to treat symptomatic patients, cancer has been ruled out, and there are no significant contraindications, all studies have shown that α-blocking agents have a significant effect on all prostates, whereas finasteride has a beneficial effect only in men with significantly large prostates and major obstructive symptoms.

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[One of the authors responds:]

The trial involving veterans, published while our article was in press, concluded that terazosin was significantly more effective than placebo, whereas finasteride was not. However, it turned out that the patients enrolled in this study had a mean prostate size identical to that in a normal population of men.[2] A meta-analysis (incorporating the results of our Canadian study) subsequently confirmed that only patients with enlarged prostates had a response significantly better than those taking a placebo.[3] It is obvious now, but not when we designed our study in 1991, that a drug whose action is to shrink the prostate only works in men with large prostates. Many of us, including Dr. Barkin, are concerned about the unacceptable failure rate of drug therapy, particularly after several years. In a long-term study of terazosin,[4] twice as many patients with small prostates (32%) as with larger prostates (16%) were still available for study after 4 years. By contrast, more than 90% of patients taking finasteride who entered open-label trials (and who presumably had a favourable response secondary to shrinkage and stabilization of their prostates) were still taking the drug and were available for study 5 years later.[5] These new and important findings allow busy clinicians such as Barkin a less confusing and more efficient, durable and evidence-based approach to the treatment of his patients who do not choose watchful waiting, who have an indication for drug therapy or who are reluctant to undergo surgery. Most men with symptoms but with normal-size prostates (50% or more of Barkin's patients) can be expected to have a favourable and durable response to α-blocking agents. Both α-blocking agents and finasteride can achieve similar results in men with larger prostates. With finasteride, we can expect the response to be durable over the long term.

Barkin was also concerned about the confusing finding of the study involving veterans that the PSA level decreased in the terazosin group, but not in the finasteride group.[1] In fact, the result was precisely the opposite. This error had passed through proofreaders, editors and multiple authors. One must question everything one reads. Even the *New England Journal of Medicine* can make a mistake.

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Wiping out measles: When to vaccinate?

The measles outbreak reported in the article "Outbreak of measles in a highly vaccinated secondary school population" (*Can Med Assoc J* 1996;155:1407-13), by Drs. Penny A. Sutcliffe and Elizabeth Rea, is one of many such outbreaks during the last several years in North America. These outbreaks prompted our southern neighbour to switch to a 2-dose measles-vaccination strategy a long time ago. The article and the accompanying editorial "Elimination of measles in the Americas" (*Can Med Assoc J* 1996;155:1423-6), by Dr. John Furesz, support a 2-dose strategy to eliminate measles. However, the timing of the 2 doses is an issue that remains to be settled.

In all Canadian provinces, the first dose of measles–mumps–rubella (MMR) vaccine is administered at 12 months of age, except in PEI, where it is given at 15 months. In the new 2-dose strategy, a second dose is given at 18 months in Newfoundland, Quebec, Saskatchewan, BC, Yukon and the Northwest Territories, and at 4 to 6 years in PEI, Nova Scotia, Ontario, Manitoba and Alberta. Both schedules are consistent with the recommendations of the National Advisory Committee on Immunization.

Our studies of measles-vaccine response, vaccine failure and waning immunity shed some light on the timing of the 2 doses. Our data show that up to 16% of children who receive the first dose of MMR vaccine at 12 months do not respond adequately and remain without protective immunity after the first dose.[1,2] This lack of immunity cannot be attributed entirely to maternal measles

antibody interfering with the live-virus vaccine, since two-thirds of the 16% of children without immunity do not have maternal antibody at the time of vaccination.[1] In addition to the immunogenicity of the vaccines used, the suboptimal response has to do with the maturity of the immune system and its ability to respond at the time of vaccination. Pools of susceptible children therefore remain after the first dose,[1–3] and this could have led to outbreaks in vaccinated children, like the one in Ontario, during the past decade. This implies that, if the first dose is given at 12 months, a second dose should be considered sooner than later. In this context, giving a second dose at 18 months appears appropriate. However, administering a second dose at 4 to 6 years of age, around the age of school entry, addresses the immediate public health concern about school-based outbreaks and is also convenient and economical. Our data indicate that 28% of children 5 to 17 years of age who received a single dose of MMR vaccine at 1 year of age have inadequate protective immunity against measles.[4] A second dose given at 4 to 6 years of age can act as a booster for those with waning immunity. Nevertheless, delaying a second dose to 4 to 6 years may not be a sound decision if the first dose was given at 12 months. A substantial proportion of preschool children would remain without adequate protection because of primary failure or suboptimal response. The question is whether these infants would form a large enough pool to allow outbreaks or simply to help sustain the transmission of measles. The alternative is to delay the first dose to 15 to 18 months to ensure a better initial response, in which case giving the second dose around school entry becomes a suitable strategy. As mentioned in the editorial, this strategy, among other factors, has been successful in eliminating not only measles but also rubella and mumps in Finland. Interestingly, the smallest Canadian province has chosen this strategy; outcomes in PEI could provide important information for the rest of the country.

Our study data also indicate that, in contrast to measles, vaccine-induced rubella immunity declines significantly only after 8 years of age.[5] In this regard, a second dose of MMR vaccine may also help prevent secondary failure of vaccination against rubella. Also, from the standpoint of sustained immunity to rubella during childbearing years, administration of the second dose around school entry or even later is likely to be more beneficial.[6] Canada is poised to achieve the goal of elimination of measles and rubella during pregnancy. Since the provinces have adopted different delivery schedules to achieve this goal, we should be able to find some answers to the question of timing in order to develop an optimal strategy for Canada.

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Can drug companies have it both ways?

The articles by Drs. Joel Lexchin ("Enforcement of codes governing pharmaceutical promotion: What happens when companies breach advertising guidelines?" *Can Med Assoc J* 1997;156:351-6), Martin F. Shapiro ("Regulating pharmaceutical advertising: What will work?" 359-61) and Jean G. Desjardins ("The PMAC Code of Marketing Practices: Time for improvement?" 363-4) are timely and provocative, and pose some fundamental questions.

For instance, can pharmaceutical companies have it both ways? They wish to be known as "partners in the health care team" (or some similar bromide) but they do not wish to be subject to the same degree of self-regulation, bolstered by considerable government interference, that is now enjoyed by the established self-regulated professions.

A second issue is the complaints process. It is inadequate to depend on complaints from professionals, who are mostly but not exclusively physicians, because it is well known that physicians often do not complain. This is not due to a conspiracy of silence but to simple inertia and heavy involvement with other matters. In the same vein, it seems ridiculous to accept complaints about a company from a rival company: the various companies would simply abuse the regulatory process for personal gain whenever possible. This is human nature, and pharmaceutical companies are run by humans.

A third issue is "direct-to-consumer" advertising, which appears to be here to stay but points to a total