TITLE: HYPERBARIC NITROUS OXIDE ANESTHESIA IN RATS FOR MAC DETERMINATION

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MAC, "the minimum alveolar concentration necessary to prevent purposeful movement in response to a painful stimulus," is a measure of volatile anesthetic agent potency. Although MAC for N_2O has been directly measured in man, in rats it has primarily been extrapolated from the previously known MAC of a volatile agent and the presumed linear relationship between MAC values for mixed agents.[1] The MAC of N_2O for rats determined in this manner has been described as ranging from 1.36 to 2.20 ATA (1 atmosphere absolute = 760 mmHg) of N_2O. Because MAC for N_2O exceeds 1 ATA we directly measured the MAC of N_2O for rats by maintaining general anesthesia with a N_2O:O_2 mix in a hyperbaric chamber.

Long Evans rats of similar age and weight were studied. Anesthesia was induced in a 2 liter plexiglass box with a gas mixture of oxygen and nitrous oxide (50:50) and 3% isoflurane. Each rat was orotracheally intubed and ventilated by a Harvard rodent ventilator. Monitoring was by compressed spectral array, somatosensory evoked potentials (Neurotrac, Interspec Medical), EKG, and end-tidal gas analysis for $ETCO_2$, ETN_2O, and ET isoflurane by mass spectrometry (Perkin-Elmer MGA 1100). Isoflurane was discontinued and the rats were compressed to 2.25 ATA with 1.8 ATA N_2O/0.45 ATA O_2. After 30 min stabilization with end-tidal isoflurane =0 and mild hyperventilation, each rat was given supramaximal, elecrical stimulii (Grass SD-5 Stimulator) subcutaneously (50 volts at 50 cycles/sec for 10 msec). The partial pressure of N_2O was decreased and allowed to equilibrate for 15 min after each negative response but chamber pressure was sustained. The MAC was taken as the N_2O partial pressure midway between that at which the rat moved purposefully and the next higher at which no response occurred. Hyperbaric N_2O depressed both somatosensory evoked potentials and the compressed spectral array. The MAC of N_2O determined for rats was 1.54±0.16 ATA.

The MAC of N_2O in rats was directly determined by combining hyperbaric general anesthesia, end-tidal gas analysis from the chamber and a controlled supra-maximal electrical stimulus. The MAC value of 1.54 is within the range determined in previous studies of the additive effects of volatile agents but markedly below that extrapolated from studies of possible nonlinear relationships.[2] Hyperbaric N_2O at levels from 1.3 to 2.0 ATA also depresses both somatosensory evoked potentials and cortical electrical activity.

References.
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2. Cole DJ, Kalichman MW, Shapiro HM. The nonlinear contribution of nitrous oxide at sub-MAC concentrations to enflurane MAC in rats. Anesth Analg 1984;68:556-62.

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TITLE: INTRAVENOUS ATP ATTENUATES SURGICAL STRESS RESPONSES AND REDUCES INHALATION ANESTHETIC REQUIREMENTS IN HUMANS

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INTRODUCTION: Intravenous Adenosine (Ado) and Adenosine Triphosphate (ATP) have potent inhibitory actions on the cardiovascular as well as the CNS; these purines inhibit catecholamine release and/or act as neurotransmitters or neuromodulators of neural activities In animal experiments,both Ado and ATP have been shown to reduce halothane requirements. In the present study, we examined whether supplemental IV ATP could suppress the circulatory, neuro-behavioral and movement responses to surgery during Enflurane (ENF)-Nitrous Oxide (N_2O)-Oxygen anesthesia.

METHODS: Following Institutional approval, 14 ASA-1 consenting patients (15-56 yrs) undergoing oral surgery were studied. After premedication (atropine 0.5 mg, pentazocine 15 mg, hydroxyzine 75-100 mg IM), anes thesia was induced with IV thiopental (4-5 mg/kg) and intubation was facilitated with succinylcholine (1 mg/kg). During surgery, anesthesia was maintained initial ly with 1.3% MAC ENF-N_2O (60%)-O_2 (40%) breathing spon taneously. No further muscle relaxants were used. Expired anesthetic gases were continuously monitored. After IV dipyridamole 0.2 mg/kg, ATP was infused continuously into a peripheral vein to maintain normotension and equi-MAC level of anesthesia. Thus, doses of ATP, ENF and N_2O were titrated, so that the lowest possible doses of ENF or N_2O were administered during surgery.

RESULTS: Main results are shown in the Table and Fig. In spontaneously breathing patients, ATP infusion at doses of 108±21 (μg/kg/min) effectively inhibited the increase of BP of intubation and surgery. ENF or N_2O could be easily reduced or totally replaced by ATP infusion when combined either with 60% N_2O alone (n=7) or 0.91±12% ENF alone (n=7). No sign of inadequate anesthesia or motor movement could be seen at any time. All patients emerged from anesthesia smoothly, and rapidly opened their eyes to verbal command. Furthermore, most patients experienced an unexpectedly sustained analgesia in the recovery room, and no patient complained of recall or any unpleasant side effect.

DISCUSSION: Our observations in humans confirm the ear lier reports in animals (1) that IV ATP when combined with inhaled anesthetics,produces suitable anesthesia for surgery. The anesthesia produced by ATP may have been mediated mostly by central adenosine receptor A_1 mechanisms, since ATP is rapidly degraded to Ado after IV administration, and it was potentiated by dipyridamole, an adenosine uptake inhibitor.

	SBP (mmHg)	HR (bpm)
Pre-induction	125±19	72±13
Intubation	147±39	88±17
Surgery	136±17	88±13
ATP: 108±21 (μg/kg/min)	123±19	94±10

Note: A_1 included in P_1 purinergic receptor

Reference:
1) Anesthesiology 71(3A):A260, 1989