



INSPIRE

الجمعية اللبنانية للأمراض الصدرية
عدد رقم ٧ - كانون الأول ٢٠٠٩

2 Continuous Medical Education

3 Editorial

4 Tuberculosis, Part IV

8 Pandemic Influenza H1N1

9 Regional Meeting: Tyre

10 ERS 2009 Report

13 LPS Annual Meeting 2009




Programme de Formation Médicale Continue – FMC 2010

Le Comité d'Education Médicale Continue vous informe que le programme 2010 consistera en une préparation des participants à l'examen HERMES de l'ERS qui se tiendra à Barcelone en septembre 2010. Cette préparation comportera des travaux à faire par Internet et un examen final. La réussite à cet examen permettra au participant d'obtenir un support financier pour s'inscrire et présenter HERMES. Ceux qui sont intéressés sont priés de s'inscrire au secrétariat de la SLP (Anne-Marie Khoury (01422582).

Continuous Medical Education Program – CME 2010

The Continuous Medical Education Committee informs you that the 2010 program will include a preparation of the participants to the ERS examination HERMES which will be held in Barcelona on September 2010. This will be done through assignments to be done by Internet, followed by a final exam. The successful participant will get a financial support to register at the HERMES exam. Those who are interested are kindly asked to register at the LPS secretary (Anne Marie Khoury (01422582).

Dr. Georges Khayat
President of the
CME Board at the LPS



Celebrating 20 years of ERS

2010 edition

HERMES

European Examination in Adult Respiratory Medicine

HERMES
Harmonised Education in Respiratory Medicine for European Specialists

Saturday, September 18, 2010
ERS Annual Congress, Barcelona



The Examination for the European Diploma in Respiratory Medicine will be on Saturday, September 18, 2010 within the framework of the Annual ERS Congress in Barcelona.

Characteristics of the examination:

- Knowledge-based
- 90 Multiple-Choice Questions
- English only
- Duration: 3 hours
- Blueprint based on the HERMES syllabus published in 2006
- Reserved to registered medical practitioners who have already obtained their national accreditation (or equivalent) to practice as a specialist in adult respiratory medicine

- Reserved to ERS members only
- Cost: €250,-
- Registration deadline: May 30, 2010
- More information, sample questions and online registration at: <http://hermes.ersnet.org>



لجان الجمعية

الهيئة الإدارية Executive Board

نديم كنج، رئيس
جورج خياط، نائب رئيس
لبنى طيارة، أمينة صندوق
طه بازارياني، أمين سر
ماري لويز كوسا كونيسكي
بانايوتي كركس
كارول يواكيم
هاني عبد الساتر
أحمد حصري

لجنة التثقيف الطبي المستمر CME Board

جورج خياط، رئيس
ميرنا واكد
جوزيف ممين
صلاح زين الدين
ميراي صفيير
بياتريس شامي
زينه عون باشا

لجنة مرض السل Tuberculosis Board

نديم كنج
مصطفى عيتاني

هيئة التحرير Editorial Board

زهير علامة
جورج خياط
ميرنا واكد



الزملاء الأعزاء

أعتقد أن الحكومة في لبنان قد تكون تشكلت عند قراءتكم لهذه الرسالة، فالخاض عسير ولكن "سياسي" الحمل لهم وسائلهم الخاصة، وفي أسوأ الأحوال القيصريّة منها.

وحالنا في الجمعية اللبنانية للأمراض الصدرية أفضل بسبب البقية الباقية من المهتمين بالشأن الطبي، الذي لا يسمّن ولا يغنى من جوع، ولكن يبقى الملاذ لمن شاء قدره أن يركب هذا الموج في بحرٍ واسعٍ بالمآسي التي نستمتع بها يومياً لحاجتنا إليها.

أما بعد

فنشاطات الجمعية مستمرة "شاء من شاء وأبى من أبى" وهي كما نأمل تحظى بتقدير المحافل الطبية، والشركات الداعمة، وأختم بأبيات أود مشاركتكم فيها وتشرح واقع الطب كما أراه:

وحكمةً للأقدمينا
وطمأنهً للخائفينا
وضغطاً للشاغليينا
سلّ، برونشيت وإمفيزينا
والطبّ نعمةً للمتمولين
أو من المؤمّنين
وكذا كل المعترينا

وطبّ كان وقاراً
ومنزلةً بين الناس
فأضحى فوضى وعجقة
ريو، جلط، سرطان
ومال مطلوب في طوارئ
أو أصحاب دعمة
والفقير متروك مكانه

وفقكم الله
والسلام

د. نديم كنج
رئيس الجمعية اللبنانية
للأمراض الصدرية

نقابة أطباء لبنان
مكتب الجمعية اللبنانية للأمراض
الصدرية

ص.ب. : ١١-١٤٠ بيروت، لبنان

تلفون/فاكس: ٤٢٢٥٨٢ ١ ٩١١

بريد الكتروني: lop_lps@yahoo.com

The scientific content of the articles in this newsletter does not necessarily reflect the opinion of the LPS

Tuberculosis (TB), part IV

Treatments, vaccines and other healings

Dr. Nadim Kanj

This is the last part of our tuberculosis saga. After having tackled in the first 3 parts the historical dimensions of tuberculosis, gone through an epidemiological journey and reviewed tests and diagnosis issues, here is, let's say the essential part, the one that interests most the patients: state of the art of the treatments

Latent Tuberculosis

The identification and treatment of persons with latent tuberculosis infection (LTBI) who are at high risk of progression to active disease is an important tuberculosis (TB) control and elimination strategy. Latent tuberculosis infection (LTBI) is a condition in which a person is infected with *Mycobacterium tuberculosis*, but does not currently have active tuberculosis disease. An estimated 10 to 15 million persons in the United States have LTBI. Because 5 to 10 percent of persons with LTBI are at risk of progressing to active disease, identification and treatment of LTBI are essential for the elimination of tuberculosis. Targeted tuberculin skin testing remains the most acceptable method of LTBI screening. New tests are being developed, the most promising of which are in vitro interferon-gamma release assays. All screened persons found to have LTBI should be offered treatment, regardless of age.

The candidates for treatment of latent TB infection are:

- Household contacts of AFB smear-positive pulmonary TB patients, who have not recently been vaccinated with BCG and who have TST induration > 10 mm; or contacts that were BCG vaccinated within the previous two years with TST induration > 15 mm
- Individuals with TST conversion (a positive test with > 10 mm induration after a previously negative test, applied 12 months earlier)
- HIV-infected individuals with a reactive TST of > 5 mm
- HIV-infected individuals that report close contact with a smear-positive TB patient, regardless of the TST response
- Individuals with a chest X-ray image consistent of residual TB, without a

history of previous anti-TB treatment Before beginning preventive chemotherapy, it is important to exclude active TB, either pulmonary or extrapulmonary, particularly in patients with moderate/severe immunodeficiency.

Recommendations call for treatment of populations at greatest risk for TB disease including immigrants from countries with high TB disease rates, persons with recent infection, persons with prior untreated TB disease, and persons with medical conditions or treatments that suppress the immune response that enforces latency.

Recommended drug regimens for treatment of LTBI:

The current first-line regimen for LTBI is isoniazid daily for 9 months. Acceptable alternatives include isoniazid daily for 6 months, isoniazid twice weekly for 9 or 6 months, and rifampin daily for 4 months.

In a recent report from USA, Four

Rational classification of anti-tuberculosis drugs*

GROUP 1/First Line Drugs: H _ isoniazid; R _ rifampicin; E _ ethambutol; Z _ pyrazinamide;
GROUP 2/Injectables: S _ streptomycin; KM _ kanamycin; AM _ amikacin; CM _ capreomycin;
GROUP 3/Quinolones: CPX _ ciprofloxacin; OFX _ ofloxacin; LVX _ levofloxacin; MOX _ moxifloxacin; GTX _ gatifloxacin;
GROUP 4/Other second line drugs: ETH _ ethionamide; PTH _ prothionamide; CS _ cycloserine; PAS _ para-aminosalicylic acid;
GROUP 5/Reinforcement drugs (poor): AMX/CL _ amoxicillin _ clavulanic acid; CFZ _ clofazimine; CLM _ clarithromycin; Th _ thiacetazone

*AJRCCM 2003, ATS & CDC

months of rifampin were found to be more effective and less expensive than standard therapy with 9 months of isoniazid, and three months course of isoniazid plus rifapentine was likely to be a cost-effective alternative if this regimen proves effective. (Holland D, AJRCC M Vol 179. pp 1055-1060, 2009).

First-line regimens for culture-positive tuberculosis caused by drug-susceptible *Mycobacterium tuberculosis*

Continuation Phase		Initial Phase	
Interval and Doses	Drugs	Drugs	Interval and Doses
days/wk for 56 doses (8wk) or 7 (days/wk for 40 doses (8 wk 5 PZA EMB	INH RIF	days/wk for 126 doses (18 7 wk) or 5 days/wk for 90 doses (wk 18)	INH/RIF
(days/wk for 14 doses (2 wk 7 then twice weekly 12 doses (wk 6) OR (days/wk for 10 doses (2 wk 5 then twice weekly for 12 doses (wk 6)	INH RIF PZA EMB	INH/RIF\$ Twice weekly for 36 doses (wk 18) INH/RPT Once weekly for 18 doses (wk 18) INH/RIF Twice weekly for 36 doses (wk 18)	
Thrice weekly for 24 doses (wk 8) PZA EMB	INH RIF	INH/RPT\$ Once weekly for 18 doses (wk 18) INH/RIF Thrice weekly for 54 doses (wk 18)	

Directly Observed Therapy (DOT)

Treatment of TB not only aims to cure the individual patient, but it also serves to prevent the spread of this potentially lethal infectious disease to others. In response to the public health threat of TB, a unique management strategy has occurred with the shift in the responsibility for adequate treatment from the patient to the medical provider, emphasizing the importance of directly observed therapy (DOT). Reported cases of TB had been declining steadily until resurgence in 1985 largely due to infections in HIV-coinfected individuals. Challenges in controlling TB in this patient population and nonadherence to treatment leading to the emergence of drug resistance prompted the adoption of DOT as a national standard of practice.

Treatment of Tuberculosis

Streptomycin and Para-aminosalicylic acid (PAS) were first discovered in the 1940s. In 1949, the efficacy of the combination of these two drugs was demonstrated in one of the first randomized clinical trials in medical history (BMJ 1949; 2:1521-5). The introduction of Isoniazid (INH) was in 1952, Ethambutol (EMB) in 1967 and Rifampin (RIF) in 1970. Later, in 1986, Pyrazinamide (PZA) was added to INH and RIF, resulting in an effective 6-month regimen.

Patients with Smear-positive pulmonary TB are contagious and should be placed in a negative-pressure room. After 2 weeks of appropriate chemotherapy for drug-susceptible TB, patients are considered no longer infectious. Most spread of infection occurs among household contacts prior to treatment being started. Multidrug regimens given for several months prevent the emergence of drug resistance and effectively sterilize disease sites. (See herein «Rational classification of anti-tuberculosis drugs» and «Drug regimens» Table)

Special Situations

Pregnancy: Greater risk, INH, RIF, and EMB (9 months) and pyridoxine. PZA is of questionable safety. Breastfeeding should not be discouraged.

Extrapulmonary Tuberculosis:

Meningitis 9 - 12 months, osteomyelitis more, corticosteroids in meningitis & pericarditis.

Evaluation of Treatment Response:

AFB smear & culture at least monthly until two consecutive specimens are culture-negative; culture status at 2 months is of significance. A positive culture after 4 months indicates treatment failure.

Monitoring for Adverse Reactions:

Liver injury (INH, RIF, and PZA). Therapy does not have to be discontinued unless liver-associated enzymes are elevated greater than five times normal or greater than three times above normal if associated with symptoms. EMB: baseline and monthly evaluations of visual acuity and color vision. Baseline and monthly audiograms (STM).

Paradoxical Response: A temporary exacerbation of symptoms, signs, or radiographic manifestations of TB (paradoxical reaction) after beginning antituberculosis therapy. More common as immune reconstitution after antiretroviral therapy in HIV. (See also herein «Promising New Anti-Mycobacterium Tuberculosis Agents...» box)

There is widespread recognition that tuberculosis treatment is too long,

Promising New Anti-Mycobacterium Tuberculosis Agents in Discovery Research

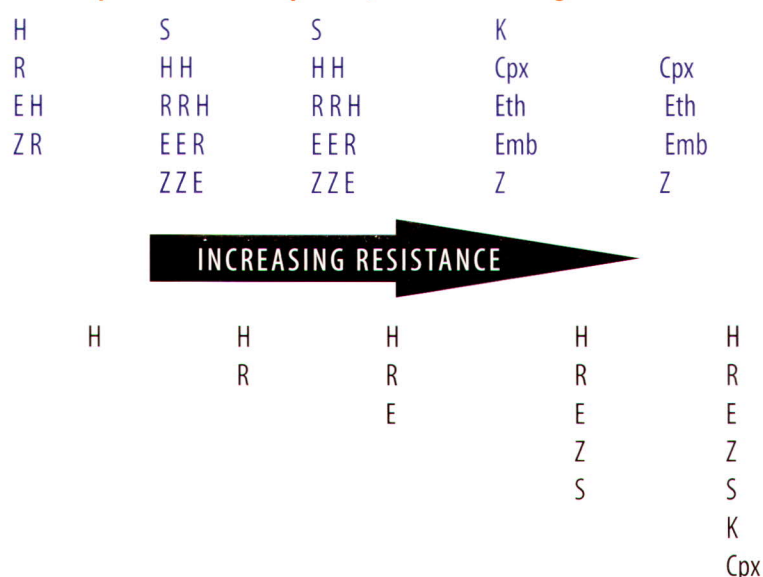
Nitroimidazoles: (Nitroimidazopyran (PA-824- and PA-1343) Nitroimidazooxazoles (OPC-((67683
(Diarylquinoline TMC207 (R207910-
Oxazolidinones: (Linezolid, DA-7157 and- (RBx8700
Ethylene diamine SQ-109-
(Pyrrole derivatives: (BM212 and LL3858-
Phenazines: Riminophenazines,-
Tetramethylpiperidine-substituted phenazines ((B4128, B4169
monosubstituted INH derivatives- '-2

currently 6 months for standard therapy, and reducing treatment duration is a global priority.

Drug-Resistant Tuberculosis

MDR-TB is defined as *M. tuberculosis* resistant to more than one anti-TB drugs (and at least Isoniazid (INH) and Rifampin (RIF)). Multidrug resistant tuberculosis is now thought to afflict between 1 and 2 million patients annually with an estimated 489,000 new cases of multidrug-resistant tuberculosis emerging each year (Publication N° WHO/ HTM/TB/2008.394). Resistance to single drug was reported to range from 2 to 41% (median 9.9%). Multiple drugs were 0 to 14.4% (prevalence 1.4%) in those who never received

Amplifier effect of repeated, standardized regimens



Example of how selective pressure of repeated standardized regimens (represented by white letters on dark background over arrow) can result in serial acquisition of resistance (represented by dark letters on light background under arrow), ultimately XDR-TB.

prior treatment. Single-drug resistance varied from 2.3 to 42.4% and Multi-drug resistance ranged between 0 and 22.1% among those who had prior treatment for tuberculosis. An estimated 489,139 or nearly 5% of all new cases of tuberculosis (TB) diagnosed in 2006 were multidrug resistant (MDR) that is resistant to Isoniazid and Rifampicin, the two most effective anti-TB agents. This represents an increase of 12% since 2004 and 56% since 2000 (see the drawing «Increasing Resistance» herein).

Suggested drug regimen for multiresistant-tuberculosis:

There is a broad spectrum of programmatic approaches to MDR-TB management, with variability in the following elements:

- (1) When to screen and treat
- (2) Whether to use empirical therapy prior to laboratory confirmation of MDR-TB
- (3) How much to individualize the regimen
- (4) How to monitor treatment response

And

- (5) Where to deliver care

Drug susceptibility testing (DST)

The most essential and controversial issues regarding the management of MDR-TB patients are:

- 1) Confirmation of diagnosis in a suspected MDR-TB patient, and determination of the value of drug susceptibility testing
- 2) The number of anti-tuberculosis drugs required to treat MDR-TB
- 3) The most rational use of effective drugs against tuberculosis
- 4) The advisable length of parenteral drug administration or of the initial phase of treatment
- 5) The contribution of surgery to the management of MDR-TB patients

And

- 6) The optimal regimen for treating MDR-TB: standardized vs. individualized regimens

The 1996 and 2003, WHO guidelines recommend at least three new drugs, similar to the recommendations of the ATS in 1993 and the BTS in 1990. This term was nevertheless changed to 'at least four drugs' in the most recent

WHO guidelines for the treatment of MDR-TB patients in 2006.

At least four medications should be selected to design a regimen, starting from Group 1 (first-line drugs for oral administration) and moving on to the next group when no adequate drug is left in the previous groups. It should be noted that in Groups 2 (injectable agents) and 3 (fluoroquinolones), only one drug should be selected from each group due to documented total or partial cross-resistance within groups.

Group 5 is composed of drugs for which anti-tuberculosis action has not been documented in clinical trials (except for thiacetazone). Their high or low efficacy has been reported only in vitro experiments or animal models. These drugs (including thiacetazone) have been designated as reserve drugs due to their low activity and high toxicity; particularly in human immunodeficiency virus (HIV) infected patients.

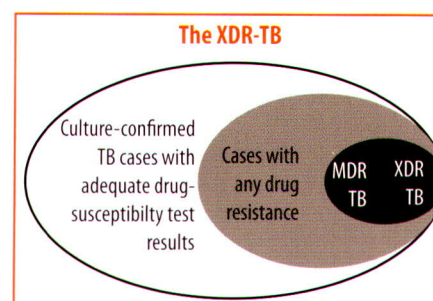
A drug that has been used to treat a patient in a failing regimen should not be included in the total four drugs in the retreatment regimen, despite an encouraging DST result. If the DST results show susceptibility to this drug, it should be added to the regimen in addition to the other four drugs.

Contribution of Surgery to the Treatment of MDR-TB Patients

For Tuberculosis, surgery is considered in the following categories:

- (1) Multidrug-resistant tuberculosis (MDR-TB)
- (2) Emergencies, almost exclusively for hemoptysis
- (3) Burnt out disease/bronchiectasis/destroyed lung
- (4) Diagnostic dilemmas where malignancy cannot be excluded

It is well known that after the discovery of effective drugs to fight TB, surgery was progressively abandoned until the 1970s, when it practically disappeared from case management. The question emerged again in patients with MDR-TB and resistance to multiple other drugs, when practically no available chemotherapy regimen ensured cure. Under these circumstances, many



patients today confront a situation very similar to that of patients in the prechemotherapy era.

Surgery for **MDR-TB** is recommended only in patients who meet the following conditions:

- 1) A fairly localized lesion
- 2) Adequate pulmonary function
- 3) A lack of sufficient available drugs (two or three with very weak action) to design a regimen potent enough to ensure cure
- 4) Persistent sputum positivity despite appropriate medical therapy; it is believed that the fibrous tissue surrounding the cavities harbors the resistant organism
- 5) High profile drug resistance to at least four drugs
- 6) Multiple previous relapses

The strongest advocates of surgical treatment recommend scheduling surgery at the time of the lowest possible bacillary load, preferably when sputum smears and culture have become negative, and suggest continuing chemotherapy after the procedure until completion of a predetermined pharmacological regimen of 18–24 months.

Extensively drug-resistant tuberculosis (**See the XDR-TB drawing**) is defined as laboratory-confirmed resistance to all of the following, at minimum: isoniazid, rifampin, any fluoroquinolone, and any second-line injectable agent. (Revision October 06 World Health Organization Emergency Global Task Force on XDR TB).

Extensively drug-resistant tuberculosis has been reported in 49 countries including the United States since it was first described in 2006, where, in KwaZulu-Natal Province, South Africa, 53 of 544 patients were defined as XDR-TB and 52 of the 53 patients died on average within 25 days, including

those on ARV therapy (Gandhi NR, et al. *Lancet* 2006; 368:1575-80).

Success in treating XDR-TB requires, aggressive protracted regimens with many drugs, at the highest tolerated doses, lasting more than 2 years in most patients. The results of drug-susceptibility testing should be used to design (and adjust) regimens containing at least five drugs that are likely to be effective whenever possible. Regimens rely heavily on Capreomycin, PAS, Cycloserine, Streptomycin, Moxifloxacin and Levofloxacin (even in patients with isolates that were resistant to ciprofloxacin), Pyrazinamide and Ethambutol (despite extensive prior exposure to these drugs), and with Amoxicillin-clavulanate, Clarithromycin, Clofazimine, and Rifabutin. Resective surgery is indicated for patients with high-grade resistance, relatively localized disease, and lack of initial response; even in patients with restricted lung volume. Medical treatment is prolonged among patients receiving surgery. Corticosteroid use might be used. Frequent contact with health care workers usually affords many benefits and finally bacteriologic assessment is integral to the above strategy. In brief Treatment for XDR TB is difficult, usually requiring at least 18–24 months of four to six second-line anti-TB drugs. Treatment success rates are generally 30–50%, with very poor outcomes in HIV-infected patients. Management of contacts to infectious XDR TB patients is complicated by the lack of a proven effective treatment for XDR latent tuberculosis infection. Recently emergence of Extensive Drug Resistance during treatment for Multidrug-Resistant Tuberculosis has been reported (*NEJM* 359:22, November 27, 2008).

Treatment continues to be limited in tuberculosis-endemic countries largely because of weaknesses in national tuberculosis health-care models. The ultimate strategy to control drug-resistant tuberculosis is one that implements a comprehensive approach incorporating innovation from the political, social, economic, and scientific realms. (*Lancet Infect Dis* 2009; 9: 19–30)

Despite the clear recommendations

made by the Global Plan to Stop TB 2006–2015, drug-resistant tuberculosis treatment and control efforts have been sadly insufficient. In 2008 alone, the overall funding gap of US\$500 million despite a total need of \$1 billion reflects the low priority given by donors and governments to combat MDR-TB. Improved laboratory capacity, rapid diagnosis, effective care, and access to medicines are urgently needed. Without immediate political commitment and mobilization of resources, transmission will continue and the proportion of MDRTB will increase.

Vaccines against Tuberculosis

Mycobacterium bovis bacillus Calmette-Guerin [BCG], is one of the most extensively utilized vaccines in the world. This live-attenuated BCG vaccine is used routinely in developing countries where high TB prevalence and incidence exist, and is usually given only once by the intradermal route during the neonatal period. BCG is inexpensive, safe and effective against severe forms of childhood TB but its efficacy appears to be limited against adult pulmonary disease in endemic areas. Thus, a more effective vaccine is needed.

New Vaccines against Tuberculosis

Three approaches have been used to produce new vaccines:

- 1- Nonliving vaccines, which include purified antigens (subunit vaccines) and DNA vaccines
- 2- Live mycobacterial vaccines, which include rationally attenuated strains of *M. tuberculosis* produced by targeted deletion of virulence genes or BCG strains that have been genetically manipulated to express immunodominant antigens (recombinant BCG)
- And
- 3- The use of viral vectors, such as adenovirus or vaccinia virus

During the next 5 years, one or more of the TB vaccines currently undergoing Phase I/II testing may be ready for Phase III testing in a high-burden country. The obvious potential advantages of pulmonary vaccination for TB have not been adequately investigated. Another currently underemphasized aspect of TB vaccine research that deserves

attention in the next 5 years is the development and testing of vaccines that are designed to be applied as an adjunct to chemotherapy to eliminate persisting tubercle bacilli and reduce the risk of treatment failure (particularly in drug-resistant TB), and vaccines that might be given to healthy individuals with long-standing latent infection to eliminate residual bacilli and reduce the risk of TB reactivation.

Conclusion

Although clinical trials have demonstrated cure in more than 95% of patients receiving regimens comprising isoniazid, rifampin, pyrazinamide and ethambutol, most countries struggled to cure 80%. In addition many HIV-infected patients were not adequately treated with a 6-month regimen, and treatment was extended to 9 months for such patients. In resource-poor nations 9-month regimens significantly tax an already overburdened healthcare system.

Finally the emergence of MDR- and XDR-TB – which are not effectively treated by the standard TB regimen – has made the search of new TB drugs imperative. A strong commitment to the use of current or existing drugs is recommended up till incorporating TB drugs in development. In particular optimizing the dose of Rifampin (or its derivative Rifapentine) is promising over the course of 6 months. It is to be considered that high dose Rifampin (or Rifapentine) may permit shorter courses. “Old” TB drugs might be reformulated. Capreomycin and Ethionamide might be in inhaled route and if successful will make the intake of these medications more desirable and less toxic. Available Quinolones as Moxifloxacin, Levofloxacin, and Gatifloxacin can potentially improve treatment of drug-susceptible and drug-resistant TB. They may permit more chance of cure and shorter course of therapy. Linezolid might have a chance in DR-TB, in spite of its well known toxicities.

Finally a host of new drugs are being discovered especially for DR-TB. If successful these will increase the chance of cure and shorten the duration of treatment.

"H1N1: "A bit early to make a judgment

European scientists and health authorities are facing angry questions about why H1N1 flu has not caused death on the scale first feared. Has pandemic been "hyped" by medical researchers and authorities to further their own cause, and to the benefits of pharmaceutical companies? ¹



Dr. Zouheir Alameh

To gather information about the clinical features and management of pandemic influenza, WHO hosted a meeting at the headquarters of the Pan American Health Organization in Washington, DC on 14–16 October.² The meeting focused on the clinical course and management of small subsets of patients who rapidly develop very severe progressive pneumonia, or marked worsening of underlying asthma or chronic obstructive airway disease. Primary viral pneumonia is the most common finding in severe cases and a frequent cause of death. Secondary bacterial infections have been found in approximately 30% of fatal cases. Bacteria frequently reported include *Streptococcus pneumoniae* and *Staphylococcus aureus*, including methicillin-resistant strains in some cases. Respiratory failure and refractory shock have been the most common causes of death. Participants who have managed such cases agreed that the clinical picture in severe cases is strikingly different from the disease pattern seen during epidemics of seasonal influenza

In severe cases, patients generally begin to deteriorate around 3 to 5 days after symptom onset. Deterioration is rapid, with many patients progressing to respiratory failure within 24 hours, requiring immediate admission to an ICU, most of them need immediate respiratory support with MV. However, some patients do not respond well to conventional ventilator support, further complicating the treatment

Risk factors for severe disease³ from pandemic (H1N1) 2009 virus infection reported to date are considered similar to those risk factors identified for complications from seasonal influenza. These include the following groups

- Infants and young children, in particular <2 years
- Pregnant women
- Persons of any age with chronic pulmonary disease (e.g. asthma*, COPD

- Persons of any age with chronic cardiac disease (e.g. congestive cardiac failure)
- Persons with metabolic disorders (e.g. diabetes, morbid obesity)
- Persons with chronic renal disease, chronic hepatic disease, certain neurological conditions (including neuromuscular, neurocognitive, and seizure disorders), hemoglobinopathies, or immunosuppression, whether due to primary immunosuppressive conditions, such as HIV infection, or secondary conditions, such as immunosuppressive medication or malignancy
- Children receiving chronic aspirin therapy
- Persons aged 65 years and older.⁴

According to a retrospective analysis of 6945 confirmed cases of H1N1 in Mexico (April 28 to July 31, 2009), the greatest mortality risk was in those aged 70 years and older (10.3%). Mortality rates for 1- to 9- year- olds was 0.3%; and 1.6% for infants younger than 1 year. Infection was transmitted mostly among young people (56%), with those aged 10 to 39 years being the most affected.⁵

The mortality rate during Australia's winter with the 2009 Pandemic influenza A (H1N1) Virus was lower-than-expected number of deaths in previous seasons. The median age of the patients who died was 53 years, as compared with 83 years. The natural history of this illness, tends to be moderate in most people rather than severe.⁶

Pregnant Women (H1N1-2009): The most significant respiratory infection that affects pregnant women with the risk of severe illness and death is influenza. The rate of seasonal influenza infection during the second and third trimester is reported to range from 2% to 22%.⁷ Epidemiological studies document increased rates of influenza in pregnant women compared with healthy non-pregnant women.^{8,9} Influenza-associated excess deaths among pregnant women were documented during the pandemic

"Spanish Flu" of 1918–1919 and the pandemic "Asian Flu" of 1957–1958,^{10, 11} with increased rates of spontaneous abortion and preterm birth reported, especially among women with pneumonia. Between April 15 and June 16, 2009, six deaths in pregnant women were reported to the CDC.¹² Pregnant women with novel influenza A (H1N1) virus infection would be expected to present with typical acute respiratory influenza-like illness, many of them will go on to have a typical course of uncomplicated influenza. However, for some pregnant women, illness might progress rapidly, and might be complicated by secondary bacterial infections including pneumonia. Fetal distress associated with severe maternal illness can occur. Ideally, pregnant women who have suspected novel influenza A (H1N1) virus infection should be tested for influenza, and treatment should not be delayed.^{12, 13}

Finally, everyone is raising the question: is Influenza (H1N1) - 2009 is a "mild" Pandemic or "severe" causing death and destruction on the scale first feared, "I think it a bit early to make that judgment

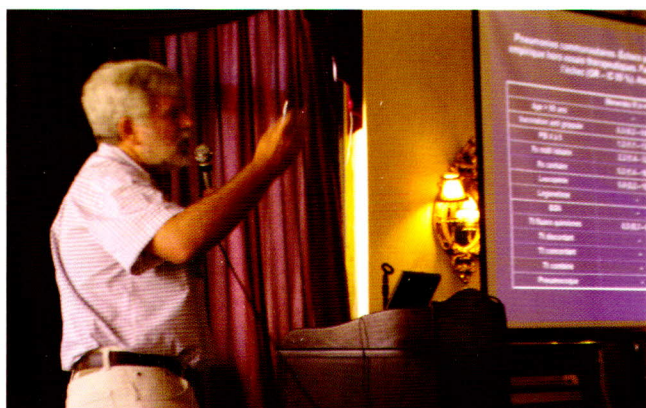
Groups at greatest risk from pandemic -*
(H1N1) 2009
LONDON (Reuters Health Information) 1-
.Nov 13, 2009
.WHO Report- OCTOBER 16, 2009 2-
WHO Report-Clinical management of 3-
human infection with pandemic (H1N1)
.2009
.N Engl J Med 2009;361:1935-44 4-
The Lancet. Published online November 5-
.12, 2009
N Engl J Med Published online, November 6-
.25, 2009
Griffiths PD, et al. J Epidemiol Community 7-
.Health 1980;34:124-8
Mullooly JP, et al. Public Health Rep 8-
.1986;101:205-11
Neuzil KM, et al. Am J Epidemiol 9-
.1998;148:1094-102
.Harris JW. JAMA 1919;72:978-80 10-
Freeman DW, et al. Am J Obstet Gynecol 11-
.1959;78:1172-5
Denise J Jamieson, et al. The Lancet, 12-
.Volume 374, 9688: 451 – 458
.CDC June 30, 2009 13-

Tyr: un week-end studieux sur fond azur méditerranéen

La réunion scientifique régionale qui s'est tenue à Tyr les 4 et 5 juillet 2009 a permis de discuter les questions de l'examen de janvier 2009 du programme de Formation Médicale Continue (Mireille Sfeir, Mirna Waked et Joseph Yammine); de présenter des mises au point sur l'asthme, la BPCO, la maladie thromboembolique et les pneumonies communautaires par des experts étrangers (Nicolas Roche, Olivier Sanchez et Patrick Petitpretz); et de discuter du rôle du Symbicort dans la BPCO (Nadim Kanj).



Nicolas Roche: COPD review



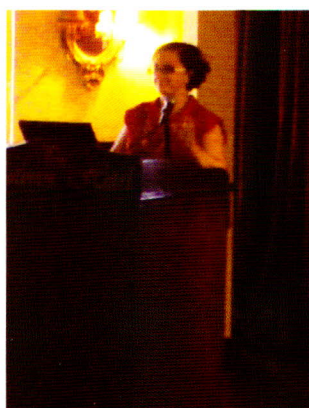
Patrick Petitpretz:
Community-acquired pneumonia

Tyre: a scholarly week-end on a navy blue Mediterranean background

During the regional scientific meeting that has been held at Tyre on the 4th and 5th of July, questions of the continuous medical education examination of January 2009 were discussed (Mireille Sfeir, Mirna Waked and Joseph Yammine); updates on asthma, COPD, thrombo-embolic disease and community-acquired pneumonia were presented by international experts (Nicolas Roche, Olivier Sanchez and Patrick Petitpretz), and the role of Symbicort in COPD was discussed (Nadim Kanj).



Olivier Sanchez: Thrombo-embolic disease



Mirna Waked:
Results of the COPD exam



Mireille Sfeir: Results of the Community-acquired pneumonia exam

European Respiratory Society (ERS) 19th Annual Congress



Dr. Mirna Waked

The scientific topics in the ERS were wide with variety, but hot topics remained focused on pulmonary hypertension (PH) and COPD. While the therapeutic protocols have been largely covered for PH and will be tackled in another issue of INSPIRE, you will find here a brief review- and not an exhaustive one- of the main interesting topics in the ERS.

September 12 - 16, 2009; Vienna, Austria

Hospitalized Patients with Community-Acquired Pneumonia Have Significantly Decreased Survival

Adult patients hospitalized with community-acquired pneumonia (CAP) have significantly shorter long-term survival than patients hospitalized for medical conditions other than CAP, according to data released at the ERS 19th Annual Congress. Importantly, the shorter survival remained significant after controlling for age and multiple co morbidities. The shorter survival was seen even after discharge with a clinical cure. "The results undermine the longstanding notion that CAP is an acute infection with a short-term impact on survival," study coauthor Paula Peyrani, MD, director of clinical research in the Division of Infectious Diseases at the University of Louisville, Kentucky, added.

Andrew Wilson, a respiratory medicine physician at Princess Margaret Hospital in Perth, Australia, told that the "study raises an interesting hypothesis and the striking association between CAP and subsequent mortality may mean that the patient has a poorly controlled underlying medical condition and/or that hospitalized pneumonias in the current age are inherently severe. He also said that future studies need to look more closely at co morbidities in hospitalized patients.

GPs Have Difficulty Distinguishing Between Asthma and COPD

Online questionnaires completed by 776 GPs aimed to determine whether GPs had difficulty differentiating between asthma and COPD.

Results of the new survey showed that 32% of GPs did not know how many patients in their practice had both

asthma and COPD. A total of 80% of GPs said that distinguishing asthma from COPD was "quite or very challenging." The data also revealed that 88% of GPs rented or owned spirometers, but that 10% of GP practices did not have staff that was trained to conduct spirometry testing and 14% of GP practices lacked staff that was trained in interpreting spirometry test results.

"I think the problem is that the diagnosis of asthma versus COPD requires more than spirometry. Spirometry is part of differentiating between asthma and COPD, but there's more to it than that," said Neil Barnes, MBBS, FRCP, professor of respiratory medicine at the London Chest Hospital in the United Kingdom. "And practitioners often don't do the things they need to do in order to distinguish between the 2 diseases", he added. The problem is compounded by the fact that the 2 diseases often do coexist, Dr. Barnes pointed out.

"So, for example, they have patients whose major problem is COPD, and they misdiagnose them with asthma," he said. "And the danger there is that you over treat them, particularly with oral steroids. And then you have the opposite problem. You'll have a young person who may be does spirometry that shows impairment and the patient gets falsely diagnosed as having COPD when, in fact, he has under treated asthma. So in secondary care, we do spend a lot of time undiagnosing incorrect diagnoses."

COPD Patients in Need of Integrated Care for Multiple Co morbidities

The recommendation was made at the European Respiratory Society 19th Annual Congress after research showed that co morbid disease - specifically,

cardiovascular disease, cerebrovascular disease, and diabetes - is extremely common in COPD patients. The associations are especially pronounced in younger patients.

The analysis showed that COPD is more common in women, smokers, older age groups, and those from lower socioeconomic classes. Overall, 40% of COPD patients had been diagnosed with at least 1 of the following: cardiovascular disease, cerebrovascular disease, or diabetes. Dr. Feary the researcher explained that it was not possible to stratify risk by disease severity because spirometry records were not available for more than a third of COPD patients.

"The fact that the investigators found a large number of COPD patients with multiple comorbidities is not surprising, given that they are often elderly and smokers. The message that you need to look at them holistically is entirely reasonable," noted Neil Barnes.

"The other thing is, of course, that across the western world, medicine has become more and more specialized, and what this really indicates is that you still have to have a body of general medical knowledge to be able to treat all the other diseases that these patients have. You don't necessarily want your patients going to 5 different doctors for 5 different conditions."

Regular Exercise Helps COPD Patients Maintain Early Benefits of Pulmonary Rehabilitation

Patients with moderate chronic obstructive pulmonary disease (COPD) can maintain the improvements they obtain from an 8-week pulmonary-rehabilitation program for at least 1 year, provided that they continue to

exercise regularly. The data, reported by an Australian group, show that benefits are similar whether patients participate in a program that combines weekly supervised outpatient-based exercise plus supervised home exercise or a program that involves standard-of-care unsupervised home exercise.

Supervised exercise provides multiple benefits, including regular patient support and encouragement, the ability to detect COPD flare-ups, and the opportunity to help patients make improvements in their exercise training.

"Fortunately, we are increasingly acknowledging the importance of exercise in respiratory diseases; the importance of exercise in cardiovascular disease has already been firmly established," Leonardo Fabbri, MD, professor of respiratory medicine at the University of Modena in Italy commented. In fact, in cardiovascular disease, exercise is probably the most effective treatment for preventing disease exacerbation and increasing life expectancy. He added that it is important that physicians recognize that the benefits of a short-term pulmonary-rehabilitation program will diminish in the absence of ongoing exercise."

Opioids Underused in Advanced COPD

Opioids are underprescribed in patients with chronic obstructive pulmonary disease (COPD) and refractory dyspnea who are nearing death, despite increasing evidence that supports the use of opioids in this population, investigators reported at the European Respiratory Society (ERS) 19th Annual Congress.

"50% of patients with advanced COPD and dyspnea are refractory to conventional treatment involving bronchodilators, steroids, and oxygen, although it is still needed to establish the prevalence and correlates of refractory dyspnea in this population. Given the known efficacy of opioids in these patients, we believe there is a potential role for carefully initiated and titrated opioids." Dr. Goodridge the researcher noted. Her colleague, Graeme Rocker, MD, recently proposed the use of a "dyspnea ladder" for the

management of breathlessness. Similar to the World Health Organization pain ladder, the first step incorporates conventional approaches to dyspnea management, with supplementation by non pharmacological approaches in step 2. These approaches include pulmonary rehabilitation, cognitive behavioral therapy, and self-management. Opioids, she added, may be helpful at step 3, when dyspnea persists at a high level despite optimal conventional therapies. A low-dose (perhaps 0.5 mg of oral morphine twice a day), measured approach to initiating opioids is important in this population, and opioid titration can occur weekly, depending on the patient's response.

However, it is often incorrectly assumed that opioid use will precipitate respiratory depression, and careful titration will prevent this complication. Both the American Academy of Pain Medicine and the American Pain Society have stated that denying patients appropriate opioids on the basis of respiratory concerns is unwarranted.

Smoking Cessation Therapy throughout Hospitalization Yields High Long-Term Cessation Rates

Australian researchers are reporting favorable results with a hospital-based program for smoking cessation. The data, presented at the European Respiratory Society (ERS) 19th Annual Congress, are from the first study of its kind to examine post discharge smoking cessation rates after the use of 2 formulations of nicotine-replacement therapy (NRT) prescribed on hospital admission for craving control.

"Hospitalization potentially provides a 'teachable moment,' but hospitals do not view smoking cessation as their responsibility," said the researchers. Hospitals are an attractive setting for starting cessation, given that they see a high number of tobacco-related admissions and given that smokers are forced to abstain during admission."

The researchers evaluated continuous abstinence post-discharge after the use of NRT during admission. Continuous abstinence was recorded at 1, 3, 6, and 12 months.

There were no statistically significant

differences between abstinence rates for the patch or the inhaler at any time point, nor was there a difference between those who used NRT and those who did not, except at the 1- and 3-month time points, at which those who did not use NRT were more likely to have resumed smoking.

The analysis revealed overall higher rates of continuous abstinence in subjects using NRT than in those who did not. Overall, 14 (38%) of 37 patients on the inhaler, 19 (38%) of 50 patients on the patch, and 9 (25%) of 36 patients on no NRT had continuous abstinence at 12 months.

"While there are no statistically significant differences between the 3 groups at any of the time points, the study was limited by a small sample size" the researchers observed. Notably, even though the study participants were highly addicted smokers, the results are at least as good as other cessation studies using NRT in a variety of community settings, they added.

Finally, the study emphasizes that every possible opportunity should be taken to discuss smoking cessation with smokers and to initiate treatment. A 30% quit rate at 1 year is not unusual, but might have been improved with ongoing community support.

Evolving Dimensions of COPD: ERS & the Lancet Symposium

Chaired by Pr PJ Barns and Pr LM Fabbri, this symposium was devoted to discuss some of the key recent developments in COPD research that are relevant to clinicians.

The importance of screening for and early detection of COPD was tackled by J Soriano emphasizing on the role of spirometry as a simple non invasive test to diagnose COPD and its severity. The more the diagnosis is early the more the patient can benefit from smoking cessation and this will lead to reduction of the social burden of the disease.

Pr Salvi talked about the emergence of non-smoking COPD and reviewed the evidence of the association of COPD with biomass fuel, occupational exposure to dusts and gases, history of tuberculosis, chronic asthma, and respiratory tract

infections in childhood, outdoor pollution and poor socioeconomic status, in those 25-45% COPD patients who have never smoked.

Pr Celli insisted on the need for management of COPD patient with holistic approach of the co-morbidities.

And finally Pr Hansel approached the new drugs for exacerbations of COPD such as improvement of existing drug classes such as long acting bronchodilators, or antioxidants, and anti-inflammatory treatments classified in different classes: 1-Statins, 2-phosphodiesterase-4 inhibitors, cytokine-directed therapy and chemokine-receptor antagonists. With extensive collaboration between scientists, clinicians and pharmaceutical industry and drug regulators it is likely that novel treatments for exacerbations of COPD can be defined.

ABOUT THE ERS AND THE IMPORTANCE TO BE MEMBERS

As the National Delegate for Lebanon in the ERS (www.ersnet.org), I want to emphasize on the growing importance that this society is having. Year after year; the ERS annual meeting is hosting more and more attendees. It is fostering scientific excellence and releasing important guidelines on major topics in respiratory medicine.

Being a full member gives access to all publications such as ERJ, the Monograph, and the Breath (www.breathe@ers.org.uk) journal which are highly appreciated for their content and their dedication for CME policy.

Being a member also gives you access to an important bulk of information, to slides about every topic in pulmonology, to a networking with famous specialists worldwide and offers also many possibilities of fellowship and researches in

European countries.

Last but not least the HERMES examination is getting a huge importance in standardization of knowledge by getting a European Board in Respiratory Medicine.

The HERMES Curriculum will be used as a basis for CME activity in the LPS and this is a project which is being considered seriously by the CME committee of the LPS.

The next meeting will be in Barcelona in 2010 September 18-22 and the next HERMES examination will be held there on the 18 of September 2010. Be numerous to attend. Hoping that we will meet soon before this date, please feel free to contact me for any additional information.



**SAINT GEORGE HOSPITAL
UNIVERSITY MEDICAL CENTER**

EMERGENCY MEDICINE TRAINING CENTER



Umedic

Saint George Hospital University Medical Center is proud to announce its new training center for emergency medicine. The training center is run, supervised, and certified by leading German authorities in the field of emergency training, and provides the highest standard of training for in-hospital staff.

The courses offered are given by fully certified instructors, and correspond with the most up-to-date protocols and recommendations. Advanced patient simulators are utilized in order to provide as much realism and hands-on training as possible, and ensures that the skills taught are integrated into the practical world.

The courses include Basic Life Support (BLS), Advanced Life Support (ALS), Basic Pediatric Life Support (BPLS), Advanced Pediatric Life Support (APLS) and Advanced Trauma Course (ATC).

Le Congrès de l'utile et de l'agréable

Le congrès 2009 de la Société Libanaise de Pneumologie (SLP) avait une saveur particulière pour plusieurs raisons. D'abord, il a regroupé des pneumologues et amis libanais, libano-français, et français grâce au concours de l'Association Franco-Libanaise de Pneumologie (AFLP) et de l'Union Méditerranéenne de Pathologie Thoracique (UMPT) et sous le regard bienveillant du Professeur Etienne Lemarié, président de la Société de Pneumologie de Langue Française (SPLF). Ensuite, sa cérémonie d'ouverture nous a permis d'apprécier la prestation émouvante de la chorale Al-Fayha. Enfin, des ateliers de pneumologie interventionnelle dirigés par des experts de stature internationale, Atul Mehta et Praveen Mathur, ont permis à certains d'entre nous de se familiariser avec des techniques de pointe

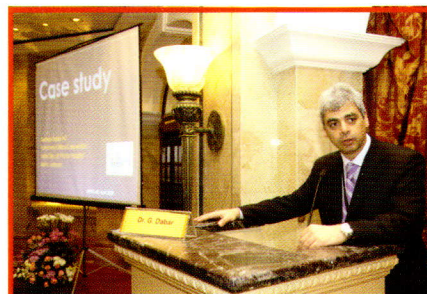
Le programme était varié puisqu'il comprenait outre les sessions «classiques» d'apnée du sommeil, d'hypertension artérielle pulmonaire et de réanimation, des sessions de sujets plus rarement discutés durant nos réunions scientifiques : génétique, prévention et physiologie. Enfin, des symposiums traitant de

maladies beaucoup plus prévalentes telles que: Asthme, BPCO, Maladie Thromboembolique et Pneumonie Communautaires, ont permis d'élargir les horizons scientifiques de cette manifestation

La cérémonie d'ouverture s'est tenue le vendredi 17 avril au soir en présence du ministre de la Santé Mohammad Khalifé qui a intervenu après le président de la Société Libanaise de Pneumologie, Wajdi Abisaleh, le président de l'Association Franco-Libanaise de Pathologie Thoracique, Youssef el-Zein, le Président de l'Union Méditerranéenne de Pathologie Thoracique, Jean-Pierre Grignet, le président de l'Ordre des Médecins de Beyrouth, Georges Aftimos et le Président de la Société de Pneumologie de Langue Française, Etienne Lemarié. Elle s'est terminée par une prestation exceptionnelle de la chorale al-Fayha

Le dîner de gala a permis à nos hôtes étrangers d'apprécier un spectacle folklorique libanais. Il a été clôturé par la dégustation d'un gâteau aux couleurs de l'UMPT, de l'AFLP et de la .SLP

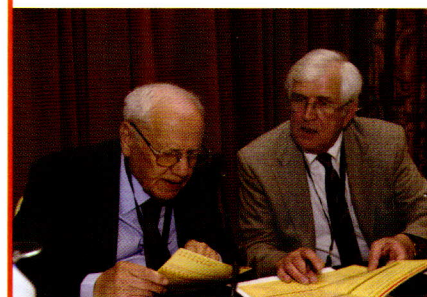
Dr. Georges Khayat



Dr. Georges Dabar: résultats de AVAIL-ME, audit de la prise en charge de la maladie thromboembolique au Liban



Drs. Darius Olivieri, Ahmad Jibbaoui et Georges Saadé: remodelage pulmonaire dans l'asthme et la BPCO, la toxicité pulmonaire des médicaments et les moyens de vaincre le tabagisme



Moderateurs: Drs. Rafic Hubeiter et Yves Rogeaux



.Quelques vues du congrès



Le gâteau découpé par Drs. Wajdi Abisaleh, Youssef el-Zein, Jean-Pierre Grignet et Etienne Lemarié



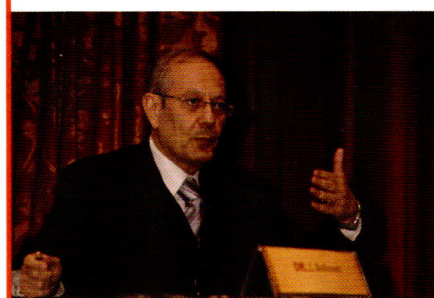
Dr. Georges Aftimos, président de l'ordre des médecins, prononçant son allocution



La Chorale al-Fayha



Une vue du gâteau



Drs. Joudy Bahous et Pierre Bou Khalil : mise au point sur l'asthme et sa prise en charge



Le modérateur est : Dr. Ahmad Hosari



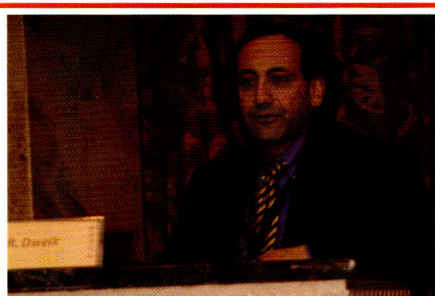
Drs. André Megarbane et Pierre Zalloua: problème génétique dans les maladies respiratoires



Modératrice: Dr. Marie-Louise Coussa Koniski



Drs. Salah Zeineddine, Raed Dweik et Joudy Bahous: physiologie respiratoire

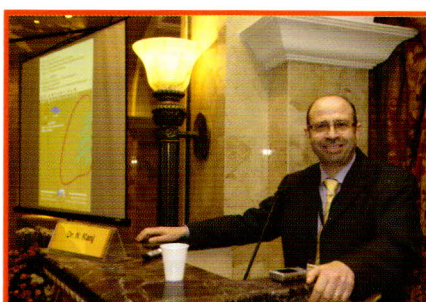
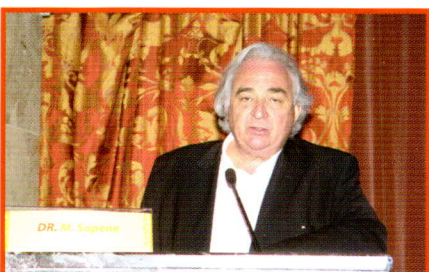


Modérateurs: Drs Toufik Kikano et Ali ben Khader

Drs. Laurent Brochard et Mme E. Shouman: problèmes de réanimation



Modérateurs: Drs. Moussa Riachi et Patrick Morin



Dr. Nadim Kanj: antibiothérapie chez les malades atteints de pneumonie communautaire

Drs. Elie Chammas, Raed Dweik et Imad Bou Akl: prise en charge diagnostique et thérapeutique de l'hypertension artérielle pulmonaire



Modérateur: Dr. Georges Khayat

Modérateurs: Drs. Georges Juvelikian et Richard Timery



Drs. Marc Sapene, Jean-Louis Racineux et Patrick Arcache: différents aspects des troubles respiratoires durant le sommeil



Dr. Peter Calverley: nouvelles données et possibilités pour l'amélioration des soins du malade atteint de BPCO

Modérateur: Dr. Wajdi Abisaleh



Modérateurs: Drs. Youssef el Zein et Pierre Eddé

UPLIFT® ...

RESULTS FROM UPLIFT®* —A LANDMARK TRIAL

A 4-year trial of tiotropium in chronic obstructive pulmonary disease

*Understanding Potential Long-term Impacts on Function with Tiotropium

UPLIFT® demonstrated significant treatment benefits with tiotropium for up to 4 years vs control

- ▶ Sustained improvements in lung function
- ▶ Sustained improvements in quality of life
- ▶ Reduced risk of exacerbations and exacerbations leading to hospitalisation
- ▶ Reduced respiratory morbidity (including a decreased risk of respiratory failure) and reduced cardiac morbidity

 **SPIRIVA®**
(tiotropium)
Life. To be continued.

Prescribing Information

Indications SPIRIVA is indicated for the maintenance treatment of patients with COPD (including chronic bronchitis and emphysema), the maintenance treatment of associated dyspnoea and for prevention of exacerbations. **Contraindications** SPIRIVA inhalation powder is contraindicated in patients with hypersensitivity to tiotropium bromide, atropine or its derivatives, e.g. ipratropium or oxitropium or to the excipient lactose monohydrate. **Special Warnings and Precautions** SPIRIVA, as a once daily maintenance bronchodilator, should not be used for the initial treatment of acute episodes of bronchospasm. Immediate hypersensitivity reactions may occur after administration of SPIRIVA inhalation powder. As with other anticholinergic drugs, tiotropium bromide should be used with caution in patients with narrow-angle glaucoma, prostatic hyperplasia or bladder-neck obstruction. Inhaled medicines may cause inhalation-induced bronchospasm. **Dosage and administration** the recommended dosage of SPIRIVA is inhalation of the contents of one capsule once daily with the Handi-

Haler device at the same time of day (for complete instructions see Instructions for use, Cleaning the HandiHaler and Blister Handling). SPIRIVA should only be inhaled with the HandiHaler device. The recommended dose should not be exceeded. **SPIRIVA capsules must not be swallowed. For full prescribing information, please read the package insert.**

*Tashkin DP, Celli B, Senn S, Burkhart D, Kesten S, Menjoge S, and Decramer M, on behalf of the UPLIFT™ (Understanding Potential Long-term Impacts on Function with Tiotropium) study investigators. A 4-year trial of tiotropium in chronic obstructive pulmonary disease. *N Engl J Med*. October 9, 2008 Vol. 359, page 1543-1554. No. 15