0749-5161/99/1506-0388
PEDIATRIC EMERGENCY CARE

Vol. 15, No. 6
Printed in U.S.A.

Continuous-flow delivery of nitrous oxide and oxygen: A safe and cost-effective technique for inhalation analgesia and sedation of pediatric patients

JAN D. LUHMANN, MD, ROBERT M. KENNEDY, MD, DAVID M. JAFFE, MD, JOHN D. McALLISTER, MD

Nitrous oxide (N_2O) safely and rapidly alleviates the pain and distress of minor procedures in the emergency department (ED). We have found self-administration in children does not consistently achieve acceptable analgesia and sedation. The equipment generally available for ED use is designed for adults and delivers 50% N_2O through a demand valve that requires an inspiratory effort of −3 to −5 cm of water to activate gas flow. This is difficult for young children who are crying, have more shallow respirations than adults, or cannot follow instructions. In collaboration with the Departments of Anesthesiology, Dentistry, and Respiratory Therapy, we constructed a continuous-flow system for delivering N_2O and oxygen (O_2). The following is a description of the components, assembly, and use of a continuous-flow machine that safely and inexpensively delivers N_2O and O_2 to children.

INTRODUCTION

Inhaled nitrous oxide (N_2O) at 50% or less has many benefits for pediatric patients undergoing brief, painful procedures in the emergency department (ED). The gas is odorless, well tolerated, and does not require intravenous access. In healthy patients, N_2O rapidly induces sedation, analgesia, and amnesia without adverse cardiopulmonary side effects (1–10).

Although the exact mechanism of action of N_2O and other inhaled anesthetics is unknown, clinical effects are determined by the partial pressure of the gas in the brain. N_2O partial pressures achieve rapid equilibration in the pulmonary alveoli and the brain. Inhalation of high concentration N_2O results in a very rapid uptake and onset of clinical effect. Similarly, rapid elimination and termination of effect occurs by pulmonary ventilation since metabolism is negligible. Owing to these characteristics, the end tidal measurement of N_2O concentration is an excellent objective measure of effective administration.

The pharmacologic and physiologic effects of N_2O may cause adverse effects in selected patients. Volume or pressure within air-filled body cavities increases as N_2O diffuses into these spaces. The magnitude of change depends upon the partial pressure of N_2O, blood flow to the cavity and the duration of administration as demonstrated in an animal model in which 75% N_2O doubled the volume of a pneumothorax in 10 minutes (11). Additionally, diffusion hypoxia may occur when administration is discontinued, in the absence of supplemental O_2, owing to the dilution of alveolar O_2 by the outpouring of N_2O from the blood to the lungs (12). For these reasons and effects on cerebral blood flow, level of consciousness and inspired O_2 concentration, the administration of N_2O is contraindicated in the presence of head injury or elevated ICP, drug intoxication, hemodynamic instability, pneumothorax, otitis media, bowel obstruction, or any other condition with a pathologic, air-filled body cavity (10). Additionally, there may be a slightly increased risk of spontaneous abortion among women exposed continuously to trace anesthetics (13), but studies have shown no teratogenic (14–16) or carcinogenic (17, 18) effects in animals.

A number of trials in pediatric patients have established a clinical safety record. After short-term exposure no major complications, unusual adverse reactions, loss of consciousness, unmanageable behavior, or change in vital signs were reported in over 1200 relatively healthy patients (19, 20). Minor side effects may occur in approximately 10 to 30% of patients (5, 10). Most commonly, these include motor excitation, nausea, vomiting, and dizziness. The possible risk of aspiration resulting from diminished airway reflexes has been noted. However, in the absence of other sedatives, clinical trials demonstrate that protective airway reflexes are intact at a concentration of 50% N_2O with O_2 (21, 22).

Fifty percent N_2O provides effective sedation for uncomplicated fracture reduction in most older children. It has also been extensively used by dentists and surgeons in pediatric outpatient settings at concentrations up to 70% (9, 23, 24). Thirty percent N_2O reduced distress in children undergoing laceration repair; however, many children were upset and required physical restraint to accomplish the procedure (5). We reported that 50% N_2O is safe and effective for alleviating distress in young children who need laceration repair (25, 26). Despite this reasonably favorable clinical and safety profile, N_2O is seldom used in young pediatric emergency patients. The availability of acceptable delivery machines may be one factor in limiting a more widespread application in these patients.

From the Departments of Pediatrics, Division of Emergency Medicine (J.D. Luhmann, R.M. Kennedy, D.M. Jaffe), and Anesthesiology (J.D. McAllister), Washington University School of Medicine, St. Louis Children's Hospital, St. Louis, Missouri.

Address for reprints: Jan D. Luhmann, MD, Department of Pediatrics, Division of Emergency Medicine, Washington University School of Medicine, St. Louis Children's Hospital, One Children's Place, St. Louis, MO 63110-1077; email: Luhmann_J@kidsA1.wustl.edu

The authors would like to acknowledge Mark Richardson and John Boehone for contributing their expertise in assembling the continuous delivery system. In addition, we would like to thank Cindy Kane and Kristine Kulage for manuscript preparation.

Key Words: Nitrous oxide, sedation, anxiolysis

The equipment most commonly used for ED administration of N_2O (eg, Nitronox® Delivery System, MDS Matrx, Inc. Ballentine, SC) delivers a fixed mixture of 50% N_2O with 50% 0_2 and uses a demand valve that requires both a tight face-to-mask seal and patient-generated negative inspiratory pressure of −1 to −5 cm of water (H_2O) to generate gas flow (10). These safety features, together with the requirement of patient self-administration of the gas mixture, function well in adults and older children but poorly in young children. Our experience in young children with this type of delivery system demonstrated that clinically effective sedation and analgesia is not achieved. Monitoring inspiratory and expiratory concentrations of N_2O with a Space Labs Medical® Capnograph 90513 (SpaceLabs Medical, Redmond, VA) confirmed end tidal concentrations of N_2O were significantly less than intended.

Commercially available equipment that delivers a continuous flow of N_2O and O_2 can cost $3000.00 to $5000.00 (27). Consequently, we collaborated with the Departments of Anesthesiology, Dentistry, and Respiratory Therapy to construct a cost-effective, continuous-flow machine for delivering N_2O and O_2 mixtures to young children via a nasal/face mask. Fifty percent N_2O with bubble-gum scent applied to the mask interior, and developmentally appropriate patient preparation, has resulted in favorable mask acceptance and sedation/analgesia in children as young as 2 years of age (25, 26). These trials suggest N_2O can be clinically effective and safely administered to young children.

MACHINE COMPONENTS AND ASSEMBLY

The gas delivery apparatus provides a continuous flow of N_2O and O_2 (Fig. 1). The design is simple, portable, and easily constructed with readily available hospital equipment; costs are illustrated in Table 1. Additionally, a number of safety features have been incorporated to minimize equipment complications and trace gas exposure. The gas delivery apparatus is composed of four main components:

1) Gas supply sources and delivery hoses for N_2O and O_2.
2) N_2O/O_2 adjustable ratio blender with gas flow meter.
3) Anesthesia circuit for gas delivery incorporating a bacterial/viral filter and optional gas-monitoring device.
4) Scavenging system to minimize escaped gas exposure in health care personnel.

The gas sources for the delivery apparatus could be medical gas cylinders or wall outlets from a piped central distribution system. Our

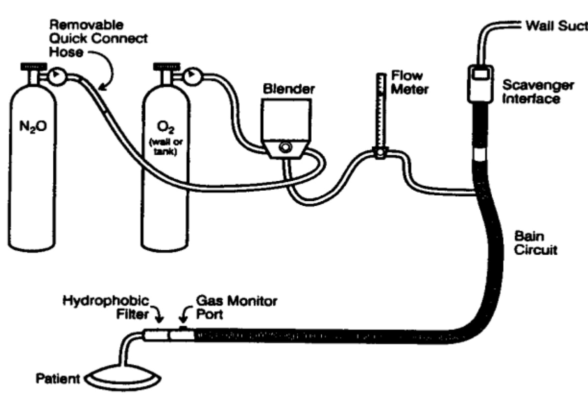

FIG 1. N_2O/O_2 continuous flow apparatus.

TABLE 1

Equipment and approximate cost for continuous delivery of nitrous oxide

Equipment	Manufacturer	Cost
Cylinder cart	Anthony Medical, 6114 R-CRO	$167.00
N_20 low flow blender (3-30LPM)	Bird Medical, 10021	$1,050.00
Vacuum Manifold	Anesthesia Associates, 00-117	$287.00
N_2O regulator	Western Enterprises, M2-326-p	$180.99
Chemtron vacuum couplers, ea (3)	Allied Medical, 11-02-0028	$51.00
Chemtron High Pressure Hose, ea (3)	Chemtron International, Inc.	$75.00
Pole mount channel clamp	Eastern Rail, 9902	$51.00
Flowmeter with 2-inch elbow	Allied Medical, 10796	$45.00
Total		$1,906.99

design uses a combination of both sources. Quick-connect couplers were used for the delivery hoses. This coupling system is unique and non-interchangeable for each type of gas/vacuum hose to prevent connection errors. A standard H or M size medical gas cylinder supplied the N_2O, and a wall outlet was used to supply O_2 at a pressure of 50 psig. The tank is bracketed to a mobile cylinder cart to facilitate transport of the unit between various clinical locations in the ED.

The N_2O cylinder is color-coded blue in accordance with the Compressed Gas Association standard (28). A pressure gauge and a hand wheel controlled N_2O regulator preset to deliver gas at 50 psig are threaded into the N_2O cylinder outlet. The regulator valve is closed by the hand wheel after each use and slowly opened prior to the next case to prevent damage to the regulator.

N_2O exists as a liquid in the pressurized medical gas cylinders. The gauge pressure on the cylinder reflects the constant vapor pressure of the remaining liquid and will not fall until all liquid is vaporized. Each H or M cylinder contains, respectively, 7,570 or 15,800 liters of N_2O when full, and when empty, the tanks weigh 63 or 119 pounds.

Chemtron® high pressure supply hoses (color-coded green for O_2 and blue for N_2O, Chemtron International, Inc., Dublin, CA) convey the gases to the N_2O/O_2 blender. A short, 8-inch extension hose threaded directly to the N_2O regulator is equipped with a female quick connect coupler which is followed in series with a longer extension to the blender. The short connecting section may be easily removed and locked after each clinical use to limit potential abuse of N_2O.

The Bird® low flow N_2O/O_2 blender (Bird Products Corporation, Palm Springs, CA) is a proportioning device (ratiometer) that has an operating flow range of 3 to 30 liters per minute and reduces the high pressures of both wall and cylinder gas sources. An adjustable rotary valve limits the FiO_2 (fractional inspired concentration of O_2) between 30% and 100% ± 4%. An audible alarm is activated if gas supply pressures differ by 20 ± 2 psi and a minimum FiO_2 of 30%. These features prevent inadvertent administration of excessive N_2O or a hypoxic gas mixture.

The desired gas mixture is conveyed from the exit port of the blender through a 2-inch elbow to a standard variable orifice Thorpe tube (Allied Medical®, Concord, Ontario, Canada) 0–15 liter per minute flow meter. The blender/flow meter unit is bracketed to the horizontal handle of the cylinder cart with a pole mount channel clamp. The desired gas flow is conveyed through a vinyl hose from the flow meter nipple to the fresh gas inlet port of the anesthesia cir-

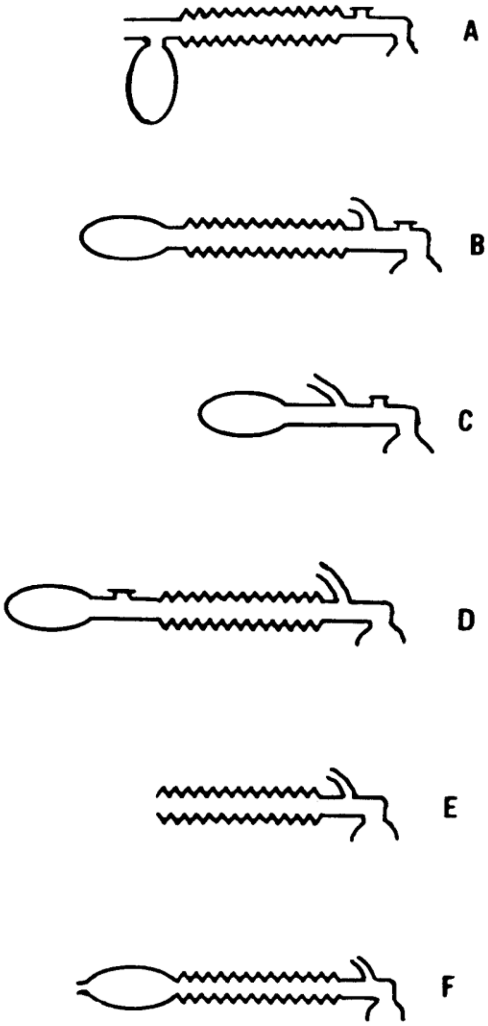

FIG 2. Mapleson Classification System.

cuit. A Bain® (Kendall Healthcare Products Co., Mansfield, MA) modification of the Mapleson D anesthesia circuit delivers the fresh gas supply to the patient and facilitates the scavenging of exhaled waste gases by the hospital vacuum system (Fig. 2).

The Mapleson breathing systems are a classification of circuits used to deliver anesthetic gases (12). They are characterized by the absence of valves or a CO_2 absorber. Since there is no separation of inspired and expired gases, the fresh gas flow must "wash out" the patient's exhaled CO_2 to prevent rebreathing and hypercarbia. The coaxial Bain® circuit supplies fresh gas through a tube located within a larger, corrugated outer exhaust tube. This decreases the bulk and weight of the circuit. Spontaneous ventilation is easily accomplished but assisted or positive pressure ventilation is not possible with our device.

A series of curves can be graphically illustrated to demonstrate the relationship between the fresh gas flow rate, patient minute volume and arterial CO_2 levels under controlled ventilation conditions (29) (Fig. 3). A similar relationship exists for spontaneous ventilation. Many different formulae to predict the fresh gas flow requirements have been developed to prevent rebreathing of exhaled gases (29). Most of these studies show that a fresh gas flow of at least 1.5 to 3 times per minute ventilation, or approximately 150 to 300 ml/kg/minute prevents rebreathing of exhaled gases in a continuous circuit. However, monitoring of end tidal CO_2 is optimal for determination of minimum fresh gas flow rates, which prevent excessive rebreathing. Gas flow rates of 5–10 liters per minute are sufficient for most children and functionally convert the circuit from partial rebreathing to nonrebreathing.

There are several advantages to this circuit design, but there are also some caveats to safe use. The equipment is rugged, simple to assemble and use, and easily accepts a gas scavenging system. The lack of valves and low resistance facilitates unrestricted spontaneous ventilation in young children. However, a separate bag-valve-mask device must be immediately available for emergencies, since positive pressure ventilation and CPAP are not possible. The adequacy of fresh gas flow is critical for oxygenation, ventilation, and patient comfort.

A sidestream gas analyzer may be used to measure the CO_2, N_2O, and O_2 levels. The end tidal gas measurements reflect pulmonary alveolar partial pressures and closely correlate with arterial samples in healthy children and adults (30). We use a Space Labs Medical® Capnograph 90513 gas monitor. Gas is continuously aspirated through a thin plastic tube from a sampling port on the connector located near the face mask. The inspiratory and end tidal partial pressures or concentrations are numerically displayed, with CO_2 graphically illustrated as a capnogram, on the same Space Labs Medical monitor recording vital signs.

A disposable Humid-Vent® HME (heat moisture exchanger, Gilbeck, Upplands, Väsby, Sweden) filter inserted between the circuit and the face mask conserves exhaled heat and humidity and is an effective bacterial/viral filter (29). This filter permits reuse of the anesthesia circuit between patients. A clear, disposable, cushioned face mask is scented with commercially available bubble gum scent applied to the interior surface to improve acceptance by pediatric patients. These two devices are the only disposable equipment items. The remainder of the circuit, including the gas sampling line, is reused.

Excess fresh gas flow and exhaled gas are prevented from flowing into the room by a scavenging system that collects the gases for removal by the hospital in-wall vacuum. The components of a scavenging system are the gas collecting assembly to capture gases from the circuit, a transfer means to convey them to an interface, and the gas disposal apparatus. A short, corrugated, kink resistant hose collects gases from the Bain® circuit and conveys the waste gas to an interface that prevents transmission of positive or negative pressure fluctuations in the scavenging system to the breathing circuit. The interface, a vacuum manifold from Anesthesia Associates® (San Marcos, CA), is mounted to a horizontal support frame of the cylinder cart and complies with American Interface Standards (29). The interface has a reservoir bag for expired gases and opens to the atmosphere for negative or positive pressure relief. Waste gases are carried from the interface to the hospital in-wall vacuum system through a black quick connect hose.

CLINICAL PREPARATION AND SET-UP

Cardiorespiratory monitors including pulse oximetry, BVM device, O_2, and auxiliary wall suction should be prepared prior to administration of N_2O. All patients are monitored in accordance with 1992 American Academy of Pediatrics and American Society of Anesthesiologists guidelines (31). An appropriately sized face

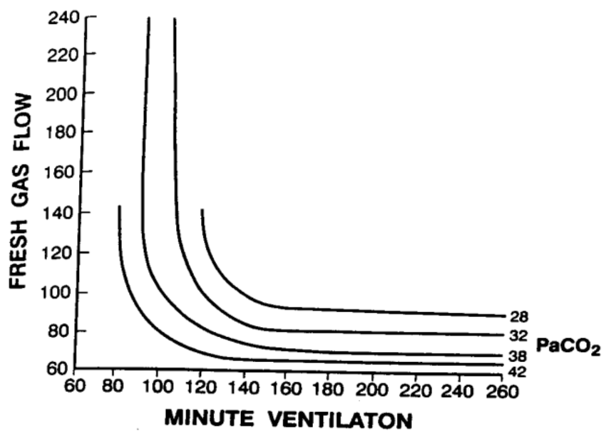

FIG 3. Relationship of fresh gas flow, minute ventilation, and $PaCO_2$.

mask scented with bubble gum, elbow connector with a gas sampling line, and HME filter are connected to the anesthesia circuit. The scavenger hose from the interface is coupled to the wall suction outlet and the green O_2 and blue N_2O delivery hoses from the blender are attached to their respective gas sources. The hand wheel valve of the N_2O tank is turned counterclockwise to pressurize the blender, which is set to 100% O_2. The gas flow meter is set to 5 or 10 l/min. After achieving mask acceptance the blender is dialed to 50% N_2O. At the conclusion of the case, in the event of vomiting, sustained desaturation below 93% or other clinical concerns the delivery of N_2O is terminated by dialing to 100% O_2 for 30–60 seconds. The mask and HME filter are removed and the N_2O cylinder valve closed after completion of the sedation.

Environmental services should confirm that the treatment areas maintain 7–10 air exchanges per hour. Ambient levels of N_2O should be measured to confirm that room air exchanges and scavenging are effective in eliminating ambient N_2O. After the initial sampling, this monitoring should be done twice a year to ensure that N_2O levels remain within acceptable limits for employee exposure. Maximum levels for 8-hour exposure recommended by the Occupational Safely and Health Administration are 50 parts per million (32). N_2O should be handled in the same manner as any controlled substance in order to prevent unauthorized use of the gas. In our ED, the short N_2O quick connect hose can be stored in a locked narcotic box between cases for this purpose.

It is crucial that physicians are thoroughly familiar with this agent and with advanced resuscitation skills prior to clinical use. In accordance with guidelines from the American Academy of Pediatrics Committee on Drugs for monitoring during sedation of pediatric patients, the practitioner who administers and monitors the sedation must have immediately available the facilities, personnel, and equipment to manage unexpected crisis situations (31). A second health care worker should be responsible for performing the procedure.

SUMMARY

A simple and relatively inexpensive machine for continuous delivery of N_2O and O_2 has been used in our pediatric ED for 4 years. We have found this to be safe and effective for selected patients. Patients, families, and emergency department staff have appreciated its clinical utility for facilitating a variety of procedures, including laceration repair, foreign body removal, intravenous cannulation, lumbar puncture, burn debridement, reduction of minor fractures or joint dislocation, and sexual abuse examinations.

REFERENCES

1. Wynne J, Mann T, Alpert JS, et al. Hemodynamic effects of nitrous oxide administered during cardiac catheterization. JAMA 1980;243:1440–1443.
2. Stewart RD. Nitrous oxide sedation/analgesia in emergency medicine. Ann Emerg Med 1985;14:139–148.
3. Thal ER, Montgomery SJ, Atkins JM, et al. Self-administered analgesia with nitrous oxide: Adjunctive aid for emergency medical care systems. JAMA 1979;242:2418–2419
4. Wattenmaker I, Kasser JR, McGravey A. Self-administered nitrous oxide for fracture reduction in children in an emergency room setting. J Orthop Trauma 1990;4:35–38.
5. Gamis AS, Knapp JF, Glenski JA. Nitrous oxide analgesia in a pediatric emergency department. Ann Emerg Med 1989;18:177–181.
6. Hennrikus WL, Simpson RB, Klingelberger CE, et al. Self-administered nitrous oxide analgesia for pediatric fracture reductions. J Pediatr Orthop 1994;14:538–542.
7. Maloney JM III, Coleman WP III, Mora R. Analgesia induced by nitrous oxide and oxygen as an adjunct to local anesthesia in dermatologic surgery. J Dermatol Surg Oncol 1980;6:939–943.
8. Braun SD, Miller GA, Ford KK, et al. Nitrous oxide: Effective analgesic for vascular and interventional procedures. AJR 1985;145:377–379.
9. Dunn-Russell T, Adair SM, Sams DR, et al. Oxygen saturation and diffusion hypoxia in children following nitrous oxide sedation. Pediatr Dent 1993;16:88–92.
10. Stewart RD. No more pain: Nitrous oxide. Emerg Med 1986; 18:49–50:52–53.
11. Eger EI, Sardman LJ. Hazards of nitrous oxide anesthesia in bowel obstruction and pneumothorax. Anesthesiology 1965;26:61–66.
12. Smith TC. Anesthesia breathing systems. In: Ehrenwerth J, Eisenkraft JB, eds. Anesthesia equipment, principles and applications. St. Louis: Mosby, 1993;89–113.
13. Buring JE, Hennekens CH, Mayrent SL, et al. Health experiences of operating room personnel. Anesthesiology 1985;62:325–330.
14. Mazze RI, Wilson AI, Rice SA, et al. Reproduction and fetal development in mice chronically exposed to nitrous oxide. Teratology 1982; 26:11–16.
15. Vieira E, Cleaton-Jones P, Moyes D. Effects of intermittent .5% nitrous oxide/air (v/v) on the fertility of male rats and the post-natal growth of their offspring. Anaesthesia 1983;38:319–323.
16. Baden JM, Rice SA, Serra M, et al. Thymidine and methionine syntheses in pregnant rats exposed to nitrous oxide. Anesth Analg 1983;62: 738–741.
17. Baden JM, Kundomal YR, Luttropp ME, et al. Carcinogen bioassay of nitrous oxide in mice. Anesthesiology 1986;64:747–750.
18. Eger EI II, White AE, Brown CL et al. A test of the carcinogenicity of enflurane, isoflurane, halothane, methoxyflurane and nitrous oxide in mice. Anesth Analg 1978;57:678–694.
19. Griffin GC, Campbell VD, Jones R. Nitrous oxide-oxygen sedation for minor surgery. Experience in a pediatric setting. JAMA 1981;245: 2411–2413.
20. Stewart RD, Paris PM, Stoy WA, et al. Patient-controlled inhalational analgesia in prehospital care: A study of side effects and feasibility. Crit Care Med 1983;11:851–855.
21. Cleaton-Jones P. The laryngeal-closure reflex and nitrous oxide-oxygen analgesia. Anesthesiology 1976;45:569–570.
22. Roberts GJ, Wignall BK. Efficacy of the laryngeal reflex during oxygen-nitrous oxide sedation (relative analgesia). Br J Anaesth 1982;54: 1277–1281.

23. Ruben H. Nitrous oxide analgesia in dentistry. A physiological and clinical study. Br Dent J 1972;132:195–196.
24. Major E, Winder M, Brook AH, et al. An evaluation of nitrous oxide in the dental treatment of anxious children. A physiological and clinical study. Br Dent J 1981;151:186–191.
25. Luhmann JD, Kennedy RM, Porter FL, et al. Nitrous oxide regimens more effective than midazolam for reducing distress during laceration repair in young children. Pediatr Res 1998;4:68A.
26. Luhmann JD, Kennedy RM, Porter FL, et al. A trial of nitrous oxide and midazolam vs comforting during laceration repair in young children. Acad Emerg Med 1998;5:518.
27. Matrix Medical Inc. 1996 Dental Catalog.
28. Dorsch J, Dorsch S, eds. Medical gas cylinders and containers. In: Understanding anesthesia equipment, ed 3. Baltimore: Williams & Wilkins, 1994;2–23.
29. Dorsch J, Dorsch S eds. The Mapleson Breathing Systems. In: Understanding anesthesia equipment, ed 3. Baltimore: Williams & Wilkins, 1994;167–189.
30. Good ML, Gravenstein N, Capnography. In: Ehrenwerth J, Eisenkraft JB eds. Anesthesia equipment, principles and applications. St. Louis: Mosby, 1993:237–248.
31. American Academy of Pediatrics, Committee on Drugs, Section of Anesthesiology: Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures. Pediatrics 1992;89:1110–1115.
32. Nitrous oxide level recommendation: National Institute for Occupational Safety and Health (NIOSH): Criteria for a recommended standard. Occupational exposure to waste anesthetic gases and vapour. Department of Health and Human Services (NIOSH) Publications No. 77–140, Cincinnati, Ohio.