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.

Accepted for publication February 28, 1964. The authors are in the Section of Anesthesiology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota. This investigation was supported in part by Research Grant No. H-4881 from the National Heart Institute, Public Health Service.

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.\textsuperscript{2} Arterial pH, $P_{\text{CO}_2}$, and $P_{\text{O}_2}$ were determined by electrodes maintained at mid-esophageal temperature. Oxygen uptake, car-

![Graph showing individual observations of oxygen uptake and esophageal temperature.](http://anesthesiology.pubs.asahq.org/pdfaccess.ashx?url=/data/journals/jasa/931630/)

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 by Boothby and associates with 4.83 (Kcal.) used as the caloric 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 premedicals 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 unpremedicated, 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 \( P_{\text{CO}_2} \) 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 unpremedicated, unparalyzed patients, carbon dioxide elimination averaged 88 ± 8 ml./minute·m.², and the mean respiratory exchange ratio was 0.70 ± 0.05. Minute volume averaged 3.93 ± 0.53 liters/minute·m.² (BTPS), and the mean \( VD/VT \) for the group was 0.36 ± 0.07. Arterial \( P_{\text{CO}_2} \) was below 40 mm. of mercury (range 23 to 35 mm. of mercury). In these patients, predicted values for arterial \( P_{\text{CO}_2} \) were calculated from knowledge of ventilatory rates (\( \dot{V} \)) and group average values of rate of carbon dioxide elimination (\( \dot{V}_{\text{CO}_2} \)) and \( VD/VT \) by means of the formula:

\[
\text{Predicted arterial } P_{\text{CO}_2} = \frac{\dot{V}_{\text{CO}_2} \times 0.859}{\dot{V} \left( 1 - \frac{VD}{VT} \right)}
\]
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° 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.5, 6 These studies were carried out in premedicated patients who underwent, in ad-

<table>
<thead>
<tr>
<th>Case</th>
<th>Alveolar, mean</th>
<th>Arterial</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>203</td>
<td>138</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>199</td>
<td>81</td>
<td>118</td>
</tr>
<tr>
<td>3</td>
<td>192</td>
<td>94</td>
<td>98</td>
</tr>
<tr>
<td>4</td>
<td>215</td>
<td>162</td>
<td>53</td>
</tr>
<tr>
<td>5</td>
<td>216</td>
<td>168</td>
<td>48</td>
</tr>
<tr>
<td>6</td>
<td>197</td>
<td>137</td>
<td>60</td>
</tr>
<tr>
<td>7</td>
<td>200</td>
<td>115</td>
<td>85</td>
</tr>
<tr>
<td>8</td>
<td>213</td>
<td>172</td>
<td>41</td>
</tr>
<tr>
<td>9</td>
<td>200</td>
<td>97</td>
<td>103</td>
</tr>
<tr>
<td>10</td>
<td>209</td>
<td>114</td>
<td>95</td>
</tr>
</tbody>
</table>

**TABLE 2. Oxygen Pressures in Alveolar Air and Arterial Blood at a Fixed $F_{IO_2}$ of 0.35**
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 in-
crease in oxygen uptake may have been due
to diminution of the influence of the premed-
ciants or thiopental (or both) on oxygen up-
taxe or to the activity of an unrevealed com-
 pensatory mechanism. This view is consist-
ent with previous demonstrations of reduced oxy-
gen uptake following premedication 2 and with
use of thiopental, 8 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 halo-
thane but hardly germane to the more general
question of specific metabolism-depressing ef-
fects of anesthetics.

Oxygen uptake averaged 100 per cent of
predicted basal values in the absence of pre-
medication, use of thiopental, or paralysis.
With paralysis, oxygen uptake was lower, a
significant relation existing between body tem-
perature and oxygen uptake, and variability in
oxygen uptake among individuals was less-
ened. Relaxants are not known, in themselves,
to be capable of reducing oxygen uptake ex-
cept through myoneural blockage and reduct-
ion of skeletal muscle activity. These findings
suggest the existence of an active oxygen-
consuming, and thereby heat-producing, mecha-
nism 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 tem-
perature (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 pa-
 tients, oxygen uptake at 37°C. averaged 76
per cent of predicted basal values (range 62
to 98 per cent). 9 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 10 stated that, “Assuming a given
anesthetic depth for any operation, the amount
of the anesthetic agent in the nerve cell re-
quired to produce that depth increases or
decreases proportionately with the increase or
decrease of metabolism.” Guedel then de-
veloped the argument that preoperative medica-
tion should be directed toward reducing meta-
bolic rate so that a given depth of anesthesia
could be achieved with a lower concentration
of anesthetic agent. 10 In the sense that the
presence of previously administered depressant
drugs permits the attainment of a given depth
of anesthesia at lower concentrations of anes-
thetic agent, Guedel’s proposal has been con-
 firmed in previous work 11 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 pre-
dictable than arterial P CO 2 . This pattern was
observed previously during methoxyflurane
anesthesia 3 and is believed to be the result
of a spread of pulmonary ventilation perfusion
ratios such that the shunt-like effect (under-
ventilated, perfused alveoli) was exaggerated
and more variable than the deadspace-like ef-
fact (overventilated, perfused alveoli). The
sizeable 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.\textsuperscript{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 \textit{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 \textit{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


\textbf{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. (\textit{Minster, J. J.: Comparison of Anesthetic Methods in Elective Surgery}, Arch. Surg. 88: 728 (May) 1964.)