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THE EFFECTS OF ETHYL ALCOHOL ON THE BLOOD VESSELS OF THE HAND AND FOREARM IN MAN

BY

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Alcohol is generally considered to have a dilator action on blood vessels, but there is little documentation of its effect on the circulation either in animals or in man. Miles (1924) and Cook & Brown (1932) reported a rise in skin temperature of the fingers and toes of normal subjects after oral administration of whisky. This was confirmed by Grollman (1942) who gave both oral whisky and alcohol as a 40% aqueous solution, and by Montgomery (1942) who observed that oral whisky had little effect on pulse rate, blood pressure or cardiac output. Abramson, Zazeela & Schkloven (1941) reported that after administration of whisky an increase in blood flow was generally seen in the hand and little or no effect in the leg or forearm. Edwards, Jones, McConnell, Pemberton & Watson (1952) described the use of infusions of ethyl alcohol into the femoral artery in the treatment of occlusive vascular disease, and observed an increase in skin temperature of the toes in one of six patients so treated. Conrad & Green (1964) found an increase in digital blood flow after ingestion of 60 ml. of 86 proof alcohol which was less marked in patients suffering from arterial disease than in normal subjects.

Horwitz, Montgomery, Longaker & Sayen (1949) postulated that, since blood pressure and cardiac output remained unchanged after oral whisky, the vasodilatation in skin must be accompanied by a vasoconstriction elsewhere, but no direct evidence of a constrictor action of alcohol on blood vessels is available.

During a recent investigation by Douglas, Fewings, Casley-Smith & West (1966) of a chronic alcoholic patient who suffered recurrent episodes of rhabdomyolysis, one of us (J. D. F.) observed that administration of alcohol into the brachial artery reduced the blood flow through the forearm. The present investigation describes the mechanism of action of alcohol on the blood vessels of the upper limbs of human subjects.

METHODS

The subjects were ourselves, our colleagues and volunteer medical students. Two patients were also studied, one who had undergone cervical sympathectomy five years previously for mild Raynaud's disease and another who had suffered unilateral brachial plexus avulsion 12 months previously. In neither case did the vessels of the limbs studied show any sympathetic reflex responses nor were they constricted by ephedrine (Parks, Skinner & Whelan, 1961 ; Fewings, Rand, Scroop & Whelan, 1966) which demonstrated that the sympathetic nerves had completely degenerated.

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The subjects lay supine on a couch in a temperature-controlled laboratory (24 to 26° C) for at least 30 min before observations began. Blood flow through the hands was recorded using the water-filled, temperature-controlled plethysmographs described by Greenfield (1954), the plethysmograph temperature being maintained at 32° C. The volume change was recorded by means of float recorders on a kymograph drum.

Capacitance plethysmographs were used to measure forearm blood flow. The plethysmographs consisted of shielded copper cylinders, formed to the shape of the forearm and separated from it by a mean spacing of 1.25 ± 0.25 cm. The copper cylinder constituted one plate of a capacitor system. The second plate, formed by the surface of the arm, was earthed to the shielding screen from surface electrodes at the wrist and upper arm. A constant current at a fixed frequency was passed across the capacitor. The volume change caused by venous occlusion produced an increase in capacity and a decrease in output voltage. The voltage change was rectified, amplified and fed to a pen-writer system (Oscilloriter, Model 323 B medium frequency recorder, Texas Instruments Inc). The details of the method have been reported elsewhere (Fewings & Whelan, 1966). A wrist cuff was inflated to 200 mm Hg during measurements of forearm flow.

Intra-arterial infusions of alcohol or of other drugs were given through a 22-gauge needle inserted, under local anaesthesia (lignocaine 2%), into the brachial artery at the elbow. The needle was connected by a 30 cm length of 0.5 mm bore polythene tubing to a mechanically driven syringe. Saline (0.9% w/v) was infused continuously at a rate of 2 ml./min throughout the experiment, being interrupted when required for the infusion of ethyl alcohol (95% ; 75 mg/ml.) or phenoxybenzamine (Dibenyline S.K.F. 250 μg/min for 8 to 10 min) diluted in saline to the desired concentration. Intra-arterial administration in this way enabled a relatively high concentration of drug to be applied to the vessels of the hand or forearm, but the amount which passed through on to the venous side and entered the general circulation was so diluted in the circulating blood volume that it had no generalized effects. The responses of the vessels thus represented the local effects of the drugs uncomplicated by any central or haemodynamic actions that they might have. The opposite hand or forearm was, therefore, used as a control. Calculation of the percent fall in blood flow during intra-arterial infusion of alcohol was made by averaging the blood flow for 3 min immediately prior to the infusion and during the last 4.5 min of the infusion. Where appropriate, correction for the spontaneous changes in the blood flow through the hand was made by reference to the control side (Duff, 1952).

In five subjects alcohol was administered in the form of 100 ml. brandy (30.9% w/v, diluted with ginger ale), which was taken over a period of 1 to 5 min. The blood flow through the forearm was recorded in one arm, and the blood flow through the hand in the other. In addition, arterial blood pressure was recorded from a 21-gauge needle inserted into the brachial artery of one arm and connected by means of 30 cm length of saline-filled polythene tubing to an electromanometer and ultraviolet light recorder (N.E.P., London). Heart rate was determined from the blood pressure record. The mean blood pressure was taken as one third of the pulse pressure added to the diastolic pressure. Hand and forearm resistance in arbitrary units was calculated by dividing the mean blood pressure in mm Hg by the blood flow in ml./100 ml./min. Samples of venous blood were withdrawn 15, 45, 75 and 105 min after alcohol, through a polythene catheter (Bardic, Intracath) inserted under local anaesthesia into a vein in the cubital fossa. The alcohol content of these samples was subsequently measured by the method of Kozelka & Hine (1958).

In two experiments the effects of alcohol (in one subject administered orally and in the other intra-arterially) on the vessels of the skin and muscle of the forearm were followed independently by determining the per cent oxygen saturation of samples of blood taken from catheters inserted into a superficial and deep forearm vein respectively (Roddie, Shepherd and Whelan, 1956, 1957a).

In two further subjects 40 ml. ethyl alcohol (76% w/v) was administered orally diluted with 110 ml. ginger ale and in a third the same amounts were given by stomach tube. In these subjects control runs were carried out in which ginger ale alone was administered. Sherry (300 ml. ; 14% w/v ethyl alcohol) was given to one subject and rum (100 ml. ; 30.9% w/v ethyl alcohol flavoured with cloves) to another. In these subjects forearm and hand blood flows alone were recorded.

RESULTS

Intra-arterial infusions

Twenty infusions of alcohol were given into the brachial artery in four normal subjects and bilateral hand blood flow measured. The amounts given ranged from 7.5 to 600 mg/min for 5 min. Doses below 150 mg/min had little or no effect on blood flow, doses between 150 and 250 mg/min caused a small reduction in flow and doses above 300 mg/min caused an intense burning sensation in the forearm and hand and a fall in blood flow through both hands which was more marked on the infused side (Fig. 1, upper frame and Table 1). An after-dilatation usually, but not always, followed cessation of the infusions.

Twenty-two infusions of alcohol were given into the brachial artery in seven normal subjects and the forearm blood flow measured on both sides. The amounts given ranged

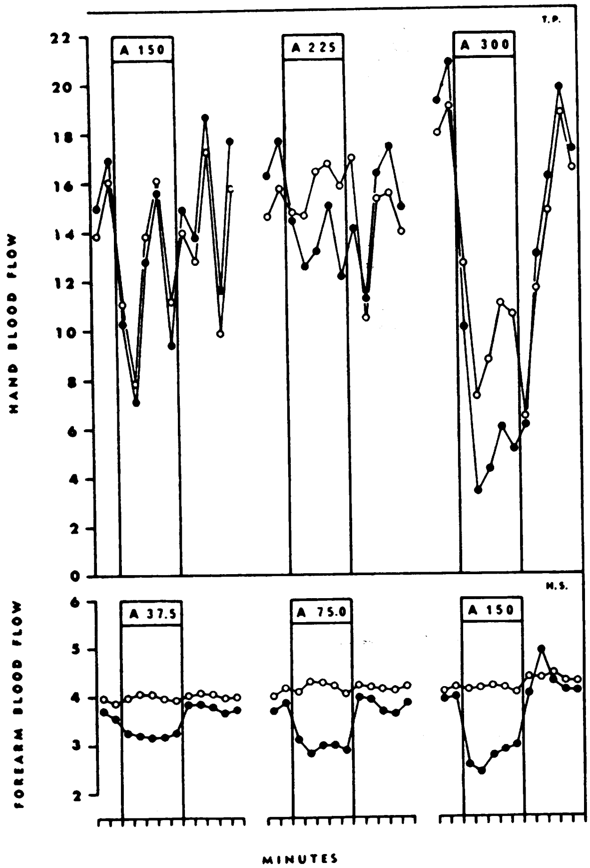

Fig. 1. The effect of intra-arterial infusions of ethyl alcohol (A, mg/min) on blood flow through the hand (upper frame) and forearm (lower frame). Blood flow in ml./100 ml./min. ●, injected side ; ○, control side.

TABLE 1

EFFECT OF INTRA-ARTERIAL INFUSION OF ALCOHOL ON HAND BLOOD FLOW

Subject	I.a. dose alcohol mg/min.	Hand blood flow ml./min. before infusion	Hand blood flow ml./min. during infusion	Per cent fall in hand blood flow†
A.R.	75	75	96	—
	300	80	87	20
	450	60	12	65
	600	60	22	34
	375*	110	28	40
T.P.	75	37	32	7
	150	60	53	9
	225	70	60	26
	300	80	25	50
D.H.	7·5	38	37	—
	18·75	32	35	8
	37·5	40	34	4
	75	33	36	5
	150	37	26	19
	225	24	15	48
	225*	115	92	16
J.F.	75	45	51	—
	150	55	40	28
	225	50	24	36
	300	40	16	54
	375	60	18	62
	450	60	23	50
	375*	115	99	13
	450*	110	94	16
W.W. cervical sympathectomy	75	17	14	19
	150	20	18	14
	225	23	18	19
	300	21	16	26

* Denotes after phenoxybenzamine.

† These values have been corrected for spontaneous changes in blood flow by reference to the opposite control side (Duff, 1952).

from 7.5 to 150 mg/min for 5 min. A constrictor effect was seen in every case, the forearm blood flow falling by 4 to 33% (Fig. 1, lower frame and Table 2). An after-dilatation was often seen.

The constrictor action of intra-arterial alcohol on the forearm vessels was not abolished by previous infusion of phenoxybenzamine (250 μg/min for 8 or 10 min), which abolished or markedly reduced the response of the vessels to intra-arterial infusion of noradrenaline (Fig. 2, Table 2). No reduction in the constrictor response of the hands to alcohol was seen after phenoxybenzamine in one subject (A.R., Table 1). In two other subjects (D.H. and J.F., Table 1) the constrictor response of the hand vessels to alcohol expressed as a percentage fall in flow from resting level was reduced but not abolished by phenoxybenzamine. Since a reduction in flow in the control hand was usually seen with doses above 300 mg/min and can be attributed to a reflex response to the painful stimulus, it seems likely that the diminution in response seen after phenoxybenzamine in D.H. and J.F. represents the blockade of this component, the residual constriction being due to a direct action of the alcohol.

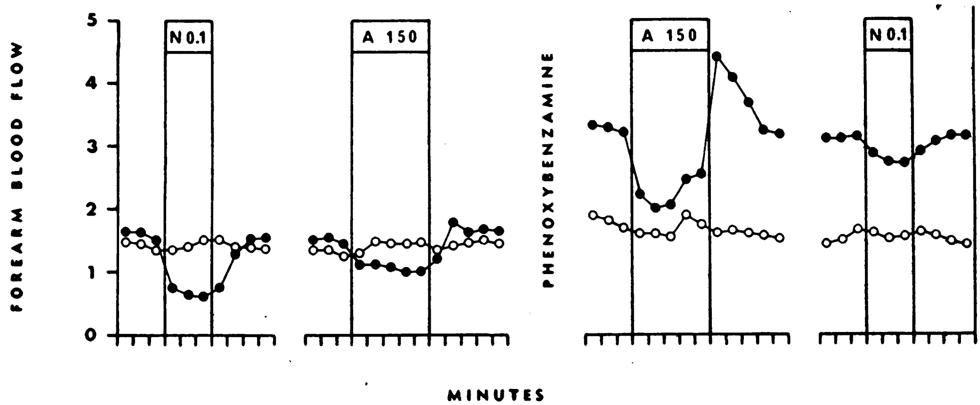

Fig. 2. The effect of intra-arterial infusion of noradrenaline (N, μg/min) and ethyl alcohol (A, mg/min) on the blood flow through the forearm before and after intra-arterial infusion of phenoxybenzamine (250 μg/min for 8 min). Blood flow in ml./100 ml./min. ●, injected side ; ○, control side.

TABLE 2

EFFECT OF INTRA-ARTERIAL INFUSION OF ALCOHOL ON FOREARM BLOOD FLOW

Subject	Forearm blood flow during infusion ml./min.	I.a. dose alcohol mg/min.	Calculated arterial alcohol concentration mg/100 ml.	Per cent fall in forearm blood flow
J.S.	32	18·75	59	4
	26	37·5	144	12
	32	75·0	234	15
G.C.	18	37·5	208	9
	19	75·0	395	6
	16	150·0	937	20
H.S.	23	37·5	163	8
	18	75·0	417	19
	20	150·0	750	32
T.P.	19	75·0	395	12
	18	150·0	833	33
J.N.	21	7·5	34	7
	21	18·75	86	7
	20	37·5	180	16
	17	75·0	426	8
	16	150·0	892	25
R.M.	11	7·5	70	13
	8	18·75	234	13
	9	37·5	417	25
	9	75·0	833	25
	8	150·0	1,875	31
	17*	150·0	882	26
L.L.	16	150·0	93	29
W.W.	18	150·0	830	16
cervical sympathectomy	16	225·0	1,406	29

* Denotes after phenoxybenzamine.

Further evidence for a direct constrictor action of ethyl alcohol on the limb vessels was obtained from the patient who had undergone cervical sympathectomy (W.W.). Intra-arterial infusions of doses ranging from 75 to 300 mg/min resulted in falls in both hand and forearm blood flow (Fig. 3, Tables 1 and 2).

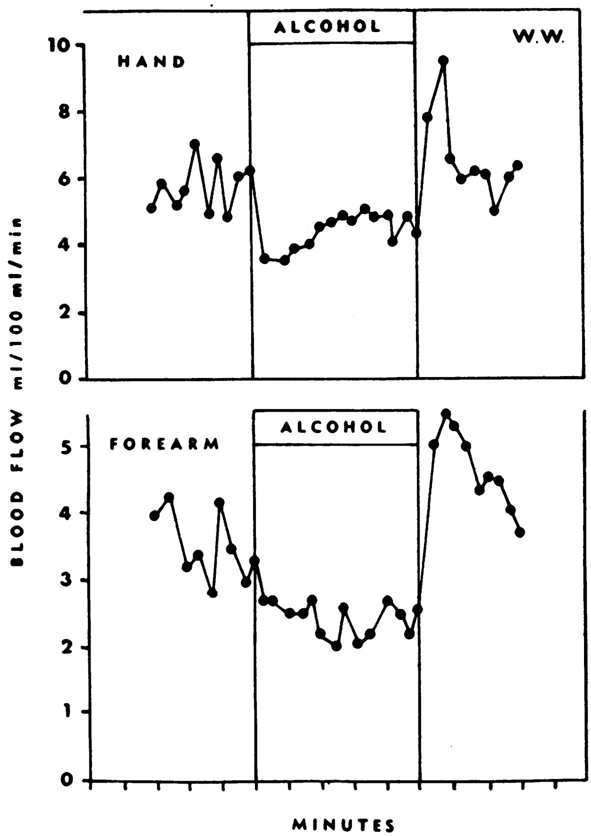

Fig. 3. The effect of intra-arterial infusion of ethyl alcohol (225 mg/min) on the blood flow through the hand and forearm of a patient whose upper limb was sympathetically denervated. The flow is expressed in ml./100 ml./min.

In one subject the effect of intra-arterial administration of alcohol on the blood flow through the muscle and skin of the forearm was determined. Ethyl alcohol (150 mg/min for 5 min) was given intra-arterially and total forearm blood flow measured. Approximately 30 min later a similar infusion of alcohol was given and venous blood samples were taken from veins which drained the muscle and skin of the same forearm and the percentage oxygen saturation of each sample estimated. Blood flow measurements and the collection of venous samples were not performed simultaneously as the collecting cuff pressure during blood flow measurements may divert skin venous blood into the muscle bed (Roddie *et al.*, 1956). Fig. 4 shows the results of this experiment. There was a fall in total forearm blood flow and the changes in venous oxygen saturation

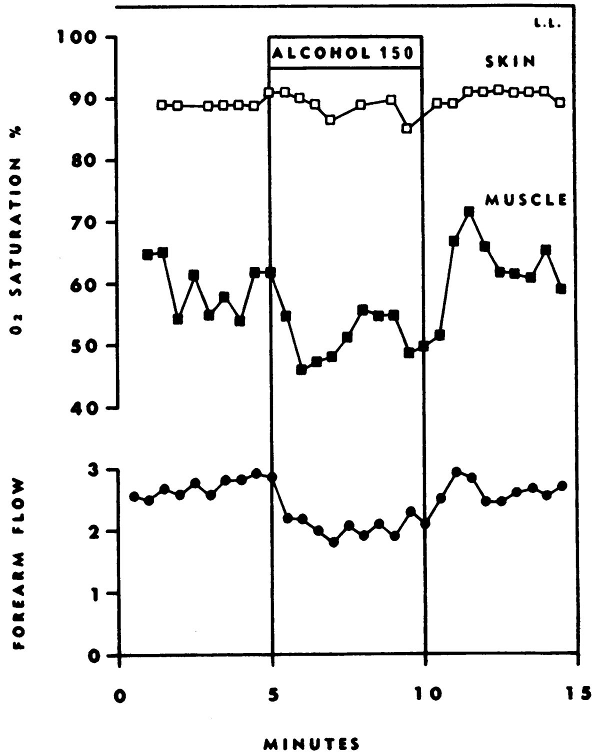

Fig. 4. The effect of intra-arterial infusion of ethyl alcohol (150 mg/min for 5 min) on the blood flow through the forearm (●, ml./100 ml./min) and on the % oxygen saturation of blood samples taken from veins which drained the skin (□) and muscle (■) of the same forearm.

indicated a fall in blood flow through muscle and skin. An after-dilatation was seen in the muscle after cessation of the infusion.

Oral administration

Five normal subjects whose body weights ranged from 65 to 80 kg, consumed 100 ml. brandy over a period of 1 to 5 min. The blood level rose rapidly to reach a peak of 35 to 60 mg/100 ml., and the increase was paralleled in every case by a rise in hand blood flow and a fall in hand vascular resistance. Forearm blood flow showed a variable response. In two subjects there was a slight increase in flow, in two there was a decrease and in one approximately a three-fold increase. Mean blood pressure fell by 6 mm Hg in one subject, rose by 4 to 8 mm Hg in three and was unchanged in one. Heart rate was increased by 5 and 9 beats/min in two subjects and was unchanged in three. The averaged data from these five experiments are illustrated in Fig. 5.

The variability of the forearm blood flow changes can be attributed to the fact that an increase in flow through the skin was accompanied by a fall in that through the underlying muscle (Fig. 6).

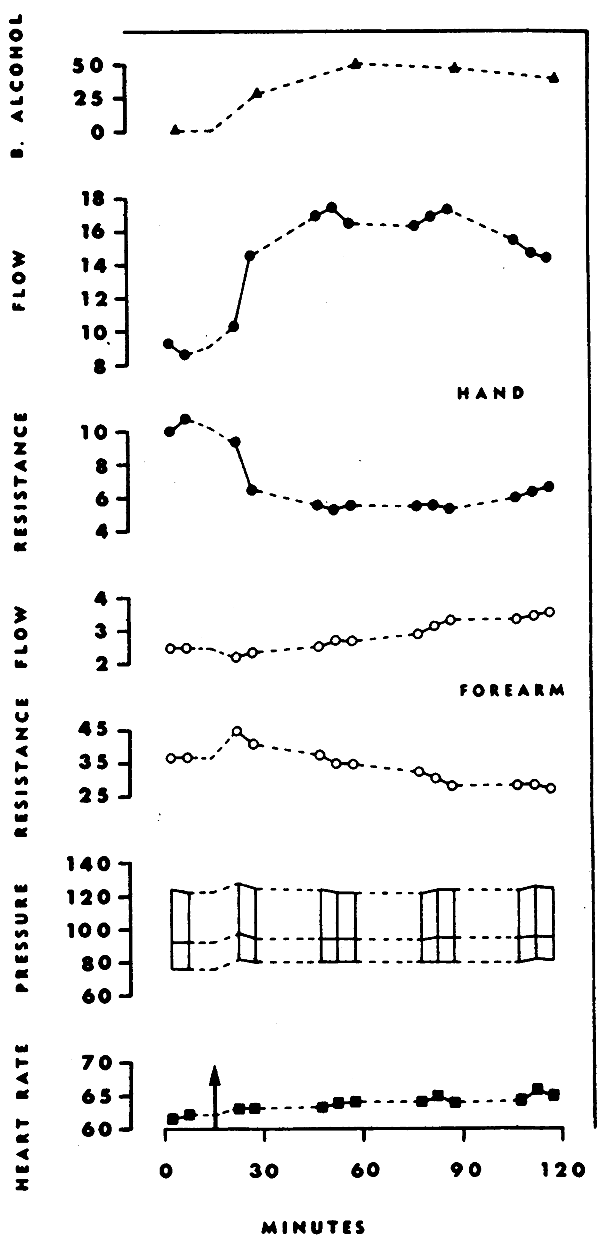

Fig. 5. The averaged data from 5 normal subjects (body weight 65 to 80 kg) who consumed 100 ml. brandy by mouth (arrow). Each point represents the mean value for a period of 5 min except for the blood alcohol estimations which were made on venous blood samples collected 15, 45, 75 and 105 min after alcohol. ▲, venous blood alcohol concentration in mg/100 ml.; ●, hand blood flow in ml./100 ml./min and hand resistance in arbitrary units; ○, forearm blood flow in ml./100 ml./min and forearm resistance in arbitrary units; arterial blood pressure in mm Hg; ■, heart rate in beats/min.

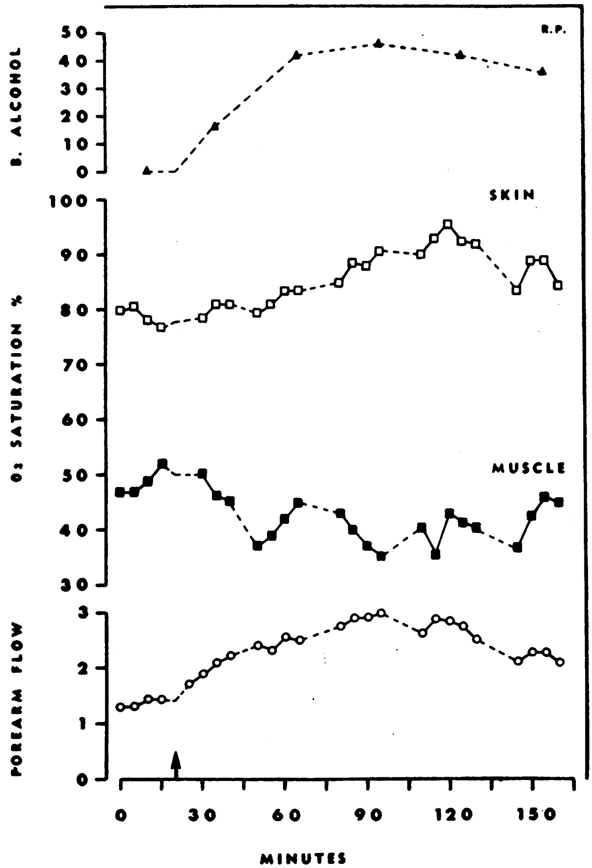

Fig. 6. The effect of 100 ml. brandy by mouth (arrow) on blood flow through one forearm (○, ml./100 ml./min) and the % oxygen saturation of blood samples taken from veins which drained the skin (□) and muscle (■) of the other forearm. ▲, venous blood alcohol concentrations in mg/100 ml.

Fig. 7 shows the response to oral brandy of the vessels of the normal and denervated hand of the patient who had suffered brachial plexus avulsion. The normal hand showed a dilator response and the flow through the denervated hand was unchanged. A less marked but similar pattern of response was seen in the forearms during a separate experiment (Fig. 8).

When brandy (75 ml.) was taken orally by the patient with bilateral sympathectomy the blood alcohol rose to a level similar to that seen in the normal subjects, but the blood flow through the hand and forearm fell slightly during the first 45 min and then rose slowly over the subsequent 90 min to a little above the pre-alcohol value (Fig. 9).

Ethyl alcohol (40 ml. 76% w/v) was given orally with 110 ml. ginger ale to two subjects, sherry (300 ml. 14% w/v) was given to one subject and rum (100 ml. 30.9% w/v flavoured with cloves) to one subject. In each case a marked increase in hand blood flow resulted with either no change or a slight rise in forearm flow. A further subject who was able to swallow only 20 ml. ethyl alcohol with 55 ml. ginger ale did not show any significant change in limb blood flow.

Ginger ale alone (110 ml.) was taken by three subjects. There was no effect on hand or forearm blood flow. Two of the subjects also rinsed out their mouths over five min

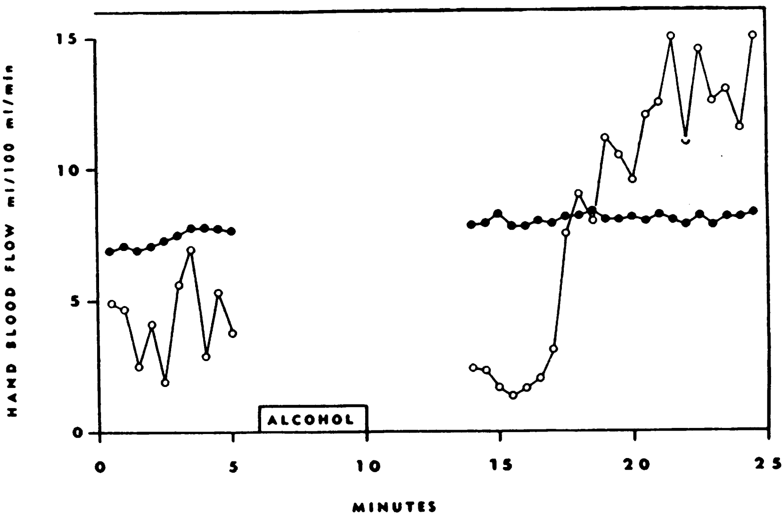

Fig. 7. The effect of 100 ml. brandy by mouth on the blood flow through a totally denervated hand (●) and the opposite normal hand (○) of a patient who had suffered unilateral brachial plexus avulsion 12 months previously. The venous blood alcohol concentration 15 min after the consumption of alcohol was 40 mg/100 ml.

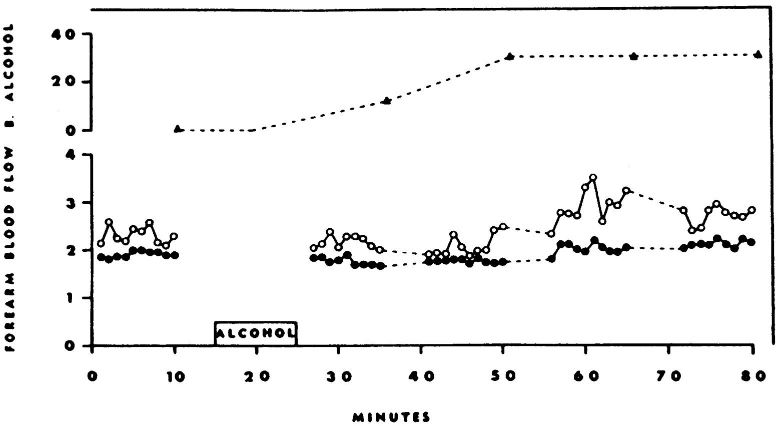

Fig. 8. The effect of 75 ml. brandy by mouth on the blood flow through the totally denervated forearm (●) and the opposite normal forearm (○) of the patient who had suffered brachial plexus avulsion. Blood flow in ml./100 ml./min. ▲, venous blood alcohol concentration in mg/100 ml.

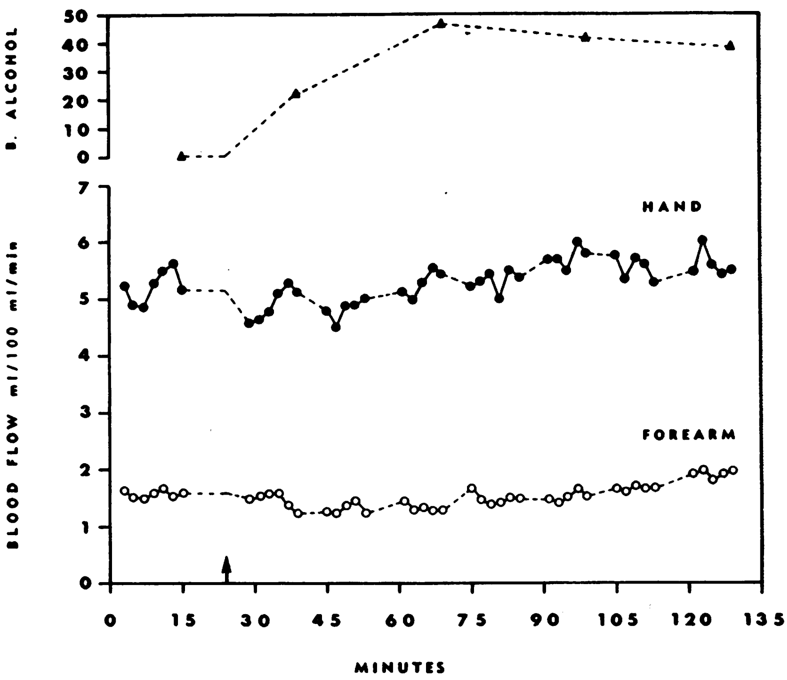

Fig. 9. The effect of 75 ml. brandy by mouth (arrow) on the blood flow through the hand (●) and forearm (○) of a patient who had undergone bilateral cervical sympathectomy 5 years previously. ▲, venous blood alcohol concentration in mg/100 ml.

with ethyl alcohol in ginger ale but did not swallow any of the mixture. This procedure did not affect the circulation in the hand or forearm.

One subject given 110 ml. ginger ale by stomach tube showed no change in hand or forearm circulation, but 40 ml. ethyl alcohol in 110 ml. water given in the same way produced a marked rise in hand blood flow and a slight increase in forearm flow.

DISCUSSION

The alcohol levels of the arterial blood arriving in the forearm during the intra-arterial infusions have been calculated to range from 34 mg/100 ml. (which represents the level produced in the blood by ingestion of about 50 ml. brandy), to 1,875 mg/100 ml. (which, if it pertained for the whole circulation, would represent the equivalent of the ingestion of more than 3 l. brandy and be more than sufficient to induce alcoholic coma). The constriction of skin and muscle vessels caused by these concentrations appeared to be a direct action of alcohol on the smooth muscle of the arteriolar walls. Sympathetic vasoconstrictor nerve stimulation or release of catecholamines from peripheral storage sites does not appear to be involved in the vasoconstrictor action since neither sympathectomy nor administration of phenoxybenzamine abolished the response.

Although intra-arterial administration of alcohol has been used in the treatment of peripheral vascular disease (Edwards *et al.*, 1952), the demonstration of a direct constrictor action on the vessels of normal limbs indicates that such administration is likely to be detrimental if alcohol has similar effects on both normal and diseased vessels. A study of the action of alcohol on the vessels of the lower limbs and of limbs exhibiting vascular disease has not yet been made.

The dilator effect on the limb vessels of moderate amounts of alcohol taken orally was found to be confined to the vessels of the skin. The response was sympathetically mediated since it was absent in the sympathectomized and denervated limbs, and was presumably due to inhibition of sympathetic vasomotor tone due to an action on either the vasomotor centres or the sympathetic ganglia. The fall in muscle blood flow which was present at the time of the skin dilatation probably represented the direct local action of the alcohol on the muscle vessels, since a fall in forearm flow occurred in the sympathectomized limb. This suggested that the dilator action of alcohol was due to a selective action on the vasomotor centres controlling the skin vessels rather than to ganglionic blockade which might have been expected to result in increased muscle flow as well as skin vasodilatation. That the skin and muscle vessels of the forearm are independently innervated and that specific controlling centres are present for the two vascular beds has been demonstrated by Roddie *et al.* (1956, 1957b). They showed that general body heating results in dilatation of the vessels of the skin without any effect on the vessels of the underlying muscles, whereas increases in pressure on the low pressure side of the intra-thoracic vascular bed cause reflex dilatation of the muscle vessels in the limbs without any such change in the skin.

This central action of alcohol to produce vasodilation appears to be the first demonstration of a drug with such a discriminating action on one part of the central controlling mechanism. Angiotensin given intravenously has been shown to cause a constriction of the vessels of the hand which is central in origin and is mediated by the sympathetic nerves (Scroop & Whelan, 1966). Whether the action of angiotensin is due to an effect on vasomotor centres or on the ganglia is not yet certain, but the former site seems the more likely.

Ethyl alcohol was not given in most of the experiments involving oral administration because it was unpleasant to the taste and not all subjects were able to ingest the required amount. However, two subjects succeeded in taking 40 ml. with 110 ml. ginger ale and a third received ethyl alcohol by stomach tube. The responses of forearm and hand vessels were similar to those seen when brandy, sherry and rum were administered orally. Ginger ale alone, orally or by stomach tube, was without effect, as was rinsing the mouth with the ethyl alcohol-ginger ale mixture. It seems reasonable to conclude that the responses of the limb vessels to the ingestion of brandy, sherry and rum can be attributed to their content of ethyl alcohol rather than to any flavouring agents or other constituents.

The fact that the blood flow through muscle is reduced after oral administration of alcohol indicates that caution should be exercised in advocating its use by mouth to improve the peripheral circulation in vascular disease. While the blood flow through the hands and digits may be enhanced, a concomitant decrease in muscle blood flow may have adverse effects in an already ischaemic muscle.

SUMMARY

1. Ethyl alcohol given into the brachial artery in normal subjects caused a reduction in the blood flow through the hand and forearm. Skin and muscle vessels were both constricted.

2. The constrictor action appeared to be a direct one on the vessels since it was present in a sympathectomized limb and in normal limbs treated by intra-arterial infusion of phenoxybenzamine.

3. Brandy, sherry, rum and ethyl alcohol given by mouth caused a vasodilatation in the hand. The skin vessels of the forearm were also dilated by oral alcohol. The dilatation was sympathetically mediated and was absent in sympathectomized and denervated limbs.

4. The blood flow through the forearm muscles was reduced after oral alcohol, probably due to a direct vasoconstrictor action.

5. Intra-arterial administration of alcohol is contra-indicated in the treatment of peripheral vascular disease. While oral administration may cause dilatation of skin vessels the accompanying constriction of muscle vessels could prove to be a disadvantage where muscle ischaemia is present.

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REFERENCES

ARAMSON, D. I., ZAZEELA, H. & SCHKLOVEN, N. (1941). Vasodilating action of various therapeutic procedures which are used in treatment of peripheral vascular disease. *Am. Heart J.*, **21**, 756–766.

CONRAD, M. C. & GREEN, H. D. (1964). Hemodynamics of large and small vessels in peripheral vascular disease. *Circulation*, **29**, 847–853.

COOK, E. N. & BROWN, G. E. (1932). The vasodilating effect of ethyl alcohol on the peripheral arteries. *Proc. Staff. Meet. Mayo Clin.*, **7**, 449–464.

DOUGLAS, R. M., FEWINGS, J. D., CASLEY-SMITH, J. R. & WEST, R. F. (1966). Recurrent rhabdomyolysis precipitated by alcohol. *Australas. Ann. Med.* (In the press).

DUFF, R. S. (1952). Effect of sympathectomy on the response to adrenaline of the blood vessels of the skin in man. *J. Physiol. (Lond.)*, **117**, 415–430.

EDWARDS, J. W. L., JONES, N. B. MCCONNELL, R. B., PEMBERTON, H. S. & WATSON, D. C. (1952). Intra-arterial injections in the treatment of peripheral vascular disease. *Br. med. J.*, **2**, 808–811.

FEWINGS, J. D. & WHELAN, R. F. (1966). Differences in forearm blood flow measured by capacitance and volume plethysmography. *J. Appl. Physiol.*, **21**, 334–340.

FEWINGS, J. D., RAND, M. J., SCROOP, G. C. & WHELAN, R. F. (1966). The action of nicotine on the blood vessels of the hand and forearm in man. *Br. J. Pharmac. Chemother.* (In the press).

GREENFIELD, A. D. M. (1954). A simple water-filled plethysmograph for the hand or forearm with temperature control. *J. Physiol. (Lond.)*, **123**, 62–64P.

GROLLMAN, A. (1942). The influence of alcohol on the circulation. *Q. Jl. Stud. Alcohol.*, **3**, 5–14.

HORWITZ, O., MONTGOMERY, H., LONGAKER, E. D. & SAYEN, A. (1949). Effects of vasodilator drugs and other procedures on digital cutaneous blood flow, cardiac output, blood pressure, pulse rate, body temperature and metabolic rate. *Am. J. med. Sci.*, **218**, 669–682.

KOZELKA, F. L. & HINE, C. H. (1958). Recognition of intoxication. Report of a special committee of the British Medical Association, 2nd Ed., Appendix B. 32–34.

MILES, W. R. (1924). Alcohol and human efficiency. Carnegie Institution of Washington, 231–235.

MONTGOMERY, H. (1942). The effect of drugs on the circulation in normal hands and feet. *Am. J. med. Sci.* **203**, 882–890.

PARKS, V. J., SKINNER, S. L. & WHELAN, R. F. (1961). Mechanisms in the return of vascular tone following sympathectomy in man. *Circulation. Res.*, **9**, 1026–1034.

RODDIE, I. C., SHEPHERD, J. T. & WHELAN, R. F. (1956). Evidence from venous oxygen saturation measurements that the increase in forearm blood flow during body heating is confined to the skin. *J. Physiol.* (*Lond.*), **134**, 444–450.

RODDIE, I. C., SHEPHERD, J. T. & WHELAN, R. F. (1957a). A spectrophotometric method for the rapid estimation of blood oxygen saturation, content, and capacity. *J. clin. Path.*, **10**, 115–119.

RODDIE, I. C., SHEPHERD, J. T. & WHELAN, R. F. (1957b). Reflex changes in vasoconstrictor tone in human skeletal muscle in response to stimulation of receptors in a low-pressure area of the intrathoracic vascular bed. *J. Physiol.* (*Lond.*), **139**, 369–376.

SCROOP, G. C. & WHELAN, R. F. (1966). A central vasomotor action of angiotensin in man. *Clin. Sci.*, **30**, 79–91.