JCI The Journal of Clinical Investigation

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J Clin Invest. 1970;49(9):1656-1667. https://doi.org/10.1172/JCI106383.

Research Article

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Effects of Hematocrit on Renal Hemodynamics and Sodium Excretion in Hydropenic and Volume-Expanded Dogs

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ABSTRACT The effects of hematocrit on renal hemodynamics and sodium excretion were studied in anesthetized dogs during both hydropenia and volume expansion. The hematocrit was decreased by isovolemic exchange with the animal's own previously harvested plasma and increased by isovolemic exchange with fresh, washed red blood cells. Renal perfusion pressure was maintained constant throughout the experiments by the adjustment of a suprarenal aortic clamp. During hydropenia, a decrease in hematocrit was associated with an increase in sodium and potassium excretion and solute-free water reabsorption. These changes were accompanied by an increase in renal plasma flow and renal blood flow and a decrease in renal vascular resistance. Glomerular filtration rate was unchanged and filtration fraction was significantly decreased as hematocrit was lowered. Increasing hematocrit during hydropenia had the opposite effects on electrolyte excretion, solute-free water reabsorption, and renal hemodynamics. In another group of animals, hematocrit was lowered during volume expansion with either saline or plasma, then returned to the control level by isovolemic exchange with washed red blood cells. This increase in hematocrit during volume expansion had a similar effect on electrolyte excretion, solute-free water reabsorption, and renal hemodynamics as during hydropenia. These results therefore suggest that acute changes in hematocrit may significantly affect sodium excretion and renal hemodynamics during both hydropenia and volume expansion. The changes in solute-free water reabsorption and potassium excretion suggest that the alterations in hematocrit may affect primarily the reabsorption of sodium in the proximal tubule. The concommitant effects of hematocrit on renal vascular resistance and filtration fraction may mediate this change in sodium reabsorption by altering hydrostatic and oncotic pressures in the peritubular circulation.

A preliminary report of this work was presented at the National Meeting of the American Federation of Clinical Research, Atlantic City, N. J., 2 May 1970 and published as an abstract (1970 *Clin. Res.* **18**: 515).

Received for publication 10 April 1970 and in revised form 18 May 1970.

INTRODUCTION

In 1925 Starling and Verney (1) demonstrated that the addition of isotonic saline to the blood perfusing an isolated heart-lung-kidney preparation resulted in increased sodium excretion which they called "dilution diuresis." These early authors did not propose which component(s) of the diluted blood may be primarily responsible for the increased excretion of sodium. Recently, Craig, Mills, Osbaldiston, and Wise (2) performed similar studies in the totally isolated perfused kidney and suggested that lowering of hematocrit may be largely responsible for the natriuresis which occurs when saline is added to the perfusion circuit. However, in the latter studies, as in those of Starling and Verney (1), the concentration of protein in the perfusing plasma was also diminished, and recent studies of several investigators, using both clearance (3–6) and micropuncture techniques (7, 8), have demonstrated a significant effect of plasma protein concentration on sodium reabsorption and excretion. Most studies in which the hematocrit has been reduced without changing the concentration of plasma protein have involved the infusion of plasma-like solutions (8–12). Under such circumstances of volume expansion, an increase in renal perfusion pressure (11, 13, 14) and renal vasodilatation (11, 15), or a change in the concentration of some humoral substance(s) affecting sodium reabsorption (16–18) could explain the natriuresis without involving an additional role of the associated changes in hematocrit. Nevertheless, the possibility has been suggested that the natriuresis which occurs during volume expansion

with saline or plasma may be related partially to consequences of the diminution in hematocrit and whole blood viscosity (11, 19).

Several investigators have attempted to define the role of hematocrit on sodium excretion, independent of volume expansion. Bahlmann, McDonald, Dunningham, and De Wardener (20) observed increased sodium excretion in anesthetized dogs as the hematocrit was decreased by circulating the dog's blood through a reservoir containing 5 g/100 ml bovine albumin. No effect on sodium excretion was observed when 2.5 g/100 ml albumin was added to the reservoir, and these authors attributed the increase in sodium excretion observed during dilution with 5 g/100 ml albumin to a pharmacological action of the foreign protein. However, Nashat and Portal (21) and Nashat, Scholefield, Tappin, and Wilcox (22) recently have demonstrated increases in urine flow, sodium excretion, and renal plasma flow as the hematocrit was decreased by an isovolemic exchange of blood for isoncotic dextran. These latter authors, however, did not demonstrate a significant decrease in sodium excretion when the hematocrit was increased by an isovolemic exchange with red blood cells which raises the possibility that the increased excretion of sodium observed during dilution of the hematocrit may have been due to some other effect of the dextran. In micropuncture studies in the dog, Knox, Howards, Wright, Davis, and Berliner (23) reported a decrease in fractional reabsorption in the proximal tubule as the hematocrit was lowered by circulating the dog's blood through a reservoir containing a 5g/100 ml human albumin, but they concluded that there was no significant effect on the excretion of sodium.

The present study was undertaken to examine further the effect of changes in the hematocrit on renal hemodynamics and sodium excretion in the absence of associated changes in renal perfusion pressure and plasma protein concentration or the infusion of foreign protein. The results suggest that changes in the hematocrit may affect renal hemodynamics and sodium excretion in the hydropenic animal and that a decrease in the hematocrit may play a role in the natriuresis accompanying volume expansion with saline or plasma.

METHODS

Experiments were performed in 18 mongrel dogs of either sex ranging in weight from 20 to 30 kg. Two of the animals had undergone a splenectomy approximately 1 wk before study. On the day of the experiments, the animals were anesthetized with intravenous pentobarbital (30 mg/kg) and ventilated automatically through an endothracheal tube connected to a Harvard respirator. Light anesthesia, as judged by preservation of corneal reflexes, was maintained throughout the experiment by the intermittent administration of pentobarbital. Pitressin Tannate in oil, 2.5 U, and deoxycorticosterone (DOCA), 10 mg, were injected intramuscularly on the evening before the experiment. Animals had free access to water, but food was withheld beginning 18 hr before the experiments. An additional 10 mg of DOCA and 2.5 U of Pitressin Tannate were administered 1 hr before the experiment. Plastic catheters were placed retrograde through bilateral retroperitoneal flank incisions into each ureter and into both renal veins for a distance of 2–3 cm. In two animals the left renal pedicle was denervated. In all animals a Blalock clamp was placed around the aorta above both renal arteries. Polyethylene catheters were inserted into the vena cava, brachial artery, and the aorta (below the level of the Blalock clamp). Aortic and brachial arterial pressures were measured continuously by pressure transducers and a direct writing recorder (Hewlett-Packard). After the surgical procedures, infusions of isotonic saline were begun at a rate of 0.5 ml/min through each renal venous catheter, as was an intravenous infusions of saline (0.5 ml/min) containing sufficient inulin and *p*-aminohippuric acid (PAH) to maintain blood levels of these substances between 15 and 25 and 1 and 3 mg/100 ml respectively. Aqueous Pitressin (50 mU/kg per hr) was also added to the maintenance infusion. At least 60 min were allowed from the completion of the surgery until the experiment was started. Urine was collected at 10-min intervals throughout the experiment, and arterial and renal venous blood samples were collected at the mid-point of alternate collections of urine.

Hydropenic experiments. In eight experiments the hematocrit was lowered by isovolemic exchange with the animal's own previously harvested plasma. Plasma (40 ml/kg) was harvested on two separate occasions from each animal at least 1 wk before the experiment. The blood was withdrawn from the jugular vein, placed in a sterile blood bag, and centrifuged at 2200 rpm. The red cells were separated and resuspended in a volume of saline comparable to the volume of plasma removed and then reinfused into the animal. The harvested plasma was stored at 4°C in sterile plastic bags with heparin added as an anticoagulant. Before use, the plasma was preheated to 37°C and then filtered through a gauze mesh. In order to avoid any change in renal perfusion pressure during these experiments (either spontaneously or due to the alteration of the hematocrit), the renal perfusion pressure was lowered 10–15 mm Hg below systemic arterial pressure before the control periods and maintained at this value throughout the experiment by appropriate adjustment of the suprarenal aortic clamp. In most of the experiments, little adjustment of the clamp was necessary after the initial setting.

The protocol on the day of the experiment was as follows. After three to five control periods, isovolemic exchange with the previously harvested plasma was achieved by infusing the plasma from a leucite reservoir at an average rate of 50 ml/min while an equal amount of blood was withdrawn from the animal and added to the reservoir. Intermittent stirring of the contents of the reservoir insured proper mixing of plasma and red blood cells. This procedure was continued for 20–30 min and resulted in lowering the hematocrit without altering the animal's blood volume. Three to five experimental periods were then obtained after this isovolemic decrease in hematocrit. In three experiments, the hematocrit was returned to control levels by isovolemic exchange with fresh washed red blood cells from a donor animal after which an additional three to five experimental periods were obtained. The donor red blood cells were washed with isotonic saline to avoid infusion of soluble foreign protein. No visible hemolysis occurred after infusing

TABLE I

Renal Hemodynamics, Cation Excretion, and Solute-Free Water Reabsorption

Time	V	GFR	RPF	RBF	RVR	FF
min	*ml/min*	*ml/min*	*ml/min*	*ml/min*	*mm Hg / ml/min*	
0–10	0.42	77	254	427	0.29	0.30
10–20	0.48	97	290	485	0.26	0.33
20–30	0.48	83	281	464	0.27	0.30
30–50	Exchange with reservoir containing 700 ml of previously harvested plasma					
50–60	0.72	88	450	659	0.19	0.20
60–70	0.73	88	448	643	0.19	0.20
70–80	0.78	93	408	583	0.21	0.23
80–90	0.78	90	327	453	0.28	0.28
90–100	0.77	83	370	523	0.24	0.22
100–110	0.73	87	378	533	0.24	0.23
110–130	Exchange with reservoir containing 500 ml of freshed washed RBC's					
130–140	0.49	91	330	531	0.24	0.28
140–150	0.40	82	306	513	0.25	0.27
150–160	0.42	93	276	465	0.27	0.34

* See Methods and Results sections for explanation of abbreviations.

the donor red cells. Furthermore, hemolysis would not be expected since naturally occurring isoantibodies to red blood cells have generally not been found in the dog (24).

Volume expansion experiments. In six animals 600 ml of isotonic saline were infused intravenously over a 20 min period after which a maintenance infusion was continued at a rate of 2–4 ml/min greater than the rate of urine flow. In four other animals 300–500 ml of the animal's own previously harvested plasma were infused intravenously over 30 min and then continued at a rate 1–2 ml/min greater than the rate of urine flow. An equilibration period ranging from 60 to 150 min after the initial infusion of saline or plasma was allowed to permit stabilization of the rate of urine flow, after which collections were made and then isovolemic exchange with fresh washed donor red blood cells was performed in the same manner described above for hydropenic animals. In all of these experiments involving volume expansion, renal perfusion pressure was maintained constant throughout by adjusting the suprarenal aortic clamp.

Analytical procedures have been described previously (11). Renal plasma flow (RPF) was calculated from the formula of Wolf (25): $RPF = V(U-R)/(A-R)$ where V = rate of urine flow and U = the urinary, R = the renal venous, and A = the arterial concentration of PAH. Renal blood flow (RBF) was calculated as RPF/1 − Hct. Renal vascular resistance (RVR) (mm Hg/ml per min) was calculated as mean arterial pressure/RBF. Solute-free water reabsorption ($T^c_{H_2O}$) was calculated as osmolal clearance (C_{osm}) minus urine flow rate (V), and filtration fraction (FF) was calculated as glomerular filtration rate (GFR)/RPF.

RESULTS

Effect of acute increases and decreases in hematocrit in hydropenic animals. Table I gives details of an experiment in a hydropenic dog in which the hematocrit (Hct) was lowered by isovolemic exchange with the animal's own plasma and then returned to control levels by isovolemic exchange with packed, washed, red blood cells. Renal perfusion pressure was maintained constant throughout these experiments, and the concentration of protein in plasma was unchanged. Lowering the Hct was associated with increases in urine flow (V), sodium excretion ($U_{Na}V$), potassium excretion (U_KV), $T^c_{H_2O}$, RPF, and RBF as RVR and FF decreased. Mean GFR was not significantly changed. Figs. 1 and 2 summarize these effects of decreasing the mean Hct from 44 to 33 vol % in 16 kidneys of eight animals. Over a wide range of control sodium excretions (Fig. 1), a decrease in hematocrit was associated with an increase in sodium excretion in each kidney. The mean $U_{Na}V$ per animal increased from 202 to 310 μEq/min ($P < 0.001$).[1] Mean U_KV also increased from 108 to 125 μEq/min ($P < 0.005$) as $T^c_{H_2O}$ increased from 1.9 to 2.4 ml/min ($P < 0.001$). Hemodynamic changes included increased RPF from 266 to 372 ml/min ($P < 0.001$) and increased RBF from 456 to 550 ml/min ($P < 0.001$) as RVR decreased from 0.32 to 0.26 mm Hg/ml per min ($P < 0.001$). GFR was not significantly changed (47–48 ml/min) and FF decreased, therefore, from 0.36 to 0.27 ($P < 0.001$). Mean E_{PAH} (not shown in Figs. 1 or 2) decreased significantly from 0.84 to 0.81 ($P < 0.001$) as Hct was diminished.

[1] Paired Student *t* test.

*in the Hydropenic Dog during Isovolemic Changes in the Hematocrit**

$U_{Na}V$	U_KV	T^cH_2O	Aortic pressure	Brachial arterial pressure	Plasma total protein	Hematocrit
μEq/min	*μEq/min*	*ml/min*	*mm Hg*	*mm Hg*	*g/100 m*	*vol %*
107	122	0.88	125	135	5.4	43.0
117	139	0.98	125	135		
118	135	0.98	125	135	5.3	42.0
		Exchange with reservoir containing 700 ml of previously harvested plasma				
170	166	1.20	125	145		
173	172	1.29	125	150	5.5	35.0
187	189	1.22	125	145		
194	187	1.24	125	145	5.4	32.0
210	200	1.31	125	145		
188	180	1.20	125	145	5.3	31.0
		Exchange with reservoir containing 500 ml of freshed washed RBC's				
125	127	1.00	125	145	5.5	42.0
86	152	1.00	130	145		
75	128	1.13	125	145	5.1	43.0

As shown in Figs. 1 and 2, increasing the Hct had the opposite effect on these parameters. When the Hct was increased from 31 to 42 vol % (average change in three animals) $U_{Na}V$ decreased from 208 to 120 μEq/min ($P < 0.001$) and U_KV decreased from 118 to 88 μEq/min ($P < 0.005$). T^cH_2O decreased from 2.2 to 1.6 ml/min ($P < 0.005$). RPF decreased from 378 to 260 ml/min ($P < 0.02$), and RBF decreased from 536 to 426 ml/min ($P < 0.05$) as RVR increased from 0.21 to 0.33 mm Hg/ml per min ($P < 0.05$). GFR was not significantly changed (50–48 ml/min), therefore FF increased from 0.27 to 0.37 ($P < 0.05$). E_{PAH} was not significantly changed as Hct was increased.

Effect of acute increases in hematocrit in volume-expanded animals. After allowing an equilibration period for stabilization of urine flow, the Hct was increased to a normal range in six animals during a continuous infusion of saline and in four animals during a continuous infusion of plasma. The Hct in the saline-loaded group increased from a mean of 32 to 40 vol % and in the plasma loaded group from 36 to 45 vol %. The concentrations of plasma protein before and after increasing the Hct were 4.6 and 4.4 g/100 ml in the saline-loaded group, and 6.2 and 5.8 g/100 ml in the plasma-loaded group. Figs. 3 and 4 illustrate saline- and plasma-loading experiments in which increasing the hematocrit resulted in an abrupt decrease in urinary sodium excretion. This diminution in sodium excretion was accompanied by a substantial decrease in RPF and an increase in RVR and FF, as GFR diminished slightly. The effects of the increased Hct on cation excretion, T^cH_2O, and renal hemodynamics for 20 kidneys in 10 animals are shown in Figs. 5 and 6. The increased Hct was associated with a mean decrease in $U_{Na}V$ per animal from 964 to 674 μEq/min ($P < 0.001$) in the saline-loaded group and from 428 to 262 μEq/min ($P < 0.005$) in the plasma-loaded group. At the same time U_KV decreased from 130 to 110 μEq/min ($P < 0.001$) in the saline group and from 144 to 100 μEq/min ($P < 0.005$) in the plasma group. The T^cH_2O decreased from 3.8 to 3.2 ml/min ($P < 0.005$) in the saline group and from 3.2 to 2.4 ml/min ($P < 0.005$) in the plasma group. These changes in cation excretion and T^cH_2O were associated with hemodynamic alterations similar to those which occurred when the Hct was increased in the group of hydropenic animals discussed above. A modest though significant decrease in GFR occurred in both the saline (106–100 ml/min; $P < 0.02$) and plasma group (124–116 ml/min; $P < 0.05$). RPF decreased from 380 to 318 ml/min ($P < 0.001$) in the saline group and from 414 to 308 ml/min ($P < 0.001$) in the plasma group. FF was increased from 0.28 to 0.33 ($P < 0.001$) in the studies during saline infusion and from 0.28 to 0.38 ($P < 0.001$) in the studies during plasma infusion. RBF decreased from 542 to 506 ml/min ($P > 0.05$) as RVR increased from 0.58 to 0.63 ($P < 0.025$) in the saline-loaded group.

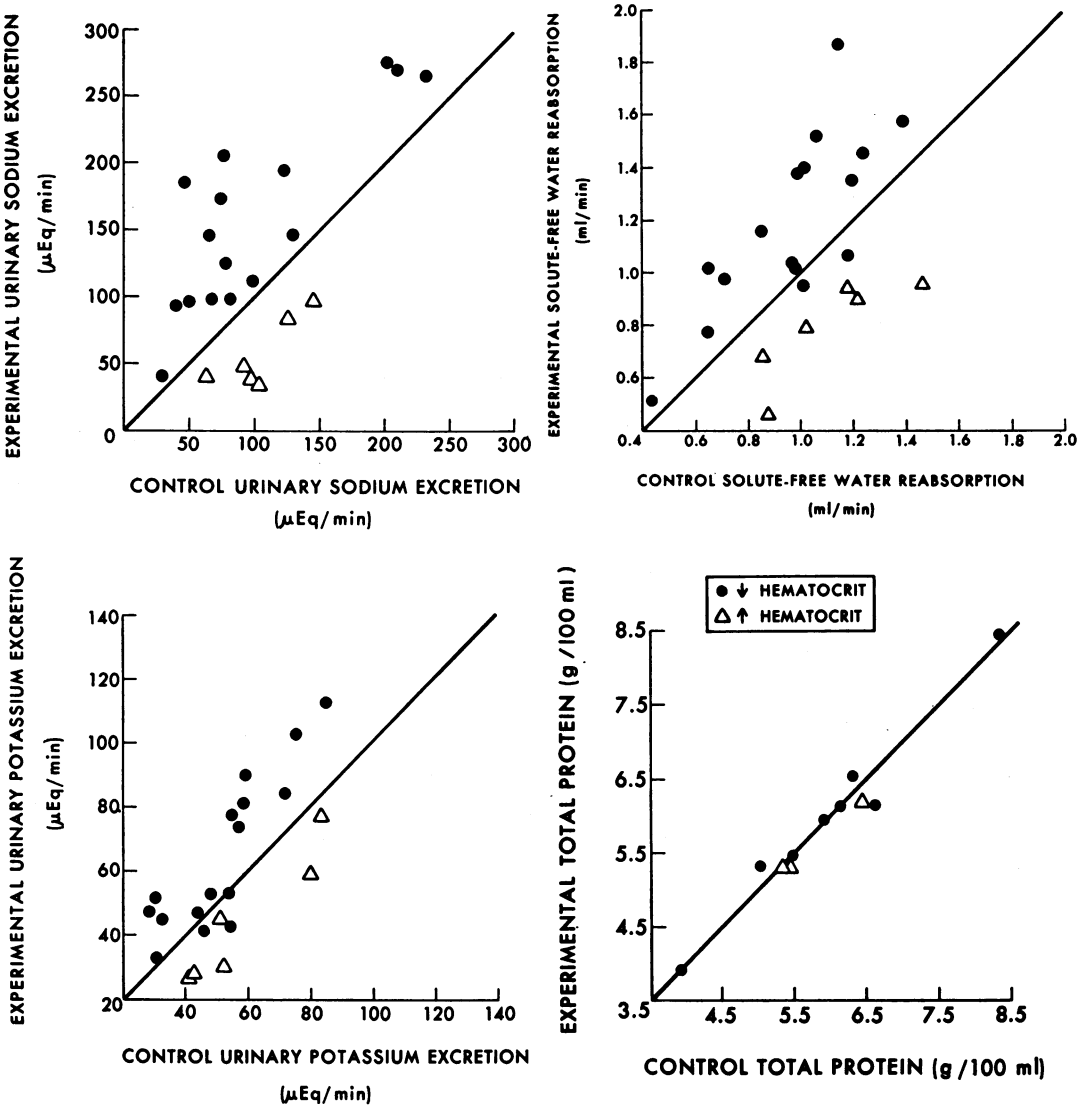

FIGURE 1 The effect of decreasing the hematocrit during hydropenia on electrolyte excretion and solute-free water reabsorption. The symbols (●) and (△) represent mean values of three to five consecutive 10-min periods in which the hematocrit was decreased and increased, respectively. Each symbol represents a mean value for one kidney except the results for plasma protein concentration which are mean values for each animal. The 45° line is the line of no change. Values which increased during the experimental period lie above this line and values which decreased during the experimental period lie below this line. Sodium and potassium excretion and solute-free water reabsorption varied inversely with changes in hematocrit as plasma protein concentration was unchanged.

RBF diminished from 622 to 518 ml/min ($P < 0.005$) as RVR increased from 0.49 to 0.58 ($P < 0.001$) in the plasma loaded group. E_{PAH} was not significantly changed by increasing Hct in either group. The results in the two splenectomized animals (a saline-loading experiment and a plasma-loading experiment) were not different from the results in the other experiments. The denervated kidneys in two plasma-loaded dogs responded in a similar manner as the contralateral innervated kidneys to increases in hematocrit.

DISCUSSION

The present observations in the group of hydropenic animals demonstrate that changes in the hematocrit may significantly affect renal hemodynamics and the excretion of sodium in the absence of volume expansion.

The effect of decreasing the hematocrit on sodium excretion in the present study was similar to that found by Bahlmann and associates in experiments in which 5 g/100 ml bovine albumin was used to decrease the hematocrit without volume expansion (20). These authors suggested that the increased excretion of sodium that they observed was due to some "pharmacologic" effect of the foreign protein. This conclusion was not entirely consistent with their observation that when the hematocrit was decreased with 2.5% solution of the same protein, there was no significant change in the rate of sodium excretion. In the present study any such dilemma in the interpretation relating to the administration of foreign protein was avoided, since the hematocrit was decreased by exchange with the animal's own plasma. Furthermore, opposite effects on renal hemodynamics and electrolyte excretion were demonstrated when the hematocrit was *increased* or *decreased,* thereby making it unlikely that the exchange procedure initiated some effect other than that attributable to the change in hematocrit per se. These observations thus seem to establish that alteration of the hematocrit in the absence of simultaneous administration of foreign protein (20, 23) or dextran (21, 22) affects sodium excretion. This is in contrast to the conclusion of Knox and associates (23) who reported no significant increase in the excretion of sodium in the dog when the hematocrit was decreased acutely by isovolemic exchange with a solution of human albumin. The anti-natriuretic state of animals undergoing micropuncture may explain the failure of Knox and associates (23) to demonstrate an effect of hematocrit on sodium excretion since the control rate of sodium excretion in most of their animals was quite low. Alternatively, in contrast to the suggestion of Bahlmann et al. (20), the administration of foreign protein could have inherent anti-natriuretic rather than natriuretic

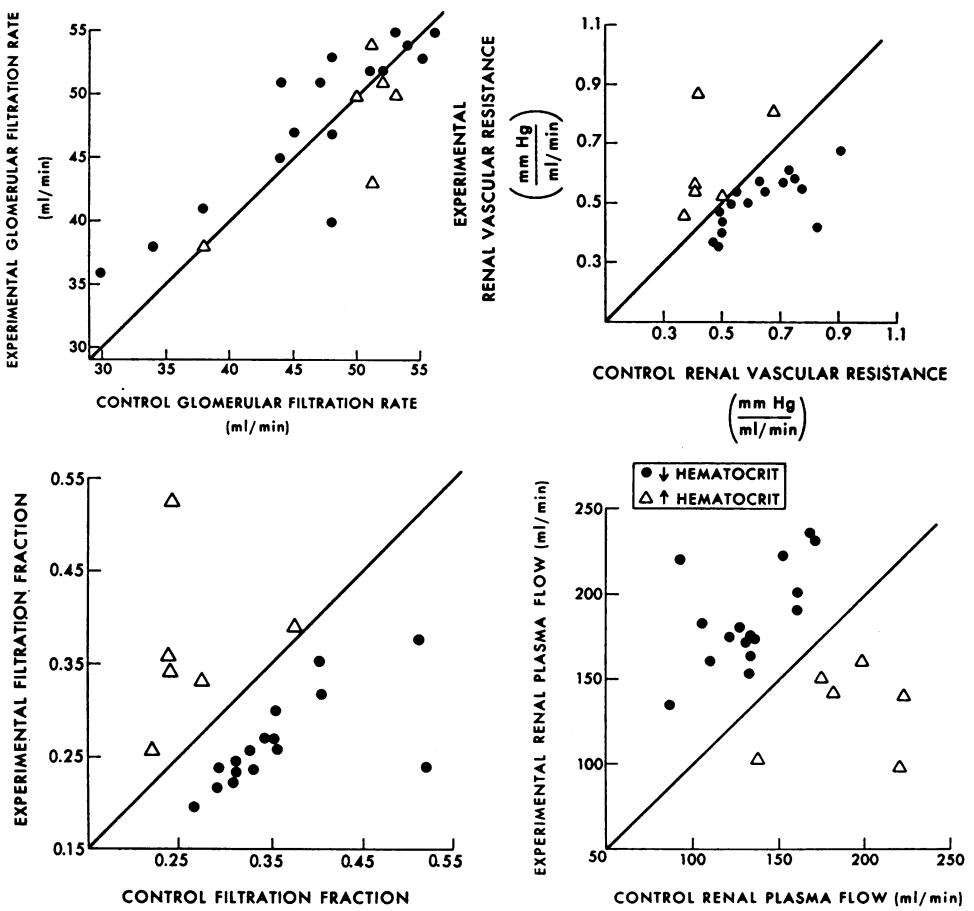

FIGURE 2 The effect of decreasing and increasing the hematocrit during hydropenia on renal hemodynamics. Values are from the same collection periods represented in Fig. 1, and the same method of display is used. GFR was not significantly changed but filtration fraction and renal vascular resistance changed directly and renal plasma flow inversely with changes in hematocrit.

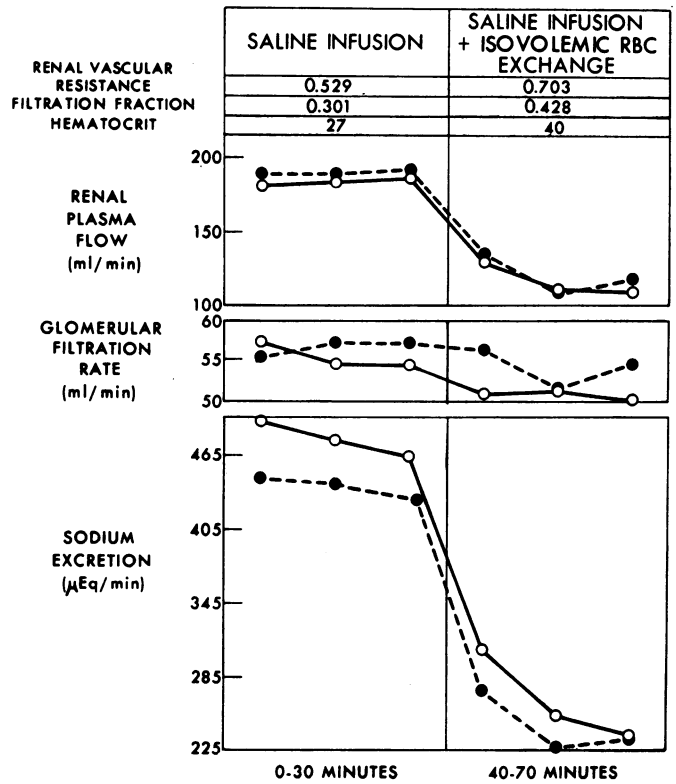

FIGURE 3 The effect of increasing hematocrit during sustained volume expansion with an infusion of isotonic saline in one animal. After stabilization of urine flow, three 10-min control periods were obtained, then isovolemic exchange with fresh, washed red blood cells was performed as the saline infusion was continued. The increase in hematocrit diminished sodium excretion and renal plasma flow as renal vascular resistance and filtration fraction increased. Values are for each kidney of a single animal.

properties. While this possibility is entirely speculative, it can be dealt with best by using native plasma as done in the present studies.

The present finding that decreasing the hematocrit in hydropenic animals increases the excretion of sodium raised the possibility that the decreased hematocrit associated with the infusion of red blood cell–free solutions, such as plasma and saline, may be a factor involved in the natriuretic response to volume expansion. The observations of de Wardener, Mills, Clapham, and Hayter (16), that natriuresis during saline infusion can be dissociated from the rate of glomerular filtration and mineralocorticoid activity, have led to investigations attempting to define further these additional natriuretic mechanisms. Recent studies have demonstrated the roles of renal perfusion pressure (11, 13, 14), renal vascular resistance (11, 26) plasma protein concentration (11, 26), and plasma sodium concentration (27, 28) in the natriuretic response to volume expansion. In the present study we examined the effect of increasing the hematocrit to normal values during sustained volume expansion with either saline or plasma. In both the saline and plasma expansion studies, increasing the hematocrit to a similar degree had a consistent effect on sodium and potassium excretion, solute-free water reabsorption and renal hemodynamics (Figs. 3–6). As in the hydropenic experiments, this effect of increased hematocrit to diminish sodium excretion was independent of changes in renal perfusion pressure or plasma protein concentration. In fact, in most of the studies the plasma protein concentration diminished slightly as hematocrit was increased, and this change alone would be expected to increase, rather than decrease, sodium excretion. This effect of an increased hematocrit to decrease the excretion of sodium during the infusion of saline or plasma is consistent with the conclusion that a decrease in the hematocrit during such infusions contributes to the natriuretic response, and adds an additional compositional factor to the mechanism of natriuresis during volume expansion.

The results of the present study also afford some information concerning potential mechanisms whereby acute changes in the hematocrit affect sodium excretion. In some experiments during both hydropenia and volume expansion, small changes in glomerular filtration rate occurred in a direction which could have accounted, at least in part, for the changes in sodium excretion. In a number of experiments however, either no change in glomerular filtration rate was measured or the change was in the opposite direction to that which could explain the effect on sodium excretion. These findings thus sugggest that the predominant effect of changes in hematocrit may be due to an effect on sodium reabsorption. This conclusion is supported by the observation of Knox et al. (23) that lowering the hematocrit in dogs was associated with a decrease in fractional reabsorption in the proximal tubule although these latter authors reported no significant change in the rate of excretion of sodium. In the present study, an effect of hematocrit on the proximal tubular reabsorption is suggested also by the increase in potassium excretion and solute-free water reabsorption which accompanied the natriuresis; changes consistent with an increased delivery of sodium to the distal nephron.

Changes in hematocrit were associated with several alterations in renal hemodynamics which have been implicated in the regulation of sodium reabsorption, including renal plasma flow or renal blood flow (15, 29), renal vascular resistance (11, 26, 30), and filtration fraction (7, 8, 31, 32). Pharmacologically induced renal vasodilatation has been shown previously to affect sodium reabsorption and excretion independent of any change in glomerular filtration rate (30, 33), and this effect has been attributed to a transmission of hydrostatic pressure to the peritubular circulation (26). It seems possible that the effects of changes in the hematocrit on sodium reabsorption could be mediated through the same pathways as induced renal vasodilatation. The influence of the hematocrit on renal vascular resistance and renal blood flow would seem to be related most likely to the known effect of hematocrit on whole blood viscosity (19, 34) rather than to a change in vascular

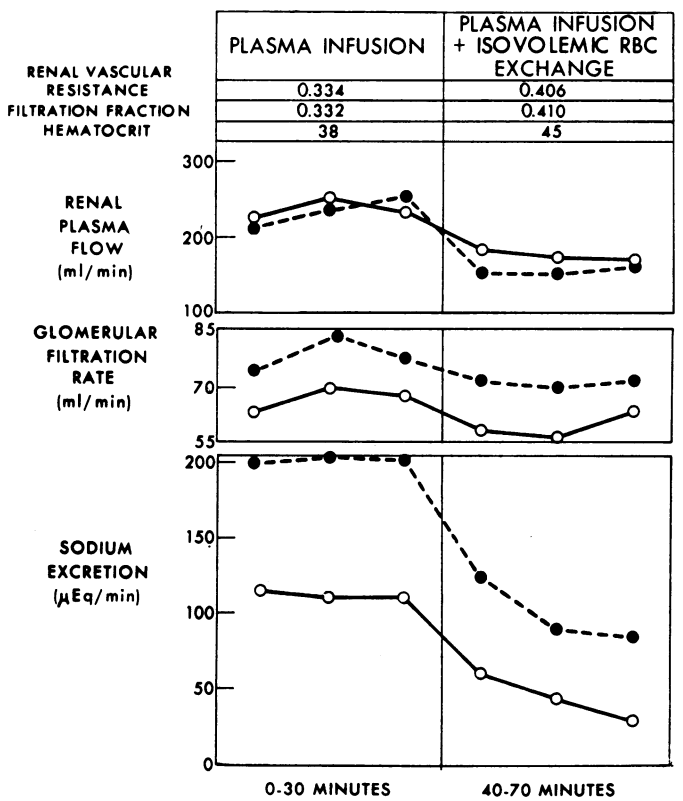

FIGURE 4 The effect of increasing hematocrit during sustained volume expansion with an infusion of the animal's own plasma. The protocol was the same as described in Fig. 3. The increase in hematocrit diminished sodium excretion and renal plasma flow as renal vascular resistance and filtration fraction increased.

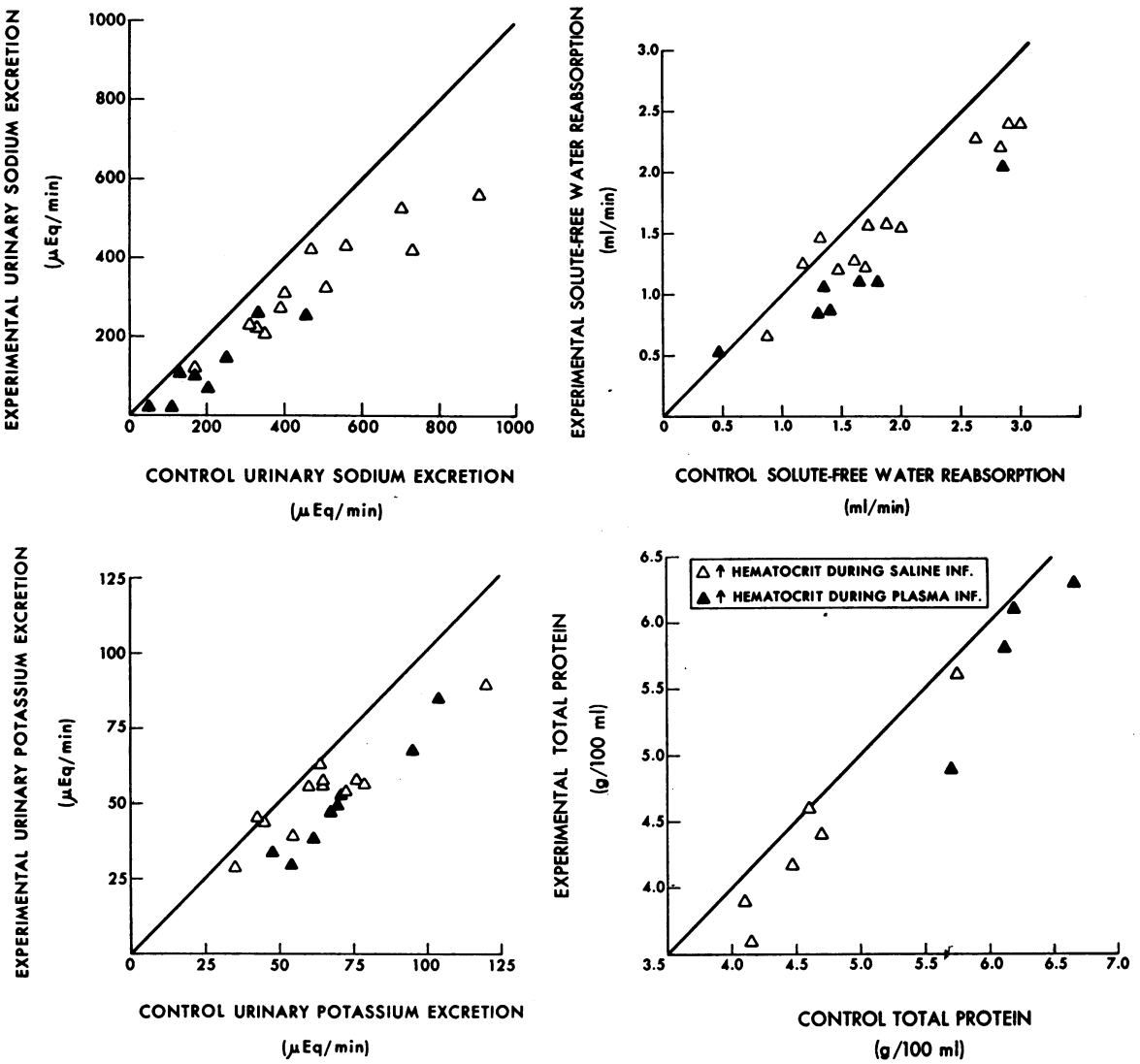

FIGURE 5 Summary of effects on electrolyte excretion and solute-free water reabsorption of increasing hematocrit during sustained volume expansion with either saline (△) or plasma (▲). Each value is the mean of three to five 10-min periods for one kidney except the results for plasma concentration of protein which are expressed for each animal. The increased hematocrit was associated with a decrease in sodium and potassium excretion and solute-free water reabsorption, as plasma protein concentration diminished slightly. These results are similar to those found when the hematocrit was increased during hydropenia (see Fig. 1).

tone. Moreover, in the present experiments, this effect of hematocrit on the renal hemodynamics was found to be independent of renal sympathetic innervation.

In addition to affecting renal vascular resistance, changes in hematocrit in the present study were associated with parallel changes in filtration fraction. Through its effect on postglomerular plasma protein concentration, filtration fraction may be a determinant of tubular sodium reabsorption (7, 8, 31, 32). These changes in filtration fraction related directly to changes in the hematocrit and could be due to an affect of the hematocrit on the resistance to flow at the level of the efferent arteriole (21). However, changes in the hematocrit also potentially may affect filtration fraction independent of an alteration in postglomerular resistance to flow. At a constant rate of total renal blood flow and glomerular filtration rate a decrease in hematocrit will result in an increase in the rate of plasma flow and a

decrease in the fraction of the plasma flow filtered. Therefore, changes in the hematocrit can result in directionally similar changes in filtration fraction in the presence of unchanged glomerular filtration pressure, postglomerular resistance, or total renal vascular resistance. In the present study, however, changes in the hematocrit were generally accompanied by alterations in renal vascular resistance and renal blood flow which also could have contributed to the observed changes in filtration fraction. These effects of the hematocrit on re-

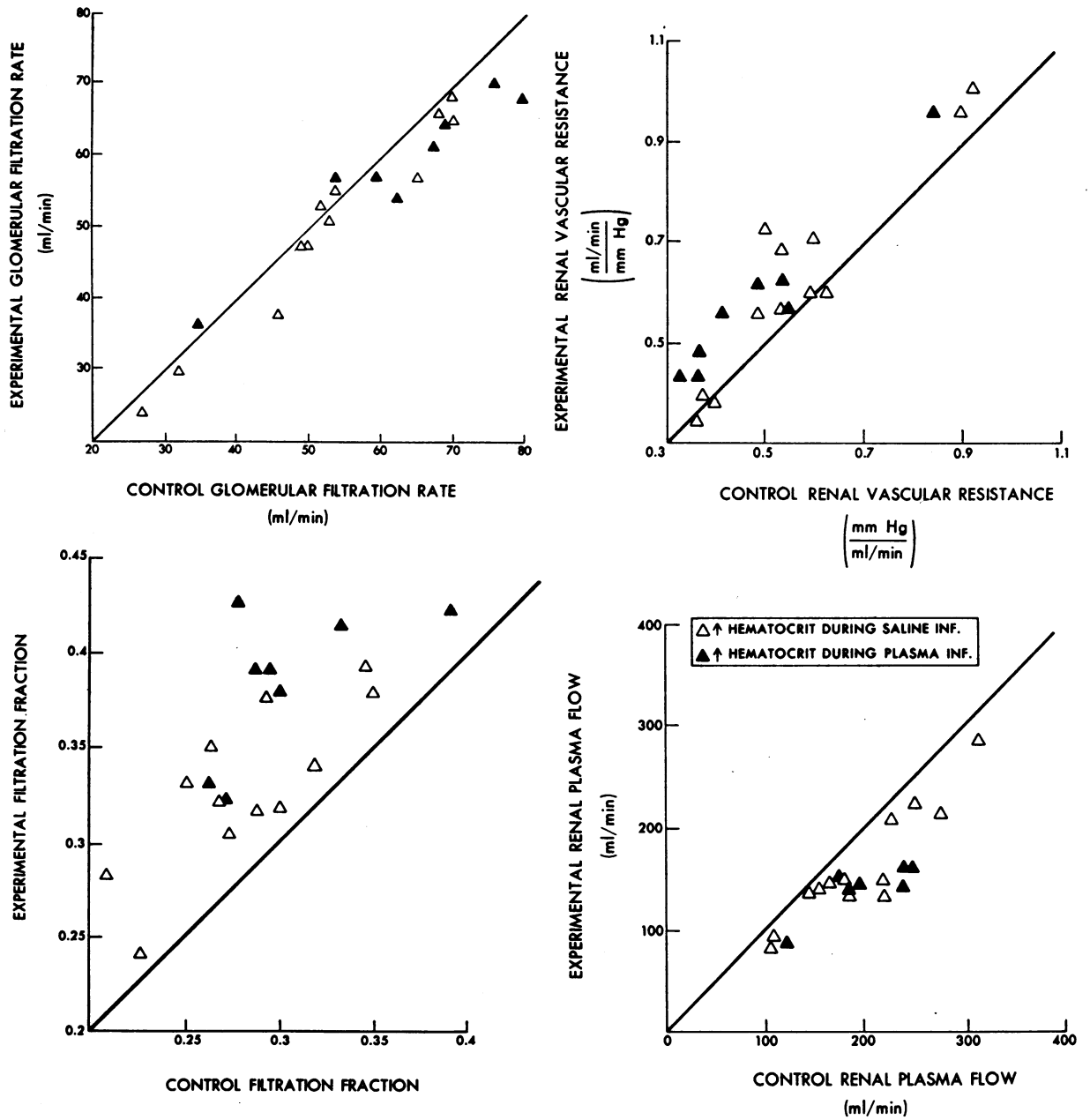

FIGURE 6 Summary of effects on renal hemodynamics of increasing hematocrit during sustained volume expansion with either saline or plasma. Representation is the same as in Fig. 5. The increased hematocrit was associated with small decreases in glomerular filtration rate in most experiments and a substantial fall in renal plasma flow as both filtration fraction and renal vascular resistance increased. These effects on hemodynamics are similar to those observed when the hematocrit was increased during hydropenia (see Fig. 2). Inf. = infusion.

nal vascular resistance and filtration fraction may significantly alter Starling forces in the peritubular circulation, including both hydrostatic and oncotic pressure and thereby possibly influence sodium reabsorption (7, 8, 11, 26).

Alternatively, the level of the hematocrit and thus viscosity in the intrarenal circulation could possibly affect the distribution of intrarenal blood flow between cortical and juxtamedullary nephrons. A redistribution of glomerular filtrate between superficial and juxtamedullary nephrons has been reported to occur during saline infusion and such an effect could increase sodium excretion by overloading the reabsorptive capacity of superficial nephrons (35). Theoretically, changes in the hematocrit could influence the excretion of sodium as a consequence of such a redistribution of intrarenal renal blood flow and glomerular filtration rate. However, recent studies by Nashat, Scholefield, Tappin, and Wilcox (36), using xenon washout curves to measure the intrarenal distribution of renal blood flow, suggest that a decrease in hematocrit primarily increases medullary, rather than cortical blood flow.

In the present investigation, the quantitative effect on sodium excretion of similar changes in the hematocrit was greater in the presence of volume expansion than in the hydropenic state, particularly at the higher rates of sodium excretion found during saline infusion. There are several potential explanations which might account for this difference. The effect of increasing the hematocrit on sodium excretion could be proportional rather than absolute in nature, so that quantitatively greater effects are found at the higher rates of sodium excretion. Secondly, the results of some studies indicate that volume expansion with saline may impose a limit on sodium reabsorption in the distal nephron (37, 38). Thus, if the effect of hematocrit on sodium reabsorption occurs primarily in the proximal tubule, a greater net effect on the urinary excretion of sodium may be found during circumstances which inhibit distal sodium reabsorption. If this effect on sodium reabsorption in the distal nephron requires a diminution in plasma protein concentration, as is implicit in other studies (39), this could also provide an explanation for the quantitatively smaller effect on sodium excretion of increasing the hematocrit during plasma infusion as compared to saline infusion. A third explanation might be that the hematocrit per se has qualitative or quantitatively different effects on variables influencing sodium excretion during volume expansion and in hydropenia. There was no evidence for this latter possibility in the present study, and, in particular, the effects of changing the hematocrit on renal hemodynamics were quantitatively similar in the hydropenic and volume expanded animals.

In summary, the results of the present investigation demonstrate an effect of hematocrit on sodium excretion during both hydropenia and volume expansion, and this effect appears to be independent of changes in glomerular filtration rate. The accompanying changes in potassium excretion and solute-free water reabsorption suggest that the influence of hematocrit on sodium excretion is due to changes in reabsorption in the proximal nephron. This effect of hematocrit on sodium reabsorption and excretion may be mediated by alterations in peritubular oncotic and hydrostatic pressures resulting from changes in filtration fraction and renal vascular resistance.

ACKNOWLEDGMENTS

We wish to express our gratitude to Lisbeth Streiff, Deborah Simmen, and Clyde Young for technical assistance and to Janice Gonsalves for secretarial assistance.

These studies were supported in part by grant AM 12753 from the National Institutes of Health; Grant NGR 05025007 from the National Aeronautics and Space Administration; and Academic Senate and Harris Robert Benjamin Grants from the University of California, San Francisco.

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