and a group of six subspecies, named the third biovariant complex (2). They are all widely distributed in soil, dust, and water and are frequently found in sputum and saliva from healthy subjects. Human pathogenicity mostly involves *M. fortuitum* and *M. chelonae*. About 50–60% of the reported infections are soft tissue abscesses or wound infections after surgery or traumatisms. Noncavitating pneumonia, endocarditis, lymphadenitis, osteomyelitis, keratitis, and fatal disseminated infections (in immunocompromised hosts) have also been reported. Cutaneous infections may occur after injections or the use of contaminated electromyography or mesotherapy needles (3).

Three cases of subcutaneous abscesses due to mycobacteria that developed in the site of insulin injections have been reported previously (1,4,5). CSII sites are appropriate portals of entry for such pathogens, the more so since patients can bathe with the inserted needle or even swim with appropriate devices. Clinicians must be aware of the possibility of mycobacterium infection even in sites of injection that have not been used for a long period of time (2 months in the present case). Recognizable growth on appropriate media can be demonstrated as early as 48 h but may take up to 12 weeks (3). Concomitant surgical excision and antimicrobial therapy is usually recommended. Testing the in vitro sensitivity to antimicrobial agents is necessary because all strains have marked resistance to classical antituberculous drugs. Combination of at least two active antimicrobial agents is advised, and treatment duration should be 3–6 months (2).

The case of our patient illustrates the possible long clinical latency of *M. peregrinum* infection. Moreover, it points out the need for careful skin disinfection before changing injection sites, especially since patients on multiple insulin injections often do not take this precaution.

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Improved Glycemic Control in a Diabetic Patient After Discontinuation of Allopurinol Administration

We report a case of NIDDM associated with hyperuricemia in which discontinuation of allopurinol was accompanied by improved glycemic control. A 60-year-old man with NIDDM was admitted to our hospital for the evaluation of diabetic complications. The patient had undergone insulin therapy for 3 years before admission. The patient also had hyperuricemia that had been controlled by the administration of allopurinol (100 mg b.i.d.). Upon admission, his fasting plasma glucose (FPG) and stable HbA_{1c} levels were 14.8 mmol/l and 8.0%, respectively. Renal function and liver function were normal. In spite of restricted food intake and an increasing dosage of insulin, his glycemic control remained poor, as evidenced by FPG >11 mmol/l and urine glucose of 15 g/day. The patient's plasma uric acid level remained relatively constant at 5.0 mg/dl, and, as a result, allopurinol was discontinued. Within a few days of discontinuation, an unexpected improvement of glycemic control was observed. FPG reduced to <11 mmol/l and urinary excretion of glucose did not exceed 5 g/day after discontinuation.

The improved glycemic control shortly after discontinuation of allopurinol strongly suggests that this drug adversely affects plasma glucose metabolism. To test this hypothesis, allopurinol was administered to this patient, who gave informed consent. A 75-g oral glucose tolerance test was performed before and after 4 weeks of allopurinol administration (100 mg b.i.d.). Results indicated reduced glucose tolerance after allopurinol treatment based on the following: fasting and post–1-h plasma glucose level increased from 7.4 to 9.8 mmol/l and from 15.3 to 19.7 mmol/l, and fasting and post–1-h plasma insulin level increased from 11 to 15 mU/l and from 27.7 to 44 mU/l. The insulin sensitivity index (1) and fasting insulin resistance index (2) calculated from the results of a glucose tolerance test were reduced 1.6-fold and elevated 1.8-fold after 4 weeks of allopurinol administration, respectively. The increased insulin response observed after treatment suggests that elevated insulin resistance, rather than impaired insulin secretion, is involved in the adverse effect of allopurinol on glucose tolerance.

Allopurinol is commonly used to reduce plasma uric acid. Although the possibility that allopurinol may reduce glucose tolerance in patients with gout was reported by Schattenkirchner and Wandrey (3), no subsequent studies have investigated the potential effects of allopurinol on glucose tolerance.

Hyperuricemia in the present patient is currently controlled by probenecid. This regimen has not adversely affected glycemic control in this patient during the 12-month administration period. The present result indicates that treatment of hyperuricemia should be considered carefully in the case of diabetic subjects with poor glycemic control.

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Diabetes and Risk of Adverse Events With Calcium Antagonists

Cardiovascular and noncardiovascular adverse outcomes associated with the use of calcium antagonists have been predominantly linked to high doses of the drugs (1,2). In certain patients, adverse events may be related to an excess pharmacological effect. Altered cellular physiology associated with disease conditions may increase the risk of adverse events even at drug doses appropriate for the normal population. Diabetes is characterized by changes in the cholesterol and phospholipid content of cellular membranes that may increase the membrane partition coefficient of calcium antagonists (3). The composition of cellular membranes affects the binding of lipophilic drugs such as calcium antagonists. A decrease in the cholesterol-to-phospholipid ratio in the membrane lipid bilayer has been shown to increase the partition coefficient of calcium antagonists and thus can magnify their pharmacological effect (4). These changes could, theoretically, affect clinical outcomes.

To assess whether diabetic patients are more susceptible to adverse events linked to calcium antagonists, we have reanalyzed the data on calcium-antagonist use and risk of mortality, cancer, and bleeding that we published in five previous studies (Table 1) (1,2,5–7). For all studies described here, diabetes was defined as either reported medical diagnosis of diabetes or use of antidiabetic drugs. In all five studies, the relative risk of adverse events associated with the use of calcium antagonists was greater in diabetic participants than in nondiabetic participants. For the outcomes of mortality and cancer, the increased relative risk with calcium antagonists was significant among diabetic patients and not significant among their nondiabetic counterparts. The interaction of calcium antagonist use with diabetes was significant in the first study ($P = 0.01$) and borderline significant in the third study ($P = 0.09$). The difference in relative risk between diabetic and nondiabetic participants was mainly evident for the outcomes of all-cause mortality and cancer. For these outcomes, we (1,2), Furberg et al. (8), and Jick et al. (9) have found a significant increase in relative risk with high calcium antagonist doses. For the outcome of bleeding, for which no significant dose-response effect was found (5,6), the difference in relative risk between diabetic and nondiabetic participants was less clear.

Although the present findings should be considered hypothesis-generating, they are in agreement with the recent results of the Multicenter Isradipine Diuretic Atherosclerosis Study (MIDAS) (10) and the Fosinopril versus Amlodipine Cardiovascular Events Trial (FACET) (11). In both trials, patients with impaired glucose metabolism or diabetes who were randomized to a calcium antagonist had a significantly increased risk of cardiovascular events compared with alternative treatments. Emerging evidence suggests that, because of physiological abnormalities that may amplify the effects of this class of drugs, diabetic patients may perhaps be particularly vulnerable to adverse events associated with calcium-antagonist use.

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Table 1—*Adverse outcomes associated with use of calcium antagonists in diabetic and nondiabetic individuals*

Study	*n*	Population	Maximum follow-up	Outcome	Comparison groups	RR (95% CI) All participants	Dose response	Diabetic	Nondiabetic
Pahor et al. (2)	906	Hypertensive subjects from EPESE	5 years	All-cause mortality	Nifedipine use vs. β-blocker use	1.72 (1.10–2.69)	Yes	3.27 (1.40–7.62)	1.36 (0.78–2.39)
Pahor et al. (7)	750	Hypertensive subjects from EPESE	5 years	Incident cancer	Calcium antagonist use vs. β-blocker use	2.02 (1.16–3.54)	Yes	3.96 (1.22–12.9)	1.74 (0.89–3.39)
Pahor et al. (1)	5,052	EPESE participants	5 years	Incident cancer	Calcium antagonist use vs. non-use	1.71 (1.26–2.33)	Yes	2.71 (1.57–4.67)	1.41 (0.96–2.06)
Pahor et al. (6)	1,636	Hypertensive subjects from EPESE	8 years	Severe gastrointestinal bleeding	Calcium antagonist use vs. β-blocker use	1.68 (1.03–2.74)	No	1.95 (0.82–4.61)	1.60 (0.87–2.94)
Zuccala et al. (5)	161	Hip replacement surgery	Hospital stay	Perioperative blood transfusion	Calcium antagonist use vs. non-use	2.05 (1.14–3.70)	No	4.53 (0.42–49.0)	1.87 (1.01–3.46)

Relative risks are adjusted for demographic variables, comorbidity, disability, and use of other medications, as indicated in the final models of the original publications. EPESE, Established Populations for Epidemiologic Studies of the Elderly; RR, relative risk.