VASCULAR RESPONSES TO ANAESTHETIC AGENTS*

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ALTHOUGH EFFECTS of anaesthetic agents on cardiac haemodynamics have been defined[1,2] until recently few data have been available concerning their actions on the peripheral circulation.

In this regard, probably the best studied agent is halothane. Among the pertinent observations are decreased hepatic artery resistance in dogs,[3] decreased resistance in the canine hind limb,[4] decreased total peripheral resistance in man[5] and increased forearm blood flow in man.[5,6] All of these observations argue for peripheral vasodilatation, although Sawyer *et al.*[7] have shown peripheral vascular resistance to be increased by halothane in the miniature swine.

On the other hand chloroform and cyclopropane have been shown to increase hepatic artery resistance[3] while cyclopropane has been reported to increase splanchnic resistance in man[8] and to increase forearm vascular resistance in man.[9,10]

There is, therefore, a body of information which suggests that some general anaesthetic agents may produce peripheral vasodilatation while others may produce peripheral constriction.

Those general anaesthetic agents which produce hypotension may do so through dilatation of peripheral blood vessels, either directly, through stimulation of beta-adrenergic receptors, or through interference with the action of endogenous noradrenaline. To explore these possibilities, selected agents were studied in clinically relevant doses on isolated rabbit veins and aortae. Possible interference with the actions of endogenously released noradrenaline was studied by inference through noting the effects of these drugs on the response to exogenously administered noradrenaline, and also by ascertaining their effects on H^3-noradrenaline washout curves; possible effects on beta-adrenergic receptors were examined by testing these agents in the presence and absence of adrenergic blocking drugs.

In the case of those drugs which, *in vivo*, produced not dilatation but constriction, the possibility of mediation through the autonomic nervous system was examined by assaying their effects in reserpine treated tissues and also by determining whether H^3-noradrenaline washout curves might give any indication of exaggerated release of endogenous noradrenaline.

METHODS

Male albino rabbits weighing between 1.5 and 2.5 kg were killed by a blow to the cervical vertebrae. The required tissues were removed immediately and placed

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into oxygenated Krebs solution which had the following composition: NaCl, 118 mM; KCl, 4.7 mM; $CaCl_2$, 2.56 mM; KH_2PO_4, 1.18 mM; $MgSO_4$, 1.24 mM; $NaHCO_3$, 25.0 mM; glucose, 11.1 mM. The pH was 7.4.

The excised vessels were rapidly cleaned of adherent tissue. The anterior mesenteric portal vein[11] was bisected longitudinally and the two halves were suspended in 20 ml organ baths under 500 mg tension. Spiral strips were cut from the descending thoracic aorta and suspended in 20 ml organ baths under 1000 mg tension. The suspended venous strips measured approximately 1.5 cm by 3.0 mm and the aortic strips measured approximately 2.0 cm by 5.0 mm. The organ baths contained Krebs solution of the composition described, which was maintained at 37° C and bubbled with 95 per cent O_2–5 per cent CO_2 gas mixture. In most experiments, two venous and two aortic strips were prepared from each animal so that one strip could serve as a control when required. In some experiments, each strip served as its own control. Periodic time controls indicated that preparations were stable over many hours.

Strips were left for 30 to 50 minutes before exposure to drugs. Halothane was administered by replacing the 95 per cent O_2–5 per cent CO_2 aeration with 95 per cent O_2–5 per cent CO_2 that was first bubbled through liquid halothane. The bath halothane concentration measured by a gas chromatographic method[12] was approximately 10 mg %. Chloroform and diethyl ether were dissolved in warmed Krebs solution and added to the bath in volumes of 0.5–3.0 ml. All other drugs were prepared in distilled water and added to the 20 ml bath in a volume of 0.2 ml. Distilled water employed in the preparation of all solutions was obtained by de-ionization of distilled water and subsequent re-distillation in a glass still; whenever distilled water was used to dissolve drugs, a control injection of distilled water alone was added to the bath in the same volume. In these experiments, halothane, chloroform, diethyl ether, chloralose, and the sodium salts of thiopentone, thiamylal, pentobarbitone, quinalbaritone, amylbaritone and methohexitone were administered in doses which produced a concentration approximating anaesthetic blood levels (see Table I). Doses of the barbiturates were calculated on the basis of their salts.

Multiple anaesthetic agents were administered to most preparations. However, the order of administration was varied, and before administration of the next agent to be examined, the preparations were washed repeatedly until all parameters had returned to control values.

In assessing the effect of these agents on the dose-response curve to noradrenaline and other sympathomimetic amines, experiments were done after ten minutes of exposure to halothane and after five minutes of exposure to the other anaesthetic drugs. The adrenergic agonists used were noradrenaline bitartrate, phenylephrine hydrochloride, metaraminol bitartrate, isoprenaline hydrochloride (as a test of beta-adrenergic blockade), and tyramine hydrochloride (as a test of reserpine activity); these sympathomimetic amines were calculated in terms of their bases. Phenoxybenzamine hydrochloride, propranolol hydrochloride and satolol hydrochloride were added in doses to produce final concentrations of 10^{-6} gm/ml, 10^{-6} gm/ml, and 10^{-4} gm/ml respectively. The periods of preliminary exposure to these drugs were 30, 15 and 15 minutes respectively and the tissues were not washed prior to the subsequent addition of the anaesthetic agents.

TABLE I

RESPONSES OF RABBIT ANTERIOR MESENTERIC PORTAL VEIN

	Drug	Effect on Vein			Effect on Noradrenaline Dose response (vein)	
		Anaesthetic Concentration	Spontaneous Activity	Basal Tone	Anaesthetic Concentration	Response
(1)	Halothane	approx. 10 mg %	decreased (21/21)	no change (16/21) increased (5/21)	10 mg %	decreased (6/6)
(2)	Chloroform	30 mg %	decreased (10/10)	no change (10/10)	30 mg %	no change (8/8)
(3)	Diethyl Ether	150 mg %	decreased (12/12)	no change (12/12)	150 mg %	no change (4/4)
(4)	Chloralose	0.3 mg %	no change (5/14) increased (9/14)	no change (12/14) increased (2/14)	0.3 mg %	no change (4/4)
(5)	Thiopentone	10 mg %	initial increase followed by decrease (23/23)	increased (23/23)	20 mg %	decreased (6/6)
(6)	Thiamylal	10 mg %	initial increase followed by decrease (7/7)	increased (7/7)	20 mg %	decreased (3/3)
(7)	Pentobarbitone	10 mg %	decreased (13/13)	no change (8/13) decreased (5/13)	20 mg %	decreased (2/2)
(8)	Quinalbarbitone	10 mg %	decreased (9/9)	no change (8/9) decreased (1/9)	20 mg %	decreased (5/5)
(9)	Amylobarbitone	10 mg %	decreased (9/9)	no change (7/9) decreased (2/9)	20 mg %	decreased (3/3)
(10)	Methohexitone	10 mg %	decreased (9/9)	no change (7/9) decreased (2/9)	20 mg %	decreased (3/3)

Figures in parentheses indicate number of rabbits.

The washing procedure consisted of complete replacement of the bathing solution at least three times. The overflow procedure was employed so that the tissues remained fully immersed at all times.

The responses were recorded isometrically using Grass force-displacement transducers (FTO3C) and a Grass model VII polygraph.

In order to deplete catecholamines, a series of rabbits were pretreated with reserpine (Serpasil®-Ciba). The animals received 0.5 mg/kg I.M. 72 hours, 48 hours, and 24 hours before use.

For experiments on noradrenaline efflux, the rabbit venous and arterial tissues were prepared as described above. They were then suspended in 10 ml organ baths and left to equilibrate for 30 to 60 minutes in oxygenated Krebs solution. The tissues were discarded if the addition of 10^{-9} gm/ml noradrenaline produced no contraction or if 10^{-8} gm/ml noradrenaline produced less than a 500 mg contraction. If a satisfactory response occurred, the tissues were washed three times and left until they returned to base line.

The volume of the bath was then adjusted to 7.5 ml and 50 μl of DL-noradrenaline-7-H^3 (specific activity 9.9–13.0 c/mM; New England Nuclear Corporation) was added. After 60 minutes the organ bath was drained and the strip was superfused at a constant rate of 6 ml/min with nonradioactive Krebs solution warmed to 38 degrees C and equilibrated with the O_2–CO_2 mixture.[13] The anaesthetics and barbiturates were added directly to the superfusing solution to produce concentrations equivalent to the final bath concentrations employed in the previous experiments.

The superfusate was collected in test tubes using an Ultrorac 700 fraction collector. The tubes were changed every two minutes. Thus, 12 ml fractions were obtained. A 3.5 ml aliquot of the collected solution was added to 11.5 ml of Aquasol universal liquid scintillation counting cocktail (New England Nuclear Corporation) and assayed for total tritium activity with a Tri-Carb liquid scintillation spectrometer. Contractility was again recorded isometrically using Grass force-displacement transducers (FTO3C) and a Grass model VII polygraph.

Results

1. Spontaneous activity:

In contrast to aortic strips, spontaneous activity is present in the rabbit anterior mesenteric portal vein.

In this venous preparation, all anaesthetic agents tested, with the exception of thiopentone, thiamylal and chloralose, consistently decreased the rate and amplitude of spontaneous activity. Thiopentone and thiamylal produced an initial increase in the rate of spontaneous activity followed by a decreased rate and amplitude; chloralose increased the rate of spontaneous activity in some preparations but had no effect in others. These results are summarized in Table I; Figure 1 gives the responses to halothane, thiopentone, pentobarbitone and chloralose respecitvely.

2. Basal tone:

The doses of anaesthetic agents used on aortic and venous strips to assess the effects of basal tone were similar with the exception that higher doses of barbi-

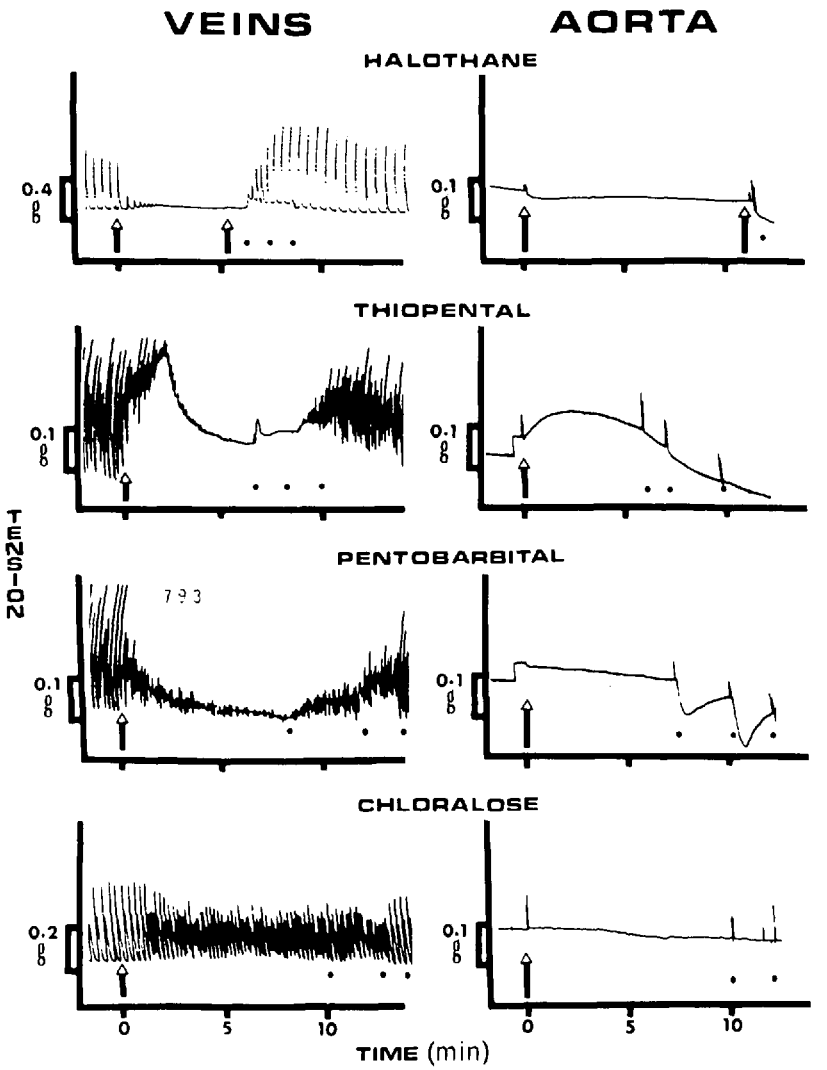

FIGURE 1. Effect of anaesthetics on isolated rabbit anterior mesenteric portal vein and aorta. The first arrow indicates the addition of anaesthetic agents. (In the case of halothane, the second arrow indicates the point at which exposure to the agent was terminated.) Circles indicate washes. (See Table I for anaesthetic concentrations.)

turates were employed in the aortic strip preparations (Table I and Table II). In these latter preparations, consistent effects on basal tone could not be produced by thiopentone and thiamylal at levels below 40 mg %; other barbiturates produced no change even at this level (Table II).

Thiopentone and thiamylal consistently produced an increase in basal tone in both aortic and venous strips. Halothane, chloroform and diethyl ether either increased or produced no change in basal tone of veins and arteries. In contrast, pentobarbitone, quinalbarbitone, amylbarbitone and methohexitone produced no change in aortic strips, and the response in veins was either that of a decrease or no change in basal tone. In the case of chloralose, there was usually no change

TABLE II

RESPONSES OF RABBIT AORTIC STRIPS

Drug	Concentration	Basal Tone	Noradrenaline Response
(1) Halothane	approx. 10 mg %	no change(5/9) increased(4/9)	decreased(6/6)
(2) Chloroform	30 mg %	no change (7/10) increased(3/10)	no change(3/3)
(3) Diethyl Ether	150 mg %	no change(5/10) increased(5/10)	no change(3/3)
(4) Chloralose	0.3 mg %	no change(9/9)	no change(3/3)
(5) Thiopentone	20 mg %	no consistent effect	decreased(7/7)
	40 mg %	increased(15/15)	not done
(6) Thiamylal	20 mg %	no consistent effect	decreased(3/3)
	40 mg %	increased(10/10)	not done
(7) Pentobarbitone	20 mg %	no change	decreased(4/4)
	40 mg %	no change(9/9)	not done
(8) Quinalbarbitone	20 mg %	no change	decreased(2/3); no change(1/3)
	40 mg %	no change(9/9)	decreased(7/7)
(9) Amylobarbitone	20 mg %	no change	no chang (2/3); decreased(1/3)
	40 mg %	no change(10/10)	no change(5/6); decreased(1/6)
	60 mg %	not done	no change(1/4); decreased(3/4)
(10) Methohexitone	20 mg %	no change	decreased(2/3); no change(1/3)
	40 mg %	no change(9/9)	decreased(4/5); no change(1/5)

Figures in parentheses indicate number of rabbits.

produced in the basal tone of veins; the basal tone of aortic strips was invariably unaltered.

The effect of these anaesthetic agents on basal tone are indicated in Tables I and II and also in Figure 1.

3. Modification of response to noradrenaline and other agents by anaesthetic agents:

Figures 2 and 3 show noradrenaline dose response curves done before, during and following exposure to anaesthetic agents. The dose response curve in both aorta and vein was depressed by halothane, thiopentone, thiamylal, quinalbarbitone, pentobarbitone and methohexitone. Amylbarbitone consistently decreased the noradrenaline response in veins, but produced a similar response in only one of six aortic strip preparations at a dose of 40 mg %. A dose of 60 mg % was required to produce relatively consistent depression of the noradrenaline response Table II).

Even when used in relatively large doses, chloroform, diethyl ether and chloralose had no effect on the noradrenaline response of either arteries or veins.

The effect of these anaesthetic agents on the phenylephrine and metaraminol dose response curve were similar to those seen with noradrenaline.

4. Adrenergic blocking agents and the response to anaesthetic agents:

The effect of adrenergic blocking agents on the responses to anaesthetic agents was tested only in veins. In these experiments phenoxybenzamine (10^{-6} gm/ml), propranolol (10^{-6} gm/ml), and satolol (10^{-4} gm/ml) were each used in preparations from five separate animals. The effects on spontaneous activity or basal tone of all the anaesthetic agents used were unaltered in the presence of either alpha, beta, or combined alpha- and beta-blockade.

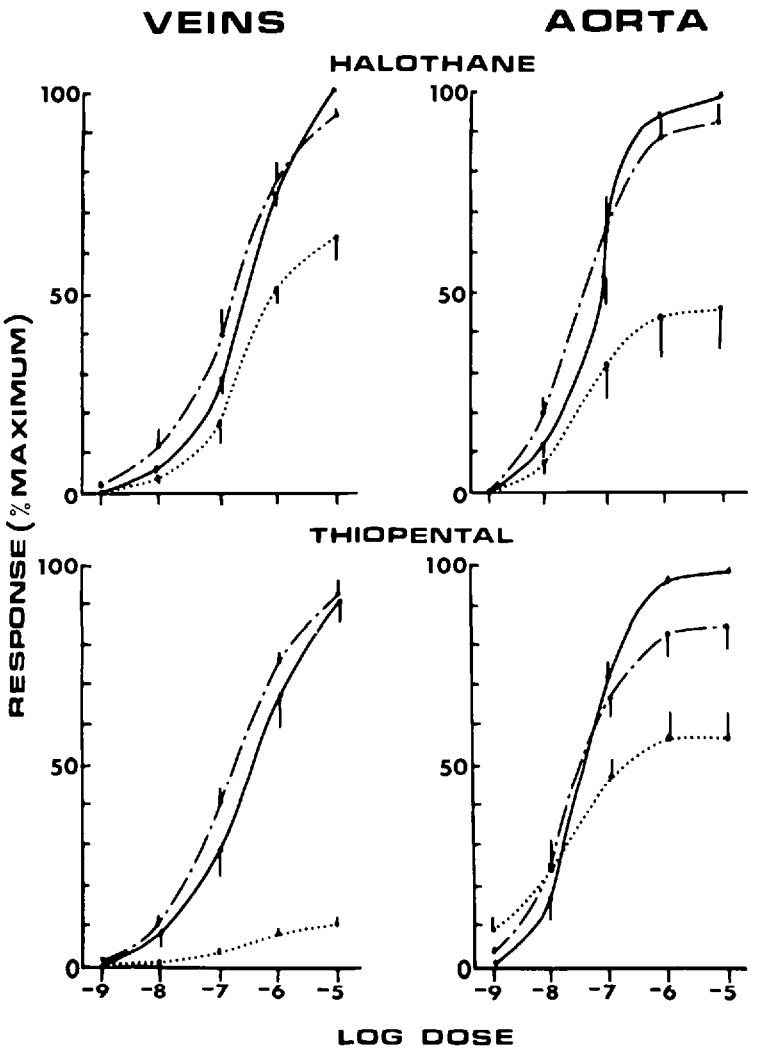

FIGURE 2. Effect of anaesthetics on noradrenaline dose response curves of isolated rabbit anterior mesenteric portal vein and aorta: — · — · — · — pre-anaesthetic; ..... anaesthetic; ——— post-anaesthetic. Each curve represents the mean of three to seven experiments. The standard error for each concentration is represented by the line extending from that point.

5. Effect of anaesthetic agents after treatment with reserpine:

The pretreatment of animals with reserpine had very little effect on the response of either veins or aortic strips to anaesthetic agents (Table III). Halothane and diethyl ether never increased basal tone in aortic strips or veins in reserpine treated rabbits; an increase in tone, however, was an occasional finding with untreated aortic strips.

It is of interest that while reserpine pretreatment totally blocked or markedly diminished the response of veins to tyramine, the responses of aortic strips to tyramine were increased.

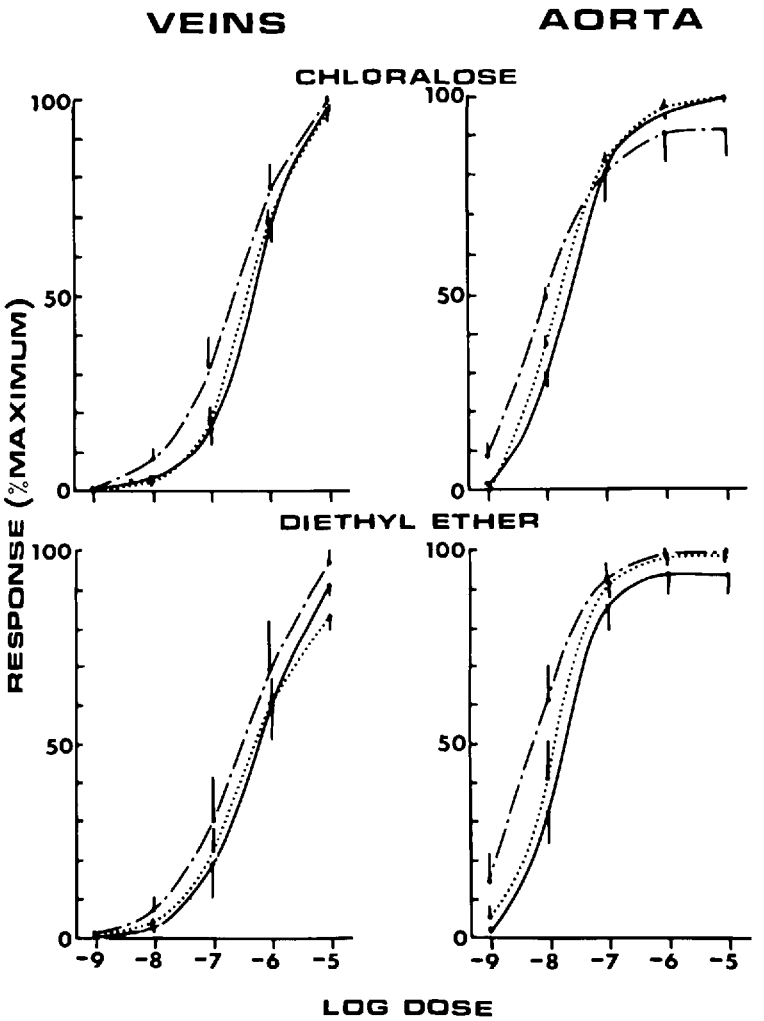

FIGURE 3. Effect of anaesthetics on noradrenaline dose response curves of isolated rabbit anterior mesenteric portal vein and aorta: — · — · — · — · pre-anaesthetic; . . . . . anaesthetic; ——— post-anaesthetic. Each curve represents the mean of three to seven experiments. The standard error for each concentration is represented by the line extending from that point.

6. Release of noradrenaline by anaesthetic agents:

Table IV indicates the lack of effect of anaesthetic agents on H^3-noradrenaline washout curves from vascular smooth muscle.

DISCUSSION

Until recently, relatively little attention had been paid to the action of anaesthetic agents and barbiturates on vascular smooth muscle. This is surprising, considering the possible importance of peripheral vascular effects in halothane-induced hypotension, in the hypotension of barbiturate overdose and in other actions of general anaesthetics on the cardiovascular system.

TABLE III

RESPONSES OF RESERPINIZED RABBIT VEINS AND AORTIC STRIPS

	Drug	Effect on Vein			Effect on Aorta	
		Anaesthetic Concentration	Spontaneous Activity	Basal Tone	Anaesthetic Concentration	Basal Tone
(1)	Halothane	approx. 10 mg %	decreased (3/4) no change (1/4)	no change (4/4)	5–10 mg %	no change (3/3)
(2)	Chloroform	30 mg %	decreased (5/6) no change (1/6)	no change (6/6)	30 mg %	no change (4/6) increased (2/6)
(3)	Diethyl Ether	150 mg %	decreased (4/5) no change (1/5)	no change (5/5)	150 mg %	no change (5/5)
(4)	Chloralose	0.3 mg %	increased (2/7) no change (5/7)	no change (7/7)	0.3 mg %	no change (6/6)
(5)	Thiopentone	10 mg %	initial increase followed by decrease (8/8)	increased (8/8)	40 mg %	increased (9/9)
(6)	Thiamylal	10 mg %	initial increase followed by decrease (4/4)	increased (4/4)	40 mg %	increased (2/2)
(7)	Pentobarbitone	10 mg %	decreased (7/7)	no change (6/7) decreased (1/7)	40 mg %	no change (8/8)
(8)	Quinalbarbitone	10 mg %	decreased (7/7)	no change (4/7) decreased (3/7)	40 mg %	no change (7/7)
(9)	Amylobarbitone	10 mg %	decreased (7/7)	no change (6/7) decreased (1/7)	40 mg %	no change (7/7)
(10)	Methohexitone	10 mg %	decreased (6/6)	no change (6/6)	40 mg %	no change (6/6)

Figures in parentheses indicate number of rabbits.

TABLE IV

EFFECT OF ANAESTHETIC AGENTS ON H^3-NORADRENALINE WASHOUT CURVES

Drug	Concentration	Vein	Response	Aorta	Response
(1) Halothane	10 mg %	6 strips (5 rabbits)	Nil*	3 strips (3 rabbits)	Nil
(2) Chloroform	30 mg %	6 strips (5 rabbits)	Nil	6 strips (4 rabbits)	Nil
(3) Chloralose	0.3 mg %	4 strips (3 rabbits)	Nil	16 strips (9 rabbits)	Nil
(4) Thiopentone	20 mg % (vein) 40 mg % (aorta)	14 strips (8 rabbits)	Nil	18 strips (11 rabbits)	Nil
(5) Pentobarbitone	20 mg % (vein) 40 mg % (aorta)	6 strips (4 rabbits)	Nil	3 strips (3 rabbits)	Nil

*Nil – No change in H^3-noradrenaline washout curves in response to anaesthetic administration.

Undoubtedly the well-established myocardial depression produced by halothane[14–16] and by other general anaesthetics[17–19] plays a role in the production of hypotension. Numerous studies, however, indicate an effect of halothane[4,20–22] and other general anaesthetics[20,23–26] on the peripheral blood vessels.

From their studies in man, Deutsch *et al*[27] concluded that the decreased total peripheral resistance accounts for all, or a large fraction, of the decrease in mean arterial pressure under halothane anaesthesia. They suggest that increased distensibility of veins may also occur in addition to arteriolar dilatation and that the observed decrease in cardiac output is attributable in part to peripheral venous pooling of blood with reduced venous return. The susceptibility to hypotension of individuals anaesthetized with halothane supports this concept. Moreover, in response to halothane in man, Caffrey *et al.*[28] observed increased forearm venous compliance and venous pressure accompanied by a significant decrease in mean arterial pressure and increase in forearm blood flow. These findings in man could suggest a depressing or dilating effect of halothane on both arteries and veins. They are supported by Longnecker and Harris'[29] finding of small artery and small vein dilation in the bat during halothane anaesthesia.

Our observations on inhibition of spontaneous activity in veins by halothane and other general anaesthetics (excepting chloralose) support the conclusion that the vascular action of these agents contributes to their hypotensive action. Halothane, as all of the general anaesthetics and barbiturates tested, except chloralose, produced inhibition of the spontaneous activity of the rabbit anterior mesenteric protal vein. Although the physiological significance of venous spontaneous activity has not been established, a decrease conceivably could result in decreased venous tone, and the possibility of venous pooling of blood.

Under the conditions of the present experiments, these agents had little effect on aortic strips (see later discussion of the thiobarbiturates, which were the exception). As was the case with veins, no consistent change in basal tension occurred. Admittedly the preparations employed are not very sensitive to relaxant drugs, but relaxation in response to halothane still could not be demonstrated when the tension on the strip was increased. Previous data by Price and Price[20] suggest that halothane produces relaxation in aortic strips. Although their results do conflict with the data presented here, they show great variability.

The actions of the general anaesthetics studied in these venous and aortic preparations would therefore support the general hypothesis that at least part of their hypotensive action is secondary to effects on peripheral blood vessels.

Price and Price[20] noted that halothane reduced the response of rabbit aortic strips to noradrenaline. Black and McArdle[6] observed that in man systemically administered halothane lessened vasoconstriction in the forearm produced by intra-arterial injection of noradrenaline. While both investigations conflict with those of Baez[30] who reported that the microcirculation of the rat mesoappendix was hyper-reactive to noradrenaline after halothane, they are consistent with our findings with respect to halothane in both venous and aortic strips. In addition, we have shown that thiopentone, thiamylal, quinalbarbitone, methohexitone and pentobarbitone all decreased noradrenaline contractions.

All of the above data might be interpreted to suggest that the hypotensive action of halothane (and possibly other drugs) might occur through modification of the alpha-adrenergic response to noradrenaline in peripheral blood vessels. On the other hand, our data suggest that the interaction between general anaesthetics and noradrenaline may be nonspecific. In considering the noradrenaline dose-response curves presented here, it is apparent that the maximal responses to noradrenaline are depressed, indicating that competitive drug inhibition at adrenergic receptor sites does not occur. Moreover, the curves are depressed and not shifted to the right, so as to make a non-competitive drug-receptor inhibition unlikely. It seems most probable that the anaesthetics are acting on the contractile mechanism at some site distal to the adrenergic receptor.

On the other hand, Klide *et al.*[31] have suggested that halothane acts not through interference with actions of noradrenaline expressed in terms of alpha-adrenergic receptors but rather by stimulating beta-adrenergic receptors, at least in the uterus and atrial muscle. (It is of interest to note that Zauder *et al.*[32] have antagonized halothane depression of the uterus with satolol but not with propranolol, possibly suggesting that the action of halothane on the uterus may not involve simple beta-adrenergic stimulation). Moreover, Price *et al.*[33] present evidence for halothane-induced beta-receptor activation of the heart in normal man. Although Sutter[11] and Guimaraes[34] have shown that the anterior mesenteric portal vein has both alpha- and beta-adrenergic receptors, our results using adrenergic blocking agents (including the newer beta blocking agent, satolol, employed by Klide[31] and Price[33]), indicate that halothane and the other anaesthetic agents studied do not stimulate beta adrenergic receptors in the rabbit anterior mesenteric portal vein.

Su and Bevan[13] have shown that H^3-noradrenaline is taken up in nerve endings of incubated tissue and can be released on stimulation of this tissue. Although this is probably not a sensitive method for detecting small differences, there was no suggestion from H^3-noradrenaline washout curves that halothane might act by reducing the amount of noradrenaline released. Greater sensitivity might be achieved by repeating these experiments during transmural stimulation.

In our experiments, the administration of thiopentone and thiamylal was associated with an increase in basal tone of both vein and artery. This observation was of particular interest since there are both clinical and animal data[20,35,36] to document that the thiobarbiturates can cause vasoconstriction (acknowledging, however, that the extreme local vasoconstriction which can ensure from inadvertent

intra-arterial administration might well be due to the high pH of these agents). The experiments reported here investigate the possibility that the thiobarbiturates release noradrenaline from tissue stores. Reserpine pre-treatment to deplete catcholamines did not prevent the thiopentone-induced contraction of either vein or aorta. Likewise, thiopentone did not alter the H^3-noradrenaline washout curves in either tissue. Thus, within the limitations of these experiments, it can be concluded that thiopentone does not release noradrenaline from tissue stores.

An apparent supersensitivity of aortic strips to tyramine was noted in our experiments in reserpine pre-treated animals. This has been reported previously by Hudgkins and Flemming.[37] It appears to be a non-specific supersensitivity insofar as it occurs with noradrenaline, acetylcholine and increased concentration of potassium ion.

Summary

Data have been presented showing that certain general anaesthetic agents such as halothane decrease the spontaneous activity of the rabbit anterior mesenteric portal vein and decrease the response of venous and aortic strips to exogenous noradrenaline. If these observations can be extrapolated to the intact animal they may indicate that the hypotension occurring with use of such agents may be due not only to cardiac effects but also to peripheral vasodilatation and muting of reflex sympathetic vasoconstriction. Although the response to noradrenaline is antagonized, this appears to be nonspecific effect and no evidence was found for interference with noradrenaline release nor for direct actions on beta-adrenegic receptors. While the thiobarbiturates increased spontaneous activity and tone of the rabbit anterior portal vein no evidence was obtained that this occurred through release of noradrenaline from tissue stores.

Résumé

Certains anesthésiques généraux, tel la halothane, diminuent l'activité spontanée de la veine mésentéro-portale antérieure du lapin et diminuent la réaction de sections de veines et d'aorte à la noradrénaline exogène. Si ces observations sont applicalbes in vivo, cela voudrait dire que l'hypotension qui survient avec ces agents d'anesthésie est due non seulement à leurs effets cardiaques mais également à une vasodilatation périphérique et à une modification de la vasoconstriction réflexe sympathique.

Le fait que la réponse à la noradrénaline soit contre-carréc, ne semble pas un effet spécifique; nous n'avons pu démontrer qu'il y ait inhibition à la libération de Noradrénaline ou qu'il y ait d'effets directs sur les récepteursβ.

Par ailleurs, les thiobarbituriques augmentent l'activité spontanée et le tonus de la veine porte antérieure du lapin. Nous n'avons cependant pu démontrer que cela était produit par une libération de noradrénaline.

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