The Pattern of the Renal Vascular Response to Epinephrine in Man[1] (34868)

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(Introduced by George W. Thorn)

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During the past decade many studies in experimental animals have demonstrated a number of circulatory pathways within the kidney (1–3). While there is little debate about the presence of separate vascular circuits in the renal cortex, the juxtamedullary area, and the medulla, disagreement continues regarding the control of flow in these vascular beds and their relative responsiveness to a wide variety of stimuli (4–6). In addition, there has been continuing controversy over the past two decades regarding the possible presence of a vascular "shunt" mechanism within the kidney (7–9). The consensus of informed opinion today appears to be that a quantitatively important shunt does not exist, but sporadic reports which suggest that such a mechanism contributes to renal functional derangements in a number of settings continue to appear (9). In the present study the effects of epinephrine have been utilized to explore the relative responsiveness of the renal cortical vasculature in man to vasoconstrictor stimuli and to assess the possibility that an intrarenal "shunt" mechanism is operative under such conditions.

Methods. The hemodynamic and arteriographic effects of epinephrine injected into the renal artery were studied in nine subjects. All had normal renal function as assessed by creatinine clearance and a symetrically normal intravenous pyelogram. They required arteriography either in their evaluation as a potential kidney donor or in the investigation of hematuria of obscure origin. None of the latter patients had a renal mass lesion or other identifiable abnormality of the kidney studied. Selective arteriography was carried out by Seldinger technique, as described in detail in previous communications (10, 13, 14). Serial films were obtained with a Schonander film changer after the manual injection of 4 to 10 ml of methylglucamine iothalamate (Conray 60%). Arteriograms were repeated at carefully timed intervals after the injection of epinephrine as a bolus into the renal artery. The dose of epinephrine selected was 6 μg calculated as the salt, which represented a dose of 0.06 to 0.12 μg/kg of body weight, calculated as the base. The intervals for restudy were 10 to 18 sec in three subjects, 20 to 35 sec in another three, and 120 to 180 sec in the last three. The arteriograms were coded and assessed without reference to the primary diagnoses in a survey of a large number of selective arteriograms in a heterogeneous population, as described in detail earlier (10).

Intrarenal hemodynamics were assessed by xenon washout after intra-arterial injection as described in detail earlier (10). These studies were also obtained at intervals corresponding to those described for the arteriograms. Mean blood flow was calculated from the initial disappearance slope. The curves were also analyzed graphically as a series of compartments.

Results. The control arteriograms were all normal. After the injection of epinephrine a

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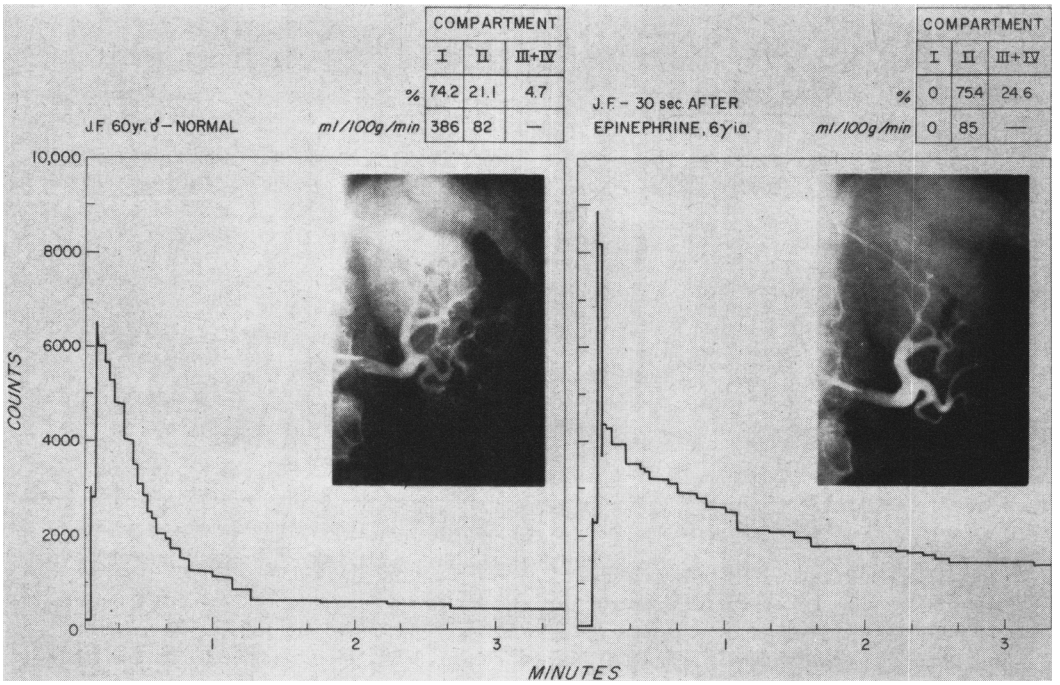

FIG. 1. Tracing of xenon washout from the normal kidney, and after the intra-arterial injection of epinephrine. Note the disappearance of the early rapid xenon washout after epinephrine. The insert shows the arteriographic features of the epinephrine effect.

profound change was found in every arteriogram. In the arteriograms repeated between 10 and 18 sec after epinephrine, vessels were unrecognizable in the renal cortex and the distal interlobar and arcuate arteries were severely attenuated. A regular, less marked attenuation of the proximal interlobar and second order arteries was also apparent. In arteriograms carried out 20 to 35 sec after the injection of epinephrine the proximal arterial vascular tree remained constricted and the cortical vessels were not identifiable, but there was a patchy reappearance of the arcuate system. By 120 to 180 sec after epinephrine injection, when renal perfusion was markedly reduced, there was a considerable slowing in the transit of contrast medium through the kidney. Contrast agent disappeared from the constricted interlobar arteries very slowly—generally requiring at least 2 to 3 sec—and the early appearance of contrast medium in the renal vein was never apparent. When renal venous opacification could be identified, it was always delayed.

In the normal kidney, the early disappearance of xenon is extremely rapid, as shown in the tracing on the left in Fig. 1. The rapid disappearance of xenon which dominates the early portion of the washout curve represents the rapid—or cortical—flow component found in compartmental analysis (Fig. 2). This component comprises 60 to 90% of total blood flow in the normal kidney, with a flow rate of 300 to 550 ml/100 g/min (10). Such a rapid flow component was demonstrable in all of the subjects studied prior to the administration of epinephrine, and was within the normal range in all but one subject, an extremely apprehensive woman whose flow was normal at the conclusion of the study. The rapid flow component was not demonstrable in the three subjects restudied between 10 and 18 sec after epinephrine and was still absent in one of the three subjects studied between 20 and 35 sec after epinephrine (Fig. 1). In the two other subjects studied between 20 and 35 sec after epinephrine, a small but recognizable, rapid flow component

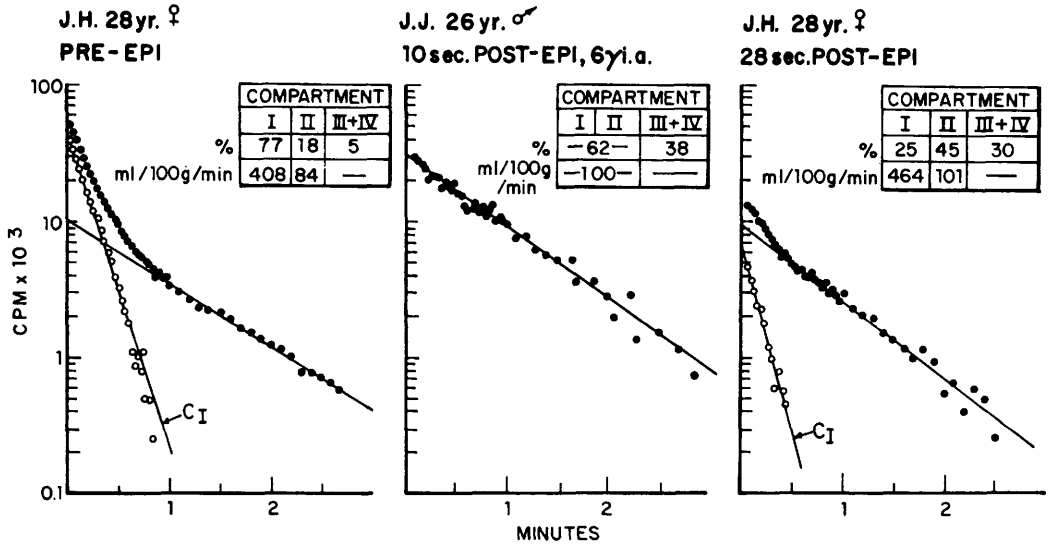

FIG. 2. Compartmental analysis of xenon disappearance from the kidney. Only the two most rapid flow components are shown. Note that the cortical flow component (C_I) which dominates the normal xenon washout curve is unrecognizable in the study carried out 10 sec after epinephrine and that a small but definite component with a normal flow rate is recognizable in the study carried out 28 sec after epinephrine.

was present, as shown in Figs. 2 and 3. The flow rate in this compartment was not significantly different from normal. By 120 to 180 sec after epinephrine the intrarenal distribution of blood flow had returned to normal.

Discussion. Several lines of evidence suggest that the rapid flow component in man, as in the dog, reflects cortical perfusion (10, 13, 14). In the present study, the absence of an identifiable rapid flow component and the failure of opacification of the cortical vasculature in the arteriogram both suggest that during the peak response to epinephrine the reduction in cortical perfusion is out of pro-

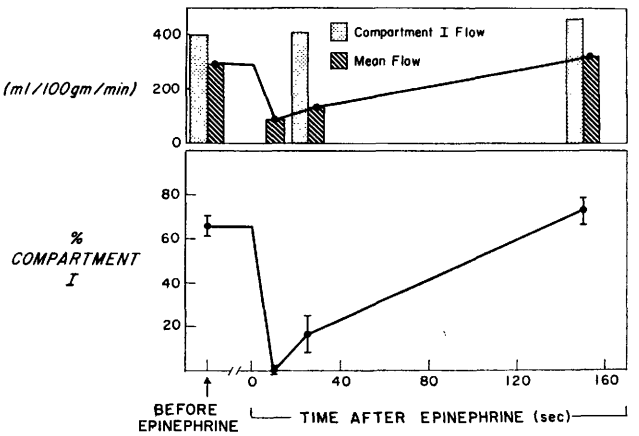

FIG. 3. The time-course of the epinephrine effect shows the reappearance of a small rapid flow component with a normal flow rate when mean flow is still markedly reduced. This pattern suggests that the disappearance of the epinephrine effect is patchy, with some areas recovering normal perfusion while others remain severly vasoconstricted. Flow returns to normal in 2 to 3 min.

portion to the reduction in overall blood flow. During early recovery from the effect of epinephrine, at 20 to 35 sec, there was the reappearance of a small rapid flow component in which the flow rate was normal. Renal perfusion returned to normal within 2 or 3 min. The pattern of recovery of renal perfusion is strikingly similar to that described by Moses in the experimental animal when a more direct method was utilized for the assessment of the effects of epinephrine on intrarenal blood flow distribution (11), and the direct observations of recovery from a prolonged period of renal artery occlusion (12). Both models revealed a patchy return of perfusion. During the disappearance of epinephrine-induced vasoconstriction in this study a small rapid flow component with a normal flow rate reappeared, suggesting that patchy areas within the cortex were perfused at a normal rate while other areas still had a very low rate of blood flow at this time. The corresponding arteriograms in this group demonstrated patchy cortical islands of opacification, lending further support to such an interpretation. Such a pattern in the response of the renal vasculature has been recognized in a large number of clinical settings in man, including allograft rejection (13), chronic glomerulonephritis, pyelonephritis, and nephrosclerosis (10, 14), and recovery from acute renal failure (10).

In the two decades which followed the appearance of Trueta's classic monograph there have been a large number of publications describing the response of the animal kidney to epinephrine (15–17). While differing in detail, all reports described cortical constriction which was either diffuse or patchy, apparently depending largely on the dose of epinephrine administered, the route of administration, the timing of the study, and the method of assessment. When massive doses were avoided and direct methods for assessing the intrarenal distribution of blood flow were used, the outer cortical vasculature generally displayed a more profound response than that of the juxtamedullary circulation (15, 17). When massive doses of epinephrine were administered diffuse vasoconstriction was described (15–17). If the assessment was delayed, outer cortical areas were frequently apparent in which perfusion appeared to be normal. More recent attempts at defining the relative responsiveness of the cortical vasculature to relatively milder stimuli and with more sophisticated methods of assessment have failed to achieve agreement. Carriere (6) reported an enhanced response of the outer cortical vasculature to norepinephrine. Direct stimulation of the sympathetic nerves to the kidney also appears to produce a dominant response of the outer cortical vasculature (4). However, Aukland (5) reported a parallel response of the cortical and juxtamedullary circulations following both renal nerve stimulation and norepinephrine infusion. The findings in the present study are consistent with the observations which suggest that the cortical vasculature is especially sensitive to this type of stimulus, and extends the observations to include man.

Evidence of a shunt mechanism could not be demonstrated with either indicator used in this study, contrast medium or radioactive xenon. Contrast medium did not show an early appearance in the renal vein, and the pattern of xenon washout ruled out the presence of a quantitatively important intrarenal shunt. Previous studies using these two indicators in patients with acute renal insufficiency of diverse etiology also failed to disclose evidence of shunting (19).

Summary. The effect of epinephrine injected into the renal artery has been studied as a model for the assessment by angiography and xenon washout of the control and relative responsiveness of the renal cortical vasculature to such stimuli in man and to ascertain whether a quantitatively significant shunt mechanism can be demonstrated in the human kidney. The findings suggested a dominant sensitivity of the cortical vasculature and rule out the presence of a quantitatively significant shunt mechanism in this setting. The pattern of recovery from the effects of epinephrine suggests that patchy areas in the cortex recover a normal rate of perfusion while other areas remain extremely vasoconstricted. This pattern of perfusion appears to be characteristic of the kidney in a large number of clinical situations.

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