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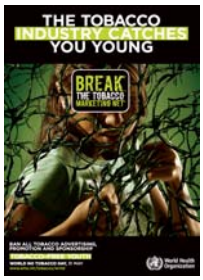
WHO aims to "eradicate" tobacco advertising

WHO proposed to ban all tobacco advertising in the frame of the World No Tobacco Day, on May 31st. WHO claims that the industry uses all communication media available to attract young children, their more vulnerable and principal target. A study conducted by WHO found that over 55% of students between 13 and 15 years old worldwide reported seeing cigarette advertising on billboard, and over 20% owned an item with a logo of a tobacco company. The World Health Statistics 2008 warns that tobacco use is a risk factor for 6 of the 8 leading causes of death.



A ban on advertising, promotion and sponsorship related to items and events is one of the five control strategies recommended by WHO. Though these have proven to be cost-effective, about half of all countries have implemented none of these initiatives.

Sources:
http://www.who.int/tobacco/wntd/2008/en/index.html
http://www.who.int/whosis/whostat/2008/en/index.html

Attempts to enhance the over to counter sales with prescription drugs

FDA rejected for the third time an application of Merck requesting the switch from prescription only to over the counter (OTC) sale of lovastatin. Merck pledges that this change would contribute to reduce the percentage of people with dyslipidemia who have an intermediate cardiovascular risk and are not receiving treatment.

FDA requires pharmaceutical companies to demonstrate proper patient management and label comprehension of a medicine to change its sales condition. The FDA´s commission based its decision on three studies of use and label comprehension of lovastatin that present worrisome features. One study tried to determine if the patients were able to take proper decisions based on the proposed label: Less than half the patients who selected over the counter lovastatin were in the target group, 20% would not benefit from treatment (risk lower than 10%) and 24% required more intensive treatment and monitoring. When asked if lovastatin was right for them, 75% of the patients were wrong (not in the target group or presence of a contraindication). We must highlight that the patients included in these studies present some advantages over the general population (highly selected individuals aware of being studied).

The FDA´s commission that rejected the application cited as some of the reasons the lack of evidence on safety and efficiency (though the company is not obligated to demonstrate efficiency or safety for changing the sales condition) and the inability of the target population to make appropriate decisions.

The laboratory can continue to present this request with minor changes. If this is approved, it would open a door for other companies to push forward the switch of other medicines for chronic diseases, such as hypertension and diabetes. Potential hazards from this possible future are numerous, as a drop in physician consultation and follow-up, indiscriminate use of potentially dangerous medication, higher medicines expenditure per patient, and unknown toxicity in a wide spread use setting of this medication without a professional supervision.

Sources:
New England Journal of Medicines, 358;25, june 19, 2008
http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4331b1-02-Merck.pdf

Contribution of Brazil against Malaria

The society conformed by the public laboratory Farmanguinhos/Fiocruz and the Medicines Initiative for Neglected Diseases (DNDi) resulted in the first medicine for a neglected disease developed and registered in Brazil: a fixed combination of artesunate and mefloquine. Besides the convenience of its administration and low cost, it is the first fixed combination of antimalarics that can be stored up to three years in a tropical climate.
The Laboratory plans to provide endemic countries with this medicine at the production cost, about U$D 2.5 for a complete adult treatment. Also, Fiocruz signed a technological transfer agreement with a generic manufacturer in India, which will act as a regional supplier for south-east Asia.

Source:
www.fiocruz.br

Failure of two combination medicines against Malaria

The development of a fixed dose combination of chlorproguanil, dapsone and artesunate (CDA) was suspended in view of the results of a Phase III clinical trial involving over 1.300 patients. This medicine was the result of a partnership between GlaxoSmithKline (GSK) and Medicines for Malaria Venture. This study compared CDA vs. lumefantrine-artemether and found a serious increase in risk of developing anemia at day 7 in patients with G6PD deficiency. Also, a combination of Chlorproguanil-dapsone (CD) was recalled due to the potential widespread use in malaria endemic zones with a high prevalence of G6PD deficiency, especially sub-Saharan Africa, where the 10-25% of the population presents this deficiency.
In 2004, WHO published a safety review of CD, reaching the conclusion that this medicine should only be used in confirmed cases of malaria, in regions with proper genetic testing for G6PD and after ruling out anemia; not a common scenario in endemic regions.
G6PD deficiency makes erythrocytes extremely sensitive to oxidative damage by reducing their capacity to regenerate glutathione. At the seventh day of treatment with dapsone a fall of about 1 g/dl of hemoglobin occurs, this effect being more marked in G6PD deficient persons.

Sources:
Review of the safety of chlorproguanil–dapsone in the treatment of uncomplicated falciparum malaria in Africa; REPORT OF A TECHNICAL CONSULTATIONCONVENED BY WHO
WHO Pharmaceutical Newsletter; No 2, 2008

Report highlights a change in trends of causes of mortality

The "World Health Statistics 2008" found a shift from infectious diseases to non communicable diseases as the leading causes of death. The report evidences that chronic conditions are consolidating as the causes of the major proportion of deaths. This may be explained by the continuous ageing of population, even in low-income countries, and the continuous decline of infectious diseases. Communicable diseases, as tuberculosis, neonatal infection, HIV and malaria still remain of vital concern, even though there is a trend towards a lower incidence.
The World Health Statistics gathers information from the 193 member states of WHO, and includes 73 health indicators. This edition also highlights the progress in the fight against malaria, the estimates of HIV burden and the difference among regions in maternal mortality per 100.000 live births (9 for developed countries, 450 for developing countries and 950 for sub-Saharan Africa), among others.

Source:
http://www.who.int/whosis/whostat/2008/en/index.html

International Seminar on antibiotic resistance in Ecuador

The international Seminar "Recovering the health of the ecosystems to contain bacterial resistance" was held in Cuenca, Ecuador on 11-13th June.
The meeting was organized by ReAct (Action on Antibiotic Resistance) in collaboration with PAHO/OMS.
In this frame professionals from 22 countries of the Region participated in a workshop, were they reached a consensus document on the subject. The lines of action agreed by the participants include the development of regional research and databases, education of the public and professionals and promotion of governmental commitment.

Source:
ReAct homepage www.reactgroup.org

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Recent trials do not evidence benefit from intensive control of glycemia beyond current recommendations

The New England Journal of Medicine published two clinical trials evaluating the effect of intensive glucose control versus standard therapy on the incidence of cardiovascular events in patients with type 2 diabetes and high cardiovascular risk.
The ACCORD trial randomized 10.251 high risk patients to receive intensive therapy targeting a glycated hemoglobin (HbA1c) level below 6.0% or standard therapy targeting a HbA1c level between 7.0% and 7.9%. Both groups received a therapeutic regimen based on the investigator´s discretion, who could prescribe medicines with no restriction, to achieve the HbA1c goal. A safety review committee terminated ACCORD because an absolute risk increase of death from any cause of 1%, an extra death per 100 patients treated for 3.5 years. The primary endpoint, a composite of major cardiovascular outcomes, presented no significant difference at the end of the study (HR CI 95% 0.78 to 1.04; P = 0.16). The intensive therapy groups presented higher rates of hypoglycemia, weight gain and fluid retention.
The ADVANCE trial randomized 11.140 patients into treatment groups with similar HbA1c targets than the ACCORD, but the intensive treatment group was treated with modified released glipizide plus other medications as required, according to the physician discretion (although a treatment protocol was provided). The primary outcome was a composite of major macro and micro vascular events. Though the study proved a reduction in the primary outcome (ARR=1.9%, 95% CI 95% 0.5-3.4; NNT=52, 95% CI 30-200), it was due to the reduction in the incidence of nephropathy (micro vascular event), and there was no effect on death from all causes. The intensive treatment group presented more events of severe hypoglycemia.
The deaths from all cause in both trials could be influenced by several factors, such as the use of thiazolinediones (widely use in ACCORD, scarcely in ADVANCE), the mean weight gain presented in the intervention group (3.5 kg in ACCORD, 0.7 kg in ADVANCE) and the rate of decrease in HbA1c (1.4% in 4 months for ACCORD vs. 0.6% at 12 months for ADVANCE).
These two trials present no evidence in favor of an intensive strategy for lowering HbA1c below the actual recommendations.
We invite you to read the last edition of "Therapeutics Initiative", which focuses on this issue (read next article).

Source:
New England Journal of Medicine, June 12, 2008

A triumph for independent information

The Therapeutics Initiative is an independent organization of The University of British Columbia dedicated to provide up to date, evidence based, practical information on rational drug therapy. Recently, a governmental office recommended its clousure, but failed after a vigourous response of the various associations and societies (BMJ 2008;336:1270, 7 June; CMAJ JULY 1, 2008, 179:1). This group achieved to raise early concern on drugs as rosiglitazone, donepezil, valdecoxib and rofecoxib.

High quality information in: www.ti.ubc.ca/

Converting academic leaders into sales representatives

Kimberly Elliott, a former sales representative of the pharmaceutical industry, unmasked the methodology for recruiting "key opinion leaders" in an article published in the British Medical Journal. This article shows how laboratories pay renowned physicians to increase sales, influence prescribing patterns and dictate biased lectures, sometimes using slides provided by the sponsor. Senior doctors are also evaluated, by monitoring prescriptions before and after their intervention; if an impact on prescribing is not noticed, the speaker may not be "invited to participate" again. Surprisingly, there also exist guidelines and even software for managing key opinion leaders.

Source:
BMJ 2008;336(7658):1402 (21 June)
Believe or not: http://kolonline.com:80/products-olms.asp

Recognized Psychiatrists failed to declare payments from the industry

Three prestigious Harvard professors "forgot" to declare around 2.5 million dollars payments from the pharmaceutical industry in the last seven years. This situation is against the rules of the University of Harvard and the National Institutes of Health (NIH), which prohibits payments over 10.000 dollars per year.
The investigators, who specialize in the field of pediatric psychiatry, wrote several articles on pharmacological treatment of attention deficit hyperactivity disorder and bipolar disorder. Dr. Biederman, one of the implicated doctors, is famous for his stout defense of the treatment of pediatric bipolar disorder with antipsychotics, sometimes promoting unapproved indications. There has been a considerable increase in the number of people diagnosed with this disease, a 40-fold increase between 1994 and 2003. It is estimated that around 500.000 children received antipsychotic medication for this condition in 2007.

Sources:
BMJ 2008;336:1327 (14 June)
www.nytimes.com; June 8, 2008

Web based pharmaceutical care on essential hypertension

The Journal of the American Medical Association (JAMA) published a study on a web-based intervention for patients with essential hypertension. The patients with uncontrolled blood pressure, a total of 778, were randomized in 3 groups:

- **Group 1**, usual care: Patients were only told that they had uncontrolled blood pressure and were encouraged to consult with a physician.
- **Group 2**, home blood pressure monitoring and access to a patient training web site: Patients were trained on home blood pressure monitoring and trained to use a web-portal, which included s part of their medical record, a health library and resources on life-style changes, among others.
- **Group 3**, home blood pressure monitoring, access to a patient training web site and pharmaceutical care delivered through internet: Besides the first two features, a clinical pharmacist telephoned the patient and defined an action plan, subsequently the pharmacist followed-up the treatment using the internet, including medication recommendations, answering specifics doubts, monitoring home blood pressure values, and other interventions.

The main outcomes were percentage of patients with controlled blood pressure (<140/90 mm Hg) and change in systolic and diastolic blood pressure at 12 months.
The pharmaceutical care group presented an important difference in all the main outcomes:

Group	Percentage of patients with controlled BP at 12 months (IC 95%)	Change in systolic BP (CI 95%)	Mean change in diastolic PB (CI 95%)
1	0.31 (0.25 to 0.37)	−5.3 (−7.1 to −3.5)	−3.5 (−4.5 to −2.5)
2	0.36 (0.30 to 0.42)	−8.2 (−10.0 to −6.4)	−4.4 (−5.4 to −3.4)
3	**0.56 (0.49 to 0.62)**	**−14.2 (−16.0 to −12.4)**	**−7.0 (−8.0 to −6.0)**

All p values regarding comparisons of group 3 with 2 and 1 were <.001

This initiative presents very positive results, documenting the impact of pharmaceutical care in leading patients with a chronic disease to treatment success. The involved clinical pharmacists, who managed up to 50 patients each, reported that only took 2-8 hours per week to successfully interact with all the patients. The adherence to the intervention is another feature to highlight, 94% of the patients completed the 12 months follow-up. The principal disadvantage of this intervention is that it requires frequent access to the internet and computer skills, characteristics not widely present in the population of the Region of the Americas.

Sources:
Effectiveness of Home Blood Pressure Monitoring, Web Communication, and Pharmacist Care on Hypertension Control A Randomized Controlled Trial
JAMA. 2008;299(24):2857-2867

Pharmaceutical intervention on dispensation of statins

A community-based intervention was developed in over 100 hundred pharmacies in Norway. The intervention consisted in the detection of co-prescription of simvastatin or atorvastatin with CYP3A4 inhibitors by the pharmacist. After the detection, the pharmacist communicated to the treating physician the potential interaction and possible alternatives.
245 co-prescriptions were detected, and in 168 cases the pharmacist achieved a positive communication with the prescriber. As a result of these 168 contacts, in 100 cases (59.5%) the prescription was changed and in 50 cases (29.8%) the physician compromised to perform a close follow up and monitoring.
This is an interesting intervention due to its simplicity, the success achieved and the promotion of an effective interaction between health care professionals in benefit of the patient´s health.

Source:
Risk Management of Simvastatin or Atorvastatin Interactions with CYP3A4 Inhibitors. Drug Safety. 31(7):587-596, 2008

Cochrane review about medication adherence

The Cochrane Collaboration published a review about interventions for improving medication adherence. Several pharmacist based interventions were included, showing promising results. This article may be useful to design or implement a pharmacist or multidisciplinary interventions on adherence.

Source:
Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence (Cochrane Review). In: *The Cochrane Library,* Issue 2, 2008

Warning in antipsychotics utilization in dementia

Two observational studies have settled evidence on a possible increase in risk of death associated with the use of classic antipsychotics for dementia-related psychosis in elderly patients, a non approved indication. Consequently, FDA is setting changes in the labeling and prescribing information to include a warning for these particular patients.
In 2005, a warning for the same reason was required for atypical antipsychotics, but due to the lack of evidence about classic antipsychotics the warning could not be extended to the entire group.

Sources:
www.fda.gov/bbs/topics/NEWS/2008/NEW01851.html
Ann Intern Med Gill et al. 146 (11): 775
CMAJ Schneeweiss et al. 176 (5): 627

Use of epoetins in cancer patients

The Committee for Medicinal Products for Human Use (CHMP) of EMEA finished a review on epoetins (analogues of human erythropoietin) when indicated for the treatment of anemia in cancer patients. The Committee concluded that epoetins are associated with an increase in risk of tumor progression, venous thromboembolism and shorter overall survival.

The Agency concluded that the benefits of epoetins outweigh their risks, however anemia in patients expected to have a long survival expectancy should be treated with blood transfusions.

Source:
http://www.emea.europa.eu/pdfs/human/press/pr/33396308en.pdf

Safety news of two immunosuppressants

Mycophenolate mofetil (MMF) and mycophenolic acid (MPA), the active metabolite of MMF, are two immunosuppressant drugs used to prevent organ transplant rejection. Two safety concerns have been put into light:

- MPA has been related with an increased risk of pregnancy loss and congenital malformations. As MMF is metabolized into MPA after administration, this warning has been extended to the first.
- Several cases of progressive multifocal leukoencephalopathy (PML) involving MMF and MPA were detected during post marketing surveillance.

Sources:
http://www.fda.gov/medwatch/safety/2008/safety08.htm#mycophenolate

Congresses and Meetings

Buenos Aires
8TH ISOP ANNUAL MEETING 2008

International society of Pharmacovigilance
"Strategies for developing Pharmacovigilance"
5th-8th October 2008, Buenos Aires, Argentina
Preliminary programme: http://www.isop2008.org/
You can apply for a half grant sending a mail to:
secretaria@mariagraziani.com

VI Pan American Conference of Pharmaceutical Education

19-21of November 2008
Radisson Victoria Plaza Hotel,
Montevideo, Uruguay

Preliminar programme: Good Pharmacy Practice, Pharmaceutical Care,Workshop "the pharmacy student in the Americas", and more.
Submission deadline: 4th of July

World Congress of Pharmacy and Pharmaceutical Sciences 2008

68th International Congress of FIP
"Reengineering Pharmacy Practice in a Changing World"

Basel, Switzerland
29th August to 4th September 2008
www.fip.org/CONGRESS/basel08/

XII Congress of the Pharmaceutical Federation of South America

"Science, technology and Pharmaceutical Services to assure the patient a better utilization of medicines"

18-21 of November 2008
Radisson Victoria Plaza Hotel
Montevideo, Uruguay
Information available in www.fefas.org/fefas08/

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