BABOON KIDNEY EXCRETION
OF $^{203}\text{Hg}$-CHLORMERODRIN DURING ISOLATED
BLOODLESS PERFUSION

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The dynamics of intrarenal localization of $^{203}\text{Hg}$- and $^{197}\text{Hg}$-chlormerodrin have been studied in a variety of experimental (1—9) and clinical (3,4,7) conditions. In the present series of experiments, these mechanisms were further characterized during bloodless perfusion in the isolated baboon kidney to distinguish the effects of relative and total anoxia on the renal mechanism for handling chlormerodrin ($^{203}\text{Hg}$).

MATERIAL AND METHODS

Thirty conditioned male and female Chacma baboons from the Stellenbosch-Hopkins Primate Colony in Bellville, Cape Province, South Africa were used. Animals were sedated before operation with 1 mg/kg Sernylan (phencyclidine hydrochloride from Parke Davis Co.), 0.6 mg Atropine and 10 mg Valium (Roche). Variations in the use of these agents during pilot experiments did not result in detectable differences in renal responses. The kidney with ureteral attachments was removed at operation under routine sterile conditions. The vascular attachments were simultaneously ligated and severed. The kidney was then gently irrigated with chilled, heparinized saline (2 ml heparin to 150 ml normal saline) until the venous effluent was clear. The average time for removal of the kidney block to the start of successful isolated renal perfusion was 6 min.

The kidneys and cannulae were weighed before institution of perfusion and were fitted into a specially made plexiglass cradle and immersed in a bath of isotonic saline maintained at 37°C in a thermostatically controlled heater and stirrer (Heidolph type PIII, Taeuber and Corssen, Cape Town). The kidneys were then connected to the primed perfusion system by the two cannulae. Arterial and venous cannulae were connected in sequence, taking care to exclude air bubbles.

Isolated Perfusion Apparatus. The apparatus has already been described in detail (10).

To maintain the in-flow solution at 37°C, a warming coil (Keatings Pharmaceutical Co., Johannesburg) was introduced into the arterial line. A calibrated Sarns roller-type pump (0—1,200 ml/min from Travenol Inc., Morton Grove, Ill.) was used to produce a pulsating perfusion flow. The optimal flow-rate was continuously monitored by a Statham flow-meter and probe (Model No. M4000). Throughout most experiments an average flow-rate of above 2 ml/min/gm was maintained by calibration of the roller pump. The entire volume of perfusion fluid was equilibrated with either oxygen or helium by an infant-size Travenol disposable oxygenator.

Bloodless perfusion solutions were used from among the many different crystalloid solutions evaluated during pilot perfusions. The solution found most suitable which was used in these experiments was Travert 5% replacement solution to which 50.0 ml of 6% clinical Dextran in saline per liter of perfusate had been added. Ionic concentration of the resultant mixture was: sodium, 103; potassium, 15; and chloride, 118 mEq/liter.

The perfusion system had a capacity of 1,000 ml. To replace losses resulting from urine production, leakage from small vessels and lymphatics and sam--
The data were statistically analyzed with the aid of an Olivetti Programma 101 desk-top computer. The principles and practices of the South African Animal Welfare Society and of the American National Society for Medical Research and Animal Care were observed throughout these experiments.

* Picker well counter, donated by S.A. Atomic Energy Board.
TABLE 1. EXPERIMENTAL GROUPS

<table>
<thead>
<tr>
<th>Group</th>
<th>Gas used</th>
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<th>Ureteral occlusion</th>
<th>Low flow</th>
<th>No. of experiments</th>
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<td>plasma perfusate</td>
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</table>

RESULTS

²⁰³Hg-chlormerodrin, regular flow (controls: Table 1, Groups 1 and 2). Blood pressure and renal resistance were increased in perfusions exposed to oxygen. Renal flows, however, were similar in perfusions exposed to both oxygen and helium. Cortical flows, as reflected in Eₚₐₐₜ results, were reduced in kidneys exposed to either gas. Oxygen consumption reflected the presence or absence of O₂ in the perfusate. Better GFR was seen with exposure to helium but with little Tₕ₂O (net solute-free water reabsorption). Percent sodium reabsorption, however, was similar, showing good preservation of proximal tubular function in both oxygen- and helium-exposed kidneys.

²⁰³Hg-chlormerodrin protein (Table 1, Groups 3 and 4). Increased blood pressure was again seen with oxygen exposure. Renal flows were similar with both oxygen or helium gas. Renal cortical flows were both reduced but were slightly better with oxygen exposure. PAH extractions, GFR rates and percent sodium reabsorption are similar in both the oxygen and helium groups.

Low-flow with ²⁰³Hg-chlormerodrin protein (Table 1, Groups 5 and 6). Lower renal flows and pressures were attained with reduction in all renal functions measured in both gas-exposure groups.

²⁰³Hg-chlormerodrin protein ureteral occlusion (Table 1, Groups 7 and 8). Ureteral occlusions (UO) with oxygen-exposed perfusion were accompanied by vasoconstriction with increased blood pressure but with little change in renal flow-rate, showing maintenance of renal autoregulatory function. Renal cortical flow, Eₚₐₐₜ and Tₕ₂O were reduced after UO with both gases. Percent sodium reabsorption was also transiently depressed with oxygen or helium. No change was seen in renal oxygen consumption in either environmental gas condition. GFR, as measured, showed recovery following release of UO in both gas-exposure groups.

²⁰³Hg-chlormerodrin ureteral occlusion (Table 1, Groups 9 and 10). Ureteral occlusions with oxygen-exposed perfusates showed the same pattern as with added plasma protein, but with a net 9% rise in renal flow immediately during and after ureteral occlusion. The basal renal flow-rates in this group were initially higher. Renal cortical flow, percent sodium reabsorption, Eₚₐₐₜ, Tₕ₂O were also depressed in both gas-exposure groups as in Table 1. A small rise in directly measured oxygen consumption was seen during the period of rise in renal flow in oxygen-exposed kidneys. Renal resistance remained elevated after release of UO during oxygen exposure. The elevation in GFR as measured by creatinine clearance reflects washout after occlusion because the extraction of creatinine showed no appreciable change.

With helium equilibration the occlusion of the ureter caused no change in blood pressure, but a
4% increase in renal flow resulted during ureteral occlusion. Effective renal cortical flow was reduced as was percent sodium reabsorption and GFR. With helium, T^3H_o also showed no consistent change in the helium-exposed kidneys.

203Hg alterations. All helium-exposed kidneys showed a rapid excretion of 203Hg-chlormerodrin with a prompt fall in arterial levels of radioactivity and its rapid appearance in the urine (Groups 1, 3, 5, Fig. 1). Ureteral occlusion (Groups 7, 9) prolonged the fall in venous 203Hg concentration, which then fell rapidly after the release of the ureteral occlusion.

With oxygen exposure and the addition of proteins, 203Hg-chlormerodrin arterial levels were elevated for a longer period of time. The responses to ureteral occlusion do not appear greatly different from the helium-exposed kidneys (Fig. 1).

Renal tissue 203Hg-chlormerodrin radioactivity was predominantly situated in the cortex (Fig. 2) with little difference between outer and inner cortex and regardless of the experimental conditions, type of perfusion gas or the addition of protein. Ureteral occlusion with helium exposure produced high renal cortical 203Hg-chlormerodrin concentrations. The addition of protein did not increase the fixation of the isotope (Groups 3, 5, 7, Fig. 2). The opposite appeared to be true with Groups 1 and 9 in Fig. 2 showing more isotope concentration in the absence of protein. Perfusion with total human plasma produced no difference in tissue radioactive distribution or concentration from the other protein-exposed kidneys (Group 11, Fig. 2).

With oxygen exposure and ureteral occlusion high renal cortical 203Hg-chlormerodrin concentrations were also noted. This was higher with protein added to the isotope than without (Groups 4, 6, 8, Fig. 2). Isolated kidneys exposed to oxygen had higher cortical radioactivity without protein than those with protein added to the system (Groups 2 and 10, Fig. 2). The radioactive concentrations in the renal cortex were also reduced by low flow-rates in the oxygen-exposed kidneys (Group 6, Fig. 2).

**DISCUSSION**

Exposure of the perfusate to oxygen or helium in isolated experiments did not affect the various measurements of renal function to any great degree. Ureteral occlusion caused slight alterations in renal blood flow; however, this was roughly the same in the presence of either oxygen or helium. Renal cortical ischemia accompanies ureteral occlusion but may be relative in that more flow is shunted to the inner cortex and medulla as the total renal flow remains unchanged. This phenomenon is different in oxygen-exposed kidneys in that a relative hypertension is also present, suggesting an oxygen-dependent release of a humoral vasoconstrictive agent, e.g. renin or angiotensin. Specific distal and proximal renal tubular impairment is seen, as shown by the changes in free-water reabsorption and percent sodium reabsorption. These are not permanent, as shown by their progressive recovery after release of the occlusion.

The distribution of radioactivity in perfusate and urine does not vary greatly between the groups exposed to oxygen and helium. Differences exist between treatments in the 1-hr anatomical distribution of radioactivity in the kidney.

The clearance of tagged isotope from the kidney was affected by ureteral occlusion but not by exposure to either gas. The exception to this was the addition of protein to the oxygen-exposed kidneys. These results in the isolated kidney are thus in contrast to those obtained previously in human or dog kidneys with renal artery stenosis (4,9). The latter results showed an apparent relationship between the levels of renal cortical 203Hg radioactivity and the aerobic function of the renal cortex (4,9). Such is not the case under these isolated, bloodless, perfused conditions (Figs. 1 and 2). The amount of radioactivity in the isolated renal tissue is also comparable to other intact studies (4,8,9). Therefore, the inability to show a difference between an oxygenated or anoxic helium environment in terms of the distribution of 203Hg-chlormerodrin cannot be on the basis of inadequate mixing or other unmonitored factors. These results suggest that other intracellular metabolic factors or possibly cellular membrane enzymatic activities such as ATP-ase are essentially concerned with the intrarenal kinetics and distribution of 203Hg-chlormerodrin. Since the renal functional measurements with this system show little difference between oxygen- and helium-exposed groups, it is not surprising that the levels of 203Hg radioactivity and distribution are similar. Whatever intrarenal factors are responsible for the similarity of 203Hg distribution in the presence of oxygen or helium are unknown. These are perhaps related to the type of perfusate or gas equilibration. Nevertheless, helium-exposed kidneys appear capable, under these isolated conditions, of handling radioactive 203Hg as well as those exposed to oxygen.

**SUMMARY**

Over 30 baboon kidneys were studied during isolated bloodless perfusion with oxygen or helium equilibration and in the presence or absence of ureteral occlusion, low perfusion rates or protein addition to the system.
Renal cortical, medullary, venous, arterial and urinary $^{203}$Hg-chlormerodrin radioactivity was monitored during these experiments. Kidneys exposed to helium excrete and concentrate $^{203}$Hg-chlormerodrin in the same manner as oxygen-exposed kidneys or as intact kidneys in other species. These results suggest that $^{203}$Hg-chlormerodrin concentration and excretion under these isolated, bloodless conditions are not oxygen dependent.

ACKNOWLEDGMENT

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REFERENCES


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