Correspondence

Nisoldipine and Myocardial Infarction

To the Editor: Estacio et al. (March 5 issue)[1] report an increased incidence of fatal and nonfatal myocardial infarction in patients with hypertension and diabetes who received nisoldipine, in a randomized, prospective, blinded study of moderate as compared with intensive control of hypertension and nisoldipine as compared with enalapril. The increased incidence of fatal and nonfatal myocardial infarction could be due to a deleterious effect of nisoldipine, a protective role of enalapril, or both, but the study design does not allow for further conclusions. Since, as the authors state, the incidence of myocardial infarction in the nisoldipine group was not significantly higher than that in previous studies, a protective effect of enalapril is plausible.

There were no follow-up data on changes in therapeutic insulin doses, antidiabetic-drug requirements, or basal insulin levels in the groups, which could differ significantly because of enhanced insulin sensitivity during treatment with angiotensin-converting–enzyme (ACE) inhibitors.[2] Hyperinsulinemia, a common finding in patients with type 2 diabetes mellitus, is an independent risk factor for coronary heart disease,[3] and plasma insulin levels are known to decrease with ACE-inhibitor therapy.[4] Hence, if enalapril treatment was associated with a significant reduction in insulin requirements or oral antidiabetic-drug requirements, or both, or in basal insulin levels, it could have a protective role by reducing not only hypertension but also hyperinsulinemia, an effect that nisoldipine may not have.

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To the Editor: Despite the authors' care not to make excessive claims, the report on the Appropriate Blood Pressure Control in Diabetes (ABCD) Trial seems incomplete. The data and safety monitoring committee noted a difference between nisoldipine and enalapril, but only in hypertensive patients. We are told, but not shown, that there was no adverse effect of treatment with calcium-channel blockers in normotensive subjects. Although there was no hypothesis that adverse effects would be limited to patients with hypertension, Estacio et al. detailed only the most worrisome part of the findings.

Could *Journal* readers be shown the rest of the data?

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To the Editor: One of the major risk factors for cardiovascular disease in patients with type 2 diabetes is the presence of microalbuminuria ($\geq$20 μg of albumin per minute),[1-5] but there were no data on urinary albumin levels or the percentages of subjects with microalbuminuria in either Table 1 or Table 2 in the article by Estacio et al. Overt albuminuria is listed in Table 2, but it is clear that the cardiovascular risk extends to the microalbuminuric range as well. Could the authors let us know whether the percentages of subjects with microalbuminuria in the two groups were significantly different?

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To the Editor: In 1989, my colleagues and I reported[1] that although nicardipine was associated with an improvement in exercise performance and a decrease in exercise-induced ischemia in 46 patients with stable angina, 6 patients (13 percent) had an ischemic event, unstable angina, or a non–Q-wave myocardial infarction over a relatively short period during treatment with nicardipine. During the placebo period, none of the patients had an ischemic event. Scheidt et al.,[2] using a comparable protocol, reported similar findings: 7 of 66 patients with stable angina had a cardiac event while receiving nicardipine therapy, as compared with 1 patient given placebo. Thadani et al.[3] found that during two weeks of therapy with nisoldipine, 6 of 137 patients with stable coronary disease had a myocardial infarction or unstable angina. No coronary events occurred in the placebo group. In the Holland Interuniversity Nifedipine/Metoprolol Trial, the risk of myocardial infarction within 48 hours was two times higher among the patients with unstable angina who were randomly assigned to treatment with nifedipine than among those assigned to placebo.[4]

I agree with Dr. Cutler's statement, in his editorial,[5] that the ABCD results need to be confirmed by additional randomized trials. However, on the basis of the available data, it is probably prudent not to use, or to use with extreme caution, short-acting dihydropyridines in patients with symptomatic coronary artery disease, particularly since many other therapies are available.

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1. Gheorghiade M, Weiner DA, Chakko S, Lessem JN, Klein MD. Monotherapy of stable angina with nicardipine hydrochloride: double-blind, placebo-controlled, randomized study. Eur Heart J 1989;10:695-701.
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4. Report of the Holland Interuniversity Nifedipine/Metoprolol Trial (HINT) Research Group. Early treatment of unstable angina in the coronary care unit: a randomised, double blind, placebo controlled comparison of recurrent ischaemia in patients treated with nifedipine or metoprolol or both. Br Heart J 1986;56:400-13.
5. Cutler JA. Calcium-channel blockers for hypertension — uncertainty continues. N Engl J Med 1998;338:679-81.

The authors reply:

To the Editor: In response to Dr. Walker: the results we reported were generated by the findings of our data and safety monitoring committee with regard to the difference in the incidence of myocardial infarction between the nisoldipine and enalapril groups in the cohort with hypertension. These findings led to the early termination of the drug comparison in the group with hypertension. The data and safety monitoring committee did not recommend early termination of the drug comparison in the cohort with normotension. These results will therefore be reported later (the study ended on June 30). It is theoretically possible that the difference between the drugs was observed only in the cohort of patients with hypertension because of their exposure to this cardiovascular risk factor for a mean of eight years, whereas the blood pressure was less than 140/90 mm Hg in the cohort with normotension.

We examined factors that may have influenced the incidence of cardiovascular events during the study. In this regard, the enalapril group had a statistically lower level of high-density lipoprotein cholesterol and a higher proportion of subjects with abnormal ankle–brachial indexes. These factors should have placed the patients in the enalapril group at higher risk for cardiovascular events. We agree with Dr. Osende's comments regarding plasma insulin levels and their possible influence on the rate of myocardial infarction in our study. Although plasma insulin levels were not measured, analyses of the use of exogenous insulin and oral hypoglycemic agents during the course of the study did not reveal any differences between the nisoldipine and enalapril groups. In response to Dr. Molitch's comments: the prevalence of microalbuminuria at base line did not differ significantly between the two groups (nisoldipine, 34 percent; enalapril, 28 percent).

The studies cited by Dr. Gheorghiade are interesting, including the study by Thadani et al.,[1] who used the short-acting form of nisoldipine. We agree that "short-acting" calcium antagonists should be used cautiously or should even be avoided, especially in patients at risk for coronary artery disease. Our study, however, used a sustained-release form of the calcium-channel antagonist (nisoldipine CC), which has been demonstrated to have a more blunted sympathetic-activation response than the short-acting forms of the medication.[2]

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1. Thadani U, Zellner SR, Glasser S, et al. Double-blind, dose-response, placebo-controlled multicenter study of nisoldipine: a new second-generation calcium channel blocker in angina pectoris. Circulation 1991;84:2398-408.
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Signal Transduction in Platelets from Patients with Polycythemia Vera

To the Editor: In the February 26 issue, Moliterno et al.[1] report on the reduced expression of the thrombopoietin receptor Mpl as a new characteristic of polycythemia vera and idiopathic myelofibrosis. On the basis of this reduced expression, they suggest a subsequent failure of activation

of the Janus kinase signaling system due to an unknown upstream defect, with subsequent loss of phosphorylation of JAK2 and STAT5. After stimulation of platelets from normal subjects with thrombopoietin or thrombin, the authors observed tyrosine phosphorylation of proteins of approximately 125, 95, and 85 kd. Interestingly, this phosphorylation pattern could be observed in the patients with polycythemia vera only after stimulation with thrombin but not with thrombopoietin. However, the identity of these proteins is not discussed.

Recently, it was shown that thrombopoietin and thrombin induce tyrosine phosphorylation of Vav, a 95-kd protein found mainly in hematopoietic cells, in the platelets of healthy subjects.[2] The same authors also observed a constitutive association of the 28-kd adaptor protein Grb2 with Vav. Another recent observation is the increased tyrosine phosphorylation of the 85-kd regulatory subunit of phosphatidylinositol 3-kinase (PI3K) after thrombopoietin stimulation of the Mpl receptor.[3] Since Vav induces tyrosine phosphorylation of PI3K in human B cells,[4] it seems likely that it is also the activating kinase of PI3K in platelets. An Mpl receptor that had completely lost its capacity to activate JAK and STAT, as a result of a deletion mutation, was shown to activate Vav and other proteins through tyrosine phosphorylation after thrombopoietin stimulation.[3]

Taken together, these observations suggest that it is very likely that the tyrosine-phosphorylated proteins observed after thrombopoietin stimulation of normal platelets are p85, PI3K, and Vav. A candidate substrate for the increased tyrosine phosphorylation of a protein of about 125 kd might be a complex composed of Vav and Grb2, since the authors also report increased phosphorylation of a protein of about 28 kd after both thrombin and thrombopoietin stimulation; another candidate substrate could be p120 Cbl, which was also tyrosine-phosphorylated after stimulation of platelets with thrombopoietin.[5]

The most likely signaling pathway downstream of the Mpl receptor is therefore first mediated by Vav and second, or alternatively, by JAK2. Lack of expression of the Mpl receptor will result in impaired signal transduction due to nonphosphorylation of signaling proteins. The reported lack of phosphorylation of proteins with apparent sizes of 125, 95, and 85 kd, as reported by Moliterno et al., fits very well in this model.

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1. Moliterno AR, Hankins WD, Spivak JL. Impaired expression of the thrombopoietin receptor by platelets from patients with polycythemia vera. N Engl J Med 1998;338:572-80.
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The authors reply:

To the Editor: We thank Lange et al. for their comments. As they indicate, the signal-transduction pathways initiated by Mpl after interaction with its cognate ligand, thrombopoietin, are both multivalent and redundant. Furthermore, thrombin can induce tyrosine phosphorylation of many of the same platelet proteins involved in the signaling cascade induced by thrombopoietin–Mpl, but presumably through a different mechanism.[1,2]

It was not our intention to imply that only the JAK–STAT pathway was involved in thrombopoietin-mediated signal transduction. Indeed, we were unable to identify the activation of TYK2 or the tyrosine phosphorylation of Shc after exposure of platelets from patients with polycythemia vera to thrombopoietin, implying that there was a generalized abnormality in signaling through Mpl that would include the pathways involving Ras, Vav, and p120 Cbl.[3,4] Since our experiments with thrombin indicated that these pathways and the mechanisms to activate them were intact in platelets from patients with polycythemia vera, and since surface expression of Mpl was reduced both functionally and immunologically, we can conclude that thrombopoietin-mediated signal transduction is globally impaired in platelets of patients with polycythemia vera.

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1. Rodriguez-Linares B, Watson SP. Phosphorylation of JAK2 in thrombin-stimulated human platelets. FEBS Lett 1994;352:335-8.
2. Cichowski K, Brugge JS, Brass LF. Thrombin receptor activation and integrin engagement stimulate tyrosine phosphorylation of the proto-oncogene product, $p95^{vav}$, in platelets. J Biol Chem 1996;271:7544-50.
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Risk of Recurrent Seizures

To the Editor: Hauser et al. (Feb. 12 issue)[1] reported on a study of the risk of recurrent seizures after two unprovoked seizures. The small number of patients (63) who had a second seizure represented a highly selected group; 41 had a third seizure, and 26 a fourth. The absence of an association between the type of seizure, age, sex, family history, or other characteristics and recurrent seizures should not be taken to suggest that these characteristics do not influence the risk of a recurrence.

Only 38 percent of the patients with a second seizure and 27 percent of those with a third seizure took their drugs as prescribed. Hauser et al. do not report recurrence rates with compliance taken into account. Patients who do not take their seizure medications as prescribed will almost certainly have higher recurrence rates than those who do — a consideration that may largely, if not completely, ac-

count for the observed relation between recurrence rates and the number of previous seizures.

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1. Hauser WA, Rich SS, Lee J R-J, Annegers JF, Anderson VE. Risk of recurrent seizures after two unprovoked seizures. N Engl J Med 1998;338:429-34.

To the Editor: Were benign childhood epilepsies (e.g., benign rolandic epilepsy) included? Inclusion of such age-specific epilepsies (along with their defining electroencephalographic abnormalities) could have altered the analysis of electroencephalographic findings and clinical classification as predictors of the risk of recurrence of seizures. It may be more useful to separate pediatric and adult age groups or to exclude age-specific epilepsies.

In addition, the identification of seizures on the basis of eyewitness accounts cannot exclude the possibility that some of the events were syncopal convulsions or pseudoseizures. Furthermore, the subclassification of seizures on clinical grounds has been described as too unreliable for use in epidemiologic research.[1]

Most striking, however, is the absence of electroencephalographic data. A study of the risk of recurrent seizures that used a rigorous analysis of electroencephalographic data, while stressing the need to improve interobserver reliability in the interpretation of such data, indicated that epileptiform abnormalities on the electroencephalogram were moderately sensitive (48 percent) and highly specific (>90 percent) in predicting the recurrence of seizures (risk of recurrence, 83 percent in patients with epileptiform abnormalities, 41 percent in those with nonepileptiform abnormalities, and 12 percent in those with normal findings).[2]

Hauser et al. suggest that people with two or more unprovoked seizures should be treated. This may be true, but it ignores the fact that studies of recurrent seizures have invariably shown that treatment with antiepileptic medication results in either no decrease in the risk of recurrence[3] or a mild increase.[4,5] Such unexpected findings have been credibly rationalized in each case,[3-5] but proof of efficacy is still lacking.

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5. Hauser WA, Rich SS, Annegers JF, Anderson VE. Seizure recurrence after a 1st unprovoked seizure: an extended follow-up. Neurology 1990;40:1163-70.

The authors reply:

To the Editor: Most people with unprovoked seizures present after multiple seizures (established epilepsy). To provide an accurate estimate of the natural history, we endeavored to identify persons with an unequivocal first seizure and then examine patterns of recurrence. We excluded persons with equivocal symptoms, as well as those with multiple episodes. The accuracy of the classification of a first seizure might be questioned, but our report deals exclusively with persons who had a second seizure. Thus, misclassification of nonseizure events as seizures was unlikely.

Pseudoseizures are rare in the general population (incidence, 2 cases per 100,000 per year) and they seldom present as a single seizure.[1] Most epidemiologic studies have relied on a clinical classification of seizures. We also had detailed data from neurologic examinations and electroencephalographic studies in all cases and brain imaging in most, which we chose to use as variables for secondary analyses.

We have no explanation for the disproportionate number of males in our study group. The incidence of a first unprovoked seizure is higher in males than in females, but the differences in our study exceed the expected difference.[2] Since the study was observational, there were no impediments to the participation of women. Sex was not a predictor of recurrence in any group.

Because of the low recurrence rate after a first seizure, the power of many analyses was limited. Electroencephalographic evidence of epileptiform activity was a strong predictor of a second seizure after the first, but epileptiform activity did not predict additional seizures after the second. The point estimates for a recurrence five years after the second seizure were virtually identical in patients with and in those without epileptiform activity, suggesting the need for an enormous sample to demonstrate a statistically significant difference, which, if it exists, is unlikely to be clinically relevant.

Observational studies have not demonstrated the efficacy of treatment, but we suspect that, as in our study, compliance is poor. The risks of recurrence after a first seizure in our study are similar to those reported by Shinnar et al. in untreated children.[3] The efficacy of antiseizure medication in patients with a first seizure is best established by the Italian First Seizure Trial Group.[4] Some antiseizure medications will induce or exacerbate seizures in patients with established epilepsy. There are no data on this effect in patients with a single seizure.

No case met the criteria for benign rolandic epilepsy. This syndrome is defined on the basis of a unique epileptiform discharge and is associated with a high risk of recurrence. Only 30 percent of such cases present as a first seizure.[5] There were few children under the age of 10 years in our series, but age analyzed as both a continuous and a dichotomous variable (<15 years and ≥15 years) did not predict recurrence. Data on nutrition and stress were not systematically collected.

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1. Sigurdardottir KR, Olaffson E. Incidence of psychogenic seizures in adults: a population based study in Iceland. Epilepsia (in press).
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Patients with Alcohol Problems

To the Editor: In their excellent review of alcohol problems, O'Connor and Schottenfeld (Feb. 26 issue)[1] discuss several ways to treat the alcohol withdrawal syndrome. Although infrequently used therapies such as carbamazepine are considered, the authors do not mention chlormethiazole (clomethiazole), a derivative of vitamin B_1 with sedative and anticonvulsant properties, which is widely used in Europe but not approved for use in the United States.[2] Like benzodiazepines, chlormethiazole can cause respiratory depression, which is the main factor limiting its use. It controls agitation and seizures effectively. The availability of solutions containing 4 g of chlormethiazole in 500 ml of water allows for continuous intravenous administration with adjustment of the dose according to the clinical symptoms, resulting in stable plasma levels.

A recent meta-analysis of therapies for alcohol withdrawal concluded that chlormethiazole was superior to placebo, but the inadequacy of the sample size did not allow for definitive conclusions about the prevention of seizures and delirium.[3] The authors also concluded that beta-blockers, carbamazepine, and clonidine, all mentioned as possible therapies by O'Connor and Schottenfeld, should not be recommended as monotherapy, since they have not been shown to reduce delirium or seizures.

Furthermore, chlormethiazole has been shown to inhibit the activity of cytochrome P-450 2E1 in humans. This activity is increased in patients with alcoholism and has detrimental effects on the liver through free-radical formation.[4]

Although data supporting the use of this drug in Europe are admittedly scanty, there may be some advantages to using chlormethiazole that justify a comparison with benzodiazepines.

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1. O'Connor PG, Schottenfeld RS. Patients with alcohol problems. N Engl J Med 1998;338:592-602.
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To the Editor: The excellent review of alcohol problems by O'Connor and Schottenfeld does not mention γ-hydroxybutyric acid (GHB) either in the management of the alcohol withdrawal syndrome or in the prevention of relapse. GHB has been shown to be effective in suppressing the alcohol withdrawal syndrome,[1] reducing the craving for alcohol,[2,3] and maintaining abstinence.[4]

In particular, a placebo-controlled trial involving 23 subjects showed that GHB (50 mg per kilogram of body weight) was very effective in suppressing withdrawal symptoms during a seven-hour observation period and was well tolerated.[1] A further randomized, placebo-controlled trial in 82 subjects showed that the same dose of GHB fractionated into three daily doses for three months was more effective than placebo in increasing the number of days of abstinence and reducing the number of daily drinks and the craving for alcohol in patients with alcoholism.[2] Recently, the same dosage was used for six months in 179 patients with alcoholism.[3] Of the 109 subjects who completed the study, 78 percent remained abstinent throughout the six-month period of drug administration. More recently, we showed that greater fractionation (into six doses) of the same dose of GHB increases the abstinence rate in patients with alcoholism who do not have a response to the conventional fractionation of the drug[4]; among the 119 patients who received this treatment, no abuse of GHB was reported.

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1. Gallimberti L, Canton G, Gentile N, et al. Gamma-hydroxybutyric acid for treatment of alcohol withdrawal syndrome. Lancet 1989;2:787-9.
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To the Editor: The article on patients with alcohol problems is both comprehensive and up to date. In recommending an approach to obtaining alcohol-related information, the authors suggest first asking about the quantity and frequency of consumption and then asking the CAGE questions. This is also the approach suggested in *The Physicians' Guide to Helping Patients with Alcohol Problems.*[1]

However, asking patients first about amounts of alcohol consumed may be confrontational and, if so, may result in

less accurate and less useful information. A small study confirmed this hypothesis, finding that when patients with alcoholism were randomly assigned to be asked the CAGE questions after an open-ended question ("Please tell me about your drinking") or after being asked about amounts of alcohol consumed, the CAGE questions were much less sensitive for detecting alcoholism in the latter group (32 percent) than in the former group (95 percent).[2] Therefore, I would recommend routinely asking the CAGE questions just after finding out that a patient drinks and before asking about amounts.

Physicians should at least be cognizant that questions about amounts of alcohol consumed can be threatening to some patients, particularly those with alcohol problems. Regardless of the order in which the questions are asked, the history should be taken in an empathetic, nonconfrontational manner.[3]

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2. Steinweg DL, Worth H. Alcoholism: the keys to the CAGE. Am J Med 1993;94:520-3.
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The authors reply:

To the Editor: Concerning the comments of Drs. Garcia-Monco and Gomez Beldarrain, chlormethiazole is an interesting agent about which there are few data. Although one study compared chlormethiazole with chlordiazepoxide and found them to be "equally effective," only 22 patients were randomly assigned to these treatments.[1] As we stated in our article, we believe that agents such as beta-blockers, clonidine, and carbamepazine are best viewed as adjunctive rather than primary therapies, especially since benzodiazepines have been established as effective in managing withdrawal symptoms and preventing severe withdrawal and seizures.

The comments of Dr. Addolorato and his colleagues concerning GHB are also of interest, given the potential of this agent for both ameliorating withdrawal and preventing relapse. As with chlormethiazole, GHB needs to be evaluated more extensively and compared with benzodiazepines in the treatment of withdrawal before it can be considered for routine use. In addition, there is no evidence that either agent is effective in reducing delirium or seizures.[2] The potential use of GHB as a therapy to prevent relapse will also require clinical trials. Finally, GHB has recently emerged as an important drug of abuse,[3] and at least one GHB-associated death has been reported.[4] Along with physical dependence, the adverse effects of GHB abuse include delirium, seizures, and coma,[3] and GHB has been identified as a potential "date rape" drug.[4]

Dr. Saitz brings up an interesting point about how to use screening instruments such as the CAGE questionnaire. Clearly, an empathetic and nonconfrontational approach is needed whenever alcohol problems are discussed. Before asking the CAGE questions, the physician needs to determine whether a patient has used any alcohol. Whether the physician should then ask the CAGE questions or obtain a detailed history of quantity and frequency may be more a matter of style than of science. Some patients may feel threatened by being asked about quantity and frequency or by being asked the CAGE questions, regardless of when they are asked. Physicians who are alert to these issues and who ask the questions in an open-ended, matter-of-fact manner might decide on the order in which the questions are asked according to the individual patient and the flow of the interview.

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Platelet Satellitism

To the Editor: With respect to the image of platelet satellitism presented by Drs. Shahab and Evans (Feb. 26 issue)[1]: complexes of platelets and polymorphonuclear neutrophils are not solely an in vitro phenomenon seen in blood treated with EDTA as an anticoagulant. Complexes of platelets and polymorphonuclear neutrophils can be observed in whole blood treated with citrate and heparin as anticoagulants.[2] Similar observations have been made in a variety of separated cell systems under static and dynamic conditions.[3] These complexes are principally dependent on the platelet alpha-granule glycoprotein CD62P (P-selectin), which is rapidly expressed on the platelet surface after exposure to a stimulus to activation. The platelet fibrinogen receptor glycoprotein IIb/IIIa and the neutrophil β_2 integrin CD11b/CD18 are also involved in the formation of polymorphonuclear neutrophils.[3] In contrast to the rosettes observed by Drs. Shahab and Evans, polymorphonuclear neutrophils are dependent on divalent cations and are abolished by anticoagulation with EDTA. Polymorphonuclear neutrophils have been observed in a number of patient populations and may reflect the extent of platelet activation in vivo.[4] Polymorphonuclear neutrophils consist of activated subpopulations of both cell types, with complexes of neutrophils having greater expression of β_2 integrins than cells that are not in complexes.[2] In view of recent work describing how immobilized platelets can support multistep inflammatory-cell adhesion and transmigration in a manner similar to that of the vascular endothelium,[5] polymorphonuclear neutrophils may be of considerable physiologic importance.

Although artifactual platelet rosetting can occur and

may be a cause of spurious thrombocytopenia, the presence of polymorphonuclear neutrophils may also lead to a decrease in free platelets in vivo, and this will not be detected by standard methods of platelet enumeration. Platelet–leukocyte interactions are important in modulating inflammation and hemostasis and should not be confused with the image presented by Drs. Shahab and Evans.

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The authors reply:

To the Editor: We agree with the comment of Peters et al. regarding platelet–neutrophil interactions in vivo and their importance in modulating inflammation and hemostasis. However, platelet satellitism as we described it is a different phenomenon. It is observed solely after blood treated with an anticoagulant is incubated at room temperature.[1] It is not reproduced if blood is incubated at body temperature or smears are made immediately from either blood treated with EDTA as an anticoagulant or capillary blood.[1,2] We agree with Peters et al. that under similar conditions, both heparin-treated blood and citrated blood have occasionally been observed to produce the same phenomenon.[1] However, others have not observed this effect with anticoagulants other than EDTA.[2]

The underlying mechanism of platelet satellitism is not fully understood. IgG autoantibodies have been implicated,[3] and more recent studies have indicated that these autoantibodies are directed against the glycoprotein IIb/IIIa complex of the platelet membrane and the neutrophil Fcγ receptor III (CD16).[4] It was postulated that at low temperatures, the chelation of calcium ions by EDTA alters the conformation of the glycoprotein IIb/IIIa complex of platelets and the Fcγ receptor III of neutrophils. This change may unmask epitopes for the IgG autoantibody, which forms a bridge between platelets and neutrophils, and hence, reveal the hematologic picture.[4] An alternative, nonimmunologic mechanism has been proposed by Christopoulos and Mattock, who suggested that thrombospondin or some other alpha-granule platelet protein had a role after they observed that adherence to neutrophils involved only platelets that stained strongly for thrombospondin.[5]

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Airbag Safety and the Distance of the Driver from the Steering Wheel

To the Editor: Actuarial data indicate that driver-side airbags reduce the overall risk of death from a car accident by 11 percent,[1] but airbag-induced injuries (both fatal and nonfatal) have been reported.[2] The driver's proximity to the airbag is an important safety issue. Under a new government policy, drivers are being encouraged to maintain a safe distance from the steering wheel or, if that is not feasible, to obtain a manual cutoff switch for their airbags.[3] Yet drivers may not properly estimate their proximity to the steering wheel.

In order to evaluate the degree of misperception, we conducted a cross-sectional survey of 1000 drivers at gas stations in the Boston metropolitan area. Proximity was defined as the distance between the center of the steering wheel and the bridge of the driver's nose, as perceived by each driver and as measured with a tape measure by trained interviewers. We compared the perceived and actual distances, documenting the number of drivers who estimated that they were or who actually were sitting with the bridges of their noses within 12 in. (30 cm) of the steering wheel.

The correlation between perceived and actual distances

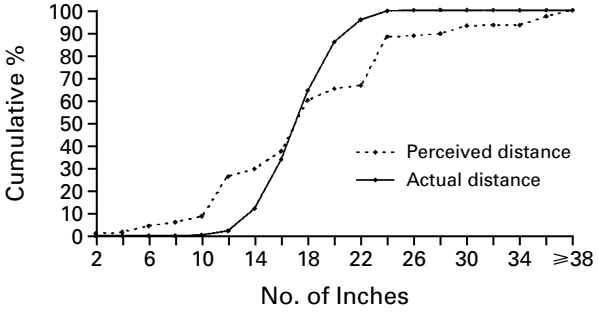

Figure 1. Perceived and Actual Distances from the Driver's Nose to the Steering Wheel.

was very low ($r=0.24$), with some drivers underestimating and others overestimating their proximity (Fig. 1). Although 234 of the drivers (mostly women) thought that they sat within 12 in. of the steering wheel, only 22 drivers (19 women and 3 men) actually did. Of these 22 drivers, only 8 correctly perceived that they sat within 12 in.

A limitation of our study is that the new regulation defines the safe distance as 10 in. (25 cm) from the breastbone to the steering wheel. We suspect that a considerable number of drivers will also misperceive their risk according to this alternative definition of safe distance.

Drivers who think they sit too close to the wheel but actually do not may be inappropriately concerned about their safety and disconnect their airbag systems, thus losing safety benefits. In contrast, drivers who actually sit too close but do not think they do may not be concerned enough. Since a petition for airbag disconnection must be submitted by the owner of the vehicle and the driver's risk status cannot be corroborated, physicians and policy makers should be aware of this problem of misperception and take a proactive approach to help identify the people truly at risk for injury from airbags. Drivers should be encouraged to measure objectively their distance from the airbag in a normal driving situation.

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