good drugs, their availability and good medical education of asthma patients. Nevertheless, near-fatal asthma continues to be a significant problem when you have to face it. There are known risk factors for severe asthma exacerbations, especially for patients in risk for asthma related death and patients with such risk factors require closer attention. The primary therapies for exacerbations include repetitive administration of rapid-acting inhaled bronchodilators, early introduction of systemic glucocorticosteroids and oxygen supplementation. When intubation is needed it's usually difficult and mechanical ventilation of asthma patient is a special issue.

PL1-4

Acute respiratory failure – role of noninvasive and invasive ventilation

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The rationale of ventilatory assistance in acute respiratory failure (ARF) is to improve oxygenation and/or alveolar ventilation. Both goals can be achieved with noninvasive (use of mask) or invasive (use of endotracheal tube) ventilation. Choice of ventilation depends on local expertise and skills of the staff, appropriate equipment and severity of respiratory failure. Noninvasive ventilation (NV) can be tried first to avoid endotracheal intubation with its discomfort and risks related to sedation, airway damage and nosocomial pneumonia. NV was used prior to invasive ventilation in 16% of cases in surveyed ICUs in Europe. Prospective survey indicates that 60% of patients with ARF can be treated successfully with NV. Absolute contraindications to NV are imminent respiratory arrest, inability to clear respiratory secretions and shock. Close monitoring is necessary during introduction and in the following hours to assess the response to NV. In the case of failure of NV endotracheal intubation should be accessible without delay. The risk of subsequent intubation varies from 20% to 80%. Invasive ventilation remains to be used in the majority of patients to treat acute respiratory failure.

PL1-5

Interventional bronchoscopy in patients with central airway obstruction because of unresectable lung cancer

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Background. Intraluminal tumour growth of the major airways, extraluminal tumour compression, or combination of both can cause central airway obstruction. It can present with life-threatening dyspnoea or haemoptysis and may require urgent intervention. Clinical examination, imaging techniques, and flow-volume curves may provide diagnostic possibilities but the most important diagnostic procedure is bronchoscopy. Almost all endobronchial therapies are palliative. The currently available methods of bronchoscopic therapy include debulking of intraluminal tumour growth, balloon dilatation, laser therapy, electrocautery, cryotherapy, argon plasma coagulation, endoluminal irradiation, or intraluminal stent placement. Endobronchial procedures could be performed under local or general anaesthesia, either with a flexible or a rigid bronchoscope. We present five years experiences with palliative bronchoscopic treatment of central airway obstruction by malignant tumours.

Patients and methods. Patients with advanced inoperable malignant tumours of central airways were admitted because of symptoms caused by tracheobronchial obstruction. Bronchoscopic examination and/or treatment were performed with flexible bronchoscope and in half of them, rigid bronchoscope was used additionally. We found the bronchoscopic intervention successful when the majority of endobronchial tumour was resected, dyspnoea was relieved and atelectatic lung parenchyma was reventilated.

Results. 102 patients (81 men, 21 women, mean age 62 years) with advanced inoperable malignant tumours were treated in five-year period. Successful improvement has been obtained in 76% (78/102) of our patients. Eleven patients required repeated procedures. No major complications were encountered.

Conclusion. Our study demonstrates that unresectable tracheobronchial tumours could be successfully removed by presented therapeutic techniques. Immediate relief of symptoms improves patient's quality of life.

PL1-6

Near drowning: fresh water, sea water or cold water – is there any difference?

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Near drowning is the survival of a drowning and can lead to secondary complications including death. The principal physiologic consequences of immersion are prolonged hypoxemia and resultant acidosis which can exist without clinical signs. All near drowning victims should be transferred to hospital for pulmonary screening. Patients without evidence of significant injury, bronchospasm, dyspnea or inadequate oxygenation can be safely discharged

from the Emergency Department after eight hours of observation. Immediate on-site resuscitation is the key to increasing the chance of survival. There is generally no difference between fresh and salt water near drowning regarding outcome or treatment. The chance of survival in warm water is much less than in cold water. The colder the water, the better chance for survival. No specific maneuvers are mandatory to expel water from the lungs. Clinical course of 46 consecutive near drowning victims treated in General Hospital in Pula was retrospectively revived. The majority of near drowning incidents involve swimmers, males, young and otherwise-healthy individuals, mainly tourists. In some cases the influence of alcohol, while in some older individuals heart attack, seizure or stroke were noted.

PL1-7

Massive haemoptysis

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Key words: massive haemoptysis, bronchoscopy, chest radiography, CT chest,

Introduction: Massive haemoptysis represents one of the most challenging conditions in clinical practice. Mortality is a function of the amount of blood lost, the underlying disease/condition and the treatment. The cause of death, as a rule, is not exsanguinations but asphyxia due to the blood flooding the bronchial system. The site and the cause of massive haemoptysis have to be determined. A chest radiogram is often not enough, and usually computerized tomography (CT) and/or bronchoscopy is usually necessary. The aims of treatment are preservation of vital function, hemostasis and dealing with the underlying cause of bleeding.

Methods and patients: A retrospective study was undertaken of 48 patients (38 males, 10 females) with massive hemoptysis admitted to the Department of Pulmonary Diseases and Allergy, University Medical Centre Ljubljana, from June 1998 through December 2008.

Results: Among the 48 patients 9 patients had lung cancer, 17 patients had pulmonary infection and/or TB, 2 patients had iatrogenic trauma with massive haemoptysis. Ten patients had other diseases such as pulmonary hypertension, AV pulmonary malphormation, pulmonary embolism, pulmonary angiectasies, and congestive heart diseases. Among 10 patients the etiology was not identified. Three patients died. Two had lung cancer and one pulmonary hypertension. CT angiography has been done in 38 patients and 17 out of them were successful. One had unsuccessful surgery procedure.

Conclusion: Massive hemoptysis may endanger the patient's life; however, with prompt and adequate treatment the prognosis is favorable.

Diffuse alveolar hemorrhage

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INTRODUCTION

Diffuse alveolar hemorrhage (DAH) is an uncommon, acute, life-threatening event presented in different ways. Repeated episodes can lead to organizing pneumonia, collagen deposition in small airways, and fibrosis. Among the many conditions it can accompany are Wegener granulomatosis, microscopic polyangiitis, Goodpasture syndrome, connective tissue diseases, antiphospholipid antibody syndrome, infectious or toxic exposures, and neoplastic disorders.

Most frequent reasons for intensive care unit admission is severe respiratory insufficiency. Diagnosis can be difficult and must be made as soon as possible since immunosuppressive therapy in most cases should be instituted immediately.

CAUSES OF DIFFUSE ALVEOLAR HEMORRHAGE

Diffuse alveolar hemorrhage can occur in three characteristic patterns reflecting the nature of the underlying vascular injury (1):

Vasculitis or capillaritis is histologic description of neutrophilic interalveolar and peribronchiolar septal vessels infiltration. This is the reason for anatomic disruption of the capillaries and for extravasation of red blood cells into the alveoli and interstitium.

Pulmonary haemorrhage without capillaritis or vasculitis (»bland« pulmonary haemorrhage) is pattern, where red blood cells leak into the alveoli without any evidence of inflammation or destruction of the alveolar capillaries, venules and arterioles. The epithelial lesions are usually microscopic and scattered geographically.

Alveolar bleeding associated with another process or condition such as diffuse alveolar damage, lymphangioleiomyomatosis, drug-induced lung injury, metastatic tumor to the lungs, mitral stenosis.

Diffuse alveolar damage is the main underlying lesion of the acute respiratory distress syndrome and is characterized by formation of an intra-alveolar hyaline membrane, by interstitial edema with minimal inflammation and by secondary diffuse alveolar hemorrhage.

CLINICAL MANIFESTATIONS

Acute or subacute (present for less than a week) dyspnea, cough and fever are the common initial symptoms. Haemoptysis as the most common clinical manifestation of DAH may be absent at time of presentation in up to a third of patients (2). Significant alveolar bleeding without haemoptysis is due to large alveolar volume which absorbs large amounts of blood. In these cases a chest radiograph indicates new unexplained bilateral alveolar infiltrates.

DIAGNOSTIC EVALUATION

Laboratory tests

Acute or chronic anemia, leukocytosis, elevated erythrocyte sedimentation rate and elevated C-reactive protein level are the most common findings in DAH. In cases of pulmonary-renal syndromes elevated blood urea and serum creatinine and abnormal findings of urin analysis are found.

Chest X-ray

The radiological pattern of DAH is characterised by diffuse, bilateral consolidation or ground-glass opacities due to alveolar filling, predominantly distributed in the perihilar regions and sparing the apices and costophrenic angles (4). The parenchymal opacities often appear suddenly, with site, extension and density changing. The opacities diminish rapidly and disappear without consequences, although a thin reticular pattern may form as they regress. In the case of recurrences, incomplete resolution of the opacities evolves into fibrosis.

CT, especially HRCT can better evaluate the extent of disease and is more sensitive in particular in identifying ground-glass opacities, but not more specific. The higher sensitivity of HRCT supports its use in patients with possible DAH and a negative chest X-ray, such as patients with connective tissue disease, vasculitis or bone marrow transplant presenting with haemoptysis and mild anaemia. The HRCT finding of ground-glass areas can guide investigations towards subsequent bronchoscopy and biopsy (4).

Pulmonary function

DAH may cause impairment of oxygen transfer and hypoxemia. In pulmonary function testing increased diffusing capacity is measured because blood in the lungs can absorb inhaled carbon monoxide. Restrictive changes are due to interstitial fibrosis. Obstructive changes are less common and are results of bronchiolitis and emphysema.

Bronchoscopy is to be done to document alveolar hemorrhage by bronchoalveolar lavage (BAL), to exclude airway sources of bleeding by visual inspection and to exclude an associated infection. The diagnostic yield of bronchoscopy is higher if the procedure is performed within the first 48 hours of symptoms.

BAL is the method of choice to diagnose the alveolar bleeding by showing free red blood cells and hemosiderin-laden, iron-positive macrophages (3). The diagnosis of DAH is with BAL and a low or falling haematocrit not difficult in patients with an acute pulmonary syndrome and pneumonic-type radiographic infiltrates. The specific diagnosis of vasculitis requires lung tissue for confirmation, particularly in those patients who present for the first time with unexplained DAH and who do not have an established diagnosis of an underlying systemic disease.

A thoracoscopic surgical biopsy is recommended when there is no evidence to suggest that diffuse alveolar haemorrhage increases operative morbidity or mortality (2). Biopsy specimens should undergo immunofluorescence staining. Serologic tests are needed, but their results are generally not available on time to guide immediate management. Antiglomerular basement membrane antibody, antineutrophil cytoplasmic antibody (ANCA), C3 and C4, anti-double-stranded DNA and antiphospholipid antibodies should to be orderd.

TREATMENT OF DIFFUSE ALVEOLAR HEMORRHAGE

Therapy for DAH is combination of treatment autoimmune destruction of the alveolar capillary membrane and the underlying condition.

Other possible management measures: supplemental oxygen, bronchodilators, reversal of any coagulopathy, intubation with bronchial tamponade, protective strategies for the less involved lung and mechanical ventilation should be done in the course of the disease if they are needed.

Immunosuppressive agents are the mainstay of therapy, especially if DAH is associated with systemic or pulmonary vasculitis, Goodpasture syndrome or connective tissue disorders.

Methylprednisolone in a dose of 250-1000mg/day i.v. for 3-5 days is recommended, followed by a gradual taper to maintenance doses of oral steroids. The treatment of small vessel vasculitis of the lung is largely the same, regardless of aetiology or whether it is isolated to the lung or a component of a systemic disease (2).

Cyclophosphamide intravenous (2mg/kg/day, adjusted to renal function) besides corticosteroids is used in DAH. It may be continued for several weeks. Prolonged cyclophosphamide therapy has a high incidence of side effects including infection, haemorrhagic cystitis, transitional cell carcinoma of the bladder and myelodysplasia. Alternative immunosuppressive drugs such as azathioprine, mycophenolate mofetil and etanercept may be used in DAH besides corticosteroids, especially when the condition is severe or specific underlying causes are present (Wegener granulomatosis, Goodpasture syndrome, systemic lupus erythematosus).

Especially in patients with pulmo-renal syndrome therapy should be started as soon as possible to prevent irreversible renal failure.

Plasmapheresis is of definite clinical benefit in Goodpasture syndrome. It also has the place in therapy of DAH in vasculitic processes in which the titers of pathogenetic immunoglobulins and immune complexes are very high.

The role of intravenous immunoglobulin therapy in DAH is still unclear.

Recombinant activated human factor VII has been successful in several case reports (5) of treating alveolar hemorrhage due to allogeneic hematopoietic stem cell transplantation, ANCA associated vasculitis, systemic lupus erythematosus or antiphospholipid syndrome.

PROGNOSIS

Prognosis of DAH depends on the underlying disease which is the reason for DAH. Recurrent episodes are the reasons for interstitial fibrosis.

CONCLUSION

DAH can be a catastrophic illness if recognition and treatment are delayed. Diagnosis is often aided by other systemic findings, associated illness and serological results. Patients with unexplained isolated DAH should undergo a lung biopsy with immunofluorescent studies and routine histological tests. During therapy close monitoring, due to potential complications of treatment and the possibility to relapses, is needed.

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PL1-9

Acute mediastinal conditions

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The mediastinum contains many vital structures. Disturbances to this compartment can endanger a patient rapidly. Main causes of acute mediastinal conditions are exogenous (trauma and infection) and endogenous (perforation or enlargement of mediastinal structures). Acute mediastinitis can result from perforation of hollow structures or from spreading from adjacent compartments, most commonly the neck. It is a mortally dangerous condition that must be dealt with rapidly and aggressively with combined surgical and antibiotic treatment. Mediastinal hemorrhage is most commonly caused by trauma, aortic rupture or thoracic procedures. Therapy is aimed at evacuating the clot and repairing the underlying lesion. Superior vena cava obstruction can be caused by any expanding lesion in the superior mediastinum or thrombosis. Treatment includes endovascular stenting, chemo- or radiotherapy and anticoagulation or thrombolysis.

The talk focuses on acute necrotizing mediastinitis and discusses its epidemiology, causes, diagnostic modalities and treatment. With the mortality of acute mediastinitis still reaching as high as 33% in recent reports, special emphasis is given to its early recognition and aggressive treatment in order to improve survival.

Key words: mediastinum, emergency, mediastinitis.

PL1-10

Pleural disorders

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Diseases of pleural space can occasionally present as a medical emergency. In this group of diseases are tension pneumothorax, massive pleural effusion and hemothorax. The first two conditions endanger patients by positive pleural pressure, which reduces venous return and therefore cardiac output. Large quantities of blood can be lost in pleural space in hemothorax, which can lead to hemorrhagic shock and death.

TENSION PNEUMOTHORAX is a presence of air in the pleural space at intrapleural pressure, which exceeds atmospheric pressure during inspiration and expiration. Large – bore needle should be immediately inserted in the pleural space to reduce the tension and to improve cardiac output.

MASSIVE PLEURAL EFFUSION can be of different aetiologies, but most of them are malignant. Pleural fluid can accumulate in pleural space and generate positive pleural pressure with mediastinal shift to the opposite hemithorax. Urgent thoracentesis is needed to reduce the pleural pressure.

HEMOTHORAX is the presence of blood in the pleural space with the hematocrit level at 50% or more by comparison with the peripheral blood. Chest tube should be inserted to remove the blood and to monitor the bleeding. Intravenous fluid or blood and its components should be replaced at the same time to prevent hemorrhagic shock. If bleeding through chest tube exceeds 100 ml/hr, emergency thoracotomy should be performed.

All above mentioned conditions can be manifestation of the underlying disease or can be caused iatrogenically. Careful monitoring of patients and early recognition of complications should be a standard after each invasive procedure.

PL1-11

Anaphylaxis: rapid recognition and treatment

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Anaphylaxis is a potentially deadly acute allergic reaction. Recognition can sometimes be difficult since the typical symptoms and signs may be absent. Three clinical criteria for the diagnosis have been proposed and the diagnosis is made when the patient is fulfilling any one of them. The most important is to begin treatment as soon as we set the diagnosis since anaphylaxis is most responsive to treatment in its early stage. Immediate actions in the management of patients with anaphylaxis include removing the inciting agent, placing the patient in the supine position with his legs elevated and administering epinephrine intramuscularly unless the patient already has i.v. access (hospitalized patients). This is followed by inserting at least two large-bore i.v. catheters and infusing large amounts of fluids. We intubate patients with inspiratory stridor or respiratory arrest. Epinephrine is a life-saving drug in anaphylaxis since it blocks the pathophysiologic processes that lead to shock; it also has beneficial

hemodynamic effects. There are no absolute contraindications for its use in anaphylaxis. Other treatments include H1 antihistamines for cutaneous symptoms and inhaled beta-2 agonists for bronchoobstruction. Other drugs do not have any proven effect in the initial treatment of anaphylaxis.

PL1-12

Acute right and left heart failure

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PL1-13

Cachexia in patients with COPD, CHF and cancer

Stefan D Anker

Obstructive Pulmonary Diseases, Saturday, May 9, 09:00-12:30

PL2-1

Diagnostic methods in asthma

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Summary

Asthma is a common disease, which prevalence is increasing for 50% each decade, and if this trend sustains World health organization (WHO) estimates that it will be more than 100 billion new asthma patients until 2050.

Asthma pathogenesis involves some mechanism that changes each bronchial layer, mucous membrane infiltration with inflammatory cells, hyperplasia of bronchial muscles, and circulation including angiogenesis. Inflammation of airways could be measured by number of inflammatory cells, particularly eosinophils in sputum and peripheral blood smear, eosinophilic cationic protein (ECP), as well as fractionated exhaled nitric oxid (FE_{NO}). This airway remodelling and bronchial hyperresponsiveness causes typical clinical presentation, symptoms that are included in the asthma definition. The role of rhinitis as part of the united airway concept is emphasized in the asthma medical history. As the third part of asthma diagnosis stress out bronchial obstruction, variability and reversibility, spirometry, PEF measurements and bronchodilator tests are explained.

Integral part of asthma diagnostic should be detection of risk factors and triggers, such are allergens, exercise, medications etc. This is not possible without partnership between a patient and a physician.

There are still lot of unknown and unpredictable facts in asthma, and lot of work to disclose the asthma mystery.

PL2-2

ASTHMA- how to choose and interpret lung function tests – a view of referring physician

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Spirometry is mandatory to measure degree of obstruction in asthma. In obstruction, BD test is mandatory and in case of negative test it is feasible to repeat it after the course of antiinflammatory treatment. Metacholine test is mainstay of diagnosis with a high negative predictive value. The positive test is less reliable in obstruction, acute respiratory illness and in obese subjects. NO as a marker of airway inflammation adds little to diagnosis in positive BD test, but is useful in very probable eosinophilic inflammation with negative metacholine test.

Repeated measures of NO to monitor adequacy of treatment add very little to ACT-guided asthma management. Decrease in NO after treatment follows after 2 days, while decrease in EOS can follow after few months. Eosinophilic airway inflammation, regardless of being asthma or not, requires antiinflammatory treatment

PL2-3

COPD – how to choose and interpret lung function tests – a view of referring physician

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Spirometry is used in diagnosis, but has a limited value in regular visits in nonsmoking COPD. It poorly correlates with prognosis, correlates well with symptoms and is of little value in severe COPD, where blood gas analysis is more important. Bronchial reversibility test: approximately half of the patients with COPD in stable state are reversible after bronchodilator if we use change in **FVC** (and not FEV1) more than 12% or 200 ml. It is not so if we use **FEV1** since only one quarter of patients is reversible. It is inappropriate to repeat bronchodilator test.

Metacholine test in COPD is feasible to rule out asthma. We should look at FVC instead of FEV1, because in COPD both FEV1 and FVC drop without any change in FEV1/FVC. Effect is due to air trapping, airway closure and hyperinflation. BODE index is used to assess survival and includes FEV1 (% predicted), 6MWD, MRC dyspnea scale and BMI. Eosinophilic inflammation in COPD is related to smoking, latter by itself increases bronchial eosinophilia. Induced sputum eosinophilia shows favourable response to short term oral GK. Exacerbations are linked with sputum eosinophilia.

PL2-4

COPD and heart failure

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Chronic obstructive pulmonary disease (COPD) and heart failure (HF) are both global epidemics in the Western World with substantial burden on both morbidity and mortality and present major challenges to healthcare providers. Few reports have addressed this often ignored combination. Multiple interactions exist between these conditions. COPD is often responsible for delayed diagnosis of HF and vice versa, since both conditions have similar symptoms such as dyspnea and poor exercise tolerance based on skeletal myopathic response rather than the primary organ failure. Also, patients with COPD have an increased risk for developing heart failure and higher hospitalisation and death rates compared with HF patients without COPD. Echocardiography and pulmonary function tests along with natriuretic peptides should be performed and carefully interpreted. Diagnostic assessment of both conditions present in the same patient is often difficult, but

therapeutic approach is also often non-adherent to current guidelines. For example, patients with coexisting COPD and HF receive beta-blockers at disappointingly low rates below 10%. Greater collaboration is required between cardiologists and pulmonologists to better identify and manage concurrent COPD and HF.

PL2-5

Bronchiectasis

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Bronchiectasis is abnormal dilatation of bronchi and bronchioles that results in chronic cough, sputum production and recurrent infections. Bronchiectasis result in progressive loss of lung function, increased morbidity, hospitalisations and may contribute to premature mortality. Prevalence increases with age, more common are in women. Development requires initial infection in connection with impairment of bronchial drainage, airway obstruction and / or defect in individual's defence. Initial diagnostic evaluation should include: radiographic confirmation by HRCT, functional assessment and identification of treatable causes.

The goals of therapy are to reduce the number of exacerbations and to improve the life quality. Potentially treatable causes should be corrected. Antibiotics according to antibiogram are the mainstay of exacerbation treatment. Preventive antibiotics are sometimes required in patients with frequent exacerbations. Anti-inflammatory treatment should be considered. All patients need physiotherapy for mobilization of airway secretions and improved airway clearance. Surgery and lung transplantation are required in selected patients.

PL2-6

New interventions in the rehabilitation of patients with COPD

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The principal goal of pulmonary rehabilitation is to increase everyday activities. To accomplish this goal, several extrapulmonary problems have to be covered by non-pharmacological interventions. Among these topics, dynamic training to improve exercise capacity is the most important.

In non-hypoxemic COPD patients with severe airflow limitation (FEV₁:31-35 ref%) investigations were carried out to evaluate the effect of 1) oxygen supplementation during exercise on dynamic hyperinflation (DH), 2) 7-week long cycle training with room air or oxygen on the exercise capacity, and 3) high intensity exercise training on the breathing pattern and exercise tolerance.

There was a dose response relationship between the amount of oxygen supplemented and symptoms, DH and endurance of patients. Beneficial effect was observed at FiO₂: 0.3 and plateaued at FiO₂: 0.5. Compared to room air, higher exercise tolerance and lower breathing frequency were observed in patients exercising with oxygen supplementation. After high intensity training,

isotime variables of breathing frequency, minute ventilation were lower, while inspiratory capacity was higher, indicating improved physiological adaptation. Therapeutic interventions resulting in attenuated DH may result in improved exercise capacity in patients with severe COPD.

PL2-7

Quality of life and functional capacity improved (walking tests, SGRQ questionnaire, BORG and MRC scales) in the group of patients with COPD, who participated pulmonary rehabilitation

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The goals of rehabilitation are to reduce the symptoms, disability, and handicap and to improve functional independence in people with lung disease. The rehabilitation process incorporates a programmed of physical training, disease education, nutrition assessment and advice, and psychological, social, and behavioral intervention.

We analyzed results of all the patients who have participated pulmonary rehabilitation between January 2006 and including May 2008 .Pulmonary rehabilitation was performed on nonacute department of University clinic for lung diseases and allergy KOPA Golnik.

From the group of 38 patients, two did not finish the pulmonary rehabilitation because of the aggravation of their illness and 1 female patient was eliminated from the study because of the lack of data. One patient has left the rehabilitation on personal decision. The total of 34 patients completed the program. Continuity of the rehabilitation was 3 or 4 weeks (average 3,4 weeks). The rehabilitation was passing 5 days per week Patients have spent their weekends at home. Programme of the rehabilitation was determined in advance (all the patients received the timetable). The therapeutic approaches and techniques of respiratory physical therapy were detailed describe in internal clinical therapeutically records. Average age of the patients participated in this study was 69 years. Portion of the women participated in our study was 38% (13). FEV1 of the patient was 800ml/s (30%); SD 300ml/s (15%).

RESULTS:

	Before rehabilitation (A)	After rehabilitation (B)	Difference (B-A)
6MWT (meter)	233,9m	323,2m	89,3m
ISWT (meter)	163,7m	217,8m	54,1m
MRC SCALE (points)	4,15	3,12	1
BORG SCALE (points)	7	5	2
SGRQ questionnaire (points)	58,5	52,5	6

PL2-8

Adult cystic fibrosis-multiple inhalation therapy

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Almost half of CF patients survive into adulthood and at that point require regular inhalation therapy. No clinical research data are available to support the combination of inhalation agents, although much of information is present for each agent by itself. Bronchodilator (SABA, LABA or saba/ACH) is most commonly prescribed. In addition, hypertonic saline should be titrated to up to 7% conc.. Inhaled tobramycin (TOBI, BRAMITOB) is reserved for Pseudomonas colonised patients. Mucolytic (dornase alfa - PULMOZYME) significantly reduce the exacerbation rate and decline in lung function even in mild disease. Amiloride has no long-term benefits in CF and should be abandoned. The combination of above drugs in adult patients in our centre is well tolerated and without significant side effects.

PL2-9

Patients with lung disease and air travel

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Commercial air travel is a popular way of transport despite escalating ticket prices. The exact number of aircraft passengers is unknown, but doctors are frequently asked by patients with chronic lung disease if they are fit to fly. Commercial flights aren't pressurized to the sea level and there's always reduction in partial pressure of oxygen, which may result in hypoxia in otherwise asymptomatic patients. Patients who become hypoxic during a flight may travel with supplemental oxygen but provision of oxygen is dependent on individual airline policy and there is a considerable variation in that policy.

There have been a number of different assessment methods to evaluate flight fitness and different guidelines to help doctors give informed advice and one seems to be superior to other.

Air travel is generally safe for patients who are under specialist respiratory care, but there are only a small number of studies that assessed which patients at risk to develop hypoxia and the exact level of hypoxia during the flight.

O1-1

Hemoptysis – analysis of 154 cases

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BACKGROUND: Hemoptysis is an important symptom with a number of diagnostic possibilities.

OBJECTIVES: The purpose of the study was to evaluate relative frequency of different causes of hemoptysis and the role of bronchoscopy and chest imaging methods in the evaluation.

METHODS: We retrospectively analysed 154 patients (93 males / 61 females, 43 smokers / 55 ex smokers / 56 non – smokers) with hemoptysis treated in University Hospital Golnik.

RESULTS: The main causes of hemoptysis were: chronic bronchitis (19,5%), lung cancer (14,3%), bronchiectasis (11,0%) and pneumonia (7,8). Severe bleeding (> 200 ml/day) was observed in 1,3% of patients, moderate bleeding (< 200 ml/day) in 25,3% and blood – stained sputum in 73,4% of patients. 81 (52,6%) of patients had pathological chest x – ray. Bronchoscopy was performed in 91 (59,1%) patients and endobronchial bleeding was found in 19 (20,9%) of them. CT scan was performed in 85 (55,2%) patients with pathological findings in 69 (81,2%) of them.

CONCLUSIONS: 85,7% of all hemoptysis in our group of patients had benign cause and the main diagnosis was chronic bronchitis. Extensive evaluation with bronchoscopy and CT scan is indicated in patients with positive smoking history and age over 50 years to exclude lung malignancy.

O1-2

The COPD plays role in lung carcinogenesis

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The circle of evidence linking COPD to Lung Cancer (LC) emerges rapidly, along with the growing interest from both bench and bedside. Epidemiologic studies suggest a strong, smoking-independent, association between COPD and LC. Recent evidence indicating a common genetic susceptibility locus on the nicotinic AchR receptor provides a possible genetic association for these two smoking-related diseases. Additionally, COPD has been suggested to play a direct, causative role in lung carcinogenesis. Chronic inflammation, a hallmark of COPD, enhance LC development in mice while antiinflammatory approaches reduce LC risk in humans. Molecular pathways linking chronic airway inflammation to lung carcinogenesis may also serve as novel biomarkers and therapeutic targets for both COPD and LC. Therefore, we hypothesized that coexisting COPD interferes with the lung carcinogenesis and changes the histology, stage of LC patients. We

analyzed digital and paper-based medical documentation of LC patients (n=460) of Semmelweis University from 2006 for the concomitant diagnosis of COPD, LC histology, stage with a telephone-based follow-up survey in randomly selected patients of squamous and small cell histology for accurate smoking history. Our results indicated that COPD causes a shift in histological subtypes favoring squamous cell carcinomas which was not dependent on the smoking habits.

O1-3

The role of erythropoietin in the treatment of non small cell lung cancer in experimental animal models

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It is well documented that the hypoxic tumor tissues are less sensitive to different oncological therapies, and hypoxia itself promotes malignant progression. Recombinant human erythropoietins (rHuEPOs) are widely used for the correction of haemoglobin level in cancer patients but the experimental and clinical data on the effects of rHuEPO treatment are inconsistent. One of the main reasons of this conflict could be the expression of EPO receptor in tumor cells which may influence their proliferation.

In our experiments we studied the effect of exogenous rHuEPO α in different non-small cell lung cancer (NSCLC) cell lines and xenograft models. Immunocytometric and flow cytometric data showed that EPO receptors are expressed by different NSCLC cell lines but rHuEPO has no effect on in vitro cell proliferation and in vivo tumor growth. However, rHuEPO administration in animal models has increased the effect of antitumor therapy (gemcitabine). Since rHuEPO significantly increased the proliferation of intratumoral endothelial cells causing vessel enlargement, the resulted better perfusion of tumor tissues could be in the background of therapy effectiveness.

This study was sponsored by OTKA K76293.

O1-4

Prognostic value of C-reactive protein in patients with advanced non-small cell lung cancer

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Background: Prognostic factors may help with treatment decision making. Significance of C-reactive protein (CRP) as negative prognostic factor has been shown in patients with several malignancies. However surprisingly until now only

few studies have analyzed CRP as prognostic factor in patients with advanced non-small cell lung cancer (NSCLC).

The aim of this study was to evaluate prognostic value of CRP before initiation of chemotherapy in a group of unselected population of patients with advanced NSCLC treated with palliative chemotherapy.

Methods: The retrospective study was conducted by reviewing 53 medical files of advanced NSCLC patients treated with platinum/gemcitabine at the University Clinic Golnik between May 2004 and November 2008. Median age of patients was 65 years. Majority of patients were males (75%), smokers or ex-smokers (81%), with performance status 1 (64.2%) and with stage IV disease (83%). Collected data included laboratory characteristics (Hb, platelet count, CRP, LDH) before chemotherapy, information on each individual patient therapy and outcome. Median number of chemotherapy cycles received was 4 (range, 1-6).

Results: Median progression free survival (PFS) for the entire group was 4.8 months (range 0-20 months). At the onset of treatment 60.4% patients had elevated levels of CRP > 20 mg/l. CRP value was found to be significant prognostic factor in univariate analysis ($p < 0.05$). Patients with elevated levels of CRP > 20 mg/l had inferior progression free-survival compared to patients who had lower values of pretreatment CRP (median PFS 8.4 vs. 3.6 months, $p < 0.05$). In a multivariate analysis with Hb comorbidity included CRP proved to be independent prognostic factor. Pretreatment hemoglobin values also proved to be independent prognostic factor.

Conclusion: Survival of patients with advanced NSCLC treated with chemotherapy is significantly influenced by patient's pretreatment value of CRP. The major strength of this study is that it was done on an unselected population of patients, but still uniform with respect to diagnosis, stage and agents used in chemotherapy treatment schedule.

O1-5

The role of angiogenin and apelin molecule in non small cell lung cancer

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Anti-angiogenic therapies have been included into clinical practice in the last few years. In addition to well-known cytokines (e.g. VEGF and bFGF), several new angiogenic molecules and their receptors have been identified, such as apelin, which has been detected in almost every normal tissue and different tumours. We tested apelin and its receptor's (APJ) presence on human melanoma, Kaposi's sarcoma, squamous cell carcinoma, colon carcinoma and non-small lung cancer (NSCLC) cell lines and tumour samples with immunocytochemistry, flow cytometry and quantitative PCR. We studied the effects of apelin peptides (apelin-12, -36) on in vitro proliferation of tumour cells and on in vivo growth and vessel density of tumours. We analyzed the possible correlation between apelin expression and clinicopathological variables or angiogenic activity of human tumours.

We found different apelin expression levels in human tumours, which were associated with the clinical behaviour in NSCLC patients. Although cell lines

expressed apelin and APJ at different levels, apelin-12 and -36 did not influence their proliferation. However, in vivo growth of tumour xenografts was promoted by exogenous apelins. Moreover, subcutaneous tumours transfected with apelin gene contained significantly more intratumoral vessels than controls. These results suggest that apelin affects mainly tumour stroma.

O1-6

Diagnosing of lung cancer: can the entire process from diagnosis to treatment be shortened?

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Background. In Slovenia, lung cancer is the first most common cancer disease among men and the fourth among women. Some patients experience a long diagnostic delay. Delay in the diagnosis of lung cancer is either due to patient delay or delay within the health care system.

The aim of the study was to explore the time spent diagnosing of suspicious lung lesions in a specialized outpatient clinic, which was established in order to speed up the diagnosis of lung cancer.

Methods. Patients with suspicious lung cancer who were examined at the outpatient clinic between January and December 2008 were consecutively analyzed. Clinical data, dates of patients' first outpatient visits, dates of final diagnoses and of the beginning of treatment were reviewed.

Results. 159 patients participated in the study; mean age was 67 years (range 20–88). 74 (53 male, 21 female) of them were diagnosed with lung cancer. The median time from onset of symptoms to the first outpatient unit visit was 67 days, 9 days from the first visit until the diagnosis and 13 days from the diagnosis to the beginning of the therapy.

Conclusion. The results show that patients in Slovenia wait too long before seeking appropriate medical assistance. However, when referred to our specialized outpatient clinic, the diagnose time of lung cancer and the time from the diagnosis to the beginning of treatment were both shorter compared to other similar analyses.

O1-7

Activation of T-Lymphocytes in lung cancer

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Few data are available on how effector T, NK, Treg-s(foxp3+) and NKT cells respond to lung cancer (LC) or cancer treatment.

Blood was drawn from 28 pts suffering from LC. Since 60% of LC pts also suffered from chronic obstructive pulmonary disease (COPD), one control group was formed from COPD pts (n=12) and another one from healthy individuals (n=16). Blood mononuclear cells were separated and analysed by FACS using labeled monoclonal antibodies.

Counts of measured cell fractions of COPD pts did not differ significantly from healthy individuals and there was also no difference between FACS data of

NSCLC and SCLC pts. Before treatment, LC pts had significantly higher neutrophil ($p < 0.05$) but unchanged total lymphocyte counts. Within lymphocytes, the CD4⁺CD45RO⁺ and the CD4⁺CD45RO⁻ subsets, the mature effector memory fractions were more than higher in LC versus healthy individuals ($p > 0.05$). At the same time, CD4⁺CD45RA⁺ and CD4⁺CD45RA⁻ cells, naive immature subsets, became diminished in cancer pts as compared to the healthy group ($p < 0.05$). LC is a stimulus for immune response. Greater fraction of effector/memory and smaller fraction of immature T cells characterize LC pts both prior to and after cancer treatment.

O1-8

Diagnostic value and safety of transbronchial biopsy in critically ill patients

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Critically ill patients often have multiorgan failure. Every invasive procedure can be life threatening. But on the other hand, transbronchial biopsy (TBB), which is also invasive, is a bedside procedure, that can guide us in further diagnostic and therapeutic decisions.

Between 2005 and 2008 we performed 66 TBB at 16 bronchoscopies in 13 patients. Two of them were breathing spontaneously, other were mechanically ventilated. We confirmed lung pathology at 9 (56,%) procedures. On the base of histologic findings, we changed or abandoned therapy after 37,5% of bronchoscopies with TBB and after 66,7% of bronchoscopies with pathologic findings.

There was only one major complication, pneumothorax. After every biopsy minor bleedings were appeared, but they were always stopped after topic endobronchial adrenalin application.

The conclusion is, that TBB is relatively safe, bedside procedure, also in critically ill, ventilated patients.

The histologic findings guide us in further therapeutic decisions in approximately one third of patients.

O1-9

Fluoroscopic versus endobronchial ultrasound-guided transbronchial biopsy of peripheral pulmonary lesions

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Background. The bronchoscopic lung biopsy under fluoroscopic guidance is the standard procedure for the diagnosis of peripheral pulmonary lesions. However, peripheral lesions can also be approached by endobronchial ultrasound (EBUS) guidance, which eliminates the risk of radiation exposure for both patients and the staff. Diagnostic yields of EBUS- and fluoroscopy-guided bronchoscopic lung biopsy (BLB) in every day clinical circumstances were compared.

Methods. Patients with peripheral pulmonary lesions who underwent fluoroscopy-guided or EBUS-guided transbronchial lung biopsy (TBB) were evaluated. Diagnostic yields were compared for both modalities.

Results. We examined 223 patients (mean age 66 years) with peripheral

pulmonary tumor who underwent EBUS- (95 patients) or fluoroscopy-guided (145 patients) TBB in a tertiary teaching hospital between January and December 2006. Diagnostic material was obtained in 75.8% of patients with EBUS and in 73.9% of patients with fluoroscopy. Mean diameter of peripheral lesions in the EBUS group was 39.7 mm and 45.7 mm in the fluoroscopy group. The difference between diagnostic outcomes of both methods measured by the true or false assessment of tumor presence was statistically insignificant, although the absolute difference in this sample indicates EBUS to be better than fluoroscopy in terms of sensitivity, when tumor is detectable by EBUS.

Conclusion. EBUS-guided TBB appears to be at least equivalent to fluoroscopy, when tumor is visible by EBUS miniprobe. The other advantage of the method is reduced radiation exposure for patients and bronchoscopy personnel.

Fluoroscopic and EBUS guided TBB are methods, which should be regarded as complementary in diagnosis of peripheral tumors.

O1-10

Various neurological paraneoplastic symptoms - but where is the primary tumor?

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The 58-year-old heavy smoker male patient with a four month history of relapsing nystagmus and fluctuating desorientation was suspected to have a paraneoplastic syndrome based on the humoral intrathecal activity in the cerebrospinal fluid and the electromyographically diagnosed Lambert-Eaton myasthenic syndrome. Brain CT scans were negative, chest computed tomography and whole body PET/CT fusion imaging showed evidence of pulmonary malignancy. Multiple bronchoscopic sampling revealed no definitive results, CT-guided transthoracic biopsy was refused by the patient.

After episodes of fluctuating neurological symptoms and clinical stability, severe respiratory failure developed with grand mal convulsions and need for mechanical ventilation. Repeated brain CT scans were negative, the suspected pulmonary malignancy showed progression on the chest CT scan, but due to the rapid deterioration of the patient, further diagnostic procedures were not. Autopsy revealed small cell lung cancer in the left lung, neuropathologic processing confirmed limbic paraneoplastic encephalitis which is often associated with this type of malignancy.

O2-1

Steroid responsiveness of natural killer T cell mediated airway inflammation

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The role of natural killer (NK) and NKT lymphocytes in airway inflammation and hyper-responsiveness (AHR) is uncertain. The effects of single, intranasal NKT stimulant α -galactosyl-ceramide (GalCer; 2?g) and dexamethasone (Dex; 5mg/kg subcutaneous, 24h after GalCer) were examined in C57Bl6 mice. AHR was assessed, and cell counts in bronchoalveolar lavage (BAL) were determined by flow cytometry, including the identification of CD3⁻/NK1.1⁺ (NK), CD3⁺/NK1.1⁺ (NKT) lymphocytes. BAL cytokine concentrations were also measured.

Eosinophil inflammation and AHR developed, NKT and especially NK cell counts were elevated in BAL 48h after GalCer treatment. Of note, AHR correlated only with the NK cell numbers. AHR completely abolished, but eosinophil inflammation remained unchanged and NKT cells even further proliferated after Dex. IL-4, IL-6, IL-17, IFN- γ and TNF- α levels were increased by GalCer, and diminished by Dex, while the elevated IL-5 failed to decrease after steroid treatment. IL-10 levels were reduced by GalCer, and remained low after Dex.

Single dose of NKT-stimulating GalCer generated a phenotype that mimicked allergic airway disease, but was partially resistant to steroid treatment. Our results also propose, that NK lymphocytes – induced secondary by NKT cells – may participate in pathogenesis of AHR.

O2-2

Pulmonary arterial pressure response during exercise in COPD and healthy subjects

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Rationale: Pulmonary arterial pressure rise (Δ PAP) during exercise in patients with COPD is unpredictable from lung function data. The non-invasive assessment of pulmonary hemodynamics may be useful in pulmonary rehabilitation (PR).

13 %pred) and 13 \pm Methods: 34 COPD patients (C; FEV1: 40 healthy subjects (H) performed semi supine echocardiography with PAP measurement. Serum hsCRP level was determined in COPD.

Results: In COPD, the systolic PAP (PAPs) was higher at rest (C: 41 \pm 7 vs. H: 31 \pm 2 mmHg, p<0,001) and elevated more during exercise (C: 34 \pm 10 vs. H: 19 \pm 6 mmHg, p<0,001). In 20 COPD patients Δ PAPs increased >25 mmHg and hsCRP was 15,4 \pm 7,0 mg/L compared to 6,9 \pm 8,9 mg/L in other COPD patients. Right

ventricular systolic function was normal in both COPD and healthy groups.

Conclusion: Some COPD patients (with higher hsCRP) have high Δ PAPs during exercise. For this COPD group, interval exercise training is a better option in PR.

O2-3

Rapid corticosteroid effect on long-acting beta2-agonist disposal in the airway: a new paradigm of inhaled combination therapy

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Inhaled corticosteroids, in addition to suppress asthma-associated airway inflammation, could improve beta2-adrenergic bronchodilation. In our in vitro experiments, we report a novel immediate form of interaction of corticosteroids and beta2-agonists to further explore the beneficial effects of combined inhalation therapy. The study provides evidence of a specialized transport mechanism for cationic drug elimination in airway smooth muscle. Transport measurements with two long-acting beta2-agonist bronchodilators, the cationic formoterol and the lipophilic salmeterol, suggest that cationic beta2-agonists are also carried by the same disposal mechanism in airway smooth muscle cells. Budesonide and fluticasone were shown to acutely (within 15 minutes) interfere with the cellular uptake of formoterol in these cells. In contrast, no interaction was revealed for corticosteroids with salmeterol uptake. We suggest that increased airway tissue retention of inhaled bronchodilators due by the corticosteroid-sensitive disposal mechanism could acutely improve responses to cationic beta2-agonist bronchodilators (i.e. formoterol). The study demonstrates an immediate interplay of corticosteroids and beta2-agonists for which previously only genomic interactions were shown. Nevertheless, whether inhaled corticosteroids potentiate beta2-adrenergic responses by inhibiting airway drug disposal mechanisms remains to be explored in vivo.

O2-4

Seasonal fluctuation of C-reactive protein level in stable COPD patients

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In stable COPD, factors resulting in elevated C-reactive protein (CRP) levels have not been clearly established.

Therefore high sensitivity CRP (hsCRP) data of 219 stable COPD patients were collected in the period between 07/2006 and 09/2008. The number of CRP and lung function measurements was 327. Average age of the subjects was 65 ± 12 (SD) years, $FEV1\% = 45 \pm 22\%$, CRP: 13.7 ± 24.2 mg/L.

No significant correlation was found between CRP and FEV1. By using a new point of view, analyses indicated that CRP levels increased systematically at the beginnings of Januarys and become lower again in Mays. Thus the period was

divided into 5 segments by separating data from January to April and from May to December. During the 2 winter segments, only 6 and 19% of subjects had lower CRP levels than 4 mg/L. In the other segments, these proportions were 47, 72 and 67%, respectively.

In conclusion, considerable seasonal fluctuation in CRP levels was found in COPD patients. The explanation of this phenomenon is not yet known.

O2-5

Exhaled nitric oxid in pregnant healthy and asthmatic women

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Measurement of fractioned exhaled nitric oxide (FENO) is useful for monitoring airway inflammation in asthma. Asthma is one of the most common diseases complicating pregnancy and FENO may also be helpful for monitoring pregnant asthmatic patients. However no study assessed the usage of this measurement in pregnant asthmatic subjects.

Our aim was to evaluate the safety and repeatability of FENO measurement in pregnant women compared to non-pregnant subjects. A total of 102 female subjects (35 healthy non-pregnant and 27 healthy pregnant females; 20 non-pregnant and 20 pregnant asthmatic women) were included in this cross-sectional study. Two FENO measurements were performed in each subject using an electrochemical sensor based device (NIOX MINO®). Data are given as median with range.

The repeatability of FENO measurement was similar in pregnant and non-pregnant subjects. FENO levels did not differ significantly between healthy pregnant vs. non-pregnant subjects. FENO levels were significantly increased in asthmatic women compared to healthy female (non-pregnant asthmatics: 38 [9, 54] ppb, $p < 0.001$ vs. healthy non-pregnant; pregnant asthmatic patients: 28 [10, 56] ppb; $p < 0.05$ vs. healthy pregnant) .

The NIOX MINO® is safely applicable during pregnancy and provides repeatable readings.

O2-6

Interaction between asthma and pregnancy

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The effect of pregnancy on the course of asthma is unpredictable but not accidental. We have demonstrated peripheral blood T lymphocytosis and increased number of interferon-gamma synthesizing lymphocytes (T1) in uncontrolled asthmatic pregnant women (n=42). Higher T1 lymphocyte counts correlated significantly with worse airway function and decreased birth weight of newborns. Those three pregnant women who suffered from the most severe airway obstruction developed preeclampsia, gave birth to very small newborns (1000-1200 g) and had the highest fractions of T1 cells. In contrast, among well

controlled asthmatic pregnant women (n=24) the ratio of activated T and B cells remained unchanged as compared to healthy pregnant women. Immunological interaction between pregnancy and airway allergy was confirmed in previously sensitized pregnant mice exposed to secondary allergen provocation. Pregnant mice responded with diminished IL-4, IL-5 and IL-13 synthesis as measured in bronchoalveolar lavage fluid. Foetal development was not altered. In contrast, in pregnant mice undergoing spontaneous abortion the development of airway hyperresponsiveness to inhaled methacholine was observed. These data point to multiple immunological and physiological interactions between pregnancy and asthma.

O2-7

Adult patients with cystic fibrosis (CF)

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With development of basic CF therapy and arms to detect a disease in the first months of life, most CF patients survive into adult life. Once they reach into their adulthood, they are being followed at different clinics in Slovenia.

In the University Clinic for Respiratory and allergic diseases Golnik we have treated 21 CF patients since October 1993 (13 females and 8 males). The age of the patients at the first visit at our clinic ranged from 13 to 44 years (median 22 years). The duration of the follow up ranged from one visit to 16 years (median three years). There was a huge variability between the frequency of hospital or out-patient department visits and the severity of exacerbations, on average there were two visits per patient yearly.

Pseudomonas aeruginosa was isolated in 14 patients, MSSA in 11, MRSA in one, *Haemophilus influenzae* in five. We isolated *Burkholderia cepacia* in two patients, *Stenotrophomonas maltophilia*, *Citrobacter coseri* and *Serratia marcescens* in one.

In nine patients severe chronic respiratory insufficiency developed during follow up and continuous oxygen treatment was demanded, six of them received lung transplant in Vienna. Three patients have died.

O2-8

Exercise tolerance of patients with cystic fibrosis

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Thanks to increasing therapeutic opportunities, the lifespan of patients with cystic fibrosis has extended. The predicted average survival rate was 37.4 years in 2007. Our institute is responsible for the care of adult cystic fibrosis patients in the region since 2004.

Patients and method: 8 patients (age:19-26) were followed by spirometry and spirometry with BMI calculation.

Results: FEV1 (ref%): 30-83 (avg: 60 SD: \pm 21), body mass index: 17.3-22 (avg: 19,7 SD: \pm 1,3) and working capacity (ref%): 45-82 (avg: 67, SD: \pm 12) were mostly under the normal range, however, desaturation was not observed. There was no correlation between age and working capacity. Decreased working capacities correlate primarily with the FEV1 (ref%).

Conclusion: Although the number of subjects was low, the patients with better compliance /regular use of inhalative drugs, calorie intake and physical activity/ had better functional conditions and achieved performance.

O2-9

Typing of *Pseudomonas aeruginosa* from Cystic Fibrosis Patients: Comparison of Susceptibility and Genotype

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BACKGROUND: *Pseudomonas aeruginosa* is the leading cause of morbidity and mortality in patients with cystic fibrosis (CF). Typing techniques are essential for understanding hospital epidemiology, permitting the explanation of the source of infection and routes of bacterial transmission.

RESULTS: In present study, antibiotypes (susceptibility profiles) were compared to genotypes established by restriction fragment length polymorphism (RFLP) analysis by pulse-field gel electrophoresis (PFGE) in 18 *P. aeruginosa* clinical isolates from the expectorations of 10 CF patients attending our hospital over a period of three years (2006-2008). PFGE allowed the typing of 100% of strains, revealing the presence of six different patterns of *SpeI*-digested genomic DNA. Susceptibility and restriction profiles were discrepant in more than 50% of the cases, and many antibiotypes were observed among isolates from the same genomic pattern. Furthermore, susceptibility profiles did not allow the distinction of isolates from unrelated genomic patterns.

CONCLUSION: We conclude that at a given time, patients with CF attending our clinic were colonized or infected by phenotypically and genotypically distinct strains of *P. aeruginosa* which has an implication in the management of these patients and gives us feed-back on infection control procedures.

O2-10

Smoking with asthma in Hungary

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Cigarette smoking represent an increased risk for the development of asthma and clearly associated with asthma death. Exposure of cigarette smoke is correlated with more frequent asthma attacks, more asthma symptoms, a lower lung function, an accelerated decline in lung function, high rates presenting to hospital emergency departments with acute asthma compared to nonsmoking asthmatic patients.

The aim of our study was to evaluate asthma control and factors determining it on Hungarian previously diagnosed and treated asthmatic group of 133 outpatients. Methods consisted of using Asthma Control Test and a self developed questionnaire describing factors influencing asthma control. Results showed that 50% of our asthmatic patients were partially controlled or uncontrolled. Many risk factor could influence asthma control. We found high prevalence of smoking, 55% of our asthmatics are active or exsmokers. At the time of study 14% of patients were active smokers, while 41% has already stopped smoking. Those patients who are active smokers – are haevy or moderate smokers. Environmental tobacco smoke (ETS) – passiv smoking at workplace were present in 38% of our patients, at home ambiente 20%, at hobby ambient passive tobacco smoke exposure were present at 19% of our asthmatic population. All this smoking factors could attribute – besides other known risk factors – to the persistence of asthma symptoms and the lack of therapeutical success.

O2-11

Tuberculosis in lung transplant recipients: the Slovenian experience

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Immunosuppression is a risk factor for the occurrence of tuberculosis (TB). Transplant patients are becoming an important group at risk due to an increased number of organ transplantations. Lung transplant patients represent a specific subgroup with reported TB incidence 0,8-6,5%, depending on epidemiological situation. Infection can be caused by reactivation of primary infection, transmitted from donor to recipient, or acquired after transplantation. TB occurs most frequently in the first 6 months after transplantation, often preceded by augmentation of steroid therapy due to organ rejection. Atypical presentation and disseminated infection are more common in immunosuppressed patients and therefore more challenging to detect and manage. Standard treatment regimens are successful when initiated early enough.

In our center we recorded two cases of TB after lung transplantation (2/17, 11,8%). In one case it was due to reactivation of primary infection and in the other transferred with donated organ. Although symptoms were not specific,

detection was early, and thus treatment was successful. Maintaining adequate immunosuppression was difficult due to rifampicin and tacrolimus/cyclosporine interactions.

In conclusion, vigilance of TB is required in immunocompromised patients as the incidence is much higher than in general population and delayed treatment is associated with significant mortality and morbidity.

P-1

Healthcare-associated pneumonia

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Introduction: Healthcare – associated pneumonia (HCAP) was recently introduced into classification of pneumonia to describe a nonhospitalized population at risk for colonization of multidrug – resistant bacteria. Risk factors for HCAP are hospitalization within 3 months of infection, residence in a nursing home, antibiotic therapy, chemotherapy and immunosuppressive therapy within 30 days of current infection, hemodialysis treatment, home infusion therapy or home wound care and family member with infection due to MDR bacteria. In our study we wanted to identify patients with HCAP, evaluate their clinical picture and laboratory results and identify causative microorganisms.

Material and methods: Patients with HCAP are included into analysis. They were hospitalized in the period January – March 2009 in Hospital Golnik. All data are from patients' files.

Results: 46 patients met the inclusion criteria, 67% men, their average age was 76 years. 41% of patients were previously hospitalized within 3 months, 33% of patients were nursing home residents, 24% of patients were receiving antibiotics, chemotherapy or steroids within 30 days of current infection and 1 patient underwent hemodialysis treatment. 80% of patients had more than one accompanying chronic disease.

76% of the patients were dispnoic at the admittance, 57% were febrile, only 4% had chills. 7% of the patients were confused, 17% of them had thoracic pain. 56% of patients were coughing and 39% expectorate. In laboratory results we found elevated CRP in 91%, leucocytosis in 63% and elevated blood urea in 43% of the patients.

Causative microorganisms were isolated from sputum in 13%, tracheal aspirate in 13%, hemoculture in 2% and pleural effusion in 2% of the patients. We isolated *S. pneumoniae* in 5 patients, *P. mirabilis* in 4 patients, *K. pneumoniae* and MSSA in 2 patients each and *P.aeruginosa*, *H. parainfluenzae*, *M. catarrhalis* and *Str. sanguis* in one patient.

Average length of hospital stay was 11,6 days. The mortality rate was 30,4%.

Conclusion: Patients with HCAP are defined by older age and numerous comorbidities. Typical clinical signs of pneumonia are frequently missing. HCAP differs from CAP with respect to pathogens and prognosis. The mortality rate in this group of patients is very high.

In case of severe form of CAP risk factors for HCAP have to be considered and broader empirical antimicrobial therapy prescribed.

P-2

Lung cancers in 2008 at Pulmonary department, University Clinical Centre Maribor

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Methods: Due to frequently observed advanced stages of lung carcinoma at admission to our department and short survival of these patients, we performed the retrospective analysis of newly diagnosed lung cancers in 2008. We evaluated patients' age, symptoms, time from onset of complaints until seeking medical help, smoking status, location, histology, stage of tumour and planned treatment.

Results: 136 were diagnosed with lung cancer, 98(72%) men (age 64 ± 10). Median time from onset of symptoms was 4 weeks (0 to 52). In 59%, upper lobes were involved. Microcellular carcinoma was present in 18%. At the time of diagnosis, 35% of our patients had locally advanced disease and 52% had metastatic disease. There was significant difference between men and women regarding histological type of tumour and smoking status. 9% of the patients died during the first hospitalization.

Conclusions: The main difference between our patients and the data from Slovenian Cancer Registry was higher percentage of metastatic disease at the time of diagnosis. If this influences overall survival of lung cancer patients in our hospital needs to be confirmed in further studies.

P-3

Comparison between 6 minute walk test and shuttle walk test in COPD patients

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Introduction: 6 minute walk test(6MWT) and shuttle walk test(SWT) are two of the most performed tests to evaluate exercise performance in patients with pulmonary diseases. Both tests are technically easier to perform than any other cardiopulmonary test. Furthermore studies show that the 6MWT is easy to administer, better tolerated, and more reflective of activities of daily living than the other walk tests.

Methods: We performed both 6MWT and SWT in 39 patients that were hospitalized in COPD rehabilitation program in our hospital between years 2006 and 2008. We retrospectively analysed and compared walking distances from both tests. We also analysed if FEV1 or BMI can predict or influence on walking distance.

Results: Comparison of walking distances in 6MWT and SWT reached correlation 0,763. and $p=0.000$. BMI and FEV1 didn't reach statistical significance on walking distance with $p=0,118$ and $p=0,067$.

Conclusion: We found out that results from both tests can be compared. Therefore we suggest that in COPD patients 6MWT should be used for evaluation of exercise performance because of its simplicity to perform and no

need for technical accessories. Of course standardized guidelines must be when performing 6MWT.

P-4

Depression in patients with COPD and lung cancer

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Background: Depression is frequent in patients with COPD and lung cancer. Usually patients with malignant disease get more attention in terms of psychological support. The aim of our study was to compare the prevalence of depression in patients with COPD, lung cancer and in the control group.

Methods: 17 successive patients with COPD, 13 with lung cancer on chemotherapy and 15 hospitalized for other reasons were included. Depression was assessed by PRIME – MD questionnaire, dyspnoea with MRC scale and performance status with Karnofsky score.

Results: 10 patients (22%) had depressive disorder. There was no statistically significant difference in prevalence of depression between the groups. Depressed patients had significantly worse performance status ($p=0,012$) and experienced worse dyspnoea ($p=0,006$). There was no difference in prevalence regarding sex and age.

Conclusions: Prevalence of depression was higher than in general population; however we did not confirm a difference between COPD and lung cancer patients, nor was there a difference regarding control group. All depressed patients should get some psychological support in order to improve their quality of life. Main determinants of depression are performance status and dyspnoea.

P-5

Our experience with the differential diagnosis of pleural fluid

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The differential diagnosis of pleural fluid does not belong to the easy ones. Etiology can be pulmonary, extrapulmonary and sometimes pleural per se. In the presented case we thought of cardiac origin first because it seemed to be that pulmonary causes could be excluded. Later a chest CT was requested due to the observed increased pressure in the right ventricle, but it did not help the diagnostic work-up. Our next suspicion was prostate cancer however the patient developed renal insufficiency in the mean time. Firm diagnosis was only established post mortem. The fluid was caused by plasmocytome.

Key-words: pleural fluid, CT, plasmocytoma

P-6

Pulmonary manifestations in systemic lupus erythematosus

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Respiratory involvement in systemic lupus erythematosus (SLE) is common, however only few data are available about the frequency and composition of different lung manifestations.

Since September 2008, 20 patients were included into the analysis (age 43.3±17.0 years, female:male ratio 16: 4, SLE diagnosis 7.7±7.9 years). Patients were divided into two groups: SLE patients treated because of severe lung manifestation (LM, N=8), and controls (N=12) consisting of SLE patients in immunological care, sent for screening to assess pulmonary involvement of the disease. Physical examination, chest X-ray, complete lung function test, in some cases CT scan, as well as laboratory tests were performed.

The most common pulmonary involvement in LM patients was obstructive ventilatory disorder (88%) followed by pulmonary embolism due to antiphospholipid syndrome (38%). In controls serositis was the most frequent (38%), obstructive ventilatory disorder was observed in (31%).

According to our results the most common pulmonary manifestation in SLE is obstructive ventilatory disorder, possibly due to underlying bronchiolitis obliterans. Detailed lung function test is recommended in all SLE patients to assess small airway involvement in this autoimmune disease.

P-7

A patient with severe dyspnea and fever

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A 51 year old male, two weeks after coming back from trip to Kenia, seaked for help in Emergency Unit of Murska Sobota hospital for having severe dyspnea, dry cough and right sided chest pain. He also reported thighthtness in lower limbs which lasted from the time beeing on trip, but his condition was recognised as pneumonia because of presence of leucocytosis, high inflammation parameters and pathologic radiogram of the chest which showed slight infiltrate in left lower lobe. He was prescribed Amoxiciline with clavulanic acid and sent back home.

After three days his symptomes were getting worse and hemoptisys apeared. He was admitted to pulmonary unit of Murska Sobota hospital and reexamined. With CT angiography of the chest we diagnosed pulmonary embolisms with left sided pulmonary infarction and effusion, complicated with inflammation.

For one year we treated him with anticoagulation therapy and after that we controled CT angiorahy of the chest which showed normal vascularisation of the lungs.

Above mentioned case report is showing us pulmonary emboly hiding with signs and symptoms of pneumonia.

We didn't proved antiphospholypid activity in our case. We are also considering a possibility of a conection with a long plane trip that we can't prove. Yet we are seeking for a potential genetic cause of thrombophilia.

P- 8

Pemetrexed-CDDP as a first line treatment of malignant pleural mesothelioma

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Malignant pleural mesothelioma is a rare tumour of poor prognosis. Pemetrexed-CDDP treatment improved the overall survival and the quality of life patients suffering mesothelioma. In our institute at 20 patients were diagnosed malignant pleural mesothelioma. 13 patients were fit for chemotherapy (ECOG 0-1). Mean age of the patients was 59,8 years. Results: In 3 cases treatment was finished because of disease progression. Mean overall survival was 13,5 months. Severe toxicity was observed only in 2 cases (1 neutropenia, 1 anaemia).

Conclusion: PEM-CDDP is a well-tolerated and efficient treatment option for patients suffering pleural malignant mesothelioma

P-9

Lung cancer seeding along needle track after FNAB - case report

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BACKGROUND: Transthoracic fine needle aspiration biopsy (FNAB) is usefull diagnostic method in evaluation of lung malignancies. The incidence of chest - wall implantation metastasis after FNAB is extremely rare. However, we report a case of cancer seeding along needle track after CT guided transthoracic FNAB. CASE REPORT: A 71 – year old male, ex – smoker was managed with FNAB in diagnostic workup of squamous cell carcinoma of the lung, stage T3N0. A small metastasis was discovered in a left humerus after PET – CT. Patient was treated with chemotherapy and irradiation of bome methastasis. 4 months after initial evaluation we repeated CT – scan of the lungs. A tumour progression with tumour growth along needle biopsy track was found from primary site in left upper lobe to pectoral muscle.

CONCLUSIONS: Although the frequency of chest - wall implantation metastasis after transthoracic FNAB is very rare, attentive follow – up is recommended. Early intervention with resection and irradiation is often curative in previously radically treated patients.

P-10

Second line pemetrexed monotherapy in non-small cell lung cancer

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Lung cancer is the leading cause of cancer death worldwide and in Hungary too. Although a lot of new active drugs are available now for lung cancer, the reported response rates in second-line setting have generally been less than 10%.

Docetaxel, pemetrexed and erlotinib are recommended as single agent chemotherapy regimens for NSCLC patients in second line treatment.

In a phase III study pemetrexed has been shown to have equivalent efficacy with docetaxel but with less toxicity.

Between 1st January 2007 and 28th February 2009 we treated 32 patients with non-small cell cancer, who have experienced disease progression during first-line therapy or within 6 months after the last treatment. Histological types of tumour in 8 cases were squamous cell carcinoma, in 17 cases adenocarcinoma and in 7 cases NSCLC. The patients received pemetrexed at the dose of 500 mg/m², during 10 minutes as an intravenous infusion, with folic acid and vitamin B12 supplementation, every 21 days for maximum 4 cycles. The therapeutic response was partial response in 2 cases, in 10 cases stable disease and in 17 cases progressive disease, in 3 cases the therapeutic response was not evaluable. Side effects of the treatment were usually mild, we did not experience any life threatening adverse event.

We found that the single agent pemetrexed is a well tolerable and effective second line therapy option for NSCLC patients.

P-11

Outcome of patients with limited-stage small cell lung cancer (LSCLC) in a routine clinical setting

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Introduction: In Europe the most common cause of cancer death is lung cancer, which accounts for one fifth of the total number of cancer deaths. LSCLC carries a median survival of approximately 18 months from diagnosis when treated by chemoradiotherapy. Cisplatin plus etoposide (PE) is the regimen of choice because of its possibility to be combined with radiotherapy and slightly superior activity compared with doxorubicin/cyclophosphamide-containing regimens (CEV). The objective of this retrospective study was to define the median survival (MS) of unselected LSCLC patients treated at the University Clinic Golnik in a routine clinical practice.

Patients and methods: The retrospective study was conducted by reviewing 251 medical files of SCLC pts treated at the University Clinic Golnik, between 2002 to 2007. Out of 251 104 (41 %) had limited disease. Sixty-nine pts (66 %)

were younger than 70 years, 35 patients (34%) were 70 years or older (range 42 - 82). Majority of pts were male (65 %), smokers (95 %), with performance status 0 or 1 (87%). Collected data included pts characteristics (age, sex, performance status, comorbidity) before starting chemotherapy as well as the information on treatment and outcome. Comorbidity was assessed by weighted index of comorbidity.

Results: MS of the entire group of pts with limited disease was 16 months (95% CI: 14 -17 months). MS of 90 pts treated by concurrent chemoradiotherapy (PE or CEV) was 16 months while the MS of 14 pts treated by chemotherapy alone was only 10 months ($p= 0.001$). Similarly in pts receiving PE chemotherapy, median survival of pts treated by chemoradiotherapy was found to be better compared to MS of pts treated by chemotherapy alone (16 months vs. 10 months). The only factor significantly correlated abandoning was age ($p= 0,012$). In a univariate analysis age (under or over 70 years) and comorbidity, but not sex, were found to have a significant prognostic value (both $p<0,005$), while in a multivariate analysis (factors analyzed were radiotherapy, age, sex and comorbidity) comorbidity and radiotherapy emerged as significant independent prognostic factors ($p=0,010$).

Conclusion: In a majority of our routinely treated pts (86%) concurrent chemoradiotherapy as a preferable method of therapy in LSCLC was feasible and resulted in satisfactory MS rates. Comorbidity and radiotherapy were found to be the only independent prognostic factors in our pts, regardless of treatment (concurrent chemoradiotherapy or chemotherapy only). To further improve our MS rates it is important to pay our attention to older pts and not to abandon chemoradiotherapy just because of over 70 years of age.

P-12

Ramel needle biopsy as a useful diagnostic tool in malignant pleural mesothelioma

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The correct diagnosis of malignant pleural mesothelioma requires immunohistochemistry, which has an important role in the distinction between mesothelioma and pleural metastases. Various antibody panels are recommended for the diagnosis of malignant mesothelioma. Pleural biopsy made with a Ramel needle is an easy, cheap and generally safe procedure, it can be the next diagnostic step after thoracocentesis. In the last 3 years we have performed 165 blind pleural biopsy with Ramel needle; in 12 cases we found malignant mesothelioma.

P-13

Different types of small bore catheters in the treatment of pleural fluids.

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We compare two types of catheters used for pleural drainage produced by B. Braun.

The first is the Mathys Pleuracan, which is frequently used in Hungary; the second is the Cystofix, produced originally for suprapubic urine bladder puncture, but we have successfully used it for pleural drainage for 10 years.

The tube of Pleuracan will be inserted through a 3 mm thick and 75 mm long needle; after removing the needle the part with two valves, a 3-way stopcock and a cone connector at the end can be attached.

The smallest cross section is 1,8 mm². The catheter often gets clogged at this point, or at the valves, which have no real function.

The Cystofix comes in two sizes; Ch10 and Ch15. It is a simple plastic tube with a cone connector part at the end.

The inserting needle is splittable; its length is 120 mm. The cross section of the Ch10 is 3,5 mm² and 15,9 mm² for the Ch15. The Cystofix has no valves or stopcocks.

The insertion is simple. The Ch10 Cystofix is suitable for treating iatrogenic or primary spontaneous pneumothorax, or evaluating the expandability of the lung before pleurodesis. The Ch 15 Cystofix can be used for treating emphysema or for pleurodesis.

P-14

Communication as a part of palliative care in COPD patients

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Introduction

Chronic obstructive pulmonary disease (COPD) with its progressive air flow limitations and repetitive acute exacerbations is a major cause of morbidity and mortality. The COPD patients were identified with poor quality of life, severe dyspnoea, and psychological burden of clinically relevant anxiety or depression. Palliative care approach should focus on symptom management, maintenance of a reasonable quality of life, good communication (patients, family members and physicians), increasing physical activities to maintain independence and practical support of emotional, spiritual and psychosocial support for patients and caregivers.

Communication is needed to establish the therapeutic relationship, obtain relevant information about problems and discuss diagnosis, prognosis and treatment options according to the patient's goals to ensure quality end-of-life care.

The aim is to introduce goals of communication and barriers to effective communication with COPD patients and their family members. It is important to be aware of the fact that severe COPD is a progressive and terminal illness. In communicating with a patient the seriousness of the illness (current stage), the expected course (exacerbations, LTOT), treatment options, risks and benefits and also the decision-making (CPR, mechanical ventilation, DNR) should be discussed.

Discussion

Goals of communication should be: respect and understanding for the patient; information about illness, its likely course and treatment options; providing empathy, support and appropriate hope; developing a plan in context of patient's goals, values and notions of quality of life.

A 9-step approach can be a useful tool in such communication.

1. Start the meeting: find a private place, introduce yourself and ask everybody else to do the same and explain relationship to the patient.
2. Agree on the purpose of the meeting: to update the news, to break bad news, to discuss decision-making, to provide support.
3. What does the patient/family know? Explore what they already know and understand.
4. How much do they need to know to make decisions around end-of-life issues? Diagnosis, likely course, prognosis; treatment alternatives, risks, benefits; effects on quality of life, goals, values; symptom palliation, expected and anticipated decisions; dying process.
5. Sharing information/responding to emotions: simple, clear, appropriate to level of understanding, show empathy and compassion. Non-verbal communication is very important.
6. Discover their goals, expectations, hopes, values.
7. Address their needs: show empathy and provide support.
8. Develop a plan: When will more information be known? Who will be consulted? What decisions are anticipated? What are we going to do?
9. Arrange follow-up: provide contact information and time of next meeting.

Barriers to effective communication can be due to patients and families or to health care providers. Many patients misunderstand the illness, treatment options and prognosis, lack support and coping mechanisms. Health care providers can be under physical, emotional or psychological stress, can have fears of confronting their own mortality and fears of death.

Conclusions

Whether the COPD patient is in terminal phase of his disease or not physician-patient communication is very important. Communication is a skill like any other medical procedure that needs to be learned and practiced. Proper use of communication skills improves palliative care received by severe COPD patients.

C-1

Acute respiratory failure

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We present an older patient, who was admitted at our department because of asthma exacerbation. After a few days, he was already experiencing some subjective improvement, when despite medications his health status deteriorated and his respiratory failure worsened. The cause of deterioration was not readily recognizable, i.e. there were several possible causes that could have worsened his condition. After careful history and physical examination, the possible trigger for respiratory failure was suggested. The patient had to be transferred to ICU, where suggested diagnosis was confirmed. After appropriate treatment patient's health status improved and he was discharged from hospital with no sequelae.

C-2

Hemoptysis; an unusual presenting symptom of the rupture of the pseudoaneurism of thoracic aorta

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Hemoptysis is a rarely described symptom of the rupture of the aneurism of thoracic aorta. We present a case of the 76 years old patient who underwent in the past grafting of the aneurism of thoracic aorta and in the same session CABG on LCX. Later he developed chronic atrial fibrillation and he was on chronic anticoagulant treatment. He presented with the symptom of hemoptysis for the first time at the end of December 2008 and on that occasion CT scan of the thorax and bronchoscopy was performed but without conclusive reason for hemoptysis. In February 2009 he was admitted again for hemoptysis and he was hemodynamically stable. During this hospitalization a CT angiography of the thorax was done and revealed bleeding from the pseudoaneurism of the aorta with hematoma at the site. Endovascular stenting of the graft was performed and soon after stenting hemoptysis disappeared. Later patient presented some brownish sputum, endoscopic examination revealed extramural compression of distal part of trachea and proximal part of left main bronchus but no sign of active bleeding. The patient is well and still on anticoagulant treatment.

C-3

Invasive pulmonary mycosis in AIDS

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C-4

An usual disease – unusual treatment

Case history of a lungtransplantation

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Case history of a 51 years old woman is presented. Her complains began at age 21, (in 1975.), diagnosis of COPD was set up at age 39, in 1993.

Her disease was quiecent with some ebb and flow during the next 7 years, although co-morbidities of COPD appeared: hypoxia, circulatory failure, GORD, erosiones in stomach, depression.

From November 2004 her condition was getting worse and worse: FEV₁ was 0.74 l, pressure of arteria pulmonary was 80 mmHg). Decompensation set in repeatly in spite of oxygen (during 24 hours/day), LABA, inhaled, sometimes systemic steroid, inhaled parasympatholytic, diuretic, ACE inhibitor, selective beta blocker, proton pump inhibitor therapy.

She was sent to the Lungtrasplantation Committee in June 2005., and in October 2005. lungtransplantation was performed in Vienna.

After 40 months she is well, her lung function test is normal, her circulation is compensated, she works and lives a normal life .

C-5

COPD and tracheobronchial amyloidosis (case report)

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The 78 years old women had metabolic X syndrome, COPD and hyperthyreosis. She had been examined with progressive dyspnoe at our clinic at November of 2005. We diagnosed antibiotics refracter bilateral infiltrations at chest X-Ray and we indicated a bronchoscopy. By the bronchoscopy, we showed inflammated mucosa hyperplasia in both main bronchus and yellow tissue infiltrations in the trachea. The histology result was not showed malignancy and tuberculosis, but bronchial amyloidosis. We planned other examinations, because suspicions of a systemic amyloidosis, but the patient refused that. The Colchicin therapy was effective. Both clinical features and the bronchoscopy pictures were improved during the therapy.

We did not see the patients until 2008. She was urgently hospitalized at our ICU with pneumonia and cardiac decompensation. Caused by long lasting mechanical ventilation, we tracheostomized her. Both endobronchial findings and radiological

features had progression during the last 3 years.

Tracheobronchial amyloidosis is a very rare and slowly progressive disease which is hardly diagnosed by the non specific symptoms and radiological findings. In our case, we suggested the diagnosis by bronchoscopy and this was supported by the histological examination.

C-6

An unusual pulmonary infection (case report)

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We report a case of pulmonary nocardiosis in a patient who presented with fever, cough and chest pain. Chest X-ray and CT showed nodular patchy infiltrates in the lungs. Empirical treatment with levofloxacin (500mg OD) was started, but the symptoms and the chest X-ray findings showed progression. The patient was hospitalized and bronchoscopy was performed. After the suspicion of TB, samples were sent to microbiology and the diagnosis confirmed nocardiosis. The patient showed remarkable recovery after treatment with trimetoprim/sulphamethoxazole. Quick identification of this uncommon pathogen in the cytological material using special stains helped in timely diagnosis and successful treatment of the patient.

C-7

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C-8

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