in my article[1] about personally and closely observing the nurses during mixing of the paste, then immediately applying the paste. It was apparent to me at the time of our conversation that these items were *not* being given his careful attention. I told the orthopedic surgeon that he was ignoring my method. He would not know if the right amounts of the drugs involved were mixed or if they might have been contaminated in the mixing process. My technique is not merely a recipe but a method. The epidural paste must be mixed under the surgeon's eye and immediately applied. The field should be dry and the dura intact. The lumbar fascia should be closed in a watertight way. This ensures that the liquid reservoir of morphine stays in the subfascial space and keeps the epidural paste away from the fascia and skin. It has long been known that Avitene molecules should be kept away from skin.

My clear impression after talking with the orthopedic surgeon was that my detailed method was not being followed. Although "hospital A" was never identified in Kramer's article,[3] it is my belief it is the same orthopedic hospital where my paste was misused. In the article, Kramer et al indicated that sometimes the paste was premixed (*not* under the eye of the surgeon) and applied later (in one case as much as 45 minutes later). A neurosurgeon putting a foreign body (eg, a shunt) into the human body does not leave it open, exposed to the air, etc. He takes the shunt out of its sterile package, fills it with fluid to test it, then immediately puts it into the body.

I devised the paste 3 years ago, to be used in lumbar laminectomy for ruptured discs and stenosis cases, not for large orthopedic instrumented cases where the orthopedist will use metal, screws, or cages, where the surgery lasts many hours, where blood loss and blood transfusions are common, and where drains are employed. A bloody field, the use of drains, and many hours, as well as foreign bodies, increase the risk of infection. The use of drains because of bleeding also removes the liquid morphine reservoir that separates the closed lumbar fascia from the epidural paste. The use of drains therefore shortens the effectiveness of the nerve paste, which itself contains only 1 µg of morphine. As Dr. Hurlbert points out, "hospital A" may have problems unique to it, related to sterilization techniques, staffing, etc.

When the method I described in my paper in 1996 is carefully followed, as it was in the double-blind study at the Barrow Neurological Institute in Phoenix, Arizona, the results are generally excellent. No increase in wound problems should be anticipated, and postoperative pains are usually eliminated. This was shown in the double-blind, controlled Barrow study.

A recipe is not just a list of ingredients. A specific method for safe application of the paste was set forth. When the method is not followed with care then problems may occur.

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The authors reply.

Hurlbert and colleagues have published the results of a randomized placebo-controlled trial in which they assessed the efficacy of morphine nerve paste for postoperative analgesia after decompressive lumbar laminectomy.[1] Their findings show that morphine nerve paste significantly improves postoperative pain control and reduces overall analgesic consumption. However, we believe that their study, like our investigation, raises some important issues about the safety of this new analgesic preparation.

In their trial, Hurlbert et al studied a total of 60 patients: 30 received paste and 30 received placebo. Of 30 patients who received paste, 1 developed serious drainage, and 2 had superficial surgical-site infections, complications similar to those experienced by patients in our report. No such complications were observed among the control group. Furthermore, the rate of surgical-site complications among the patients who received the paste in Hurlbert's study (10%) was similar to the rate detected among the paste recipients in our investigation (11.5%).[2] We found that the rate of complications was significantly higher in patients who received the paste than in those who did not (11.5% vs 1.5%, $P<.001$). In Hurlbert's study, the difference in the rate of surgical-site complications between the treatment (10%) and nontreatment (0%) groups did not reach statistical significance, suggesting that the number of patients studied in their trial may have been adequate to assess the efficacy of the paste, but not necessarily adverse events of low frequency.

We also believe that Hurlbert's report highlights the variability in procedural practices that may occur when the paste is used. First, neither Hurlbert's trial nor the original case series describing the paste[3] specified the amount of paste used on a single patient. Similarly, we could not document the amount of paste used during procedures in our investigation. Second, Hurlbert et al report the need for thorough irrigation of the subcutaneous tissues after closure of the lumbodorsal fascia to prevent sterile fluid accumulation, a recommendation not made in Needham's original publication regarding the paste. Lastly, all of the procedures in Hurlbert's trial were done by a single surgeon, and the paste was always applied by the same person. By contrast, in our investigation, multiple surgeons performed the procedures in which the paste was used. We agree that variability in procedural practices likely influences the risk of surgical-site complications when the paste is used and that the surgical-site complications described in our article may be attributable to institution-specific conditions. Nevertheless, we believe that the circumstances at this hospital more likely represent the variability in surgical technique and other surgical practices that exist within and between institutions than do the circumstances described in Hurlbert's controlled trial.

Morphine nerve paste appears to be an innovative and efficacious approach to postoperative pain control after laminectomy. However, conclusions about the safety of the product can not be appropriately made until the use of the paste becomes more widespread or larger multicenter studies are done. Our report was intended to alert the medical community about the possibility of surgical-site complications when morphine nerve paste is used. Our findings and those reported by Hurlbert et al are an important contribution to the scientific discussion about the potential benefits and risks

associated with this new analgesic formulation and its application. At a minimum, the cumulative experience to date underscores the need for standardized protocols for the preparation and use of morphine nerve paste and for systematic monitoring of patients who receive it.

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Implementation of a Practical Antibiotic Policy in the Czech Republic

To the Editor:

We read with great interest the article by Kolár and Látal reporting the implementation of an antibiotic policy at Olomouc Faculty Hospital in the Czech Republic.[1] We agree with them that an antibiotic policy should be based on the responsible administration of antibiotics and regular monitoring of bacterial resistance. However, we want to express our concerns about the effectiveness of their policy in the urology and the neonatology department, and for the whole hospital.

In the urology department, the authors reported a 14.5% decrease in ofloxacin resistance in *Pseudomonas aeruginosa* between 1995 and 1996 following enforcement of the antibiotic policy by strict control of ofloxacin prescriptions. However, this decrease must be viewed in light of the concomitant increase in ceftazidime resistance (from 2% to 6%) and, more concerning, the emergence of meropenem resistance (from 0% to 8%) observed during the same period. Unfortunately, the level of significance of these variations is impossible to measure, since the number of *P aeruginosa* isolates tested for antimicrobial susceptibility in 1996 was not mentioned. Another problem is that data were not reported on antimicrobial use in the urology department. If, like these authors, we agree that "the selective pressure of antibiotics and their excessive use combine to constitute the driving force behind bacterial resistance," then we would like to know if restriction of fluoroquinolones did not lead to an increase in the use of other antimicrobials, possibly third-generation cephalosporins and carbapenems, resulting in an increase in resistance to these antimicrobials.

In the neonatology department, the authors reported the control of an outbreak of extended-spectrum β-lactamase–producing bacterial infections by restriction of the administration of third-generation cephalosporins. As an alternative, the Antibiotic Center recommended the use of piperacillin, combinations of β-lactam and β-lactamase inhibitor, and aminoglycosides, which were mainly found in the list of controlled antimicrobials. Unfortunately, data on antimicrobial use in this department and data on the evolution of antimicrobial resistance in other microorganisms were not reported.

It seems like the experiences of these two departments do not represent examples of the effectiveness of the antibiotic policy, but only examples of what can be achieved by the antibiotic-control program when specific restrictions are used in addition to the policy. Moreover, it is likely that these interventions only resulted in cycling from one class of antimicrobials to another class without reducing global antimicrobial pressure in these units and that this cycling was performed within the group of controlled drugs.

As mentioned by Kolár and Látal, resistance continued to occur in Olomouc Faculty Hospital despite control efforts. During 1995 and 1996, for the whole hospital, ceftazidime resistance among *P aeruginosa* isolates increased from 6% to 12% ($P<.0000001$). Among other gram-negative bacteria, ceftazidime resistance increased from 12% to 23% in *Acinetobacter baumannii* isolates ($P=.0002$), from 17% to 31% in *Enterobacter cloacae* isolates ($P<.02$), and from 4% to 29% for *Klebsiella pneumoniae* isolates ($P<.0000001$), the latter probably being related to the outbreak observed in the neonatology department. With the exception of gentamicin resistance in *K pneumoniae,* there was a decrease or a stability in the percentage of these gram-negative isolates that were resistant to aminoglycosides during the same period. Unfortunately, data on fluoroquinolone and carbapenem resistance were reported only for the urology department and not for the whole hospital. As mentioned earlier, it is also unfortunate that antimicrobial-use data were reported only for 1996 and were not stratified by units, which makes it difficult to make hypotheses on the origin of the variations in the percentages of resistance. Ceftazidime use was low in 1996; however, as stated by the authors, third-generation cephalosporins were among the most frequently used antimicrobials in the hospital. Although gentamicin was part of the group of controlled antibiotics, it was the second most commonly used controlled drug in 1996. Imipenem represented only a small fraction of controlled antimicrobials used in 1996; however, we do not know if there was an increase in imipenem use between 1995 and 1996.

The effectiveness of the antibiotic policy presented by Kolár and Látal should be questioned, since it looks like it did not control antimicrobial resistance when used alone, even with the requirement of approval from the Antibiotic Center for controlled drugs. A clear reduction in the percentage or control of resistance was achieved only when specific and localized restrictions were used in addition to the antibiotic policy. One reason for this might be that the microbial ecology of their hospital necessitates the use of broad-spectrum antimicrobials and if (for example) a restriction is placed on fluoroquinolones, other antimicrobials, such as third-generation cephalosporins and carbapenems, are still needed for the empirical treatment of suspected infections. In other words, to maintain provision of adequate patient care, the Antibiotic Center has no other choice than to approve the use of these drugs even if they are controlled. As a result, the antibiotic policy may only work as cycling of antimicrobials,[2] thus leading to a decrease in resistance to the drugs that are effectively controlled, while resistance to other drugs is maintained or continues to increase. Unfortunately, data on the use of noncontrolled antimicrobials in 1995 and 1996 were not provided, and it is impossible to verify that controlled