

# Arterial Oxygen Tension Measurements During Nitrous Oxide–Oxygen Anesthesia

E. M. Slater, M.D.,\* S. E. Nilsson, M.D.,† D. L. Leake, D.M.D.,‡ W. L. Parry, M.D.,§  
M. B. Laver, M.D.,¶ J. Hedley-Whyte, M.D.,¶ H. H. Bendixen, M.D.‡

Arterial oxygen tensions were determined while commonly used mixtures of nitrous oxide and oxygen were administered. These mixtures were administered in random order to 60 patients without clinical evidence of cardiac or pulmonary disease. The patients were divided into 3 equal groups according to whether they were undergoing upper abdominal, lower abdominal, or peripheral operations. Intermittent positive pressure ventilation was provided by means of a respirator. Each ratio of N<sub>2</sub>O:O<sub>2</sub> was administered for 10 minutes, and at the end of this period an arterial blood sample was withdrawn. Arterial oxygen tension, arterial carbon dioxide tension and arterial pH were determined. All patients had arterial carbon dioxide tensions of less than 40 mm. Hg. Arterial oxygen tensions were found lower than expected in almost all patients. Because suboptimal oxygenation occurred so frequently when N<sub>2</sub>O in excess of 66 per cent was administered to patients undergoing intra-abdominal operations, it is strongly recommended that during surgery of this type anesthetic mixtures contain at least 33 per cent oxygen.

INCREASED physiologic shunting has been recognized as a cause of hypoxemia during anesthesia and surgery.<sup>1-10</sup> These findings suggest that higher inspired oxygen concentrations than previously thought necessary may be required when nitrous oxide and oxygen anes-

thesia is administered. The present study examines arterial oxygenation during N<sub>2</sub>O:O<sub>2</sub> anesthesia when commonly employed ratios of N<sub>2</sub>O and O<sub>2</sub> are used, and attempts to determine the influence of age and operative site on arterial oxygenation during N<sub>2</sub>O:O<sub>2</sub> anesthesia.

## Methods

Sixty patients without clinical evidence of cardiopulmonary disease were studied while undergoing elective anesthesia and surgery. Twenty patients (group I) underwent upper abdominal surgery, another twenty (group II) had lower abdominal surgery, and the remaining twenty (group III) had "peripheral" (*i.e.*, nonabdominal, nonthoracic, nonneurosurgical) procedures performed. The distribution of patients in the three groups, according to age and sex, is presented in table 1.

Anesthesia was induced with thiopental sodium (dose range 100 to 400 mg.) following premedication with pentobarbital sodium (100–150 mg.) and atropine (0.6 mg.). The tracheas of all patients were intubated with cuffed endotracheal tubes to insure an airtight fit. Intubation was facilitated by succinylcholine (60–80 mg.). Anesthesia was maintained by means of a semiclosed system with nitrous oxide of known concentrations, and relaxation was provided by intermittent injections of *d*-tubocurarine (20–50 mg.). Ventilation was controlled by pressure regulated mechanical respirators adjusted to maintain moderate hyperventilation (table 2). Tidal volumes ranged from 600 to 1,000 ml. at respiratory frequencies ranging from 12 to 20 per minute. Once adjusted at the beginning of the procedure, the pattern of ventilation remained constant. The constancy of tidal volumes delivered was spot checked with a ven-

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\* Instructor in Anaesthesia, Harvard Medical School.

† Visiting Lecturer in Anaesthesia, Harvard Medical School. Present Address: University of Lund, Lund, Sweden.

‡ Research Fellow in Oral Medicine, Harvard Medical School.

§ Assistant in Anaesthesia, Harvard Medical School. Present Address: University College Hospital, London, England.

¶ Clinical Associate in Anaesthesia, Harvard Medical School.

# Assistant Clinical Professor of Anaesthesia, Harvard Medical School.

tilometer. No deep breaths were administered before or during the study period. Body temperature was measured continuously with an esophageal or nasopharyngeal electrode. By clinical criteria the circulatory status remained stable for the duration of the study in all patients.

In groups I and II the period of study began after intra-abdominal packs and retractors had been in position for 20 minutes. In group III the study period started 20 to 30 minutes after the skin incision had been made. Thus anesthesia and artificial ventilation had been administered for approximately 45 to 60 minutes prior to the start of the study period. Nitrous oxide uptake was considered constant at this time.<sup>11</sup>

The amounts of nitrous oxide and oxygen supplied as fresh gas in liters per minute were 3:3, 4:2, 6:2, and 4:1. The concentration of oxygen in the inspired gas was not measured, but gas flows of all anesthetic machines were checked with a Fisher and Porter Master Flow-rator. Total flows of each gas were found to be correct to within 100 ml. The mixtures were administered in random order to each patient. After each mixture had been administered for five to ten minutes 8 ml. of arterial blood was withdrawn into 10-ml. syringes wet with heparin from a Cournand needle placed in a radial artery. It is estimated that in five minutes the change in alveolar nitrous oxide concentration was 90 to 95 per cent complete at the lowest of the gas flows used.<sup>11</sup> Syringes were then capped and stored in ice for approximately one hour before analysis.\* Values for arterial pH, oxygen tension and carbon dioxide tension were obtained in each patient for each gas mixture.

Arterial carbon dioxide tension ( $P_{aCO_2}$ ) was measured with a Severinghaus electrode. Arterial pH was measured with a Radiometer microcapillary glass electrode. Arterial oxygen tension ( $P_{aO_2}$ ) was measured with a modified Clark electrode (0.001 or 0.0008 inch platinum cathode) using a Sanborn polarization cell. All measurements were made with electrodes kept at 38° C. The accuracy

\* Analysis of arterial blood samples before and one hour after storage in ice have shown insignificant falls in oxygen tension (av. 1-2 mm. of mercury).

TABLE 1. Distribution of Patients

	Age		Sex	
	Mean	Limits	Male	Female
Group I Upper abdominal procedures	52	36-73	11	9
Group II Lower abdominal procedures	52	20-72	9	11
Group III "Peripheral" procedures	48	16-75	10	10

of the Severinghaus and Clark electrodes was repeatedly checked against water equilibrated with known percentages of oxygen and carbon dioxide. For  $P_{O_2}$  and  $P_{CO_2}$  the reproducibility of any particular sample was found to be within 2 per cent.

All  $P_{aCO_2}$ ,  $P_{aO_2}$  and arterial pH values were corrected to the temperature of the patient.<sup>12</sup> Temperature corrections for  $P_{aO_2}$  above full saturation of hemoglobin (*i.e.*,  $P_{O_2} = 150$  mm. of mercury or high) were performed according to the nomogram of Hedley-Whyte, Radford and Laver.<sup>13</sup> For  $P_{aO_2}$  values below 150 mm. of mercury corrections were applied as given by Severinghaus.<sup>†</sup><sup>12</sup>

The statistical analysis of the oxygen tension data was complicated by the shape of the oxyhemoglobin dissociation curve. Changes in oxygen content of blood caused by changes in physiologic shunt effect oxygen tension of

† The errors inherent in the use of the Severinghaus nomogram have recently been discussed.<sup>9</sup> For a 3° C. temperature gradient between patient and electrode the probable error in corrected  $P_{aO_2}$  is  $\pm 5$  per cent under the conditions of this study.

TABLE 2.  $P_{aCO_2}$  and pH Values

	Average $P_{aCO_2}$	S.D.	Average pH	S.D.
Upper abdominal group	30	$\pm 4.4$	7.48	$\pm 0.06$
Lower abdominal group	29	$\pm 4.6$	7.47	$\pm 0.05$
Peripheral group	27	$\pm 6.2$	7.52	$\pm 0.07$
Three groups combined	29	$\pm 5.1$	7.49	$\pm 0.07$

TABLE 3. Arterial Oxygen Tensions in Millimeters of Mercury

		Percentage Oxygen in Fresh Gas Mixture			
		50	33	25	20
Group I Upper abdominal procedures	Median	126	92	66	58
	90th percentile	234	128	102	93
	10th percentile	59	62	44	38
Group II Lower abdominal procedures	Median	197	99	85	67
	90th percentile	287	160	98	82
	10th percentile	93	66	50	43
Group III "Peripheral" procedures	Median	206	125	92	74
	90th percentile	317	176	127	96
	10th percentile	128	71	68	56

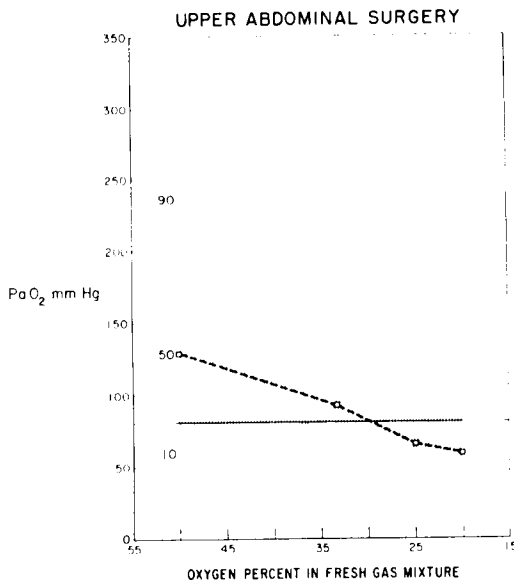


FIG. 1. Shows the relation between the fraction of oxygen in the  $N_2O:O_2$  mixture and the arterial oxygen tension ( $Pa_{O_2}$ ). The figures 10, 50 and 90 to the left of the stippled area mark the tenth, fiftieth (median) and ninetieth percentiles of the  $Pa_{O_2}$  measurements, *i.e.*, 80 per cent of the measurements of  $Pa_{O_2}$  fall within the stippled area. At an  $O_2$  concentration of 50 per cent the horizontal line representing a  $Pa_{O_2}$  of 80 mm. of mercury is on the twenty-fifth percentile. Therefore, in a quarter of the patients having upper abdominal surgery even 50 per cent oxygen does not lead to an arterial oxygen tension ( $Pa_{O_2}$ ) of over 80 mm. of mercury.

blood by different amounts at different points on the oxyhemoglobin dissociation curve.<sup>14</sup> We therefore preferred not to assume a specific form for the distribution of  $Pa_{O_2}$  but instead employed percentiles.<sup>15</sup> For further details of statistical methods see appendix.

A horizontal line representing a  $Pa_{O_2}$  of 80 mm. of mercury has been drawn in each figure to indicate the arbitrary border between normal and abnormal oxygenation.<sup>16</sup> The intersection of this horizontal line with the tenth percentile line thus indicated the  $N_2O:O_2$  mixture required to give a  $Pa_{O_2}$  of 80 mm. of mercury or over in 9 out of 10 patients. The intersection of this horizontal line with the line joining the medians shows the  $N_2O:O_2$  mixture required to give a  $Pa_{O_2}$  of 80 mm. of mercury or over in half of the patients.

## Results

Patients undergoing upper abdominal surgery and those to whom  $N_2O:O_2$  mixture containing 20 per cent or 25 per cent oxygen was administered had the lowest arterial oxygen tensions. In table 3 values of the median, ninetieth and tenth percentiles are given for each  $N_2O:O_2$  mixture in each of the three groups. In figures 1, 2, and 3 the distribution is shown graphically.

A  $N_2O:O_2$  mixture containing at least 25

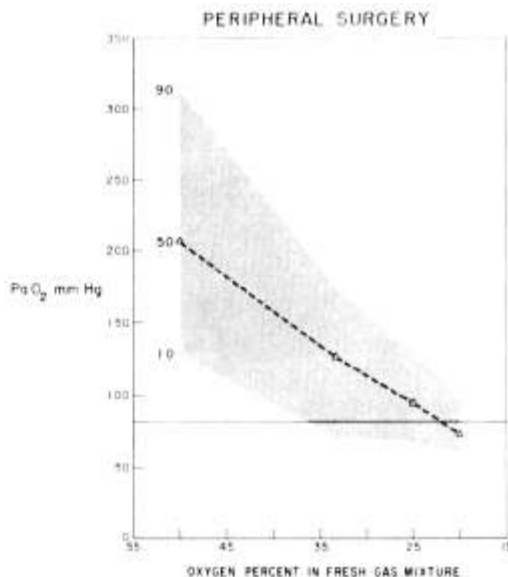
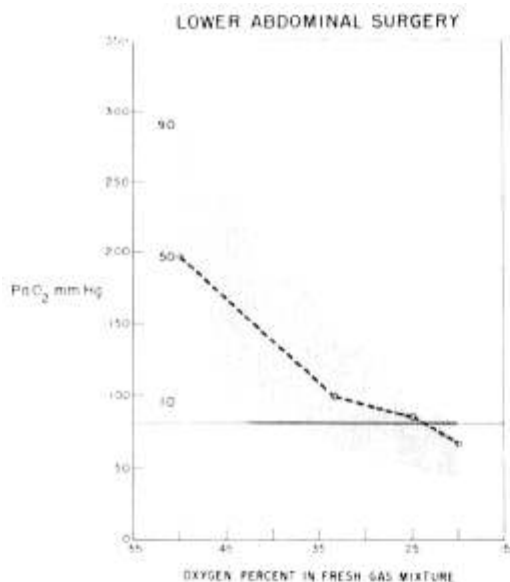


FIG. 2. During lower abdominal surgery the arterial oxygen tension ( $Pa_{O_2}$ ) is higher than during upper abdominal surgery (fig. 1) but lower than during peripheral surgery (fig. 3).

FIG. 3. During intermittent positive pressure ventilation of patients undergoing peripheral surgery for each  $N_2:O_2$  mixture the arterial oxygen tension ( $Pa_{O_2}$ ) is higher than the corresponding  $Pa_{O_2}$  during abdominal surgery (figs. 1 and 2).

per cent  $O_2$  was required to achieve a  $Pa_{O_2}$  greater than 80 mm. of mercury in half of the patients undergoing peripheral and lower abdominal surgery (table 3). An  $N_2:O_2$  mixture containing an oxygen concentration of 33 per cent was necessary for this degree of oxygenation in patients undergoing upper abdominal surgery. Achievement of a  $Pa_{O_2}$  of 80 mm. of mercury in 90 per cent of patients, required that the fresh gases supplied contain approximately 35 per cent  $O_2$  in the "pe-

ripheral" group and 40 per cent in the lower abdominal group (table 3). A fresh gas mixture containing 50 per cent oxygen failed to provide a  $Pa_{O_2}$  of 80 mm. of mercury in 25 per cent of patients undergoing upper abdominal surgery (fig. 1).

The site of operation appears to be of major importance in determining the ease with which arterial blood can be oxygenated. Statistical tests for the significance of this finding were applied, and the results are shown in

TABLE 4. Statistical Tests

Value of <i>P</i> for Difference Between:*	Per Cent Oxygen in Fresh Gas Mixture			
	50	33	25	20
Upper abdominal procedures versus "peripheral" procedures	<0.001	<0.01	<0.001	<0.01
Upper abdominal procedures versus lower abdominal procedures	<0.025	<0.05	<0.05	<0.05
Lower abdominal procedures versus "peripheral" procedures	<0.05	<0.05	<0.025	<0.025

\* One sided significance levels found when testing for equality versus the alternative that the two groups of  $Pa_{O_2}$ 's differed. The tests of significance are not, of course, statistically independent either from row to row or column to column.

table 4. The differences between upper abdominal procedures and peripheral procedures are highly significant.

The influence of age was tested in similar fashion and did not reach statistical significance ( $P = 0.05$ ) in any group for any  $N_2O:O_2$  mixture. The average body temperature was  $36.5^\circ C$ . The range was from  $35^\circ C$ . to  $37^\circ C$ .

### Discussion

Many patients in whom there was no evidence of pre-existing cardiopulmonary disease had arterial oxygen tensions considerably below the accepted normal range of 80 to 100 mm. of mercury.<sup>16</sup> This occurred in spite of increased oxygen concentrations in the inspired gas, and in spite of alveolar hyperventilation as defined by arterial carbon dioxide tension.

This study was designed to show the arterial oxygen tensions which result when different proportions of nitrous oxide and oxygen are administered by standard anesthesia machines. The greater part of the discrepancy between the concentration of oxygen thus administered and the arterial oxygen tension is caused by physiologic shunting. A small part of this discrepancy is caused by the admixture of expired gas to inspired gas in the semiclosed system. The effect of allowing less than ten minutes for equilibration in 5 of 60 patients is a random error and probably insignificant.<sup>11</sup>

An arterial oxygen tension of 80 mm. of mercury results in 95 per cent arterial oxygen saturation, at normal pH and body temperature. This level of arterial oxygenation is arbitrarily taken as the lower limit of normal in this study. An oxygen concentration of 25 per cent in the fresh gas mixture was required to achieve this degree of arterial oxygenation in 50 per cent of patients undergoing peripheral and lower abdominal surgery. It was not until the fresh gas mixture contained at least 33 per cent oxygen that the median value of  $Pa_{O_2}$  surpassed 80 mm. of mercury in the upper abdominal group. It should not be overlooked that 25 per cent of patients in the upper abdominal group had arterial oxygen tensions below 80 mm. of mercury even when 50 per cent oxygen was administered. The fact that abdominal patients required higher concentrations of oxygen in the inspired mixture to

maintain adequate arterial oxygenation than the peripheral patients indicated that shunting is increased by intra-abdominal packing and retraction.

This study deliberately omitted periodic passive deep-breathing but employed large tidal volumes. Had periodic passive deep-breaths been provided one would predict that the component of the total shunt caused by atelectasis of recent origin would have been reduced, although perhaps not eliminated entirely. The degree or duration of the beneficial effect of deep-breathing is not known with certainty, but the oxygen tension certainly starts a downward trend immediately following the deep breaths.<sup>17</sup> Consequently we advise the use of large tidal volumes, the use of intermittent sustained deep breaths, and the use of at least 33 per cent oxygen in the fresh gas mixture when patients with normal lungs are subjected to intra-abdominal surgery.

### Summary

Arterial oxygenation during  $N_2O:O_2$  anesthesia was studied in 60 patients who were without clinical evidence of cardiorespiratory disease. Arterial oxygen tensions were found to be lower than expected in almost all patients. Suboptimal oxygenation was more marked in patients subjected to abdominal surgery than in those subjected to peripheral procedures. On the basis of these results we strongly recommended that at least 33 per cent oxygen be utilized in the anesthetic mixture when patients are subjected to intra-abdominal surgery with anesthetic techniques which employ intermittent positive pressure respiration.

### APPENDIX

The tenth and ninetieth per cent points joined to give the tenth and ninetieth percentile curves shown in figures 1, 2 and 3 were calculated in two stages:

- (1) The observations of  $Pa_{O_2}$  were ordered and used to furnish estimates of the  $\frac{100i}{n+1}$  per cent points ( $i$  is the rank of an observation, counting from least to greatest,  $n$  is the size of the sample which was ordered and, of course, also the rank of the largest measurement).
- (2) The estimates of the tenth and ninetieth per cent points shown in figures 1, 2 and 3 were calculated

by linear interpolation from the per cent points furnished in stage 1, by using the equation:<sup>14</sup>

$$\bar{X} \frac{P}{100} = X_i + \frac{\frac{P}{100} - \frac{i}{n+1}}{\frac{1}{n+1}} (X_{i+1} - X_i)$$

where  $n$  is the sample size and  $\frac{P}{100}$  is the interpolated empirical  $P$  per cent point lying between the ordered observations  $X_i$  and  $X_{i+1}$ , (the subscripts  $i$  and  $i+1$  give the order of the observations  $X_i$  and  $X_{i+1}$ ). Here  $i$  is the largest rank such that  $\frac{100i}{n+1}$  is less than the desired  $P$ .

The statistical significance of operative site on the  $Pa_{O_2}$  for each  $N_2O:O_2$  proportion and for each pair of operative sites was evaluated by the Mann-Whitney test<sup>18</sup> and shown in table 4. Similarly the oxygen tensions observed in patients over 50 years of age were compared with the oxygen tension in patients under 50 years of age.

It should be noted that the median points shown in figure 1, 2 and 3 are sample medians. The shaded areas in figures 1, 2 and 3 show the 80 per cent range, *i.e.*, four-fifths of the observations of  $Pa_{O_2}$  fell within these shaded areas.

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