PERIPHERAL CIRCULATORY REACTIONS AS A BASIS FOR EVALUATING ANESTHETIC AGENTS *

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Introduction

Surgeons and anesthetists, from their clinical experience, have long been aware of the significance of anesthesia in the maintenance of vasomotor circulatory adjustments during operative procedures. Even under the most favorable conditions, the physiologic effects of anesthesia, when superimposed on those of trauma and blood loss, are essentially undesirable. The numerous discussions of the proper anesthetic control of the shocked patient testify both to the variable influence anesthetic agents can exert and to the inadequacy of the available data dictating the selections of such agents (1, 2).

Laboratory evidence has indicated that anesthetic drugs are an important contributory variable in experimentally induced shock (3, 4, 5) and to some extent has quantitated this factor. The importance of the compensatory reactions of the peripheral vascular system in conditions such as shock or hemorrhage led to a study of peripheral circulatory dynamics through direct observation of these vessels (6, 7, 8). This study clearly demonstrated that anesthetic agents have a profound influence on the integrated activity of the peripheral circulation and that the reactions observed were sufficiently definitive to permit their use as a basis for the comparison of different anesthetic procedures (6).

The present report on hemorrhage attempts to correlate typical clinical cases with comparable animal records on the basis of changes observed in the peripheral circulation in dogs during ether, cyclopropane and pentothal anesthesia. The two sets of data not only supplement one another but substantiate general clinical impressions by placing them on a factual basis.

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MATERIALS AND METHODS

The influence of anesthesia on the overall changes in the peripheral circulation after hemorrhage has been treated previously in an analysis covering 168 experiments in dogs (6, 7). Material included in the present study represents selected records of typical dogs from three different anesthetic groups, together with average data from 22 representative experiments. These dealt with the effects of graded hemorrhage in dogs subjected to ether, cyclopropane or pentothal anesthesia.

The shock syndrome was followed by direct microscopic observation of the peripheral blood vessels in the exteriorized omentum, the details of which method were described elsewhere (9). It was possible to integrate the reactions of these peripheral vessels with the compensatory mechanisms activated by blood loss. The specific vascular criteria evaluated were: (1) blood flow, as the rate and extent of distribution through the capillary network; (2) the presence of intermittent periodic changes in the caliber of the terminal arterioles and their precapillary side branches, an activity which regulates the distribution of blood through the capillary bed and which has been termed vasomotion; and (3) the response of these terminal vessels to a physiologic stimulus, epinephrine.

In addition, these circulatory changes were related to several more commonly used criteria: (1) hematocrit, (2) plasma protein, (3) blood pressure, (4) mixed venous oxygen, (5) blood uric acid, and (6) the development of humoral principles, vasoexcitor and vasodepressor substances in the blood of the bled dogs.

The bleeding procedure was designed to inflict comparable circulatory trauma in each animal, and not to withdraw a given volume of blood according to body weight or to exsanguinate the dog over a given time interval. Maximal blood loss was determined on the basis of a clear-cut and typical response in the peripheral circulation; namely the point at which the bleeding produced a complete, transient cessation of peripheral blood flow. A uniformly light plane of anesthesia was maintained throughout with brisk corneal and lid reflexes and no depression of respiration. The to and fro carbon dioxide absorption technic was utilized to maintain anesthesia. An endotracheal airway was employed.

Clinical data were selected from anesthesia study records of patients anesthetized at Bellevue Hospital. Management of these patients was a clinical routine, and completely apart from the laboratory studies. No attempt was made to include a statistical analysis of the available clinical material. Each case illustrated a frequently observed characteristic of the anesthetic agent employed in its relation to hemorrhage in the operating room.

ETHER

Clinicians have agreed, for a long time, that ether does not afford the shocked patient a wide margin of safety. This conviction has been re-

peatedly confirmed in the laboratory (3, 4, 5, 6). Ether tends to produce acidemia, fluid imbalance, interference with carbohydrate metabolism, and of itself brings about many of the circulatory disturbances characteristic of shock. Patients undergoing long surgical procedures during ether anesthesia frequently develop a cool, moist skin exhibiting an uneven patchy pallor. Often, they do not look normal despite comparatively high blood pressures; they withstand further blood loss poorly and their response to transfusion is delayed and inadequate. The effects attributable to ether are illustrated in case records of two patients who had suffered considerable hemorrhage; the first before and the second during operation.

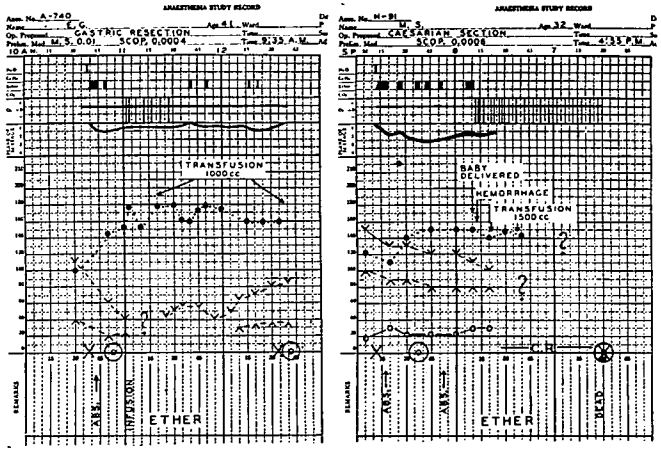


FIG. 1. Anesthesia study record during ether anesthesia. The patient was a 41 year old white male who had an emergency gastric resection for bleeding peptic ulcer. He died in shock twelve hours after operation.

FIG. 2. Anesthesia study record during ether anesthesia. The patient was a 32 year old white female, in labor, who had a cesarean section because of pelvic disproportion. She died of hemorrhage during operation.

Case 1 (fig. 1): The patient was a 41 year old white male with a bleeding peptic ulcer. Gastric resection was performed during ether anesthesia. This patient was admitted twenty-four hours before operation in his first episode of gastric hemorrhage and presented a typical clinical picture of shock. He received 1250 cc. of whole blood as three transfusions, but continued to bleed intermittently. Each of these transfusions seemed to improve his condition and just prior to operation his blood pressure was 110 mm. Hg systolic and 40 mm. Hg diastolic, and pulse rate 102. On being anesthetized with ether, his condition, as can be seen in figure 1, deteriorated rapidly. During operation, it was neces-

sary to support the patient by the administration of another liter of blood. His response to this therapy was slow and unimpressive. Toward the close of surgery, his blood pressure rose gradually to 90 mm. Hg systolic and 34 mm. Hg diastolic. This improvement was not sustained postoperatively in spite of further transfusion of two liters more of blood and the patient died in shock twelve hours later.

This case calls attention to the deleterious effects accompanying ether anesthesia, especially the poor response to transfusion. Ether interfered with this response to the extent that the beneficial action of transfusion during anesthesia was considerably less, even before surgery was begun, than that obtained prior to the onset of anesthesia. The rising blood pressure following transfusion was no index of the degree of restoration of circulation. At the completion of surgery the patient was still in shock despite an improved blood pressure and adequate fluid replacement. Further transfusion in the postoperative period was of no avail.

This next case illustrates the inability of the patient to cope with severe hemorrhage during ether administration. As in the previous case, the poor response of this patient to fluid replacement therapy stresses the rapid deterioration of the vasomotor adjustments of the circulation following the onset of circulatory collapse.

Case 2 (fig. 2): This was a 32 year old white female, in labor, who had a cesarean section for pelvic disproportion. Ether anesthesia was administered. Preoperatively, there was nothing unusual about this patient in labor. During surgery, she suffered a massive hemorrhage from an atonic uterus after a normal baby was delivered. In the ten minute period after hemorrhage, her blood pressure fell slightly from 110 mm. Hg systolic and 80 mm. Hg diastolic to 100 mm. Hg systolic and 80 mm. Hg diastolic. In this time, bleeding was controlled. In the next eighteen minutes, her pulse was counted at 140 to 150 but no blood pressure was obtainable. In this interval, she received 1500 cc. of whole blood by syringe. Efforts at resuscitation failed. She never recovered and was dead at the close of operation.

Strikingly similar changes were noted in dogs subjected to hemorrhage during ether narcosis. Studies of the peripheral circulation revealed that its functional integrity was impaired by ether in the unbled animal and considerably disrupted after severe hemorrhage. Vasodepressor substances were also present in the blood of shocked animals during ether narcosis.

Figure 3 is the record of a typical ether experiment and presents in detail the changes observed in such animals. It should be noted that the withdrawal of as little as 2.5 per cent of blood by body weight resulted in a serious curtailment of visceral blood flow. The compensatory activity of the peripheral circulation attending hemorrhage was relatively ineffective in reducing the capacity of the peripheral vascular bed. Peripheral blood flow was sluggish with an inefficient return of blood to the venous system and pronounced capillary stagnation. Dur-

ing this period, the physiologic mechanisms regulating peripheral blood flow became progressively deranged and were finally abolished. The rapid precipitation of this condition is seen in the accompanying chart where reactivity to epinephrine and vasomotion became suppressed within ninety minutes following the initial bleeding. In this interval, the depression of blood pressure was only moderate and completely out

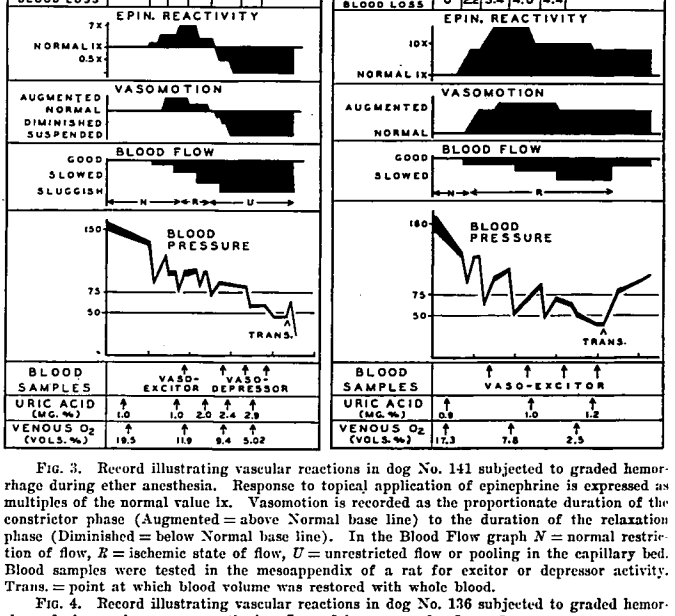


FIG. 3. Record illustrating vascular reactions in dog No. 141 subjected to graded hemorrhage during ether anesthesia. Response to topical application of epinephrine is expressed as multiples of the normal value 1x. Vasomotion is recorded as the proportionate duration of the constrictor phase (Augmented = above Normal base line) to the duration of the relaxation phase (Diminished = below Normal base line). In the Blood Flow graph N = normal restriction of flow, R = ischemic state of flow, U = unrestricted flow or pooling in the capillary bed. Blood samples were tested in the mesoappendix of a rat for excitor or depressor activity. Trans. = point at which blood volume was restored with whole blood.

FIG. 4. Record illustrating vascular reactions in dog No. 136 subjected to graded hemorrhage during cyclopropane anesthesia. Legend is same as for figure 3.

of proportion to the degree of circulatory degradation. It was significant that during the phase of peripheral circulatory inadequacy the blood uric acid increased, venous oxygen decreased and vasodepressor substances in considerable amounts accumulated in the blood. Transfusion at this time produced a moderate rise in blood pressure but had no beneficial effect on the omental circulation and total collapse ensued shortly. The lack of response to transfusion was referable invariably to the disorganized state of the peripheral circulation.

CYCLOPROPANE

Cyclopropane, since its introduction, has achieved wide clinical usage and has been subjected to extensive laboratory investigation. After some years of clinical observation, there has been established here the conviction that this agent affords the shocked patient, especially one who had suffered hemorrhage, a wider margin of safety than other drugs used for general anesthesia. Numerous instances have demonstrated that anesthesia with this agent need not await shock therapy but that both may proceed simultaneously with no apparent detriment to the individual. During long operative procedures with cyclopropane, the patient's skin usually remained warm with good color. When pallor was evident, the skin was evenly blanched and did not present the uneven coloration seen during hemorrhage with ether anesthesia. Laboratory evidence suggests that metabolic and functional effects of cyclopropane are relatively innocuous, with the exception of its sensitization of cardiac automatic tissue. The satisfactory adjustment to blood loss and to fluid replacement therapy when cyclopropane was administered can be seen in the following case.

Case 3 (fig. 5): This patient was a 60 year old white female who had a gastric resection for bleeding peptic ulcer. Cyclopropane was used. She had been bleeding for three days prior to operation and was supported by 2000 cc. of blood during this time. Special studies just before surgery showed a 25 per cent re-

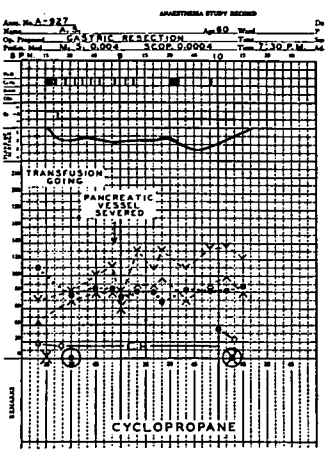


FIG. 5. Anesthesia study record during cyclopropane anesthesia. The patient was a 60 year old white female who had an emergency gastric resection for bleeding peptic ulcer. She recovered uneventfully.

duction in blood volume, a twenty-two per cent hematocrit and a lowered cardiac output. Another 500 cc. transfusion was started preoperatively. Just prior to induction of anesthesia with cyclopropane, the blood pressure was 70 mm. Hg systolic and 44 mm. Hg diastolic, and pulse rate 110. During operation with blood being transfused slowly, her blood pressure rose gradually in the next forty minutes to 110 mm. Hg systolic and 80 mm. Hg diastolic, and pulse fell to 80. At this time, a pancreatic vessel was accidentally severed permitting considerable blood loss. The blood pressure fell to 80 mm. Hg systolic and 60 mm. Hg diastolic but recovered quickly and later rose to 130 mm. Hg systolic and 90 mm. Hg diastolic, the pulse remaining relatively unchanged. At the close of surgery, her blood pressure was 120 mm. Hg systolic and 80 mm. Hg diastolic, and pulse 86. No further transfusions were required and recovery was uneventful.

Little or no impairment in the patient's ability to respond to transfusion was noted. The satisfactory response characteristic of the unanesthetized state was maintained during anesthesia and surgery as well as in the postoperative period. Further accidental blood loss was well tolerated.

Recent experimental studies in traumatic and hemorrhagic shock are unanimous in concluding that cyclopropane provides a wider margin of safety and less interference with compensatory mechanisms than any other anesthetic agent used (2, 4, 5, 6, 10). The most striking difference between dogs given ether and cyclopropane was the ability of the latter to maintain an efficient peripheral circulation with little or no impairment of its vasomotor adjustment mechanisms. Animals so narcotized withstood more severe hemorrhage when compared with those given ether or pentothal. They responded better to transfusion and showed better capillary blood flow at comparable levels of hypotension. Vasodepressor substances could not be detected in the blood of any of these animals. The circulatory dynamics during cyclopropane anesthesia, both before and after hemorrhage, most closely resembled those seen in unanesthetized dogs.

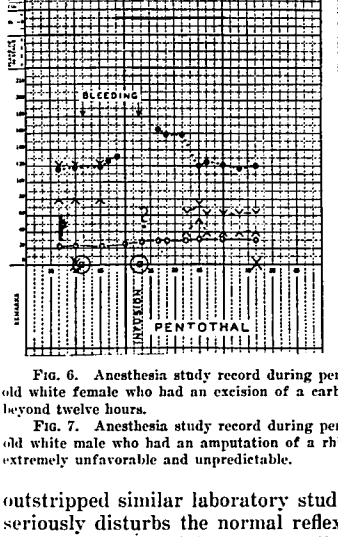
The dog's ability to maintain adequate peripheral blood flow when subjected to hemorrhage during cyclopropane anesthesia is illustrated by figure 4. In contrast to ether, blood loss as high as 4 per cent was attained without interfering with the return of blood to the venous vessels. Compensatory activity in the omental circulation was pronounced and served to restrict the flow to the most direct arteriolar-venular channels. Although the capillary bed was markedly ischemic, no stagnation of blood was present. The peripheral regulatory mechanisms remained intact. At the time of maximal blood loss, the venous oxygen was very low, blood uric acid had increased only slightly and no vasodepressor substances could be detected in the blood.

Following each bleeding, there was a considerable and rapid rebound in blood pressure from its low level during the bleeding period. This was in marked contrast to ether treated animals in which the blood pressure rebound was small and progressively disappeared with in-

creasing blood loss. After maximal blood loss in the cyclopropane experiment, transfusion was followed by a rapid improvement in both blood pressure and peripheral blood flow. The absence of functional deterioration of the vascular bed is of extreme significance in explaining the striking differences between the ether and cyclopropane studies.

PENTOTHAL

Pentothal has received extensive clinical application. Most qualified observers agree that great caution must be exercised when pentothal is used in circumstances of shock or hemorrhage, perhaps indicating a narrow margin of safety for such patients. Because of its singular adaptability and ease of administration, its clinical use has far



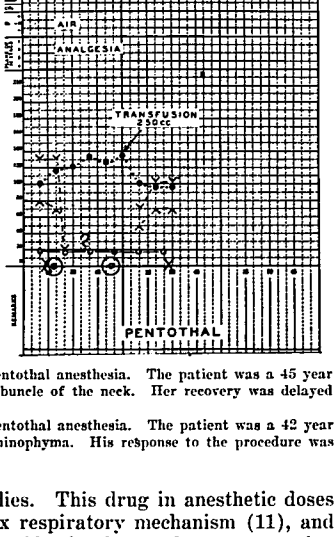


FIG. 6. Anesthesia study record during pentothal anesthesia. The patient was a 45 year old white female who had an excision of a carbuncle of the neck. Her recovery was delayed beyond twelve hours.

FIG. 7. Anesthesia study record during pentothal anesthesia. The patient was a 42 year old white male who had an amputation of a rhinophyma. His response to the procedure was extremely unfavorable and unpredictable.

outstripped similar laboratory studies. This drug in anesthetic doses seriously disturbs the normal reflex respiratory mechanism (11), and in hemorrhage exhibits an unpredictable circulatory depressant action (12). Two case records of pentothal (fig. 6 and 7) were included to illustrate the sudden deterioration of the compensatory circulatory mechanisms and the relatively poor adjustment to sudden blood loss which was characteristic of these patients.

The first case represents a condition of fairly extensive hemorrhage well tolerated for a time, after which rapid circulatory collapse ensued. Response to infusion and transfusion was only fair and considerably delayed.

Case 4 (fig. 6): The patient, a 45 year old white female, was scheduled for an excision of a carbuncle of the neck. She was not diabetic. Narcosis was obtained with a 5 per cent solution of sodium pentothal. The operation lasted thirty-five minutes and required 20 cc. of pentothal. It entailed protracted, fairly copious bleeding which did not affect the blood pressure or pulse for twenty minutes, at which time pulse rose to 160 and the blood pressure was suddenly unobtainable. A glucose and saline infusion was started, and twenty-five minutes later the blood pressure was 64 mm. Hg systolic and 40 mm. Hg diastolic, and pulse rate 120. Two hours and twenty minutes later, a transfusion was given and it elevated the blood pressure to 84 mm. Hg systolic and 60 mm. Hg diastolic. Almost twelve hours later in spite of 2500 cc. of saline and 650 cc. of blood, her blood pressure was 80 mm. Hg systolic and 50 mm. Hg diastolic, and pulse rate 114. She recovered uneventfully after this.

The second case illustrates the development of an abrupt circulatory depression following moderate blood loss during pentothal anesthesia, without spontaneous recovery until restoration of blood volume had been accomplished.

Case 5 (fig. 7): This was a 42 year old white male who was to have a rhinophyma removed. A total of 13 cc. of a 2.5 per cent solution of sodium pentothal was used. The nasal mass bled profusely from the start but the blood pressure and pulse rate were relatively unaffected by the hemorrhage for five minutes. Without warning, the blood pressure fell abruptly to 20 mm. Hg systolic and 0 mm. Hg diastolic in the next five minutes and then was no longer obtainable. Bleeding was controlled rapidly, the pulse continued at 120 to 130, but blood pressure was unobtainable until seven minutes after rapid transfusion of 250 cc. of blood when it was heard at 70 mm. Hg systolic and 50 mm. Hg diastolic. Several minutes later, it was 102 mm. Hg systolic and 70 mm. Hg diastolic, and the pulse rate 98. Recovery was uneventful.

The alarming reaction of this patient could be compared with a corresponding behavior noted in a definite proportion of dogs exhibiting an unfavorable response to pentothal.

Animals, subjected to intestinal trauma during pentothal narcosis, survive for longer periods than those receiving ether (3). Recent studies of the peripheral circulation during hemorrhage have indicated that pentothal exerts a less deleterious effect than does ether, but it was not as effective as cyclopropane in maintaining an adequate peripheral circulation (6).

The functional capacity of the capillary bed in dogs given pentothal was not seriously disturbed by moderate blood loss but was extensive and rapid when blood loss became severe despite relatively high blood pressure levels. In addition, considerable variability in reactions to pentothal administration was obtained, both with respect to its effect

on blood pressure and peripheral blood flow. Perhaps the most significant feature in the pentothal experiments was the abrupt deterioration of the peripheral circulation, resulting in a state increasingly refractive to transfusion. During this depressed stage, vasodepressors in considerable amounts appeared in the blood.

The reactions of dogs to pentothal itself and to hemorrhage during pentothal narcosis were extremely variable. This occurred despite the cautious administration of very small doses of dilute solution (9.6 mg./

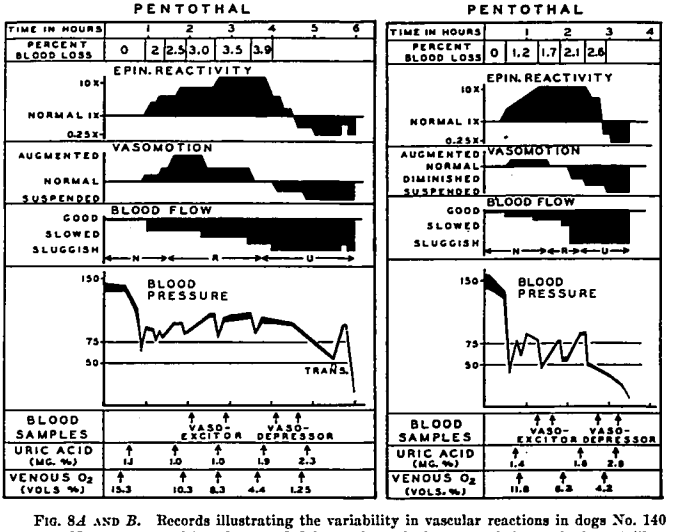


FIG. 8*A* AND *B*. Records illustrating the variability in vascular reactions in dogs No. 140 (*A*) and No. 135 (*B*) subjected to graded hemorrhage during pentothal anesthesia. *A* illustrates the type of response in which the blood pressure remains high and the animal appears to compensate well for almost four hours before rapid deterioration of the circulation occurs. *B* demonstrates the type of poor response noted in a definite proportion of the pentothal experiments. Legend same as for figure 3.

Kg./hr. as 1 per cent solution). Some animals, even before bleeding, showed definite disturbance in the omental circulation evidenced by subnormal vasomotion and dilatation of the small veins. Dog 140 (fig. 8*A*) demonstrates the average response to hemorrhage and pentothal anesthesia. It should be noted that blood pressure which remained relatively high throughout was a poor guide to the extent of existing circulatory disturbance. Vasomotion was inhibited relatively early resulting in the trapping of appreciable quantities of blood in the capillary bed. Toward the end of the experiment, complete capillary stag-

nation developed. The blood pressure remained relatively high and only fell to a very low level precipitously some time later. Transfusion at this time was completely ineffective. It is interesting to note that vasodepressors appeared in the blood concomitantly with vascular stagnation. A record of dog 135 (fig. 8*B*) is included to illustrate the type of unfavorable response noted in a definite proportion of the pentothal animals following hemorrhage.

DISCUSSION

The profound effects exerted by anesthetic agents on the circulation, especially the peripheral vascular bed, make this aspect of the problem of extreme importance in surgical procedures where the limits of circulatory adjustment are often the decisive factor. It is, therefore, necessary to make a direct comparison of these circulatory changes observed in the laboratory with those seen in the operating room.

Ordinarily, the clinical circulatory criteria taken into account include blood pressure readings, pulse rates, respiration and skin temperature and color. In terms of circulation, these are actually indirect measurements. As such, they reflect the circulatory status resulting from disturbances already in effect. These criteria might be termed end points rather than progressive guides to changes in circulation. Although the blood pressure is an important diagnostic guide in the operating room, blood pressure records were found to be a poor index of changes developing in the periphery. The decrement in blood pressure level during observation of the development of the shock syndrome was more an end-result of pre-existing circulatory impairment rather than a concomitant progressive change. It was an especially poor prognostic guide when hemorrhage was severe. Sudden collapse occurred repeatedly with the blood pressures giving no indication of the precarious state of the animal. This might assume serious significance during an operation because the so-called critical blood pressure levels varied from animal to animal and according to the anesthetic agent used.

The definitive circulatory criteria established by direct microscopic observation represent measurements of fundamental components of the vascular system. These measurements have been found valid in a wide variety of circulatory disturbances; namely those seen in hemorrhagic, traumatic and anaphylactic shock, neurogenic hypotension and hypertension, general or locally induced toxemia and narcosis. In all these circumstances, these criteria served as highly discriminating indices of the syndrome. Since circulatory collapse during surgery and anesthesia is in large measure peripheral in nature, direct studies of the peripheral circulation also should provide basic information for evaluating anesthetic drugs.

It was significant that though the laboratory and clinical data cited were obtained through different means, they yielded essentially similar

results. The experimental material also provided substantiation of the clinical observations by relatively quantitative evidence.

The utility of this type of laboratory approach to an appraisal of anesthetic drugs serves to stress the lack of comparable methods for obtaining such direct information in the operating room. Lately, DiPalma (13) has applied, with promising results, quantitative measurements of skin reactions in the shocked patient. Changes in the skin, which are reflections of the circulation in it, become fully developed rather early in the shock syndrome because of prompt intense compensatory vasoconstriction. For this reason, they may not distinguish the progressive peripheral vascular changes occurring late in the syndrome. Continuous plethysmographic studies of the digits offer another direct circulatory measurement that has been applied clinically (14). It is interesting to entertain, also, the possibilities which the circulation of the eye might afford, for this organ possesses both a cutaneous and visceral type of blood supply which is available for uncomplicated visualization (15).

The concensus from existing evidence indicates that in hemorrhagic and traumatic shock, cyclopropane serves well and ether poorly. There is division of opinion concerning pentothal. Bennett, Bassett and Beecher (4) using the changes in blood flow as a circulatory criterion in hemorrhage, concluded that cyclopropane had a wider margin of safety than did ether or evipal. Evans (5), in a brief report of his work, also found that cyclopropane was best when traumatic shock was followed by operation. He also found the effects of ether were poor but those of pentothal, when carefully administered, compared favorably with cyclopropane except when operation was undertaken.

This present study, in considering the changes in the smallest components of the peripheral circulation, indicated that cyclopropane gave better results than ether or pentothal. When cyclopropane was used, dogs maintained an adequate rate of peripheral blood flow which was functionally restricted. No trapping of blood occurred in the capillary bed and venous outflow was good. Vasodepressors were not detected. In contrast, ether gave the poorest results. Functional deterioration and disruption of the capillary circulation occurred early and was extensive. The ultimate disorganization of the peripheral circulation which developed during ether narcosis was related to the early appearance of depressor substances. Pentothal, in its effects on the capillary circulation, gave intermediary results. Early in the syndrome, it compared rather favorably with cyclopropane. Later, changes developed similar to those seen in the ether experiments. The transition from one type of reaction to the other was indefinite and unpredictable. When deterioration set in, it was abrupt and progressed rapidly.

In patients, the administration of cyclopropane did not interfere appreciably with their compensatory circulatory responses to hemorrhage. Improvement from supportive therapy was also in proportion to the

treatment. Laboratory animals given cyclopropane showed greatest maximal blood loss volumes. When transfused, these dogs recovered easily. During ether anesthesia, blood loss was a greater hazard. Furthermore, transfusion was less effective and in many cases reached a point of complete ineffectiveness. For pentothal, both tolerance to hemorrhage and response to transfusion were extremely variable, resembling both cyclopropane and ether at the extremes.

In any hospital or laboratory population, the resistance to hemorrhage or trauma varies widely with the individual. Their behavior in this respect is conditioned by a tendency toward compensatory or decompensatory responses or an in-between pattern. Such distribution curves have been plotted for shock experiments in the laboratory (16). It is impossible, for the most part, to predict the category into which any given patient will fall. But it has been shown, experimentally, that some phase of treatment, by affecting compensatory mechanisms, can shift the normal mode in either direction (16). This makes the borderline cases especially vulnerable to such therapy. On the basis of peripheral circulatory mechanisms, some anesthetic drugs seem to have the capacity to shift responses toward the decompensatory side. The choice of anesthesia for poor-risk patients, particularly, is therefore an important factor in their management, for by influencing the peripheral circulation, the patient's ability to cope with hemorrhage and to improve his condition with transfusion is altered.

From such interpretation of direct measurements of the peripheral circulation, the significance of clinical impressions becomes clearer.

CONCLUSION

Ether, by dampening the compensatory responses in the capillary bed, is to be avoided in circumstances of hemorrhage. Cyclopropane, not exerting the undesirable hemo-dynamic effects of ether, seems much better suited for such operative conditions. Pentothal, having effects between cyclopropane and ether, has limited safety. Its most striking feature is the unpredictability of its influence on the capillary circulation. Much more laboratory information is needed about this drug to evaluate it properly.

SUMMARY

Utilizing peripheral circulatory criteria obtained by microscopic visualization of the peripheral vessels, the effects of ether, cyclopropane and pentothal following hemorrhage in dogs were compared with those in similar clinical cases. Ether anesthesia predisposed animals to early and extensive deterioration of the peripheral compensatory mechanisms, decreased their tolerance to hemorrhage and their response to transfusion. Cyclopropane did not produce these effects. Pentothal gave variable and unpredictable results, generally intermediate between

those of ether and cyclopropane. The clinical records agreed with the laboratory data in respect to resistance to blood loss and response to fluid replacement.

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Wesley Bourne, M.D., of McGill University, Montreal, Canada, will deliver the first of the annual series of Osler Lectures of the University of Vermont College of Medicine at the Fleming Museum, Burlington, Vermont, July 5th and 6th at 8:00 p.m. and July 7th at 10:00 a.m. His subject will be "Anesthesia—Some Contemplations." Published monographs will be available.