The Heartbreak of Drug Pricing

TO THE EDITOR: Dr. Davidoff’s appeal to the kind hearts of the pharmaceutical industry to restrict drug pricing (1) is fatally flawed. First, the captains of the drug industry have a fiduciary duty to their stockholders. Unlike health care professionals, they have taken no oath to place the interests of their patients before their own. This is the hallmark of our profession as compared with a corporation. The bottom line is the care of patients, not profits.

Second, the idea that reducing prices will increase revenues ignores the fact that our prescriptions determine the product and quantity of drugs sold. Because of this, drug manufacturers have hired 1 drug representative for every 10 doctors, schmoozing and bribing us on a daily basis. (For an enlightening and amusing review of this situation, try the Web site www.nofreelunch.org.)

If the marketplace were a drug in a trial to cure the diseases of high health care costs and poor access to care, the trial would be stopped as a dismal failure. The United States needs a national health insurance program, with everybody in and nobody out, to bring public accountability to our “nonsystem” of sickness care, including the pharmaceutical industry. Three out of four Americans support health care for all. When will the American College of Physicians–American Society of Internal Medicine join the American Public Health Association, Physicians for a National Health Program, American Medical Women’s Association, National Medical Association, American Medical Student Association, American Academy of Family Physicians, and our patients in calling for a national health insurance program?

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Reference

IN RESPONSE: As Dr. Ross notes, companies do, of course, have a fiduciary obligation to their stockholders, but my editorial was intended to appeal to forces in corporate life other than purely fiscal ones. In fact, many pharmaceutical companies, as well as those in other sectors of the economy, take seriously their nonfinancial obligations, including those to their customers and other parts of the community, not just because it’s the “right thing” to do but because it makes good, hard business sense. A well-known example is Johnson & Johnson’s credo, which begins: “We believe our first responsibility is to the doctors, nurses and patients, to mothers and fathers and all others who use our products and services” (1). This policy is widely credited with helping the company make good business decisions during the so-called Tylenol crisis (2), which suggests that it is more than just window dressing.

The number of prescriptions written is, to be sure, driven primarily by doctors’ willingness to write them. But lower drug prices could very well encourage doctors to write prescriptions, to their patients’ benefit, in just those discretionary situations where they now hold back because they know patients would have trouble paying for them. Moreover, because of high costs, patients frequently fail to fill, or refill, prescriptions that could do them good. On this account as well, lower prices would almost certainly increase the actual volume of drug sales.

I agree totally with Dr. Ross about the need for universal health care, as I’ve stated previously (3). The College is also on record as supporting universal access.

Dr. Lisker provides a number of important insights on drug
sales and promotion, including the role of the FDA. The cost of FDA approval clearly influences drug prices, but the degree to which it does so is a complex subject. It does seem, however, that the current system, in which manufacturers’ fees help pay for drug approval, muddies the regulatory waters, since it potentially provides industry with a kind of leverage that may not always be in the public’s best interest.

Frank Davidoff, MD
Editor Emeritus

References

Molecular Genetic Evidence of an Association between Nasal Polyposis and the Peutz–Jeghers Syndrome

TO THE EDITOR: The Peutz–Jeghers syndrome is an autosomal dominant disorder characterized by hamartomatous polyposis of the gastrointestinal tract, melanin pigmentation of the skin and mucous membranes, and an increased risk for cancer (1, 2). It is caused by a germline mutation in the STK11/LKB1 gene on chromosome 19p13.3 (2). Hamartomas and carcinomas in patients with the Peutz–Jeghers syndrome show loss of heterozygosity at chromosome 19p13.3, indicating inactivation of the wild-type STK11/LKB1 gene (3).

Peutz described the first family with the Peutz–Jeghers syndrome as having “a highly remarkable combination of polyposis of the mucosa of the intestinal tract and of the nasopharynx, together with typical mucocutaneous pigmentation” (1). Although nasal polyposis in affected patients has been mentioned occasionally (4, 5), it is not a recognized extraintestinal manifestation of the disease. Consequently, we used a molecular genetic approach to investigate the association between nasal polyposis, the Peutz–Jeghers syndrome, and STK11/LKB1.

We studied 4 patients with the Peutz–Jeghers syndrome who came from 3 families with known germline mutations in STK11. Twelve nasal polyps from these 4 patients were available for study. We also analyzed 28 sporadic nasal polyps from 28 controls without evidence of the Peutz–Jeghers syndrome, the Kartagener syndrome, cystic fibrosis, or aspirin sensitivity. Polyp DNA was isolated from microdissected polyp epithelium, and wild-type DNA was isolated from stromal inflammatory cells. Loss of heterozygosity was assessed by comparing polyp DNA with normal DNA, as described elsewhere (3). The markers used were D19S886 and D19S565 (www.gdb.org), flanking the STK11/LKB1 gene on chromosome 19p13.3. Blood samples for haplotype analysis were collected from affected and nonaffected family members of a patient with the Peutz–Jeghers syndrome and nasal polyposis to determine which 19p13.3 allele segregates with the Peutz–Jeghers syndrome. The medical ethics committee of the University Hospital Rotterdam, Rotterdam, the Netherlands, approved the protocol, and all participants provided informed consent.

Figure. Loss of heterozygosity at 19p13.3 in nasal polyp DNA, and haplotype analysis confirming loss of the wild-type allele.

A. Loss of heterozygosity with marker D19S886 in nasal polyp DNA compared with normal DNA from patient III.1, analyzed with the ABI377 sequencer and Genescan software (PE Biosystems, Foster City, California). The peaks represent the two alleles (179 base pairs and 187 base pairs). In polyp DNA, the allele with 179 base pairs is lost; the small peak represents contamination with normal DNA from inflammatory or stromal cells. B. Marker D19S886 was used to analyze normal DNA from patient III.1, his spouse, and affected and nonaffected offspring. The allele with 179 base pairs from patient III.1 does not segregate with the Peutz–Jeghers syndrome; that is, the allele with 187 base pairs (*) contains the germline mutation responsible for the Peutz–Jeghers syndrome. Consequently, loss of heterozygosity in the nasal polyp of patient III.1 results in retention of only the mutant allele.
In two unrelated patients with the Peutz–Jeghers syndrome, four of eight nasal polyps showed loss of heterozygosity at 19p13.3. In contrast, loss of heterozygosity was not found in 23 sporadic nasal polyps (P = 0.002). Haplotype analysis showed that loss of heterozygosity comprised deletion of the wild-type allele (Figure). Our findings indicate that nasal polyps related to the Peutz–Jeghers syndrome lack the functional STK11/LKB1 tumor-suppressor gene, suggesting a causal relationship between nasal polyp development and the Peutz–Jeghers syndrome. Loss of heterozygosity at 19p13.3 in nasal polyps of affected patients corresponds with reports of loss of heterozygosity in gastrointestinal hamartomatous polyps (3). Loss of heterozygosity at the STK11/LKB1 locus in nasal polyps related to the Peutz–Jeghers syndrome suggests that these lesions may be neoplastic in nature. This may also be reflected by the co-occurrence of nasal polyposis and nasopharyngeal squamous-cell carcinoma in a patient with the Peutz–Jeghers syndrome (4). We provide molecular genetic support for the initial observation of Dr. Peutz: Nasal polyposis can be an extraintestinal manifestation of the Peutz–Jeghers syndrome.

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References
1. Peutz JL. A highly remarkable combination of polyposis of the mucosa of the intestinal tract and of the nasopharynx, together with typical mucocutaneous pigmentation of the skin and mucous membranes [Dutch]. Nederlandsch Maandschrift voor Geneeskunde. 1921;10:134-46.

Correction: Update in Infectious Diseases

In the 2001 Update in Infectious Diseases (1), the fourth sentence under the heading "Unusual Infections and Modes of Transmission" should read "The patients died 5 to 17 days after symptoms developed" rather than ". . .after having been bitten."

Reference