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## Jahrestagung 2013 der Österreichischen Gesellschaft für Pneumologie

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### Abstracts

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## Fall des Jahres 2013

### F01

#### Bilaterale Infiltrate bei immunkompromittierten Patienten mit EML4-ALK-Translokation

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Ein 63-jähriger Patient mit fortgeschrittenem pulmonalem Adenokarzinom mit zerebralen und hepatalen Metastasen und EML4-ALK-Translokation klagt unter der seit 4 Wochen laufenden Therapie mit Crizotinib plötzlich über zunehmende Ruhedyspnoe, verbunden mit unproduktivem Husten und Fieber.

Eine schwere Oxygenierungsstörung ist mit einer Sauerstoffsättigung von 86 % nachweisbar. Im Thorax-Röntgen zeigten sich bilaterale Infiltrate. In der weiteren Abklärung mittels HR-CT finden sich Milchglasverschattungen und Crazy-paving in beiden Oberfeldern. Laborchemisch sind eine deutliche CRP- und LDH-Erhöhung feststellbar. Eine HIV-Infektion wird ausgeschlossen.

Mittels Bronchoskopie und nachfolgender Aufarbeitung des Materials kann die Diagnose gestellt und der Patient behandelt werden.

Die Behandlung führt zur Regredienz der radiographischen Veränderungen als auch der Oxygenierungsstörung.

röntgen nur schwer zu erkennen. Computertomographie und Bronchoskopie spielen eine zentrale Rolle in der Diagnose. Deswegen sollten sie bei Patienten mit therapierefraktären Asthmasymptomen durchgeführt werden.

Das Verhalten eines pleomorphen Adenoms wurde bisher selten beschrieben aufgrund der geringen Zahl der Fälle. Es hat jedoch zwei Fälle gegeben, wo der Tumor ein malignes und aggressives Verhalten zeigte.

Deswegen müssen solche Tumore als potentiell maligne betrachtet werden und ein Follow-up sollte erfolgen.

Zusammenfassend ist festzustellen, dass ein pleomorphes Adenom als Differentialdiagnose zu einem Asthma bronchiale ohne Therapieerfolg in Erwägung zu ziehen ist, obwohl nur wenige Fälle verzeichnet sind. Computertomographie und Bronchoskopie sind wichtige Diagnosestützen.

### F02

#### Therapierefraktes Asthma bronchiale?

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Eine 35-jährige Patientin wurde zur Abklärung eines inspiratorischen Stridors zugewiesen. Sie wurde bislang mit einer inhalativen broncholytischen Therapie bei Verdacht auf Asthma bronchiale behandelt. In einer flexiblen Bronchoskopie imponierte ein exophytischer Tumor mit glatter Berandung. Er füllte das Tracheallumen fast vollständig aus. In einer starren Bronchoskopie wurde dann eine endoskopische Schlinge angelegt und das Tumorgewebe abgetragen. Die Formation konnte in weiterer Folge mittels Zange geborgen werden. Nach Abtragen war letztendlich die Trachea wiederum vollständig frei. Im Vergleich zur eingangs durchgeföhrten Atemfunktion, wo sich eine deutliche extrathorakale Stenose zeigte, bestanden postinterventionell wiederum normale lungenfunktionelle Daten.

Primäre Tumore der Trachea betragen nur 2 % aller Tumore der oberen Atemwege.

Das pleomorphe Adenom ist der häufigste Tumor der Speicheldrüse. Es entwickelt sich sehr selten in der Trachea mit bisher nur 33 Fällen in der Literatur. Das Durchschnittsalter dieser Patienten war 48 Jahre und die Geschlechterverteilung war gleich. Aufgrund des langsamem Wachstumes dieser Tumore sind Symptome wie Husten, Dyspnoe und Stridor heimtückisch. Die Patienten präsentieren sich mit Asthma und dadurch ist eine Verzögerung in der Diagnose häufig. Unsere Patientin wurde langjährig mit einer inhalativen Therapie bei Verdacht auf Asthma bronchiale behandelt, bis die Diagnose eines Trachealtumors gestellt wurde. Diese Tumore sind im Thorax-

### F03

#### Unklarer Pleuraerguss sucht Diagnose

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Eine 36-jährige Patientin wird erstmals im Mai 2011 vom niedergelassenen Lungenfacharzt zur Abklärung eines rezidivierenden Pleuraergusses links zugewiesen. Anamnestisch besteht ein allergisches Asthma bronchiale mit Z. n. Desensibilisierung. Weiters war bereits 2008 ein Pleuraerguss mit positivem Tuberkulin-Hauttest bekannt, die Patientin erhielt damals eine 3-monatige tuberkulostatische Therapie. Anschließend war der Erguss nicht mehr nachweisbar.

Im auswärtigen Thorax-CT findet sich ein 3 Querfinger hoher Pleuraerguss links mit Dystelektasen des Unterlappens. Sonographisch ist der Pleuraerguss zum Aufnahmepunkt hierorts nicht punktabel. Laborchemisch finden sich gering erhöhte Entzündungsparameter, die sich auf Antibiotikagabe wieder normalisieren. Bronchoskopisch bestehen unauffällige Verhältnisse, die spezifischen Kulturen sowie die weiteren Befunde sind negativ.

Klinisch besteht kein Hinweis auf Systemerkrankung, die serologischen Parameter (ANA, ANCA) zeigen ebenfalls keine Auslenkung.

Bei anschließenden ambulanten Kontrollen ist der Erguss nicht mehr nachweisbar. Ein im August 2011 durchgeföhrtes PET-CT ergibt keinen Hinweis auf gesteigerten Traceruptake, sodass vorerst weitere Kontrollen vereinbart werden.

In weiterer Folge entwickelt die Patientin links eine Pleuraschwiele, sowie zusätzlich einen diskreten basalen Erguss rechts. Sie wird daraufhin im AKH Wien zur VATS zugewiesen und so letztendlich die Diagnose gestellt und die Patientin einer Behandlung zugeführt.

## F04

## Das trojanische Pferd

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**Fallbericht:** Ein 57-jähriger Patient wird im Oktober 2011 im Landeskrankenhaus Feldkirch mit Fieber und Husten vorstellig. Es besteht ein Status post Nierentransplantation 2009 aufgrund einer Refluxnephropathie.

Im CT-Thorax zeigen sich fleckförmige Infiltrate in der Lingula und im dorsobasalen Unterlappen links. Der Erreger nachweis aus Blutkultur und bronchoalveolären Lavage ergibt Rhodococcus equii. Unter nierenadaptierter i.v.-Antibiose mit Meropenem und Clarithromycin normalisieren sich die ursprünglich erhöhten Entzündungswerte. Es erfolgt die Umstellung auf orale Gabe von Moxifloxacin und Azithromycin, woraufhin sich der Patient zwar klinisch beschwerdefrei, die Infiltrate aber unverändert präsentieren. Aufgrund der Vermutung einer organisierenden Pneumonie wird die Steriodosis gesteigert und initial Linezolid, bei weiterer bildgebender Verschlechterung dann additiv Meropenem verabreicht. Hierunter ist eine nur minimale Befundverbesserung zu erzielen. Wir übernehmen den Patienten im Mai 2012 zur Diagnosesicherung an unsere Abteilung. Sämtliche weitere infektiologische Abklärung bleibt ohne pathologischen Befund.

Wegen eines erhöhten OP-Risikos wird von einer thorakoskopischen Intervention abgesehen und eine transbronchiale Biopsie favorisiert. Diese erbringt zu wenig repräsentatives Material, sodass eine CT-gezielte Punktions des Infiltrates durchgeführt wird. Postpunktionell fiebert der Patient, und in der Blutkultur wird neuerlich Rhodococcus equui nachgewiesen.

Nach Rücksprache mit den Infektiologen erfolgt eine 3fach-Therapie mit Clindamycin, Doxycyclin und Azithromycin, worunter es zu einer Stabilisierung kommt und der Patient nach Hause entlassen werden kann. Aufgrund der Bakterämie ist der Patient einer operativen Sanierung gegenüber negativ eingestellt und entscheidet sich für alternativmedizinische Maßnahmen. Im Februar 2013 verstirbt der Patient an einer Rhodococcus equui-Sepsis mit Abszess der Thoraxwand und Pericarditis per continuitatem.

**Schlussfolgerungen:** Rhodococcus equui ist ein grampositives, partiell säurefestes, fakultativ intrazelluläres kokkoides Stäbchen und Hauptverursacher von Bronchopneumonien bei Pferden, kann aber auch selten bei Immunsupprimierten opportunistische Infektionen verursachen. Anamnestisch war zu erheben, dass der Patient neben einer Reitbahn wohnte. Diese Kasuistik zeigt die Gefährlichkeit dieses seltenen Keims und das Risiko einer Keimverschleppung und potentiellen Sepsis durch eine transthorakale Punktion.

## F05

## Mediastinale Raumforderung

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Bei Herrn XY, 54 Jahre, wurde im Rahmen einer Routineuntersuchung im Lungensrötgen eine mediastinale Verschattung diagnostiziert, diese einer weiterführenden Untersuchung mittels Computertomografie zugeführt.

An unserer Abteilung wurde Herr XY zur bronchoskopischen Abklärung vorstellig. Der Patient präsentierte sich in gutem Allgemeinzustand, pulmonal vollkommen beschwerdefrei. Anamnestisch waren eine arterielle Hypertonie, Hyperlipidämie und ein Zustand nach Nikotinabusus zu erheben.

In der mitgebrachten Computertomografie des Thorax zeigten sich im rechten Mediastinum eine, der Trachea anliegende Raumforderung ( $43 \times 46 \times 51$  mm), sowie eine mediastinale Lymphadenopathie. Zusätzlich waren zwei intrapulmonale Rundherde sowie eine Raumforderung im Bereich des Milzpolys auffällig.

Lungenfunktionell bestanden altersentsprechend normale Flow- und Volumenparameter. Blutgasanalytisch lag eine gute Oxygenierung vor, mit Anstieg der  $\text{PO}_2$  unter Belastung.

In weiterer Folge wurde eine Bronchoskopie (mit EBUS) durchgeführt, in dieser konnte eine große zystische Formation paratracheal dargestellt werden. In der zytologischen Aufarbeitung fanden sich zahlreiche kleine isomorphe lymphatische Zellen mit eingestreuten Histiozyten.

Differentialdiagnostisch kam neben Dermoidzysten, Struma und Teratomen auch eine Thymuszyste in Frage. Auch eine primäre Tumorerkrankung der Lunge konnte nicht mit Sicherheit ausgeschlossen werden.

Im Rahmen der weiteren Durchuntersuchung wurde ein PET Scan angefertigt, in diesem waren keine hypermetabolen Herde nachweisbar.

Die histologische Untersuchung ergab ein lymphozytenreiches Punktat mit Nachweis kleiner, spindeliger epithelialer Zellen. Das morphologische Bild sprach für das Vorliegen einer thymogenen Zyste.

Die Therapie der Wahl ist eine operative Sanierung, sodass der Patient an der thoraxchirurgischen Abteilung des AKH vorgestellt wurde. Ein Operationstermin wurde für Herbst 2013 vereinbart.

**Schlussfolgerungen:** Die zweithäufigste Ursache für mediastinale Raumforderungen sind Veränderungen des Thymus.

Diese sind meistens gutartig. Thymuszysten sind mit einer Prävalenz von 3% eine seltene, gutartige Ursache für mediastinale Raumforderungen.

Typisch ist, dass Thymuszysten als Zufallsbefunde diagnostiziert werden und die betroffenen Patienten häufig beschwerdefrei sind.

## F06

## Lungenkarzinom in der Schwangerschaft

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**Anamnese:** Übernahme aus KH der Barmherzigen Brüder Linz unter der Verdachtsdiagnose einer Tuberkulose. Die 29-jährige Büroangestellte ist in der 26. SSW und klagt über seit 9 Wochen therapieresistenten Husten mit intermittierenden Hämoptyseen, sowie Schmerzen in der BWS (Th2/3). Bis auf eine bekannte substituierte Hypothyreose unauffällige Anamnese und bisheriger Schwangerschaftsverlauf. 3 Jahre Gelegenheitsraucherin. Passivrauchexposition.

**Diagnostik 05/2012: Labor:** Normozytäre, normochrome Anämie (Hb 10,2 g/dl), CRP 8,8 mg/dl, Lymphopenie 12 %.

**Thorax-Röntgen:** Infiltrationszone rechts pulmonal mit Maskierung des rechten Hilus, sowie flache Infiltrate linksseitig.

**Tuberkulosebefunde** (MMT, Quantiferon, Flüssig- und Festkulturnen) allesamt negativ.

**Bronchoskopie:** Ödematöse Einengung des anterioren Oberlappensegments rechts und des Mittellappenostiums - 6 Probeexzisionen aus dem Oberlappen und Bronchialspülung.

**Histologie:** Großzelliges Karzinom, aus immunmorphologischer Sicht in erster Linie Adenokarzinom - ERCC1 und Thymidylat-Synthase negativ.

**Tumormarker** (Ca19.9, CEA, Cyfra 21-1, Ca125) deutlich erhöht.

**Staging mittels MR (Thorax, Abdomen, Schädel):** Raumforderung rechts zentral mit Stenosierung OL- und ML-Bronchus mit intrapulmonalen Metastasen; Wirbelkörper-Filialisierung Th2/3 mit V. auf epidurale Infiltrationszone; multiple zerebrale Filiae supratentoriell.

**Diagnose:** Adenokarzinom der Lunge mit multipler Metastasierung - CT4NxM1b - Stadium IV.

**Therapie/Verlauf:** Einleitung einer Chemotherapie mit Carboplat/Taxotere (1 Zyklus AUC 5-90 %) unter gynäkologischer Kontrolle 6. 6. 2012.

Bestrahlung der Region Th1-3 mit 3000 cGy in 12 Fraktionen von 11.6-27.6. 2012.

**20. 6. 2012:** Exon 19 Mutation des EGF-Rezeptors mit Wahrscheinlichkeit eines guten Ansprechens auf Anti-EGFR-Therapie.

**2. 7. 2012:** Entbindung eines gesunden Mädchens (1441 g, 41 cm) mittels Sectio in der 31.(+0)SSW nach Lungenreifung mit Solo-Celestan.

**Ab 4. 7. 2012:** Beginn mit Gefitinib (Iressa<sup>®</sup>) 250 mg 1x tgl. nach Abstillen mit Dostinex.

**07/2012:** CT HWS/BWS: instabile Kompressionsfraktur BWK2 mit Kompression des Myelons.

**6. 7. 2012:** ventrale Korpporektomie Th1/2+dorsale Osteosynthese C6/7 auf Th3/4

**Restaging 08/2012:** Klinisch stabil, Iressa assoziierte Dermatitis; thorakal und cerebral partielle Remission.

**Follow-up:** 08/2012 klinisch und radiologisch regredient unter Gefitinib.

**03/2013:** klinisch und radiologisch stabiler Befund unter laufender Gefitinibtherapie.

## F07

### Ein Fleck, drei Diagnosen

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Bei einem 1956 geborenen Patienten wurde nach Angabe von B-Symptomatik eine pulmonale Raumforderung im li. OL diagnostiziert. Nach Biopsie wurden lediglich Veränderungen einer Anthracosilikose festgestellt. Bei jedoch weiterhin bestehender B-Symptomatik und TBC in der Anamnese wurde bei positivem Quantiferontest der Verdacht auf eine atypische Mycobakteriose oder Superinfektion vermutet, weshalb eine Therapie mit Klacid und Rifoldin über eingeleitet. Aufgrund des unveränderten Zustandes wurde nach einigen Monaten eine offene Biopsie durchgeführt. Dort wurde ein Plattenepithelkarzinom festgestellt, weshalb eine Lobektomie 09/2012 durchgeführt wurde. Der Zustand des Patienten besserte sich daraufhin. Jedoch wurde in der Kontrolluntersuchung eine sternförmige Narbenregion rechts entdeckt. Auch hier ergab die Biopsie eine Anthracosilikose!

## F08

### Junger Patient mit akutem Abdomen – beinahe fataler Verlauf

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**Anamnese und Klinik:** Ein 27-jähriger Mann wird aufgrund akuter kolikartiger Bauchschmerzen, Übelkeit und Stuhloverhalt an einem auswärtigen Krankenhaus vorstellig. Anamnestisch erwähnenswert eine cystische Fibrose (Genotyp Phe 508 del homozygot), eine Leber- und Inselzelltransplantation 2002 sowie ein Adhäsionsileus 2010.

**Diagnostik und Differentialdiagnosen:** Im Abdomen-Leer-Röntgen imponieren multiple Spiegelbildungen, eine Abdominal-CT zeigt weite Dünndarmschlingen, impaktierten Stuhl distal davon und einen Kalibersprung im Ileum, außerdem einen Hungerdarm ab der linken Colonflexur.

Es handelt sich um ein distales intestinales Obstruktionssyndrom (DIOS), eine Obstruktion vorwiegend von terminalem Ileum und Coecum durch zähe, eingedickte mucofäßale Massen. Differentialdiagnostisch kommen Invagination, Obstipation, Volvulus, entzündliche Alterationen und letztlich auch Malignome in Frage. Typisch ist eine palpable Stuhlwalze im rechten Unterbauch, sowie die oben erwähnten radiologischen Befunde.

**Verlauf:** Gastrografingabe via Magensonde ist aufgrund von Erbrechen unergiebig. In Unkenntnis eines DIOS wird der konservative Weg nicht weiter forciert und wegen Verschlechterung des Allgemeinzustands und Fieber schließlich laparotomiert. Es besteht eine Obstruktion des distalen Dünndarms durch Stuhlmassen weswegen manuell dekomprimiert wird.

Im Anschluss Übernahme an die Intensivabteilung intubiert und beatmet. Die Beatmungsdrücke steigen stetig (Spitzendruck 38 cm H<sub>2</sub>O, PEEP 15 cm H<sub>2</sub>O), die Oxygenierung wird trotz mehrmaliger bronchoskopischer Absaugung immer schlechter und ein Weaning ist nicht möglich. Schließlich nach einer Woche Überstellung an unsere Intensivabteilung zur Weiterbetreuung und eventuellen ECMO. Nach Anlage eines Tracheostoma gelingt unter konsequenter endoskopischer Bronchialtoilette, initial bis zu viermal täglich, eine rasche Reduktion der Beatmungsdrücke und nach zwei Wochen ist die Entwöhnung vom Respirator möglich. Aufgrund von allgemeiner Schwäche besteht nach wie vor eine relevante Clearanceproblematik, es muss für weitere zwei Wochen, bis zum Tracheostomaverschluss, täglich, insgesamt knapp 70 mal bronchoskopiert werden. Anschließend rasche Erholung und Entlassung nach sechs Wochen Spitalsaufenthalt.

**Schlussfolgerungen:** Ein DIOS ist eine bei CF-Patienten, insbesondere jenen mit schwerem Genotyp, häufige Komplikation, welche in der Regel konservativ (PEG p. o. sowie Gastrografin p. o. und als Einlauf) gelöst werden kann (> 90 % Effektivität). Eine Operation ist Ausnahmefällen vorbehalten, zumal bei diesem Patientenkollektiv mit einer hohen peri- bzw. postoperativen Morbidität und Mortalität zu rechnen ist.

## F09

### Ein Triathlet mit akuter Dyspnoe und Hämoptysen

K. Pintscher, M. Hubner, M. Kneussl

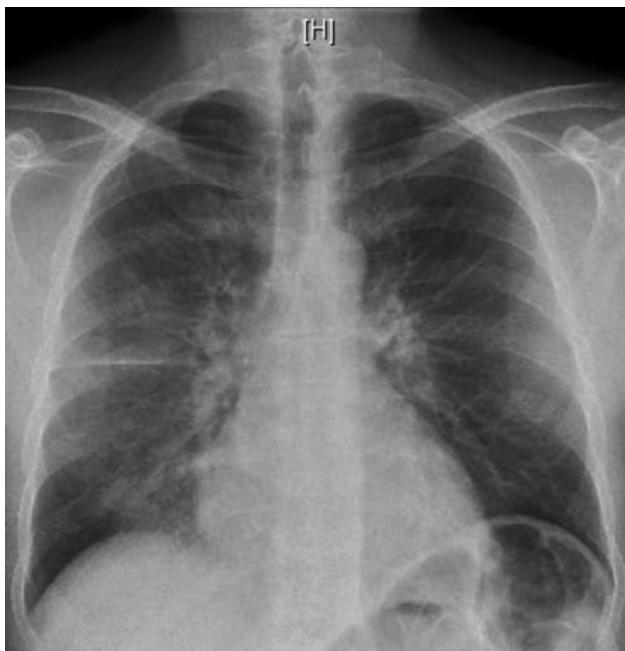
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## abstracts

Während der Schwimmdisziplin im Rahmen eines Triathlons kam es bei einem 50-jährigen Mann zum Auftreten von Dyspnoe und Hämoptysen. Laborchemisch zeigten sich eine Linksverschiebung bei normalen CRP sowie ein erhöhtes D-Dimer. In der arteriellen Blutgasanalyse fand sich eine Partialinsuffizienz unter Raumluftatmung. Das Thoraxröntgen ergab ein infiltratsuspektes Areal im rechten Oberlappen sowie Stauungszeichen Grad I. Computertomographisch fand sich kein Nachweis thromboembolischer Füllungsaussparungen, allerdings beidseitige alveolare Verdichtungsareale. Drei Tage danach war der Patient ohne Therapie völlig beschwerdefrei; radiologisch zeigte sich eine vollständige Rückbildung der alveolären Veränderungen, das Labor war unauffällig. Die Lungenfunktion mit DLCO ergab einen Normalbefund.

Zusammenfassend sprachen die spontane Reversibilität der pulmonalen Veränderungen sowie der klinische Verlauf mit spontaner Beschwerdefreiheit innerhalb von 48 h für ein Swimming Induced Pulmonary Edema (SIPE), einer seltenen Form eines nicht kardio-genen Lungenödems.

Ursächlich wird ein „pulmonary capillary stress failure“ durch Integritätsverlust der Kapillarwand mit konsekutivem Flüssigkeitseinstrom in die Alveolen während intensiver körperlicher Belastung mit übermäßigem Anstieg des transmuralen Drucks in den Kapillaren angenommen. Das SIPE ist selbstlimitierend. Die Therapie ist supportiv mit Sauerstoffgabe und eventuell Inhalation eines Beta-2-Agonisten. Diuretika haben basierend auf dem pathophysiologischen Mechanismus keinen Nutzen [1].



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## F10

### Therapie eines pleuraständigen Tumors mit Cortison

T. Efsthathiades, A. Fazekas, M. J. Hochmair, M. Vesely, M. K. Breyer, C. Pirker, O. C. Burghuber

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Eine 73-jährige Patientin kommt wegen epigastrischer Schmerzen und Emesis zur stationären Aufnahme. Laborchemisch zeigt sich ein erhöhtes hs-Troponin-T bei unauffälligem EKG und fehlendem Enzymanstieg. Eine Koronarangiographie liefert die zugrundeliegende Ursache des NSTEMI – eine Stenose eines Seitenastes der ACX.

Als Zufallsbefund findet sich im Thoraxröntgen eine Raumforderung im linken dorso-basalen Unterlappen, welche sich in einer anschließenden CT Thorax ( $\varnothing 3$  cm) sowie in einem PET Scan bestätigt. Zusätzlich zeigte sich im CT Thorax eine hiläre, bronchiale Einengung, einer möglichen intrabronchialen Tumormasse entsprechend.

In einer diagnostischen CT-gezielten Punktion der beschriebenen Raumforderung findet sich nach histologischer Aufarbeitung der gewonnenen Materialien ein *inflammatorischer myofibroblastischer Tumor (IMT)*.

IMTs sind Weichteiltumore, die in nahezu allen Bereichen des Körpers vorkommen können. Die Altersverteilung ist relativ breit, jedoch finden sich bei Kindern vorwiegend abdominelle IMTs, während die pulmonalen bevorzugt beim Erwachsenen auftreten. Im Detail sind IMTs Spindelzelltumoren mit einem unterschiedlich stark ausgeprägten, überwiegend plasmazellulären Entzündungsinfiltrat, die nur in seltenen Fällen maligne sind. Die Inzidenz beträgt weniger als 1% aller resezierter Tumore [1, 2]. Die Pathogenese ist aufgrund des seltenen Vorkommens völlig unklar. Diskutiert wird ein primär entzündlicher Prozess oder ein niedermaligner Prozess mit nachfolgender entzündlicher Reaktion [2]. In über der Hälfte der Fälle ist immunhistochemisch ein ALK-Re-arrangement detektierbar [3]. In unserem Fall war die ALK-Testung aber negativ.

Aufgrund des kardiovaskulären Risikos der Patientin und der hochwahrscheinlich benignen Natur des Tumors wurde eine Kortikosteroidtherapie, die in einigen Fällen zu guten Ergebnissen führte, eingeleitet. Unter jener zeigt sich in einer CT-Thorax Verlaufskontrolle eine deutliche Regression des Tumors ( $1,7 \times 2,4$  cm). Die einst beschriebene hiläre bronchiale Einengung konnte ebenso nicht mehr nachgewiesen werden und ist am ehesten als reaktive Lymphknotenvergrößerung zu werten. Die Patientin ist subjektiv seither beschwerdefrei.

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## F11

### Expansion im Pankreas + Raumforderung an der Wirbelsäule + Lungenrundherde = einfache Diagnose!?

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**Anamnese:** Ein 53-jähriger Patient suchte wegen zunehmender Lumbalgie und unproduktiven Hustens den Hausarzt auf. Eine MRT der LWS zeigte degenerative Veränderungen. Wegen Persistenz des Hustens und der Infektzeichen trotz antibiotischer Therapie wurde eine CT des Thorax veranlasst.

**CT-Thorax:** Mehrere noduläre Rundherde beidseits mit radiären Ausläufern bis max. 1,8 cm im Durchmesser. Nebenbefund: paravertebraler Weichteiltumor in Höhe TH IX-XI; Nebenbefund: 2,5 cm große Expansion im Pankreaskopf.

**DD:** Metastasierendes Karzinom mit Primum in der Lunge oder im Pankreas. Die Pankreasenzyme und die Tumormarker waren unauffällig, CRP 124 mg/l. Die Raumforderung im Pankreas wurde biopsiert.

**Histologie:** Schwere chronische nekrotisierende, zum Teil epitheloidzellig-granulomatöse Entzündung mit V. a. TBC.

**Verlauf:** Der Patient wurde deshalb an unsere Abteilung transferiert. In der Abklärung zeigte sich im bronchoskopisch gewonnenen histologischen Material eine epitheloidzellige granulomatöse Entzündung verdächtig auf eine Tuberkulose. Retrospektiv interpretierten die Radiologen die beschriebene Raumforderung an der Wirbelsäule als tuberkulöse Spondylodiscitis. Eine antituberkulöse 4-fach Therapie wurde eingeleitet. Der Quantiferon-TB-Gold Test blieb negativ, im Bronchialsekret konnte keine mykobakterielle DNA nachgewiesen werden, die Kultur war noch ausständig. Nach 4-wöchiger spezifischer Therapie waren die Rückenschmerzen und der Husten progredient, zudem traten abdominelle Beschwerden hinzu. Die nodulären Läsionen in der Lunge waren radiologisch großenprogredient mit zentralen Kavernen, ebenso verdoppelte sich die Größe des Pankreastumors.

**Diagnose:** Es erfolgte die Bestimmung der spezifischen Autoantikörper, welche hochpositive c-ANCA-Titer (1:1280) und Pr3-ANCA-Titer (155) ergaben, sodass nun die Diagnose einer Granulomatose mit Polyangiitis (GPA – ehem. Wegener-Granulomatose) gesichert war. Der Weichteltumor an der Wirbelsäule wurde nun als Periaortitis gewertet.

**Therapie:** Nach 6 Stößen einer leitliniengerechten Therapie mit Cyclophosphamid i. v. und Prednisolon p. o. kam es zu einer radiologischen Vollremission und zur Normalisierung der ANCA bei subjektiver Beschwerdefreiheit des Patienten.

**Fazit:** Pankreasbeteiligung als auch Periaortitis im Rahmen einer GPA sind für sich bereits äußerst selten, ein kombiniertes Vorkommen wurde noch nie beschrieben.

## F12

### Ungewöhnliche Lungenembolie – Palacos Embolie nach Vertebroplastie

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Perkutane Zementaugmentationssysteme haben sich in den letzten 10 Jahren als eine effektive Behandlungsmethode bei Wirbelkörperkompressionsfrakturen durchgesetzt.

Bei der mit der perkutanen Vertebroplastie verwandten Kyphoplastie (KP) werden expandierbare Ballons in den Wirbelkörper eingebracht und nachfolgend die entstandene Kavität mit Zement gefüllt.

Wesentliche Komplikationen einer Zementauflösung sind ähnlich wie bei der Vertebroplastie Austritte des flüssigen Knochenzements aus dem Wirbelkörper. Bei der (Ballon)-Kyphoplastie kann durch die Formung eines Hohlraums ein etwas dickflüssigerer PMMA-Zement verwendet werden, so dass insgesamt die Rate an Zementaustritten im direkten Vergleich zur Vertebroplastie geringer ist.

**Fallbeispiel:** Wir berichten über eine 78-jährige Patientin, bei welcher aufgrund osteoporotischer Wirbelkörpereinbrüche im Jahr 2003 eine perkutane Wirbelkörperaugmentation im Bereich LWK 2 und LWK 4 durchgeführt wurde.

Zehn Jahre später wurde aufgrund von zunehmender Belastungs-dyspnoe eine Multislice CT des Thorax (ohne Kontrastmittel bei chron. Niereninsuffizienz) durchgeführt. Mit dem Befund von mul-

tiplen vor allem in der rechten Lunge gelegenen Subsegmentembolien wurde die Patientin an unserer Institution vorstellig.

Die Zementembolie nach Vertebro- bzw. Kyphoplastie wird als oft asymptomatische, aber ernstzunehmende Komplikation beschrieben. Die Häufigkeit von pulmonalen Zementembolien nach perkutanen Wirbelkörperaugmentationen variiert in der Literatur zwischen 3,5–23 %.

Es gibt derzeit in der Literatur keine klaren Therapieempfehlungen. Die meisten Autoren tendieren zu einem konservativen Vorgehen im Sinne einer Antikoagulation für ca. 6 Monate zur Vermeidung von Appositionsthromben. Ein postinterventionelles Lungenröntgen als Screeningmethode wird von einigen Zentren empfohlen.

Die operative Embolektomie als einzige kausale Therapieoption sollte aufgrund der damit verbundenen Risiken nur bei ausgedehnten zentralen Embolien durchgeführt werden.

## F13

### Fieber, Husten, Dyspnoe: banale Symptome, exotische Ursache

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**Anamnese:** Eine 63-jährige Patientin wird wegen persistierendem Husten mit klarem Auswurf, subfebriler Temperatur, Belastungsdyspnoe sowie Muskel- und Gelenksschmerzen an die pneumologische Abteilung überwiesen. Vorbekannt sind eine COPD, langjähriger Nikotinkonsum, Diabetes mellitus II und eine Hausstaubmilbenallergie.

**Verlauf:** In der CT des Thorax zeigen sich Oberlappen-betonte, mikronoduläre Strukturveränderungen beidseits, außerdem bestehen leicht erhöhte Entzündungsparameter. In der Lungenfunktion zeigt sich eine bronchiale Obstruktion mit Überblähung, entsprechend einer COPD GOLD III, eine verminderte Diffusionskapazität sowie eine erhöhte AaDO<sub>2</sub>.

Zur Gewebsgewinnung wird eine Bronchoskopie durchgeführt. Histologisch besteht das Bild einer respiratorischen Bronchiolitis mit peribronchiolarer Fibrose ohne Anhaltspunkte auf eine EAA oder Sarkoidose, präzipitierende IgG liegen nicht vor. Auch die Autoimmundiagnostik, Quantiferonserologie sowie PCR-Analyse auf säurefeste Stäbchen sind unauffällig. Zusätzlich wird eine Serologie auf systemische Pilzinfektionen durchgeführt. Überraschenderweise findet sich ein erhöhter IgM-Titer für Coccidioides (0,415), IgG war negativ. Somit konnte histologisch zwar keine Diagnose gesichert werden, in Zusammenschau mit den Symptomen besteht allerdings ein hochgradiger Verdacht auf eine seltene akute Coccidioides-Infektion.

Nach einer dreimonatigen oralen Therapie mit Fluconazol haben sich die Konsolidierungen vollständig rückgebildet. In der Lungenfunktion ist eine deutliche Besserung der Obstruktion zu verzeichnen, die Diffusionskapazität hat ebenfalls zugenommen. Nach weiteren vier Monaten ist der IgM-Titer noch schwach positiv, eine Serokonversion hat allerdings (noch) nicht stattgefunden.

**Take Home Message:** Coccidioides Sporen sind aus dem Erdreich stammende Pilze, welche ein diffuses Spektrum an Symptomen verursachen können, von mildem Fieber bis zu schweren disseminierten Verläufen.

Die Endemiegebiete befinden sich vornehmlich in den südlichen USA sowie Teilen Südamerikas. Häufig kommt es zu Lungenbeteiligungen mit Atemnot, Thoraxschmerzen, Husten und Fieber; oft können auch Arthralgien auftreten, sodass diese Erkrankung auch

den Namen „desert rheumatism“ und „San-Joaquin-Valley-fever“ (als Hochrisikogebiet) bekommen hat. Die Kultivierung des Pilzes ist problematisch und erfordert spezielle Sicherheitsmaßnahmen. Eine histologische Diagnose gelingt gelegentlich, empfohlen wird der serologische Nachweis von Antikörpern. Die Therapie sollte jedenfalls ein Konazol für mindestens 3–6 Monate beinhalten.

**F14****33 jährige Frau mit großer thorakaler Raumforderung**

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**Fallbericht:** Eine junge Patientin wurde über die Notaufnahme (EBA) an unserer Abteilung vorstellig. Zuweisungsdiagnose „Sero-thorax“. Anamnestisch bestand ein fiebigerhafter Infekt vor etwa 2 Wochen mit persistierenden atemabhängigen linksseitigen Thoraxschmerzen, Leistungsminderung sowie ein „Plätschern in der Brust“ beim Joggen. Die weitere Anamnese war unauffällig.

**Status:** 33a, weiblich, leicht red. AZ guter EZ, afebril. Pulmo: verschärftes VA bds., abgeschwächtes Atemgeräusch li. Mittelfeld, aufgehobenes Atemgeräusch und Dämpfung li. Unterfeld. Des Weiteren auch Klopfsschmerzhaftigkeit in diesem Bereich. Der weitere Status war unauffällig.

**EKG:** Sinusrhythmus 73/min, keine pathologischen Veränderungen.

**Labor:** Blutbild, Leber, Niere, Gerinnung, Elektrolyte, Herzfermente und Entzündungsmarker waren völlig bland.

**CT-Thorax:** 7,5 cm haltender Pleuraerguss li. Ca. 11 × 10,8 × 11,5 cm rundliche, gut umschriebene, arteriell teilvaskularisierte, inhomogene Expansion in der li. Lunge basal. Die Dichtewerte teils inhomogen mit flüssigkeitsäquivalenten und soliden

Anteilen. Mediastinalshift nach re. Keine pathologisch vergrößerten mediastinalen Lymphknoten. Pleuraspitzenschwielen re. Ansonsten die re. Lunge unauff. (Abb. 1).

**PET:** Pathologisch große rundlich konfigurierte Expansion inhomogen FDG-metabolisierend beinahe gesamthaft im linken Lungenunterlappen.

**Pleurapunktion li.:** Entzündlicher unspezifischer Erguss, ZN negativ.

**CT-gezielte Punktion, li. Unterlappen:** Anteile eines Schwannoms. Kein Hinweis auf Malignität.

**Therapie:** Operative Komplettentfernung und endgültige Diagnose eines Schwannoms als seltene Ursache eines intrathorakalen Tumors. Ein postoperativer Fluidopneumothorax wurde erfolgreich drainiert. Die Patientin konnte schließlich in gebessertem Allgemeinzustand entlassen werden.



**Abb. 1:** CT-Thorax bei Vorstellung

## Poster

Die mit \* markierten Poster wurden in einem anonymisierten Reviewerverfahren als beste Poster ausgewählt.

### P01

#### Quantitative determination of lung vessel tortuosity, but not fractal dimension correlates with lung function parameters of PH patients

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**Background:** Pulmonary hypertension (PH) can result in decrease of volume of blood vessels, vascular pruning and increased tortuosity of the blood vessels. In this study we examined whether automatic calculation of tortuosity and 3D fractal dimension of the segmented lung vessels can provide information about the lung function of PH patients.

**Methods:** Twenty patients with PH were examined with contrast-enhanced chest computed tomography (CT) following their diagnostic lung function test. Images of the whole thorax were acquired with a 128-slice dual-energy CT scanner. After lung identification an automatic vessel extraction algorithm with a vessel enhancement filter was used to detect lung vessel segments. From these the vascular trees were generated. The tortuosity of each vessel segment (distance metric) was calculated by dividing its length with the Euclidean distance between the end points. 3D fractal dimension (FD) was computed using the box counting method on the vessel centerlines. Lung function data was used for correlation.

**Results:** Vessel tortuosity quantification resulted in a significant, negative correlation of distance metric with total lung capacity (TLC, Spearman correlation coefficient:  $r = -0.44$ ) and other relevant clinical parameters, like functional vital capacity ( $r = -0.48$ ) or forced expiratory volume in 1 s ( $r = -0.46$ ). However, distance metric did not correlate with diffusing capacity. A positive correlation of 3D FD was found with the TLC ( $r = 0.49$ ), whereas no other correlations with the lung function parameters were observed. Conclusion: Automatic segmentation of the lung vascular tree can provide measures of blood vessel properties. Non-invasive quantification of pulmonary vessel tortuosity may be useful in monitoring the functional status of the lung.

### P02

#### Endoscopic placement of fiducial markers for real-time tumor-tracking radiotherapy in 50 patients with lung cancer: a feasibility study

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**Background:** Fiducial markers can be used for real-time tumor-tracking radiotherapy in patients with lung cancer. CT-guided placement is associated with a substantial complication rate (15–30% pneumothorax). In this retrospective study we examined the feasibility and safety of bronchoscopic placement of fiducial markers (gold coils) into/nearby solid lung lesions.

**Methods:** We placed 137 gold coils (35 by needle:  $0.5 \times 5$  mm, and 102 by brush:  $1.2 \times 3$  mm) in 50 consecutive patients with lung lesions. We used electromagnetic navigation bronchoscopy (ENB) and/or fluoroscopy for guidance. 74% of patients were male, mean age was 71.6a, mean FeV1 was 1.7 l (60% of predicted). Anatomical distribution of lung lesions was mostly in the inner-third of the lung parenchyma (38%), followed by peripheral lesions (34%) and lesions located in the mid-third of the lungs (28%).

**Results:** Migration rate of the fiducial markers was 20%. We did not observe any severe complications throughout bronchoscopy, e.g. pneumothorax or haemoptysis. Three (=8%) of the patients developed radiotherapy-associated pneumonitis.

**Conclusions:** Placement of fiducial markers through ENB or fluoroscopy guided bronchoscopy is a safe and effective method without complications. Real-time tumor-tracking radiotherapy with fiducial markers decreases the risk of pneumonitis.

### P03

#### Airflow obstruction in the general population: bronchodilation makes the difference

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**Background:** Although recommended, most lung function studies in the general population abandon bronchodilation when defining airflow obstruction and evaluating the prevalence of chronic obstructive lung diseases. The aim of the present study was to evaluate the prevalence of airflow obstruction pre and post bronchodilation in a general population.

**Methods:** The ongoing Austrian LEAD study intends to evaluate the natural decline in lung function in a general population. Participant's lung function was assessed pre and post bronchodilation. Airflow and fixed airflow obstruction were defined as FEV1/FVC < 0.7 pre and post bronchodilation. Reversible airflow obstruction was defined as FEV1 ≤ 85% pre bronchodilation and an increase ≥ 200 ml or ≥ 12% of FEV1 pre bronchodilation.

**Results:** In total 1268 participants (male: 46%, age:  $53 \pm 17$  years) were included. Airflow obstruction was diagnosed pre and post bronchodilation in 15.3 and 10.4%, respectively ( $p < 0.01$ ). Of those 15.3% having airflow obstruction pre bronchodilation, 63.9% had fixed airflow obstruction and 54.6% had reversible airflow obstruction, repre-

## abstracts

senting 9.8 and 8.4 % of the total population, respectively. Both, fixed and reversible airflow obstruction was seen in 36.6 %.

**Conclusions:** When defining airflow obstruction in the general population, lung function including bronchodilation should be performed in order to accurately evaluate the prevalence of chronic obstructive lung diseases.

### P04

#### Prevalence of smoking in the Austrian general population

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**Background:** Smoking is the main preventable cause of premature death and the main risk factor for chronic obstructive pulmonary disease. According to the Eurobarometer 2010, the prevalence of ever smoking in Austrian is higher compared to other European countries (57 vs. 51%, respectively). An underlying cause might be the failure of national smoke ban actions.

**Methods:** We aimed to investigate the prevalence of active and second hand smoking in Austrian male and female participants of the Austrian LEAD study, an ongoing, longitudinal, observational, population based cohort study.

**Results:** Interim analysis ( $n=1.314$ ; male 47%; age  $51.9 \pm 17$  years) showed that in Austrian male and female participants ever smoking (65 and 56%; respectively) as well as second hand smoking (70 and 70.8%; respectively) in childhood and/or adulthood are highly prevalent. Second hand smoke in adulthood lasts on average  $17.4 \pm 13.3$  years and happens predominantly at work (20.6%). Interestingly, ever-smokers have a higher prevalence of second hand smoking compared to never smokers in both, childhood and adulthood ( $p < 0.01$ ).

**Conclusions:** Active smoking and second hand smoking are highly prevalent in Austria and national smoke ban actions have to be executed more strictly in order to reduce smoking itself as well as smoking related morbidity and mortality.

### P05

#### Evaluation of Fatigue in COPD patients

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**Background:** The aim of this study was to investigate the perception of fatigue in patients with COPD and to determine the relationship between fatigue and exercise tolerance measured with Six-Minute Walk Test (6MWT).

**Methods:** The study included 140 patients with stable COPD (70 GOLD stage II and 70 GOLD stage III), 90 men and 50 women, aged 42–80 years. Spirometric measures of pulmonary function and 6MWT were carried out in each patient. Fatigue was measured with the Fatigue Assessment Scale, questionnaire consisting of 10 items (FAStotal): five questions reflecting physical (FASphysical) and five

mental fatigues (FASmental), respectively. The patient was also asked to indicate his/her level of fatigue by using a Borg scale (from 0 to 10) at the beginning and at the end of the 6MWT. The results of fatigue measurements were correlated with 6MWT results.

**Results:** Patients with severe COPD (GOLD III) had significantly higher FAStotal score, FASphysical and FASmental ( $P < 0.05$  for all). There was no significant gender difference in FAStotal score and FASmental, but FASphysical was significantly ( $P = 0.0078$ ) greater in women. GOLD III group had significantly higher Borg fatigue score after 6MWT ( $P = 0.0037$ ). There was also a significant difference between the two groups in change in Borg fatigue score from baseline ( $P = 0.0367$ ), indicating that patients with severe COPD feel greater fatigue difference than patients with moderate COPD. Exercise tolerance showed significantly weak negative correlation with FAStotal score, FASphysical and FASmental ( $P < 0.05$  for all) in the whole group of 140 patients, GOLD II group and in a group of men. In group of women 6MWT showed significantly strong negative relationships with FAStotal score and FASphysical ( $P < 0.05$ ).

**Conclusions:** Based on these results, fatigue is an important symptom requiring evaluation and management in patients with COPD.

### P06

#### Impact of the p22phox dependent NADPH-oxidase on hypoxia-induced pulmonary vasoconstriction and hypertension\*

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**Background:** The prime function of the non-phagocytic NADPH oxidase family of enzymes is the generation of reactive oxygen species. They have been suggested to play a major role in physiological and pathophysiological conditions of hypertrophy, remodelling, and angiogenesis in the pulmonary circulation. p22phox (22 kDa Protein) is one of vital and integral part of NOX1, NOX2, NOX3 and NOX4. These NADPH oxidase are functionally inactive to produce ROS when they do not form a functional protein complex together with p22phox.

**Aim:** Our objectives in this study were to determine the precise role of NADPH oxidase in hypoxia induced pulmonary arterial vasoconstriction (HPV) and pulmonary arterial hypertension (PH).

**Methods:** p22phox knockout mice (KO,  $n \geq 8$ ) and wild type littermate (WT,  $n \geq 10$ ) were used in isolated perfused mouse lung model to study HPV. For hypoxia induced PH the mice were exposed to 10% hypoxia for 5 weeks. Later hemodynamic parameters were assessed by Right heart catheterisation, immunohistological staining and gene expression studies were made on lung and heart tissues to characterize the hypoxia induced vascular remodelling.

**Results:** The p22phox KO showed a impaired HPV compared to their wild type litter mates. In specific the second phase of HPV and flow induced increase in the pulmonary pressure was significantly reduced in p22phox KO. In chronic hypoxic setting p22phox KO showed significant reduction in hypoxia induced Right ventricular systolic pressure and a non significant reduction right ventricular hypertrophy compared to the wild type litter mates. Furthermore the

parameter for right ventricular contractility assessment like maximum and minimum dP/dt was significantly reduced in p22phox KO compared wild type mice under hypoxia. Nonetheless the lung vascular remodelling was also significantly reduced in p22phox ko.

**Conclusions:** p22phox knockout mice were protective against pulmonary hypertension under hypoxia. Further p22phox dependent NADPH oxidases plays crucial role in the maintaining sustained HPV.

## P07

### Right ventricular hypertrophy in hypoxia-exposed mice is fully compensated and has a distinct molecular expression profile

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**Objectives:** To clarify the relationship between invasively and non-invasively measured functional parameters of right ventricular function and the corresponding morphological and molecular changes in the early stages of right ventricular hypertrophy.

**Background:** Right ventricular function is the critical clinical parameter governing the survival of pulmonary hypertension patients. Assessment of right ventricular function represents a significant diagnostic challenge. Although right heart catheterization is the current gold standard, echocardiography is used for screening purposes but there are few echocardiographic parameters with a high prognostic value.

**Methods:** We assessed the progression of right ventricular hypertrophy in a mouse model of hypoxia-induced pulmonary hypertension by combining echocardiography measurements with invasive hemodynamic assessment and histological and molecular examination of the heart.

**Results:** Numerous echocardiographic parameters were significantly changed during the course of right ventricular hypertrophy, including right ventricular wall thickness, right ventricular end diastolic diameter, eccentricity index, tricuspid annular plane systolic excursion and pulmonary artery acceleration time. However, invasive and histologic assessment demonstrated increased right ventricular contraction with unchanged contractility index, increased right ventricle weight and no increase in right ventricular fibrosis, suggesting a fully compensated right ventricular hypertrophy phenotype. On the molecular level, we observed significant changes in expression of calcium handling proteins (Serc2a2) and tissue remodeling markers (alphaSMA, ET-1, apelin and tenascin C).

**Conclusions:** In hypoxia-induced pulmonary hypertension of the mouse, echocardiography clearly indicates increased right ventricular afterload and hypertrophy but also indicates right ventricular dysfunction where it is not present. Invasive functional and molecular parameters are needed to demonstrate right ventricular dysfunction. This may also be true in human pulmonary arterial hypertension.

## P08

### Respiratory infection in patient with Kearns-Sayre syndrome: case report

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**Background:** Kearns-Sayre syndrome (KSS) is a rare neuromuscular disorder with onset usually before the age of 20 years. It is the result of abnormalities in the DNA of mitochondria. From 1992 there were only 226 cases reported in published literature. There is currently no effective way to treat mitochondrial abnormalities, so we can only treat manifestations of this disease.

**Case report:** Diagnosis of KSS was established 12 years ago in our 33 years old male patient. Due to KSS he has progressive external ophtalmoplegia, skeletal and proximal muscle weakness which resulted with paralysis, heart block due which pacemaker was implanted, short stature, hearing loss, ataxia, impaired cognitive function. He was admitted to our hospital with radiographic features of bilateral pneumonia. Clinically he was presented with high temperature which lasted for two months and positive factors of inflammation CRP 48.3, sedimentation rate 56, leucocytosis 19.23. Breathing sound was abnormal with rare inspiratory crackles on lung bases. There were no gas exchange abnormalities. Sputum was smear negative, Löwenstein-Jensen cultures were negative. Patient was treated with third-generation cephalosporin and second-generation fluoroquinolone antibiotics, bronchodilatators and with physical rehabilitatation measures as well. After two days the temperature was normal, CRP decreased (10.5), normal value of leucocytes 7.6, auscultatory and radiografic findings showed almost complete regression. Endocranial CT showed expressed old atrophic and lacunar lesions with leucoencephalopathy. Patient was discharged completely recovered regarding respiratory infection.

**Conclusions:** Proper treatment of respiratory infection in patient with KSS can be achieved in a few days with no complication. Patient's condition increases the risk of aspiration pneumonia, so it should be taken in consider as possible cause of respiratory infection.

## P09

### Poster-Nummer nicht vergeben

**P10****Determinants of smoking behavior in 2466 teens of upper Austria 2012**G. Ennsberger<sup>1</sup>, P. Flink<sup>1</sup>, J. Thaler<sup>1</sup>, H. Schinko<sup>2</sup><sup>1</sup>Upper Austrian Krebshilfe, Linz, Austria<sup>2</sup>Division of Pulmonology, General Hospital Linz, Linz, Austria

Smoking, an individual as well a social behavior dynamically develops in the teens. Cancer and dozens of other diseases are associated with incomplete combustion of tobacco. The Upper Austrian Krebshilfe is active in tobacco prevention at schools based on information gained by representative random checks of students, again in May 2012. 2466 interviews in 1226 males and 1214 females, aged 12–19, covered 14 topics. The different school types of Austria represent at least three educational careers. The one from Hauptschule (HS—Secondary Modern School, age 12–14 years) to Polytechnicum (15) and Berufsschule (Vocational years/School, 16–19 years) lead to 72% smokers (regular use 50%), while the one in grammar school (12–18 years) in 20% and students of Berufsbildende Höhere Schulen (~ Colleges) in 25%. The educational level is one of the driving Forces in smoking. The second determinant is the number of smokers in the household. Offsprings of non-smoking families remain non-smokers in 88%, while with two or more smokers the rate of smoking in teens rises to 50%. Third, teens are surrounded by smoking peers. Even the majority of those refraining from tobacco are exposed to cigarette smoke in 75%, smoking youngsters in 97%. Peer-pressure is extreme. Asking how pocket money is spent, the close association between smoking and alcohol reveals alcohol as the fourth important factor by itself correlating with disco-experience. Regular cigarette use is found in 3% at age 12 and 44% at age 19. The percentage of irregular use remains always below 10%. The latency between the first cigarette tried and daily consumption is only 1.8 years. The survey by SPECTRA and Krebshilfe OÖ is the largest to our knowledge ever done. It contains still more details about smoking Austrian teens.

**P11****Apelin isoforms and GDF-15 are promising biomarkers for pulmonary hypertension\***V. Foris<sup>1,2</sup>, G. Kovacs<sup>1,2</sup>, M. Tscherner<sup>1,2</sup>, A. Avian<sup>1,3</sup>, A. Olschewski<sup>1,4</sup>, H. Olschewski<sup>1</sup>Ludwig Boltzmann Institute for Lung Vascular Research, Graz, Austria<sup>2</sup>Division of Pulmonology, Department of Internal Medicine, Medical University of Graz, Graz, Austria<sup>3</sup>Institute for Medical Informatics, Statistics and Documentation, Medical University of Graz, Graz, Austria<sup>4</sup>Experimental Anaesthesiology, Medical University of Graz, Graz, Austria

**Background:** Apelin and growth differentiation factor 15 (GDF-15) are endothelial factors playing a role in the pathological mechanism of pulmonary hypertension. The level of different apelin isoforms in pulmonary hypertension has not been studied yet. GDF-15 was already investigated in idiopathic pulmonary arterial hypertension (IPAH) but not in other forms of the disease.

**Aims:** In this prospective pilot study we aimed to determine the serum level of the apelin isoforms and GDF-15 in patients with IPAH, chronic thromboembolic pulmonary hypertension (CTEPH) and age- and sex-matched controls.

**Methods:** Peripheral venous blood was taken from 10 patients with IPAH, 10 patients with CTEPH and 15 healthy age- and sex-matched controls. All the subjects gave their informed consent and the study was approved by the local ethic committee. The serum levels of Apelin-13, Apelin-17 and Apelin-36 and GDF-15 were determined using commercially available enzyme-linked immunosorbent assay (ELISA) kits.

**Results:** The major isoform, Apelin-13 was not associated with patient groups, however, in IPAH it was negatively correlated with cardiac output ( $r=-0.6$ ). Apelin-17 was significantly elevated in CTEPH as compared to control (18.32 pg/ml vs. 16.99 pg/ml,  $p<0.02$ ). Apelin-36 was significantly lower in CTEPH as compared to control (17.93 pg/ml vs. 32.77 pg/ml,  $p<0.05$ ). In IPAH, patients showed the same tendency (NS). Apelin-36 levels in IPAH patients were strongly correlated with right atrial pressure ( $r=0.9$ ). As expected, GDF-15 was significantly elevated in IPAH as compared to control (839.62 pg/ml vs. 418.8 pg/ml,  $p<0.007$ ) and in CTEPH (2076.62 pg/ml vs. 418.8 pg/ml,  $p<0.001$ ) as compared to control.

**Conclusions:** These preliminary results suggest that elevated Apelin-17 and decreased Apelin-36 may be characteristic for CTEPH patients suggesting a possible role as biomarkers. GDF-15 is not only elevated in IPAH but also in CTEPH. Adequately powered prospective studies are warranted.

**P12****Neutrophil extracellular traps (NET's) formation in chronic obstructive pulmonary disease (COPD)\***F. Grabcanovic-Musija<sup>1</sup>, G. Weiß<sup>1</sup>, M. Klappmacher<sup>2</sup>, A. Perl-Obermeyer<sup>2</sup>, W. Krautgartner<sup>2</sup>, M. Studnicka<sup>1</sup><sup>1</sup>Department of Pulmology, Paracelsus Medical University Salzburg, Salzburg, Austria<sup>2</sup>Arbeitsgruppe Licht- und Elektronenmikroskopie, Naturwissenschaftliche Fakultät, Salzburg, Austria

**Background:** Chronic obstructive pulmonary disease (COPD) is an airway disease characterized by persistent and progressive airway inflammation [1] and tissue infiltration of neutrophils [2]. Persistent chronic inflammation together with the infiltration of neutrophils and bacterial challenge has been repeatedly shown to involve neutrophile extracellular trap formation(NET's) [3].

**Aims:** The aim of this pilot study is to examine the formation of NETs in patients with chronic obstructive pulmonary disease and healthy smokers.

**Methods:** We examined induced sputum samples of 14 outpatients with stable disease, and 14 patients hospitalized for acute COPD exacerbation. The control group consists of healthy smokers. Sputum induction is performed according to the protocol of the ECLIPSE study.

**Results:** NET's are present in 50% of patients with stable COPD, and in 93% of patients with acute exacerbation of COPD, however are also present in 29% of healthy smokers.

**Conclusions:** NET's are closely associated with tobacco induced chronic airways inflammation.

**References**

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3. Remijnen et al. Cell Death and Differentiation 2011, 18, 581–588.

**P13****Der Kremser Index****S. Handzhiev, P. Errhalt**

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**Background:** We assume that if the level of carcino-embryonic antigen (CEA) in a pleural effusion of unknown etiology is higher than in a blood test, this could be related to a malignant disease.

**Methods:** CEA levels were measured in pleural effusion and serum. We compared the CEA effusion/ serum ratio (CEA E/S Ratio) with the final pathological results.

**Results:** Fifty-eight cases met the inclusions criteria. There were 27 cases with higher CEA level in pleural effusion than in the serum. In 24 (88 %) of them we found a malignant disease, in 20 cases (74 %) we could proof a malignant pleural effusion. Only 2 Patients (7.4%) had CEA E/S Ratio > 1 because of Inflammation.

**Conclusions:** If the CEA level in pleural effusion is higher than in the blood test (CEA E/S Ratio > 1), there is about 74 % likelihood to detect malignant effusion. We would suggest the CEA E/S ratio to be called Kremser Ratio.

**P14****Quality of customer informations in product problems of point of care tests and analysers for blood gases and electrolytes published by BfArM 2005–2011****J. Hannig, R. Siekmeier**

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**Background:** The European Directive 98/79/EC on In-vitro Diagnostics (IVD) regulates marketing and post market surveillance of IVD in the European Economic Area. In cases of incidents and field safety corrective actions (FSCA) manufacturers have to inform the responsible Competent Authority (CA; D: BfArM for most IVD) and the public by field safety notices (FSN). Here we analysed FSN of IVD for point of care testing of blood gases and electrolytes.

**Methods:** FSCA and FSN published by BfArM 2005–2011 (<http://www.bfarm.de/DE/Medizinprodukte/riskinfo/kundeninfo/functions/kundeninfo-node.html>) for the included products were analysed in respect to the MEDDEV 2.12-1 rev 8.

**Results:** Thirty-four FSCA regarding the included products were published. German and English FSN were found in 32 and 31 cases, respectively. FSN were clearly characterized as FSN in 26/30 cases and product names were provided in 32/31 cases. Lot numbers were provided in 10/7 cases and other information for product characterization was available in 22/19 cases. Detailed information regarding FSCA and product malfunction were found in 32/31 and 30/29 cases. Information on product related risks with previous use of affected IVD was provided in 24/24 cases. In 32/30 cases manufacturers provided information for mitigation of product related risks including retesting in 2/2 cases. Requests to pass FSN to persons needing awareness were found in 9/6 cases. Contact data were provided in 22/16 cases. Confirmation that a CA was informed was found in 5/3 cases and in 21/16 cases a customer confirmation was included.

**Conclusions:** Most FSN fulfill the MEDDEV criteria. Typically there are differences between German and English FSN, e. g. regarding the distribution to persons needing awareness, missing statement that a CA was informed and missing customer confirmation. Due to

the importance of FSN for reduction of product related risks in FSCA type and content of FSN should be further improved.

**P15****Quality of customer informations in product problems of tests and reagents for diagnostics of infective diseases published by BfArM 2005–2011****J. Hannig, R. Siekmeier**

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**Background:** The European Directive 98/79/EC on In-vitro Diagnostics (IVD) regulates marketing and post market surveillance of IVD in the European Economic Area. In cases of incidents and field safety corrective actions (FSCA) manufacturers have to inform the responsible Competent Authority (CA; D: BfArM for most IVD) and the public by field safety notices (FSN). Here we analysed FSN of IVD for tests and reagents for infection diagnostics (except analyzers and general consumables).

**Methods:** FSCA and FSN published by BfArM 2005–2011 (<http://www.bfarm.de/DE/Medizinprodukte/riskinfo/kundeninfo/functions/kundeninfo-node.html>) for the included products were analysed in respect to the MEDDEV 2.12-1 rev 8.

**Results:** One hundred and ten FSCA regarding the included products were published. German and English FSN were found in 106 and 100 cases, respectively. FSN were clearly characterized as FSN in 88/81 cases and product names were provided in 106/100 cases. Lot numbers were provided in 83/80 cases and other information for product characterization was available in 88/80 cases. Detailed information regarding FSCA and product malfunction were found in 106/99 and 65/88 cases. Information on product related risks with previous use of affected IVD was provided in 65/65 cases. In 104/98 cases manufacturers provided information for mitigation of product related risks including retesting in 37/42 cases. Requests to pass FSN to persons needing awareness were found in 64/45 cases. Contact data were provided in 80/84 cases. Confirmation that a CA was informed was found in 16/17 cases and in 83/73 cases a customer confirmation was included.

**Conclusions:** Most FSN fulfil the MEDDEV criteria. Typically there are differences between German and English FSN, e. g. regarding the distribution to persons needing awareness, missing statement that a CA was informed and missing customer confirmation. Due to the importance of FSN for reduction of product related risks in FSCA type and content of FSN should be further improved.

**P16****In a general population there seems to be a link between subclinical atherosclerosis and lung hyperinflation****A. Hartmann<sup>1</sup>, R. Breyer-Kohansal<sup>1</sup>, M. Breyer<sup>1</sup>, A. Schrott<sup>2</sup>, S. Hartl<sup>1</sup>, O. Burghuber<sup>1</sup>**<sup>1</sup>Ludwig Boltzmann Institute for COPD and Respiratory Epidemiology, Vienna, Austria<sup>2</sup>Statistik Ambulanz, Vienna, Austria

**Background:** It has been shown in patients with COPD that there is a correlation between the degree of lung hyperinflation and subclinical atherosclerosis measured by carotid-femoral pulse wave

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velocity (PWV). We wondered if we could demonstrate this correlation in a general population cohort.

**Methods:** In an interim analysis of the ongoing Austrian LEAD (Lung hEart sociAl body) study, a single-center, longitudinal, open labeled, observational, population based cohort study, 1,147 participants were included (female 54.9 %, mean age 52.8 years). In addition to PWV, age, parameters of lipid profil (HDL plasma level), systemic inflammation (hsCRP) and lung hyperinflation (RV%/TLC) were measured.

**Results:** In total 7.2% ( $n=83$ ) of participants showed elevated levels of PWV, defined as  $>12$  m/s indicating subclinical atherosclerosis. Compared to participants with normal PWV, those with elevated PWV were older ( $67.2 \pm 8.0$  vs.  $51.7 \pm 15.7$ ;  $p=0.0051$ ), had higher HDL plasma levels  $67.3$  mg/dl  $\pm 18.6$  vs.  $62.1$  mg/dl  $\pm 16.9$ ;  $p=0.05$ ), higher hsCRP plasma levels ( $3.2$  mg/dl  $\pm 4.4$  vs.  $2.1$  mg/dl  $\pm 3.9$ ;  $p=0.001$ ), and increased RV%TLC post lysis ( $40.8\% \pm 6.8$  vs.  $34.9\% \pm 7.7$ ;  $p=0.000$ ). However, in a multivariate analysis, only age correlated significantly with PWV, possibly due to small sample size.

**Conclusions:** In a general population cohort, subclinical atherosclerosis seems not only to be linked to age, lipid profil and systemic inflammation, but also to lung hyperinflation.

### P17

#### Von Willebrand factor a marker for hepatopulmonary syndrome\*

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**Background:** Hepatopulmonary syndrome (HPS) occurs in 20–30 % of patients with liver cirrhosis and is associated with a >2-fold increased mortality. Pulmonary angiogenesis and endothelial dysfunction seem to play a central role in its pathogenesis. von Willebrand factor antigen (vWF-Ag), a marker of endothelial dysfunction, is significantly elevated in patients with liver cirrhosis and is associated with increased pulmonary angiogenesis in a rat model of HPS. Therefore we aimed to evaluate the role of vWF-Ag in patients with HPS.

**Methods:** One hundred and twenty-eight patients with liver cirrhosis were included in this prospective study. vWF-Ag was assessed by ELISA. Patients were screened for presence of clinically significant HPS according to the established consensus guidelines (presence of cirrhosis,  $AaDO_2 > 15$  mmHg &  $PaO_2 < 80$  mmHg, intrapulmonary vasodilatation in contrast enhanced echocardiography) [1].

**Results:** Criteria of HPS were fulfilled in 27 patients. vWF-Ag level was significantly higher in patients with HPS compared to patients without HPS ( $483 \pm 123$  vs.  $331 \pm 100$ %;  $p < 0.05$ ). vWF-Ag correlated significantly with gas exchange abnormalities in the total cohort by means of  $AaDO_2$  and  $PaO_2$  ( $r = 0.47$ ;  $p < 0.05$ ). ROC AUC of vWF-Ag for detection of HPS was 0.825. The best cut off with maximal sensitivity was 327 % (sensitivity: 100 %, specificity: 51.5 %; positive predictive value: 34.2 %, negative predictive value: 100 %). vWF-Ag levels were significantly associated with HPS (OR: 1.016, 95 % CI: 1.009–1.023,  $p < 0.05$ ) and remained significantly associated with HPS after correction for sex, age, MELD score and hepatic venous pressure gradient (OR: 1.019, 95 % CI: 1.002–1.036,  $p < 0.05$ ).

**Conclusions:** vWF-Ag is a significant predictor for presence of HPS, independently of severity of cirrhosis. vWF-Ag using a cut-off level  $>327$  % may help to identify HPS in patients with cirrhosis.

#### References

- Rodriguez-Roisin. Eur Respir J 2004.

### P18

#### Hemoptysis in the patient with vascular malformation and *Pasteurella multocida* infection: case report

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*Pasteurella multocida* is a Gram neg. coccobacillus that colonizes the upper airways of many animals. Infections in humans are usually a consequence of an animal bite or scratch. 60-year-old patient was admitted for evaluation of hemoptysis. Physical examination on admission was unremarkable; in blood: higher CRP and blood sedimentation rate. On chest x-ray the mediastinal shadow was shifted to left, highlighted TB sequelae. Smears for AFB were negative. Bacteria *Pasteurella multocida* was present in sputum culture. The patient denied fiberbronchoscopy. Another notable point of this case is that CT scan revealed the congenital malformation—tortuous bronchial artery, reduced diameter of left pulmonary artery and left lung. The treatment with ciprofloxacin was successful and she was discharged from hospital, advised to avoid contact with infected animals and followed at our outpatient clinic. The nasopharyngeal swabs for the members of her family were negative for this bacteria. But *P. multocida* were isolated from nasopharyngeal swabs of the her dog and cats. So, the infection was caused by the contact with her dog and cats. We describe the patient with *Pasteurella multocida* infection caused by the contact with her domestic animals. The vascular arterial malformation and TB sequelae contributed to hemoptysis because of direct blood supply from the systemic to bronchial circulation.

### P19

#### Highflow-oxygen treatment in patients with severe COPD: effects on breathing rate and lung volumes

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**Background:** COPD is one of the leading causes of death worldwide. While the benefit of long-term oxygen treatment (LTOT) has been verified in numerous studies, data concerning high-flow oxygen therapy (HFOT), where a warm, humidified air/oxygen mix is administered at high flow rate, exist only for the treatment of OSAS. The study was designed to examine the safety and efficacy of HFOT in treatment of severe COPD and to compare the effects on breathing rate and lung volumes with the established LTOT.

**Methods:** Inclusion criteria were the following: patients aged 30 to 80, with stable COPD III–IV and indication for LTOT, no exacerbations in the last 14 days and  $Hb > 8.5$  g/L. Oxygen supplementation was performed in 10 min intervals, with an augmentation of 0.5–1 L/min, for both established LTOT and high flow TNi® 20 oxy System at 15 L/min, until a  $PaO_2 \geq 60$  mmHg was achieved.

**Results:** Eight patients were included, 4 men and 4 women with a mean age of 64.25 years. High flow treatment showed no significant changes in measured lung volumes (Raw, ERV, IC, VC, TLC, FVC, FEV1 and DLCO) in comparison to LTOT. Most notably, HFOT showed no negative effects on RV or RV/TLC as markers for the emphysema. Furthermore, no significant changes in the patients breathing rate were observed ( $\Delta BR$  after 1 h LTOT –  $0.4 \pm 2.19$  breaths per minute to  $\Delta BR$  after 1 h HFOT –  $1.2 \pm 1.79$  breaths per minute).

**Conclusions:** Concerning its effects on lung volumes and breathing rate, transnasal high flow oxygen treatment is a safe and well tolerated alternative to the established oxygen treatment. Further trials with more patients and for longer periods are needed to verify our results.

## P20

### Physical activity and optimal asthma treatment: a beneficial combination

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**Background:** Asthmatic patients often avoid physical activities because they might lead into exacerbations. However, studies demonstrated the ability of asthmatics to exercise safely and therewith significantly improve their cardiovascular fitness, asthmatic symptoms and quality of life.

**Methods:** A prospective, multicenter, non-interventional study (NIS) was conducted in pulmonary and general practices all over Austria in 2012. Asthmatics treated with a pMDI fixcombination of extrafine 100 µg beclomethasone/6 µg formoterol were monitored over twelve weeks regarding asthma control, symptom scores and tolerability. In the screening phase a patient-check was performed to determine asthma control status. Pulmonary function, the number of asthma attacks as well as the severity of asthma symptoms and exacerbations were assessed.

**Results:** Two hundred and six patients (mean age 49 years, 53 % female, 26 % smokers, 40 % physically active) were analysed. Asthma control, pulmonary function (PEF, FEV<sub>1</sub> and FVC) and symptom scores significantly improved ( $p < 0.01$ ) after 12 weeks of treatment with BDP/F extrafine. In physically active patients ( $n = 80$ ) a significant improvement towards well controlled asthma was observed in 63.8 % (vs. 2.5 % at baseline) while the exacerbation rate decreased significantly ( $p < 0.01$ ). Pulmonary function and symptom scores were significantly enhanced in the subgroup of smokers ( $n = 52$ ;  $p < 0.01$ ) after receiving the study medication. In patients pretreated with other ICS/LABA fixcombination ( $n = 120$ ) the rate of nocturnal symptoms decreased from 64.2 to 10.3 % and FVC significantly increased ( $p < 0.01$ ). Three cases of undesirable side effects were reported (headache, tremor, palpitation), all transient and without sequelae.

**Conclusions:** The NIS shows effective increases of patients' asthma control by decreasing asthma symptoms, reliever usage as well as exacerbations and improvement of lung function parameters and patient reported outcomes due to treatment with extrafine BDP/F. These results indicate that physical activity can be recommended safely for well controlled and stable asthmatics.

## P21

### Heterogeneity in prevalence and underdiagnosis of COPD: Results from BOLD, EPI-SCAN, PLATINO, and PREPOCOL

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**Background:** We evaluate heterogeneity in prevalence of COPD and factors associated with underdiagnosis using data from four general populations surveys: BOLD (Burden of Obstructive Lung Disease), EPI-SCAN (Epidemiologic Study of COPD in Spain), PLATINO (Proyecto Latinoamericano de Investigación en Obstrucción Pulmonar), and PREPOCOL (Prevalencia de EPOC en Colombia).

**Methods:** Representative samples of adults aged  $\geq 40$  years were randomly selected from well-defined administrative areas at studied sites. Post-bronchodilator spirometry and face-to-face interviews were performed. Post-BD FEV<sub>1</sub>/FVC  $<$  LLN was used to define chronic airflow limitation consistent with COPD. Doctor-diagnosed COPD was self-reported. Underdiagnosed COPD was considered when participants had a FEV<sub>1</sub>/FVC  $<$  LLN and did not report previous diagnosis of COPD by a doctor or health professional.

**Results:** Among 30,874 participants with a mean age of 56 years, 55.8 % were female, and 22.9 % were current smokers. Prevalence of reported doctor-diagnosed COPD ranged from 0.1 % in Pune (India) to 22.4 % in Lexington (US). 26.4 % of all participants reported having had a lung function test before, with a major rate of 97.6 % in Norway and the lowest rate of 0.5 % in Nigeria. Prevalence of COPD ranged from 3.6 % in Baranquilla (Colombia) to 19.0 % in Cape-Town (SA). 81.4 % were undiagnosed with the highest rate in Ile-Ife, Nigeria (98.3 %) and the lowest rate in Lexington, US (50.0 %). Male gender, lower age, current smoking, and less severe airflow limitation were associated with underdiagnosis.

**Conclusions:** There is substantial heterogeneity in prevalence and underdiagnosis of COPD worldwide. The majority of COPD cases remain undetected.

## P22

### Singen als neue Therapieform für die Behandlung der COPD – eine Vorstudie

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**Grundlagen:** Singen in der Gruppe hat in der Behandlung der Alzheimererkrankung und Demenzkranken einen Stellenwert im therapeutischen Spektrum erlangt. Singen beeinflusst die Stimmung und die Lebensqualität. Eine spezielle Wirkung des Singens auf die Atemmuskulatur und die Atemkontrolle ist vorstellbar und wurde in ersten Studien erhärtet.

**Methodik:** In der SKA Weyer wurde eine Vorstudie an PatientInnen mit COPD GOLD II und III durchgeführt. Während des 3- bis 4-wöchigen Aufenthaltes in der Rehabilitation wurde eine Singgruppe mit 4 Sitzungen (je eineinhalb Stunden) angeboten. Das Angebot bestand aus Atemübungen, Gesangsübungen und dem gemeinsamen Singen von bekannten Liedern. Am Ende der letzten Gruppe wurde Fragebogen ausgefüllt, der für die Vorstudie ausgewertet wurde.

**Ergebnisse:** An der Befragung nahmen 117 TeilnehmerInnen teil. In der 10-stufigen Skala (10 = bester Effekt, 0 = keine Effekt) haben mehr als 2/3 der TeilnehmerInnen die Fragen „Wie hat Ihnen das Singen gefallen, Hat Ihnen das Singen eine Verbesserung

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gebracht, Helfen die Übungen beim Einatmen, helfen sie beim Ausatmen, helfen sie bei körperlicher Belastung, helfen sie in Stresssituationen' mit den höchsten Einstufungen von 8 bis 10 beantwortet. Von 40 PatientInnen, die ein Sekretproblem angaben, haben 32 (oder 80 %) angegeben, dass das Singen die Sekretolyse positiv beeinflusst hat. 114 PatientInnen gaben an, dass sie die Übungen zuhause weitermachen wollen.

**Schlussfolgerungen:** In der Vorstudie gab es ein überwiegend positives Echo auf das therapeutische Singen. Höchstbewertungen erreichte das Singen bei der Hilfe beim Einatmen und bei der Hilfe bei körperlichen Belastungen.

### P23

#### Efficacy of recruitment manoeuvre with or without anti-derecruitment strategy in ARDS patients: a prospective study

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**Background:** In acute respiratory distress syndrome (ARDS), adequate positive end-expiratory pressure (PEEP) may recruit collapsed alveoli and reduce repetitive opening and closing that causes shear stress. Recruitment manoeuvre (RM) opens up collapsed segments of the lung in many patients with ARDS whereas some patients do not respond to RM. In the responders, the collapse may reappear once the RM is complete and the patient is returned to his pre-RM PEEP level. Oxygenation benefit achieved by the RM may be partially lost soon after the RM. The level of PEEP, i. e., an antiderecruitment strategy in mechanical ventilatory support, could be important in preserving the effect of the ARM.

**Objective:** To evaluate the outcome of setting the PEEP using decrement PEEP titration after an alveolar recruitment manoeuvre and its effects on the clinical outcome in patients with ARDS.

**Methods:** Twenty four patients with early ARDS were assigned in this study. Initially recruitment manoeuvre was given using pressure control ventilation to determine the responders or non-responders. Responders were randomly assigned to 'antiderecruitment RM' group and 'only RM' group. The 'antiderecruitment RM' group received RM using volume control ventilation and optimal PEEP was set after RM using decremental PEEP titration method. The 'only RM' group patient was put on baseline ventilator settings after manoeuvre.

**Results:** Out of the total 24 patients, 12 showed an improvement in oxygenation (P/F) in response to the initial recruitment manoeuvre by more than 20 % from baseline. When the change in P/F ratio was correlated with survival, it suggests that a P/F ratio <90 at admission (baseline) is associated with mortality.

**Conclusions:** Only half of the patients with ARDS respond to recruitment manoeuvres with an improvement in oxygenation. In most responders, the improvement is sustained irrespective of whether RM only or ADRM was used.

### P24

#### Biomarkers in routine diagnostic of pleural effusions

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**Background:** Measurements of many pleural biomarkers are available to help physicians searching the ethiology of pleural effusion. Our purpose was to analyze the utility of biomarkers used at our clinic in routine diagnostic of pleural effusions.

**Methods:** We retrospectively reviewed the pleural effusion levels of proteins, LDH, alpha amilasis, pH, glucose, cholesterol in 333 patients treated in Clinic Golnik in 2011 and compared their values to the final identified ethiology of effusions.

**Results:** The majority of effusions were recognized to be a consequence of malignancy (120 cases: 66 carcinoma, 11 mesothelioma, 9 KLL or lymphoma, 34 paramalignant) or infection (82 cases: 65 bacterial pneumonia, 9 tuberculosis, 8 empiema). In 73 cases the etiology of the effusions was heart failure, in 58 other reasons. Considering Light criteria (LDH, proteins) 243 effusions were characterized as exudates and 90 as transudate. The vast majority of the effusions were correctly classified in the two ethiological subgroups of exudate and transudate, only few effusions were misclassified according to the final diagnosis (4.5 %). There were significant higher values of pleural fluid LDH ( $p=0.005$ ) and proteins ( $p=0.026$ ) in effusions in confirmed carcinoma or mesothelioma compared to the effusions of paramalignant origin. Alpha amilasis, pH and glucosidase were determined in most cases but there were no differences in their values in malignant or other ethiologies, additionally, they rarely influenced the treatment decisions.

**Conclusions:** We found out that pleural LDH and proteins are the biochemical parameters that are most helpful in our routine diagnostic of pleural effusions and correctly narrow the ethiology specter. Further, significantly higher pleural LDH and protein values could additionally help us in distinguishing paramalignant effusions from pleural malignancy. Parameters such as pH, glucosidase and alpha amilasis are useful in selected cases and have no place in the routine diagnostic.

### P25

#### Bronchial sleeve resections in the treatment of lung cancer: a comparison of different suture materials and techniques

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**Background:** Sleeve resections offer parenchyma-sparing alternatives to pneumonectomy in patients with centrally located lung cancer. Though it is a modern standard procedure, there is no consensus on the optimal bronchial suture material and technique. The aim of this study was to compare two suture materials and techniques in patients with complete bronchial sleeve resections.

**Methods:** We retrospectively analysed records of 85 patients who underwent bronchial sleeve lobectomy between January 2002 and December 2011. Data included type of operation, suture material (Vicryl vs. PDS) and technique (interrupted stich vs. continuous), and post-operative complications. Chi-square and Fisher's exact test were used to compare suturing materials and techniques with respect to complications. A  $p$ -value  $<0.05$  was considered statistically significant.

**Results:** In 85 patients (age  $64.4 \pm 12.8$  years; 72.9% male) 74 bronchial and 11 bronchovascular sleeve lobectomies were performed. Continuous and interrupted stich suture techniques were used in 52 (67.1%) and 33 patients (32.9%), respectively. PDS was used in 56 patients, Vicryl in 29. Post-operative complications were recorded in 22 patients (13 PDS vs. 9 Vicryl,  $p = 0.435$ ; 12 continuous vs. 10 single,  $p = 0.459$ ) with no difference with respect to suturing material or technique: bronchopleural fistulas ( $n = 4$ ; 3 PDS + continuous vs. 1 Vicryl + interrupted,  $p = 0.999$  for both), atelectasis ( $n = 10$ ; 6 PDS vs. 4 Vicryl,  $p = 0.729$ ; 6 continuous vs. 4 interrupted,  $p = 0.999$ ), empyema ( $n = 3$ ; 2 PDS vs. 1 Vicryl,  $p = 0.999$ ; 1 continuous vs. 2 interrupted,  $p = 0.560$ ), emphysema ( $n = 2$ ; 1 PDS + continuous vs. 1 Vicryl + interrupted,  $p = 0.999$  for both) and pneumonia ( $n = 6$ ; 3 PDS vs. 3 Vicryl,  $p = 0.406$ ; 3 continuous vs. 3 interrupted,  $p = 0.673$ ). All patients survived a 30-day post-operative follow-up period.

**Conclusions:** Bronchial sleeve resection is a safe method in the treatment of bronchial malignancies independent of the suture technique and material used.

## P26

### Depression in COPD patients

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**Background:** The effective control of COPD requires a treatment regimen that may be compromised by psychological factors, such as anxiety and depression. Depression is associated with poor self-care and medication adherence, continued smoking, and increased COPD exacerbations.

**Aim:** To estimate the prevalence of anxiety and depression among COPD patients.

**Methods:** We analyzed the data from seventy two patients with stable COPD (GOLD II-IV) (group A). Fifty adult patients with persistent asthma were the control group (group B). The pulmonary function test was performed by spirometry and expressed as FEV1 (%pred). Depression and anxiety were assessed by Hospital Anxiety and Depression Scale and expressed as score. The prevalence of anxiety and depression was calculated in both groups and the difference between groups was estimated.

**Results:** The anxiety score in Group A was  $7.92 \pm 4.34$  and in Group B  $6.2 \pm 2.3$ . The depression score in Group A was  $7.91 \pm 4.11$  and in Group B  $4.9 \pm 2.4$ . The difference between groups was significant ( $p < 0.05$ ). There was no correlation between psychological status (anxiety, depression score) and post bronchodilator FEV1 in group A ( $p > 0.05$ ) and no correlation between psychological status and post bronchodilator FEV1 in group B ( $p > 0.05$ ).

**Conclusions:** This research suggests the importance of psychological distress screening for COPD patients. Further studies are needed to examine the correlations between the severity of the disease and mental status and to target the psychological factors that contribute COPD exacerbations.

## P27

### Delays in the diagnosis and treatment in lung cancer patients in Slovenia in 2012

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**Background:** In Slovenia lung cancer (LC) is the fourth most common cancer among men and women accounting for almost 10% of all cancers. 5-year survival is 14.5%. The most important factor affecting survival is stage at the diagnosis. We assume, that delays in the diagnosis and treatment can result in diagnosing more advanced stages of LC. The aim of our study was to determine the delays between the onset of symptoms and the first treatment in newly diagnosed LC patients in Slovenia.

**Methods:** We retrospectively analysed records of 416 patients with microscopically confirmed LC in 2012 in four hospitals in Slovenia. The following intervals were determined: symptom to doctor interval (SDI), doctor to pulmonologist interval (DPI), pulmonologist to diagnosis interval (PDGI), diagnosis to treatment interval (DgTI) and symptom to treatment interval (STI). The relationship between the interval from the first symptom to diagnosis (SDGI) and the degree of invasion in LC was determined. Recommended intervals are <30 days for SDI, <14 days for DPI, PDGI, DgTI, <72 days for STI and <58 days for SDGI.

**Results:** Data of 416 (65% men) patients were evaluated. Median intervals in days were as follows: SDI 13 (3-730), DPI 13 (3-730), PDGI 8 (3-365), DgTI 23 (3-163) and STI 77.5 (12-1155). Patients with SDGI shorter than 58 days were diagnosed in significantly more advanced stages of LC compared to patients with SDGI longer than 58 days.

**Conclusions:** All the intervals are in line with the British and Swedish recommendations except for the interval between the diagnosis and treatment, what reflects current organisation of Slovenian healthcare system. Patients diagnosed faster have more advanced stages of LC. More severe symptoms probably bring the patient faster to the doctor and to the diagnosis.

## P28

### Comparison between dual-energy computed tomography and standard lung perfusion scintigraphy in preoperative evaluation of lung cancer patients

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**Background:** In the pre-operative assessment of lung cancer patients functional evaluation of operability is a crucial step. It includes, apart from spirometry, measurement of diffusion capacity and exercise testing, split function studies by means of lung perfusion scintigraphy. Using this approach it is possible to predict postoperative lung function and therefore assess resection limit and operability. As computed tomography (CT) is essential for pre-operative evaluation in every patient, a recently advanced CT-protocol, the so called dual-energy computed tomography (DECT), by which lung

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tissue perfusion gets visible, might be a new and better alternative to radioactive scintigraphy.

**Objectives:** To compare calculated percentage values for perfused lung tissue, as measured on the one hand by lung perfusion scintigraphy and on the other hand gathered by DECT.

**Methods:** Seven patients (five female, two male) were included in this pilot project. All patients had to undergo lung perfusion scintigraphy, as well as dual-energy computed tomography (DECT) a few days before surgery. Lung function testing and assessment of diffusion capacity was performed in all patients preoperatively.

**Results:** Patients (mean age  $61 \pm 8$  years) were investigated by scintigraphy and DECT. Split studies revealed no significant difference in calculated percentages for lung perfusion between both methods ( $p > 0.05$ ). Values for the FEV1 ppo did not differ between scintigraphy or DECT results which served as basis for calculation.

**Conclusions:** There is no significant divergence between the use of dual-energy CT and lung perfusion scintigraphy for pre-operative evaluation of lung cancer patients.

### P29

#### Accelerated right ventricular diastolic dysfunction in the ABCG2 knockout mouse

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**Background:** Recent studies are primarily focusing on treatment of lung vasculature in pulmonary hypertension (PH) nonetheless molecular mechanisms leading to right heart dysfunction in PH remains poorly investigated. ABCG2 is a membrane transporter which maintains cell survival under hypoxia via effluxing accumulated toxic metabolites.

**Aim:** To investigate the role of ABCG2 transporter in hypoxia induced right ventricular (RV) dysfunction.

**Methods:** Wild type and ABCG2 knockout mice were exposed to 10% hypoxia for 5 weeks. Haemodynamic parameters—including RV end-diastolic pressure (RVEDP)—were assessed by cardiac catheterisation. Characterisation of heart in particularly the right ventricular and lung tissues was performed by immunohistochemical staining.

**Results:** Hypoxia induced pulmonary vascular remodelling, RV systolic pressure elevation and RV hypertrophy in wild type animals. Furthermore RVEDP was also increased in wild type animals under hypoxia as compared to the normoxic group ( $p < 0.001$ ). ABCG2 knockout mice under hypoxia showed pulmonary vascular remodelling, RV systolic pressure elevation and RV hypertrophy in the same extent as it was observed in the wild type counterpart. However, loss of ABCG2 significantly elevated the RVEDP after hypoxic exposure compared to wild type controls ( $p < 0.001$ ) with preserved systolic function. Nonetheless the left heart function was not affected under hypoxia in wild type and ABCG2 knockout mice compared to respective normoxic control. To further elucidate the elevated RVEDP in ABCG2 in the observed phenotype, collagen content analysis was performed on heart sections. Hypoxia treated ABCG2 knockout mice showed markedly increased fibrosis in RV as compared to wild type controls ( $p < 0.05$ ).

**Conclusions:** The enhanced RVEDP and fibrosis observed under hypoxia in ABCG2 knockout mice show the crucial role of ABCG2 in preserving the right ventricular function under stress or pathophysiological condition.

### P30

#### A young female from Kosovo with pleural sarcoma

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**Case Report:** The patient F. M, 28 years old, female, was admitted in the ER of our hospital. Her complains were effort dyspnoea and pain in the right hemithorax since last April 2012. Without any previous pathologies. She has been under treatment with antibiotics several times but without any improvement. Since September 2012 she was under empiric treatment with antitubercular drugs full dose. Several examinations, laboratory and radiologic was performed to her, such as: Chest X-ray: Large opacity of right hemithorax with compression of the mediastinum and the heart in the left side, right minimal pleural effusion. Thorax CT with i/v contrast: It was confirmed the large opacity. It was suspected malignant mesothelioma, pleural sarcoma? Blood counts: Slight anemia (Hb 11 g/dl). Abdomen and head CT free of pathologies. ABG: Respiratory alkalosis. FBS: The entire right hemisystem compromised in the left side. Right hemisystem without signs of infiltration. FNA under CT scan was performed to take biopsy sample. Immunohistochemical result: High grade undifferentiated Sarcoma. After the consultation with thoracic surgeons and the oncologists the case resulted inoperable. Radiotherapy was tried but without success. The patient deteriorated with dyspnea grade MRC 3–4. She was discharged from the hospital from her relatives against doctors' recommendations. After one week from her discharge her family informed us that the patient had done exitus lethalis.

**Conclusions:** It is very important early diagnostication of these cases. We are not in grade to know the etiologic factors in this case. Because of the rarity of pleural sarcoma and its similarity (clinical and histological) to other pleural neoplasms, particularly sarcomata's Mesothelioma, diagnosis is often difficult especially in low income or development country. Optimal treatment for pleural sarcoma has not been defined. Multimodal therapy of surgery, chemotherapy and radiation has been used.

### P31

#### High-flow oxygen insufflation—effect on blood gases in severe COPD

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**Background:** COPD is marked by an airflow limitation, which is preventable, partially treatable and mostly progressive. In severe stages it is related to chronic hypoxemia and also often to chronic hypercapnia. Long term oxygen treatment (LTOT) is established as a standard therapy in COPD treatment. A new therapeutic approach is High-Flow Oxygen Therapy (HFOT), where warm and humidified air is insufflated with a flow of up to 50 L/min. HFOT is rated among non-invasive ventilation and is well established in the therapy of acute respiratory disorders in newborn.

**Aim:** This study was designed to explore efficacy and safety of HFOT in patients with severe COPD. Changes in blood gas param-

eters (as pH,  $\text{paO}_2$ ,  $\text{paCO}_2$ , bicarbonate and  $\text{AaDo}_2$ ) were analyzed after HFOT and standard oxygen treatment (SOT).

**Methods:** Patients were treated with SOT and HFOT for 60 min each. The oxygen flow was increased every 10 min by 0.5 L/min until a  $\text{paO}_2$  of >60 mmHg was reached or a rise of more than 10% of baseline  $\text{O}_2$  was detected. According to the study protocol blood gas analysis were taken from the hyperaemic earlobe. Inclusion criteria: severe COPD, age: 30–80 years, indication for LTOT, stable disease (no exacerbation for 2 weeks), Hemoglobin >8.5 g/l.

**Results:** So far 7 patients were included in our study: three males, four females, mean age:  $65.7 \pm 8.1$ ,  $\text{paO}_2 < 55$  mmHg, COPD III or IV (GOLD). HFOT was tolerated in all patients and all of them regarded it as pleasant. Within one hour of HFOT we observed further a significant reduction of  $\text{paCO}_2$ . For the other observed parameters ( $\text{paO}_2$ , pH and bicarbonate) no significant changes were documented. In conclusion we can postulate that there are seen no disadvantages for patients using HFTO, even an improvement of ventilation can be observed.

## P32

### Pseudomonas infection of the lung in cystic fibrosis and non cystic fibrosis patients: epidemiology, risk factors and antibiotic resistance

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**Background:** *Pseudomonas aeruginosa* infections are the major cause of morbidity and mortality in patients with CF. *P. aeruginosa* is the major cause of ventilator-associated pneumonia (VAP) and the second most common cause of nosocomial pneumonia in general. Antibiotic treatment of *P. aeruginosa* infections is complicated by its multiple resistance mechanisms.

**Methods:** We retrospectively analysed data of 289 patients with *P. aeruginosa* infection/colonisation of the respiratory tract. We examined resistances to 37 antibiotic drugs in CF-patients and non-CF-patients. Furthermore we were interested in accompanying diseases, prior hospitalisation and ICU stays. In CF-patients we examined whether they are more frequently coinfected with *Staphylococcus aureus* and whether there are differences in resistances to antibiotics compared to non-CF-patients.

**Results:** Highest susceptibilities for single antibiotics were found for tobramycin (95.8%), amikacin (95.7%) and colistin (92.1%). The most effective combination preparations were ciprofloxacin plus colistin (100%), colistin plus ciprofloxacin (100%) and tobramycin plus ceftazidim (100%). Most significant differences between susceptibility rates in CF-patients and non-CF-patients were found for aztreonam (61.4% higher in CF-patients), doripenem (25% less in CF-patients) and imipenem (24.3% less in CF-patients). A highly significant correlation was found for *S. aureus* coinfection and cystic fibrosis compared to non CF patients. In nearly half of our patients *Pseudomonas* was detected while staying on ICU. Most of them where intubated. Among accompanying diseases COPD, CF and bronchiectasis were the most common ones.

**Conclusions:** Stays on ICUs and intubation are common risk factors for acquiring *Pseudomonas*. Although antibiotic resistances are rising, there are still some highly effective antibiotics, especially in combination preparations. Significant differences concerning susceptibilities in CF and non CF patients have to be considered in antibiotic treatment.

## P33

### The good and bad of smoking. Acrolein inhibits antibody formation and allergic sensitization, but promotes tumor growth

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**Background:** Allergic sensitization has been linked to active and passive smoking in exposed individuals and even their pets. We here investigated the contribution of acrolein, a compound generated in large amounts during smoking, during nasal sensitization and—based on the surprising preliminary results—on tumor growth. As a model antigen we used KLH with or without acrolein.

**Methods:** BALB/c mice were nasally sensitized five times in biweekly intervals with KLH alone or with KLH in conjunction with acrolein. Airway hyperreactivity was measured according to change of enhanced pause and KLH-specific anaphylactic reaction was monitored in vivo. Levels of specific antibodies as well as cytokine profile of KLH-stimulated splenocytes were analyzed by ELISA. Further, mouse D2F2-tumor cells were grafted to the flanks and tumor growth monitored in mice previously exposed to acrolein or buffer.

**Results:** Nasal application of KLH as model antigen induced specific IgG1-, IgG2a-, IgA- and IgE-levels. The same mice secreted elevated levels of IL5, IL13, IL10 and IFN- $\gamma$  from their splenocytes. They showed increased airway-hyperreactivity and had a significant drop in body temperature upon allergen challenge. Pointing towards tolerance, and against our expectations, presence of acrolein in the KLH-antigen significantly reduced specific antibody-titers, resulted in lower splenocyte cytokine production and prevented anaphylaxis. However, the impaired immune response simultaneously led to a significantly higher tumor growth in mice exposed to acrolein than in the control group.

**Conclusions:** Acrolein in smoke—best known for its carcinogenic effect—decreases the risk of sensitization towards a specific antigen by inhibiting immune activation. Our data further suggest that Acrolein via the same mechanism acts tumor promoting in smokers.

## P34

### Smoking trends of the adult Austrian population 2005–2008–2012

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In 2005, 2008 and 2012 representative random checks of adult Austrians ( $N=1.031, 1.027, 1.035$ ) age 15 or older were performed. The survey was funded by the Austrian Krebshilfe and carried out by SPECTRA Marketing Research Institute. Regular smokers were male in 43, 34 and 38% and female in 31, 23 and 27% in 2005, 2008 and 2012. Women, individuals above 50 years and non-smokers found smoking more harmful than smokers. Men consumed on the average more than women (20 vs. 15 cigarettes/day). 47%–48%–42% smoked their first cigarette within 30 min, signalling tobacco dependence.

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Regular cigarette consumption was taken up by the older generations about 4 years later than by teens 2012. The denial to quit rose from 15–16% 2005–2008 to 27% last year. But a trend towards less cigarettes a day was observed. Smoking was associated with professional activity in 59%, no activity corresponded with non-smoking in 53%. The number of regular smokers peaks at 20 years (43–46%). On the other hand is the daily consumption of cigarettes rising with age. Surprisingly does the number of ever smokers (ex- and present ones) reach 72% in males and 63% in females between 40–60 years. This contrasts with 33% regular and 5% occasional smokers at the survey 2012. The BMI did not correlate with the smoking status—male active, ex- or never smokers having 25.6, 25.0 and 24.8 and female ones 24.4, 24.0 and 24.6 kg/m<sup>2</sup>.

**Conclusions:** Males still smoke more than females. The percentage of ever smokers is unexpectedly high. Lifetime cigarette consumption could be significantly underestimated in regard to related diseases. Weight is not influenced by smoking in contrast to the experience, that quitting is associated with a weight gain. The number of 42% dependant smokers corresponds well with the denial of quitting.

### P35

#### Overdiagnosis of COPD: results from the BOLD study

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**Background:** Also Chronic obstructive pulmonary disease (COPD) is often underdiagnosed, there are also a number of persons with a diagnosis of COPD who spirometrically do not have an obstructive lung function. We aimed to identify determinants of COPD overdiagnosis within different countries.

**Methods:** We analyzed data from 24 countries, participating in the international, population based Burden of Lung Disease (BOLD) study. Overdiagnosis of COPD was classified when lungfunction showed FEV1/FVC > LLN post bronchodilator (post-BD), together with a self-reported doctor diagnoses of COPD.

**Results:** Among 16,218 participants between the age of 40 and 70, 51.3% were female. 14,302 had a post-BD non obstructive lung function. Out of this population, 570 (4.0%) had a self reported doctor diagnosis of COPD. This finding ranged from 0.0% in Pune, India to 17.4% in Lexington, USA. In multivariate analysis, female gender, older age, higher Body Mass Index (BMI) and respiratory symptoms, especially wheeze and also a prior diagnosis of Asthma or Heart disease were significantly associated with an overdiagnosis of COPD.

**Conclusions:** COPD overdiagnosis varies between different countries, but overall show higher rates in High Income Countries. Within this questionable diagnosis of COPD the risk of overtreatment and unnecessary medical expenses exists.

### P36

#### Inhalation of macrolides: a novel approach for treatment of respiratory infections?

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**Background:** Inhalation of antibiotics is of increasing interest for treatment of infectious pulmonary diseases, e. g. cystic fibrosis (CF) and bronchiectasis both causing recurrent pulmonary infections by various bacterial strains, in particular *Pseudomonas aeruginosa*. Inhalative administration has the advantage of high local drug doses and avoidance of systemic side effects. Prerequisites are adequate delivery resulting in sufficient pulmonary deposition and usability of the compound for inhalation (e. g. sufficient stability, no local toxicity). Various antibiotics have received market approval or are subject of clinical studies. However, data regarding macrolide inhalation are sparse even though these are important in treatment of infective lung diseases and bear an additional anti-inflammatory effect.

**Methods:** Publications on preparation and administration of aerosols of macrolide antibiotics were analysed focusing on recent publications.

**Results:** Up to now there are only few publications regarding macrolide aerosols. Both aerosol types solutions and dry powder aerosols (DPI) were investigated. A number of publications investigated physicochemical properties of aerosols. In brief, it was demonstrated that macrolide aerosol particles may serve for inhalation and will achieve sufficient lung deposition (Hickey, J. Aerosol Med. 2006, azithromycin; Pilcer, J. Pharm. Sci. 2013, tobramycin-clarithromycin). The bitter taste of macrolides can be masked by microencapsulation (Sollohub, Acta. Pol. Pharm. 2011; roxithromycin). Animal experiments demonstrated that higher concentrations in alveolar macrophages and epithelial lining fluid than in plasma were achieved after aerosol administration than after oral administration (Togami, Drug Dev. Ind. Pharm. 2010, telithromycin; Togami, Pharm. Dev. Technol. 2010, azithromycin; Togami, J. Aerosol Med. Pulm. Drug. Deliv. 2012, clarithromycin; Zhang, Int. J. Pharm. 2010, azithromycin).

**Conclusions:** Data demonstrate the feasibility of macrolide inhalation. Modern methods of aerosol administration will allow deposition of high local doses for local antiinfective/antiinflammatory treatment without systemic side effects improving treatment of patients, e. g. with CF or bronchiectasis.

### P37

#### Short-term effects of chest physiotherapy on ventilation inhomogeneity in cystic fibrosis patients with moderate to severe lung disease

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**Background:** Cystic fibrosis (CF) lung disease is characterized by both airway infection and airway inflammation involving the peripheral airways already in the early stages of the disease. The lung clearance index (LCI) is a measure of ventilation inhomogeneity determined during multiple breath washout (MBW). Studies in CF patients have shown that the LCI is more sensitive at detecting lung disease than conventionally used lung function parameters. We sought to determine the short term effect of chest physiotherapy (CPT) in adolescents and adults with CF and moderate to severe lung disease on the LCI and conventional lung function parameters.

**Methods:** We used a validated open-circuit N2-MBW hard- and software package (Exhalizer D and Spiroware 3.1, Eco Medics AG) to measure LCI. Two to three successful tests followed by conventional lung function were done before and 30 min after CPT.

**Results:** So far 19 patients (10 f), mean age 24 years (range 13.3–43.4), 12 colonized with *Pseudomonas aeruginosa*, were measured. For the group, LCI (mean; range) before (15.7; 7.4–19.5) and after CPT (15.7; 7.1–20.5) was not different, but 6/19 patients showed a differ-

ence of more than 3 LCI units (increase in 3/19: 3.1, 3.4, 5.6; decrease in 3/19: -3.69, -4.8, -4.84). LCI coefficient of variation before and after CPT was 3.7 and 3.3 %. FEV1 (mean; range) before (67%; 34-89) and after CPT (69%; 38-89) differed significantly ( $p=0.016$ ) for the group.

**Conclusions:** In CF patients with established lung disease the short-term effect of CPT may be variable. By opening up previously poorly ventilated lung regions, CPT may either increase or decrease ventilation inhomogeneity.

## P38

### Integrierte telemedizinische Versorgung von COPD-Patienten in Kärnten – erste Ergebnisse einer europaweiten kontrollierten Studie RENEWING HEALTH – Telemonitoring der COPD (REgioNs of Europe WorkING Together for HEALTH)

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**Grundlagen:** Telemonitoring mit Feedback zu den behandelnden Ärzten und Krankenhäusern stellt eine moderne Behandlungs- und Präventionsmethode dar. Diese Methode wurde bisher nicht systematisch studiert und soll auf ihre Wirksamkeit und Kosteneffizienz bei COPD Patienten getestet werden.

**Methodik:** Multizentrische, randomisierte Pilot-Studie zur Implementierung eines lebenslangen Telemonitoring in der Überwachung von Patienten mit COPD III und IV im Rahmen einer EU-weiten Telemonitoring und Krankheitspräventionsstudie (Grant EU 250487). In mehreren europäischen Clustern werden COPD-Patienten europaweit in unterschiedlichen Monitoring-Protokollen. Randomisierung 2:1 in Interventionsgruppe versus Kontrollgruppe. Plan 300 Patienten in Kärnten. Endpoints: Hospitalisationsrate, Mortalität, Lebensqualität SF 36 und CAT-Fragebogen, ökonomische und informationstechnologische Outcome Parameter Intervention: Patienten mit COPD 3 und 4 werden in 3 Untergruppen einer Telemonitoringstudie eingeschleust: 1. Web-basierter CAT-Fragebogen über Online Zugang, 2. Telefonisch automatisierter CAT-Fragebogen 3. Pflege-assistiertes Monitoring und Internetzugang. Es erfolgt eine tägliche Evaluation des CAT Fragebogens und eine automatisierte Auswertung. Bei Grenzwertüberschreitung (>8 Punkte) erfolgt eine elektronische Information des Behandlungsteams (Studienzentrale). Routinedatenübermittlung in das Krankenhaus-IT-System alle 30 Tage. Die Studiendauer beträgt ein Jahr nach Randomisierung. Ende der Patientenrandomisierung ist der 31.03.2012.

**Vorläufige Ergebnisse:** In den 3 österreichischen Zentren wurden bisher xx Patienten in die Studie eingeschleust. Xx% werden über webportal, xy % über automatisierte Telefonbefragung und yy % über Pflegeassoziiertes Monitoring betreut. Bis 6 Monate nach Randomisierung führen xx Patienten das tägliche Monitoring mit einer Compliance von % (Dokutage/Plantage)durch. Die Möglichkeit eines Telemonitorings bei COPD-Patienten zeigt bei den Studienteilnehmern eine hohe Akzeptanz. Endgültige Daten stehen bis Juli 2013 zur Verfügung.

## P39

### Results of an internet-based COPD awareness program

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**Grundlagen:** COPD ist unterdiagnostiziert. Nur etwa 80 % der Patienten mit einer obstruktiven Ventilationsstörung sind auch als COPD-Patienten identifiziert. Neue Initiativen sind erforderlich, um einerseits das Bewusstsein für die Erkrankung COPD zu erhöhen und damit in weiterer Folge den Anteil der nicht diagnostizierten Erkrankungen zu reduzieren.

**Methodik:** Wir berichten über eine Initiative, die in Zusammenarbeit mit netdoktor.at durchgeführt wurde. Auf einer Internetplattform wurde ein COPD-Fragebogen zur Verfügung gestellt und Personen via die Initiative „Atmen statt Husten“ aufgefordert, diesen Risiko-Fragenbogen zu benutzen. Der Fragebogen setzte sich aus mehreren Items zusammen, die zu respiratorischen Symptomen und zum Zigarettenrauchen abgefragt wurden. Die Auswertung erfolgte unter Verwendung eines Algorithmus, der im Rahmen der BOLD-Studie für Personen jenseits des 40. Lebensjahres entwickelt wurde.

**Ergebnisse:** 7.614 Personen haben im Zeitraum von 11. März 2013 bis 17. April 2013 den Fragebogen ausgefüllt. Von diesen waren 32 % Raucher und 38 % Ex-Raucher. 22 % berichteten von einer Einschränkung durch Atemnot im Alltag, und 28 % gaben an, bereits bei der Bewältigung eines Stockwerkes in Atemnot zu geraten. 46 % berichten über ein pfeifendes Atemgeräusch ihrer Lunge und 71 % berichten Husten. 29 % der Personen möchten diese Ergebnisse verwenden, um einen Lungenfacharzt zu kontaktieren. Die Altersverteilung zeigt, dass jüngere Personen deutlich vermehrt angesprochen wurden als ältere; so waren 35 % der Studienteilnehmer zwischen 40 und 50 Jahren alt.

**Schlussfolgerungen:** Unsere Ergebnisse zeigen, dass Internet basierte Fragebögen geeignet sind, Personen für COPD zu sensibilisieren und damit das Wissen um diese Erkrankung in der Bevölkerung zu erhöhen.

## P40

### Prevalence of tricuspid regurgitation in patients with heart failure and preserved ejection fraction

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**Background:** Heart failure (HF) with preserved ejection fraction (HFPEF) is commonly observed in elderly female patients and is responsible for approximately 50 % of all HF cases. An elevated left ventricular end-diastolic pressure leads to a rise in pulmonary arterial pressure, resulting in right ventricular dilatation, and the development of tricuspid regurgitation (TR). Little is known about the prevalence and characteristics of TR in HFPEF patients.

**Methods:** Consecutive patients with HFPEF diagnosed according to ESC guidelines were enrolled in our prospective Viennese registry, which was approved by the local ethics committee of the Medical University of Vienna. All patients underwent invasive hemo-

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dynamic work-up. According to TR severity, patients were dichotomized into two groups: TR < moderate and TR ≥ moderate. Groups were compared with Student's t-test and a Chi-square analysis for categorical data.  $P < 0.05$  indicated statistical significance.

**Results:** Between December 2010 and January 2013, a total of 102 patients (71f/31 m, mean age  $71 \pm 9$ ) were enrolled, of whom 62 (61%) were diagnosed with ≥ moderate TR. Patients with TR ≥ moderate were characterized by older age in years ( $72 \pm 8$  vs.  $68 \pm 10$ ,  $p = 0.024$ ) and higher NT-proBNP values in pg/ml ( $2,113 \pm 2,388$  vs.  $1,233 \pm 1,235$ ,  $p = 0.034$ ). Atrial fibrillation (79 vs. 40%,  $p < 0.001$ ) was more prevalent among patients with TR ≥ moderate. With respect to echocardiographic parameters a larger left atrial diameter in mm ( $67 \pm 8$  vs.  $63 \pm 8$ ,  $p = 0.037$ ), a larger right atrial diameter in mm ( $68 \pm 11$  vs.  $60 \pm 7$ ,  $p < 0.001$ ), and a larger right ventricular end-diastolic diameter in mm ( $40 \pm 8$  vs.  $36 \pm 6$ ,  $p = 0.004$ ) were detected. Furthermore patients with TR ≥ moderate displayed a higher pulmonary capillary wedge pressure, pulmonary vascular resistance and transpulmonary gradient compared with the remaining group.

**Conclusions:** Relevant TR is present in more than half of patients with HFPEF and is associated with poor pulmonary hemodynamic parameters.

### P41

#### Predictors of adverse outcome in patients with heart failure and preserved ejection fraction

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**Background:** Patients with heart failure and preserved left ventricular ejection fraction (HFPEF) face an adverse outcome. The aim of the present study was to identify factors that determine prognosis.

**Methods:** Consecutive patients with HFPEF diagnosed according to current ESC guidelines were recruited in our prospective registry. Death and/or hospitalization for HF were defined as primary outcome variables. Outcome groups were compared with respect to potential prognostic predictors using the Student's t-test and Chi-square test. Multivariable logistic regression analysis was applied to determine whether parameters of interest were associated with adverse outcome.  $P < 0.05$  indicated statistical significance.

**Results:** Between December 2010 and January 2013, 102 HFPEF patients (71f, mean age  $70 \pm 8$  years) were registered. After a mean follow-up of  $13 \pm 9$  months, 24 (24%) patients were hospitalized or died. Patients in the adverse outcome group were characterized by a shorter 6-minute walk distance in m ( $254 \pm 117$  vs.  $347 \pm 112$ ,  $p = 0.002$ ), a higher borg dyspnea score (BDS,  $6 \pm 2$  vs.  $3 \pm 2$ ,  $p < 0.001$ ), lower haemoglobin values in g/dl ( $11.6 \pm 1.3$  vs.  $12.7 \pm 1.9$ ,  $p = 0.011$ ), higher NT-proBNP in pg/ml ( $2107 \pm 1409$  vs.  $1363 \pm 1243$ ,  $p = 0.017$ ), a higher mean pulmonary arterial pressure in mmHg ( $39 \pm 9$  vs.  $33 \pm 9$ ,  $p = 0.009$ ), a higher mean right atrial pressure in mmHg ( $16 \pm 7$  vs.  $12 \pm 5$ ,  $p = 0.008$ ) and a higher transpulmonary gradient (TPG  $> 12$  mmHg, 83 vs. 55%,  $p = 0.013$ ) at enrolment. Diabetes mellitus II (DM II, 58 vs. 27%,  $p = 0.005$ ) was more prevalent among patients with adverse outcome. In the multivariable regression model, DM II (odds ratio: 5.5 [95% confidence interval 1.5–20.2];  $p = 0.010$ ), the BDS (odds ratio: 6.2 [95% confidence interval 1.7–22.1];  $p = 0.005$ ), as well as TPG  $> 12$  mmHg (odds ratio: 3.9 [95% confidence interval 1.0–15.1];  $p = 0.046$ ) remained independent predictors of adverse outcome.

**Conclusions:** Presence of DM II, a higher BDS and a TPG  $> 12$  mmHg predict adverse outcome in HFPEF patients.

### P42

#### High-flow oxygen therapy in COPD patients: optimised oxygen delivery

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**Background:** COPD is a leading cause of death and is often related to chronic hypoxemia. Long-term oxygen therapy (LTOT) is a well established treatment. High-Flow oxygen treatment (HFOT), the nasal insufflation of warm, humidified air at a high flow rate, is a new and simplified method in not-invasive ventilation. Until now, no data concerning HFOT in COPD patients are available.

**Aim:** Our studies were designed to assess the safety and efficacy of HFOT in COPD patients compared to conventional oxygen therapy and to examine possible changes in oxygenation.

**Methods:** Inclusion criteria: COPD °IV, indication for LTOT, 30–80 year, clinical stable and Hb  $> 8.5$  g/l. Oxygen ( $O_2$ ) supplementation was performed with a TNi® 20s oxy-system (15 L/min) or with a standard oxygen delivering system.  $O_2$  adaptation was performed in 10 min intervals until a  $paO_2 \geq 60$  mmHg was achieved. Blood gas analyses were performed from the hyperaemic earlobe.

**Results:** Sixty patients were enrolled: 45 male, 15 female, mean age: 66.3 year, FEV1 (pred): 12–49%. HFOT was well tolerated and was sensed as comfortable. A significant decrease of  $paCO_2$  could be measured ( $-1.45$  mmHg;  $p = 0.018$ ) when compared to conventional oxygen administration. Oxygen delivery trends to be lower with HFOT ( $-0.23$  L/min). By using the high-flow system with 15 L/min the delivered mean  $FiO_2$  was 31.7% compared to the  $FiO_2$  of 100% delivered by conventional oxygen treatment ( $p = 0.0001$ ).

**Conclusions:** Treatment with high-flow nasal insufflation is safe in patients with severe COPD on LTOT treatment. Lower amounts of delivered  $O_2$  seem to be necessary to oxygenate the patient. Trials for longer periods are planned to further prove efficiency of HFOT.

### P43

#### Lipocalin 2 modulates inflammation and impairs host defense against *Streptococcus pneumoniae*\*

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**Background:** Lipocalin 2 (Lcn2) is an antibacterial protein, known to interfere with the siderophore-dependent iron acquisition of pathogens such as *E. coli* and *Mycobacteria*. However, most bacterial species constituting the lung microbiome do not utilize siderophores. Likewise, *Streptococcus pneumoniae*, the major cause of community acquired pneumonia, utilizes siderophore-independent mechanisms of iron acquisition. Despite this fact, infection with *S. pneumoniae* induces tremendously high lung levels of Lcn2 in mice and humans—and the biological role of this finding remains elusive. We therefore investigated the function of Lcn2 during pneumococcal pneumonia.

**Results:** Studying a murine pneumonia model, we found Lcn2<sup>-/-</sup> mice to display an enhanced bacterial clearance, accelerated resolution of lung inflammation and improved survival. As an explanation for this improved host defense we found the early inflammatory response (6h after induction of pneumonia) to be augmented with a significantly increased neutrophil influx in Lcn2<sup>-/-</sup> animals. Mechanistically, Lcn2<sup>-/-</sup> macrophages exhibited an enhanced secretion of pro-inflammatory cytokines and decreased induction of IL-10 in response to *S. pneumoniae* both in vivo and in vitro. Consistently, recombinant mouse Lcn2 dampened the macrophage's response to TLR ligands. Over-expression studies disclosed that Lcn2 mediated these effects via induction of IL-10 and the blocking of IL-10 abolished the difference in bacterial clearance between WT and Lcn2<sup>-/-</sup> in vivo.

**Conclusions:** We postulate that Lcn2 modulates the early inflammatory response upon *S. pneumoniae* infection through induction of IL-10 and deactivation of lung macrophages, which ultimately results in impaired bacterial clearance and survival.

#### P44

#### Endothelin-1 stimulates dendritic cell migration via the ETA and B receptors

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Endothelin-1 (ET-1) is a peptide that is engaged in tumor growth, metastasis, pulmonary vascular disorders like PAH and inflammation. Thus, ET-1 stimulates migration of inflammatory cells, i. e. basophils or monocytes. Dendritic cells serve as key cells in inflammatory and immunological processes. Whole blood dendritic cells, plasmacytoid and myeloid dendritic cells were isolated from EDTA-anticoagulated venous blood, followed by subpopulation specific MACS isolation protocols. For the chemotactic assays modified 48-well microrhometaxis chambers were used. Dendritic cells migrated through a 8 µm pore sized cellulose membrane filter for 240 min in a humified atmosphere (37°C, 5% CO<sub>2</sub>) against a gradient of the substances tested (ET-1, fMLP, MCP-1). For blocking experiments dendritic cells were preincubated with specific receptor antagonists for 30 min. Migration depth of the cells in the filter was quantified microscopically by measuring the distance [µm] from the surface of the filters to the leading front of the cells. ET-1 significantly stimulated migration in a dose-dependent manner revealing a maximal effect at 10–8 M. The effect was comparable with maximal stimulation of migration

elicited by the well known chemoattractants fMLP (10–8 M) and MCP-1 (10–8 M). ET-1 stimulated as well the whole blood dendritic population as the two subtypes. To further evaluate the engaged receptor mediating this process blocking studies were performed. As well the ETA receptor antagonist (BQ-123) as the ETB receptor antagonist (BQ-788) abolished the ET-1 effect in all tested dendritic cell populations to a similar extent. In a third step, both the ETA and the ETB receptor mRNA were detected in dendritic cells. ET-1 not only exhibits vasoconstrictive or proliferative activity, but also directly stimulates migration of immunologic cells like dendritic cells. Thus, it can be suggested that Endothelin-1 is directly involved in innate and adaptive immunological responses.

#### P45

#### The migration of monocytes is stimulated by Jagged-1 and DLL-4 via the Notch pathway

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The notch signaling system is a highly conserved signaling system that functions to regulate tissue homoeostasis and morphogenesis of stem cells in adults. Monocytes serve as key cells in inflammatory and immunological processes. Monocytes were isolated from EDTA anticoagulated venous blood. For the chemotactic assays modified 48-well microchemotaxis chambers were used. Monocytes migrated through an 5 µm pore sized cellulose membrane filter for 45 min in a humified atmosphere against a gradient of the substances tested (fMLP, Jagged1, DLL4, DAPT). For blocking experiments monocytes were preincubated with specific ligands for different durations. Migration depth of the cells in the filter was quantified microscopically by measuring the distance [µm] from the surface of the filters to the leading front of the cells. The notch ligands DLL4 and Jagged1 significantly stimulate migration in a dose dependent manner revealing a maximal effect at [100 ng/ml]. The effect was comparable with maximal stimulation of migration elicited by the well known chemoattractant fMLP (10–8 M). A significant inhibition of migration was observed by pre-incubating the cells with the γ-secretase inhibitor DAPT [10–4]. Interestingly, priming of cells with the ligands also elicited monocyte migration [maximal effect at 100 ng/ml]. Different preincubation times with the ligands revealed that at least a preincubation time of 30 min is necessary to stimulate monocyte migration. Jagged1 and DLL4 directly stimulate migration of human monocytes in vitro. For activation of migration a cell-cell interaction for about 30 min seems to be necessary. In conclusion, it can be suggested, that Jagged1 DLL4 are involved in inflammatory processes.

#### P46

#### 7 year old boy with cough: diagnosis? A case study

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**Background:** Since 1997, blood spot immunoreactive trypsin (IRT) determination is used for new-born screenings (NBS) to detect Cystic Fibrosis (CF) in Austria. In case of values above 65 ng/ml, a second measurement is carried out at the fourth week of life. Results

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above 50 ng/ml in the repeated testing require the implementation of a sweat test. Reasons for false negative results are largely unknown, and happen at a rate of one case per year (excluding meconium ileus patients) in Austria (number of births 2012: 77.700).

**Case report:** This is a case of an Austrian-born, male, term infant without pathological findings at newborn screening. At the age of 2 months, the boy contracts pneumonia. Subsequent respiratory infections require frequent antibiotic treatments. Unfortunately, the boy does not present at any routine paediatric check-up visits and only receives treatment during acute respiratory infections. Despite failure of thrive being diagnosed and further workup being recommended by the family doctor, these procedures are not carried out due to language barriers, socioeconomic disadvantage and finally change of residence. Again, the boy is solely treated for acute respiratory infections in an out-patient setting. At the age of seven years, he is admitted to a children's hospital due to acute pneumonia. At that time, his body weight and length is below the first percentile. A sweat test is carried out and yields the diagnosis of CF.

**Conclusions:** This case report demonstrates the necessity for taking into consideration CF as possible differential diagnosis, even if NBS is negative.

### P48

#### Vascular endothelial growth factor receptor-2 blockade as a new experimental model of pulmonary arterial hypertension\*

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**Background:** Pulmonary arterial hypertension (PAH) is a severe and progressive disease characterized by obstruction of small pulmonary arteries leading to increased pulmonary vascular resistance. The key pathologic finding in this disease is a negative pulmonary vascular remodeling process with total vessel occlusion and a monoclonal expansion of collateral endothelial cells. It has been proposed that impaired vascular endothelial growth factor (VEGF) signaling plays a significant role in this process. Aim of our study was to investigate whether inhibition of VEGFR-2 (KDR) by direct gene manipulation may replicate classical pulmonary vasculopathy.

**Methods:** We utilized mice with conditional VEGFR-2/KDR knock-out in endothelial cells (KDR-/-). KDR<sup>flox/flox</sup>/Tie-2Cre and KDR<sup>flox/flox</sup>/Tie-2 mice were injected intraperitoneally with tamoxifen for three weeks to induce the knock-out. KDR-/- mice and wild type littermates were held in an environmental chamber with FiO<sub>2</sub> of 10 % or under normoxia for 2, 4, and 6 weeks. We investigated the effect of KDR deletion and chronic normobaric hypoxia on pulmonary hemodynamics and right ventricular hypertrophy.

**Results:** KDR-/- mice showed significantly increased right ventricular pressures (RVSP's) and Fulton indices after 2, 4, and 6 weeks under normoxic conditions, compared with wild type controls. Both KDR-/- and wild type mice showed increased right ventricular pressures under normobaric hypoxia. KDR-/- mice revealed significantly higher right ventricular pressures (Fig. 1) and Fulton indices than controls after 4 and 6 weeks. Knockout mice showed a significant increase in pulmonary arterial wall thickness after chronic hypoxia compared to control mice. Lung histologies demonstrated neointimal thickening and vessel occlusions in lungs of KDR-/- mice resembling human pulmonary arteriopathy.

**Conclusions:** Classical pulmonary arterial hypertension was induced in C57/BL6J mice by direct ablative gene manipulation of KDR.

### P47

#### Notch signaling in idiopathic pulmonary fibrosis

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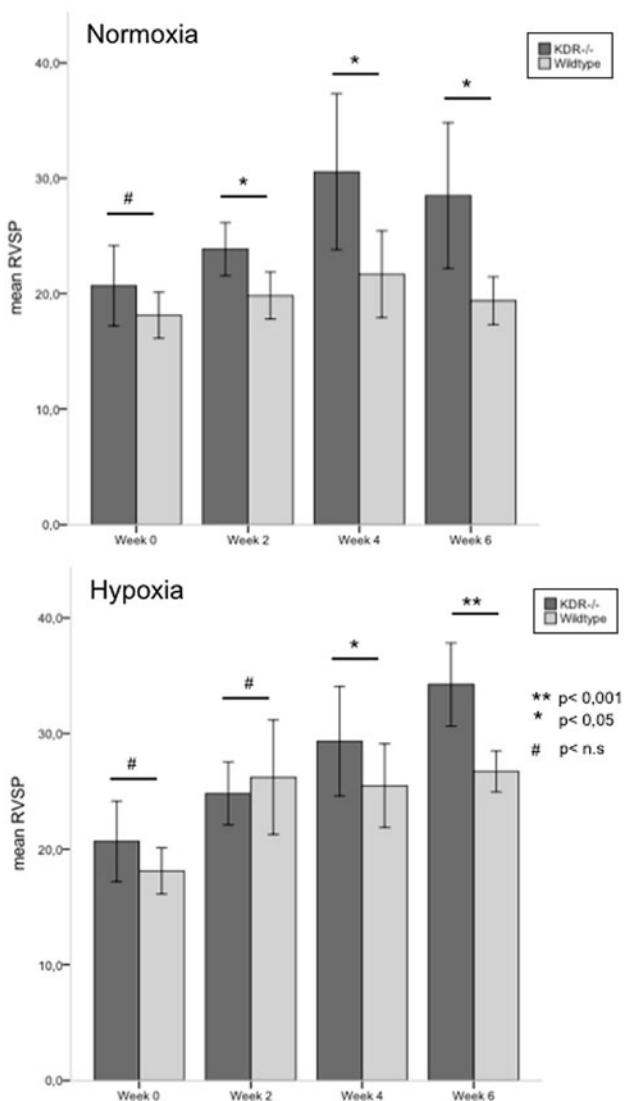
**Background:** Idiopathic Pulmonary Fibrosis (IPF) is a chronically progressive interstitial lung disease of unknown origin. It is believed so far that proliferation of lung fibroblasts with synthesis and alveolo-capillary deposition of collagen as well as cytokine-mediated interstitial infiltration by inflammatory cells seems to play a prominent role in IPF pathogenesis. Thus, this study aims to further decode the underlying molecular signaling which might lead to enhanced fibroblast activity in IPF.

**Aims:** The evolutionary conserved Notch signaling pathway is an essential one regarding the establishment of patterns of gene expression, the maintenance and differentiation of (stem) cells and the binary regulation of cell fate choices. However, less is known on the role of Notch on fibroblast proliferation, so far. Therefore, we examined the effects of Notch ligand-receptor-interaction on human lung fibroblast proliferation.

**Methods:** We conducted experimental in-vitro trials with human pulmonary fibroblasts from PromoCell and the Notch ligands Jagged-1 and Delta-like-4. Cells were cultured in Fibroblast Growth Medium under humified conditions. After 24 hours of G0-starving, cells were incubated with either 0.2 % FCS (negative control), 20 % FCS (positive control) or the test substances in 0.2 % FCS in a 96 well microplate (25000cells/ml). To analyze cellular proliferation we used the fluorometric EZ4U proliferation assay (Biomedica).

**Results:** Jagged-1 and Delta-like-4 significantly stimulated proliferation of human fibroblasts in a dose dependent manner, revealing a maximal effect of both ligands at a concentration of 100 ng. The observed effect was comparable with maximal proliferation elicited by the positive control of 20 % FCS.

**Conclusions:** Herewith, we report for the first time that the Notch signaling pathway is affecting human pulmonary fibroblasts proliferation in vitro. This might be a promising target for therapeutic strategies in pulmonary fibrotic diseases.



(Wohlkoenig et al., Cancer Letters 308 (2011) 134–143). It is unknown if this is also true for cancer drugs using the nr4a1-pathway. Therefore we investigated the effects of cytosporone B, a fungal metabolite, the first naturally occurring agonist for NR4A1, on lung cancer cells in normoxia and hypoxia.

**Methods:** For investigating hypoxia-induced apoptosis resistance of cytosporone B, A549 cells were preincubated for 3 days in normoxia and hypoxia (1% O<sub>2</sub>). Then cells were splitted and after 24 h treated with predefined concentrations of cytosporone B. DMSO was included as vehicle control. After another 24 h cell growth and viability was assessed by pulse area analysis (CASY® cell counter). Induction of apoptosis was investigated with the PhiPhiLux® assay following flow cytometry.

**Results:** Cytosporone B induced a concentration-dependent and statistically significant growth inhibition and reduction of viability ( $p<0.001$  for both). This effect was not affected by hypoxia ( $p=0.35$  for growth and  $p=0.53$  for viability). Cytosporone B (200 μM) caused  $83.7\pm9.3\%$  and  $86.3\pm3.3\%$  apoptosis rate with characteristic nuclear fragmentation after 24 h in normoxia and hypoxia, respectively ( $p=0.81$ ).

**Conclusions:** Unlike cisplatin, cytosporone B effects are not oxygen-dependent in A549 lung cancer cells. This suggests that cytosporone B may have superior anticancer properties in hypoxic tumors.

## P50

### Cytokines in chronic thromboembolic pulmonary hypertension

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**Background:** CTEPH is a progressive occlusive pulmonary vascular disease, where inflammatory factors, misguided vascular remodelling and endothelial dysfunction contribute to major and small vessel obliteration. In CTEPH inflammatory factors such as C-reactive protein, tumor necrosis factor-alpha, and MCP-1 have been found to be elevated. The correlation of these factors with hemodynamic parameters indicates the important role of inflammation in the progression of the disease. In our study we have investigated IL-8, IL-6, MCP-1, IP-10, MIG, Rantes, CX3CL1, MIP1alpha, CXCL12 and HMGB1 at three different levels (PEA tissue, PEA supernatant and serum) and correlated these factors with clinical parameters in order to throw light on the role of inflammation in the development of this obliterative disease.

**Methods:** The supernatant of PEA samples from CTEPH patients ( $n=8$ ) and age and sex matched serum samples from 16 healthy controls and 16 CTEPH patients were collected. IL-8, RANTES, MIG, MCP-1, IP-10, IL-6, Fractalkine and MIP-1alpha were determined by FACS or ELISA.

**Results:** We observed a significant up-regulation of IL-8, IL-6, MCP-1, IP-10, MIG, Rantes, MIP1alpha and HMGB1 in the PEA tissue compared to healthy human lung and in the supernatant of the PEA

## P49

### Cytosporone B, an nr4a1 specific cytotoxic agent, is not prone to hypoxia-induced apoptosis resistance in A549 cells

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**Background:** The overall survival rate of lung cancer patients is still poor and consequently the need for new therapeutic options is high. NR4A1 is an orphan nuclear receptor that was recently found to be a promising target for cancer therapy. Preclinical studies revealed four different mechanisms how apoptosis can be induced through NR4A1. However, these studies were done in ambient oxygen conditions whereas in solid tumours *in vivo* hypoxic conditions prevail. We have previously shown that the efficacy of the gold standard in NSCLC treatment, cisplatin, is significantly reduced under hypoxia

## abstracts

tissue. The presence of IL-8, IL-6, MCP-1, IP-10, CXCL12, HMGB1 and MIP1alpha was validated in the PEA tissue by immunohistochemistry. In addition, we detected significantly increased levels of IL-8, IL-6, IP-10, MIG, HMGB1 and MIP1alpha in the serum of CTEPH patients in comparison to healthy controls. IP-10 and IL-6 were correlated ( $p<0.05$ ) with hemodynamic deterioration and decreased physical capacity (6MWD).

**Conclusions:** The increase of IP-10 and IL-6 may indicate active remodelling within PEA tissue contributing to deterioration of pulmonary hemodynamics and may represent biomarkers in CTEPH.

### P51

#### Outcome of multidrug-resistant tuberculosis treatment in a cohort of 57 patients at Otto-Wagner-Hospital (Austria) from 2004 to 2010

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**Background:** MDR-TB is caused by Mycobacterium tuberculosis strains which are at least resistant to rifampicin and isoniazid. This fact leads to a long-standing and extensive therapy associated with a high potential of toxic sideeffects. All WHO recommended drugs are available in Austria. All therapies were established immediately after hospitalisation based on recent WHO guidelines and if necessary adapted according to results of resistance testing.

**Methods:** We retrospectively analysed the clinical records of 57 patients(pts) infected with MDR-TB. All of them were treated at the ward Karlshaus, Otto-Wagner-Hospital.

**Results:** During six years 34 men and 23 women suffering from MDR-TB were treated. The median age was 30.52 years (min=16, max=60). The majority of them were citizens of the Russian Federation (36, includes Chechnya 31), Georgian Republic (7) and Romania (4). Every patient received resistance testing. The following baseline resistances were detected: Streptomycin (S=52), rifabutin (Rfb=50), pyrazinamide (Z=34), ethambutol (E=29), prothionamid (Pto=23), amikacin (Am=21). Resistance against cycloserine, linezolid and para-aminosalicylic-acid is rare, nevertheless resistance against fluoroquinolones (Fqn) is emerging (9). Under fully established therapy 6 pts developed resistance(E=2, Fqn=2; Z=1; Lzd=1). After the inclusion of drug resistance results, drug tolerability is a major element in treating MDR-TB pts. 80.7 % of our pts developed gastrointestinal sideeffects, 57.9 % elevation of liverenzymes (ALT/AST), 57.9 % polyneuropathy. Less than 10 % suffered from changes in their haemogramm, rash, erectile dysfunction and dysgeusia. Depression was the major comorbidity (54.38%) followed by caries (52.63%). 46 pts (80.7 %) were cured, proved by sputum conversion. The median length of therapy was 22.41 months (min=14, max=34). 6 pts returned into their country with medical support and were lost to follow-up, 3 pts escaped and 2 pts died (1 TB associated; 1 lung cancer).

**Conclusions:** The successful cure of 46(80.7 %) patients suggests that access to efficient therapy, high patients' adherence and therapy control lead to a significant cure rate. This cure rate is comparable to other resource-rich settings worldwide.

### P52

#### Jagged-1 and DLL-4 stimulate the migration of T-cells via the NOTCH pathway

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The Notch pathway is a signaling system, which regulates cell fates. It includes 4 different Notch receptors and 5 ligands, which are transmembrane proteins. T cells belong to a group of white blood cells known as lymphocytes, and play a central role in cell-mediated immunity. We want to uncover, which role the notch signaling pathway plays in the pathogenesis of immunological processes. T-cells were isolated from EDTA-anticoagulated venous blood, taken from healthy donors and with their informed consent. The isolation was carried out according to MACS isolation protocol (Miltenyi Biotec Bergisch Gladbach, Germany). For the chemotaxis experiments, a 48-well microchemotaxis chamber was used. The isolated T-cells migrated through a 5  $\mu$ m pore sized cellulose nitrate filter. Incubation time was 90 min, in a humidified atmosphere. As chemokines were used fMLP, and gradients of DLL4, and Jag1. Migration depth of the cells in the filter was quantified microscopically by measuring the distance [ $\mu$ m] from the surface of the filters to the leading front of the cells. Findings are expressed as 'Chemotactic Index (CI)', which is the ratio between the distance cells migrated towards chemoattractants and that towards medium. DLL4 and Jag1 significantly stimulated migration of the isolated T cells in a dose-dependent manner, revealing a maximal effect at [100 ng] of both Notch ligands. The effect was comparable with maximal stimulation of migration elicited by the chemoattractant fMLP (10-8 M). Jag1 and DLL4 directly stimulate migration of T-cells. Thus, it can be suggested that Jag1 and DLL4 are involved in innate and adaptive immunological responses.

### P53

#### Pneumonia in a tertiary care center: analysis of a 3-year period

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Pneumonia is a serious condition being the primary diagnosis in about 1.6% (2434/ 151820) of patients hospitalized in a tertiary care center. Pneumonia takes the third place at the pulmonary department. While 87 % of pulmonary infiltrates were considered pneumonias themselves, 13 % were of other etiologies. A three year period at the AKH Linz was analyzed for admission of patients with pneumonia—the majority (90.9 %) either at the pulmonary or an internal medicine department—68.2 % and 22.8 % respectively. Pneumonias occurred in 2 % in neurological, 1.9 % with surgical or ENT-patients. In orthopedics and traumatology as well as urology (0.9 %) pulmonary infiltrates were frequently considered a complication. The rest at other specialties amounts to 1.1 %. The incidence of pneumonia rises with age up to 80 years—the median age being 68 years and the mean 64 years with a mortality rate of 2,45 % between 31–35 years and 8,59 % between 71–75 years. In the age groups 76–80 years, 81–85 years and 86–90 years the lethal outcome increases to 23.93, 16.56, and 17.18 % respectively, but in % of the age-group it goes continuously up until 90 years. In these periods pneumonia is most often the terminal event of life associated with a number of comorbidities. About 4 % of patients need a transfer to intensive or intermediate

ate care units. In over 90 % either a conventional biplanar CXray or a chest-CT has been done within the day of admission. The hospital stay increases with age, too. It rises from 4–5 at 20 years to 12 days between 80–90 years, and lies on the average around 7,57 days. Death occurs around day 10–11, but there is no correlation between age and time to death. In the future quality assessment of care will be based on statistics of outcome. Pulmonary specialists should be prepared and know their facts and figures.

## P54

### The Austrian Severe Asthma Net (ASA-Net)

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Severe asthma represents a heterogeneous group of patients probably consisting of specific subtypes which are neither well defined nor understood yet. It is estimated that 5 to 10 % of patients

with asthma suffer from severe asthma. This group of patients has a high burden of disease, high risk for work disability, needs specialized care and cause relevant health care costs.

The Austrian Severe Asthma Net (ASA-Net) was initiated in January 2012. The aims of ASA-Net are to increase awareness and knowledge about (severe) asthma and improve quality of care of severe asthmatic patients, both children and adults in Austria. The ASA-Net supports and addresses physicians as well as patients. This project entails several components with the clinical registry as its core component:

- A web-based clinical registry for patients with severe asthma
- The ASA-Net homepage with information and communication tools for physicians and patients ([www.asa-net.at](http://www.asa-net.at))
- Supply of clinical support materials and services (guidelines, questionnaires, clinical reference pocket cards and posters, etc.) for centers and partners of ASA-Net

In a pilot phase of four years, the Austrian network should be established consisting of about twenty centers and partners with a special focus on asthmatic patients. Currently, six centers and one partner are participating in ASA-Net and recruiting patients for the clinical registry. Due to the poor awareness of (severe) asthma and the missing integration of the clinical and research field in asthma in Austria, the permanent establishment of this network is a major goal. The clinical registry is run in cooperation with the German Asthma Net e. V. (GAN) and is about to become the largest international registry for patients with severe asthma.

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