SALUD COLECTIVA, Buenos Aires, 11(1):5-8, January - March, 2015

The medication cycle: its impact on access to and adequate use of drugs

El ciclo de los medicamentos: su impacto en el acceso y el uso adecuado

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As the consumption and the cost of medicines increase, there is a better understanding of the impact of these tendencies on health. The evidence is not always encouraging. Global expenditure on medicines grows faster than other components of total health expenditures. In 2013, the global pharmaceutical market reached US 870,200 million dollars.(1) In spite of this, half of the residents from middle-income and low-income countries and those affected by more than 5,000 known rare diseases do not have access to the medicines they need. At the other end of the spectrum, several countries, especially middle-income and high-income countries, bear the consequences of overmedicalization and inappropriate medication use.

While many patients might not be able to live without their medications, approximately 328,000 patients die each year in the USA and Europe as a result of consuming properly prescribed medicines; that is to say, this figure does not include deaths caused by incorrect prescriptions, maladministration, or drug interactions. It is estimated that in the USA, medicines cause almost two million hospitalizations, and a single hospitalization accounts for thirty people affected by adverse reactions.[2] Moreover, the continuous increase in the price of new medicines renders doctors and healthcare administrators resistant to ordering and/or including these products in pharmaceutical formularies, especially when other therapeutic alternatives with equal effectiveness are available at a lower price.[3,4]

Maximizing the benefit that medications can bring to society is not a simple task because all the actors participating in the medication cycle must work properly, in a coordinated manner and for the best interest of society. Those actors include the following: those who decide the type of drugs that are to be researched and developed; those who design and conduct basic and clinical research studies; those who analyze and disseminate the results; those who approve the commercialization of new medications; those who set the prices, prescribe, distribute or dispense the drugs; and, finally, those who consume and discard the unused medications. Unfortunately, during the last decades, a number of well documented reports have unveiled how conflicts of interest affect the behavior of these actors and have created a context that does not facilitate access to medications and their appropriate use.

Evidence shows that the research and development of new drugs is not primarily aimed at generating remedies for the health problems with no treatment options (for example, infections resistant to

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available antibiotics, rare and neglected diseases) but at developing products for lucrative markets, which are expected to yield high returns for the pharmaceutical industries and their investors. This evidence, which scandalizes public health specialists, is compatible with the business model of the pharmaceutical companies listed on the stock exchange and their fiduciary duties to the shareholders. When a company announces that the clinical trials of a new product with prospects of blockbuster sales (more than one billion dollars in sales a year) have shown promising results, a publicity campaign is vigorously launched, the share's price of the company soars.[5] If the results of the trials are negative, companies have to cancel the research and development effort around the new product. Thus, companies will use all resources at their disposal to display optimism over the quality of the products under investigation and the benefits of the commercialized products, although, on occasion, they might compromise the health of consumers. The case of rofecoxib (Vioxx), an anti-inflammatory drug that in theory posed a lesser gastrointestinal bleeding risk than the classic nonsteroidal anti-inflammatory drugs (NSAID), was important to clearly appreciate many of these interactions and relationships.[6-10]

The authors of the articles in this thematic issue represent different disciplines (law, economy, pharmacology, medicine, sociology), and through examples taken from Latin America they illustrate the factors that restrict access to pharmaceuticals and their appropriate use. Dr. Allard clearly illustrates the contradictions present in international treaties and their impact on universal access to medications. Countries that are members of the World Trade Organization (WTO) subscribed the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement, which grants patents. And patents allow price monopolies that restrict the access of governments and residents of middle-income and low-income countries to medications. Governments accepted TRIPS despite the fact that they had previously subscribed and ratified the International Covenant on Economic, Social and Cultural Rights (ICESCR) of the United Nations (UN) that compels them to facilitate access to medications. It also describes the commitments undertaken by these countries after subscribing and/or ratifying those agreements. Moreover, the article shows that in spite of the efforts that some countries had made to guarantee access to medications through the Doha Declaration and the use of TRIPS flexibilities, disputes were presented before the Dispute Settlement Body (DSB) of the WTO and of those related to the bilateral or regional trade agreements. These bilateral and regional trade agreements include clauses known as TRIPS Plus because they provide additional protection to the intellectual property rights of companies, facilitate pharmaceutical price increases, and prevent signatory members from complying with the commitments undertaken through ICESCR.

Dr. German Velázquez describes how the current medication research and development (R&D) system, based on intellectual property incentives, has failed to offer the pharmaceutical products that humankind needs, especially to the residents of middle-income and low-income countries. The article, in addition to stating the advantages and the principles that must govern the creation of an international binding treaty on pharmaceutical research and development to be negotiated with the support of the WHO, analyzes the advances in its constitution, including the interests and views of its opponents and advocates.

A different alternative to improving access to available treatments is controlling the drug prices. The article written by Joan Rovira describes the different components in the final price of medicines, not only of those protected by a patent but also of the generic versions, and the strategies that countries can use to control the prices of these products and facilitate their access.

The article written by Dr. Eduardo Goronazky analyzes the strain between scientific advance and the respect towards the rights of the volunteers who participate in clinical research studies. Based on historical data, the article proves that the existence of laws and regulations has not sufficed to guarantee respect for the dignity of the participants. The economic interests of research sponsors and those of the clinical researchers contribute not only to violating the participants' rights, but also the integrity of the research process, data gathering and analysis, and the dissemination of results. Rising doubts are cast on the capacity of regulatory agencies to protect research study participants as well as the quality and integrity of the study results.

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Antonio Ugalde and Núria Homedes explain the hurdles that innovative pharmaceutical firms face in attracting shareholders by paying substantial dividends. The problem results from the expiration of the patents on blockbuster drugs and the difficulties that the firms have in bringing new blockbuster drugs to the market. One solution devised by these companies is to accelerate the implementation of clinical trials in order to obtain, in record time, the commercialization approval of new drugs, the facto lengthening the period during which they can sell the new drugs under monopoly conditions. The authors discuss how innovative pharmaceutical firms accelerate the implementation of clinical trials in Latin America and the consequences that such actions have on the quality of the collected data, the protection of the human rights of the clinical trial participants, and the compliance with the ethical principles approved in universal declarations.

One of the interests of the pharmaceutical industry is the development of the vaccine market. Dr. Juan Carlos Tealdi enumerates the contributions that vaccines have brought to health and presents the bioethical and human right problems that have arisen while conducting clinical research with these products. Although these problems are not new, their magnitude has no precedent, since vaccine prices render them unaffordable to many, including the residents of rich countries that do not offer universal health care coverage. Nevertheless, the industry's rush to include expensive vaccines in the immunization schedules, occasionally through rather unethical means, has aroused suspicions and increased the mistrust of those who question their safety and cost-effectiveness. The article presents the bioethical problems that have been documented while conducting vaccine clinical trials in Argentina, and it proposes the creation of a national committee to review clinical trials with vaccines and to systematically monitor those studies.

A group of Brazilian researchers documents how placebo controlled clinical trials are being conducted in Brazil despite the fact that, in 2008, Brazil's Federal Council of Medicine (CFM) [*Consejo Federal de Medicina*] banned the participation of Brazilian doctors in studies using placebos when treatment is available. The authors compare the clinical trials implemented between 2003 and 2007 with those conducted between 2009 and 2013 and conclude that the pharmaceutical industry was the main sponsor of placebo-controlled clinical trials; there was also a predominance of clinical trials involving chronic diseases compared to those for neglected diseases or for other Brazilian health priorities.

Finally, Dr. Pol Yanguas states how the lack of integrity in the research of psychiatric disease treatments and in the dissemination of the results affects the treatment of those patients. This author also criticizes those health professionals who impose their treatment preferences and do so under the influence of an ideological-commercial construct and at the expense of patient's freedom.

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CITATION
Homedes N, Ugalde A. The medication cycle: its impact on access to and adequate use of drugs. Salud Colectiva. 2015;11(1):5-8.

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The translation of this article is part of an inter-departmental and inter-institutional collaboration including the Undergraduate Program in Sworn Translation Studies (English < > Spanish) and the Institute of Collective Health at the Universidad Nacional de Lanús and the Health Disparities Research Laboratory at the University of Denver. This article was translated by Braian Castaño and Verónica Dall'Ospedale under the guidance of Mariela Santoro, reviewed by Audrey Adler under the guidance of Julia Roncoroni, and prepared for publication by Aldana Micaela Schöenfeld under the guidance of Vanessa Di Cecco. The final version was approved by the article author(s).