Effects of Gemfibrozil on Triglyceride Levels in Patients With NIDDM

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Hyperlipidemia in Diabetes Investigators

OBJECTIVE — Patients with NIDDM have a two- to fourfold increased risk of macrovascular disease. The constellation of elevated TGs and decreased HDL cholesterol are recognized as risk factors and constitute the major dyslipidemia in NIDDM. We therefore sought to determine if gemfibrozil (600 mg b.i.d.) was effective in correcting the dyslipidemia of NIDDM.

RESEARCH DESIGN AND METHODS — After 8 wk of placebo stabilization, 442 patients from 46 study centers were randomized to double-blind treatment; in a designated 2:1 ratio, 295 received gemfibrozil and 147 received placebo for 20 wk. The primary end point was plasma TG; secondary end points were TC, LDL cholesterol, VLDL cholesterol, HDL cholesterol, and HbA1c. No baseline differences were noted between groups in sex, age, weight, type of diabetic therapy, fasting plasma levels of TGs, HbA1c, or C-peptide. About two-thirds received oral hypoglycemic drugs, one-third insulin.

RESULTS — TG fell 26.4% in the gemfibrozil group and rose 7.4% in the placebo group (P < 0.023), by an intent-to-treat analysis. When patients who were noncompliant or with inadequate data were excluded, similar results were found—a 30.4% fall with gemfibrozil and a 4.8% increase with placebo (P < 0.0001). TG levels fell within 4 wk and remained low for 20 wk (P < 0.001). Mean HDL cholesterol rose by 4 wk and increased further at 12 wk (8–12%), P < 0.0001. TC fell. We observed a significant rise in LDL cholesterol in both gemfibrozil- and placebo-treated groups, with no significant differences between these groups. Changes in HbA1c were similar in gemfibrozil and placebo groups. No differences were observed in responses in groups treated with insulin and or oral hypoglycemic drugs. Overall AE s that were clinically important occurred in 6.1% in the gemfibrozil group vs. 2.0% in the placebo group (NS).

CONCLUSIONS — We conclude that gemfibrozil is an effective and safe agent in combating the dyslipidemia of NIDDM, irrespective of type of diabetic therapy.


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NIDDM, non-insulin-dependent diabetes mellitus; TG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very-low-density lipoprotein; TC, total cholesterol; NS, no significance; CAD, coronary artery disease; ANCOVA, analysis of covariance; AE, adverse event.

The role of hypertriglyceridemia as a risk factor in CAD has been the subject of considerable debate. Although hypertriglyceridemia may not be an independent risk factor, elevated TG levels certainly amplify CAD risk in patients with high TC/HDL-cholesterol ratios.

In the Prospective Cardiovascular Munster (PROCAM) Study, the rate of CAD per 1000 was nearly twice as high after just 4 yr of follow-up in men who had hypertriglyceridemia (≥200 mg/dl) and TC/HDL-cholesterol ratios >5.0 compared with men with normal TG levels and the same TC/HDL-cholesterol ratios (1). In hypertriglyceridemic men with TC/HDL-cholesterol ratios >5.0 who also had HDL-cholesterol levels <35 mg/dl, the incidence of CAD was more than eightfold higher than in normotriglyceridemic men with the same TC/HDL-cholesterol ratios and HDL-cholesterol levels >35 mg/dl (1). In the Framingham Heart Study, patients with hypertriglyceridemia were at high risk for CAD if their TC/HDL-cholesterol ratios were >4.5 (2).

Such findings in the general population have prompted experts to recommend that TG levels ≥200 mg/dl warrant investigation and possible intervention (3). Very often, hypertriglyceridemia clusters with other CAD risk factors, notably low HDL-cholesterol levels, hypertension, obesity, and insulin resistance.

Diabetes and dyslipidemia

The high-risk profile of hypertriglyceridemia and low HDL cholesterol is particularly prevalent in patients with NIDDM*. About 50% of all NIDDM patients are dyslipidemic (4); the hallmark abnormalities are elevated plasma TG levels (>150 mg/dl, i.e., diabetic dyslipidemia) and reduced HDL-cholesterol levels (<45 mg/dl). Less commonly, plasma LDL-cholesterol concentrations also may be elevated (≥130 mg/dl, i.e., mixed dyslipidemia).

Dyslipidemia substantially in-
creases the likelihood of serious cardiovascular problems in NIDDM patients, a population already at high risk of adverse cardiovascular changes associated with hypertension and hyperinsulinemia (5).

CAD is two to four times more common in diabetic than in nondiabetic individuals (6), and coronary atherosclerosis accounts for ~60% of all deaths in diabetic subjects (7). In fact, >75% of all hospitalizations for diabetic complications are attributable to CAD (8). Diabetic women are at particularly high risk for CAD (6) and myocardial infarction (9) as diabetes removes the protection that premenopausal women appear to have against CAD.

Therefore, the presence of mixed dyslipidemia in diabetic patients—especially those with NIDDM—superimposed on hyperinsulinemia and hypertension, often seen in these patients, constitutes an especially atherogenic profile. This, in turn, may be magnified by qualitative lipoprotein changes in diabetics, such as glycosylation and oxidation (10).

Diet, exercise, and glycemic control are first-line measures for managing dyslipidemia in the diabetic patient (8). These measures, although often beneficial, may not normalize lipid levels, because they do not necessarily completely correct the metabolic derangements, particularly in NIDDM patients (11–17).

In view of the high incidence of persistent dyslipidemia and CAD coincident with diabetes, greater attention must be given to correcting dyslipidemia in diabetic patients with lipid-lowering therapy, even in those patients with good glycemic control. Although the beneficial effects of normalizing lipids in NIDDM patients have not been studied in terms of reduced CAD morbidity/mortality, correction of dyslipidemias has been shown to significantly reduce cardiac end points in nondiabetic patients with elevated plasma LDL cholesterol and TG and low HDL-cholesterol levels (18).

To achieve similar benefits in diabetic patients, however, consideration should be given to tailoring lipid-lowering therapy to the specific needs of this patient population. Of particular concern is the effect of hypolipidemic therapy on glucose control. An agent that improves lipid levels while negatively affecting glucose control may offer less overall benefit in diabetes treatment.

In this study, we examined the efficacy of gemfibrozil in reducing TG levels in patients with NIDDM, independent of changes in nutritional regulation and glycemic control.

RESEARCH DESIGN AND METHODS

Study design
Patients were recruited from the general population served by each participating site. Initial screening was for patients with NIDDM (defined by national diabetes data group criteria) who were being treated with diet and either oral hypoglycemic agents or insulin. All patients were required to sign informed consent, and the study was approved by the committees for protection of human rights and the institutional review boards at each site.

A minimum of 10 patient visits were scheduled during the screening, placebo lead-in, and double-blind treatment phases. A timetable of clinic visits is given in Fig. 1.

Before entering the double-blind treatment phase, subjects completed an 8-wk placebo lead-in period to establish baseline lipid values and glycemic control during a prescribed dietary regimen (American Diabetes Association diet). For entry into the double-blind phase, patients had to have mean stable TG levels of 150–500 mg/dl and good glycemic control (HbA1c <10%) 1 wk before randomization.

Patients who met these criteria were randomized to receive either gemfibrozil (600 mg b.i.d.) or matched placebo (b.i.d.) (2:1 ratio) for a 20-wk double-blind period. Patients were stratified according to their current treatment with oral agents or insulin.

During double-blind treatment, efforts were made to maintain, rather than intensify, diabetic control. Therefore, changes in diabetic treatment were permitted only if a patient became symptomatically hypo- or hyperglycemic.

Serum lipid levels and clinical chemistries were measured at wk 4, 12, and 20. Data were analyzed for TG levels as the primary end point with HDL cholesterol, TC, and LDL cholesterol as secondary end points. Safety indexes included adverse clinical events, clinical laboratory measurements, and physical examination data.
Table 1—Prestudy clinical characteristics of patients randomized to treatment

<table>
<thead>
<tr>
<th></th>
<th>GEMFIBROZIL</th>
<th>PLACEBO</th>
<th>ALL PATIENTS</th>
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<tbody>
<tr>
<td>N</td>
<td>295</td>
<td>147</td>
<td>442</td>
</tr>
<tr>
<td>SEX (MEN/WOMEN)</td>
<td>149/146</td>
<td>76/71</td>
<td>225/217</td>
</tr>
<tr>
<td>AGE (YR)</td>
<td>58.6 ± 9.8 (36–84)</td>
<td>58.4 ± 10.0 (38–82)</td>
<td>58.5 ± 9.9 (36–84)</td>
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<tr>
<td>WEIGHT (LB)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>MEN</td>
<td>203.8 ± 32.1</td>
<td>214.7 ± 33.1</td>
<td>207.5 ± 32.7</td>
</tr>
<tr>
<td>WOMEN</td>
<td>175.5 ± 27.6</td>
<td>175.3 ± 35.4</td>
<td>175.4 ± 30.3</td>
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<tr>
<td>DIABETIC THERAPY TYPE* (%)</td>
<td></td>
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<tr>
<td>ORAL</td>
<td>192 ± 65.1</td>
<td>96 ± 65.3</td>
<td>288 ± 65.2</td>
</tr>
<tr>
<td>INSULIN</td>
<td>99 ± 33.6</td>
<td>49 ± 33.3</td>
<td>148 ± 33.5</td>
</tr>
<tr>
<td>TGs (MG/DL)</td>
<td>273.1 ± 84.8</td>
<td>270.8 ± 110.4</td>
<td>272.3 ± 94.2</td>
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<tr>
<td>HbA1c (%)</td>
<td>6.85 ± 1.51</td>
<td>6.61 ± 1.45</td>
<td>6.77 ± 1.49</td>
</tr>
<tr>
<td>C-peptide (NG/ML)</td>
<td>3.31 ± 1.48</td>
<td>3.18 ± 1.31</td>
<td>3.27 ± 1.43</td>
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</tbody>
</table>

Values are means ± SD, with ranges in parentheses. n, number of patients.
*Six patients were on oral and insulin therapies or on neither therapy.

before discontinuation (if tested within 7 days of final treatment dose). Additional analyses were performed using the subgroup of patients who adhered to the protocol and had valid data. Efficacy data were not included in analyses if a patient visit did not occur within 7 days of the scheduled appointment. Patients were removed from the study for repeated noncompliance or missing all scheduled doses of study medication for 72 h. Only four patients were excluded on the basis of compliance using the criterion of missing ≥25% of study medication during the double-blind phase.

Single-point analysis used final baseline and final end-of-treatment values.

In three-point averaging, the values used in the preliminary trend analysis were averaged to obtain baseline and end-of-treatment data.

The constant group included only those patients with valid data at wk 4, 12, and 20 of double-blind treatment, to better depict any time trends using the same patients. Percentage changes in lipid levels from baseline to end of treatment were evaluated by using a three-way ANOVA model including treatment group, diabetic therapy, and study center as main effects, and treatment by diabetic therapy interaction. Changes at wk 4, 12, and 20 were also assessed by using the three-way ANOVA model. ANOVA and ANCOVA models were used to determine if age, sex, or baseline TG levels affected changes in TG levels, and to assess the relationship between glycemic control and TG changes. All statistical tests were two-sided with α = 0.05. All underlying assumptions were tested, and pertinent analyses were performed. Intent-to-treat and single-point analysis results are given for the secondary end points.

Laboratory measurements
Total TGs in serum were measured using an enzymatic method. TC and HDL cholesterol were measured in serum by automated chemistry. LDL cholesterol was calculated by the following formula: LDL cholesterol = TC − HDL cholesterol − (0.2 × TGs). Although this formula gives spurious values when TGs are >350–400 mg/dl, the cohort included few such patients, and they were equally distributed in the treatment and placebo groups. HbA1c was measured with the Bio-Rad Diamat fully automated analyzer, which uses ion exchange chromatography (Richmond, CA).

RESULTS—A total of 442 patients were randomized to treatment at 46 centers: 295 to gemfibrozil, 147 to placebo. Baseline patient characteristics are summarized in Table 1. The two groups were evenly matched with regard to sex, age, and previous therapy with oral agents or insulin. Of all randomized patients, 380 completed the study (248 gemfibrozil [84.1%]; 132 placebo [89.8%]). All enrolled patients were analyzed in the intent-to-treat analysis. Because of protocol violations and insufficient data, only 73% of patients are included in the other analyses (Table 2).

Efficacy TG. Mean baseline TG levels were 273.1 mg/dl for the gemfibrozil group and 270.8 mg/dl for the placebo group. Table 3 shows the mean plasma TG changes from baseline to end of treatment. By all methods of analysis, the decreases in TGs were statistically (P < 0.0001) significantly greater for the gemfibrozil-treated patients than the placebo-treated patients who experienced a statistically significant increase in TG levels using the intent-to-treat analysis. Figure 2 shows the changes in TG levels over the 20-wk treatment period with the constant group patients. At wk 20, plasma TG levels had fallen to 177 mg/dl in the gemfibrozil group, but had increased significantly (P < 0.05) in the...
Gemfibrozil effects on triglyceride levels

Table 2—Patients evaluated for changes in TGs (inclusions and exclusions)

<table>
<thead>
<tr>
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<th>GEMFIBROZIL</th>
<th>PLACEBO</th>
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<tr>
<td><strong>N</strong></td>
<td>295</td>
<td>147</td>
</tr>
<tr>
<td><strong>%</strong></td>
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<td>100</td>
</tr>
<tr>
<td><strong>Total Randomized</strong></td>
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<tr>
<td><strong>Excluded</strong></td>
<td>81</td>
<td>38</td>
</tr>
<tr>
<td><strong>Excluded</strong></td>
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<tr>
<td><strong>Compliance exclusion</strong></td>
<td>40</td>
<td>22</td>
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<tr>
<td><strong>Insufficient data</strong></td>
<td>41</td>
<td>16</td>
</tr>
<tr>
<td><strong>Included</strong></td>
<td>214</td>
<td>109</td>
</tr>
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</table>

*From single-point and three-point averaging analysis.

placebo group. Using single-point analysis, the differences between the gemfibrozil and placebo groups were significant ($P < 0.001$) at wk 4, 12, and 20. After 4 wk, gemfibrozil had reduced plasma TG levels by 31.6%. This reduction was sustained for the duration of the study and was independent of type of diabetic therapy (Fig. 3). In contrast, plasma TG levels in the placebo patients rose significantly at wk 20 of the study.

**HDL cholesterol.** Gemfibrozil treatment was associated with significant increases in HDL cholesterol ($P < 0.001$ vs. baseline; Fig. 4). Whereas the peak effect of gemfibrozil on TGs had occurred by wk 4, HDL-cholesterol levels continued to increase with sustained gemfibrozil therapy, peaking at the 12-wk measurement. HDL-cholesterol levels increased 8.4% by wk 4 and 12.2% by wk 12 of gemfibrozil treatment (Fig. 4). Using single-point analysis, statistically significant increases in HDL-cholesterol levels with gemfibrozil were seen regardless of diabetic therapy (Fig. 5). In patients taking insulin, the increase in HDL cholesterol tended to be slightly lower than that in patients taking oral agents at wk 12 and 20. By wk 20, insulin-treated placebo patients experienced a statistically significant increase in HDL cholesterol.

**Figure 2**—Mean TG levels at wk 4, 12, and 20 of double-blind treatment period. The fall in TGs with the gemfibrozil-treated group was significant ($P < 0.05$) from baseline at wk 4, 12, and 20. Differences between the gemfibrozil-treated group and the placebo-treated group were significant ($***P < 0.001$) at wk 4, 12, and 20. A significant ($^*P < 0.05$) rise occurred in TGs at wk 20 of placebo treatment.

**Figure 3**—Mean changes in TG levels by diabetic therapy (oral versus insulin) at wk 4, 12, and 20 of double-blind treatment period (gemfibrozil, $n = 197$; placebo, $n = 100$; $§P < 0.001$ from baseline in the gemfibrozil-treated group at wk 4, 12, and 20, irrespective of diabetic therapy. Differences between gemfibrozil and placebo were significant ($^*P < 0.001$) at wk 4, 12, and 20.

Table 3—Mean plasma TG changes from baseline

<table>
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<tr>
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<td><strong>INTENT TO TREAT</strong></td>
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</tr>
<tr>
<td><strong>Baseline</strong></td>
<td>273</td>
<td>271</td>
</tr>
<tr>
<td><strong>Mean (mg/dL)</strong></td>
<td>295</td>
<td>147</td>
</tr>
<tr>
<td><strong>% Change</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Baseline</strong></td>
<td>-26.4*</td>
<td>+7.4</td>
</tr>
<tr>
<td><strong>Mean (mg/dL)</strong></td>
<td>266</td>
<td>269</td>
</tr>
<tr>
<td><strong>% Change</strong></td>
<td>-27.9*</td>
<td>+8.1</td>
</tr>
<tr>
<td><strong>Baseline</strong></td>
<td>179</td>
<td>273</td>
</tr>
<tr>
<td><strong>Mean (mg/dL)</strong></td>
<td>214</td>
<td>109</td>
</tr>
<tr>
<td><strong>% Change</strong></td>
<td>-30.4*</td>
<td>+4.8</td>
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<tr>
<td><strong>Baseline</strong></td>
<td>180</td>
<td>265</td>
</tr>
<tr>
<td><strong>Mean (mg/dL)</strong></td>
<td>214</td>
<td>109</td>
</tr>
<tr>
<td><strong>% Change</strong></td>
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* $P < 0.0001$ (paired Student's $t$ test for changes from baseline).

$^*P < 0.05$ (paired Student's $t$ test for changes from baseline).
Figure 4—Mean HDL-cholesterol levels at wk 4, 12, and 20 of double-blind treatment period. The rise in HDL cholesterol was significant (§P < 0.001) from baseline at wk 4, 12, and 20 in the gemfibrozil-treated group and were significantly (***P < 0.001) different than the placebo-treated group. A significant (†P < 0.05) rise occurred in HDL cholesterol at wk 20 of placebo treatment.

TC. As Fig. 6 shows, mean decreases in TC were statistically significant in gemfibrozil-treated patients at weeks 4, 12, and 20, whereas placebo-treated patients experienced statistically significant increases in TC at wk 12 and 20. By wk 12 and 20, TC levels tended to rise in both placebo and gemfibrozil-treated patients (P < 0.05).

LDL cholesterol. In the gemfibrozil and placebo treatment groups, LDL-cholesterol levels rose and were significantly (P < 0.05) above baseline at wk 12 and 20 in gemfibrozil-treated patients and at wk 4 and 12 in placebo-treated patients. The differences between gemfibrozil and placebo, however, were not significant (Fig. 7).

Glycemic control. As measured by HbA1c levels, glycemic control increased from baseline in the placebo-treated group (from 6.53 to 6.94%) and the gemfibrozil-treated group (from 6.8 to 7.31%). The percentage changes, 7.2 and 8.6, respectively, were not significantly different.

Safety
Of the 442 patients randomized to treatment, 64.7% on gemfibrozil and 55.1% on placebo reported AEs (P < 0.05; Table 4). Generally, side effects tended to be mild. The most frequently reported associated side effects were headache (1.8% of patients), diarrhea (1.6%), nausea (1.6%), abdominal pain (1.4%), and asthenia (1.4%).

Gastrointestinal side effects were more common with gemfibrozil, although only for patients on insulin therapy. Statistically significant weight loss (1.5 lb) occurred in the gemfibrozil-treated group.

A greater number of patients treated with gemfibrozil than placebo had AEs that led to withdrawal from the study (8.5 vs. 3.4%, respectively; P < 0.05). However, only 6.1% of the patients on gemfibrozil and 2.0% of those on placebo had AEs that were considered clinically important (NS). Placebo and gemfibrozil treatments had similar incidences of associated AEs—i.e., AEs with definite, probable, or possible relation to treatment (gemfibrozil, 12.2 vs. placebo, 13.6%).

CONCLUSIONS
This study is the largest to date to examine the specific effects of gemfibrozil or any hypolipidemic agent in patients with NIDDM. In this multicenter study, 442 patients were randomized to receive either gemfibrozil or matched placebo for 20 wk of double-blind treatment. Our results demonstrate that gemfibrozil is effective in correcting the two most common lipid abnormalities of NIDDM, i.e.,
hypertriglyceridemia and low HDL-cholesterol levels. In our study, the lipid-lowering effects of gemfibrozil were independent of type of concomitant therapy for glycemic control.

This study was carefully designed so that the specific effects of gemfibrozil treatment on lipid levels could be analyzed without interference from such confounding variables as diet and glucose control. To qualify for inclusion, patients had to have verifiable NIDDM and elevated G (in the range encountered in NIDDM) and demonstrate reasonable glycemic control as measured by HbA1c.

An 8-wk placebo lead-in period before double-blind treatment allowed monitoring and stabilization of glycemic control and lipids. Patients with unstable TGs were excluded from consideration. Patients were closely monitored for compliance with the study regimens. Trend analysis in the placebo lead-in period showed no tendency for TGs to change.

There was, however, a 26% dropout from placebo treatment and 27% from gemfibrozil (Table 2), raising concern as to the validity of the analysis. To test the validity of the results and determine whether they were affected by patient dropouts, several analytical methods were used, including intent-to-treat, evaluable results, and constant group (patients in whom all data was available). By all analyses, gemfibrozil significantly lowered plasma TG and TC levels, and an increase in HDL-cholesterol levels, without a significant effect on diabetic status (19–28). However, these were short-term studies of small numbers of patients. Furthermore, they were not controlled for such confounding factors as diet and glycemic control, nor were patients carefully screened to provide a well-defined population of patients with both NIDDM and hypertriglyceridemia.

A major concern in clinical studies of this nature is the tendency for biochemical parameters to regress towards the mean. To eliminate this possibility, we established an 8-wk baseline period. Trend analysis revealed no significant change over this period, indicating that these values are constant and that the late rise in TG values in placebo-treated patients represents a real change. This is a paradoxical study effect, wherein patients entered into a study who receive any drug may have relaxed dietary and diabetic therapy with the consequent rise in TGs. Active lipid-lowering drug presumably masks this tendency.

We also noted a significant, albeit small (mean 1.5 lb) weight loss in the gemfibrozil-treated group. Analysis of the relationship between weight and changes in TGs showed no correlation, and it is unlikely that this small weight change in a largely obese group accounted for the plasma TG change.

Our findings of an increase in HDL cholesterol induced by gemfibrozil are consistent with those reported in the study of a generally nondiabetic population (18). However, others have reported an effect of gemfibrozil to increase LDL cholesterol (29). Our data demonstrate a slight rise in LDL cholesterol in both placebo and gemfibrozil-treated patients. However, between the two groups, the differences were not significant. Factors such as diet and diabetic therapy may have an impact on LDL cholesterol, and the rise in TG as well as LDL cholesterol in the placebo group may reflect subtle changes in diabetes treatment. On the other hand, treatment with gemfibrozil may be sufficient to mitigate these negative effects on TG, but not those on LDL cholesterol. This speculation should be formally tested.

Although the inclusion rates were similar for the gemfibrozil and placebo groups, the reasons for patient withdrawals from the study differed. More patients treated with gemfibrozil with-

### Table 4—Patients with AEs

<table>
<thead>
<tr>
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<th>GEMFIBROZIL (n = 295)</th>
<th>PLACEBO (n = 147)</th>
<th>P VALUE</th>
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<tbody>
<tr>
<td>OVERALL</td>
<td>191</td>
<td>81</td>
<td>0.041</td>
</tr>
<tr>
<td>CLINICALLY IMPORTANT</td>
<td>18</td>
<td>6.1</td>
<td>3</td>
</tr>
<tr>
<td>LEADING TO WITHDRAWAL FROM STUDY</td>
<td>25</td>
<td>8.5</td>
<td>5</td>
</tr>
<tr>
<td>ASSOCIATED WITH TREATMENT†</td>
<td>36</td>
<td>12.2</td>
<td>20</td>
</tr>
</tbody>
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*Serious or requiring hospitalization.
†Definite, probable, or possible relation to treatment.
drew because of AEs, abnormal laboratory results, or lack of compliance than with placebo (72.3 vs. 53.3% of each treatment group’s dropouts, respectively).

As yet, no primary prevention trial has specifically examined the effects of lipid-lowering therapy on macrovascular end points in NIDDM patients. However, in the 5-yr Helsinki Heart Study of 4081 dyslipidemic men, gemfibrozil raised HDL cholesterol and reduced plasma TG, LDL-cholesterol, and non-HDL-cholesterol and TC levels (18). These improvements in the lipoprotein profiles were associated with a 34% reduction in the incidence of fatal and non-fatal coronary heart disease events. In a subset analysis, the effectiveness and safety of gemfibrozil were found to be similar for the NIDDM and nondiabetic patients (30). These results strongly suggest that the correction of the specific dyslipidemias associated with NIDDM via the use of gemfibrozil may confer life-prolonging benefits in diabetes patients. The use of lipid-lowering as a surrogate end point for progression or regression of macrovascular disease must be considered necessary but not sufficient to establish a role for gemfibrozil in managing the dyslipidemic diabetic patient. What is needed now is a prospective study to explore the role of gemfibrozil in slowing progression of macrovascular disease in NIDDM.


References