reflect a positive impact of the genogram. Yet type I error seems equally plausible given the number of correlations computed.

Finally, Blossom may be correct that the "newer qualitative research modes" will show how using genograms can improve clinical practice. Still, if genogram encounters have the educational and therapeutic "impact" he claims, we expect this will someday be demonstrated by traditional scientific means as well.

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Treatment of Pharyngitis

To the Editor: In a letter recently published in *JABFP*, Dr. McIntyre criticizes the use of rapid streptococcal antigen tests and asks, " . . . why use a test that identifies less than one-half of the treatable organisms?"[1] From his letter it appears that he assumes mycoplasma organisms and groups C and G streptococci to be antibiotic-responsive, in addition to group A streptococci. A review of his references provides little support for his implied view that antibiotic treatment is demonstrably beneficial to patients whose throats are infected with agents other than group A streptococci. Corson, et al.[2] expressed the opinion that "treatment of non-group-A streptococcal pharyngitis may be warranted" but offered no supporting evidence. McCue[3] was unable to demonstrate clear benefit from treatment of group G streptococcal pharyngitis with penicillin V potassium or erythromycin in his relatively small series. The other papers cited by McIntyre were essentially silent on the subject of antibiotic treatment. Dr. McIntyre has called to my attention the paper by Gerber, et al.[4] in which group G streptococci appeared to be responsive to penicillin, but this study is inadequately controlled.

There has been a long controversy in the medical literature whether antibiotics shorten the clinical course of even group A streptococcal pharyngitis. Randolph, et al.[5] are probably correct in asserting that antibiotics may shorten symptoms in group A infected children to whom they are given shortly after the onset of symptoms, but I have not seen convincing evidence for effectiveness in adults, especially those who have had symptoms for more than 3 days (the question of preventing rheumatic fever is a separate issue that will not be addressed here).

The physician's desire to help patients can understandably tempt us to prescribe antibiotics for all sore throats, but there are good medical and economic reasons to avoid their use without good evidence that they are effective. Pharyngitis is so common and the economic benefit to drug companies of wide antibiotic use so substantial that studies to demonstrate their effectiveness in this context must surely have been attempted in the half century since penicillin became available. The fact that pharmaceutical representatives are not inundating us with evidence that antimicrobials benefit patients with non-group-A pharyngitis suggests that they have not been proved effective for that purpose.

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The above letter was referred to the author of the letter in question, who offers the following reply:

To the Editor: Dr. Gillette's comments are most appreciated to extend the discussion on the scientific approach to the patient with pharyngitis. My original letter clearly does not suggest physicians "prescribe antibiotics for all sore throats." The intent of the letter, however well articulated, was to point out that using the rapid strep tests encourages clinicians to evaluate pharyngitis as "strep or nothing," without considering the multiple causes of pharyngitis.

The large amount of human suffering and economic loss from pharyngitis should force us to seek out carefully with the history and physical any treatable cause of pharyngitis. Although thoughtless overtreatment exposes the patient unnecessarily to drug reactions, undertreatment has a cost also in human suffering, patient dissatisfaction, and lost time from work. In my practice, sinusitis is the most common final diagnosis in patients who present with "sore throat," and of course the standard therapy includes antibiotics. Whether due to Stoicism or parsimony in my private patients, I see very few viral-appearing upper respiratory tract infections.

Other treatable causes of pharyngitis include oral candidiasis, allergic rhinitis, pharyngeal gonorrhea, reflux esophagitis, Stevens-Johnson syndrome (if an offending agent can be withdrawn), *Corynebacterium hemolyticum*,[1] *Corynebacterium diphtheriae* (thankfully rarely), *Yersinia enterocolitica*,[2] *Chlamydia psittaci* (TWAR subspecies),[3,4] Lyme disease,[5] and probably a host of rarer diseases. Causes of pharyngitis that are recognizable (and thus reassuring to the patient) include Coxsackie virus, mononucleosis, and the primary attack of herpes simplex type I. It is not practical in moderately ill outpatients to try to elucidate the rare causes of pharyngitis, but group C streptococcal[6] and group G streptococcal[7] pharyngitis

may be found to be as common as group A streptococcal pharyngitis when modern culture and typing methods are used. The rapid strep tests, of course, do not recognize any of these entities, being antigen specific for only group A streptococcal infections.

Turner, et al.[6] studied 232 college students with pharyngitis and 198 age-matched controls for more than 2 years to minimize the chance of contamination of their data by an outbreak of nongroup A streptococcal infections. They found 26 percent of the symptomatic patients had group C streptococcus, with cases spread throughout the academic year. Patients with group C streptococcus had fever, exudative tonsillitis, and adenopathy much more often than patients with negative cultures.

Dr. Gillette referred to a study by Randolph, et al.[8] that showed symptom response to antibiotic therapy in patients with group A streptococcal pharyngitis. I would differ with Dr. Gillette's interpretation of that study. Although 80 percent of the patients were treated within 24 hours of symptom onset, the response rate reported was not stratified to be able to conclude that patients treated after a longer period of symptoms responded either better or worse than the entire group. The study by Randolph was a randomized, blinded, placebo-controlled study with 260 participants and showed that symptomatic group A streptococcal pharyngitis responds to antibiotics. It seems unlikely that anyone would conduct a study to enroll enough patients to stratify to statistical power the different subgroups of patients presenting with varying lengths of symptoms, different age groups, different races, smokers versus nonsmokers, or any other possibly confounding issues. Having seen Zomax™, Oraflex™, and Suprol™ blossom and wither on the medical landscape, I respect Dr. Gillette's healthy skepticism but think there is clear, convincing proof that group A streptococcal pharyngitis is a treatable illness, as clear proof as any we use in clinical medicine. Pichichero, et al.[9] also has presented a more recent double-blinded study that reported symptom reduction with the use of antibiotics for group A streptococcal pharyngitis in a study designed to overcome some of the perceived methodological defects of earlier studies.

The study by Gerber, et al.[7] does not use a placebo arm but carefully compares the symptom response to antibiotics of 56 patients with group G streptococcal pharyngitis with the symptom response of 91 patients with group A streptococcal pharyngitis (which I believe can be considered a known benchmark after the above studies). They found that in 5 of 6 measures the patients with group G streptococcal pharyngitis responded more favorably to antibiotic therapy than patients with group A streptococcal pharyngitis. This large, carefully conducted study is at least strongly suggestive that group G streptococcal pharyngitis responds to antibiotics. There are very few symptomatic bacterial infections that we don't treat with antibiotics, and I believe after a study like Gerber's we should treat group G streptococcal infections until an equally convincing study proves otherwise.

In the section on chlamydial infection in the 1990 edition of *Internal Medicine*,[4] Dr. Schachter notes that seroprevalence rates of *Chlamydia pneumoniae* (previously called *Chlamydia psittaci*, TWAR subspecies) in many communities are 30 to 40 percent, making *C. pneumoniae* infections a very common and usually undiagnosed illness. The symptoms include a severe pharyngitis in a considerable proportion of patients, and the pharyngitis can precede the other respiratory symptoms. The severe pharyngitis seen in *C. pneumoniae*[3,4] infections illustrates the difficulty in assessing older trials of antibiotics in nonstreptococcal pharyngitis.[10] Modern tissue culture techniques are necessary to identify the subgroup that has a tetracycline-sensitive organism, and older trials that used penicillin or erythromycin would not have shown a response in the chlamydial group. Clinicians faced similar frustration when *Chlamydia trachomatis* was discovered as a cause of pelvic inflammatory disease but wasn't routinely diagnosable without tissue culture techniques. Hopefully, further research will provide an estimate of the frequency of *C. pneumoniae* pharyngitis and an outpatient test to diagnose it in a timely fashion.

Rather than treating all patients with pharyngitis with antibiotics, I would suggest that a brief but broad review of associated symptoms will provide the basis for the appropriate diagnostic or therapeutic approach. The rapid strep test would be uniquely useful if positive in a patient with expected noncompliance in whom injectable penicillin is being considered as a treatment. If a throat culture is indicated, other patients would be better served with the more sensitive throat culture for all β-hemolytic organisms. If the culture is negative and the patient has improved, antibiotic therapy is obviated. If the culture shows group A streptococcal infection, antibiotics are indicated for the prevention of rheumatic fever, regardless of symptoms. If the patient's sore throat has worsened considerably and the culture is negative, the diagnosis of *C. pneumoniae* should be considered. If the culture is negative and a rash has appeared, *Corynebacterium hemolyticum* should be considered, as Miller, et al.[1] estimate that a case of pharyngitis with rash in a person 11 to 20 years of age is almost as likely to result from *C. hemolyticum* infection as from streptococcal scarlet fever. In contrast to the immediate treatment fostered by the rapid strep tests, the delay of holding antibiotics for 1 or 2 days in nontoxic patients while waiting for a throat culture can be beneficial in mild or recurrent pharyngitis. Several studies have suggested that early treatment of group A streptococcal pharyngitis fosters same-season recurrence.[9,11]

Despite having antibiotics for a half century, as Dr. Gillette notes, the recent research cited above shows that our body of knowledge about pharyngitis continues to change. Although familiarity breeds con-

tempt, we should use our full clinical acumen in assessing a patient with pharyngitis.

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So. Dennis, MA

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Phase IV Drug Studies

To the Editor: I have serious concerns about the ethical appropriateness and scientific accuracy of a paper that recently appeared in *JABFP*, a report from the Clinical Experience Network exploring a variety of coronary heart disease risk factors in patients with high cholesterol levels. The study is billed as an epidemiologic study of the demography of a heterogeneous and representative group of dyslipidemic patients to be followed by a subsequent report of the efforts of diet, exercise, and gemfibrizol therapy. Parke-Davis paid for the study and also purchased a three-page advertisement for gemfibrizol in the same issue of *JABFP*, an advertisement that directly precedes the article in question. Even though this is probably a coincidence, the juxtaposition of the study and the advertisement exemplifies the dangers inherent in drug company funding of research evaluating drugs manufactured by the sponsoring company.

Let's discuss the science first. The major justification for publishing this manuscript is that the patient sample is representative of the general population and that the findings are generalizable. But what evidence do we have for this assertion? We know relatively little about the 327 family physicians who are part of the Clinical Experience Network, how they were selected, and whether they are, in fact, representative of the universe of American family physicians. We know nothing about the extent to which the patients studied are representative of other patients in their respective practices. What percentage of all patients with high cholesterol were enrolled, and how many refused to be studied? How many were excluded from the study based on the various exclusion criteria established by the authors? How many patients were enrolled from each practice, and does the sampling strategy actually yield a study population that represents the geographic and demographic distribution of hypercholesterolemic patients in the United States? The discussion of this critical element of the study is incomplete at best.

But the ethical considerations are even more troubling than the inadequate science. The involvement of the pharmaceutical company would appear to introduce a serious potential for conflict of interest in the sponsorship and administration of the study. It is impossible to know whether actual or potential conflict of interest exists because we are given no information about the relationships among the involved individuals and organizations. What are the commercial, contractual, and financial links between the Clinical Experience Network, Health Learning Systems, and Parke-Davis? Did any of the listed authors of the study receive financial compensation from any of the above organizations? Who owns the Clinical Experience Network and Health Learning Systems? Do any of the authors have investments in any of the involved organizational entities? How were the participating physicians recruited, and did they receive any inducements or compensation for participating?

In my opinion, this paper is of limited scientific value and raises serious ethical questions about the propriety of drug company sponsorship of research in primary care. Clinical networks have an important role to play in research, but it is critical that there be no possibility that the commercial interests of the sponsors influence the design of the studies, the analysis of the data, or the presentation of the results. Full disclosure of potential conflicts of interest should be part of the review of all manuscripts, and papers that may be tainted by such actual or potential conflicts should be rejected. Any lesser standard demeans our discipline and undermines the probity of