

BLOOD FLOW AND OXYGEN CONSUMPTION OF THE
HUMAN BRAIN DURING ANESTHESIA
PRODUCED BY THIOPENTAL* †

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THE mechanism of action of anesthetic agents remains a challenging and largely unanswered question. One of the theories of narcotic action involves the concept of interference with cellular oxidations (1). Studies *in vitro* of the effect of narcotics on the oxygen consumption of nervous tissue have, however, yielded equivocal results (1, 2, 3, 4, 5). Studies on the rhesus monkey *in vivo* (6) have demonstrated a definite decrease in cerebral consumption of oxygen during deep anesthesia with thiopental. Earlier studies in man (7) (8) have shown a decreased arteriovenous oxygen difference across the brain during anesthesia with barbiturates; this suggests a depression in utilization of oxygen, but without a simultaneous measurement of cerebral blood flow valid conclusions cannot be drawn.

The introduction of the nitrous oxide method for estimating cerebral blood flow has permitted more accurate measurement of cerebral oxygen consumption under a variety of circumstances (9) (10). Thiopental in seminarcotic doses, sufficient to increase the accessibility of schizophrenic patients, was without effect on the circulation or oxygen consumption of the brain as a whole (11). With anesthetic doses, however, Himwich and co-workers reported a decrease in cerebral consumption of oxygen in man (12). On the assumption that the cortical and subcortical regions of the brain drain separately into opposite internal jugular veins, these workers interpreted their results as indicating that thiopental produced an earlier and more intense depression of the cerebral cortex than of the rest of the brain.

Because the assumption of a difference in origin of blood in the two jugular veins was at variance with results obtained by one of us (10) on subjects in the waking state, and because Himwich's series of studies was relatively small, it was decided to repeat these observations

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upon a larger number of cases during surgical anesthesia induced by thiopental.

METHODS

These studies were carried out prior to some minor surgical procedure upon 11 females and 1 male, varying in age from 17 to 41 years. All had preoperative medication consisting of demerol (75 to 100 mg.) and scopolamine (0.4 mg.), or morphine sulfate (10 mg.) and atropine (0.4 mg.). They were then given thiopental sodium intravenously, the total dosages ranging from 0.5 to 1.6 gm. Needles were successfully placed in both internal jugular veins in 10 patients and in only one jugular vein in 2 patients. Cerebral blood flow (CBF) was then measured by means of the nitrous oxide method (9). Pulse rate and mean arterial blood pressure (MABP) were recorded before and during each flow determination. Blood gas analyses were made with the Van Slyke-Neill manometric apparatus (13). Measurement of the hydrogen ion concentration of the blood was made anaerobically at 37 C. by means of a closed glass electrode and a Cambridge potentiometer. Values for arterial and venous carbon dioxide tension were calculated from the nomograms of Peters and Van Slyke (13). Cerebral metabolic rate in terms of cerebral oxygen consumption ($CMRO_2$) and cerebrovascular resistance (CVR) were calculated as previously described (9).

RESULTS

The pertinent data obtained in these 10 bilateral and 2 unilateral studies during thiopental anesthesia are presented in tables 1 and 2. One study was repeated for reasons which will be discussed. The most striking result was a significant ($p < 0.05$) depression of cerebral utilization of oxygen from the normal (10) value of 3.3 to a mean of 2.1 ml. of oxygen per 100 gm. of brain per minute. The average cerebral arteriovenous oxygen difference of 3.7 volumes per cent is very significantly ($p < 0.001$) lower than the normal of 6.3 volumes per cent. In spite of the lowered mean arterial blood pressure of 71 mm. of mercury (normal = 85 mm. of mercury) the cerebral blood flow was slightly higher than normal, with a mean value of 61 ml. per 100 gm. per minute (normal = 54). An explanation for this finding lies in the cerebrovascular resistance, a measure largely of the tone of cerebral vessels. This was significantly ($p < 0.01$) lower than the normal (1.3 units compared with a normal mean of 1.6 units). This low value for cerebrovascular resistance was probably caused partially by the slight anemia present in most of these patients, but also by the vasodilator effects on cerebral vessels of the increased tension of carbon dioxide in arterial and internal jugular blood. Although no measurement of respiratory ventilation was made in this study, some degree of respiratory depression is generally recognized as an effect of thiopental

TABLE 1
EFFECTS OF PENTOTHAL ON BLOOD GASES

Patient	Age	Sex	Mean Arterial Blood Pressure	Hemoglobin	Arterial				Internal Jugular				pH				
					mm. Hg	gm. per cent	Oxygen Content	Carbon Dioxide Content	Carbon Dioxide Tension	pH	vols. per cent		mm. Hg		Right	Left	
											Right	Left	Right	Left			
Bilateral	years		mm. Hg	gm. per cent	vols. per cent	vols. per cent	mm. Hg										
H. W.	28	F	75	11.6	13.2	58.4	69	7.23	9.8	10.6	63.1	61.8	80	73	7.20	7.23	
R. G.	35	F	63	12.8	14.9	52.8	50	7.35	10.1	10.1	57.9	58.2	50	58	7.31	7.32	
A. B.	24	F	63	9.9	12.5	48.8	47	7.31	8.3	9.1	52.6	51.7	55	54	7.27	7.28	
H. L.	26	F	71	10.5	13.7	49.8	47	7.33	10.4	10.5	52.6	52.9	54	60	7.29	7.29	
D. W.	19	F	68	11.6	14.7	52.6	53	7.30	10.0	11.5	56.0	55.5	60	60	7.27	7.26	
W. R.	24	F	80	12.6	15.1	53.9	56	7.29	11.9	11.6	56.6	57.4	62	63	7.26	7.26	
J. B., I*	17	M	72	13.4	16.5	51.9	58	7.28	12.8	15.0	51.9	55.1	66	64	7.22	7.22	
J. B., II	17	M	73	9.7	11.5	57.3	58	7.29	9.0	8.7	50.9	60.6	67	66	7.24	7.25	
E. G.	32	F	63	11.1	14.4	53.8	56	7.29	10.3	10.1	56.8	57.7	62	64	7.26	7.24	
L. S.	30	F	68	12.4	15.8	49.9	52	7.20	11.2	11.2	53.9	53.6	60	60	7.26	7.26	
M. B.	41	F	82	11.6	14.2	50.1	52	7.28	10.4	10.2	53.4	54.1	60	59	7.25	7.26	
Mean			71	11.4	14.0	52.7	54	7.30	10.2	10.4	55.1	53.2	61.8	61.0	7.26	7.27	
Unilateral																	
R. G.	35	F	81	10.7	13.0	44.8	42	7.33	10.0		48.3		48		7.30		
L. R.	32	F	101	12.7	15.0	50.3	50	7.28	11.7		58.8		64		7.26		

* This study was not included in the mean values for reasons given in the text.

anesthesia and was undoubtedly responsible for the retention of carbon dioxide which was observed. The arterial oxygen content was 10 per cent lower than that to be expected from complete saturation of the hemoglobin present, another reflection of ventilatory inadequacy.

The cerebral respiratory quotient was significantly ($p < 0.05$) depressed from a normal value of unity (10) to 0.89. At the present state of our knowledge there is little basis for speculation as to the significance of this alteration.

TABLE 2
EFFECTS OF PENTOTHAL ON CEREBRAL FUNCTIONS

Patient	Cerebral										Total Dose gm.
	Respiratory Quotient		Arteriovenous Oxygen Difference		Cerebral Blood Flow		Cerebral Metabolic Rate (Oxygen)		Cerebrovascular Resistance		
	Right	Left	vols. per cent		cc. per 100 gm. per minute		cc. per 100 gm. per minute		mm. Hg. cc. per 100 gm. per minute		
			Right	Left	Right	Left	Right	Left	Right	Left	
H. W.	0.72	0.72	3.2	2.6	111	117	3.5	3.0	0.7	0.6	1.6
R. G.	1.06	1.12	4.8	4.8	41	40	2.0	1.9	1.6	1.6	0.8
A. B.	0.91	0.85	4.2	3.4	52	45	2.2	1.5	1.2	1.4	1.1
H. L.	0.85	0.97	4.2	4.3	69	66	2.3	2.1	1.0	1.1	0.7
D. W.	0.83	0.90	3.1	3.2	52	50	1.6	1.6	1.3	1.3	0.6
W. R.	0.84	1.00	3.2	3.5	64	80	2.1	2.8	1.3	1.0	1.1
J. B., I*	0.87	0.87	3.7	1.5	95	81	3.5	1.2	0.8	0.9	—
J. B., II	1.04	1.18	2.5	2.8	75	82	1.9	2.3	1.0	1.1	1.2
E. G.	0.73	0.91	4.1	4.3	54	50	2.2	2.2	1.2	1.3	0.5
L. S.	0.88	0.80	4.6	4.6	41	33	1.9	1.5	1.7	2.1	0.6
M. B.	0.87	1.00	3.8	4.0	43	45	1.6	1.8	1.9	1.9	1.1
Mean	0.87†	0.95†	3.7†	3.6†	60.2	60.8	2.1†	2.1†	1.3†	1.3†	
Unilateral											
R. G.	0.9		3.9		49		1.9		1.7		0.7
L. R.	0.8		3.3		74		2.4		1.4		0.7

* This study was not included in the mean values for reasons given in the text.

† These mean values vary significantly from the normal mean ($p < 0.05$).

The results of the bilateral measurements are interesting. Mean values for arteriovenous oxygen difference, blood flow, oxygen consumption and vascular resistance obtained from the right internal jugular vein were practically identical with those obtained from the left side. Furthermore, in the individual cases the differences in cerebral blood flow or oxygen consumption between the two sides were within the experimental error of the method as measured by duplicate determinations on the same side (10) (with F values of 1.05 and 1.53 for blood flow and oxygen consumption respectively).

DISCUSSION

These results indicate that thiopental depresses cerebral oxygen consumption even though the quantity of oxygen available to the neurons by way of the arterial blood flow is not impaired. This suggests an interference with intracellular mechanisms responsible for the normal utilization of oxygen. These results and inferences are compatible with those of Quastel (2) and others, who demonstrated *in vitro* that anesthetic concentrations of barbiturates reversibly inhibit, in brain tissue, the oxygen consumption associated with the oxidation of glucose, lactate or pyruvate.

The decrease in oxygen utilization observed in the present studies on the intact human brain confirms the results of Himwich and associates (12). In one important respect, however, these results and conclusions are quite divergent. The previous group found what they considered to be a significant difference between results derived from simultaneous sampling of the two internal jugular veins in the same individual although no statistical analysis was carried out. They assumed that this difference was real and represented the difference between cortical and subcortical venous blood, each draining predominantly into one or the other jugular vein. Their results were interpreted as indicating a greater effect of thiopental on the cerebral cortex than on subcortical regions.

It is difficult to substantiate a difference in histologic origin of the blood in the two internal jugular veins. If the anatomic observation that the superior and inferior sagittal sinuses appear to drain into opposite jugulars is to be used as evidence for a difference between the two sides (12), it should also be mentioned that the superior sagittal sinus goes toward the right in the majority of individuals. One of us has recently reported a series of ten bilateral studies in unanesthetized individuals (10). In this as well as in the present series the mean value for oxygen consumption in blood obtained from the right internal jugular was identical with that from the left, a finding difficult to reconcile with the concept of poor mixing of cerebral venous blood. Moreover, in the present series during anesthesia, as well as in the former studies performed with the patient in the waking state, the individual differences between determinations obtained from the right and left jugular veins were well within the experimental error of the method. It is difficult to avoid the conclusion, on the basis of these 20 cases, that in practically all individuals there is adequate mixing of cerebral venous blood from the cortex and subcortical areas before entrance into the jugular veins.

In one study (J. B., I) there was a considerable difference between values for cerebral oxygen utilization from the right and the left jugular veins. This appeared to be related to a disproportionately low arteriovenous oxygen difference on one side, the cerebral blood

flows showing considerably less discrepancy. It appeared that at last we had encountered one of those individuals in whom cortical and sub-cortical areas were represented differently in the two jugular veins. There was an equally good possibility, however, that this result was caused by some technical error. We were presented with an opportunity for testing these possibilities when, four weeks later, a second operation on this patient was necessary. The second study (J. B., II) did not show this divergence between the two sides. Since a real anatomic anomaly should have been present the second time as well as the first, we believe that the discrepancy found in the first study was caused by a technical error in the analyses of blood oxygen, and have therefore not included this study in our averages.

These studies merely indicate an over-all depression of cerebral metabolism caused by a rapidly acting barbiturate. Little is known of the effect of these drugs on the intermediate metabolic processes within the cells of the brain. Since this organ is believed to utilize carbohydrate almost exclusively, determination of the intermediary products of carbohydrate metabolism in the arterial and internal jugular blood is indicated. Such studies are now being actively pursued with the hope that a more exact localization of the action of these drugs will thus be made possible.

SUMMARY

The effects of the intravenous administration of sodium thiopental in anesthetic doses were studied on blood gases, hydrogen ion concentration of the blood, cerebral blood flow, cerebral oxygen consumption and cerebrovascular resistance.

Sodium thiopental significantly depressed cerebral utilization of oxygen in spite of the maintenance of an adequate blood flow.

There was no statistically significant difference in the values obtained from the right or left internal jugular veins under anesthesia. Thus, there is adequate mixing of cerebral venous blood from cortical and subcortical areas before it enters the jugular veins.

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Tissue Changes Following the Use of Plasma Substitutes.

Frank W. Hartman, M.D., Detroit, Mich.

Present Status of Plasma Volume Expanders in the Treatment of Shock: Clinical Laboratory Studies.

Walter L. Bloom, M.D., Emory University, Ga.

Present Status of Plasma Volume Expanders in the Treatment of Shock: Clinical Results in Surgery.

Winchell McK. Craig, M.D., Howard K. Gray, M.D., and John S. Lundy, M.D., Rochester, Minn.

THURSDAY

Business Meeting

Election of Officers

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F. Paul Ansbro, M.D., Francis S. Latteri, M.D., and Benson Bodell, M.D., Brooklyn, N.Y.

Preoperative and Postoperative Respiratory Studies.

Carl S. Hellijas, M.D., Hartford, Conn.

Studies of the Minute Volume Respiration During Anesthesia.

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Chairman's Address: Professional Obligations.

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A Controlled Study of the Treatment of Pain by Intravenous Procaine.

A. S. Keats, M.D., G. L. D'Allessandro, M.D., and Henry K. Beecher, M.D., Boston, Mass.

Intravenous Propyl-Methyl-Carbonyl Allyl Barbituric Acid for Hypnosis During Nitrous Oxide Anesthesia.

V. K. Stoelting, M.D., and J. P. Graf, M.D., Indianapolis, Ind.

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