Whole Body Oxygen Consumption in Awake, Sleeping, and Anesthetized Dogs

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To study the metabolic effects of anesthesia, whole-body oxygen consumption ($\dot{V}O_2$) was compared on 242 occasions in six dogs under standard conditions while awake, sleeping, or anesthetized. The dogs were trained to lie unrestrained in the lateral position for the measurement of $\dot{V}O_2$ (STPD) in the unanesthetized state. Arterial blood gas tensions, pH_a, heart rate, and blood pressure also were determined. The maximum $\dot{V}O_2$ of the alert resting and the minimum of the drowsy resting state averaged (±SE) 5.57 ± 0.48 and 3.97 ± 0.41 ml·kg^{-1}·min^{-1}, respectively. $\dot{V}O_2$ was lowest and least fluctuating during natural sleep (2.46 ± 0.2 ml·kg^{-1}·min^{-1}). During deep anesthesia with methohexital, thiopental, and etomidate, $\dot{V}O_2$ averaged (±SE) 4.68 ± 0.26, 4.26 ± 0.28, and 4.77 ± 0.35 ml·kg^{-1}·min^{-1} during spontaneous ventilation (open-circuit flow-through technique) and 3.54 ± 0.27 ml·kg^{-1}·min^{-1} during controlled ventilation (open-circuit collection technique) with 2% halothane. Anesthesia reduces $\dot{V}O_2$ relative to the resting values of the alert state but increases it relative to that of natural sleep. Accordingly, anesthetics should not be considered general metabolic depressants without qualification. (Key words: Anesthetics, intravenous: etomidate; methohexital; thiopental. Anesthetics, volatile: halothane. Metabolism: oxygen consumption. Sleep: oxygen consumption.)

ANESTHESIA is said to decrease whole-body oxygen consumption ($\dot{V}O_2$), but the magnitude of this effect is still in doubt. In one of the earliest reports, the decrease in $\dot{V}O_2$ correlated closely with the preanesthetic measurements, which, however, were appreciably greater than the estimated basal metabolic rates, and the level of $\dot{V}O_2$ during anesthesia (cyclopropane or pentothal/N_2O anesthesia) was considered as being "of similar order as in sleeping men."[1] A decrease in $\dot{V}O_2$ relative to standard tabulated basal values also has been demonstrated during anesthesia in humans for halothane[2,3] and methoxyflurane.[4] However, in comparing the effects of anesthesia with individual measured basal metabolic rate, three reports documented an increase rather than a decrease in

$\dot{V}O_2$ in humans (cyclopropane and ether)[5] and in dogs (hexobarbital, pentobarbital, chloralose, and ether).[6,7]

Thus, the issue remains undecided and cannot be resolved from a review of published work, in part due to differences in experimental conditions and lack of basic information such as body weight, height, and temperature. Therefore, we measured $\dot{V}O_2$ in trained dogs under standard conditions and found that $\dot{V}O_2$ was greater during anesthesia than in either a drowsy or sleeping state.

Methods

Six mongrel dogs weighing between 19 and 25 kg were studied on a total of 242 occasions for the determination of resting $\dot{V}O_2$ (201 experiments) and of the effects of various anesthetics (41 experiments).

In all animals the common carotid arteries were chronically exteriorized in skin loops for blood sampling and recording of blood pressure. The animals, familiar with the research personnel and the laboratory, were trained to lie quietly and unrestrained in the lateral position during all experiments.

They were treated in accordance with the guidelines of the American Physiological Society.

MEASUREMENTS

$\dot{V}O_2$ (STPD) was measured by two methods:

1. During spontaneous breathing for the determination of resting values and of the effects of injectable agents, $\dot{V}O_2$ was measured continuously by an open-circuit flow-through technique similar to that described by Kappagoda et al.[8] and Webb and Hilstand.[9] The dog's head and upper trunk remained under a transparent plastic hood through which a constant flow of ambient air is sucked with a precision pump, the dog breathing freely from it.[10] Room air enters the hood at the edges of the hood, whereas the expired gas/air mixture is removed at the top of the hood. $\dot{V}O_2$ then is derived from the air flow and the O_2-difference (paramagnetic principle) between in- and out-flowing gas mixtures. The apparatus has a time constant of 30 s and an error of maximally 5%. Any escape of expired air into the ambient atmosphere is prevented by a sufficiently high air flow. This was verified further by measuring CO_2 concentration with a mass spectrometer at the edges of the hood. The CO_2 concentration was the same as in room air and did not show any fluctuation when the dog expired.

2. During controlled ventilation for studying halothane effects, $\dot{V}O_2$ was determined minute by minute using the open-circuit collection technique described by Herr and co-workers.[11] The expired volume was collected with a spirometer (Ohio 840, Airco Corp.), and the inspired and mixed expired concentrations of O_2, CO_2, N_2, and halothane were measured by mass spectrometry (Perkin-Elmer MGA 1100 A). N_2 was used as an inert gas assuming net N_2 exchange as zero. The sampling period (filling and dumping of the spirometer and the sequence of gas analysis) was controlled by a computer. The mass spectrometer was calibrated prior to each experiment with test gases. The error with this method of $\dot{V}O_2$-measurement is less than 4%. In the halothane study, the animals were ventilated with a Starling pump at a frequency of 16 min^{-1} and a tidal volume adjusted to maintain an end-expiratory P_{CO_2} of 35 ± 2 mmHg. The inspiratory port of the pump was connected to a reservoir bag kept filled by a continuous flow of compressed air. By passing the air through a vaporizer (Drägerwerke Lübeck, Germany), any desired halothane concentration could be maintained in the bag and thus in the inspired air.

Blood pressure was determined electromanometrically via a cannula inserted into a carotid loop and heart rate from the pulse pressure with the aid of a cardiotachometer. Both variables were recorded continuously. Arterial blood gas tensions and pH_a were determined intermittently at specified time intervals.

DETERMINATION OF THE RESTING LEVELS OF $\dot{V}O_2$

$\dot{V}O_2$ was measured repeatedly in each dog under standard conditions, i.e., in the fasting state (food withheld for at least 12 h before an experiment), at thermoneutral room temperature of 24° C, usually in the morning in the same quiet room, and in the unrestrained lateral position on a cushioned table. Under these conditions $\dot{V}O_2$ was measured continuously for 2–5 h. During this time the animals calmed down and occasionally even fell asleep. Throughout an experiment the dog's state of vigilance was assessed from its behavior and classified as "alert," "drowsy," or "sleeping" by the research personnel who were aware of the dog's $\dot{V}O_2$ levels at all times. From the $\dot{V}O_2$ readings, the maximum of the alert and minimum of the drowsy resting state or, if possible, also the "sleep" values were differentiated for each dog and experiment.

EXPERIMENTAL PROTOCOL FOR THE STUDY OF THE EFFECTS OF ANESTHETICS

The dogs were studied again under the same standard conditions as described above. In addition, blood pressure, heart rate, blood gas tensions, and pH_a were measured.

Anesthesia was induced whenever $\dot{V}O_2$ reached an apparent awake minimum or, in the halothane study, when the animals actually were sleeping. Immediately after induction, a rectal temperature probe was placed. During anesthesia, rectal temperature was kept at 36.8 ± 0.2° C by surface heating with an infrared lamp.

1. Halothane: The control period was extended up to 5 h, i.e., until the animals fell asleep. To facilitate the intubation of the trachea, thiopental (10 mg·kg^{-1}) was injected and controlled ventilation with air at any desired halothane concentration instituted, the inspired halothane concentration being increased stepwise from 0.5% to maximally 2.0%. Each concentration was maintained for approximately 45 min, i.e., until the mixed expired halothane concentration had reached a plateau.

2. Injectable anesthetics: After control periods of about 3 h in the awake state, either methohexital (4 mg·kg^{-1}), thiopental (10 mg·kg^{-1}), or etomidate (0.8 mg·kg^{-1}) were injected either three times, or, in the case of etomidate, four times, at 9–14-min intervals, while the recording of $\dot{V}O_2$ and the circulatory variables continued until the animals had recovered from anesthesia.

DATA EVALUATION

Averages (±SE) were plotted against time. The measurements during anesthesia were tested for significance in relation to the maximum and minimum resting values prior to anesthesia (injectable agents) or in relation to maximum resting values and sleep values (halothane). This was done by one-tailed Bonferroni t tests for paired samples,[12,13] because the effects are always compared in the same animal. Since there were multiple experiments in the same dog, variances for the t test were estimated by analysis of variance.[12,13] As two comparisons (maximum vs. anesthesia and minimum vs. anesthesia) were made, significance conventionally is accepted if $P < 0.025$, yielding a type I error less than 5%.

Results

DETERMINATION OF THE RESTING LEVELS OF OXYGEN CONSUMPTION

Whole body $\dot{V}O_2$ varied considerably in resting dogs, in spite of standard conditions not only from day to day but also during the course of most experiments. In figure 1, $\dot{V}O_2$ is more than halved during the transition from a maximum in the alert resting state to a period of natural sleep over a period of 1 h. Variability was similar in all other experiments. Accordingly, three $\dot{V}O_2$ levels were extracted from the recordings of each experiment: the maximum and minimum resting, and, if it happened, also the "sleep" values. As shown by the histograms in figure 2, $\dot{V}O_2$ ranged widely from 1.6 to 10 ml·kg^{-1}·min^{-1},

$[ml \cdot min^{-1}]$ Dog "NINA", 24 kg

O_2-
CONSUMPTION
(STPD)

150

100

ALERT
$(\dot{V}O_2 - 5.5 \, ml \cdot kg^{-1} \cdot min^{-1})$

50

SLEEPING
$(\dot{V}O_2 - 2.0 \, ml \cdot kg^{-1} \cdot min^{-1})$
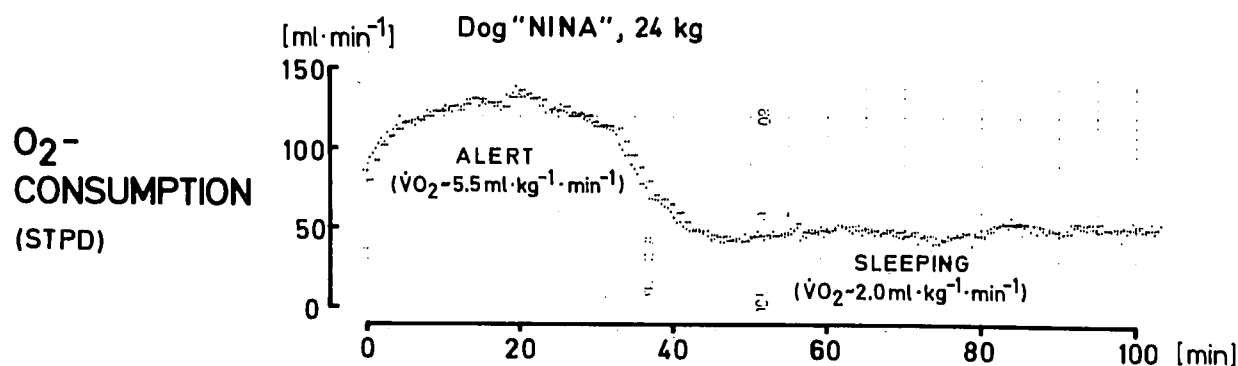
0

0   20   40   60   80   100 [min]

FIG. 1. Effects of vigilance on $\dot{V}O_2$. Representative experiment. Note that $\dot{V}O_2$ is more than halved during the transition from the alert resting state to a period of natural sleep.
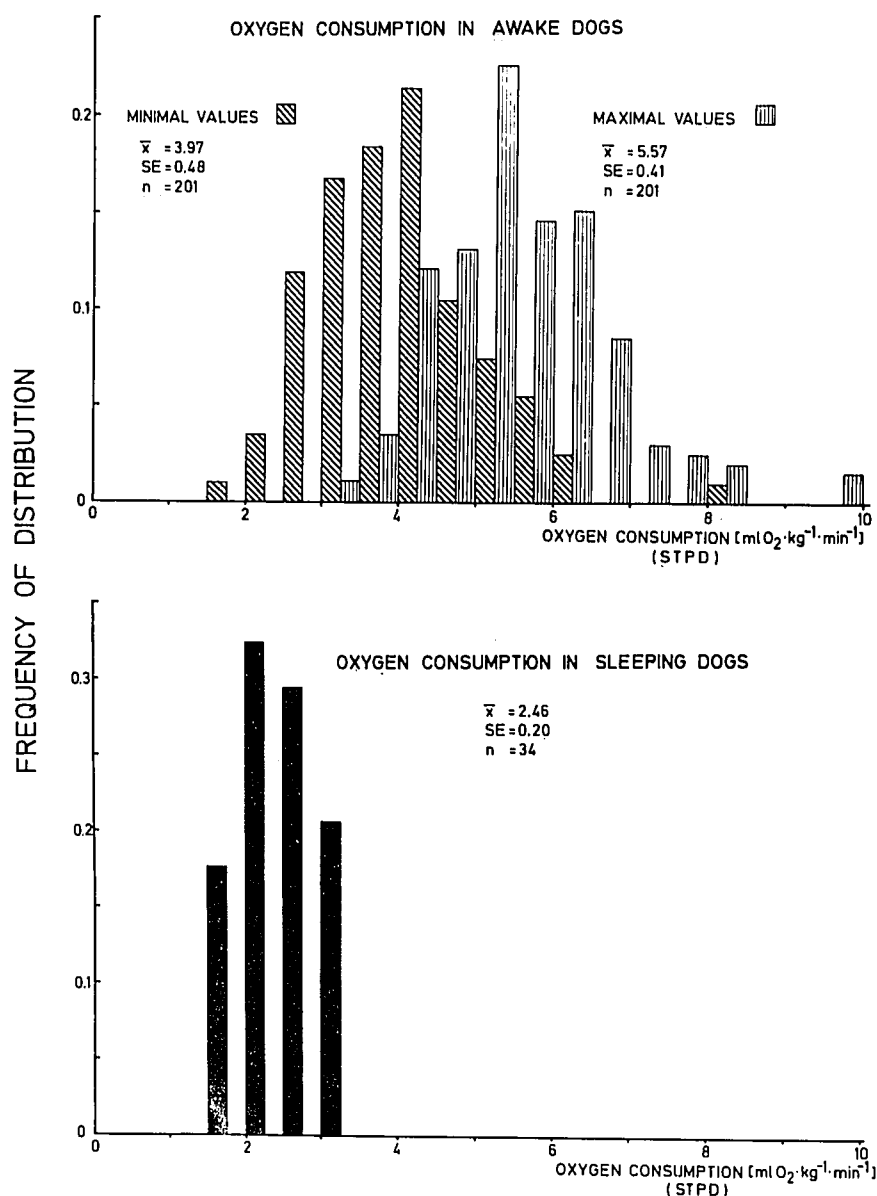
FREQUENCY OF DISTRIBUTION

OXYGEN CONSUMPTION IN AWAKE DOGS

MINIMAL VALUES ▨
$\bar{x}$ = 3.97
SE = 0.48
n = 201

MAXIMAL VALUES ▥
$\bar{x}$ = 5.57
SE = 0.41
n = 201

0.2

0.1

0

0   2   4   6   8   10
OXYGEN CONSUMPTION $[ml \, O_2 \cdot kg^{-1} \cdot min^{-1}]$
(STPD)

OXYGEN CONSUMPTION IN SLEEPING DOGS

$\bar{x}$ = 2.46
SE = 0.20
n = 34

0.3

0.2

0.1

0

0   2   4   6   8   10
OXYGEN CONSUMPTION $[ml \, O_2 \cdot kg^{-1} \cdot min^{-1}]$
(STPD)

FIG. 2. Frequency distribution of $\dot{V}O_2$ for various states of vigilance. Means (±SE) from 201 experiments on six trained dogs under standard conditions. Maximum = alert resting, minimum = drowsy resting. Despite standard conditions and differences in sample size, $\dot{V}O_2$ fluctuates least in natural sleep.

FIG. 3. $\dot{V}O_2$ during halothane anesthesia. Means (±SE). Maximum (alert) and minimum (sleep) preanesthetic $\dot{V}O_2$ readings are indicated by dashed lines. Even in deep stages of halothane anesthesia, $\dot{V}O_2$ is higher than during natural sleep.
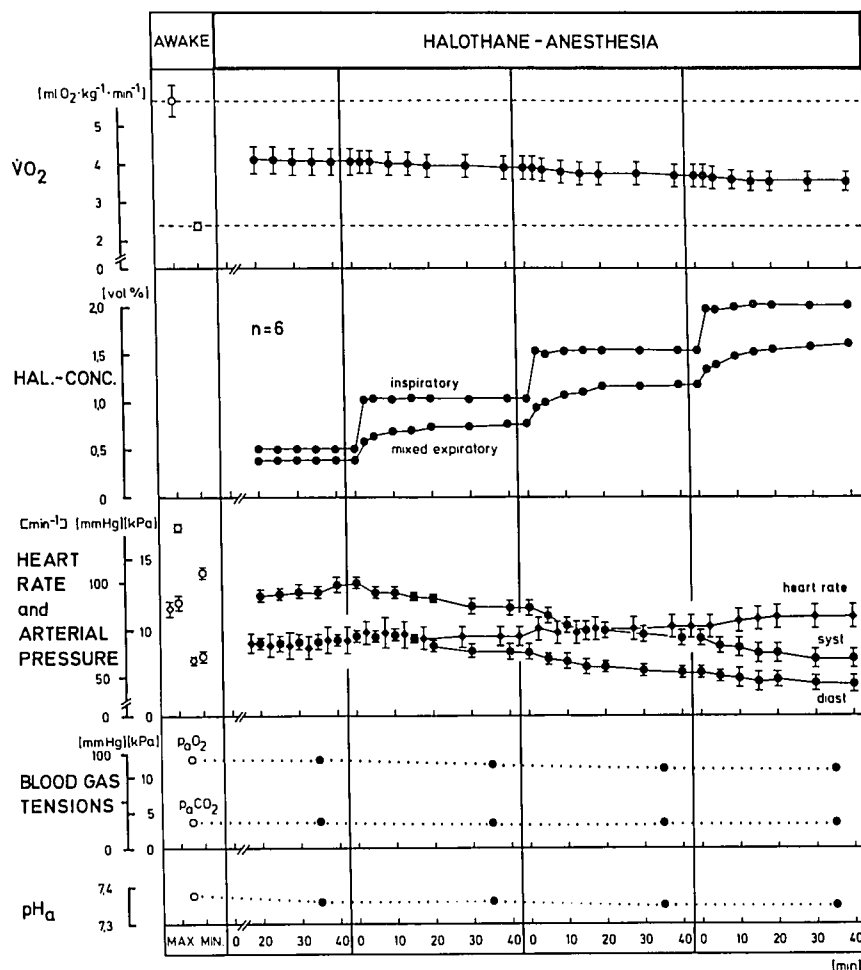
and there was also appreciable variability both in the maximum and minimum values with mean values (±SD) of 5.57 ± 1.18 and 3.97 ± 1.01 $ml \cdot kg^{-1} \cdot min^{-1}$. The large standard deviations presumably reflect day-to-day differences in the state of vigilance. In sleep, when vigilance had reached its lowest physiologic limit, the mean $\dot{V}O_2$ of 2.46 $ml \cdot kg^{-1} \cdot min^{-1}$ was the least and, in spite of the small sample size (n = 34), also the least variable (SD ± 0.48).

Difficulties in evaluating the effects of anesthesia on $\dot{V}O_2$ are therefore largely a matter of the control conditions one happens to encounter. Averaged nonanesthetized "control" values are likely to blur the effects of anesthetics. To avoid this problem we compared $\dot{V}O_2$ during anesthesia with the maximum, minimum, or "sleep" values that were measured in each experiment before anesthesia.

HALOTHANE ANESTHESIA

In all dogs, halothane decreased $\dot{V}O_2$ conspicuously relative to the maximum control values (5.66

$ml \cdot kg^{-1} \cdot min^{-1}$ ± 0.38 SE), but even during deep halothane anesthesia (1.5%, expired), $\dot{V}O_2$ (3.54 $ml \cdot kg^{-1} \cdot min^{-1}$ ± 0.27 SE) remained well above the preanesthetic "sleep" values (2.41 $ml \cdot kg^{-1} \cdot min^{-1}$) (fig. 3). Differences of $\dot{V}O_2$ during sleep and halothane anesthesia ranged from 0.08 to 2 $ml \cdot kg^{-1} \cdot min^{-1}$. The largest decrease in $\dot{V}O_2$ (in relation to the maximum control value) occurred at the lowest inspired halothane concentration of 0.5%, which was sufficient along with the induction dose of thiopental to render the animals unresponsive to noxious stimulation (tail clamping with a hemostat). Doubling and even tripling of the halothane concentration had comparatively little additional effects. It appears, therefore, that $\dot{V}O_2$ responds primarily to the change of state from nonanesthetized to anesthetized rather than to the concentration of halothane.

It should be stressed that in these experiments the preanesthetic control readings were extended for up to 5 h until the dogs fell asleep, as indicated also by the concomittant low heart rate and blood pressure levels. During halothane anesthesia, $\dot{V}O_2$ obviously remains well above that of natural sleep. Blood–gas tensions and pH_a
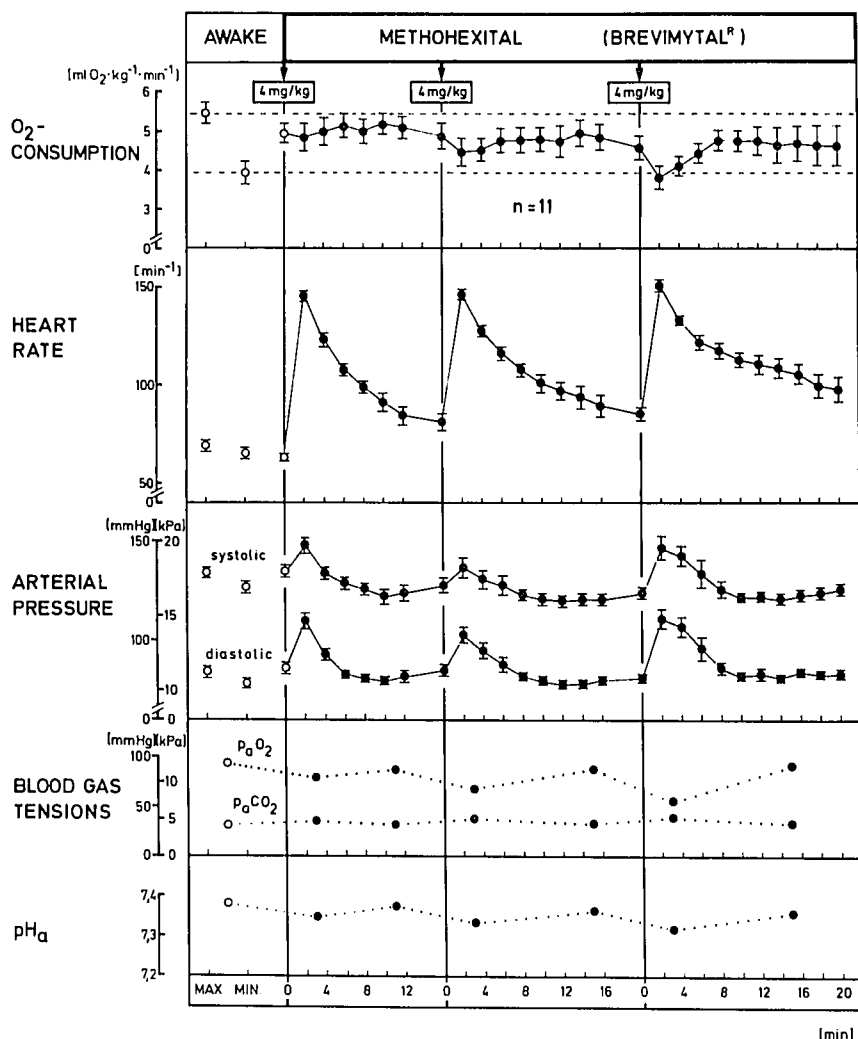
FIG. 4. $\dot{V}O_2$ during methohexital anesthesia. Means (±SE). Dashed lines indicate maximum (alert) and minimum (drowsy) preanesthetic $\dot{V}O_2$ readings. $\dot{V}O_2$ values remain between the maximum and minimum preanesthetic readings during steady state anesthesia.

did not change significantly during the course of these experiments.

INJECTABLE ANESTHETICS

Injectable anesthetics affect $\dot{V}O_2$ similar to halothane. For methohexital this is shown in figure 4. With the second and third injection there was a transient decrease of measured $\dot{V}O_2$ for about 4–7 min because of a transitory apnea. During apnea, however, $\dot{V}O_2$ cannot be measured reliably with the method employed, and measured $\dot{V}O_2$ therefore deviates from actual $\dot{V}O_2$ during these first minutes after injection. With the resumption of adequate breathing, as indicated by the concomittant normalization of the arterial blood gas tensions, $\dot{V}O_2$ always reached a plateau between the maximum and minimum control values. These plateaus reflect the metabolic demands during methohexital anesthesia. All animals remained unresponsive to noxious stimuli throughout the entire recording period shown in the graph. Heart rate and blood

pressure were low in the quiet resting state but increased strikingly during anesthesia.

$\dot{V}O_2$ during thiopental anesthesia also remained between the maximum and minimum awake values in all dogs, while heart rate and blood pressure changes were minimal. $\dot{V}O_2$ during etomidate anesthesia was always greater than the minimum awake value, whereas the maximum awake values were exceeded during anesthesia in several experiments. Heart rate and blood pressure remained unchanged during etomidate anesthesia.

The principle observations for the four anesthetics are summarized in figure 5, which contrasts the measurements during anesthesia with the controls as defined. $\dot{V}O_2$ reflects the readings during deep anesthesia at a mixed expired halothane concentration of 1.5% and the measurements 10 min after the last injection for the injectable agents. With each agent, $\dot{V}O_2$ is greater than the minimum of the drowsy resting state or, in the case of halothane, definitely greater than during natural sleep. With the exception of etomidate, $\dot{V}O_2$ during anesthesia is also

FIG. 5. $\dot{V}O_2$ during anesthesia as compared with the maximum and minimum preanesthetic values. Means (±SE) from multiple experiments on six trained dogs. With all agents, $\dot{V}O_2$ is greater than the minimum (drowsy) preanesthetic values but also less (exception: etomidate) than the maximum (alert) values. In the case of halothane, the minimum value refers to natural sleep.
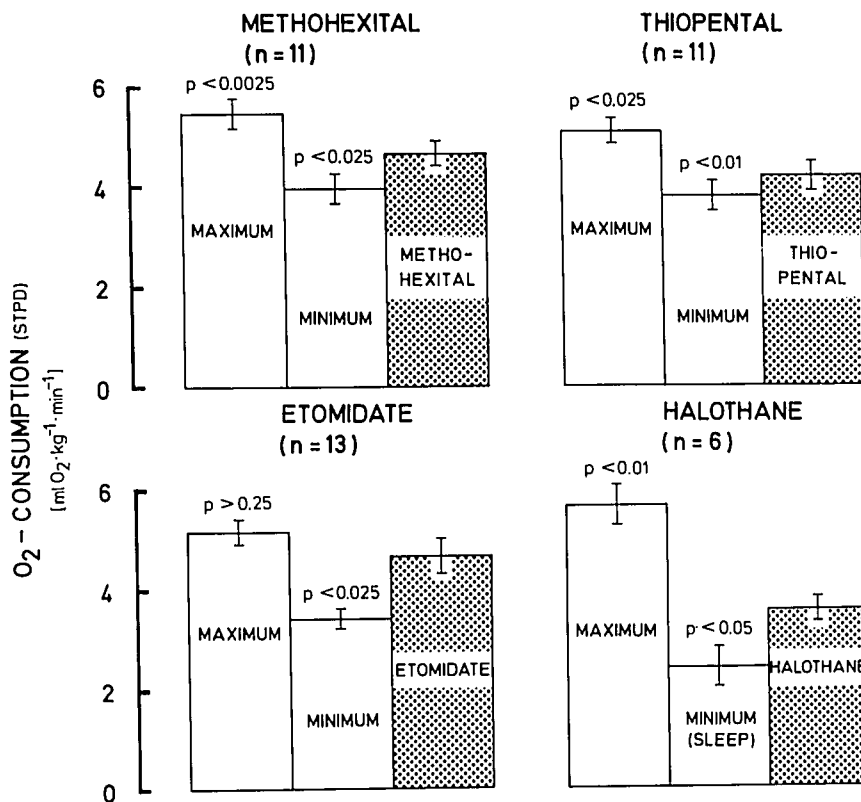
less than the maximum of the alert state. Although mean $\dot{V}O_2$ during etomidate anesthesia was less than the maximum control value, this difference was not significant $(P > 0.25)$. This was due to the occurrence of myoclonia in several cases accompanied by a marked increase in $\dot{V}O_2$.

Discussion

Evaluation of whole body $\dot{V}O_2$ effects of anesthesia as reported in the literature is hampered by differences in experimental protocols and also by the choice of a control reference. This is evident from examination of table 1. Experimental conditions differ in regard to premedication, use and kind (depolarizing vs. nondepolarizing) of muscle relaxants, and ventilation (spontaneous vs. controlled). In addition, such basic information as body weight, height, or body and environmental temperature often are not reported. Premedication with opiates potentiates anesthetic action,[20] $\dot{V}O_2$ increases with thermoregulatory efforts[21] and following intravenous succinylcholine[22] but decreases with mechanical ventilation[3] and, depending on the anesthetic used, also with curare-type relaxants.[23] Perhaps most important, most authors, who reported a decrease in $\dot{V}O_2$ during anesthesia, compared the anesthetic effect on $\dot{V}O_2$ with either estimated basal values derived from metabolic rate tables or with $\dot{V}O_2$ measured just prior to induction of anesthesia. Those authors, however, who reported an increase in $\dot{V}O_2$ dur-

ing anesthesia, used for comparison the individual metabolic rate measured in each individual under standard conditions.

Our own observations could be used in support of either view, depending on the control reference one prefers to choose: the maximum of the alert resting state, the minimum of the drowsy resting state, or the $\dot{V}O_2$ during natural sleep. The accepted reference for the evaluation on metabolic effects is the basal metabolic rate.[24] Estimated with Brody's formula ($\dot{V}O_2 = 10.15$ $kg^{0.73}$), it should range between 4.3 and 4.5 $ml \cdot kg^{-1} \cdot min^{-1}$ in our dogs. These figures roughly correspond to the averaged $\dot{V}O_2$ for the awake state but are markedly less than the maximum (5.57 $ml \cdot kg^{-1} \cdot min^{-1}$) and greater than the minimum (3.97 $ml \cdot kg^{-1} \cdot min^{-1}$). But even the maxima and minima of the resting state, which arbitrarily were chosen to show the influence of changing vigilance on $\dot{V}O_2$, varied considerably from day to day, even in the same animal. The provision of basal conditions alone is apparently not a sufficient precondition for the evaluation of metabolic effects unless it takes into account also the state of vigilance. This is supported by our observation that $\dot{V}O_2$ is lowest (2.46 $ml \cdot kg^{-1} \cdot min^{-1}$) and least fluctuating in natural sleep when vigilance reaches its lowest physiologic level. For this very reason, $\dot{V}O_2$ during sleep may be—as had been suggested already by Benedict[25]—a more reliable standard for the evaluation of metabolic effects than the "basal metabolic rate."

TABLE 1. Survey of the Effect of Anesthetics on Whole Body Oxygen Consumption ($\dot{V}O_2$) in Humans and Dogs in Relation to Various Reference Values

Anesthetic	n	$\dot{V}O_2$ during Anesthesia	Change (%)	Reference Value	Relax-ation	Premedi-cation	Venti-lation	Ref.
Humans								
Cyclopropane Pentothal + N_2O	23	168 ml·min^{-1}	−22	Preinduction (224)*	—/C	+	CMV	1
Cyclopropane Ether	23	222 ml·min^{-1} 222 ml·min^{-1}	+15 + 9	Day before (193)* Operation (202)*	—	—	SV	5
Halothane	6	144 ml·min^{-1}	−13/−14	Table	—	+	SV	2
Halothane	5	169 ml·min^{-1}	−22	Table (217)*	—/C	+	CMV	3
Methoxyflurane	20	96 ml·m^{-2}·min^{-1}	−19 −16	Table (118)* Before premedication (114)*	—	+	CMV	4
Halothane	6	161 ml·min^{-1}	−35	Preinduction (249)*	—	+	SV	14
Droperidol/fentanyl + N_2O	6	130 ml·min^{-1}	−32	Preinduction (223)*	C	+	CMV	14
Thiopental	8	Not reported	− 7	Preinduction	—	—	SV	15
Dogs								
Hexobarbital	12	3.7 ml·kg^{-1}·min^{-1}	+28	Preinduction (2.9)*	—	—	SV	6
Halothane 2.5%	10	119 ml·m^{-2}	−16	Halothane 0.8% (142)*	S	—	CMV	16
Halothane 1.5%	8	4.7 ml·kg^{-1}·min^{-1}	−27	Halothane 0.2% (6.5)*	S	—	CMV	17
Halothane 1.5% + N_2O	23	4.6 ml·kg^{-1}·min^{-1}	—	None	—	+	CMV	18
Methoxyflurane 0.5% + N_2O	17	3.9 ml·kg^{-1}·min^{-1}	—	None	—	+	CMV	18
Various barbiturates	25	5.1 ml·kg^{-1}·min^{-1}	—	None	—	+	CMV	18
Ketamine + N_2O	?	7 ml·kg^{-1}·min^{-1}	—	None	—	+	CMV	18
Ether	9	7 ml·kg^{-1}·min^{-1}	+19	Preinduction (5.7)*	—	—	SV	7
Thiopental + N_2O	12	7.8 ml·kg^{-1}·min^{-1}	—	None	—	—	CMV	19
Own Data								
Thiopental	11	4.3 ml·kg^{-1}·min^{-1}	+ 8	Preinduction (3.8)*	—	—	SV	
Methohexital	11	4.7 ml·kg^{-1}·min^{-1}	+15	Preinduction (4.0)*	—	—	SV	
Etomidate	13	4.8 ml·kg^{-1}·min^{-1}	+28	Preinduction (3.4)*	—	—	SV	
Halothane 2% (insp.)	6	3.5 ml·kg^{-1}·min^{-1}	+32	Preinduction (sleep) (2.4)*	—	—	CMV	

* $\dot{V}O_2$ dimensions as in third column.

c = curare-type relaxant, s = succinylcholine, sv = spontaneous ventilation, cmv = controlled mechanical ventilation.

By the same token, sleep values may be a better choice of reference than awake control values when evaluating variables like cardiac output, heart rate, blood pressure, or the CO_2 response curve during anesthesia.

In order to not obscure the individual responses, we preferred to compare the anesthetic effects in relation to the maximum and minimum resting or the "sleep" values in each single experiment. With these precautions, anesthesia can be said to reduce $\dot{V}O_2$ relative to the maximum values in the alert resting state, *i.e.*, when $\dot{V}O_2$ is well above the estimated basal metabolic rate. It is also true, however, that $\dot{V}O_2$ even in deep stages of anesthesia, is greater than in natural sleep. This agrees with the older literature.[6]

Mean $\dot{V}O_2$ during halothane anesthesia was markedly less than with any of the injectable agents. This is not unexpected because mechanical ventilation[3] and a profound arterial hypotension in all likelihood decreased O_2 demand in the halothane group. It is worth stressing that,

in relation to the maximum preanesthetic control values, $\dot{V}O_2$ decreased most conspicuously with the lowest concentration of halothane following thiopental induction, whereas higher halothane concentrations had only slight further effects. Consequently, $\dot{V}O_2$ seems to respond primarily to the change in state from awake to anesthetized rather than to increasing halothane concentrations.

It is not too surprising, therefore, that with the exception of ketamine and ether in particular, the reported $\dot{V}O_2$ values during anesthesia are in the same range (table 1). The differences between agents are explained perhaps by their special effects on individual organs. The relatively high $\dot{V}O_2$ during ketamine[18] and etomidate anesthesia (this study) are, in all likelihood, due to the peculiar effects on skeletal muscle, as the former enhances skeletal muscle tone and the latter induces myoclonia. By the same token, $\dot{V}O_2$ is probably relatively increased with agents such as barbiturates, althesin, and other injectable agents, which, because of a central vagolytic action, quicken the heart[26]

and correspondingly increase its O_2 demand. Similarly, marked tachycardia has been reported with ether anesthesia in dogs.[7]

In comparison with a report by Theye and Michenfelder,[17] $\dot{V}O_2$ during halothane anesthesia at similar anesthetic depth is markedly less in our study (4.71 vs. 3.54 $ml \cdot kg^{-1} \cdot min^{-1}$).

Although we can only speculate on the reason for this difference several explanations are available. First, the authors used intravenous succinylcholine during anesthesia, which is known to increase $\dot{V}O_2$ by 9–14% during halothane anesthesia.[22] Second, heart rate and blood pressure in their dogs were considerably greater, probably causing increased myocardial $\dot{V}O_2$. Moreover, the long control period prior to anesthesia culminating in natural sleep in all likelihood minimized sympathoadrenal activity and catecholamine secretion in our dogs. It is possible that this contributed to a low $\dot{V}O_2$ also during anesthesia. Taking these factors into account, there is a good agreement with the reported $\dot{V}O_2$ levels during halothane anesthesia, despite different methods of $\dot{V}O_2$ measurement.

Do our observations also apply to humans? This is probably the case. In humans, like in dogs, $\dot{V}O_2$ decreases in relation to the estimated tabulated basal values or to the preinduction measured controls, but it also increases in relation to the individual basal metabolic rate measured under standard conditions the day before surgery.[5] The statement[1,3] that anesthesia would decrease $\dot{V}O_2$ in humans to that occurring during natural sleep, however, is not supported by any measurements. Much to our surprise, and possibly because of the difficulty in measuring $\dot{V}O_2$ in humans without disturbing sleep, we could not find any reliable data in the literature. The problem has been discussed by Webb and Hilstand,[9] who found remarkable interindividual fluctuations between 1.59 and 6.17 $ml \cdot kg^{-1} \cdot min^{-1}$.

In conclusion, "basal metabolic rate" is difficult to define even when determined under standard conditions. Compared with sleep as the lowest physiologic limit of metabolism,[25] anesthesia markedly and without exception increases $\dot{V}O_2$. The general statement that anesthesia reduces O_2 demand, therefore, should be viewed with caution. Anesthetics do not seem to decrease cell metabolism below the physiologic range and, therefore, they are not general metabolic depressants.

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