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The Successful Implementation of Pharmaceutical Practice Guidelines

Analysis of Associated Outcomes and Cost Savings

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Background: Although approximately 2,000 medical practice guidelines have been proposed, few have been successfully implemented and sustained. We hypothesized that we could develop and institute practice guidelines to promote more appropriate use of costly anesthetics, to generate and sustain widespread compliance from a large physician group, and to decrease costs without adversely affecting clinical outcomes.

Methods: A prospective before and after comparison study was performed at a tertiary care medical center. Clinical outcomes data and times indicative of perioperative patient flow were collected on the first of two sets of patients 1 month before discussion of practice guidelines. Practice guidelines were developed by the physicians and their associated care team for the intraoperative use of anesthetic drugs. A drug distribution process was developed to aid compliance. Clinical outcomes data and times indicative of perioperative patient flow were collected on the second set of patients 1 month after institution of practice guidelines. Hospital drug costs and adherence to guidelines were noted throughout the study period and for each of the following 9 months by querying the database of an automated anesthesia record keeper.

Results: A total of 1,744 patients were studied. Drug costs decreased from 56 dollars per case to 32 dollars per case as a result of adherence to practice guidelines. Perioperative patient flow was minimally affected. Time (mean \pm SD) from end of surgery to arrival in the post-anesthesia care unit (PACU) increased from 11 ± 7 min before the authors instituted practice guidelines to 14 ± 8 min after practice guidelines ($P < 0.0001$). Admission of inpatients to the PACU receiving monitored anesthesia care increased from 6.5 to 12.9% ($P < 0.02$). Perioperative patient flow and clinical outcomes were not otherwise adversely affected. Compliance and cost savings have been sustained.

Conclusions: This study is an example of a successful physician-directed program to promote more appropriate utilization.

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tion of health care resources. Cost savings were obtained without any substantial changes in clinical outcomes. Institution of similar practice guidelines should result in pharmaceutical savings in the range of 50% at tertiary care centers around the country, with a slightly smaller degree of savings expected at institutions with more ambulatory surgery. (Key words: Anesthesia, costs. Anesthesia, recovery periods. Anesthesiology, physicians' practice patterns. Economics, drugs. Equipment, computers: information systems. Outcomes. Practice guidelines.)

THE effectiveness of much of the medical care delivered in this country is questionable because of the equivalent outcomes seen with large variations in practice.¹⁻⁴ Drug-prescribing variability is an area that has not been sufficiently studied. Pharmaceutical products generated 89.7 billion dollars for pharmaceutical companies in 1995; hospital-based drug purchases represented a 13.7% share of that market, or about 12.3 billion dollars.## Anesthesia drugs alone are expected to have sales of \$2.1 billion by 1999.*** Carefully constructed practice guidelines may increase appropriate use of costly pharmaceuticals and have a large monetary impact. This concept has generated international interest across all medical specialties.^{5,6}†††‡‡‡§§ However, definitive determination of the cost-effectiveness of drugs often is lacking. This ambiguity makes practice guideline development more difficult,⁷⁻⁹‡‡‡ and the success of practice guidelines in pharmaceutical prescribing is not well documented.¹⁰

Practice guidelines are now prevalent. The brief definition of a practice guideline is: a recommendation of how to use tests and therapies based on a combination of clinical practice consensus and evidence from the scientific literature. Overall, approximately 2,000 medical practice guidelines have been proposed, but a very limited number have been successfully implemented,

Table 1. Tenets for Successful Implementation of Practice Guidelines^{21-23,25,26,28}

Identify problems that would have substantial impact if improved.
Use specific, unambiguous language in a limited number of guidelines.
Internally develop practice guidelines that take into account both the published literature and the practice patterns at the hospital.
Allow for clinical flexibility.
Institute a point of service plan at the pharmacy's dispensary to encourage the most appropriate utilization of pharmaceuticals (i.e., release of certain drugs to attendings only; posting of guidelines at the pharmacy window).
Develop a way to use a medical information system to follow the success of implementation.
Create incentives for provider compliance.
Receive credit from the hospital for curtailing of expenses.
Measure success and publicize the results of the practice changes for the department as a whole.
Provide feedback on an ongoing basis to the individuals concerned.

their effects rigorously evaluated, and their impact sustained.¹⁰⁻¹³ There have been many review papers detailing what should be done, providing exhortations toward the "ideal" process (i.e., using the process most likely to enhance the acceptance of practice guidelines by clinicians). Unfortunately, few, if any, efforts have completely embraced the well-described multiple tenets necessary for successful implementation and sustenance of practice guidelines (table 1). No previous study of hospital based pharmaceutical prescribing has described a rigorous attempt to follow the ideal process of practice guideline development and implementation.

In the United States, anesthesia departments have been among those at the forefront of hospital-based efforts to reduce pharmaceutical costs through practice guidelines, and those initiatives can be expected to serve as templates for cost reduction in other clinical departments. Most of the anesthesia pharmaceutical cost reduction initiatives have concentrated on limiting costly drugs where no outcome differences were expected compared with the use of less costly alternatives.¹⁴⁻¹⁷ However, despite being leaders in this effort, no study in the field of anesthesiology has prospectively measured the effect on clinical outcomes after efforts at cost containment, nor have any documented long-term success maintaining those savings. We hypothesized that we could develop and institute practice guidelines to promote more appropriate use of costly drugs, generate and sustain widespread compliance from a

##IMS America 1995 Business Watch. <http://www.cpsnet.com/mmm/reprints/may96/watch95.html> (© CPSNET, Inc., Boca Raton, FL, USA) Thanks to Kelly Ahlfeld, Duke University Medical Center librarian, for locating this reference.

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large physician group by adhering to the ideal process, and substantially decrease cost without adversely affecting clinical outcomes.

Methods

Approval was obtained from the Duke University Medical Center institutional review board for the administration of patient surveys and the collection of data. Beginning in March 1994, Arkive® (Arkive Information Systems, Inc., San Diego, CA; company no longer operational), an automated anesthesia record keeper and information system, was used to identify the top anesthesia drug expenditures under the prescribing control of the anesthesiologist.

Calculating Costs

The essence of the method was to take the amounts delivered (as recorded by the anesthesia automated record keeper [AARK]) and compute the costs according to the prices that we obtained from the Department of Pharmacy. All anesthesia pharmaceutical products could be categorized into two groups with similar variables: drugs and infusion fluids in one group, anesthetic gases in another. For drugs and infusion fluids, the AARK gave us the amounts administered. Because the products are dispensed from the pharmacy in vials or infusion bags of predetermined sizes, some portions of these substances may remain unused after case completion and therefore may have to be discarded. To account for the discarded portions, we programmed our custom-designed database analysis software to round up the amounts of drugs and infusion fluids administered to the nearest vial or bag size for that particular substance before computing the costs. This custom analytic software was shown by us to be 99% accurate compared with pharmacy distribution costs.

For the inhalation anesthetics, waste was not a concern because anesthetic gases are used for multiple cases until the liquid volume in the vaporizer is exhausted. Isocalc (a custom program designed by us and written in ObjectPal code) extracted data from our AARK database on the timing and values of recorded gas flow rates and vaporizer dial settings. Isocalc then computed the interval rate of anesthetic use and converted that to dollars based on cost/ml of the inhalation agent.¹⁸

(Also see companion article¹⁹ for more detailed methodological information.)

Practice Guideline Implementation and Evaluation

In July 1994, a departmental consensus was developed regarding the need to pursue pharmaceutical cost containment directed by clinicians. During the next 6 months, educational efforts regarding the costs of drugs were begun.

During February 1995, before the development of practice guidelines, a control group of 863 consecutive elective surgery patients arriving in the post-anesthesia care unit (PACU) were evaluated. PACU nurses were given specific surveys with each patient's paperwork as they arrived in the PACU. Research nurses were available in the PACU throughout the entire day to answer questions and to provide consistency to any interpretations of the outcome measures. Patients stopping in the PACU on their way to a pre-planned surgical intensive care unit bed were not included, nor were late night emergency cases.

In the PACU, times relevant to the efficiency of perioperative patient flow and immediate clinical outcomes in the PACU were recorded. Several times were considered critical indicators of the process of patient flow. Time from the end of surgery to arrival time in the PACU was empirically considered the most useful global measure of emergence from the sedative effects of anesthesia and neuromuscular blockade reversal. Times from arrival at the PACU until the patient was judged ready for discharge and until the patient was actually discharged were noted for each patient. Incidences of unplanned admission to the hospital also were recorded.

Outcomes assessment included:

- 1) the total incidence of nausea and vomiting and the subset who required treatment for nausea and vomiting;
- 2) the incidence of unplanned postoperative mechanical ventilation; and;
- 3) any physiologic problem in the PACU causing a delay in discharge beyond the minimum mandated stay of 45 minutes. We looked at delays caused by inadequate pain control, system problems (bed not available, transporters, etc.), shivering and hypothermia, desaturation or any unplanned postoperative mechanical ventilation, cardiovascular causes (hypertension, hypotension, chest pain, or other cardiac problem), low urine output or inability to void, unplanned hospital admission, allergic responses, other anesthetic complications (oversedation, regional

Table 2. Drug Choices: Costly Drugs *versus* Less Costly Alternatives

Drug Considered	Costly Alternative	Less Costly Alternative
Induction drugs	Propofol, etomidate	Thiopental
Fluids	Hydroxyethyl starch, albumin, plasma protein fraction	Lactated ringers
Muscle relaxants	Atracurium, mivacurium, rocuronium, vecuronium	Succinylcholine, pancuronium
Benzodiazepines	Midazolam	Less midazolam, preoperative diazepam
Opioids	Sufentanil, alfentanil	Fentanyl
Inhalational agents	Desflurane	Isoflurane
Fresh gas flow	High	Low

complication, failure of block to wear off), or other surgical complications (preoperative planned delays, wound care, bleeding).

Practice Guideline Development

Only those categories of drugs that were the largest budget items (> 50,000 dollars/yr) were targeted for practice guidelines. In the month that we began our educational efforts (March 1994), the drugs that we targeted (including isoflurane at high flows) represented 86.5% of the total pharmaceutical budget. Five committees of four to six individuals were formed to agree on the most appropriate use of these costly drugs *versus* their less costly alternatives (table 2). We solicited volunteers, especially among any given drug's most ardent proponents, to serve on a committee devoted to developing practice guidelines for that class of drug. Each committee reviewed the often conflicting scientific literature and solicited comments from the entire anesthesia care team (attending anesthesiologists, resident anesthesiologists, and certified registered nurse anesthetists).

In March 1995, the practice guidelines committees developed and disseminated draft guidelines for comment. On April 5, 1995, the practice guidelines were presented to all faculty, nurse anesthetists, and resident physicians involved in the administration of the drugs, and their final comments were invited. The full practice guidelines are attached in Appendix A.

On May 1, 1995 the operating room (OR) satellite pharmacy began distributing drugs according to the practice guidelines. To request drugs outside the practice guidelines required the consent of the attending anesthesiologist supervising the case except in emergencies. Attending physicians were notified that individual drug use would be tracked by querying the automated anesthesia information system database on a periodic basis. All anesthesia care providers were notified

that pharmacy records of declared "emergencies" would be reviewed. At the beginning of June 1995, 1 month after institution of practice guidelines, 871 consecutive PACU patients were evaluated (table 3). Outcome data collection for this group of patients was performed identically to the data collection before practice guidelines were implemented.

Outcome and time analyses were performed. Clinical outcomes and times relevant to patient flow were evaluated for all PACU patients before and after practice guidelines. The study patients were divided and analyzed in the following subgroups:

- 1) Type of anesthesia—general (included combined

Table 3. Comparison of Patient Populations Surveyed before and after Institution of Practice Guidelines

	February 1995 (before)	June 1995 (after)
N	863	871
Age (yr)	42.8	42.1
ASA Physical Status	2.31	2.30
Inpatient (%)	68.0	67.1
Outpatient (%)	32.0	32.9
Female (%)	51.9	52.6
Male (%)	48.1	47.4
Case distribution (%)		
Anesthesia	0.1	0.1
Dental	0.4	0.4
Eye	12.0	11.7
General	20.0	21.8
Gynecological	7.1	6.6
Hematology/oncology	0.9	0.5
Neurosurgery	6.2	6.1
ENT	7.0	7.1
Orthopedics	19.8	17.1
Pediatric bone marrow	0.5	0.4
Pediatrics	3.1	3.0
Plastics	7.5	9.0
Cardiothoracic	10.0	9.3
Urology	5.4	6.8

There were no statistically significant differences.

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- techniques of general plus regional anesthesia); regional (*i.e.*, spinal, epidural, other nerve conduction blockade); monitored anesthesia care (MAC, sedation, and monitoring of physiologic status);
- 2) Patient designation—inpatient (patients in the hospital before surgery, patients admitted to the hospital the day of surgery, patients admitted to a 23-h observation bed) *versus* outpatient (discharged home on same day as surgery); and
 - 3) Type of anesthetic and patient designation combined.

To follow the subsequent adherence of anesthesia care providers to practice guidelines, use patterns of the following agents were catalogued: propofol, etomidate, colloid, pancuronium, sufentanil and alfentanil, and fresh gas flows.

Statistical Analysis

Data from the 1,744 patients were entered in a spreadsheet and transferred to SAS® (SAS for Windows version 6.10, SAS Institute Inc., Cary, NC) statistical system for analysis. Before calculation of the time outcomes, time variables were given exhaustive range and logic checks, and discrepancies were corrected by reference to original records. Comparisons of groups and subgroups on all categorical event outcomes were conducted with Fisher's exact test of contingency tables. SAS® gives Fisher's test with all 2×2 cross-tabulations, regardless of number of cases in each cell. If the number of cases in any cell is less than 5, Fisher's is more accurate than the usual chi-square test; otherwise results are comparable. We used Fisher's exclusively because some of our subtables had very small cell sizes, and we decided to be consistent for all tests. Continuous time outcomes were treated as "time-to-event" data and analyzed using a Cox proportional-hazards model.²⁰ This model allows testing effects of the new practice guidelines while accounting for possible differences associated with type of anesthesia and patient designation (in-patients *versus* out-patients). Costs were compared using two tailed independent sample unequal variance *t* tests.

As regards multiple comparisons, the *P* value was set at 0.05. This would tend to overstate the statistical significance of any findings attributed to the institution of practice guidelines. Given our hypothesis that no change in clinical outcomes would occur with institution of practice guidelines, we believed that overreporting of possible effects was a better approach than adjusting for the dozens of comparisons made and possi-

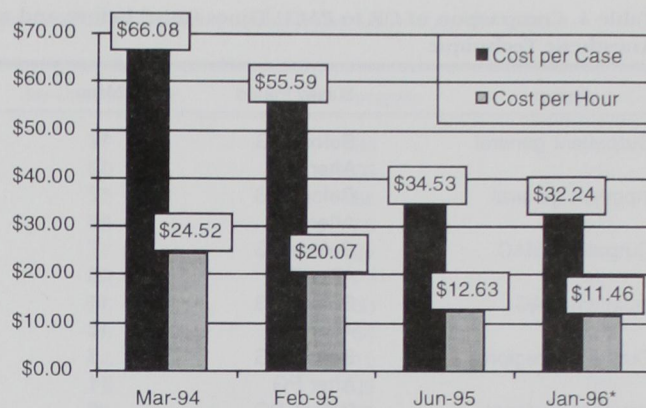


Figure 1. Costs per case and costs per hour. Cost per case: intravenous drugs and fluids given rounded up to vial size costs plus inhaled agents costs. Costs per hour: total monthly drug costs divided by total monthly hours of anesthesia. *P* value: compared with previous time period. * Cost difference due to marked decrease in cost of isoflurane. *P* = NS for cost calculation at June 1995 prices.

bly underestimating the importance of a detrimental change in patient outcome.

Results

Pharmaceutical Savings as a Result of Practice Guidelines

The effects of practice guidelines on the nominal costs per case and costs per h of anesthetic care are shown in figure 1. (Nominal costs are dollar costs not adjusted for inflation). A baseline mean pharmaceutical cost of 66.08 dollars \pm 62.25 per case, 24.52 dollars per h in March 1994 was measured. A 1-yr general educational effort reduced costs 16% ($P < 0.0001$) to 55.59 dollars \pm 50.04 per case, 20.07 dollars per h (February, 1995). Immediately after the institution of practice guidelines, pharmaceutical costs per case declined an additional 38% to 34.53 dollars \pm 27.53 per case and 12.63 dollars per h ($P < 0.0001$). This level of expenditure has been sustained. Drug costs per case decreased slightly ($P < 0.01$) from 34.53 dollars in June 1995 to 32.24 dollars \pm 26.69, 11.46 dollars per h of anesthesia in January 1996.

Annualized savings of 647,000 dollars could be attributed directly to the institution of practice guidelines for the 27,728 anesthetics administered in 1995. Savings of 938,000 dollars per yr for our institution could be ascribed to the preceding educational effort combined with the firm implementation of the guidelines.

Table 4. Comparison of OR to PACU Times (min) before and after Practice Guidelines According to Patient Designation and Anesthetic Technique

Group	Survey Period	Mean	Standard Deviation	25th Percentile	75th Percentile
Outpatient general	Before PG	12	7	8	15
	After PG	13	7	8	17
Inpatient general	Before PG	12	7	7	15
	After PG	16	8	10	20
Outpatient MAC	Before PG	7	4	3	9
	After PG	10	5	8	12
Inpatient MAC	Before PG	11	10	6	11
	After PG	15	7	11	19
Outpatient regional	Before PG	7	4	4	10
	After PG	11	6	7	12
Inpatient regional	Before PG	9	5	5	12
	After PG	14	7	9	15

PG = practice guidelines.

Outcomes Analysis

Time Outcomes. Time (mean \pm SD) from the end of surgery to arrival time in the PACU (OR to PACU Time) was 11 ± 7 min before we instituted practice guidelines *versus* 14 ± 8 min after ($P < 0.0001$). Time until the patient was judged ready for discharge (Ready for PACU Discharge Time) was 99 ± 66 min before *versus* 97 ± 75 min after ($P = \text{NS}$). Time until the patient was actually discharged (Actual PACU Discharge Time) was 127 ± 80 min before *versus* 126 ± 84 min after ($P = \text{NS}$; tables 4-6). Subgroup comparisons yielded results similar to the group as a whole; no differences were statistically significant before *versus* after practice guidelines.

Unplanned Hospital Admission. Unplanned hos-

pital admissions for ambulatory patients were negligible before and after practice guidelines, 1.1% *versus* 0.7% ($P = \text{NS}$).

MAC Admissions to the Post-anesthesia Care Unit. Inpatients receiving MAC required admission to the PACU (as opposed to being directly discharged back to their hospital room) more frequently after practice guidelines compared with before practice guidelines: 18/277 (6.5%) before *versus* 37/288 after (12.9%; $P < .02$).

Physiologic Outcomes. Pulmonary Events. The incidence of unplanned postoperative mechanical ventilation before practice guidelines for those receiving general anesthesia was 0.6%, with 95% confidence intervals of 0.2-1.7%. The incidence of unplanned postoper-

Table 5. Comparison of Ready for PACU Discharge Times (min) before and after Practice Guidelines According to Patient Designation and Anesthetic Technique

Group	Survey Period	Mean	Standard Deviation	25th Percentile	75th Percentile
Outpatient general	Before PG	146	75	105	176
	After PG	132	82	70	175
Inpatient general	Before PG	85	53	45	105
	After PG	84	73	45	100
Outpatient MAC	Before PG	79	36	60	95
	After PG	92	64	55	110
Inpatient MAC	Before PG	100	100	45	100
	After PG	80	60	45	85
Outpatient regional	Before PG	131	87	70	165
	After PG	118	59	75	145
Inpatient regional	Before PG	101	74	45	120
	After PG	94	60	45	120

PG = practice guidelines.

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Table 6. Comparison of Actual PACU Discharge Times (min) before and after Practice Guidelines According to Patient Designation and Anesthetic Technique

Group	Survey Period	Mean	Standard Deviation	25th Percentile	75th Percentile
Outpatient general	Before PG	185	87	135	225
	After PG	172	90	105	225
Inpatient general	Before PG	111	72	65	135
	After PG	108	79	65	125
Outpatient MAC	Before PG	107	37	85	125
	After PG	127	69	77	145
Inpatient MAC	Before PG	123	96	60	130
	After PG	109	78	60	120
Outpatient regional	Before PG	169	94	110	208
	After PG	163	75	105	185
Inpatient regional	Before PG	121	75	65	155
	After PG	115	62	70	150

PG = practice guidelines.

ative mechanical ventilation after practice guidelines for those receiving general anesthesia was 0.3%, with 95% confidence intervals of 0.1 - 1.1% ($P = \text{NS}$).

The incidence of pulse oximetry arterial hemoglobin desaturation less than 90% in the PACU delaying discharge was 2.2% before *versus* 2.3% after practice guidelines ($P = \text{NS}$). Subgroup comparisons did not reveal any significant differences.

Nausea and Vomiting. The incidence of nausea and vomiting requiring treatment (PONV + RX) was 10.2% before practice guidelines and 9.5% after ($P = \text{NS}$). The incidence of any postoperative nausea and vomiting (ANY PONV) was 12.7% before *versus* 14.4% after ($P = \text{NS}$; tables 7, 8). When broken down by the type of

anesthesia and disposition of the patients, after practice guidelines, ANY PONV increased approximately two-fold for patients undergoing outpatient MAC and regional anesthesia. This increase in ANY PONV was not found to be statistically significant ($P = 0.044$ when MAC and Regional patients grouped; NS because P value was corrected for multiple comparisons). The incidence of PONV + RX in patients undergoing MAC and regional anesthesia did not increase as much and was less than 10% after practice guidelines were introduced.

Other Post-anesthesia Care Unit Physiologic Events. There were no significant differences before *versus* after practice guidelines for any of these clinical outcome parameters. There were no statistically sig-

Table 7. Incidence of Nausea and Vomiting Requiring Treatment before and after Practice Guidelines According to Anesthetic Technique

Group	Survey Period	N	%	P Value
Outpatient general	Before PG	18	13.1	NS
	After PG	24	12.6	NS
Inpatient general	Before PG	59	12.3	NS
	After PG	45	9.6	NS
Outpatient MAC	Before PG	3	3.7	NS
	After PG	3	5.7	NS
Inpatient MAC*	Before PG	0	0	NS
	After PG	3	8.1	NS
Outpatient regional	Before PG	2	3.5	NS
	After PG	3	7.0	NS
Inpatient regional	Before PG	6	6.8	NS
	After PG	5	6.4	NS

PG = practice guidelines; NS = not significant.

* Most inpatient MAC cases were sent directly back to the hospital room.

Table 8. Any Incidence of Nausea and Vomiting in All PACU before and after Practice Guidelines According to Anesthetic Technique

Group	Survey Period	N	%	P Value
Outpatient general	Before PG	28	20.4	NS
	After PG	44	23.2	NS
Inpatient general	Before PG	69	14.3	NS
	After PG	59	12.6	NS
Outpatient MAC	Before PG	4	4.9	NS
	After PG	6	11.3	NS
Inpatient MAC*	Before PG	0	0	NS
	After PG	5	13.5	NS
Outpatient regional	Before PG	2	3.5	NS
	After PG	5	11.6	NS
Inpatient regional	Before PG	7	8.0	NS
	After PG	6	7.7	NS

PG = practice guidelines; NS = not significant.

* Most inpatient cases were sent directly back to the hospital room.

nificant changes in frequency of grouped PACU physiologic events delaying discharge before *versus* after practice guidelines (fig. 2).

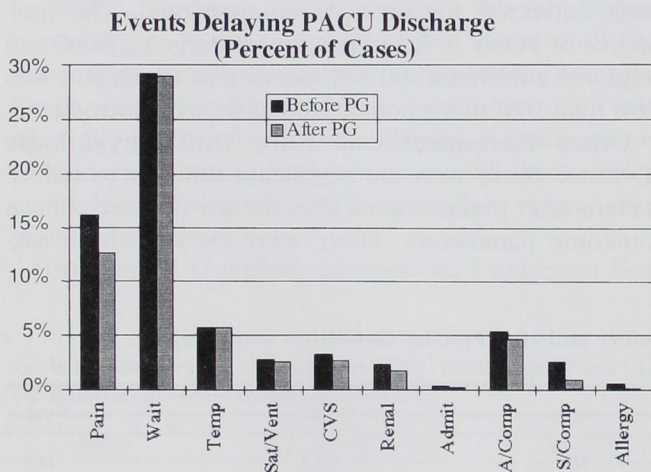


Figure 2. Events delaying PACU discharge (percent of all cases affected by the delay). PACU = post-anesthesia care unit (recovery room); PG = practice guidelines; Pain = delay because of inadequate pain control; Wait = any wait for system problems (bed not available, transporters, etc.); Temp = delay because of shivering hypothermia; Sat/Vent = delay because of desaturation or any unplanned postoperative mechanical ventilation; CVS = delay because of cardiovascular causes—hypertension, hypotension, chest pain, or other cardiac problem; Renal = delay because of low urine output or inability to void; Admit = unplanned hospital admission; Allergy = allergic responses; A/comp = other anesthetic complications (oversedation, regional complication, failure of block to wear off); S/comp = other surgical complications (preoperative planned delays, wound care, bleeding, etc.).

Comparison of System Problems to Physiologic Events Delaying Discharge. Approximately one half of all noted delays occurred as a result of system problems (*i.e.*, administration of patient flow) unrelated to patient health. More than 25% of time spent in the PACU was a result of system problems (Actual Time minus Ready Time).

Adherence to Practice Guidelines. More marked changes were seen in the reports generated after practice guidelines were instituted (June 1995) compared with changes reported before practice guidelines (educational period from March 1994 to March 1995; table 9). Fresh gas flows had the least adherence to the practice guidelines; no distribution control was possible because fresh gas flow through each anesthetic machine is dialed in at each anesthetizing location by each provider and because specific feedback for the provider was not initially programmed. Compliance with fresh gas flow practice guidelines improved when accurate feedback was given to each member of the anesthesia care team after October 1995.

Table 10 details the statistically significant differences in the percentage of patients receiving propofol before practice guidelines *versus* after practice guidelines. Subgroup comparisons revealed a marked decrease in the percentage of inpatients receiving bolus (a single dose parenteral administration) or infusion of propofol, and less change in the use for outpatients. Changes in the use of propofol infusions were most dramatic, significantly dropping in every category of patient except outpatients receiving general anesthesia (table 11).

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Table 9. Changes in Drug Utilization Patterns

Date	Propofol	Etomidate	Colloid (%)	Pancuronium (%)	Alfentanil/Sufentanil (%)	Fresh Gas Flow (L/min)
March 1994	40	5 (39)	13	20	3	4.02
February 1995	40	5 (34)	12	35	0.5	3.53
June 1995	32	2 (62)	4	75	0.1	3.22
January 1996	27	3 (85)	3	70	0.8	2.67

Propofol = percent of patients receiving bolus and/or infusion propofol; Etomidate = the percentage of patients overall receiving etomidate (in parentheses, the percentage of those patients receiving etomidate who were ASA 3E, 4 or 5); Pancuronium = for cases >90 min, the number of patients who received pancuronium divided by the number of patients receiving non-depolarizing muscle relaxants; Colloid = the percentage of patients receiving any albumin, hetastarch, or plasma protein fraction; Alfentanil/Sufentanil = percent of patients receiving either drug; Fresh Gas Flow = average fresh gas flow for each minute that inhalation anesthetics were in use.

Discussion

It should be noted that anesthesia costs are but 5.6% of the perioperative costs incurred by a hospital.²¹ However, the institution of practice guidelines to limit the inappropriate use of drugs produced large savings at our tertiary care hospital without adversely impacting clinical outcomes. Institution of similar practice guidelines should result in pharmaceutical savings in the range of 50% at tertiary care centers around the country, with a slightly smaller degree of savings expected at institutions with more ambulatory surgery. This is because of an inability to markedly decrease the use of intermediate acting neuromuscular blockers and propofol when short outpatient surgeries are performed. If

we assume that all surgeries had the same profile of drug use as Duke University Medical Center, the magnitude of national implementation would be on the order of 1 billion dollars.

Our methods of practice guidelines development mirrored the ideal methods of those who have published reviews on guidelines development (table 1).²²⁻²⁴ We actively pursued each of these ideas, and the success of this program should be attributed to the overall approach to utilization review.^{13,22-29} Merely transplanting these guidelines to another institution and announcing that they are being implemented would ignore one of the most important tenets of successful implementation—grassroots development and consideration of local practice patterns. Implementation from the top down would negatively impact the success of the program.

We purposefully chose a nonrandomized before and after observational prospective comparison study de-

|||||Prager LO: Obstacles seen in physician use of guidelines. *American Medical News*, February 19, 1996; pp 3, 26.

Table 10. Percentage of Patients Receiving Propofol before and after Practice Guidelines According to Anesthetic Technique

Group	Survey Period	N	%	P Value
Outpatient general	Before PG	61	44.5	NS
	After PG	91	47.9	NS
Inpatient general	Before PG	193	40.1	<0.0001
	After PG	109	23.2	<0.0001
Outpatient MAC	Before PG	60	73.2	NS
	After PG	36	67.9	NS
Inpatient MAC*	Before PG	9	50.0	<0.0001
	After PG	11	29.7	<0.0001
Outpatient regional	Before PG	27	47.4	NS
	After PG	20	46.5	NS
Inpatient regional	Before PG	48	54.5	<0.0001
	After PG	15	19.2	<0.0001

PG = practice guidelines; NS = not significant.

* Most inpatient MAC cases were sent directly back to the hospital room.

Table 11. Percentage of Patients Receiving Propofol Infusion before and after Practice Guidelines According to Anesthetic Technique

Group	Survey Period	N	%	P Value
Outpatient general	Before PG	21	15.3	NS
	After PG	20	10.5	NS
Inpatient general	Before PG	65	13.5	<0.0001
	After PG	12	2.6	<0.0001
Outpatient MAC	Before PG	37	45.1	<0.01
	After PG	12	22.6	<0.01
Inpatient MAC*	Before PG	7	38.0	<0.0001
	After PG	3	8.1	<0.0001
Outpatient regional	Before PG	19	33.3	<0.05
	After PG	11	25.6	<0.05
Inpatient regional	Before PG	37	42.0	<0.0001
	After PG	9	11.5	<0.0001

PG = practice guidelines; NS = not significant.

* Not corrected for multiple comparisons.

signed to test the hypothesis that practice guidelines effectively and safely reduce costs. We carefully considered whether we could introduce guidelines to half of our 58 faculty and make sure that they were evenly divided by anesthetic subspecialty practice. Because supervision of anesthesia care team personnel was the primary mode of practice, we would have had to randomize and then limit residents and CRNAs to work with the control group *versus* the practice guidelines group. We did not believe that we could adequately achieve separation or equality of the groups. Also, we could not guarantee that some of the practice guidelines would not be adopted by the control group. Having the pharmacy staff identify to whom they were to distribute drugs according to the practice guidelines would have been a daunting, if not impossible, task. Finally, the lack of scheduling flexibility inherent in joining certain residents and CRNAs to anesthesia care teams involving only certain attending physicians would have been impractical considering the demands of 40 anesthetizing sites per day. A recent editorial by Berwick³⁰ echoed our sentiments that much knowledge about medical processes and outcomes can be gained from studies that are not randomized controlled trials. It is extremely unlikely that a control group would have demonstrated any significant changes in practice during the few months' time frame of this study. A similar tertiary care institution 8 miles from ours measured their costs per case and costs per h during the time frame of this study (October 1993 to June 1995) and found no change.³¹ At our institution, no operational changes occurred in the ORs or in the PACU, nor did any change occur in

anesthesia care team personnel during this period. Also important is the fact that clinical outcomes were measured the first month after adoption of the practice guidelines. This would have most likely resulted in a higher incidence of adverse events requiring intervention because learning and becoming familiar with the new practice guidelines takes time.

The institution of practice guidelines to limit use of costly drugs produced savings markedly in excess of that reported previously using educational initiatives.^{15,17} Although substantial financial savings can initially be generated by educational efforts, physicians have a tendency to revert to old practice parameters after time.^{11,17} Base pharmaceutical costs per case and per h,^{14,15,32} the 10–23% savings reported using educational initiatives^{17,33} and the 40–50% savings reported after institution of practice guidelines with distribution control for neuromuscular blocking drugs^{34,35} are consistent with our results. It is interesting to note that the one practice guideline for which we were unable to control distribution (fresh gas flows) was the one with the least change noted, and the level of change was consistent with that expected for a purely educational initiative. After we were able to extract individual performance information for this parameter from our information system database and give accurate feedback to the practitioners, fresh gas flows decreased an additional 15%.

Institution of guidelines in our department was not without expenses. The time that anesthesia care providers worked on practice guideline teams was not calculated. The teams scheduled their meetings so as not to

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interfere with the OR caseload, and attending caregivers used nonclinical time, but a full counting of the cost would have to factor in the administrative expenses of arranging meetings, searching the literature for articles, writing and revising the guidelines, etc. Also, as this article and its companion piece make apparent, we relied heavily on the database created by an AARK for initially identifying areas of expense that would be worth cutting, and then we used the database to track our success and to provide feedback to the anesthesia care team. The authors estimate that about 50% salary support for 1 yr of the AARK system administrator's time would need to be figured into the start-up costs, plus about 5% thereafter to update the drug database and to generate reports. Also, it would be appropriate to add 3–10% of the cost of an administrative secretary or staff assistant—accounting for the approximately 2 days of work necessary to generate each feedback report—monthly initially, then quarterly. If commercial AARK manufacturers were to include cost analysis database software with their products, it may only require cost updates by Pharmacy with some oversight review by an anesthesiologist; in that scenario, costs would be negligible. If this monitoring were done by hand, the cost would be high, probably amounting to a clerical full-time equivalent on an ongoing basis. The cost of buying and installing the AARK itself was approximately 600,000 dollars (about 15,000 dollars per site). The list price for some systems as of October 1996 is approximately 20,000 dollars per site for software plus another 5,000–10,000 dollars per site for computer hardware.

We analyzed costs from the provider perspective. The patient's perspective, insurance company's perspective, and society's perspective would additionally include the minor increased anesthesiology provider costs associated with the 3-min increase in OR to PACU times. Additionally, the increased charges associated with the fact that MAC cases more often required PACU care would add cost in the instances wherein care was not covered under a case pricing structure (e.g., with the Health Care Financing Administration [HCFA], no additional charges would be recognized or paid if the patient went to the PACU as the payment is solely based on the Diagnosis Related Group [DRG]). Costs to society would need to additionally account for the impact (should similar guidelines be adopted by more hospitals across the country) on the pharmaceutical industry, its employees, and related microindustries.

The increase in time from end of surgery to arrival in the PACU was not believed to be clinically significant.

Operating rooms would not be forced to cancel or delay cases³⁶ or pay overtime as a result of the small 3-min change noted. The authors and their colleagues initially suspected that the single greatest factor leading to this outcome difference was a delay in the complete antagonism of neuromuscular blockade. However, analysis of the data suggests that times from the OR to the PACU after regional and MAC cases were even more affected, probably as a result of fewer propofol infusions and a greater reliance on narcotics and methohexital.

The increased rate of PACU admissions for patients receiving MAC would not have any effect on staffing costs. The burden of approximately one extra patient per day would not change PACU nursing requirements given the semifixed nature of PACU personnel costs.

It is interesting to note that system problems delaying discharge accounted for approximately 25% of the time patients spent in PACU. Although personnel costs in the PACU are semifixed (*i.e.*, it requires discrete steps of large numbers of patients for changes in patient volume to affect the numbers of personnel needed in the PACU),³⁷ it is certainly true that if all system problems were eliminated, PACU staffing could be proportionately downsized by some approximation of wasted time. A 25% annual savings of the 1.6 million dollar variable PACU nursing personnel costs at our institution (data: Transition One Accounting System, Transition Systems Inc., Boston, MA) would be 400,000 dollars, a substantial amount in relation to the 1 million dollars saved as a result of improved drug utilization. As we consider strategies such as practice guidelines that place limitations on physician practice, we should first consider initiatives that have no impact on clinical care.

We were careful not to let the anticipated system delays mask differences that may be found in more efficient operations. Times when the patients were judged ready for discharge were measured specifically to discount operational factors that were separate from the effects of practice guidelines; those times were identical before and after practice guidelines. There was a trend toward significance in the increased incidence of nausea and vomiting in outpatients receiving MAC and regional anesthesia. This was probably a result of decreased use of propofol infusions (for outpatient MAC cases, 45% before *versus* 23% after practice guidelines received propofol infusions) and substitution with methohexital with or without opioids. This drop occurred despite the practice guideline suggestion to consider propofol infusions routinely for outpatient MAC and regional cases. Although managing a case of nausea

and vomiting can be a small expense (approximately 1 dollar/patient variable costs)^{38,39} and although the observed increase in nausea and vomiting did not translate into increased average PACU times, we would recommend a greater utilization of propofol for sedation of outpatients during regional and MAC anesthesia or consideration of prophylactic antiemetics, such as perphenazine,⁴⁰ which are not sedating. We do not anticipate any savings from this change (for example, being able to downsize PACU staff),^{37,41} but the increased cost to the hospital for the propofol or prophylactic antiemetic is, and should be, overshadowed by considerations of patient comfort. If propofol use was extended to all appropriate patients as per the practice guidelines' suggestions, this would add about 1 dollar per patient (about 3% of current costs) for our group as a whole.

Regarding inpatients discharged from the PACU to the ward, it is possible that some increased complications, in particular nausea and vomiting, may have occurred only after they reached their hospital ward beds. Given the trend (statistically nonsignificant) toward an increased incidence of nausea and vomiting in outpatients receiving MAC and regional anesthesia, a follow-up study of inpatients after they are discharged to the wards merits further attention. Outpatients are monitored closely for a longer period of time than inpatients, and it is conceivable that immediate PACU outcomes may not adequately reflect the entire perioperative course for inpatients.

The use of pancuronium also was expected to be associated with a higher incidence of nausea and vomiting. Larger doses of neostigmine are necessary for antagonism of the more profound neuromuscular blockade achieved with pancuronium as opposed to the level of neuromuscular blockade associated with shorter-acting neuromuscular blocking drugs. The higher dosage of neostigmine causes increased acetylcholine release, which is probably associated with greater parasympathetic effect, and it has been previously suggested that this could cause more nausea and vomiting.⁴² Despite this theoretical concern, patients undergoing general anesthesia (*i.e.*, those most likely to receive muscle relaxants) did not experience any change in the incidence of nausea and vomiting after practice guidelines were instituted.

Pancuronium, which the practice guidelines designated as the default muscle relaxant for longer procedures, has a duration of muscle relaxation that can exceed 90 min when administered in a dose necessary to provide intubating conditions.⁴³ It was feared that the switch to pancuro-

nium would result in a markedly higher incidence of inadequate antagonism of muscle relaxation⁴⁴ and an increased risk of postoperative mechanical ventilation when compared with the newer more costly muscle relaxants it was replacing. This did not occur. Increased postoperative ventilatory problems may have been avoided because of an increased reliance on succinylcholine for use as an initial muscle relaxant to provide intubating conditions, followed by careful incremental dosing of pancuronium for surgical relaxation. (This requires a smaller total pancuronium dose.) This positive result was mirrored in a recent abstract that used self-reporting rather than prospective data collection to assess the effect of increased pancuronium use on PACU ventilatory outcomes.³⁵ Given the extremely low incidence of postoperative mechanical ventilation, this study does not have the power to conclusively rule out a statistically significant difference. However, the low incidence and narrow range of the 95% confidence limits combined with the nonmorbid nature of continuing mechanical ventilation into the early postoperative period suggests that even if there were a statistically significant difference, it would have a clinically negligible effect. A detailed repeat survey of unplanned postoperative mechanical ventilation in February 1996 revealed an incidence of 0.4% (4/966 patients), with only one case of unplanned mechanical ventilation resulting from an inability to reverse pancuronium. The hypothetical fear that patients receiving pancuronium intraoperatively would routinely arrive intubated in the PACU is apparently not a major concern.

The incidence of physiologic complications occurring in the PACU and the postoperative recovery times in this study are similar to that reported in the literature.^{35,39,41,45-47} Our cardiovascular and pulmonary complications were similar or slightly less than previous studies looking at complications occurring in the PACU.^{46,48,49} This may have been because we only recorded physiologic complications delaying PACU discharge. However, we believed events delaying discharge were more appropriate endpoints, expecting any significant morbid events to cause a delay beyond the mandatory 45 minute stay and discounting minor morbidity that does not affect patient flow.

We did not anticipate any specific complications as a result of abandoning colloid use for the majority of cases. The available literature suggests that there should be no difference in outcome when crystalloids are used rather than colloids. Some physicians were already using exclusively crystalloids as a standard of care. The prepractice guidelines colloid users were concerned about a possible increase in immediate postoperative cardiac, pulmonary,

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and renal complications, but consistent with expectations, this did not occur. Arterial hemoglobin desaturations and the incidence of oliguria, for example, were the same before *versus* after practice guidelines. No increase in any physiologic event delaying discharge from the PACU was seen. However, this study was not designed to detect complications that may be associated with the theoretical concern of greater postoperative fluid shifts as a result of greater interstitial fluid retention as a result of using larger volumes of crystalloid. Of note, the studies that have previously demonstrated an improved outcome using therapeutic regimens that included the administration of larger volumes of intravenous fluids have not demonstrated a difference between using colloids and crystalloids to achieve predetermined physiologic endpoints.^{50,51} These facts are emphasized in the guidelines.

It would be unwise to assume that all of the changes suggested here could be strictly applied with impunity to all patients without further study. Similarly, it may be imprudent to take these practice guidelines and strictly apply them to a patient population containing very sick patients (such as ICU patients or patients undergoing emergency surgery). We purposefully left a great deal of control in the hands of the attending physicians so that clinical judgment was preserved and never coerced. We believe that only physicians and their associates in the care team can make decisions on what drugs are appropriate for any patient.

The key to a successful implementation of practice guidelines lies in making it easier for physicians to change their practice than to continue in their old habits. We sustained success and prevented a relapse to previous prescribing practices by monitoring individual compliance using an advanced information management system, providing feedback to individuals practicing outside of the guidelines, and continuing distribution control. This approach previously has been shown to be successful for limited time frames.²⁵⁻²⁸

Alternative methods to limit pharmaceutical costs include formulary limitations. A recent report suggests that limitation of drug use by formulary restriction may increase, rather than decrease, total costs of care.### The lack of efficacy or acceptability⁵¹ of formulary limitations is a serious concern. As society searches for the greatest value in health care, we cannot expect the corporate culture sweeping medicine to disappear. We will eventually deal with the desire of administrators to control costs within their institutions. We believe that administrative solutions

such as formulary limitations can be effectively preempted by physician-developed practice guidelines that maximize appropriate use of health care resources.

In conclusion, we found that the institution of practice guidelines to promote the most appropriate use of anesthetic drugs reduced hospital costs 1 million dollars. The sustained success of this approach, especially its reliance on medical informatics, has great implications for those concerned with developing and instituting practice guidelines.

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Appendix A: Full Practice Guidelines Issued to the Department of Anesthesiology

I. Induction Drugs

Propofol. Only open what you are about to use. DO NOT OPEN VIALS IN ADVANCE; PUT ONE VIAL AT A TIME IN ANY INFUSION DEVICE. Only two vials (400 mg) will be distributed without attending physician approval.

Inpatients, Same-day Admissions, 23-h Admissions. General Anesthesia: Use propofol for induction in patients with a documented history of N/V or in patients having surgery that predisposes them to postoperative N/V (e.g., eye surgery, laparoscopic surgery). Do not use for infusion throughout the case. Consider use of propofol at the end of the case to increase any postoperative antiemetic effect. In cases longer than 2 h, do not use propofol for induction. Consider using propofol only for last 30 min of cases because the induction dose's antiemetic effect will probably have worn off before a long case is finished.

MAC or Regional Anesthesia with sedation: Use only if N/V is a major consideration.

Rationale for use of propofol: Inpatients/Same-day admits who have a likelihood of developing N/V would benefit from the antiemetic properties and would avoid discomfort, additional pharmacologic therapy, or longer PACU stays.

Practice Options: Consider using a methohexital infusion for cases longer than 90 min. This can be used for sedation with great success and still allow for direct discharge of patients to the floor.⁵³ For cases lasting longer than 90 min, this costs half as much as sedation with a propofol technique.

Outpatients. General Anesthesia: Consider propofol as an induction agent in all patients for cases less than 2 h. Minimize use for continuous infusion. Antiemetic effects can probably be obtained by

###Winslow R: Limiting drugs a doctor orders may cost more. Wall Street Journal March 20, 1996; p. B1.

induction doses and supplemental propofol at the end of the case, while using inhalation for the rest of the maintenance phase (at low flows!). Our clinical experience and the literature support the fact that wake up, emergence, and discharge from the hospital is not prolonged with this technique compared with a continuous propofol infusion.^{54,55}

Rationale: Outpatients benefit from the early emergence and antiemetic properties associated with propofol. This may allow faster discharge from the ambulatory surgery unit.^{55,56}

Practice Options: Use thiopental for induction in cases longer than 2 h because antiemetic effect associated with propofol induction is probably gone. Consider propofol infusion at the end of the case.

MAC or Regional Anesthesia with sedation: Consider routinely in all outpatients.

Practice Options: May consider using a methohexital infusion—see previous.

Etomidate. Consider for transplant cases (heart, lung, kidney) requiring a rapid sequence induction. May consider use when a deep plane of anesthesia is required concomitantly with maintenance of perfusion pressure. Use should require an attending signature for release from pharmacy for all cases.

Rationale: Patients receiving this drug should be so sick that attending physician input is necessary for choosing this induction agent.

Practice Options: Consider using only in patients requiring hemodynamic stability during induction and who will be extubated at the end of the case. Consider a fentanyl-based induction if patient will remain intubated. Consider a reduced dose of thiopental if some response to intubation is not detrimental.

II. Intravenous Fluids, or Colloids versus Crystalloids in the OR at DUMC

Attending physician release of colloid from the pharmacy will be necessary except when particular subspecialty sections develop plans for routine use in particular cases.

Normal saline or lactated Ringers solution followed by packed red blood cells are indicated for all fluid maintenance in the ORs. May consider use of a colloid for:

- Life-threatening massive hemorrhage; and
- Patients at high risk of developing endothelial leak (e.g., cardiopulmonary bypass, transplantation surgery, some major intravascular and intracranial surgery).

Rationale: There are no human data that demonstrate that any particular solution (colloid or crystalloid) is better than another in terms of outcome. It is pointless to give small amounts of colloid in any circumstance; small amounts (< 1 l) will not result in any change in colloid oncotic pressure.

Practice Options: To avoid tissue hypoperfusion, one needs to give enough of whatever is chosen, and it needs to be given promptly with the appropriate level of monitoring.⁵¹ A lesser volume of colloid is required than crystalloid to obtain the same amount of intravascular volume expansion. Use inflatable pressure bags to infuse crystalloid quickly to get equivalent intravascular volume expansion in the same amount of time.

III. Neuromuscular Blocking Agents

Succinylcholine and pancuronium are the default muscle relaxants and should be considered for each procedure that requires muscle

relaxation. All of the intermediate muscle relaxants remain on formulary, but the intent of this policy is to prevent the prolonged, inappropriate use of these more costly muscle relaxants when a less costly alternative is available. If more than one vial of the intermediate acting group of muscle relaxants is requested (vecuronium, atracurium, rocuronium, mivacurium), the attending physician will have to release it from the OR satellite pharmacy.

Practice Option 1: Use of pancuronium for case 60–90 min in length should be considered if succinylcholine is used for intubation, and especially if complete relaxation (i.e., ≤ 1 twitch on train-of-four monitoring) is not required throughout the case. Hints on the use of pancuronium to avoid problems:

- 1) Titrate to ≤ 1 twitch on train-of-four monitor;
- 2) Use small incremental doses (0.25 ml of 2 mg/ml = 0.5 mg at a time);
- 3) As opposed to bolus dosing of pancuronium,⁵⁷ anecdotal clinical experience suggests that titrated small incremental doses (0.5–1.0 mg) do not cause the same degree of tachycardia.

Tachycardia after pancuronium dosing also may be more limited in patients taking beta-blockers.

Succinylcholine in pediatrics. Succinylcholine in children is not recommended for routine use, but it may be considered.

Rationale: The Food and Drug Administration has rescinded its earlier hazard warning, which contained a more explicit warning notice.

Succinylcholine in adults. Succinylcholine can be used as part of the routine induction sequence in adults as long as arrhythmias are not a major concern (as they are, for instance, in Automatic Implantable Cardiac Defibrillator [AICD] implantation cases).

Rationale: Use of intubating doses of pancuronium may lead to difficulty reversing the neuromuscular blockade if case times are slightly less than expected. A high incidence of postoperative myalgias are not necessarily related to succinylcholine administration even during simple cases.^{58–60} Longer, more complex cases often will require postoperative analgesics that will mask any myalgias.

Rapid Sequence Inductions. Use succinylcholine. Use rocuronium for rapid sequence only when succinylcholine is contraindicated (e.g., full stomach considerations combined with a history of congenital muscle disease or stroke).⁶⁰

Use of vecuronium or rocuronium for cases longer than 90 min. Only where the control of heart rate is extremely important.

Practice Options: For cardiac and noncardiac surgery, if rocuronium is absolutely needed for an intubating dose, consider incremental dosing with pancuronium after the first vial.

IV. Opioids and Benzodiazepines

Opioids. Fentanyl is indicated in all cases.

Rationale: No evidence exists that suggests that any narcotic is superior (pharmacodynamically) to fentanyl.^{61,62} When opioids are used in common amounts as the analgesic component of an anesthetic (i.e., below the threshold for significant respiratory depression and not as the entire anesthetic), recovery is unaffected by choice of opioid.^{63,64} Others opioids—alfentanil, sufentanil—are markedly more costly.

Practice Options: For patients receiving high-dose narcotics who have a planned early postoperative extubation, sufentanil may be considered. However, patients who are candidates for early extuba-

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tion can usually tolerate isoflurane as part of their anesthetic (in combination with fentanyl) for an equivalent result.

Benzodiazepines. There is no acceptable substitute for intravenous midazolam currently in the United States. Midazolam will be routinely issued in a 2-mg size rather than the current 5-mg size.

Rationale: Vein irritation in the awake anxious patient with intravenous diazepam is considered unacceptable. However, judicious use of midazolam in patients requiring anxiolysis is appropriate because not every patient requires midazolam before induction of anesthesia. Analysis of Arkive® case records indicates that most patients do not receive more than 2 mg. Our anecdotal experience suggests that adequate anxiolysis and amnesia before general anesthesia can usually be obtained with this dose.

Practice Options: Consider preoperative administration of diazepam as a premedicant, especially for inpatients. Consider other benzodiazepines when administering through a central line. In cardiac surgery cases, consider other benzodiazepines if early postoperative extubation is not a critical factor.

V. Inhalation Anesthetics

1. Continue to use isoflurane as the primary agent for all inhalation anesthetics.
2. After checking for a leak-free circuit and assessing the function of an in-line oxygen monitor, use the minimal fresh gas flows that do not cause nitrous oxide-to-oxygen ratio anesthetic machine alarms.

Fresh gas flows greater than 1 l/min should not be required (0.6 l/min N₂O and 0.4 l/min O₂).

Rationale: No indication was found for desflurane.⁶⁵⁻⁶⁷

N.B. Sevoflurane was not included because it was not available at the time of this study. No cost or outcome differences could be ascribed to our current decision to use sevoflurane only for induction of anesthesia in pediatric patients and then to switch to a less costly agent, halothane or isoflurane, for maintenance.⁶⁸

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