Effects of drugs on the negative (backflow) component of velocity patterns in the dog aorta

PETER A. KOT and JOHN C. ROSE

From the Department of Physiology and Biophysics, Georgetown University Schools of Medicine and Dentistry, Washington, DC 20007, USA

AUTHORS’ SYNOPSIS Using an accurately calibrated flowmeter in the descending thoracic aorta of the dog, a study was made of alterations in aortic flow patterns following intravenous and intra-arterial injections of vasoactive drugs. When injected distal to the flowmeter, vasopressors caused marked backflow while vasodilators raised the level of the lowest portion of the pulsatile flow curve. When injected into the brachiocephalic artery, vasopressors prevented the development of a significant negative component whereas vasodilators caused the appearance of backflow, or augmented that which was already present. All acute elevations or decreases in peripheral resistance due to drugs were accompanied by increases in the negative or ‘backward’ phase of flow in diastole. A significant negative flow component was noted only during these acute adjustments. A temporary differential in resistances of the upper and lower portions of the arterial circulation protected cerebral and coronary blood flow during acute haemodynamic adjustments.

The acute alterations in arterial blood flow and the instantaneous changes in the pattern of blood velocity within each pulse provide information concerning the mechanisms by which circulatory adjustments are made. In this investigation, acute haemodynamic alterations were produced in dogs by intravenous administration of pressor agents or vasodilator substances and with selective injections of these agents into major arteries supplying large vascular beds. The descending thoracic aorta was the point of flow measurement. This single site for high frequency blood flow recording reflected the sum of regional changes in vascular resistance.

Methods

The cannulating blood flowmeter used in this study is an improved version of the acoustic flowmeter described by Kalmus and his coworkers (1954). It measures flow by comparing upstream and downstream transit times between two cylindrical transducers which are bonded to the outer wall of a thin-walled, stainless steel tube. This system is accurate and reliable and has been calibrated repeatedly with blood at physiological temperatures using a pulsatile variable-speed diaphragm pump with adjustable stroke volume. Zero flow and velocity obtained electronically were demonstrated repeatedly to agree with zero flow levels obtained either by mechanical occlusion of the thoracic aorta or by inducing ventricular fibrillation.

All observations were made in open-chest, anaesthetized mongrel dogs. Intravenous sodium pentobarbital, 25 mg/kg, was the anaesthetic agent. Generalized alterations in peripheral vascular resistance were induced by giving single, rapid injections of vasodilator and vasoconstrictor agents into a femoral venous catheter. For determining changes in the aortic flow and velocity patterns resulting from regional alterations in vascular resistance, injections of several vasoactive agents

1 Supported by grants from the American Heart Association, Washington Heart Association, and USPHS grants RR 5360 and RR 5306.
were given in the brachiocephalic artery and/or in the descending thoracic aorta immediately distal to the flow cell.

To determine the effects of vasoactive agents on blood flow distribution to the 'upper' and 'lower' segments of the arterial system, the left ventricle was bypassed by a method previously described (Rose et al, 1955). All pulmonary venous return was diverted into a reservoir from whence it was pumped into a Y-tube which connected the extracorporeal pump to the proximal and distal segments of the transected descending thoracic aorta. The cannulating ultrasonic flow probe was inserted into either limb of the Y-tube so that blood flow to the upper or lower portions of the arterial system could be continuously measured. Arterial pressures in both sections of the circulation were constantly monitored along with mean right atrial pressure. Bolus injections were made into the pump tubing proximal to its bifurcation into the limbs leading to the proximal and distal segments of the descending thoracic aorta. This assured complete mixing of the drug before it reached the respective segments of the circulation.

Results

Intravenous injection of vasoactive agents

Fourteen injections of phenylephrine were given intravenously in 13 animals. There was a consistent fall in mean thoracic aortic blood flow in the immediate post-injection period. Peak flow and velocity usually increased at the time blood flow in the aorta had diminished. Negative or backflow became pronounced in every instance. Maximum changes in velocity and flow appeared slightly earlier than in the control tracings in relation to the systolic peak of the simultaneous pressure pulse contour. The decrease in heart rate noted in each instance provided a flow pattern with prolonged diastolic plateau that resembles aortic flow patterns obtained in human studies (Spencer et al, 1958).

Nine animals were given intravenous injections of norepinephrine. In all but one of the animals mean thoracic aortic blood flow temporarily diminished in the immediate post-injection period. Heart rate changes were variable when mean blood flow diminished, three showing an increase, four decreasing, and two remaining unchanged. Although maximum velocity and flow exhibited an initial decrease following four injections, this was never pronounced. Backflow was enhanced in every instance except one when it remained unchanged. The negative component was most marked during the rise and peak elevation of the arterial pressure.

Eleven animals received single, intravenous injections of histamine. Eight showed an initial increase in mean aortic blood flow. This was of short duration and was associated with an instantaneous velocity pattern which revealed greater systolic peaking of the velocity curve, but little change in the negative component. Arterial pressure at this point was just beginning to decline. With a further drop in pressure, mean thoracic aortic blood flow diminished sharply. This drop in mean flow was more prolonged and appeared to result both from a marked decline in maximum flow and velocity and from a prominent backflow phase. The most pronounced change in the configuration of the velocity pattern was the absence of a flow and velocity plateau during diastole. Velocity and flow continued to decline until the systolic upstroke of the succeeding cardiac cycle.

Satisfactory tracings following intravenous acetylcholine were obtained in six instances. Mean blood flow in the descending thoracic aorta diminished in each instance but one, in which it remained unchanged. Backflow per stroke was enhanced in every case. Changes in maximum blood flow per stroke were variable, three of the animals demonstrating an increase and three a decline in the immediate post-injection period.

Regional intra-arterial administration of vasoactive agents

A vasodilator injected distally caused a marked increase in mean thoracic aortic blood flow (Fig. 1). The most obvious change from the normal flow curve was the raising up of the lowest portion of the pulsatile flow curve with a marked reduction or complete disappearance of the backflow phase. Peak systolic velocity and flow were enhanced and minimum velocity during diastole was frequently well above zero. When a vasoconstrictor was injected distal to the point of flow measurement, mean blood flow in the thoracic aorta declined, peak systolic forward flow usually diminished and the
negative component became very prominent (Fig. 1).

When injected into the brachiocephalic artery, proximal to the point of flow measurement, the changes in the contour of the pulsatile flow curve and the mean flow rate were opposite to those obtained when the drugs were injected distally. Vasopressors prevented the development of a significant negative component and mean blood flow increased. Vasodilators caused the appearance of backflow or augmented that which was already present, and mean blood flow in the thoracic aorta declined.

**Effects of vasoactive agents on blood flow distribution to the upper and lower segments of the systemic circulation**

Blood flow distribution to the upper and lower segments of the systemic circulation was continuously measured following bolus injections of phenylephrine and acetylcholine into the pump outflow tubing. During the acute haemodynamic alterations produced by these agents the directional changes in blood flow to the two areas of the circulation were similar. Blood flow to the distal segment of the transected aorta, which essentially supplied all organs and tissues below the diaphragm was always reduced (Fig. 2, upper tracings). Blood flow to the proximal segment, which supplied the heart, cerebral and head and neck areas was always augmented (Fig. 2, lower tracings). These changes in blood flow distribution occurred regardless of whether the substance administered resulted in a depressor or pressor response.

**Discussion**

The physical characteristics of arterial blood flow have been extensively analysed by McDonald (1974) and Attinger (1964). Flow curves have been found to vary widely according to the vessel or the particular segment of a vessel in which they have been obtained (Franklin et al, 1959; Rushmer et al, 1961). Alteration in the instantaneous flow curve and the mean flow rate through any vessel reflects the vascular resistance both proximal and distal to the point of flow measurement. The influence of changes in the vascular resistance both proximal and distal to the site of measurement in the descending thoracic aorta was demonstrated by regional injections of vasoactive agents. The backflow phase in diastole could be temporarily aug-
FIG. 2 Alterations in right atrial pressure (RAP), pressure in the proximal (APP) and distal (ADP) segments of the aorta, and mean blood flow in the distal segment (upper tracings) and lower segment (lower tracings) of the transected aorta produced by injecting acetylcholine and phenylephrine into the pump outflow tubing. The arrows indicate the time of drug administration. (See text for discussion.)

imented or completely abolished by changing the relationship of vascular resistances between the upper and lower portions of the arterial circulation. Backflow was always prominent in those circumstances when resistance to flow to those areas proximal to the flowmeter was less than that distal to it.

Spencer and Denison (1956) also demonstrated marked alterations in both the contour and magnitude of the flow curve in the dog thoracic aorta by increasing or diminishing peripheral resistance. With gradual mechanical constriction of the aorta downstream to the flowmeter, mean flow and peak flow were diminished and the negative component became quite prominent. By inducing reactive hyperaemia distal to the point of flow measurement, peak flow increased above normal values and backflow did not appear even if it were normally present.

In dogs a significant backflow phase is normally present in the femoral artery. By insertion of a vein valve into the femoral artery, flow reversal was significantly reduced or eliminated in this vessel, and net forward flow was augmented (Phillips, 1971). Similar changes in the phasic flow curve have been induced in rabbit abdominal aorta. Using high-speed cinematography, McDonald (1952; 1954) was able to demonstrate a negative component in the normal flow pattern of the rabbit lower abdominal aorta. By mechanically occluding the coeliac and superior mesenteric arteries, backflow could be entirely abolished. The reactive hyperaemia occurring with release of the occlusion was associated with the appearance of a prominent negative component, often occupying the entire diastolic interval.

In the present study, the descending thoracic aorta served as an advantageous site for differentiating simultaneous alterations in the vascular resistances of the upper and lower portions of the arterial circulation. A variety of vasoactive agents were given intravenously to cause abrupt changes in total peripheral resistance. Regardless of the predominant action of these drugs, whether vasodilatation or vasoconstriction, the backflow phase in diastole became quite prominent. This increase in the negative component was most pronounced during periods when the arterial blood pressure was rising or falling, suggesting that while circulatory adjustments are taking place, there is a temporary differential in the vascular resistances of the upper and lower portions of the arterial circulation. This temporary differential appeared to be characterized by a consistently lower resistance in the cerebral and coronary regions.

This concept is supported by studies in which the systemic circulation is divided at the level of the descending thoracic aorta and the upper and lower segments of the circulation are perfused with an extracorporeal pump. During the acute haemodynamic alterations produced by acetyl-
Flow reversal in the dog thoracic aorta

Choline and phenylephrine administration, blood flow to the upper segment of the systemic circulation was always augmented while flow to the lower segment was reduced. Since arterial pressure changes in both segments of the circulation were identical, and the mean right atrial pressure was the same, vascular resistance was always altered in the upper segment of the systemic circulation to favour continuance of blood flow to structures in this area of the circulation. The temporary differential effects of vasoactive agents on the vascular resistance of the upper and lower segments of the systemic circulation account for the prominent negative flow component observed in the descending aortic flow curve of animals with an intact circulation. A prominent backflow developed because resistance to flow to those areas proximal to the flowmeter was less than that distal to it.

References


