

Faut-il encore utiliser le protoxyde d'azote ?



Pr Jean Mantz  
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INSERM U 676

OUI!

OUI!

**Merci de votre attention!**

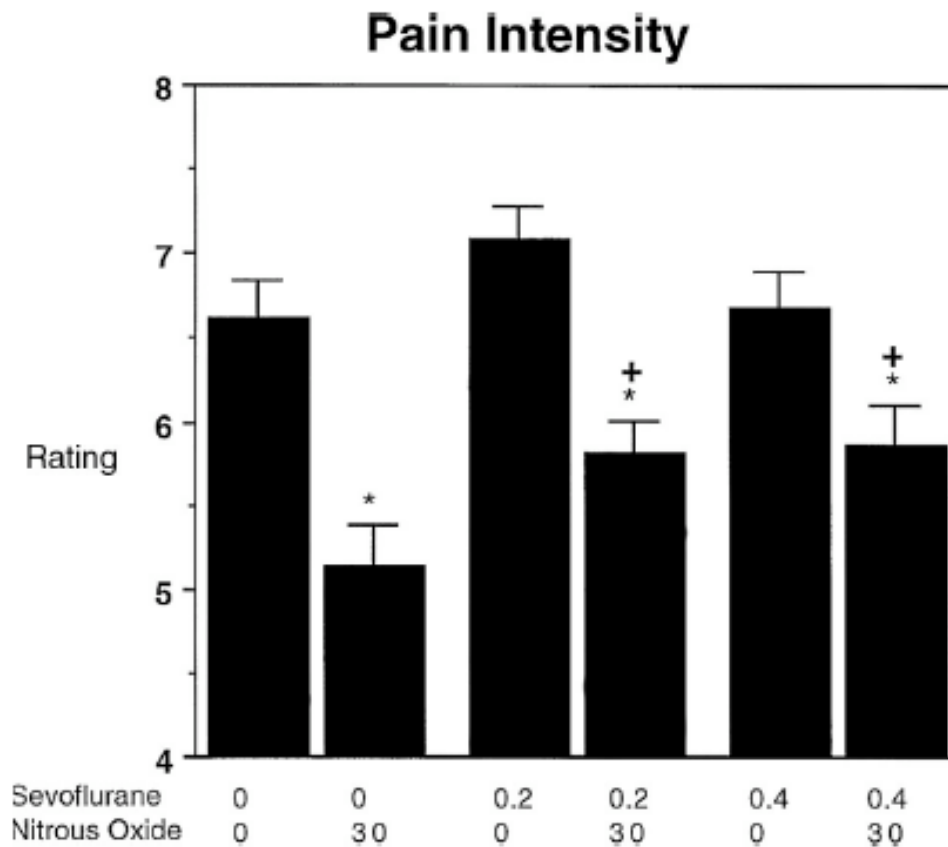
## Les atouts du protoxyde d'azote

- Gaz d'action rapide et fugace
- Anesthésique et analgésique
- Inodore (utilisation en pédiatrie)
- Très bien toléré
- Coût raisonnable

# *Biologic Effects of Nitrous Oxide*

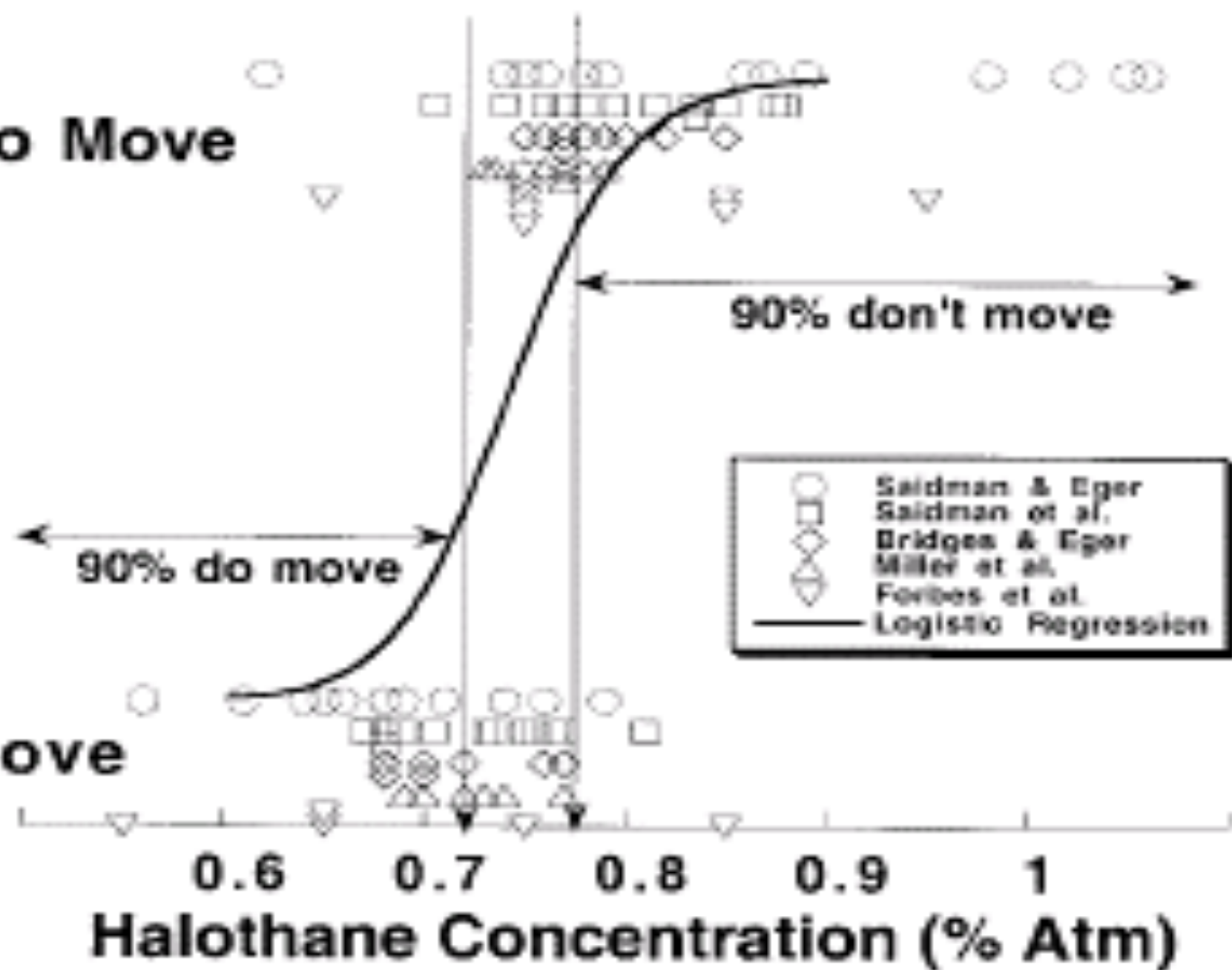
## *A Mechanistic and Toxicologic Review*

Robert D. Sanders, B.Sc., M.B., B.S., F.R.C.A.,\* Jörg Weimann, M.D., D.E.A.A.,†  
 Mervyn Maze, M.B., Ch.B., F.R.C.P., F.R.C.A., F.Med.Sci.‡



**No Move**

**Move**



« She reported she had woken up during surgery, hearing surgeon talking about politics. She spontaneously mentioned the name Schroeder » (*Luginbühl M and Schnider TW Anesthesiology 2000; 96: 241-3*)

« Realised she was awake when she should not be. She tried to get attention, tried to talk and move but was unable. Heard voices and noise from surgical instruments » (*Sandin R et al Lancet 2000; 355: 707-11*)

« The pain was like a tooth drilled without local anesthetic-when the drill hits a nerve. Multiply this pain so that the area involved would equal a thumb-print, then pour a steady stream of molten lead into it » (*Anonymous, Br J Anaesth 1979; 51: 711-2*)

« Alors, docteur, j'ai un cancer ? Mais si, j'ai entendu ce que vous disiez sur le résultat de l'examen extemporané ... » (*CHU..., 200...*)



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**Bispectral index monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial**

*P S Myles, K Leslie, J McNeil, A Forbes, M T V Chan, for the B-Aware trial group\**

**Lancet 2004; 363: 1757–63**

*The* **NEW ENGLAND**  
**JOURNAL** *of* **MEDICINE**

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**Anesthesia Awareness and the Bispectral Index**

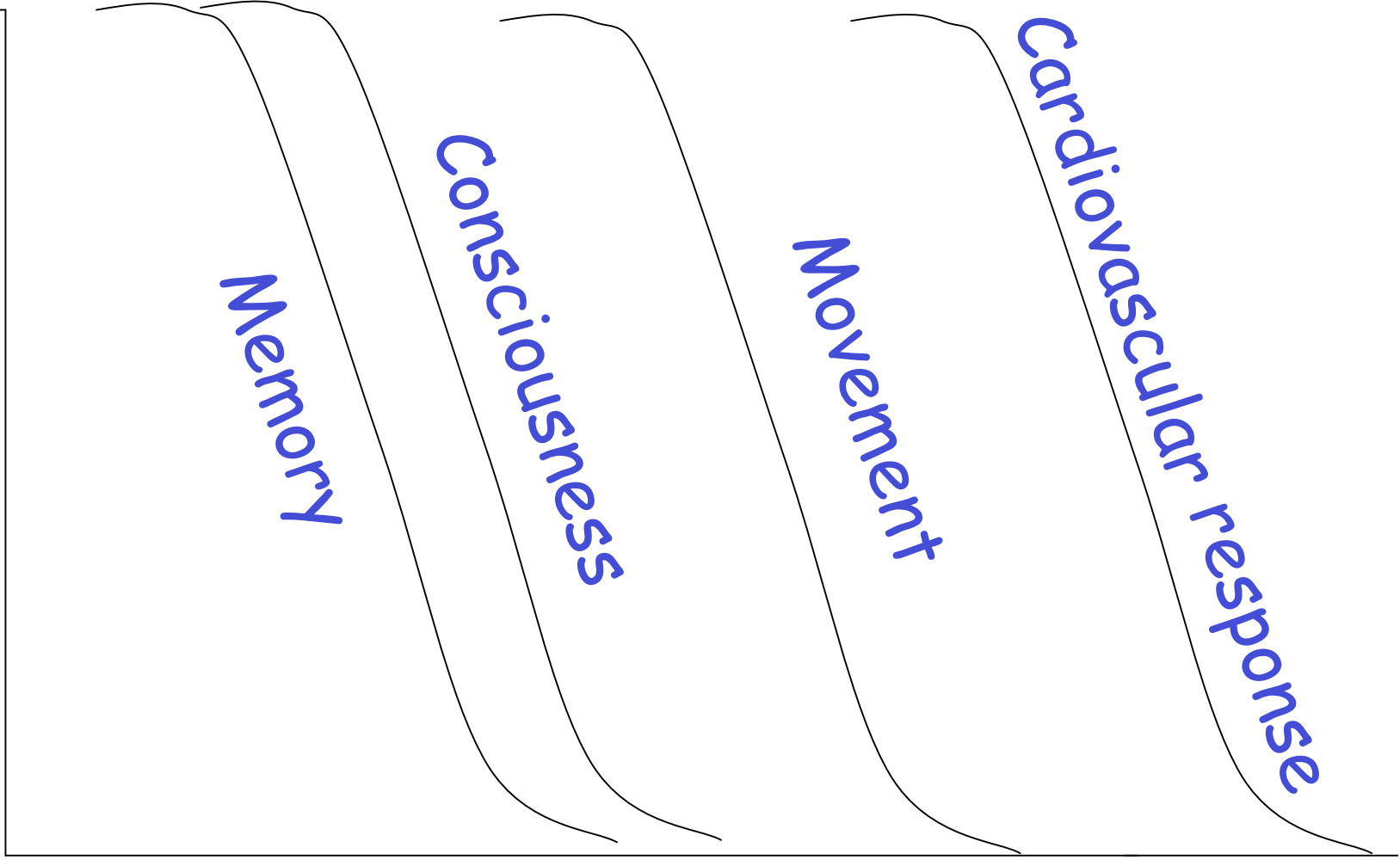
Michael S. Avidan, M.B., B.Ch., Lini Zhang, M.D., Beth A. Burnside, B.A., Kevin J. Finkel, M.D., Adam C. Searleman, B.S., Jacqueline A. Selvidge, B.S., Leif Saager, M.D., Michelle S. Turner, B.S., Srikar Rao, B.A., Michael Bottros, M.D., Charles Hantler, M.D., Eric Jacobsohn, M.B., Ch.B., and Alex S. Evers, M.D.

**N Engl J Med 2008;358:1097-108.**

*Antognini JF, Carstens E Br J Anaesth  
2002; 89: 156-66*

% patients  
responding

100



Anesthetic concentration

Tramer M, Moore A, McQuay H:

Omitting nitrous oxide in general anaesthesia: meta-analysis of intraoperative awareness and postoperative emesis in randomized controlled trials.

Br J Anaesth 1996; 76: 186-93

- ✓ 24 essais inclus (2478 patients)
- ✓ NVPO: NNT = 13 en défaveur du protoxyde d'azote
- ✓ Mémorisation: NNT = 46 en faveur du protoxyde d'azote

Tramer M, Moore A, McQuay H:

Omitting nitrous oxide in general anaesthesia: meta-analysis of intraoperative awareness and postoperative emesis in randomized controlled trials.

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- ✓ 24 essais inclus (2478 patients)
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- ✓ Mémorisation: NNT = 46 en faveur du protoxyde d'azote

## Que reproche-t-on au protoxyde d'azote ?

- ✓ NVPO+++
- ✓ Dilatation intestinale
- ✓ Dépression immunitaire
- ✓ Toxicité neurologique
- ✓ Toxicité cardiovasculaire
- ✓ Toxicité hématologique
- ✓ Toxicité sur la reproduction

# The NEW ENGLAND JOURNAL of MEDICINE

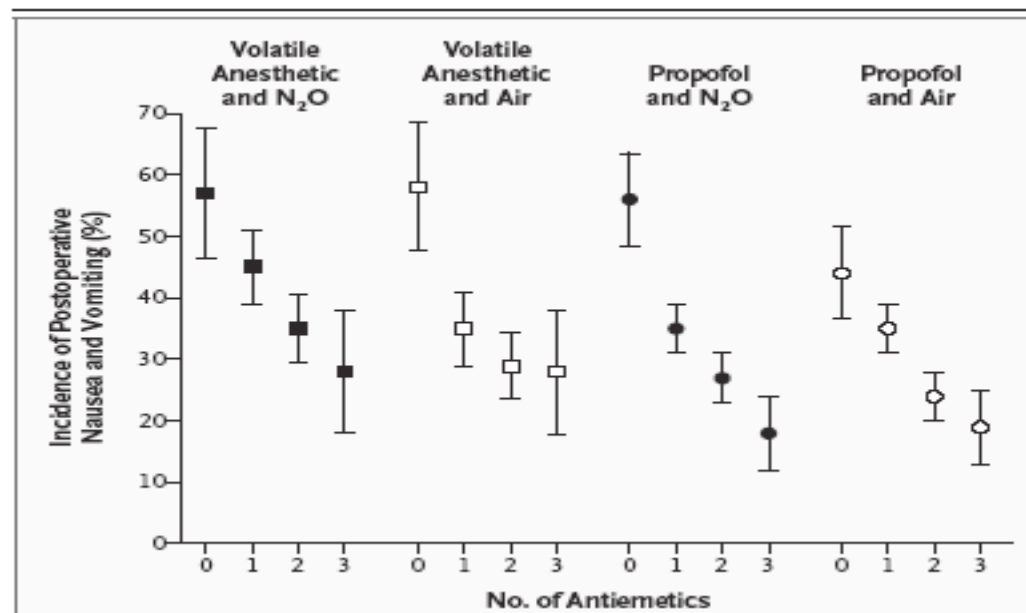
ESTABLISHED IN 1812

JUNE 10, 2004

VOL. 350 NO. 24

## A Factorial Trial of Six Interventions for the Prevention of Postoperative Nausea and Vomiting

Christian C. Apfel, M.D., Kari Korttila, F.R.C.A., Ph.D., Mona Abdalla, Ph.D., Heinz Kerger, M.D.,  
Alparslan Turan, M.D., Ina Vedder, M.D., Carmen Zernak, M.D., Klaus Danner, M.D., Ritva Jokela, M.D., Ph.D.,  
Stuart J. Pocock, Ph.D., Stefan Trenkler, M.D., Markus Kredel, M.D., Andreas Biedler, M.D., Daniel I. Sessler, M.D.,  
and Norbert Roewer, M.D., for the IMPACT Investigators\*



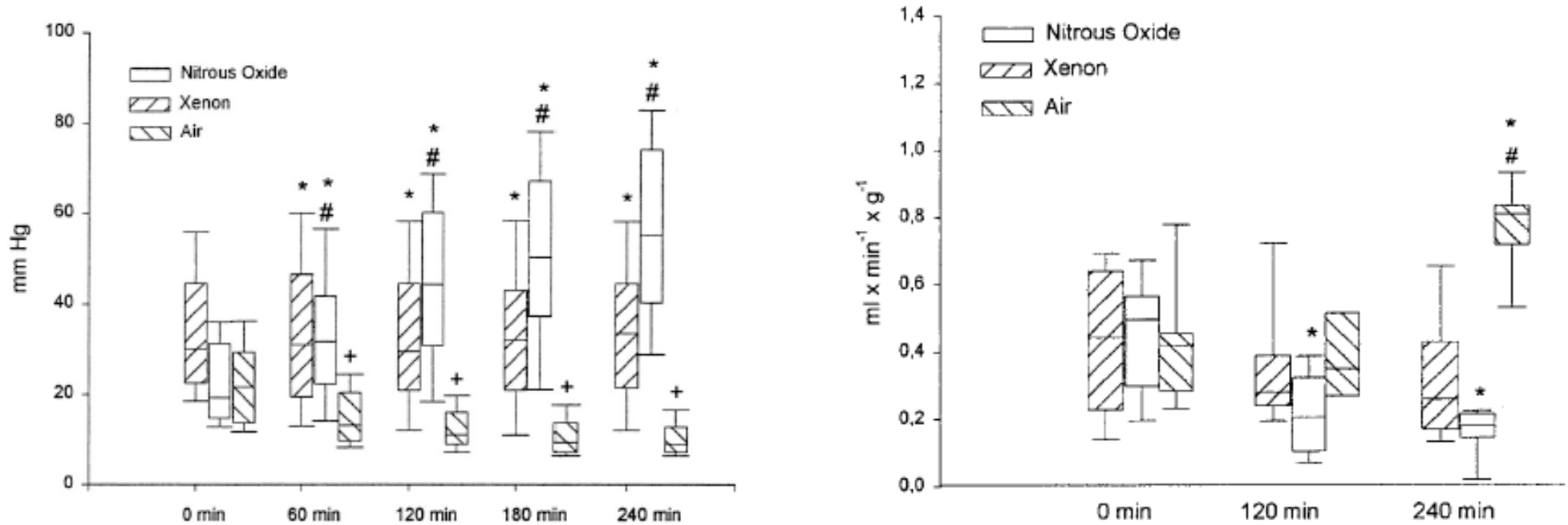
## LABORATORY REPORT

Anesthesiology 2002; 96:512-3

© 2002 American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

# Diffusion of Xenon and Nitrous Oxide into the Bowel during Mechanical Ileus

Helmut Reinelt, M.D.,\* Thomas Marx, M.D.,† Uwe Schirmer, M.D.,‡ Sibylle Luederwald,§ Pantelis Topalidis,§ Michael Schmidt M.D.\*



# Inhaling Nitrous Oxide or Xenon Does Not Influence Bowel Wall Energy Balance During Porcine Bowel Obstruction

Antje Pittner, MD\*, Marek Nalos, MD\*, Marc Theisen, MD\*, Franz Ploner, MD\*, Uwe B. Brückner, MD†, Michael Georgieff, MD\*, Peter Radermacher, MD\*, and Gebhard Fröba, MD\*

(Anesth Analg 2002;94:1510–6)

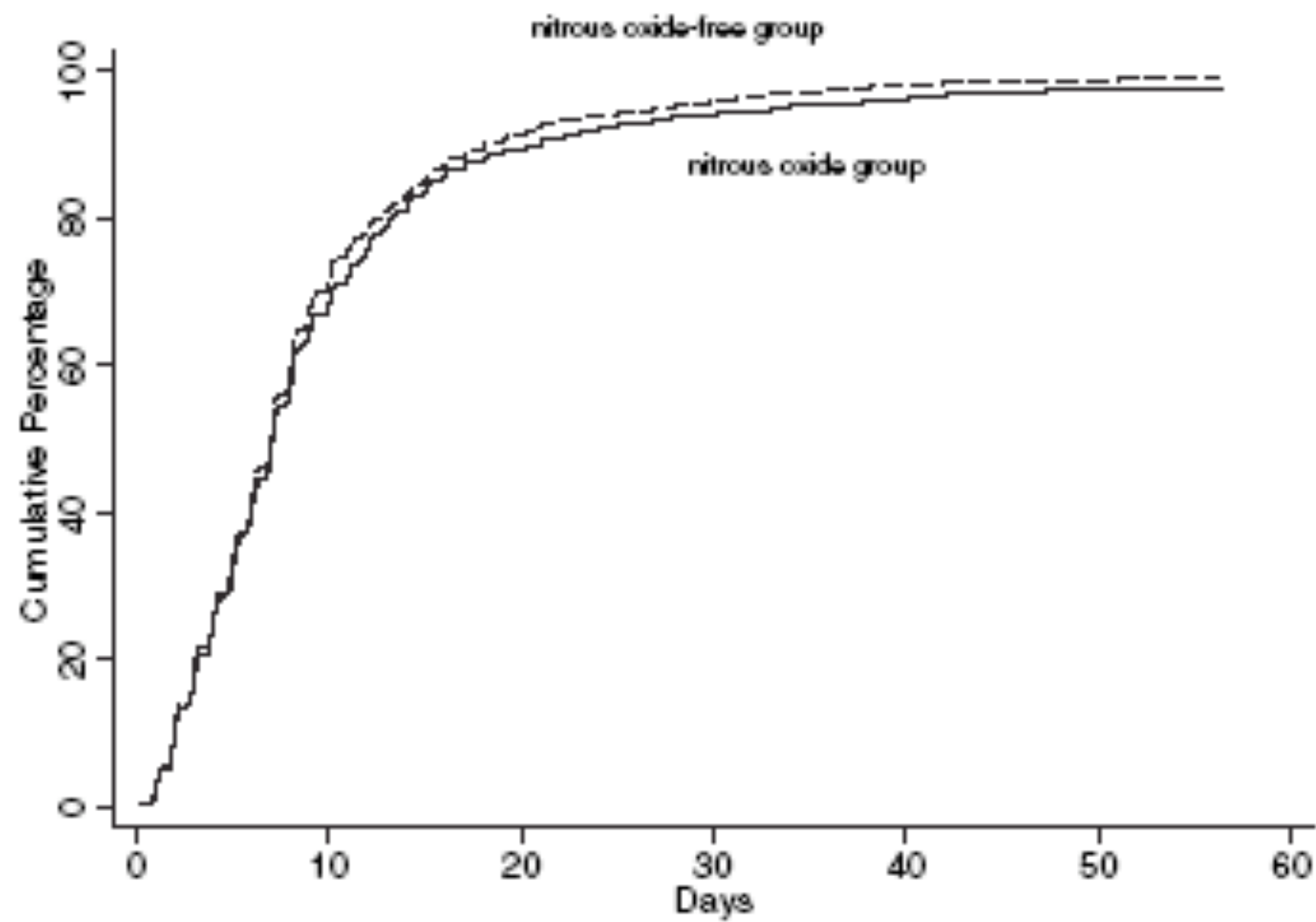
|  | Group 1 (n=12) | Group 2 (n=8) | Group 3 (n=10) |
|--|----------------|---------------|----------------|
| Intraluminal pressure (mm Hg)  |                |               |                |
| TIVA   | 9 (2–12)       | 8 (6–9)       | 10 (5–12)      |
| Xe   | 12 (9–15)      | 14 (12–18)†   | 18 (14–18)†    |
| N <sub>2</sub> O   | 9 (3–10)       | 21 (9–33)†    | 35 (25–60)*    |
| Blood flow, mesenteric artery (mL · min <sup>-1</sup> · kg <sup>-1</sup> ) |                |               |                |
| TIVA   | 2.1 (1.6–4.5)  | 2.7 (1.9–4.3) | 2.2 (1.3–3.8)  |
| Xe   | 1.5 (1.4–1.8)  | 1.9 (1.6–2.2) | 1.9 (1.4–2.5)  |
| N <sub>2</sub> O   | 1.9 (0.7–4.0)  | 2.0 (0.9–3.6) | 1.6 (1.2–4.6)  |
| Intestinal oxygen extraction (%)   |                |               |                |
| TIVA   | 32 (20–32)     | 24 (15–27)    | 26 (8–32)      |
| Xe   | 29 (15–41)     | 23 (17–38)    | 30 (19–41)     |
| N <sub>2</sub> O   | 27 (15–47)     | 27 (13–31)    | 26 (14–41)     |

# *Avoidance of Nitrous Oxide for Patients Undergoing Major Surgery*

## *A Randomized Controlled Trial*

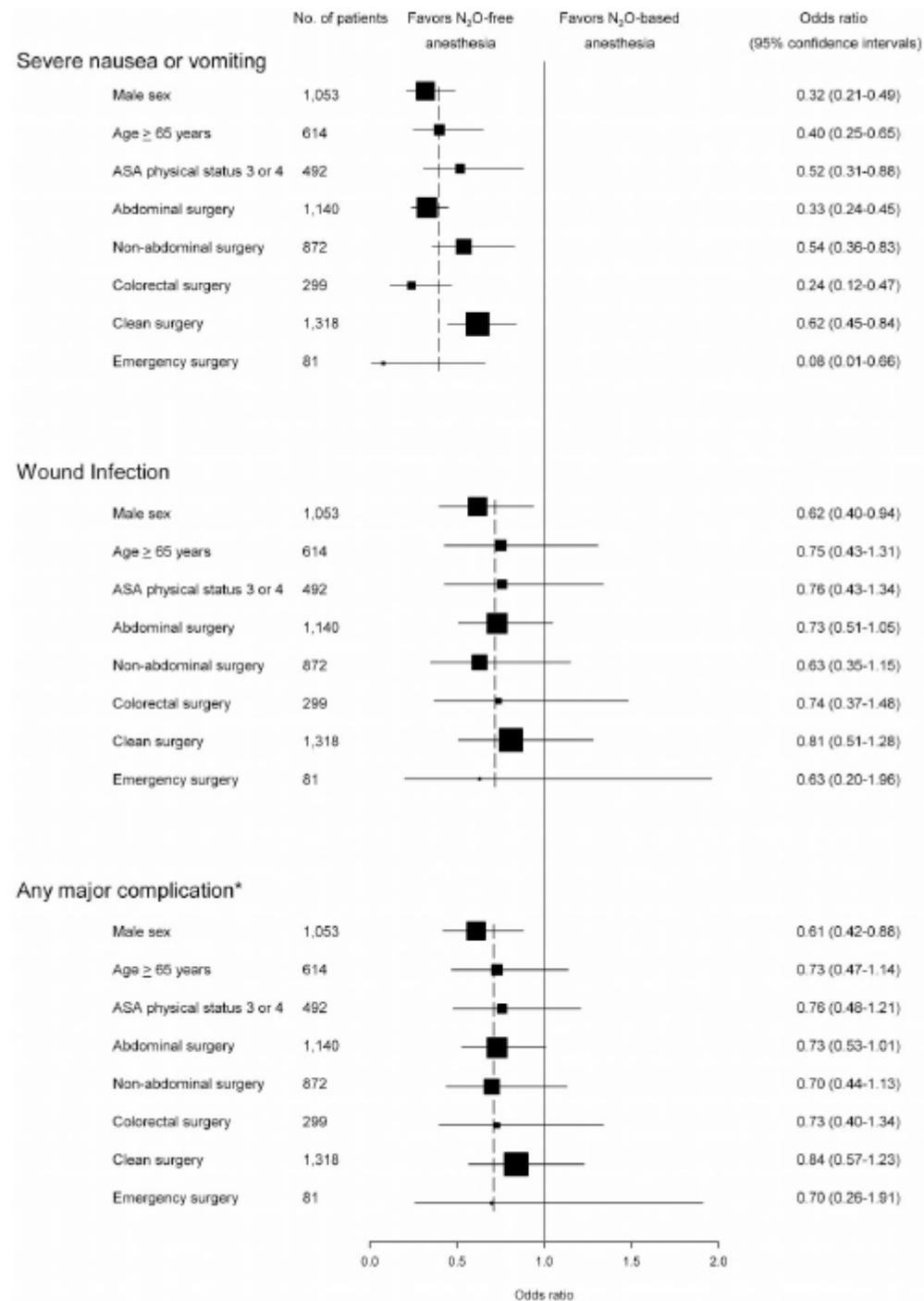
*Paul S. Myles, M.B., B.S., M.P.H., M.D., F.C.A.R.C.S.I., F.A.N.Z.C.A.,\* Kate Leslie, M.B., B.S., M.D., M.Epi., F.A.N.Z.C.A.,†  
Matthew T. V. Chan, M.B., B.S., F.A.N.Z.C.A.,‡ Andrew Forbes, M.Sc., Ph.D.,§  
Michael J. Paech, M.B., B.S., D.M., D.R.C.O.G., F.R.C.A., F.A.N.Z.C.A., F.F.P.M.A.N.Z.C.A.,||  
Philip Peyton, M.B., B.S., M.D., F.A.N.Z.C.A.,# Brendan S. Silbert, M.B., B.S., F.A.N.Z.C.A.,\*\* Elaine Pascoe, B.Sc.,†† and  
the ENIGMA Trial Group‡‡*

- ✓ Chirurgie > 2h
- ✓ Groupes O<sub>2</sub> 80% N<sub>2</sub> 20% vs O<sub>2</sub> 30% N<sub>2</sub>O 70%
- ✓ Objectif principal: durée de séjour hospitalier
- ✓ Objectifs secondaires: toute complication post-opératoire



**Table 3. Postoperative Complications**

| Variable                   | Nitrous Oxide-free Group (n = 997), n (%) | Nitrous Oxide Group (n = 1,015), n (%) | Univariate Odds Ratio (95% CI) | P Value | Adjusted Odds Ratio* (95% CI) | P Value |
|----------------------------|---|--|--------------------------------|---------|-------------------------------|---------|
| Severe nausea or vomiting  | 104 (10)                                  | 229 (23)                               | 0.40 (0.31–0.51)               | < 0.001 | 0.40 (0.31–0.51)†             | < 0.001 |
| Wound infection            | 77 (7.7)                                  | 106 (10)                               | 0.72 (0.53–0.98)               | 0.034   | 0.72 (0.52–0.98)‡             | 0.036   |
| Fever                      | 275 (28)                                  | 345 (34)                               | 0.74 (0.61–0.89)               | 0.002   | 0.73 (0.60–0.90)              | 0.003   |
| Pneumonia                  | 15 (1.5)                                  | 30 (3.0)                               | 0.50 (0.27–0.94)               | 0.031   | 0.51 (0.27–0.97)              | 0.040   |
| Atelectasis                | 75 (7.5)                                  | 127 (13)                               | 0.57 (0.42–0.77)               | < 0.001 | 0.55 (0.40–0.75)              | < 0.001 |
| Pneumothorax               | 1 (0.1)                                   | 3 (0.3)                                | 0.34 (0.01–4.23)               | 0.63    | —                             | —       |
| Myocardial infarction      | 7 (0.7)                                   | 13 (1.3)                               | 0.54 (0.22–1.37)               | 0.20    | 0.58 (0.22–1.50)              | 0.26    |
| Thromboembolism            | 16 (1.6)                                  | 10 (1.0)                               | 1.64 (0.74–3.63)               | 0.22    | 1.60 (0.72–3.55)              | 0.25    |
| Blood transfusion          | 188 (19)                                  | 202 (20)                               | 0.94 (0.75–1.17)               | 0.55    | 0.96 (0.75–1.21)              | 0.71    |
| Stroke                     | 1 (0.1)                                   | 1 (0.1)                                | 1.02 (0.01–80)                 | > 0.99  | —                             | —       |
| Awareness                  | 0 (0.0)                                   | 2 (0.2)                                | —                              | —       | —                             | —       |
| Death within 30 days       | 3 (0.3)                                   | 9 (0.9)                                | 0.34 (0.09–1.25)               | 0.10    | 0.33 (0.09–1.22)              | 0.096   |
| Any pulmonary complication | 78 (7.8)                                  | 132 (13)                               | 0.57 (0.42–0.76)               | < 0.001 | 0.54 (0.40–0.74)              | < 0.001 |
| Any major complication§    | 155 (16)                                  | 210 (21)                               | 0.71 (0.56–0.89)               | 0.003   | 0.70 (0.55–0.89)              | 0.003   |



## Nitrous Oxide and Evidence-based Medicine: Here We Go Again

Marek A. Mirski, M.D., Ph.D.,\* Allan Gottschalk, M.D., Ph.D.,  
\*Johns Hopkins Medicine, Baltimore, Maryland. mmirski@jhmi.edu

## Nitrous Oxide or Nitrogen Effect

James S. Dawson, B.Sc., M.B., Ch.B.,\* Jonathan G. Hardman,  
B.Med.Sci.(Hons), B.M., B.S., F.R.C.A., D.M. \*University Department  
of Anaesthesia, Queen's Medical Centre, Nottingham, United Kingdom.  
james@dawson.me.uk

## Nitrous Oxide Remains a Valuable Adjuvant for Surgery

Paul F. White, Ph.D., M.D., F.A.N.Z.C.A.,\* Ronald H. Wender,  
M.D. \*University of Texas Southwestern Medical Center, Dallas,  
Texas. paul.white@utsouthwestern.edu

## Nitrous Oxide: Time to Laugh It Off? Not Quite

Deepak Sharma, M.D., D.M., Hari H. Dash, M.D.\* \*All India  
Institute of Medical Sciences, New Delhi, India. drhh\_dash@yahoo.com

## Nitrous Oxide and Supplementary Oxygen: Let's Give Moderation a Chance

Gonzalo Tornero-Campello, M.D., Hospital General Universitario  
de Elche, Elche, Alicante, Spain. gtorcam@hotmail.com

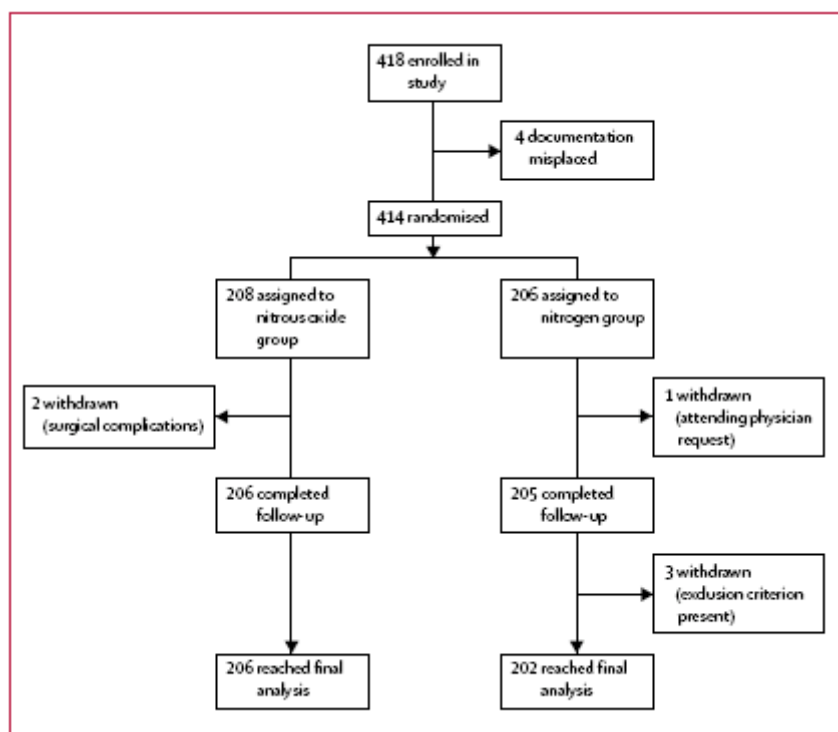
## Explanatory *versus* Pragmatic Trials? The Methods Make the Difference

Paul Merckx, M.D., Catherine Paugam-Burtz, M.D., Sandrine  
Boudinet, M.D., Agnes Bonnet, M.D., Jean Mantz, M.D., Ph.D.\*  
\*Beaujon University Hospital, Assistance Publique des Hôpitaux de Paris,  
Paris 7 University, Clichy, France. jean.mantz@bjn.ap-hop-paris.fr

# Nitrous oxide and risk of surgical wound infection: a randomised trial

Edith Fleischmann, Rainer Lenhardt, Andrea Kurz, Friedrich Herbst, Béla Fülesdi, Robert Greif, Daniel I Sessler, Ozan Akça, on behalf of the Outcomes Research Group\*

*Lancet* 2005; 366: 1101-07

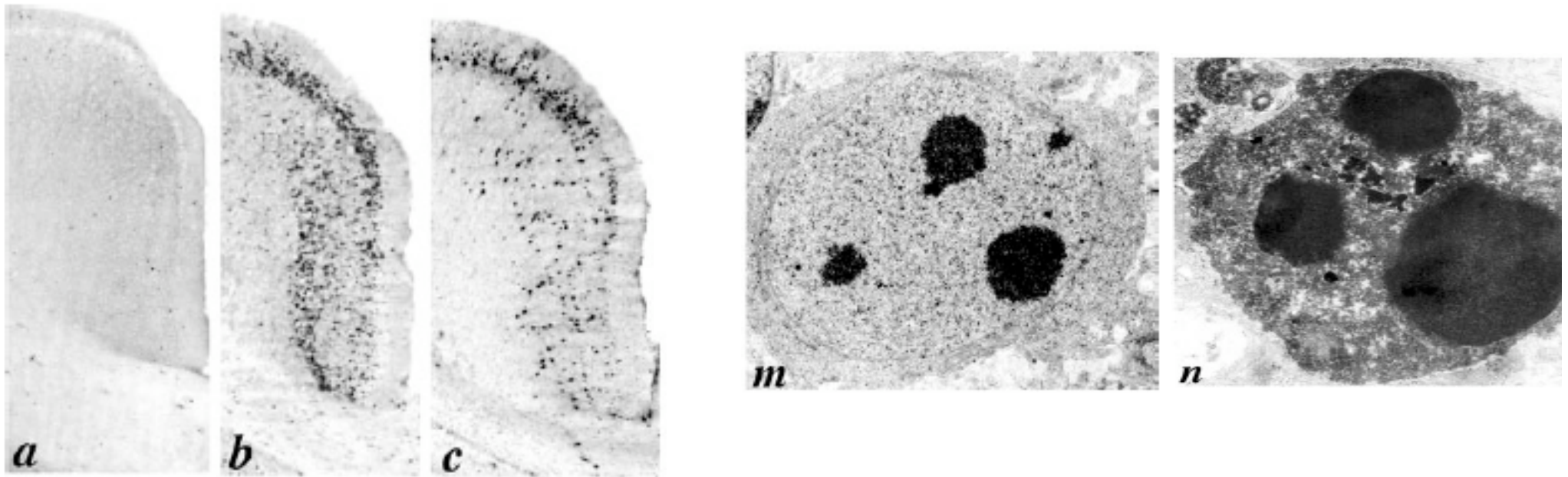


|   | Nitrous oxide | Nitrogen   | p     |
|---|---------------|------------|-------|
| Infection diagnosed by pus and positive culture | 17 (8%)       | 23 (11%)   | 0.287 |
| Infection diagnosed by CDC criteria             |               |            |       |
| Superficial                                     | 28 (14%)      | 34 (17%)   | 0.362 |
| Deep  | 9 (4%)        | 13 (6%)    | 0.355 |
| Peritoneal                                      | 2 (1%)        | 6 (3%)     | 0.145 |
| Any CDC infection                               | 30 (15%)      | 38 (19%)   | 0.250 |
| Total infection by either criteria*             | 31 (15%)      | 40 (20%)   | 0.205 |
| ASEPSIS† score                                  | 5.6 (10.1)    | 7.4 (13.5) | 0.137 |
| Wound collagen deposition, ng/mm‡               | 1.4 (0.7)     | 1.4 (0.7)  | 0.683 |
| Intensive care admission                        | 32 (16%)      | 41 (20%)   | 0.209 |
| Nausea, mm on a VAS§                            | 2 (0-24)      | 0 (0-8)    | 0.007 |
| Emesis  | 10 (5%)       | 7 (3%)     | 0.476 |
| Antiemetic rescue                               | 39 (19%)      | 26 (13%)   | 0.090 |
| First solid food, postoperative days            | 4.8 (2.4)     | 4.8 (2.0)  | 0.938 |
| Time to first flatus, days                      | 3.5 (1.7)     | 3.5 (1.8)  | 0.917 |
| Time to first bowel movement, days              | 3.8 (1.6)     | 3.9 (1.9)  | 0.533 |
| Duration of hospital stay, days                 | 11.1 (4.9)    | 11.6 (7.2) | 0.387 |
| Mortality within 15 days                        | 0             | 3 (2%)     | 0.120 |

# Early Exposure to Common Anesthetic Agents Causes Widespread Neurodegeneration in the Developing Rat Brain and Persistent Learning Deficits

The Journal of Neuroscience, February 1, 2003 • 23(3):876 – 882

Vesna Jevtovic-Todorovic,<sup>1</sup> Richard E. Hartman,<sup>2</sup> Yukitoshi Izumi,<sup>3</sup> Nicholas D. Benshoff,<sup>3</sup> Krikor Dikranian,<sup>3</sup> Charles F. Zorumski,<sup>3</sup> John W. Olney,<sup>3</sup> and David F. Wozniak<sup>3</sup>



Midazolam, nitrous oxide, isoflurane

# ***Effect of Nitrous Oxide Use on Long-term Neurologic and Neuropsychological Outcome in Patients Who Received Temporary Proximal Artery Occlusion during Cerebral Aneurysm Clipping Surgery***

Jeffrey J. Pasternak, M.D.,\* Diana G. McGregor, M.B.B.S.,† William L. Lanier, M.D.,‡ Darrell R. Schroeder, M.S.,§  
Deborah A. Rusy, M.D.,|| Bradley Hindman, M.D.,# William Clarke, Ph.D.,\*\* James Torner, Ph.D.,††  
Michael M. Todd, M.D.‡‡ on behalf of the IHAST Investigators§§

| Metric                                       | Univariate Analysis |                        |         | Multivariate Analysis |           |         |
|--|---------------------|------------------------|---------|-----------------------|-----------|---------|
|  | Nitrous Oxide Group | No Nitrous Oxide Group | P Value | Odds Ratio            | 95% CI    | P Value |
| DIND, yes or no                              |                     |                        |         |                       |           |         |
| n  | 199                 | 242                    | 0.108   | 1.78                  | 1.08–2.95 | 0.025   |
| DIND = yes                                   | 55 (28)             | 51 (21)                |         |                       |           |         |
| GOS at 3 months, 1 vs. > 1                   |                     |                        |         |                       |           |         |
| n  | 199                 | 242                    | 0.059   | 0.70                  | 0.45–1.10 | 0.123   |
| 1 (Minor or no disability)                   | 135 (68)            | 143 (59)               |         |                       |           |         |
| GOS at 3 months, 1, 2, 3, 4, 5               |                     |                        |         |                       |           |         |
| n  | 199                 | 242                    | 0.043   | 0.67                  | 0.44–1.03 | 0.065   |
| 1: Minor or no disability                    | 135 (68)            | 143 (59)               |         |                       |           |         |
| 2: Moderate disability                       | 40 (20)             | 55 (23)                |         |                       |           |         |
| 3: Severe disability                         | 12 (6)              | 23 (10)                |         |                       |           |         |
| 4: Vegetative state                          | 0 (0)               | 0 (0)                  |         |                       |           |         |
| 5: Death                                     | 12 (6)              | 21 (9)                 |         |                       |           |         |
| Rankin Score at 3 months, 0 or 1 vs. > 1     |                     |                        |         |                       |           |         |
| n  | 199                 | 242                    | 0.078   | 0.74                  | 0.47–1.16 | 0.192   |
| 0 or 1: Mild or no neurologic disability     | 137 (69)            | 147 (61)               |         |                       |           |         |
| NIHSS at 3 months, 0, 1–7, 8–14, > 14, death |                     |                        |         |                       |           |         |
| n  | 194                 | 240                    | 0.741   | 1.02                  | 0.66–1.56 | 0.937   |
| 0: No deficit                                | 120 (62)            | 149 (62)               |         |                       |           |         |
| 1–7: Mild deficit                            | 57 (29)             | 58 (24)                |         |                       |           |         |
| 8–14: Moderate deficit                       | 3 (2)               | 8 (3)                  |         |                       |           |         |
| 15–42: Severe deficit                        | 2 (1)               | 4 (2)                  |         |                       |           |         |
| Death  | 12 (6)              | 21 (9)                 |         |                       |           |         |

## Nitrous oxide does not change the incidence of postoperative delirium or cognitive decline in elderly surgical patients

J. M. Leung<sup>1\*</sup>, L. P. Sands<sup>2</sup>, L. E. Vaurio<sup>1</sup> and Y. Wang<sup>3,4</sup>

|   | Odds ratio | 95% Confidence interval |
|---|------------|-------------------------|
| Age   | 1.07       | 1.02–1.26               |
| Anaesthetic type (N <sub>2</sub> O vs oxygen) | 1.09       | 0.57–2.07               |
| Dependence on performing $\geq 1$ IADL        | 1.54       | 1.01–2.35               |
| Postoperative analgesia                       |            |                         |
| PCA vs oral opioids                           | 3.75       | 1.27–11.01              |
| Use of benzodiazepines on POD #1 or POD #2    | 2.29       | 1.21–4.36               |

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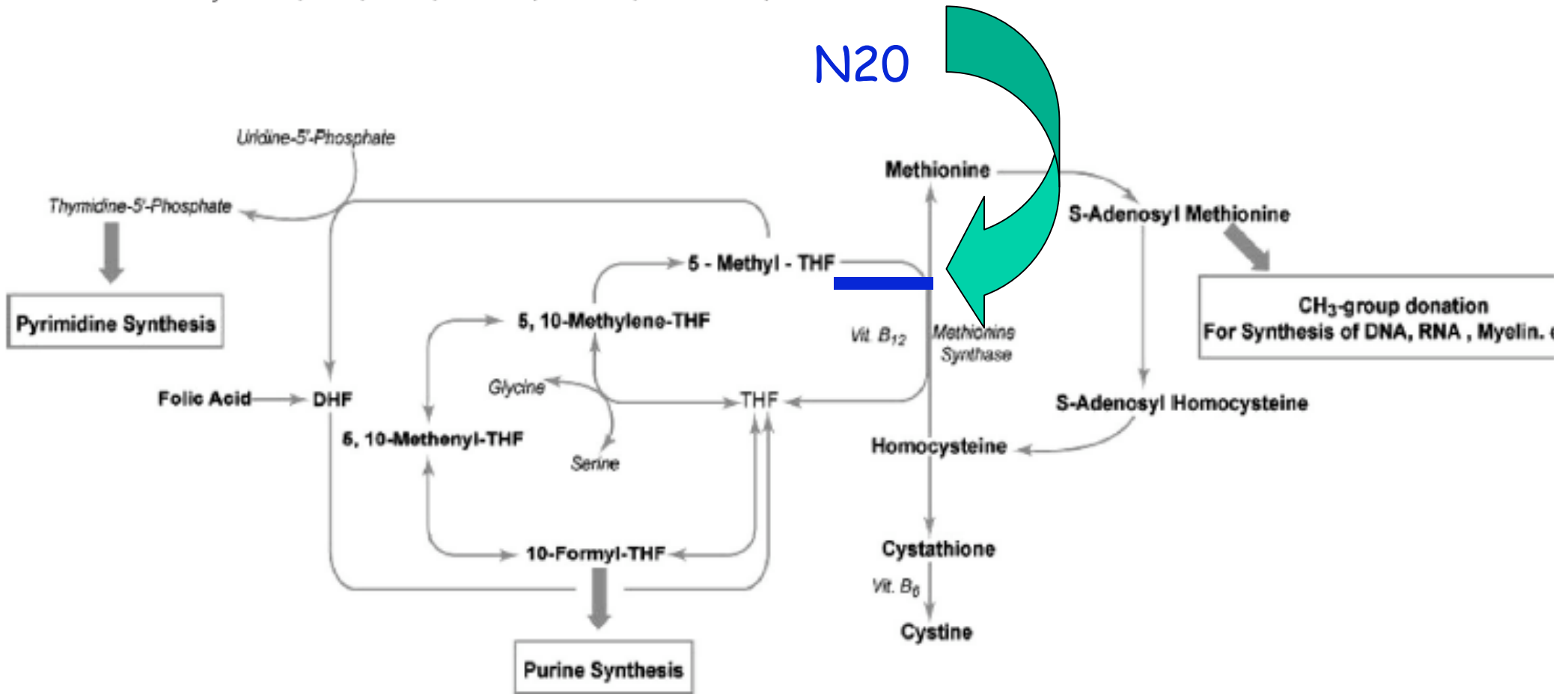
J. M. Leung<sup>1\*</sup>, L. P. Sands<sup>2</sup>, L. E. Vaurio<sup>1</sup> and Y. Wang<sup>3,4</sup>

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# Biologic Effects of Nitrous Oxide

## A Mechanistic and Toxicologic Review

Robert D. Sanders, B.Sc., M.B., B.S., F.R.C.A.,\* Jörg Weimann, M.D., D.E.A.A.,†  
Mervyn Maze, M.B., Ch.B., F.R.C.P., F.R.C.A., F.Med.Sci.‡



**Table 1. Patients at Risk from Cobalamin Deficiency**

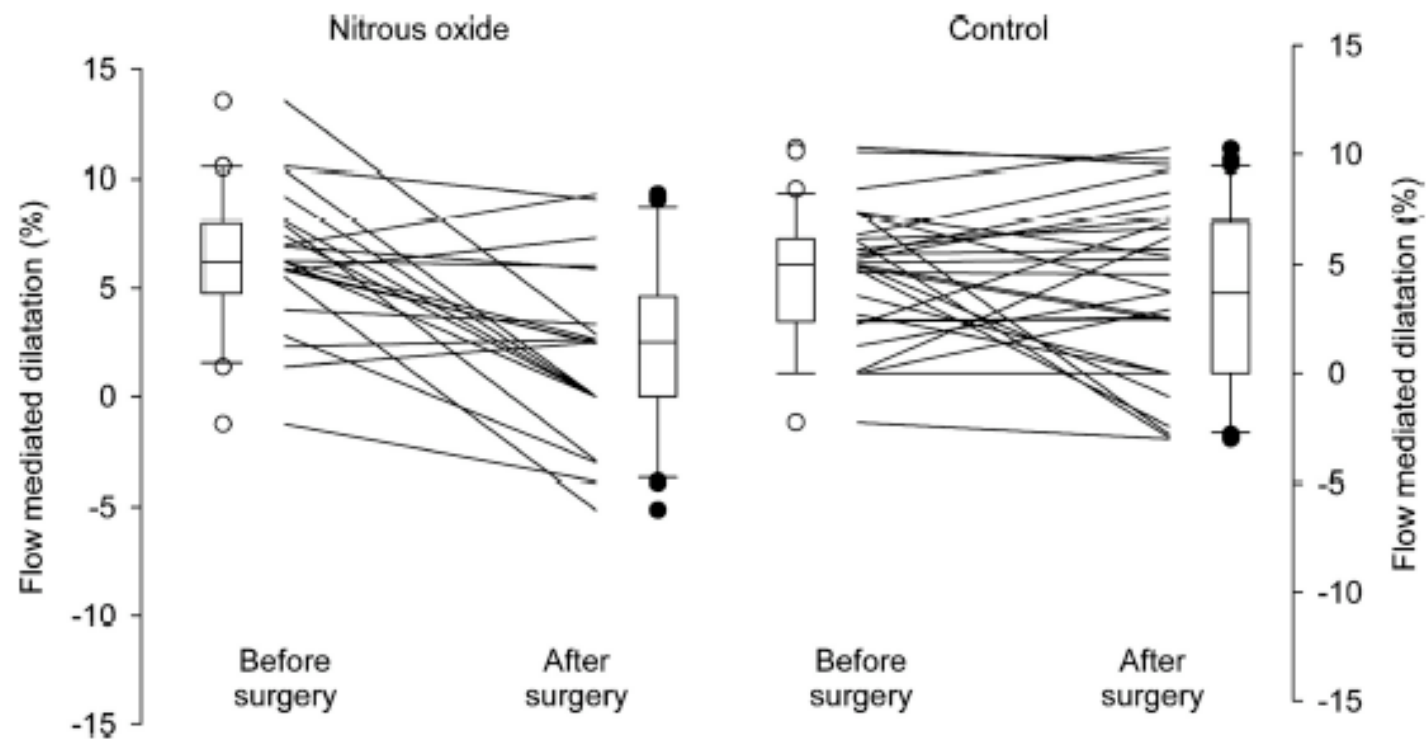
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|                         |  |
|-------------------------|--|
| Nutritional disorders   | Elderly<br>Vegans<br>Alcoholics  |
| Malabsorption disorders | Prolonged use of proton pump inhibitors or H <sub>2</sub> receptor antagonists<br>Pernicious anaemia<br>Atrophic gastritis<br>Postgastrectomy, Whipple procedure, ileal resection<br>Crohn disease |
| Infection               | Bacterial overgrowth, tapeworm   |

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# Effect of Nitrous Oxide Anesthesia on Plasma Homocysteine and Endothelial Function

Paul S. Myles, M.P.H., M.D.,\* Matthew T. V. Chan, M.B.B.S.,† David M. Kaye, M.D., Ph.D.,‡ David R. Mcllroy, M.B.B.S.,§ Chung-Wai Lau, M.B.B.S.,|| Joel A. Symons, M.B.Ch.B.,§ Shaohui Chen, M.D., Ph.D.#



## *Pharmacogenetics of Nitrous Oxide*

*Standing at the Crossroads*

**Kirk Hogan, M.D., J.D., 1**

In turn, knowing in advance who can breathe nitrous oxide without fear of clinically relevant hyperhomocysteinemia may help to sustain its safe use for a second century and a half, and beyond.

# Colton's Laughing Gas Broadside



**Table 4. Recommended Indications and Contraindications for Nitrous Oxide Use in Anesthetic Practice**

| Indications  | Inhalational analgesia/sedation   |
|--|---|
| Absolute contraindications   | Known deficiency of enzyme or substrate in methionine synthase pathway<br>Potential toxicity from expansion of gas filled space, e.g., emphysema, pneumothorax, middle ear surgery, pneumocephalus, air embolus |
| Relative contraindications   | Raised intracranial pressure<br>Pulmonary hypertension<br>Prolonged anesthesia(> 6 h)<br>First trimester of pregnancy*<br>High risk of postoperative nausea and vomiting  |
| Putative relative contraindications<br>(requiring further investigation) | Risk of myocardial ischemia   |

\* Based on the theoretical (but unproven) detrimental effect.

# Conclusion

- Il n'y a pas d'argument clinique crédible pour recommander l'abandon du protoxyde d'azote.
- Le protoxyde d'azote possède des avantages indiscutables en tant qu'agent d'anesthésie.

L'hôpital sans proto...

L'hôpital sans proto...

C'est du pipo!