A STUDY OF THE "SHOCK-DELAYING" ACTION OF THE BARBITURATES

WITH A CONSIDERATION OF THE FAILURE OF OXYGEN-RICH ATMOSPHERES TO DELAY THE ONSET OF EXPERIMENTAL SHOCK DURING ANESTHESIA

HENRY K. BEECHER, M.D., JANE D. MCCARRELL, Ph.D.,

AND

EVERETT I. EVANS, M.D.

BOSTON, MASS.

FROM THE ANESTHESIA LABORATORY OF THE HARVARD MEDICAL SCHOOL AT THE MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASS.

IT HAS BEEN SHOWN REPEATEDLY that there is a concentration of the cellular elements of the blood under ether and a dispersion of them under various barbiturates; the blood has thus been described as concentrated under ether and "diluted" under barbiturates. Because of these and other observations, Seeley, Essex and Mann[15] (1936) set out to determine by experiment whether the onset of traumatic shock would occur after the same interval under ether as under a barbiturate. A first step in their work was to develop a "standard method" of producing trauma.

We have repeated this work, insofar as their two major groups of dogs are concerned. The possibility that barbiturates will delay the onset of shock is of great importance if it is applicable to the shock problem in general, and of considerable importance if this effect can be shown to hold even under special circumstances. We have examined the effect of a barbiturate and compared it with ether in circumstances where shock is produced by bleeding. We have also studied the effects on "shock-time" of respiration of room air compared with oxygen-rich atmospheres under the conditions of these experiments.

METHODS.—*Experimental Animals:* Forty mongrel dogs were used in this study.

Anesthesia.—A freshly prepared 5% solution of sodium amytal was injected into the saphenous vein in an initial dose of 50 mg. per Kg. Ether was induced in a closed cabinet and then maintained as described by Hardenbergh and Mann[7] (1927) in order to repeat the experiments of Seeley, Essex and Mann. Particular effort was made to maintain comparable levels of anesthesia under the two anesthetics. The level chosen was that in which the corneal reflex persisted but was very sluggish. In about half of the experiments of each group the level of anesthesia was controlled further by means of comparable records of the flexion reflex of the leg when the central end of the cut sciatic nerve was stimulated by a Grass stimulator (condenser type); see Beecher and Moyer,[3] 1941.

The Production of Shock.—The intestinal manipulation experiments were carried out as described by Seeley, Essex and Mann (1936). They produced trauma in the following way:* "The entire length of small intestine was delivered outside the abdominal cavity and gently manipulated by a continuous rolling motion between the hands of the operator. After 30 minutes of manipulation the intestines were spread out on towels on the anterior abdominal wall. The intestines were turned every 30 minutes to remove fibrin and to avoid unequal exposure of the loops. The blood pressure in the femoral artery was recorded at intervals on a standard kymograph. When the blood pressure had declined to a level of 70 Mm. of mercury, the animals were considered to be in a state of shock." Blood concentration studies were made.

In the bleeding experiments which we carried out, the first blood was drawn from the femoral artery as soon as the control samples and measurements had been taken. The first hemorrhage amounted to 1.0% of the body-weight. Thirty minutes later a second hemorrhage of 0.5% body-weight was carried out. Every half-hour following this, until death, blood to the extent of 0.25% body-weight was withdrawn.

"Shock-time" was measured from the beginning of intestinal manipulation, or in the bleeding experiments from the beginning of bleeding, until the mean arterial blood pressure had fallen to 70 Mm. Hg. and had remained at this level or below for one-half hour. "Death-time" was measured from the beginning of intestinal manipulation, or from the beginning of bleeding in the bleeding experiments, until death occurred.

Blood Data.—Mean arterial blood pressure was determined and recorded through a cannula placed in the femoral artery. Hematocrit determinations in the bleeding experiments were made by the method of Sanford and Magath[13] (1929) on 6 cc. arterial samples. Blood withdrawn routinely in the course of the experiment was utilized for this determination. In the intestinal manipulation experiments the hematocrit was determined on 1.25 cc. venous blood by the method of Rourke and Ernstene[12] (1930). Serum protein measurements were made with the Zeiss refractometer. This instrument had been repeatedly checked against Kjeldahl protein determinations. Arterial and venous blood oxygen measurements were made by the method of Van Slyke and Neill[19] (1924). When ether was present in the blood the modifications of Shaw and Downing[16] (1935), and Snyder[17] (1938) were used in determining oxygen content of the blood.

RESULTS.—The data of Table I have been compiled from the results of Seeley, Essex and Mann. Tables II and III present our results on repetition of the same experiment. It can be seen that in the case of the ether shock time we are in remarkably close agreement: Our data differ from theirs by

* Parsons and Phemister[10] (1930) used exposure and repeated manipulation of the intestine to produce shock, apparently under barbiturates and ether, but they record few details of their study.

only 5%.* It is worth observing that in this case both groups had the same number of experiments, seven. In the case of the sodium amytal (alone) experiments we had the same number of experiments as with ether, seven; while Seeley, Essex and Mann had three. Possibly this may account in part at least for our failure to agree better with their amytal data. A further explanation probably lies in depth of anesthesia. Seeley, Essex and Mann gave, apparently, a single initial injection of the barbiturate without later supplement.†

TABLE I

DATA COMPILED FROM ARTICLE BY SEELEY, ESSEX AND MANN[15]

Anesthetic Agent	Number of Dogs	Time for Shock to Develop Hrs.	Death-Time Hrs.
Ether alone	7	Average 3.88	Average 5.88
Sod. amytal, alone, 50 mg./Kg.	3	Average 11.55	Average 14.73
Sod. amytal 25 mg./Kg., preceding ether	5	Average 10.50	Average 13.50
Ether followed by 25 mg./Kg. sod. amytal	2	One animal 6.42	One animal 10.25
		One animal 11.42	One animal 15.08

TABLE II

SHOCK BY INTESTINAL MANIPULATION

Ether and Room Air

No.	Wt. Kg.	Sex	Shock-Time Hrs.	Death-Time Hrs.	Hematocrit Control %	Hematocrit Shock %	Serum Protein Control %	Serum Protein Shock %
1.	7.2	♀	10.25	14.17	50.0	69.4	6.94	6.34
2.	7.9	♀	1.00	4.83	56.6	67.6	6.90	7.13
3.	11.0	♂	8.16	10.33	56.3	66.1	7.93	7.61
4.	8.8	♀	4.91	5.55	57.7	70.4	7.70	6.90
5.	12.6	♂	2.28	8.58	50.0	60.4	6.68	6.75
6.	12.2	♂	1.00	5.16	47.0	69.0	6.25	7.70
7.	8.8	♂	1.00	1.50	55.1	80.8	7.11	7.91
Average			4.09	7.16	53.2	69.1	7.07	7.19
			4.1 ± 1.5	7.2 ± 1.6				

*This should dispose of any possible objections that differences between the average room temperatures, mean barometric pressures, or mean relative humidities would, in altering evaporation rates, make it impossible to compare data obtained in these different parts of the country. It is our policy to observe and record such data twice daily, in the middle of the morning and in the middle of the afternoon. These factors are too often neglected. A further control on this point is the fact that both types of experiments, ether and barbiturate, were made in each place; so differences between the two should emerge, if present.

† A recent letter from Dr. Mann supplied the following information: "While in our original article we presented the data on only three dogs in which amytal was used, before the paper was published we had enlarged the number and to date have a fairly large series. We failed to state in the article that occasionally it was necessary to give small amounts of amytal when the animal became light, until shock had developed. It is also our practice to decrease ether as soon as the animal is definitely in a condition of shock (suggested by Meltzer) so that the time of action of the two anesthetic agents does not differ greatly."

TABLE III

SHOCK BY INTESTINAL MANIPULATION

Sodium Amytal and Room Air

No.	Wt. Kg.	Sex	Shock-Time Hrs.	Death-Time Hrs.	Hematocrit Control %	Hematocrit Shock %	Serum Protein Control %	Serum Protein Shock %	Na Amytal mg./Kg. Initial	Na Amytal mg./Kg. Suppl.	No. Inject.
8.	9.8	♀	11.41	14.83	32.3	57.2	7.13	8.33	51	5.1	2
9.	18.6	♂	9.00	15.58	39.6	62.6	7.13	7.72	51	24.8	18
10.	6.8	♂	9.16	10.30	40.4	52.0	6.20	6.18	50	14.7	5
11.	8.5	♂	2.17	5.83	37.6	46.5	6.66	6.10	50	19.4	5
12.	11.0	♂	9.00	18.50	39.8	60.2	7.89	8.18	50	30.0	16
13.	8.4	♂	10.50	11.16	40.4	74.8	7.09	7.70	50	11.3	4
14.	28.4	♂	6.58	8.90	53.8	67.3	—	—	50	30.0	6
Average.....			8.26	12.16	40.6	60.1	7.02	7.37	50	19.3	8
			8.3 ± 1.2	12.2 ± 1.7							

In our experience, it was not possible to maintain a level of barbiturate anesthesia that was comparable with that of the ether experiments by this single injection (except in one out of 20 amytal experiments). In our experiments, following this initial injection, sometimes sooner than an hour, the animal's anesthesia would become very light, so that the dogs could not truly be considered as anesthetized unless supplementary doses of barbiturates were given. It seems to us that Seeley, Essex and Mann were comparing ether anesthesia with, in the latter part of their barbiturate experiments, a state in which hardly any anesthesia produced by the drug itself was present, but what depression there was was chiefly the depression of the shock state. We have made particular efforts to maintain comparable levels of anesthesia. Because of the larger number of our amytal experiments and the particular efforts we have made to maintain comparable levels of anesthesia in the two groups we are inclined to believe that our values more nearly express, than does the other series, the shock-delaying properties of the barbiturates: Shock was delayed twice as long under barbiturates as under ether (our data) rather than three times as long (Seeley, Essex and Mann). There is no point in dwelling on this quantitative difference, of much more importance is the fact that we confirm their observation that the barbiturates *under the conditions of this experiment* do delay the onset of shock, and that death will occur later if barbiturate anesthesia be used than if ether is the agent employed.

We next set out to test whether or not barbiturates would delay the onset of shock produced by bleeding, with the belief that this might help to round out the picture of possible usefulness of the agents in seriously wounded individuals. From Tables IV, V, VI and VII it is apparent that no significant shock-delaying action has been demonstrated when hemorrhage constitutes the trauma.

We had planned to compare the effects of barbiturates and ether in muscle trauma experiments but decided not to, in view of the failure of barbiturates to delay shock produced by bleeding in our experiments and the failure of barbiturates to delay, in comparison with ether, the shock produced in the muscle trauma experiments of Parsons and Phemister,[10] and of Bla-

lock.[4] Parsons and Phemister (1930), in a large series of experiments (70) upon anesthetized dogs, studied the effects of stimulation of the nerves of the limb, of traumatization of the limb, and of bleeding. For anesthetics they employed ether and morphine in 24 cases, ether alone in 17 cases, morphine and barbital in 18 cases, and barbital alone in 11 cases. They report that except where morphine was used, the effects under ether or barbiturate were very similar.

TABLE IV
SHOCK BY HEMORRHAGE
Ether with Room Air

No.	Wt. Kg.	Sex	Shock-Time, Hrs.	Death-Time, Hrs.	Hematocrit Control %	Hematocrit Shock %	Serum Protein Control Gm. %	Serum Protein Shock Gm. %	Arterial O_2 Content Control Vols. %	Arterial O_2 Content Shock Vols. %	Venous O_2 Content Control Vols. %	Venous O_2 Content Shock Vols. %
1.	6.4	♂	4.50	4.85	42.1	30.5	7.96	6.19	13.7	10.4	6.0	2.9
2.	9.7	♀	2.05	4.32	51.9	39.8	6.64	5.18	19.9	16.8	6.2	4.7
3.	8.0	♀	4.00	5.09	51.8	36.8	6.55	5.45	18.1	13.4	10.8	1.8
4.	8.2	♀	1.50	2.00	49.4	41.5	6.77	5.56	18.9	14.0	8.8	2.1
5.	6.0	♀	1.63	2.67	58.9	51.5	7.22	5.94	19.0	18.5	12.0	8.6
6.	7.0	♀	1.67	4.57	46.9	43.4	6.89	5.90	18.1	16.7	16.8	9.1
	Average.....		2.56 2.6± 0.6	3.92 3.9± 0.5	50.2	40.6	7.01	5.70	18.0	15.0	10.1	4.9

TABLE V
SHOCK BY HEMORRHAGE
Ether with 100% Oxygen

No.	Wt. Kg.	Sex	Shock-Time, Hrs.	Death-Time, Hrs.	Hematocrit Control %	Hematocrit Shock %	Serum Protein Control Gm. %	Serum Protein Shock Gm. %	Arterial O_2 Content Control Vols. %	Arterial O_2 Content Shock Vols. %	Venous O_2 Content Control Vols. %	Venous O_2 Content Shock Vols. %
7.	11.0	♂	0.50	1.08	45.3	42.8	6.89	6.62	—	—	—	—
8.	7.3	♀	4.18	4.49	59.1	44.0	5.88	4.16	24.8	19.8	19.1	7.9
9.	7.0	♂	4.40	4.45	45.6	35.1	7.50	5.79	19.3	15.2	13.1	5.0
10.	7.8	♂	4.33	4.44	52.0	43.7	7.07	5.72	19.0	15.7	14.4	7.3
11.	9.0	♂	4.05	4.48	63.3	52.9	8.08	5.70	26.6	23.6	21.0	13.2
12.	12.5	♂	2.75	3.68	58.6	51.1	6.73	5.58	24.6	21.8	16.5	14.4
13.	9.2	♀	3.00	6.77	60.6	55.0	7.68	6.27	24.2	22.6	23.8	13.3
	Average.....		3.32 3.3± 0.5	4.20 4.2± 0.6	54.9	46.4	7.12	5.69	23.1	19.8	18.0	10.2
	Combined ether Average.....		2.8± 0.4	4.1± 0.4								

TABLE VI
SHOCK BY HEMORRHAGE
Sodium Amytal with Room Air

No.	Wt. Kg.	Sex	Shock-Time, Hrs.	Death-Time, Hrs.	Hematocrit Control %	Hematocrit Shock %	Serum Protein Control Gm. %	Serum Protein Shock Gm. %	Na Amytal mg./Kg. Initial	Na Amytal mg./Kg. Suppl.	No. Inject.	Arterial O_2 Content Control Vols. %	Arterial O_2 Content Shock Vols. %	Venous O_2 Content Control Vols. %	Venous O_2 Content Shock Vols. %
14.	8.6	♂	1.55	—	35.6	33.8	6.98	5.97	50	0	1	14.0	14.1	10.6	6.0
15.	11.0	♂	4.90	—	29.1	28.6	5.46	4.94	50	41	7	11.0	11.1	5.9	1.6
16.	11.8	♀	4.72	—	38.4	32.9	7.27	6.12	50	13	4	11.4	13.0	7.4	2.0
17.	8.5	♀	1.55	—	39.4	39.2	4.96	4.05	50	12	3	14.2	16.0	9.6	8.2
18.	12.2	♀	0.75	1.58	38.9	54.7	6.49	6.32	50	8	2	14.9	18.8	9.1	1.6
19.	10.7	♂	5.00	7.38	42.7	53.8	6.05	5.34	56	15	5	15.8	20.1	9.0	2.2
20.	11.2	♀	5.50	6.53	43.7	42.7	5.90	4.81	54	12	9	17.7	17.3	15.5	5.6
	Average...		3.42 3.4± 0.8	5.16	38.0	40.8	6.16	5.36	51	14	4	14.1	15.8	9.6	3.9

TABLE VII

SHOCK BY HEMORRHAGE

Sodium Amytal with 100% *Oxygen*

No.	Wt. Kg.	Sex	Shock-Time, Hrs.	Death-Time, Hrs.	Hematocrit Control %	Hematocrit Shock %	Serum Protein Control Gm. %	Serum Protein Shock Gm. %	Na Amytal mg./Kg. Initial	Suppl.	No. Inject.	Arterial O_2 Content Control Vols. %	Arterial O_2 Content Shock Vols. %	Venous O_2 Content Control Vols. %	Venous O_2 Content Shock Vols. %
21.	9.0	♀	4.50	5.36	42.9	38.8	7.57	6.68	50	47	11	18.7	16.5	10.1	2.8
22.	9.0	♀	3.00	6.60	44.0	48.0	7.11	5.70	55	24	8	19.6	21.8	14.7	9.6
23.	7.0	♀	0.50	6.77	43.7	53.4	5.05	4.73	54	20	6	18.7	22.7	12.5	7.0
24.	9.7	♀	2.50	6.07	37.9	37.1	5.53	4.51	54	16	7	13.7	16.6	9.8	6.2
25.	8.2	♀	4.00	5.67	43.0	42.7	7.27	6.14	54	28	13	15.8	15.3	14.5	6.5
26.	8.0	♂	4.50	5.20	32.4	39.4	6.93	6.01	52	18	8	14.0	16.6	11.8	5.7
Average...			3.17	5.95	40.7	43.2	6.58	5.63	53	26	9	16.8	18.3	12.2	6.3
			3.2± 0.6	6.0± 0.3											
Combined Na amytal Avg.....			3.3± 0.5	5.7± 0.6	39.3	41.9	6.35	5.49	52	20	6				

Blalock (1942), in his study of the comparison of the effects of the local application of heat and cold in the prevention and treatment of shock produced by pounding an extremity, records among other data the following when heat was added to the injured member (Table VIII):

TABLE VIII

Anesthetic Agent	Nembutal	Barbital	Morphine and Ether
Number of dogs	14	6	5
Av. diff. in wt. of traumatized and nontraumatized parts, in per cent body-wt.	3.80	4.05	3.40
Death-time	5° 52′	5° 44′	5° 50′

It is clear that the barbiturates do not prevent in comparison with morphine and ether the loss of fluid into the traumatized extremity, under the conditions of this experiment, nor do they delay the death-time over that produced under morphine and ether. Therefore, considering our hemorrhage data, and Parsons and Phemister and Blalock's muscle trauma data, we have not continued with the traumatization of limb experiments.

Conflicting reports have been made concerning the usefulness of oxygen in shock. We wished to test whether or not breathing of an oxygen-rich (about 100%) atmosphere would be of value in delaying shock under conditions where these two widely different types of anesthesia were employed. From the data, it is apparent that it is possible nearly to double the venous oxygen,* and yet we do not find any significant delay in the onset of shock as a result of using an oxygen-rich atmosphere. Since this was so, we have combined the high oxygen and the room air data.

* For these experiments blood was withdrawn from the femoral vein. It seemed to us that the question of whether the oxygen content could be raised in this peripheral venous blood constituted a severer test than that provided by mixed venous blood from the right heart. We, of course, would have added such determinations had we not failed to get delay in the shock-time as a result of the high oxygen atmosphere, notwithstanding the great increase in the oxygen content of the femoral venous blood.

DISCUSSION.—While it is true that most of the methods employed for producing experimental shock involve a complicated and confusing variety of traumatic stimuli in a single procedure, it is evident that the method of Seeley, Essex and Mann has this objection. The fact that clinical shock may be due to several simultaneous causes in a given patient, is no indication for needlessly complicating experimental procedures. Admittedly, the problem of how to produce experimental shock is a most difficult one; however, it can be pointed out that the intestinal manipulation method of producing traumatic shock involves at least four types of stimuli well known to lead to or aggravate the condition of shock: Tissue trauma, harmful nerve stimulation, chilling, plasma loss and dehydration. The last factor appears to be of major importance in the shock developed by this method. The multiplicity of these factors perhaps accounts for the variability of results obtained from one experiment to another, not only in our hands, but in the experiments reported by the originators of the method (cf. the large standard errors of the mean).

We have available the data of Seeley, Essex and Mann, and the confirmatory data of Kendrick[8] (1939). These studies seem to have demonstrated that real delay in the onset of shock *under the special circumstances of this experiment* can be effected by barbiturates *in comparison with ether.* Our own data support this conclusion.

The major purpose of this communication, and the questions we wish to raise, are concerned primarily with the important assumptions that have been made by others concerning the implications of the work of Seeley, Essex and Mann. It has been assumed by numerous writers, on the basis of the report by Seeley, Essex and Mann, (although not by these men) that it is safe, and desirable, to recommend the use of barbiturates in wounded men with the aim of delaying shock, however it may be caused. Various references to bear this out could be given. More to the point in the present military situation is the official report of the Tenth International Congress of Military Medicine and Pharmacy held in Washington, D. C., May 7–15, 1939. On page 188, the statement is made that *"these experiments* (of Seeley, Essex and Mann) *indicate that patients to whom sodium amytal is administered early, more often survive the exposure, delay and transportation incident to their evacuation to installations of definitive treatment."* (Italics ours). This report goes on to say that *"with these facts in mind it seems advisable to equip battalion surgeons and collecting company personnel with sodium amytal*—(to delay) *the onset of shock . . . ."* The experiments under discussion may or may not be applicable to man subjected to the common types of shock producing trauma of the battle field.

Transference of the findings of Seeley, Essex and Mann, obtained from studies on anesthetized dogs to a general recommendation concerning the equipment of battalion surgeons and collecting company personnel for widespread application to seriously wounded soldiers, involves a good many assumptions. The interpreters of the Seeley, Essex and Mann data make at least two major suppositions that are difficult, if not impossible, to uphold:

First, to have made the recommendations mentioned, it must have been assumed by the interpreters that the findings of Seeley, Essex and Mann (which they obtained in their specialized method of producing shock) hold for battle field shock in general; at least they must have supposed that the recommended barbiturate will not of itself constitute a real hazard. Evidence directly opposing both of these opinions is at hand. Second, use of the data obtained from the anesthetized dogs as a guide for treating wounded but unanesthetized men requires the assumption that the etherized dog represents unanesthetized man and that the dog under the influence of the barbiturate is comparable to man following the administration of barbiturates. In other words, it must be recognized by those who wish to transfer these findings to man that the data of Seeley, Essex and Mann do not compare an unanesthetized group of dogs with a group of dogs under a barbiturate. The comparison is between dogs under ether and dogs under a barbiturate. It would be a more accurate transference of the data in question if those who wish to apply these data to man would conclude that the wounded soldiers would be better off on receiving barbiturate than he would be if he received ether. Unfortunately, data are not available which permit the comparison of shocking stimuli with and without anesthesia; the available data merely present comparisons between the effects of one anesthetic agent and another. It seems apparent that recommendation of the general use of barbiturates for the prevention of shock in severely wounded soldiers, by battalion surgeons and collecting company personnel, is not securely founded, and there is considerable evidence that such use of the barbiturates may be dangerous.

While barbiturates delay the onset of shock in the intestine-manipulating experiments of Seeley, Essex and Mann, of Kendrick, and in ours, it must be recognized further that this is a special type of trauma, and all subjects are under anesthesia. As pointed out by Seeley, Essex and Mann, the method is probably effective chiefly through its dehydrating effect. The barbiturates appear to be more effective in preventing water and plasma loss from the exposed intestines than is ether. The chance that the difference between the two agents may appear simply because ether may increase this loss above normal or above that which is the case under barbiturates must be kept in mind. Seeley, Essex and Mann observed, as we have also, that the loss of fluid from the surface of the traumatized intestines was much less rapid under the barbiturates than under ether.

Other evidence could be cited to support the view that the plasma volume tends to be preserved or increased under the barbiturates whereas the reverse is true under ether. (Ref. Hamlin and Gregerson[6] (1939), McAllister[9] (1938); Searles and Essex[14] (1936), Adolph and Gerbasi[1] (1933), Bourne, Bruger and Dreyer[5] (1930), Barbour and Bourne[2] (1923) and others). Polderman and Beecher[11] (1942) have shown that the volume flow of cervical lymph is usually about 70 per cent greater under ether than under barbiturates. This adds one step to the probable explanation of the greater loss of fluid under ether and the more rapid decline in the

subject's condition under this agent than when under the barbiturates, under the special circumstances of this experiment.

It must be emphasized, that if the barbiturates are effective only by virtue of their antidehydrating effects, then one could hardly expect them to be of value in shock due to other causes, as hemorrhage, tissue damage and so on, unless rapid fluid loss from large surfaces was a complicating factor. In these other types of shock it is reasonable to suppose that the barbiturates might be distinctly harmful, for their typical effects are undesirable—depression of the respiratory volume, decrease in, even loss of effectiveness of the normal respiratory stimulant, carbon dioxide (ref. Beecher and Moyer[3] (1941) for a discussion of this and references to other papers on the subject), depression of blood pressure, depression of the cardiac muscle, *etc.* These and many other effects of the barbiturates could be listed to emphasize that unless specifically indicated these agents had better be avoided in the seriously wounded.

SUMMARY AND CONCLUSIONS

1. We have confirmed the observation of Seeley, Essex and Mann that shock produced in dogs by exposure and manipulation of the intestines is slower to appear when barbiturate (sodium amytal) anesthesia is used than when ether anesthesia is employed.

2. No significant delay was found in the onset of shock produced by hemorrhage when barbiturate (sodium amytal) anesthesia was compared with ether anesthesia. This observation coupled with those of Parsons and Phemister, and Blalock, who found similar effects under barbiturate and ether anesthesia when shock was produced by muscle trauma, indicates that the barbiturates as compared with ether anesthesia are not useful in delaying all types of shock.

3. On the basis of the available evidence, the barbiturates appear to delay shock in comparison with ether, only when the chief shocking trauma is dehydration or plasma loss from wound surfaces.

4. Numerous recommendations have been made, on the basis of the work of Seeley, Essex and Mann (but not by these men), that barbiturates be administered to all wounded men if the development of shock is anticipated. Such recommendations involve two major assumptions, both of which, on the basis of the available information, are untenable: First, the numerous recommendations that barbiturates be administered routinely to all seriously wounded men involves the assumption that the barbiturates will be of value in shock, *however caused*; if one can judge by the results in dogs, this is not the case (see above); or at least the assumption is made that such administration of barbiturates will not be dangerous. Abundant evidence is available to indicate that this is not the case. Second, direct application as a shock preventive, of the observation mentioned in paragraph 1, above, requires the assumption that comparison of the barbiturate data with the ether data is the same thing as a comparison of barbiturate data with a condition of no anesthesia, certainly not the case. No data are available to indicate that the onset

of shock is slower under barbiturates than in unanesthetized subjects.

5. In the experiments presented here, the administration of approximately 100% oxygen did not significantly delay, in comparison with room air, the onset of shock due to bleeding under either a barbiturate or ether, notwithstanding great elevation in peripheral venous blood oxygen content as a result of breathing the high oxygen atmosphere.

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