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THE RENAL BLOOD FLOW IN COARCTATION OF THE AORTA

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Arterial hypertension in the upper extremities has long been recognized as a frequent accompaniment of coarctation of the aorta (1), and has been produced experimentally by constriction of the aorta above the level of the origin of the main renal arteries in rats (2, 3) and in dogs (4, 5, 6, 7).

Pickering (8), studying the peripheral resistance in hypertension, and using a method which measured blood flow through heat elimination from the hand, examined three cases of coarctation. In these, as in all other examples of persistent hypertension which he studied, an abnormally high resistance to the flow of blood continued after influences from the nervous system had been released. Thus, pressor effects mediated through the nerves were excluded as a major cause of the increased peripheral resistance. Pickering believed that "a chemical abnormality of the blood" could be excluded also, because of the differences in blood pressure readings between the upper and the lower extremities. He concluded, by exclusion of the factors mentioned, that the vascular narrowing in the upper limb was accounted for best by a local change in its vessels.

The findings of other investigators are significant in relation to these conclusions. Lewis (9), and Blumgart, Lawrence and Ernstene (10) have shown that the blood supply is normal to both the upper and the lower extremities in patients with coarctation. Graybiel, Allen and White (11) found no evidence of muscular hypertrophy in the small arteries of the upper limb in coarctation.

Prinzmetal and Wilson (12) also studied the effect of the release of vasoconstrictor nervous influences in hypertension by means of the plethysmograph. They measured blood flow through the forearm under conditions of increased temperature, and in some cases following the injection of novocain into the upper dorsal sympathetic ganglia. They concluded that the hypertension

found in coarctation of the aorta was caused by a neurogenic increase in the peripheral vascular resistance. They were not in agreement with Pickering in this respect. For technical reasons, however, they did not attempt novocain injection into the dorsal sympathetic ganglia of patients with coarctation of the aorta.

In the experimental animal, Goldblatt and his associates (4, 5) demonstrated that constriction of the abdominal aorta just above the origin of the main renal arteries had little or no immediate effect on the blood pressure above the site of the clamp; the immediate effect below the clamp was a lowering of blood pressure. In about 24 hours, however, it was observed that a hypertension developed above the site of the clamp. Further, it was found that with elevation of the carotid blood pressure there was a concomitant rise above normal in the femoral artery pressure, despite a substantial constriction of the aorta.

Likewise, Steele (6) found that constriction of the aorta above the renal arteries in dogs resulted in hypertension both in the femoral and in the carotid arteries. He also found, by direct measurement, a definite diastolic hypertension in the femoral artery of a patient with coarctation (13). Page (7), studying the blood pressure in dogs in which the aorta was constricted above the diaphragm, noted little or no hypertension developing proximal to the occlusion but he found a hypotension distal to the occlusion which tended to return toward normal levels. However, if the aorta also was constricted below the origin of the renal arteries, "hypertension of renal origin" developed. Page believed that the inability to produce a sustained hypertension by constriction of the thoracic aorta was due to the development of sufficient collateral circulation to insure the prevention of substantial renal ischemia.

The reports quoted above make it clear that, in the experimental animal, constriction of the

abdominal aorta above the renal arteries is capable of producing systemic hypertension of renal origin. Constriction of the thoracic aorta in dogs, however, was followed by equivocal effects on the arterial pressure.

In humans, moreover, there has not been agreement as to the mechanism of the hypertension associated with coarctation of the aorta, nor has the important factor of renal ischemia been determined in these patients. In this communication, measurements of the effective renal blood flow in six cases of congenital coarctation of the aorta are reported.

METHODS

The work of Smith and his associates (14) has made available the technique of measuring the "effective renal blood flow" by means of the clearance of diodrast by the kidneys from the circulating plasma. The determination of both the effective renal blood flow and the rate of glomerular filtration in the six cases of coarctation studied was accomplished by the employment of both diodrast and inulin in the same general manner as described by these authors.¹

Briefly, a preliminary priming infusion of diodrast and inulin in normal saline solution was given for 10 minutes and was followed by a sustaining solution of the same chemical in normal saline solution in lesser concentration. The iodine level of the blood was maintained at 0.5 to 2 mgm. per cent, and the inulin concentration varied from 40 to 60 mgm. per cent. Thirty minutes were allowed to elapse after the initiation of the sustaining infusion before urine collections were made. There were four urine collections, each of 20 minutes' duration. A blood sample was taken at the beginning, middle and end of each one. All tests were made on fasting patients in the recumbent position. Urine was obtained by catheter.

The urine and blood samples were analyzed for iodine according to the technique reported by White and Rolf (15). The inulin content of the urine and blood samples was determined by the colorimetric method described by Alving and his associates (16).

The renal plasma flow and the glomerular filtration were also determined from these specimens. The total renal blood flow was calculated by the addition of the volume of red cells, as obtained by hematocrit readings. All reported quantities are corrected to 1.73 square meters.

CASES

Six patients with definite coarctation of the aorta were studied. Brief abstracts are given below which present only the positive data establishing the diagnosis of coarctation.

¹ In addition, similar measurements were made on eleven individuals without evidence of any renal or circulatory abnormality.

Case 1, W. D., male, age 52 years

Blood pressure: brachial (right) 230/85; popliteal (right) 135/110. Left ventricular enlargement. Pre-cordial and interscapular systolic murmur. Normal retinal arteries. Palpable intercostal artery pulsations. Femoral artery pulsations weak and retarded. Scalloping of lower rib margins by x-ray. Urinary findings normal except for 1 to 2 erythrocytes per high dry field.

Case 2, J. G., male, age 7 years

Blood pressure: brachial (right) 140/90; brachial (left) 140/75; popliteal, not obtainable. Left ventricular enlargement. Systolic apical and interscapular murmur. Retinal arteries normal. Intercostal artery pulsations palpable. Femoral artery pulsations not palpable. Roentgenologic evidence of rib margin erosions and narrowing of the aortic arch. Urinary findings negative.

Case 3, F. P., male, age 9 years

Blood pressure: brachial (right) 305/110; (left) 172/105; popliteal (right) 134/?, (left) 106/?. Left-sided cardiac enlargement. Retinal arteries spastic and sclerotic. X-ray evidence of scalloped rib edges. Aortic arch not visualized by x-ray. Urinary findings negative.

Case 4, M. J., female, age 33 years

Blood pressure: brachial (right) 240/100; (left) 225/100; popliteal (left) 140/90. Spastic retinal arteries. Left ventricular enlargement. Soft interscapular systolic murmur. Palpable intercostal artery pulsations. Femoral artery pulsations retarded and barely palpable. Roentgenologic evidence of rib margin erosion and narrowing of the aortic arch. Urinary findings negative.

Case 5, F. H., male, age 37

Blood pressure: brachial (right) 210/105; (left) 205/100; popliteal not obtainable. Left ventricular enlargement. Interscapular systolic murmur. Retinal arteries slightly spastic. Femoral artery pulsations not palpable. Roentgenologic evidence of aortic arch narrowing and erosions of the inferior margins of the ribs. Urinary findings negative.

Case 6, A. T., female, age 41 years

Blood pressure: brachial (right) 220/110; (left) 210/110; popliteal (right) 130/?. Left ventricular enlargement. Palpable intercostal artery pulsations. Femoral artery pulsations not palpable. Urinary findings negative.

Thus it will be seen that these patients, of whom four were males and two females, and whose ages ranged from 7 to 52 years, in each case presented definite clinical and x-ray evidences of aortic coarctation.

RESULTS

Determinations of effective renal blood flow and inulin clearance were performed in eleven sub-

jects without circulatory or renal disturbances. This group was composed of six men and five women. The ages of the men ranged from 22 to 50 years, and the women from 25 to 40. The renal blood flows, inulin clearances, and filtration fractions in the six male subjects are tabulated in Table I-A. The renal blood flow averaged 1288

TABLE I
Clearance determinations in normal individuals

A. MALE

| Case number | Age | Blood pressure (brachial) | Renal plasma flow | Hematocrit | Effective renal blood flow | Renal inulin clearance | | Filtration fraction |
|-------------|-----|---------------------------|-------------------|------------|----------------------------|------------------------|----------------|---------------------|
| | | | | | | cc. per minute | per cent serum | |
| 1. P. L. | 22 | 130/80 | 815 | 57 | 1285 | 110 | 15 | 17.8 |
| 2. G. S. | 25 | 110/75 | 573 | 63 | 910 | 122.5 | 22.7 | |
| 3. S. B. | 25 | 120/75 | 987 | 60 | 1640 | 128 | 12.9 | |
| 4. A. E. | 47 | 120/68 | 667 | 59.5 | 1125 | 137 | 20.5 | |
| 5. S. L. | 50 | 120/70 | 764 | 55 | 1390 | | | |
| 6. J. N. | 50 | 110/70 | 760 | 55 | 1380 | | | |
| Average | | | 761 | 58 | 1288 | 124.4 | 17.8 | |

B. FEMALE

| | | | | | | | | |
|-----------|----|--------|-----|------|------|-------|------|--|
| 7. E. H. | 25 | 95/75 | 695 | 70 | 990 | 153 | 22 | |
| 8. L. D. | 28 | 105/70 | 582 | 68 | 855 | 117 | 20.1 | |
| 9. M. C. | 30 | 118/70 | 575 | 71.5 | 805 | 124.5 | 21.6 | |
| 10. N. C. | 40 | 125/78 | 710 | 68 | 1045 | 116.5 | 16.4 | |
| 11. E. M. | 30 | 95/70 | 787 | 64 | 1230 | 118 | 15 | |
| Average | | | 669 | 68.3 | 986 | 125.8 | 19.0 | |

cc. per minute (range 910 to 1640). The average inulin clearance was 124.4 cc. per minute (range 110 to 137), and the average filtration fraction was 17.8 per cent (range 15.0 to 22.7). The clearance values for the five women studied are given in Table I-B. It was found that the renal blood flow averaged 986 cc. per minute (range 805 to 1230). The average inulin clearance was 125.8 cc. per minute (range 116.5 to 153) and the average filtration fraction was 19.0 (range 15 to 22.0). These values are similar to those obtained by Smith and his associates (17) in normal men and women.

The clearance measurements obtained in the six cases of coarctation are shown in Table II. The average effective renal blood flow in the four male cases was 795 cc. per minute (range 742 to 840), and 661 cc. per minute (range 595 to 727) in the two females. Thus, in all six cases, the renal

TABLE II
Renal clearance determinations in coarctation

A. MALE

| Case number | Age | Blood pressure (brachial) | Renal plasma flow | Hematocrit | Effective renal blood flow | Renal inulin clearance | | Filtration fraction |
|-------------|-----|---------------------------|-------------------|------------|----------------------------|------------------------|----------------|---------------------|
| | | | | | | cc. per minute | per cent serum | |
| 1. W. D. | 52 | 230/85 | 412 | 53 | 775 | 118.5 | 28.8 | |
| 2. J. G. | 7 | 140/95 | 531 | 63 | 840 | 121.0 | 22.8 | |
| 3. F. P. | 9 | 172/105 | 445 | 60 | 742 | 129.5 | 29.0 | |
| 5. F. H. | 37 | 210/95 | 470 | 57 | 825 | 119.0 | 25.3 | |
| Average | | | 464.5 | 58 | 795 | 122 | 26.5 | |

B. FEMALE

| | | | | | | | | |
|----------|----|---------|-----|----|-----|-------|------|--|
| 4. M. J. | 33 | 240/100 | 370 | 62 | 595 | 121.0 | 32.7 | |
| 6. A. T. | 41 | 220/110 | 488 | 67 | 727 | 110.0 | 22.5 | |
| Average | | | 429 | 64 | 661 | 115.5 | 27.6 | |

blood flow was markedly less than the average normal flow and in each one was lower than the smallest flow recorded in any normal individual studied. In these six cases, then, substantially reduced renal blood flow was demonstrated. However, the inulin clearances of these six cases were within the normal limits. As a result of the maintenance of a normal inulin clearance despite the reduction in renal blood flow, the filtration fraction was high, averaging 26.5 per cent (range 22.8 to 29.0) in the males, and 27.6 per cent (range 22.5 to 32.7) in the females.

DISCUSSION

It is of prime interest that each of the six cases of coarctation showed a partial renal ischemia, as demonstrated by definite reduction in diodrast clearance. The demonstration of this ischemia does not necessarily prove the renal etiology of the hypertension present in these cases. In view of the fact that Lewis (9) found that the hypertension in aortic coarctation could not be explained on the basis of anatomical obstruction to aortic blood flow, and in view of the fact that hypertension occurs in dogs and in rats when the abdominal aorta is constricted above the renal arteries, it appears highly possible that the renal ischemia found in these six cases was the initiating factor in the production of the hypertension present.

It seemed quite important to us that, although these six patients showed a significant reduction in the blood flowing through the kidneys, the rate of glomerular filtration, as measured by inulin clearance, remained essentially normal. This maintenance of a normal inulin clearance, despite the reduction in the diodrast clearance, can be explained adequately only by the assumption that there is an increase in the intraglomerular pressure which, in turn, must be caused by an increase in the resistance provided by the glomerular efferent arteriole (18).

In cases of essential hypertension, also, it has been reported (18, 19) that there is a reduction in renal blood flow, but the glomerular filtration rate may be normal. These findings have led investigators to stress the important rôle played by spasm of the glomerular efferent arteriole in this disease. Various pathological studies (20, 21, 22) have demonstrated, however, that the organic obstruction to blood flow present in the kidneys of hypertensive patients is typically proximal to the glomerular tuft. Because it is impossible at the present time to determine in cases of essential hypertension the exact onset of the renal arteriosclerosis found at autopsy, it is difficult to ascertain whether the arteriosclerosis causes a reduced renal blood flow and a secondary compensatory spasm of the glomerular efferent arteriole, or whether the reduction in renal blood flow occurs because of a primary spasm of the efferent arteriole.

In the six cases herein reported, however, it is almost certain that the reduction in renal blood flow is due to the congenital aortic atresia and, although glomerular efferent arteriolar spasm is also present, it seems clear that the latter is distinctly secondary and compensatory to the afferent reduction in renal blood flow. Otherwise one must assume that these patients were born not only with aortic atresia but also with efferent arteriolar spasm, a most unlikely possibility. This secondary glomerular efferent arteriolar spasm present in these cases of coarctation cannot be considered as indubitable evidence that the efferent arteriolar spasm present in essential hypertension is likewise secondary in nature, but it does indicate that such spasm *can occur* following a reduction of the amount of blood flowing to the glomerulus.

SUMMARY

1. The effective renal blood flow and the rate of glomerular filtration were measured by means of the diodrast and inulin clearances, respectively, in a group of eleven normal control subjects and in a group of six patients with coarctation of the aorta.

2. The findings in the cases of coarctation indicated an appreciable decrease in renal blood flow as compared to the normals. The glomerular filtration rate, however, was normal.

3. The arterial hypertension in coarctation is interpreted in the light of primary reduced renal blood flow associated with secondary glomerular efferent arteriolar spasm. A probable relationship of these factors to the pathogenesis of essential hypertension is pointed out.

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