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# Blood flow to the adrenal gland of the rat: its distribution between the cortex and the medulla before and after haemorrhage

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## INTRODUCTION

Flint (1900) published the first authoritative article on the blood supply of the adrenal gland, describing in detail the vessels of supply and venous drainage and their complex intraglandular arrangement. Since that time surprisingly little has been added to this classical description (for review, see Coupland, 1975) though more recent work has confirmed the suspicion of a number of earlier authors that a truly portal system linking cortex and medulla does not exist within the gland.

The use of variously coloured injection masses introduced from both arterial and venous sides of the circulation (Coupland & Selby, 1976) clearly showed that not only do the arteries supplying the cortex and those destined for the medulla have separate origins outside the gland, but they also supply different capillary beds. This work was fully confirmed by the elegant corrosion cast studies of the microcirculation of the rat adrenal gland by Kikuta & Murakami (1982, 1984).

The small arteries lying in the peri-adrenal region approach the capsule in which they branch repeatedly to supply a capsular plexus. Many branches penetrate the capsule as cortical arteries to form a subcapsular and glomerular plexus that is continuous with the capillary vessels that permeate the zonae fasciculata and reticularis to become the peripheral radicles of the central vein. A few cortical arteries penetrate further to join the capillary plexus of the fasciculata or to take a looped course into the gland and then back towards the surface before joining the cortical capillary plexus (Flint, 1900; Lever, 1952). The peripheral radicles of the central vein join to form progressively larger channels as they course through the adrenal medulla and these ultimately open into the central vein in most laboratory mammals – in man the more lateral parts of the central vein are surrounded by infolded cortex.

Adrenal medullary arteries arise external to the adrenal capsule and penetrate the gland to pass more or less radially through the cortex without dividing and ultimately divide within the medulla to form a medullary capillary plexus. This permeates the medullary mass of chromaffin tissue and some medullary capillaries open into the venous radicles of the central vein, through which the majority of adrenal medullary and cortical blood flows.

Because of the small size and complexity of the vessels supplying the adrenal gland, the gland's topography and lability with respect to nervous and hormonal influences, measurement of adrenal blood flow is a difficult and relatively complex procedure.

Early studies on the flow of blood to the adrenal gland have used a variety of techniques such as direct cannulation of an adrenal vein, $^{86}$rubidium ($^{86}$Rb) frac-

tionation, radioactive microsphere distribution and radiographic imaging. Almost always, however, it has been the total flow to the gland that has been measured and there is currently little information available concerning the intra-organ distribution of that flow to the various functional parts of the gland.

Kramer & Sapirstein (1967), using $^{86}$Rb uptake, reported that medullary flow per mg wet weight was 57% higher than cortical flow in anaesthetised rats. Stressing the animals, by unilateral carotid artery ligation, altered this distribution so that uptake of $^{86}$Rb increased by 130% in the cortex, but by only 50% in the medulla; this implied that a greater reduction of vascular resistance occurred in the cortex. Also using anaesthetised rats, Clark, Henderson, Balment & Mosley (1978) found that the medulla received 8% of the total adrenal flow if assessed by the $^{86}$Rb uptake technique, but that when radioactive microspheres were used, the medullary proportion was 16%. The same authors found that neither acute administration of ACTH nor chronic sodium deficiency affected the distribution of flow, whichever method was used to measure it. Hamaji, Miyata & Kawashima (1985) reported that of the non-radioactive microspheres found in the adrenal following *in vivo* administration to anaesthetised rats 4% of 10 $\mu$m diameter spheres, 9·1% of 15 $\mu$m spheres and 11·1% of 25 $\mu$m spheres were lodged in the medulla.

The adrenal appears able to maintain its absolute blood flow in the face of considerable hypovolaemic hypotension by reducing its vascular resistance (Banks, Beilin, Soltys & Davidson, 1982; Engeland, Lilly & Gann, 1985; Forsyth, Hoffbrand & Melmon, 1970; Houck & Lutherer, 1981; Slater *et al.* 1973). However, there appears to have been no study to determine whether this lowering of resistance occurs equally in both the medullary and cortical vascular beds of the gland in the rat.

This study was therefore designed to allow quantification of total adrenal blood flow in anaesthetised rats, in order to establish a baseline with respect to normal total adrenal flow in anaesthetised rats that have not been subjected to laparotomy or thoracotomy and have been stressed as little as possible, to measure the gland's response to haemorrhagic hypotension and, in particular, to determine whether such hypotension alters the intra-organ distribution of the total blood flow. For general comparative purposes the total blood flow to a series of other glandular organs (kidney, lung and pancreas) was also determined.

## MATERIALS AND METHODS

Male Wistar rats of between 335 and 385 g body weight were used. They were housed at a temperature of 21 $\pm$ 0·5 °C under a 12 hour light–dark cycle and allowed to feed *ad libitum* on standard rat pellets (Heygates diet 41B modified). Drinking water was freely available.

Anaesthesia was achieved using a intraperitoneal injection of sodium pentobarbitone (75 mg/kg, Sagatal). A catheter was introduced into a tail artery and advanced for about 10 cm so that its end lay in or near the distal abdominal aorta. In conjunction with a Gould P50 pressure transducer this was used to record blood pressure and heart rate on a Lectromed MX216 oscillograph. The right common carotid artery was then exposed and carefully dissected free of adjacent nerves and vessels. A catheter was passed via the artery into the left ventricle, correct placement being verified by observing the characteristic change in pressure waveform as the catheter tip crossed the aortic valve. The position of the catheter tip was adjusted, if necessary, to avoid initiating premature beats. A further catheter was advanced for about 2 cm along the right external jugular vein. In all cases polythene catheters of internal diameter

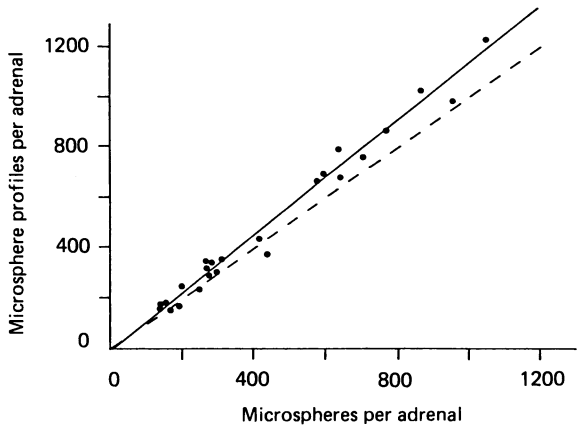


Fig. 1. The relationship between the number of microspheres present in an adrenal gland as calculated from the radioactivity of that gland and the total number of microsphere profiles seen after the same gland had been completely serially sectioned. The solid line is that of best fit. It is described by the equation $y = 1{\cdot}14x - 5{\cdot}0$ ($r = 0{\cdot}99$, $P < 0{\cdot}001$). The broken line is the line of identity.

0·28 mm and external diameter 0·61 mm (Portex) were used and filled with heparinised saline (1 unit/ml). Deep body temperature was maintained throughout at 37·6 °C using a heating blanket and rectal probe.

The animals were allowed to stabilize for 30 minutes after surgery. Those in the control group received no further treatment. Those in the hypotensive group were bled through the jugular catheter so that, over approximately three minutes, their systolic blood pressure fell by about 30%. Cardiac output and regional blood flows were then immediately measured in both groups by the administration of radioactive microspheres.

Each batch of microspheres ($11{\cdot}1 \pm 0{\cdot}3$ $\mu$m diameter, $^{57}$Co label, New England Nuclear) was carefully washed to remove leached nuclide before being resuspended in 0·9% NaCl. About 3000 microspheres were allowed to dry on to a cover slip and then counted accurately using a microscope. The cover slip was broken up and its radioactivity measured on an Ames Gammacord II. This allowed an accurate determination of the counts per minute per microsphere. Hence the radioactivity of other samples could be used to calculate precisely the number of microspheres in that sample.

About 280000 microspheres in 0·2 ml were vortexed to eliminate clumping (confirmed microscopically on a number of samples) and immediately injected through the ventricular catheter over about 20 seconds. Preliminary work had demonstrated that at least 4 infusions of this kind could be made successively on the same animal without any detectable change in heart rate or blood pressure either during or after the procedure. A flush-through of 0·2 ml of saline over a further 20 seconds followed. Blood was withdrawn through the tail artery catheter at a rate of 0·43 ml/min starting just before microsphere injection and continuing for a further 60 seconds after completion of the flush. This provided a reference sample from which cardiac output could be calculated. The animals were then killed by an intravenous overdose of anaesthetic.

Both adrenal glands were excised, dissected free from fat (for comparison, portions of kidney, lung and pancreas were treated similarly), weighted and placed in 10% buffered formalin for fixation. Their gamma emission was then quantified along with that of the reference sample and the caudal and ventricular catheters and their

associated syringes; care was taken to ensure that the samples were correctly centred in the counting well. Cardiac output and blood flows were calculated from these data using the method described previously (Heymann, Payne, Hoffman & Rudolph, 1977).

The adrenal glands, after fixation in the 10% buffered formalin for 24 hours, were dehydrated in graded alcohols, cleared in xylene and embedded in paraffin wax (Fibrowax, Gurr, congealing point 56 °C); they were then serially sectioned at 10 $\mu$m and stained with haematoxylin and eosin. Each section was examined for microsphere profiles and the position of any seen recorded.

Results were evaluated using an unpaired Student's *t*-test or linear regression analysis. 'Adrenal flow' was calculated as the sum of the flows to both glands of an animal except when comparing optically and radioactively derived estimates of the number of microspheres present (Fig. 1). Each adrenal was then considered separately.

## RESULTS

Systolic blood pressure, measured immediately prior to microsphere injection, was 32% lower in the hypotensive group ($165 \pm 8$ mmHg in the control group, $113 \pm 10$ mmHg in the hypotensive group: Table 1) while diastolic pressure was 39% lower ($105 \pm 5$ mmHg in the control group, $64 \pm 6$ mmHg in the hypotensive group). Pressure readings were accepted only if a dicrotic notch could clearly be seen on the oscillograph trace.

Cardiac output was 35% lower in the hypotensive group ($23{\cdot}1 \pm 1{\cdot}2$ ml/min/100 g in the control group, $15{\cdot}0 \pm 0{\cdot}8$ ml/min/100 g in the hypotensive group).

Pancreatic flow was lower in the hypotensive group. Expressed in absolute units it was 63% less ($150 \pm 22$ ml/min/100 g in the control group, $55 \pm 4$ ml/min100 g in the hypotensive group) while expressed as the percentage of cardiac output per 100 mg of pancreas it was 47% less ($0{\cdot}19 \pm 0{\cdot}03$% cardiac output/100 mg pancreas in the control group, $0{\cdot}10 \pm 0{\cdot}01$% cardiac output/100 mg pancreas in the hypotensive group). Renal blood flow and heart rate were unchanged.

In one rat from each group total pulmonary radioactivity was measured by removing both lungs completely. In the control group this amounted to 2·7% of the injected radioactivity whilst in the hypotensive group it was 3·4%. The radioactivity per 100 mg in the samples of lung tissue from the remaining rats was not different between the two groups (data not shown). This radioactivity arises from microspheres which have arrived directly via the bronchial arteries and those which have lodged in pulmonary capillaries after having passed through the systemic capillary bed.

### *The effect of haemorrhage on total adrenal flow*

Total adrenal blood flow was significantly higher in the hypotensive group despite the lower cardiac output and reduced blood pressure of these animals (Table 1). The total flow, as measured by the radioactivity of both intact glands, was $470 \pm 56$ ml/min/100 g in the control group and $715 \pm 66$ ml/min/100 g in the hypotensive group, an increase of 52%. When total flows were expressed as a percentage of the animals' cardiac output the difference was more pronounced. There was a rise of 122% from $0{\cdot}27 \pm 0{\cdot}04$% of cardiac output in the control group to $0{\cdot}60 \pm 0{\cdot}08$% of cardiac output in the hypotensive group.

### *Microsphere profiles*

Using a magnification of × 100 microsphere profiles were easily visible in the serial sections. Although not quantified the great majority of profiles had a diameter close to that of the injected spheres.

Table 1. *The effects of hypovolaemic hypotension on adrenal blood flow and other haemodynamic variables*

| | Body weight (g) | Heart rate (beats/min) | Blood pressure (mmHg) | | Cardiac output (ml/min/100 g) | Adrenal weight (mg) |
|---|---|---|---|---|---|---|
| | | | Systolic | Diastolic | | |
| Control group $n = 6$ | 354 ± 8 | 370 ± 8 | 165 ± 8 | 105 ± 5 | 23·1 ± 1·2 | 45·7 ± 3·3 |
| Hypotensive group $n = 6$ | 362 ± 9 | 349 ± 25 | 113 ± 10** | 64 ± 6*** | 15·0 ± 0·8*** | 46·1 ± 2·6 |

| | Adrenal blood flow | | Pancreatic blood flow | | Renal blood flow | |
|---|---|---|---|---|---|---|
| | ml/min/100 g | Cardiac output (%) | ml/min/100 g | Cardiac output 100 mg (%) | ml/min/100 g | Cardiac output 100 mg (%) |
| Control group $n = 6$ | 470 ± 56 | 0·27 ± 0·04 | 150 ± 22 | 0·19 ± 0·03 | 614 ± 36 | 0·76 ± 0·04 |
| Hypotensive group $n = 6$ | 715 ± 66* | 0·60 ± 0·08** | 55 ± 4 ** | 0·10 ± 0·01* | 539 ± 62 | 1·01 ± 0·12 |

Values are given as means ± standard error.
* $P < 0·05$; ** $P < 0·01$; *** $P < 0·001$.

Table 2. *Distribution of microsphere profiles seen in serially sectioned adrenal glands. The percentage distribution between the zones.*

| | Zona glomerulosa | Zona fasciculata and zona reticularis | Medulla |
|---|---|---|---|
| Control group | | | |
| $n = 6$ | 91·7 ± 1·0 | 1·0 ± 0·2 | 7·4 ± 1·0 |
| Hypotensive group | | | |
| $n = 6$ | 93·5 ± 0·8 | 0·8 ± 0·1 | 5·7 ± 0·8 |

Values expressed as mean % ± S.E.M.
Profiles from both adrenals of a particular animal are summed prior to calculating the percentage distributions.

Table 3. *Distribution of microsphere profiles seen in serially sectioned adrenal glands. The number of profiles seen in the zona glomerulosa and the medulla.*

| | Zona glomerulosa | Medulla |
|---|---|---|
| Control group | | |
| $n = 12$ | 233 (150–415 ) | 17 (11–24) |
| Hypotensive group | | |
| $n = 12$ | 697 (323–1131) | 42 (14–83) |

Values are means (ranges in parentheses). Each adrenal gland is considered separately.

Figure 1 shows the correlation between the number of profiles seen and the number of microspheres calculated to be present in each gland from its radioactivity. Data from both control and hypotensive groups have been pooled and each point represents a single gland. The two measures were very highly correlated. The slope of the regression line indicated that the number of microsphere profiles seen was 1·14 times the number of microspheres calculated to be present.

*Zonal distribution of microsphere profiles – control group*

No spheres were seen to have lodged in the capsule. Very many were scattered throughout the thickness of the zona glomerulosa, there being no apparent preference for a subcapsular location or for one close to the glomerulosa–fasciculata boundary. Those seen in the medulla were likewise scattered evenly throughout that portion of the gland. Profiles were only very occasionally seen in the zona fasciculata or the zona reticularis and in consequence these zones were amalgamated.

Of the total number of profiles seen in the control group 7·4 ± 1·0 % were in the medulla, 91·7 ± 1·0 % in the zona glomerulosa and 1·0 ± 0·2 % in the remainder of the cortex (Table 2).

The actual number of profiles counted was 17 (range 11–24) in the medulla and 233 (range 150–415) in the zona glomerulosa (Table 3). Between 2 and 9 profiles were seen in the combined zona fasciculata and zona reticularis.

*Zonal distribution of microsphere profiles – hypotensive group*

Despite the higher total flow to the adrenal glands of the animals subjected to haemorrhagic hypotension the proportional distribution of the microsphere profiles was not altered. The medulla received 5·7 ± 0·8 % of the increased total flow, the zona glomerulosa 93·5 ± 0·8 % and the remainder of the cortex 0·8 ± 0·1 % (Table 2).

The actual number of profiles counted had increased threefold in the zona glomerulosa to 697 (range 323–1131) and by almost as much in the medulla to 42 (range 14–83). Between 4 and 17 profiles were seen in the combined zona fasciculata and zona reticularis.

Profiles were distributed within these zones as described for the control group.

## DISCUSSION

Early work on the response of the adrenal vascular bed to haemorrhagic hypotension tended to show that as blood pressure fell so too did adrenal blood flow (Frank *et al.* 1955; Herman, Mack & Egdahl, 1971; Johnson *et al.* 1971; Mack & Egdahl, 1970; Monos *et al.* 1972; Walker, Shoemaker, Kaalstad & Moore, 1959). However these experiments were carried out on acute preparations and blood flow was measured directly by cannulating an adrenal vein and collecting the venous effluent, a procedure likely to affect normal haemodynamics. Furthermore extra-adrenal tributaries of the adrenal vein, such as the inferior phrenic, were generally not mentioned and probably not ligated and the resistance to flow of the narrow-bore tubing used for cannulation was often not considered.

Such factors presumably affected the values of adrenal flow obtained since other and subsequent studies have shown the gland able to maintain its blood flow (and substantially increase it if measured as a percentage of cardiac output) in the face of haemorrhagic hypotension, by lowering its vascular resistance. These experiments either avoided manipulations in the abdomen by using radioactive microspheres (Banks *et al.* 1982; Forsyth, Hoffbrand & Melmon, 1970; Houck & Lutherer, 1981; Slater *et al.* 1973) or used carefully or chronically implanted catheters in an adrenal or lumbo-adrenal vein (Dempsher & Gann, 1983; Engeland *et al.* 1985; Feuerstein, Feuerstein & Gimmon, 1980). The compensatory response did not always appear to be immediate. For instance Engeland *et al.* (1985) used anaesthetised dogs which had been cannulated at least 48 hours previously and removed 20% of their blood volume over 3 minutes. This produced prolonged hypotension and presumably reduced cardiac output (although this measurement was not made). They found that adrenal flow declined initially and did not regain pre-haemorrhage levels until 8 minutes after the commencement of bleeding. This level of flow was then maintained for the remaining 22 minutes of the experiment. Similar results were obtained by Dempsher & Gann (1983) and Feuerstein *et al.* (1980) who also used cannulas, in anaesthetised dogs and anaesthetised cats respectively.

The present results demonstrate the ability of the adrenal gland of the rat to maintain its blood flow in the face of haemorrhagic hypotension: although similar results have been obtained previously in various larger animals, we have been unable to find any recent reference to such work in rats. Unlike Engeland *et al.* (1985), who used dogs, we observed not a decrease, but an increase in adrenal flow early in the hypotensive period in the rat. This may be a species specific reaction and whether it represents an early additional response to the stress of hypotension over and above that of the surgical preparation which would be maintained for some time or whether it is merely a transient effect with flow soon returning to pre-haemorrhage levels is currently under investigation. It may be that cannulas, even when chronically implanted, impair the response of the gland. Banks *et al.* (1982), using conscious rabbits and radioactive microspheres, reported that 5 minutes after a haemorrhage sufficient to reduce cardiac output by 22% adrenal flow had increased by 13%: however the change recorded was not statistically significant.

The relationship between the number of microsphere profiles seen in the serial sections and the number of microspheres calculated to be present from the radioactivity of the gland is interesting. Given that the section thickness was 10 $\mu$m and that the microspheres had a mean diameter of $\pm 11{\cdot}1$ $\mu$m, application of Abercrombie's correction (Abercrombie, 1946) would lead one to expect to count 2·1 times as many profiles as there were microspheres present. That many fewer profiles were seen (1·14 times the number of microspheres) may be due to several factors. Thin sections of microspheres may not be visible, the 'optically lost cap' effect (Aherne & Dunnill, 1982); such thin sections may be lost from the tissue during processing or the spheres may be sufficiently hard to be pushed into or out of a particular section without being cut. A combination of these effects may be involved. A microsphere might be cut if hit by the microtome knife along or near an equator but might be pushed without being cut if hit near a pole.

Nevertheless there is evidence (Fig. 1) of a good correlation between the number of profiles counted and the number of microspheres present. Thus total blood flow per adrenal could be calculated from the total number of profiles seen by applying a correction factor of 1·14. We therefore believe that the distribution of profiles within the gland can be used as an indicator of the flow received by each region. Does this then mean that in the control group the zona glomerulosa receives a full 91·7% of the blood delivered by the adrenal arteries (Table 2), the medulla 7·4% while the combined zonae fasciculata and reticularis are apportioned a meagre 1·2%? No, these data must be interpreted in the light of knowledge of both adrenal vascular anatomy and of microsphere behaviour in a vascular bed.

The great majority of microspheres in arterial blood will, if appropriately sized, lodge in the first capillary bed which they encounter. Any which do not and are 'shunted' into the venous side of the circulation will reach the capillary bed of the lung and lodge there. In the present work radioactivity in the lungs was found to be only 2 or 3% of the total injected, an amount constituting both 'shunted' microspheres and those which had arrived via the bronchial arteries. Thus under the conditions used here 10 $\mu$m microspheres are, in general, satisfactorily trapped on their first transit.

To determine directly whether any were being shunted through the adrenal would require collection of the adrenal venous effluent with the associated undesirable manipulations that would almost certainly affect vascular tone. Alternatively different sized microspheres could be used to determine whether larger microspheres, which would be shunted less, gave a higher measured flow. This was done by Saxena & Verdouw (1985) who showed that measured adrenal blood flow in anaesthetised pigs was the same whether 10, 15, 25 or 35 $\mu$m diameter microspheres were used. Similarly in our hands the use of 10 or 15 $\mu$m diameter microspheres in anaesthetised rats gives comparable results for total adrenal flow (Sparrow & Coupland, unpublished). Hamaji *et al.* (1985) have reported that 10 $\mu$m microspheres may be less well trapped in the medulla of anaesthetised rats than those of 15 or 25 $\mu$m diameter.

When the adrenal arteries reach the gland they divide to form numerous cortical arteries. These divide beneath the capsule and supply a subcapsular capillary plexus. This invests the whole gland and the capillaries arising from it join capillaries of the zona glomerulosa that are themselves continuous with the larger capillaries and sinusoids of the zonae fasciculata and reticularis. Occasional cortical arteries have been described by Lever (1952); these penetrate the gland to supply directly the capillaries of the zona fasciculata. However these must be very few and were not observed by Kikuta & Murakami (1982). Effectively, therefore, the blood supply to the inner cortex flows first through the subcapsular and glomerular capillaries. In the rat four to six medullary arteries arise peripherally and penetrate the cortex without any

capillary branches finally to supply the capillary plexus in the medulla. Thus those microspheres trapped in the zona glomerulosa are representative not of the flow to that zone alone, but rather the proportion of the total flow which is to supply the whole of the cortex. Likewise the number of microspheres lodged in the medulla represents the flow reaching the medulla directly through the medullary arteries. It seems unlikely that any microspheres that might have traversed the cortical capillary bed would have lodged in the medulla since the vessels forming the inner part of the cortical capillary network are not connected in series with the medullary capillaries but, rather, represent the peripheral radicles of the central vein, ie are larger diameter venous capillaries or sinuses that penetrate the medulla and unite to form the 10–20 radicles that open into the central vein (Coupland, 1975; Coupland & Selby, 1976; Kikuta & Murakami, 1982, 1984). Supporting this analysis is the report of Hamaji *et al.* (1985) on the localisation of non-radioactive microspheres in the rat adrenal following orthograde (arterial) and retrograde (venous) injection. In particular these authors present evidence for large diameter anastomoses between the cortical sinusoids and tributaries of the adrenal vein.

It has been suggested by Ishise *et al.* (1980) that a minimum of 200 microspheres should be present in a sample from a conscious rat to give a reliable measure of flow. In the present work there were sometimes fewer microspheres per sample in the zona glomerulosa and always fewer in the medulla (Table 3). Nonetheless total flow values in the control group are similar to those of other authors and small numbers of microspheres, similar to those seen here in the medulla, have been considered sufficient in several studies on pancreatic islet blood flow (Jansson, 1985; Jansson & Sandler, 1985; Lifson, Lassa & Dixit, 1985; Vetterlein, Senske, Bornkessel & Schmidt, 1985). Supporting the view that the numbers of microspheres used and trapped in the medulla is acceptable is the fact that the standard error of the mean was only 14% of the mean for both groups.

The medullary arteries of the control group in the present work carry 7·4% of the total flow directly to the medulla, the remainder passing into the cortical capillary network at the level of the zona glomerulosa (Table 2). The few profiles seen in the zonae fasciculata and reticularis may represent either those microspheres which escaped entrapment at the commencement of the cortical capillary bed or those which entered a penetrating cortical artery (Lever, 1952). Our value for medullary flow is similar to that obtained by Clark *et al.* (1978) using $^{86}Rb$ uptake in anaesthetised rats (i.e. 8%) but considerably less than the value they found when they used microspheres (i.e. 16%). However, they did not use serial sections to assess distribution but, instead, attempted to dissect the gland into its constituent parts.

The stress of haemorrhage, while increasing the total flow to the glands, did not significantly alter its distribution in our animals (Table 2). Thus it would appear that both the cortical and medullary vascular beds reacted similarly to this degree of haemorrhagic hypotension, decreasing their vascular resistance sufficiently not only to compensate for the fall in blood pressure but actually to increase their flow. We have found only one previous publication in which an attempt was made separately to quantitate medullary and cortical blood flow in rats under conditions of acute stress. Kramer & Sapirstein (1967) stressed rats by ligating the 'carotid' artery. They reported that medullary flow increased by 50% while cortical flow rose by 130%, implying, unlike the present results, a selectively greater alteration of vascular resistance in the latter bed. Since they did not measure cardiac output it is impossible to say whether the absolute flow (as opposed to flow expressed as percentage uptake) rose or fell and thus whether the vascular resistance rose, fell or remained the same.

Since this work was completed a report has appeared concerning the effects of acute

haemorrhage on zonal blood flow in the adrenal gland of the anaesthetised dog (Breslow, Mennen, Koehler & Traystman, 1986). This work, using radioactive microspheres and blunt dissection of the gland into its constitutent parts, indicates that, in the dog, total adrenal flow decreases initially but that this is the net effect of a substantial reduction in cortical blood flow combined with a 100–400% increase in flow to the medulla. Thus it would appear that there may be a species difference in the response of the cortex, though the increase in medullary flow is observed in both animals.

Our results lend no support to the work of Harrison & Hoey (1960) who suggested that, under stress, cortical perfusion was increased by constriction of medullary arteries. This was based upon the questionable assumption that cortical vascularisation was proportional to cortical blood flow. Likewise we find no evideence for the 'vasoconstrictive block' in the cortical arterioles as a result of hypotension proposed by Mack, Wyler & Egdahl (1969) following silicone rubber infusions.

## SUMMARY

This study has investigated the flow of blood to the adrenal gland of the anaesthetised rat under basal conditions and after the induction of haemorrhagic hypotension. By combining the use of radioactive microspheres with subsequent serial sectioning we have been able not only to assess total adrenal blood flow but also to determine its distribution within the gland.

In normal anaesthetised rats approximately 7·4% of the adrenal blood flow passes directly to the medulla, the remainder being distributed to the cortex. This proportional flow is also observed immediately after withdrawal of sufficient venous blood to cause a 32% reduction in systolic blood pressure. However, the latter procedure results in a 52% increase in the total blood flow to the gland despite the associated fall in cardiac output.

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