Oxygen Uptake During Light Halothane Anesthesia 
in Man

Richard A. Theye, M.D., and Gerald F. Tuohy, M.D.

Oxygen uptake was measured during light halothane anesthesia, controlled ventilation, and operation. In the absence of premedication and without thiopental, oxygen uptake averaged 84 per cent of predicted basal values in paralyzed patients and 100 per cent in unparalyzed patients. The difference is attributed to increased oxygen consumption of skeletal muscle in the unparalyzed state. With premedication and thiopental, oxygen uptake averaged 84 per cent initially but increased with time. With premedication alone, oxygen uptake averaged 88 per cent initially and increased to 94 per cent in 2 to 5 hours. The return of oxygen uptake to basal values in both groups is attributed primarily to diminution of the effect of the previously administered drugs. Significant effects of halothane concentration per se on oxygen uptake were not observed. An association between oxygen uptake and esophageal temperature was demonstrated only in paralyzed patients.

Oxygen transfer and transport requirements of the pulmonary and circulatory systems depend, in major part, on the rate of oxygen consumption by the tissues. Currently available information about oxygen consumption in anesthetized man is conflicting in many respects, primarily because of the technical difficulties in carrying out oxygen uptake determinations during anesthesia with gaseous anesthetic agents, and, to a lesser extent, because of the lack of a suitable standard for expression of results. These difficulties have been mitigated by the introduction of gas chromatographic techniques for quantitative analysis of oxygen and carbon dioxide in the presence of anesthetics and by the use of predicted basal oxygen uptake values from a standard table.

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to compare results. With this background, an analysis of the influences on oxygen uptake of halothane anesthesia in man has been carried out.

Materials and Methods

Adult patients free of known metabolic disorders were studied during operative treatment of varicose veins. Each received ethchlorvynol (Placidyl) (500 mg. orally) the night before operation and atropine sulfate (0.4 mg. subcutaneously) 1 hour before induction of anesthesia. Premedics consisting of pentobarbital (100 mg. orally) 2 hours before and meperidine (50 to 100 mg. intramuscularly) 1 hour before induction of anesthesia were given to 19 unselected patients. In all others no premedication (other than atropine) was given. Thiopental (100 to 250 mg. intravenously) was used for induction in nine of the 19 premedicated patients. In the other premedicated patients and in all unpremedicated patients, anesthesia was induced with halothane without thiopental induction.

An orotracheal cuffed tube was placed in each patient with the aid of succinylcholine (20 to 40 mg.), and anesthesia was maintained with halothane in oxygen (35 per cent) and nitrogen. The inspired mixture was delivered from a Bird (Mark IV) ventilator. Patients referred to as "paralyzed" received d-tubocurarine chloride (15 to 25 mg. initially and 6 mg. each 20 minutes thereafter, intravenously) or succinylcholine (400 mg. per hour by intravenous drip). The first hour was used to establish nitrogen equilibrium, a ventilatory steady state, and a steady depth of anesthesia. Inspired-halothane concentration was adjusted, as required, to arrive at the lowest concentration compatible with anesthesia and freedom from movement. Intravenous fluids (5 per cent glucose in 0.2 per cent sodium chloride) were
administered at approximately 2 ml./kg./hour. Room temperature averaged 21° C. (range 20 to 25° C.). Blood loss approximated 75 ml./hour and was not replaced. No studies were carried out in the presence of arterial hypotension. Expired air was collected with a closed non-rebreathing system for 10 minutes at intervals of 20 or 30 minutes and analyzed as previously described. Arterial pH, $P_{\text{a}CO_2}$, and $P_{\text{a}O_2}$ were determined by electrodes maintained at mid-esophageal temperature. Oxygen uptake, car-

<table>
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<th>Description of Group</th>
<th>Premedication</th>
<th>Thiopental</th>
<th>Paralysis</th>
<th>Duration, hour</th>
<th>Patients</th>
<th>Total Observ.</th>
<th>Oxygen Uptake, % of Predicted Basal Mean</th>
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Fig. 1. Oxygen uptake and esophageal temperature during halothane anesthesia in patients not receiving relaxants. Fifty-eight individual observations in 10 patients are illustrated.
bon dioxide elimination, exchange ratio, expired volumes, ratio of dead space to tidal volume, and mean alveolar $P_{O_2}$ were calculated as previously described. Predicted basal oxygen uptake (ml./minute/m$^2$) was obtained by applying the age and sex of the patient to a table adapted from Boothby and associates with 4.83 (Kcal.) used as the calorific equivalent of oxygen (L). Body surface area (m$^2$) was obtained from a height-weight nomogram (Dubois). Observed oxygen uptake is reported as percentage of predicted basal value.

**Results**

Observations of oxygen uptake are presented in table 1 and in figures 1 to 4. The most striking finding was a significant difference in oxygen uptake among groups having as a common denominator the same clinical depth of anesthesia. In addition, in each group the highest average oxygen uptake was associated with the highest average halothane concentration, and the lowest oxygen uptake was associated with the lowest halothane concentration. In the absence of premedication and without thiopental, average oxygen uptake in unparalyzed patients was 100 per cent of predicted basal values (range 84 to 124 per cent). In paralyzed patients who received no premedicants or thiopental, mean oxygen uptake was lower (84 per cent of predicted basal values). The average expired-halothane concentration was lower in the paralyzed group. Significant correlation existed between oxygen uptake and esophageal temperature in paralyzed patients but not in those unparalyzed. In each way examined, variability in oxygen uptake was less in the paralyzed group. These values and relationships did not change significantly over the 1 to 5 hours of observation. In three additional paralyzed patients (not in table), the administration of neostigmine (1 mg. preceded by atropine sulfate 0.4 mg.) was followed within 1 hour by an increased oxygen uptake which averaged +9 per cent of the predicted basal value.

In premedicated patients not receiving thiopental and not paralyzed, oxygen uptake averaged 88 per cent of predicted basal values during the first hour of anesthesia with halothane; 1 to 4 hours later, oxygen uptake had increased to 94 per cent. During this period little change occurred in mean expired-halothane concentration or esophageal temperature. Initial and final average oxygen uptake and expired-halothane concentration in this group were significantly lower than in the unpremedicated, unparalyzed group. The administration of meperidine (50 mg. intravenously)
in an unmedicated, unparalyzed patient was associated with a fall in oxygen uptake from 93 to 81 per cent in 1 hour, with a return to 94 per cent in 1 additional hour.

In premedicated patients who received thiopental for induction and were not paralyzed, average oxygen uptake during the first hour was 84 per cent. This was slightly lower (not highly significant) than that observed in the premedicated group not receiving thiopental. Observations after the first hour in premedicated patients receiving thiopental were available in three of the nine patients. In each patient, oxygen uptake increased with time. The average oxygen uptake 3 to 6 hours after thiopental induction in these premedicated patients was 95 per cent of predicted basal values; this was comparable to the value (94 per cent) observed at a similar time in premedicated patients not receiving thiopental. No association between oxygen uptake and mean expired-halothane concentration or arterial $P_{CO_2}$ was demonstrated in any of the individuals or groups studied. Esophageal temperature was below normal in each patient and averaged about 35.3° C. in each group.

Ventilatory performance was similar in each of the groups. In unmedicated, unparalyzed patients, carbon dioxide elimination averaged $88 \pm 8$ ml./minute/m.$^2$, and the mean respiratory exchange ratio was 0.70 \pm 0.05. Minute volume averaged $3.93 \pm 0.53$ liters/minute/m.$^2$ (BTPS), and the mean $VD/VT$ for the group was 0.36 \pm 0.07. Arterial $P_{CO_2}$ was below 40 mm. of mercury (range 23 to 35 mm. of mercury). In these patients, predicted values for arterial $P_{CO_2}$ were calculated from knowledge of ventilatory rates ($\dot{V}$) and group average values of rate of carbon dioxide elimination ($\dot{V}_{CO_2}$) and $VD/VT$ by means of the formula:

\[
\text{Predicted arterial } P_{CO_2} = \frac{\dot{V}_{CO_2} \times 0.850}{\dot{V}(1 - \frac{VD}{VT})}.
\]
Predicted values and observed values were not systematically different. The mean difference without regard to sign was 2.4 ± 2.0 mm. of mercury. Values for arterial $P_{O_2}$ (table 2) were more variable (range 81 to 172 mm. of mercury) than those for arterial $P_{CO_2}$. The variability was based on a wide range of alveolar-arterial $P_{O_2}$ gradients (41 to 118 mm. of mercury). No association between alveolar $P_{O_2}$ and arterial $P_{O_2}$ was demonstrated over the range of values for alveolar $P_{O_2}$ (192 to 216 mm. of mercury). No pattern of change was observed in alveolar-arterial $P_{O_2}$ gradient with time in individual patients. Average hourly differences for the first 5 hours between inspired and expired-halothane concentrations were 0.21, 0.22, 0.16, 0.13, 0.10 ml. halothane vapor per 100 ml. gas, respectively.

Discussion

During clinical anesthesia with halothane, oxygen uptake apparently was influenced to a considerable extent by premedicants, thiopental, and relaxants, and only slightly, if at all, by the actual concentration of halothane.

Oxygen uptake was related to body temperature over the range of 34 to 36°F C. only in the totally paralyzed state. In two previous studies of oxygen uptake in man anesthetized with halothane, average values of about 83 per cent of predicted basal values were obtained. These studies were carried out in premedicated patients who underwent, in ad-

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dition, induction with thiopental; the results are similar to the initial observations under the same circumstances of the present study. It is therefore likely that oxygen uptake in premedicated patients early after thiopental induction will average about 80 to 85 per cent of predicted basal values. In the present study oxygen uptake increased with time and approached predicted basal values. The increase in oxygen uptake may have been due to diminution of the influence of the premedicants or thiopental (or both) on oxygen uptake or to the activity of an unrevealed compensatory mechanism. This view is consistent with previous demonstrations of reduced oxygen uptake following premedication and with use of thiopental, and consistent also with observations in the unparalyzed patients of the present study. Accordingly, the 80 to 85 per cent value is considered to be a useful estimate of oxygen uptake during a specific circumstance of clinical anesthesia with halothane but hardly germane to the more general question of specific metabolism-depressing effects of anesthetics.

Oxygen uptake averaged 100 per cent of predicted basal values in the absence of premedication, use of thiopental, or paralysis. With paralysis, oxygen uptake was lower, a significant relation existing between body temperature and oxygen uptake, and variability in oxygen uptake among individuals was lessened. Relaxants are not known, in themselves, to be capable of reducing oxygen uptake except through myoneural blockade and reduction of skeletal muscle activity. These findings suggest the existence of an active oxygen-consuming, and thereby heat-producing, mechanism during these studies which depends in major part upon an intact myoneural junction. Increased activity probably took the form of increased muscular tone since neither gross shivering nor movement was observed. It is not known to what extent low room temperature (21°C.) and the absence of premedicants and thiopental contributed to the activity of this mechanism, what the oxygen uptake would have been if body temperature had remained at 37°C., or whether this mechanism was operative in the premedicated patients. It is apparent, however, that halothane anesthesia and lowered body temperature do not, in themselves, ensure reduced rates of oxygen consumption. In those clinical situations in which a reduction in oxygen consumption is required, for example a period of circulatory arrest or embarrassment, the use of relaxants to eliminate muscle activity may be indicated.

During whole-body perfusion and halothane anesthesia in premedicated, unparalyzed patients, oxygen uptake at 37°C. averaged 76 per cent of predicted basal values (range 62 to 98 per cent). In this circumstance body temperature was maintained by extracorporeal warming of the blood. It is not certain whether the lower oxygen uptake at normal body temperature in this circumstance reflects the absence of a compensatory heat-producing mechanism, the lower than normal systemic blood flow rates, the nonpulsatile nature of the flow, or some other peculiarity of whole-body perfusion.

Guedel stated that, “Assuming a given anesthetic depth for any operation, the amount of the anesthetic agent in the nerve cell required to produce that depth increases or decreases proportionately with the increase or decrease of metabolism.” Guedel then developed the argument that preoperative medication should be directed toward reducing metabolic rate so that a given depth of anesthesia could be achieved with a lower concentration of anesthetic agent. In the sense that the presence of previously administered depressant drugs permits the attainment of a given depth of anesthesia at lower concentrations of anesthetic agent, Guedel’s proposal has been confirmed in previous work and in the present study. It should be emphasized, however, that the findings of the present study deny the implication that a given depth of anesthesia is associated with a given metabolic rate.

Arterial \( P_{O_2} \) was more variable and less predictable than arterial \( P_{O_2} \). This pattern was observed previously during methoxyflurane anesthesia and is believed to be the result of a spread of pulmonary ventilation perfusion ratios such that the shunt-like effect (underventilated, perfused alveoli) was exaggerated and more variable than the deadspace-like effect (overventilated, perfused alveoli). The sizable alveolar-arterial \( P_{O_2} \) gradients seen in both studies are probably ascribable in major part to the contribution of a fixed, unchanging
tidal volume to the collapse of alveolar air spaces.12

Summary
A variety of influences on oxygen uptake have been demonstrated in studies carried out during halothane anesthesia, controlled ventilation, and operations for varicose veins. In the absence of premedication and induction with thiopental, oxygen uptake averaged 84 per cent of predicted basal values in paralyzed patients (that is, those who received d-tubocurarine chloride or succinylcholine) and 100 per cent in unparalyzed patients. The difference is believed to be the result of increased activity and oxygen consumption of skeletal muscle in the unparalyzed patients. With premedication and thiopental, oxygen uptake averaged 84 per cent of predicted basal values initially and increased with time. With premedication alone, oxygen uptake averaged 88 per cent initially and increased to 94 per cent by 2 to 5 hours. The return in oxygen uptake toward basal values in both groups is believed to have been the result primarily of diminution of the effect of the previously administered drugs. The findings were consistent with the proposals of Guedel in the sense that premedication was associated with reduced halothane concentrations at equivalent depths of anesthesia. Significant effects of halothane concentration per se on oxygen uptake were not observed. An association between oxygen uptake and esophageal temperature was demonstrated only in paralyzed patients.

The authors are indebted to Dr. T. T. Myers and Dr. K. A. Lofgren, Section of Peripheral Vein Surgery, who carried out the operative procedures during which these observations were made.

References

INTUBATION Patients having elective hernia operations and orchiopexies were grouped according to the anesthesia used: regional, general with masks, general with endotracheal tube. Postoperative pulmonary complications occurred most often in the group with endotracheal anesthesia. The need for sterilization of endotracheal tubes, and aseptic technique during the procedure, is emphasized. (Minster, J. J.: Comparison of Anesthetic Methods in Elective Surgery, Arch. Surg. 88: 728 (May) 1964.)