electrode polarized and thus permit it to calibrate immediately when turned on. This current (table 4) is normally about half the "on" current in air, or a smaller fraction of the current in O_2. A theoretical additional source of trouble arises from this situation, in that a battery might weaken during use, go undetected, and regenerate its potential in the "off" position sufficiently to pass all tests, including the N_2O test, when first turned on. The manufacturer states that approximately 60 batteries were subjected to tests to examine for this potential problem, disclosing that when the batteries are discharged two or three times, there is a possibility that it may arise.

The malfunction in Case 2 was not detected at the beginning of the anesthetic procedure using the manufacturer's criteria. The specifications suggest that calibration is needed only every eight hours, yet, in both cases, failure occurred one to two hours after calibration.

This sensitization to N_2O occurring with battery failure is due to a design problem that the manufacturer recognized in 1976 (after an FDA report), and corrected in those model IL 402 and 404 O_2 sensors manufactured after October 1976. In the revised instruments, polarization voltage decreases with battery failure, and N_2O will never be sensed. Clearly this is a highly desirable modification for instruments manufactured before November 1976, which needs only a change of two resistors and relocation of one of their leads. Due to the potentially lethal results of interpreting N_2O as O_2, we believe all of the older instruments should be recalled and modified to prevent such failure.

Since 1976, communication with the manufacturer about this problem has been undertaken by two individuals at our institution. Two notices of the problem have been filed with FDA as well. The manufacturer maintains that the revised check list mounted on the monitor's side, which includes the statement "Check anesthetic sensitivity, <1 per cent, suffices to discharge this obligation. Considering that N_2O is not specifically mentioned, nor is the possibility that it will be detected by batteries that are low but check "OK," or that it may progressively fail with time during use, we cannot agree that these instruments are safe for use in anesthesia where closed-system operation may depend on them for proper O_2 concentration maintenance. We therefore submit this report to alert users of IL 402 and/or IL 404 oxygen monitors to this defect and potential danger. We consider dangerous instruments bearing the following serial numbers:

IL 402: all below 02570
IL 404: all below 02812
Ohio[¶] Model 200: all below BAF-D-00918, all BAF-C, all BAF-B, all AAB-A, all AAA-A
Ohio Model 400: all below BAF-D-01287, all BAF-E, all BAF-B, all AAB-A, all AAA-A
Air-Shields**: all oxygen analyzers of IL type

At present, they may be returned for modification at a modest charge.

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Addendum

Since submission of this article to Anesthesiology (and to the manufacturers), the manufacturer has altered the daily check list procedure and offered to modify the polarizing voltage circuit so that nitrous oxide sensitivity is no longer obtained by battery discharge. Clearly this is a highly desirable modification, and the authors strongly recommend that all IL machines manufactured prior to November 1976 have this modification made.

[¶] Ohio Medical Products, Division of Airco, Inc., P.O. Box 7550, 3030 Airco Drive, Madison, Wisconsin 53707.

** Narco Air-Shields, Division of Narco Scientific, Hatboro, Pennsylvania 19040.

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Pain Relief by Intrathecally Applied Morphine in Man

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In recent animal experiments, opiate receptors were identified autoradiographically in the brain and the substantia gelatinosa of the spinal cord.[1] In a corollary study, morphine administered directly into the spinal subarachnoid space of the rat produced potent analgesia.[2] Subsequent studies confirmed this finding and showed that repeated intrathecal injections of mor-

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TABLE 1. Clinical Results with Intrathecally Applied Morphine

	Age (Years), Sex	Number of Injections	Agent and Dose (mg)	Pain	
				Mean Change in Intensity (Scale of 0 to 10)	Mean Duration of Relief (Hours)
Patient 1	56, M	3	Morphine (0.5)	7, 1	18
		2	Saline solution	6, 1	6
Patient 2	60, M	2	Morphine (0.5)	7, 1	12
		2	Saline solution	8, 8	No relief
Patient 3	57, F	2	Morphine (0.5)	5, 0	22
		1	Saline solution	6, 5	No relief
Patient 4	68, M	2	Morphine (1.0)	5, 0	20
		2	Saline solution	5, 4	No relief
Patient 5	66, M	2	Morphine (0.5)	5, 1	14
		1	Saline solution	6, 7	No relief
Patient 6	71, M	2	Morphine (0.5)	3, 1	10
		1	Saline solution	3, 1	8
Patient 7	51, M	3	Morphine (1.0)	4, 0	24
		2	Saline solution	5, 4	No relief
Patient 8	62, M	1	Morphine (0.5)	4, 0	21
		1	Saline solution	5, 5	No relief

phine did not cause adverse tissue reactions of the spinal cord.[3] Also, an opiate-like analgesic effect was reported to occur after the injection of methionine[5]-enkephalin (Met[5]-enkephalin) and its analogs.[4] The results of these animal experiments prompted us to study the effect of intrathecally applied morphine in eight patients suffering from intractable pain of inoperable cancer.

METHODS AND MATERIALS

Eight patients who had severe intractable pain in the back and legs secondary to malignancies of the genitourinary tract with invasion of the lumbosacral plexus were selected for study. Systemically administered narcotic analgesics had not suppressed the pain when given at reasonable dose levels and frequencies (5–10 mg every four to six hours), whereas high, clinically effective doses (10–20 mg every two to four hours) were almost always complicated by depression of the central nervous system.

All procedures and possible risks pertaining to this study were explained to the patients, and each signed a written informed-consent form. Systemic narcotics were not given for at least two hours before treatment. Neurologic examinations were performed immediately before and one hour after the morphine injections.

Each patient was shown the visual pain scale (0 to 10) and instructed in its use by a person who was unaware of the pattern of double-blind study. The baseline pain intensity was determined 30 min before intrathecal injection. Patients then received physiologic saline solution intrathecally at the second and third lumbar interspace with or without morphine, 0.5 to 1.0 mg. After administration of the agent, the intensity of pain was assessed at 15-min intervals for one hour. Vital signs were carefully monitored during this hour. When the pain was relieved, patients were told to record, at hourly intervals, whether relief was still present.

The injections were given in random order, so that neither the patient nor the person evaluating the pain knew which type of agent was used. The intervals between injections ranged from four to 48 hours, depending on the patient's response. Each patient received both saline control and morphine injections. They were repeated as many times as the patient was willing to participate. Totals of 17 injections of morphine and 12 of physiologic saline solution were given.

RESULTS

Two of the eight patients (Patient 1 and Patient 6) reported complete relief of pain after separate injections of morphine and physiologic saline solution, although the mean duration of relief after morphine injection was 15 hours, whereas that after injection of physiologic saline solution was seven hours (table 1). The other six patients reported complete relief from pain after the morphine injections. Relief lasted 12 to 24 hours, the average duration being 20 hours. Elapsed times from instillation of the drug to its maximal effect ranged from about 15 to 45 min. Increasing the dose of morphine to 1.0 mg did not prolong the relief proportionately. In contrast to the good response to morphine, there was no improvement after nine injections of physiologic saline solution. The results of repeated injections of either morphine or physiologic saline solution in the same patient were strikingly reproducible. The typical pattern of changes in intensity of pain, from three patients, is shown in figure 1.

The intrathecal injection of morphine was accomplished with little discomfort to the patient. Complete relief of pain allowed greater ease in use of the lower extremities. Although patients experienced noticeable enhancement of their feelings of well-being, they showed no sign of sedation, respiratory depression, or other behavioral changes. During the periods of complete pain relief, perception to pinprick and light touch remained intact, as did all other neurologic functions.

DISCUSSION

The small number of cases studied renders our observations preliminary. Another limitation is that eval-

uation of methods for controlling pain lacks standardized means for measuring pain.

After abandoning the McGill Pain Questionnaire[5] because of the grossly obvious analgesic effect of intrathecally administered morphine, we settled on the visual pain scale,[6,7] and found it to be workable, although all it does is quantitate pain intensity. Repeated application of the scale did not seem to affect the rating significantly, for neither patients nor evaluating personnel were familiar with the ramifications of a double-blind study. To try to avoid placebo reactions from doctor–patient interaction, we had the same person administer the morphine and the physiologic saline solution.

Notwithstanding the limitations of this study, we were sufficiently impressed by the results to submit the data for publication in the hope that others will be stimulated to evaluate independently this potential mode of symptomatic therapy for incurable cancer problems. Six of our eight patients were clearly able to distinguish morphine from placebo, did so on repeated occasions, and believed they had obtained satisfactory and relatively long-lasting relief. In none was there any demonstrable evidence of side-effects on the central nervous system. Relief of pain after injections of physiologic saline solution in two of the patients came as no surprise, since as many as 40 per cent of cancer patients may obtain substantial relief of pain from placebo medications.[8]

Although the absence of depression of the central nervous system suggests that intrathecally administered morphine acts on the spinal cord alone—perhaps on the substantia gelatinosa—our study does not exclude an interaction between morphine and receptors in the brain. If narcotics or endogenous opiate-like substances can be repeatedly administered intrathecally, prolonged control of pain by application of a drug reservoir or an indwelling cannula may be possible. The advantage of this method would be to provide predictable relief from pain without attendant loss of motor or sensory function. It is tempting to speculate that this technique may be used for obstetric analgesia or postoperative pain. However, further studies are needed to establish the clinical applicability of intrathecal injections of morphine, especially with regard to the risk to the spinal cord of repeated administration and the effects on tolerance to and dependency on the drug.

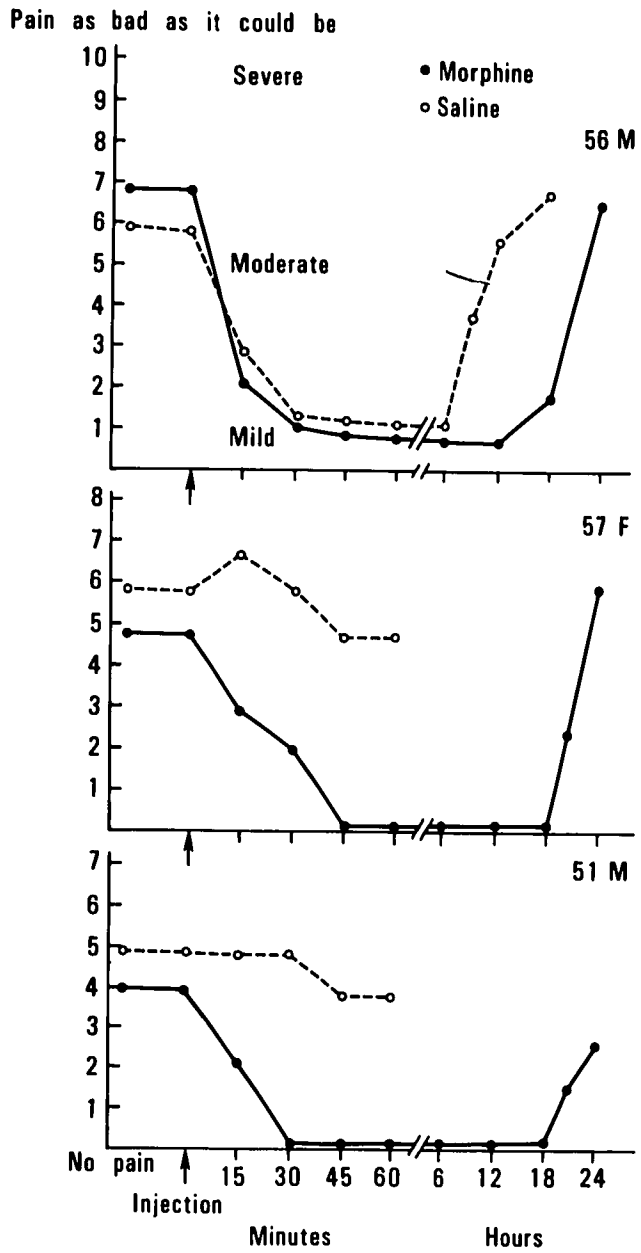

FIG. 1. Changes in intensity of pain after intrathecal injection of physiologic saline solution or morphine.

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