EDITORIALS

The Social and Economic Influences on Medication Use and Misuse

Robert A. Aronowitz, MD

University of Pennsylvania, Philadelphia, PA, USA.

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Considered together, two reports in this issue suggest that some serious adverse effects of medications arise from the social and economic conditions in which medications are marketed, prescribed, and used.

Bennett et al. review the history of three serious adverse drug reactions (ADR): aspirin and Reye's syndrome, epoetin and pure red cell aplasia, and gadodiamide and nephrogenic systemic fibrosis.¹ In each case, astute clinicians recognized the link between the drug and the ADR, but long after the drug was introduced into practice. Gaining scientific consensus about these links and enacting regulations have also been slow and problematic processes.

ADRs may not be apparent in phase 3 trials of new drugs because the numbers of subjects are small and follow-up intervals are short. But these historical case studies underscore that serious ADRs are often *new*, not just newly discovered, phenomena. Once released into the real world, medications can take on new lives. They may be given to individuals very different from those who were initially tested. They are often prescribed for new indications and administered by new routes and in different doses. Unlike the conditions that usually exist in clinical trials, patients may already be on multiple medications for multiple diagnoses. All these factors, and others, were apparent in the three case studies reviewed by Bennett et al.

A 19th century adage reminded physicians that “all medicine is experimental.” Something novel often occurs when a standardized medication meets an individual with his or her unique biology, life experience, and social conditions. But many ADRs are not simply unanticipated or idiosyncratic. They are also the predictable consequence of the social and economic conditions shaping modern medical practice and health consumption. The ADRs that Bennett et al. review underscore the minimal oversight of OTC medications that occurs in the context of mass marketing of consumer goods, and the wide berth given to clinicians for off-label use, dosage, and mode of administration of prescription medications. These practices follow

from the lack of regulation and surveillance of medicines in their post-marketing existence.

These contexts are what link Bennett et al.'s ADR case studies with Wolf et al.'s demonstration of the potential misuse of acetaminophen-containing OTC medications.² Wolf et al. show that consumers are often unaware that different OTC medications—pitched to different markets, advertised for different problems, given different names and physical characteristics—contain the same active ingredients. The authors point to confusing labeling and patient illiteracy as underlying and remediable causes.

While improving labeling and addressing patient literacy are important goals, these efforts will not change the underlying structural conditions from which these errors arise, especially the “tower of babel” character of the OTC medication market with its proliferation of proprietary products and the staggering numbers of doses consumed. Some estimate that over 29 billion doses of acetaminophen are consumed yearly in the U.S.³ and that 28% of Americans have used an acetaminophen containing product in the previous week (similar to this study's 20% result).⁴ The nature and size of this market is the direct consequence of relentless and relatively unfettered marketing. This marketing has led to the great number of confusing brand names, varying pill sizes and shapes, and the cacophony of redundant combination pills. From all of this there is demonstrable harm and little or no evidence of benefit.

So there would seem to be a good argument for more stringent restrictions on the approval and marketing of acetaminophen and other OTC medications rather than current regulatory practice which is largely limited to how these products are labeled. Similar issues have surfaced recently about consumer confusion over identical but differently marketed generic medications. Patients often recognize their pills by shape and color. These very features also lead to brand identity and loyalty. So it is understandable that the producers of once-patented medications fiercely protect their right to ward off new generics by demanding that they have different sizes and shapes. Similar to what Wolf et al. demonstrate about OTC medications, these are also the very conditions which produce misuse and overuse.⁵ In the case of generic and OTC medications, there is a compelling health argument for more restrictive marketing practices, regulations, and norms.

Unfortunately for effective reform, as the article by Wolf et al. points out, OTC medicine labeling is the province of the FTC while safety and efficacy concerns are under FDA jurisdiction. Perhaps clinical evidence that marketing *is* a safety issue, as Wolf et al.'s study suggests, can lead to legislation that reforms this antiquated regulatory structure.

There are of course benefits to the marketing of cheap and accessible OTC medicines. Acetaminophen-containing OTC medications, for example, relieve pain, reduce inflammation, and bring down uncomfortable fevers. Bennett et al. note the remarkable decline in Reye's syndrome in the years after the aspirin-virus-liver-brain disease link was made. How did this change happen? Some fraction must have been due to the diffusion of epidemiological insights by clinicians and public health authorities and consequent behavior change by parents. But there is another old saw in public health that anything that depends on the individual is bound to fail. It is not inconceivable that the aggressive marketing of OTC acetaminophen as the safe alternative to aspirin played an important role in the rapid decline in childhood aspirin use. I was taken aback by an informal poll I recently conducted among some non-health care colleagues. This group has a very high awareness of aspirin's gastrointestinal side effects as well the prohibition on giving it to febrile children. But they had no awareness of acetaminophen's dangers or that acetaminophen was a leading cause of serious medication overdose. The ironies are potentially rich. The high numbers of Reye's cases flowed from aggressive marketing of OTC aspirin and the reduced numbers of cases may have resulted from the successful marketing of OTC acetaminophen products—which then created the conditions for new patterns of misuse.

OTC and prescription medications have other efficacy than their presumed physiological effects. They also have social and psychological efficacy. Parents of children sick with febrile illnesses seek relief of their children's symptoms but also want to behave and be perceived as good parents, exercise some control over a potentially frightening illness, shorten the amount of time missed at school or work, etc.⁶ Medications have been developed and marketed to do this kind of work.

Most clinicians are acutely aware of the social and psychological work medicines do for them, from increasing patient trust or getting patients out the door more quickly. What has been missing from clinical and policy discussion is whether the social and psychological work done by medications might be brought out into the open and perhaps creatively deployed at an aggregate level for health rather than for market gain alone (as is usually the case). One half-serious idea I have imagined concerns a

potential remedy for antibiotic overuse. Instead of largely ineffective educational campaigns aimed at individuals to prescribe and consume fewer antibiotics, why not substitute a less harmful (and perhaps even physiologically effective) practice or product that satisfies parental and physical social and psychological need to do something for an upper respiratory or middle ear infection, such as promoting acupuncture?

Overall, the policy challenge for prescription drug misuse is that our regulatory response occurs only after significant development and investment (making it exclusively after-the-fact rather than proactive), and is typically focused on narrow, idealized indications and the context of initial use rather than the many real world contexts in which drugs are eventually used. Nor are the broad social and economic factors shaping medication use the object of health policy. For prescription and OTC medications, their post-marketing, aka real world, lives are inadequately understood and regulated.

Reducing medication error is at the same time not only about regulation and surveillance. Early in my medical training, I was taught by a pharmaco-epidemiologist to learn everything about a few medications and focus on using them appropriately. Effectively disseminating such general principles and heuristics to clinicians, patients, and consumers are also needed to improve the effectiveness and safety of medication use.

Corresponding Author: Robert A. Aronowitz, MD; University of Pennsylvania, Claudia Cohen Hall, Rm. 324, Philadelphia, PA 19104-6304, USA (e-mail: aronowitz@wharton.upenn.edu).

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