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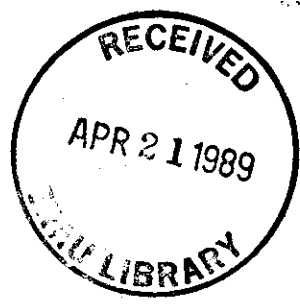
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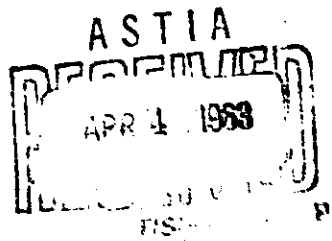
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THE DEVELOPMENT OF
 REVERSIBLE HEMATURIA
 AND OLIGURIA
 FOLLOWING ELEVATION OF
 RENAL VENOUS PRESSURE



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FEDERAL AVIATION AGENCY
 AVIATION MEDICAL SERVICE
 AEROMEDICAL RESEARCH DIVISION
 CIVIL AEROMEDICAL RESEARCH INSTITUTE
 OKLAHOMA CITY, OKLAHOMA

JANUARY 1963

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2. Renal Function
3. Hematuria

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FOREWORD

Proteinuria (the presence of albumin and other proteins in the urine in quantities exceeding the usual values) may be disqualifying for aviation medicine certification purposes, if the underlying cause for the proteinuria is an active or advanced nephritic condition (inflammation of the kidney). Other causes of proteinuria may or may not be disqualifying.

This report deals with a category of proteinuria which is not disqualifying if accurately diagnosed. This category is that of reversible proteinuria found in certain persons following the assumption of various postures. If the mechanism underlying this category of proteinuria is clarified, improved diagnostic criteria can be applied in resolving questionable certification cases.

This study provides information on the mechanism of reversible proteinuria, and indicates the direct relationship between the renal venous pressure and proteinuria. The study also describes the matter of hematuria (a number of red blood cells in the urine above the "normal" level) and its appearance following a sufficiently elevated renal venous pressure.

In addition to the postural effects leading to proteinuria, rapid changes of altitude may result in temporary or prolonged increases in inferior vena caval pressure (and consequently renal venous pressure) and proteinuria. In this respect, the Aviation Medical Examiner should be alert to the possible influence of an applicant's recent physical activity and flight experience on the urine chemistry as noted above.

This type of research will help the FAA to develop more accurately the aeronautical standards regarding proteinuria in airmen applicants. There is some disparity in this area at present, as evidenced by the fact that postural proteinuria is considered disqualifying by the U.S. Air Force, but not so by the FAA Aviation Medical Service.

THE DEVELOPMENT OF REVERSIBLE HEMATURIA AND OLIGURIA FOLLOWING ELEVATION OF RENAL VENOUS PRESSURE

T. E. Emerson
L. B. Hinchaw
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ABSTRACT

An investigation was completed to study the acute effects of elevated renal venous pressure in the development of reversible gross hematuria and oliguria. Both isolated and intact dog kidney preparations were utilized. Results demonstrate that gross hematuria was produced as renal venous pressure was elevated, but not until a relatively high pressure was produced. The degree of hematuria increased as the pressure was further elevated, but disappeared rapidly following restoration to control pressure. The effect of renal venous pressure elevation on urine flow rate was one of progressive oliguria after a critical pressure was reached, and eventually anuria at the highest pressures. This effect was also reversible.

Proteinuria has been reported following exercise and during radical changes in body posture (1). Winton (2) also noted its presence in some instances in the isolated perfused kidney following limited elevation of renal venous pressure. A number of explanations have been suggested (1) to account for this phenomenon, but its cause remains obscure. A series of experiments was therefore carried out on the isolated and intact dog kidney to investigate the acute effects of renal venous pressure elevation. The experimental preparations utilized in the present study are of particular value in that varied conditions of pressure are carefully controlled.

METHODS. *Isolated Kidneys:* Male and female dogs were intravenously anesthetized with sodium pentobarbital, 30 mg/Kg. Isolated dog kidneys were perfused with heparinized whole blood from an isolated heart-lung system (3). The kidney was transferred to the perfusion circuit without interruption of blood flow (4). The system was primed with whole blood from a donor dog, a kidney was taken from another, and a third dog supplied the heart and lungs. A constant renal artery pres-

sure was maintained with a Starling shunt device (range 100-150 mm Hg). Urine samples were collected from the catheterized ureter and urine flow rates were measured with a graduated cylinder and stopwatch. Renal venous pressure was elevated by progressively tightening a screwclamp on a length of large bore polyethylene tubing secured in the renal vein. All pressures were recorded using Statham pressure transducers connected to a Sanborn direct-writing recorder.

Intact Kidneys. The left kidney was exposed through a flank incision. The renal vein was either (a) cannulated and venous blood continuously returned to the jugular or femoral vein by a pump or (b) isolated, but otherwise undisturbed. In the first instance, venous pressure was elevated with a screwclamp on the tubing and pressure monitored through the tubing proximal to the clamp. In the latter case, a number 27 gauge needle was secured in the vein for pressure measurements and venous pressure was elevated by applying tension on the vein with a ligature placed distal to the needle. The ureter was catheterized with a small bore polyethylene tube and urine flow

rates were measured as described above. Mean systemic arterial pressure was monitored from a catheterized femoral artery and registered on a Sanborn direct-writing recorder.

Urine samples were collected in centrifuge tubes during a five or ten minute period and 1 cc samples of each collection period were centrifuged in Wintrobe tubes for urine hematocrit determination.

The renal venous pressure elevations were sustained for five or ten minutes at each pressure level.

RESULTS. The experimental data are summarized in Table 1. Results show that hematuria was present in all experiments following venous pressure elevation. The volume of red blood cells present in the urine is seen to be small and variable (0.1-1.8%). Urine flow rate decreased in all experiments to a variable degree (7 to 87% of control values). The large vein pressure necessary to produce hematuria appeared to be similar in both isolated (mean 53 mm Hg) and intact (mean 53 mm Hg) kidneys. Hematuria disappeared following return to control pressure. Figure 1 shows the decrease in urine flow rate for a wide range of renal venous pressures expressed on a percentage basis. Hematuria was not observed in either group until the urine flow rate was significantly reduced (mean of both groups: 44% of control).

Discussion. Results show that gross hematuria, including red blood cells and hemoglobin, appears when a relatively high venous pressure is produced. If the pressure is further elevated, the degree of hematuria increases and is sustained until control venous pressure is restored, at which time it disappears. Hemoglobinuria, present in the isolated kidney, was not present in the intact organ under conditions of increased renal venous pressure. Although absent at low venous pressures in the isolated organ, the subsequent appearance of hemoglobinuria at elevated pressures could be accounted for by increased levels of plasma hem-

oglobin (due to the perfusion pumps) or decreased tonicity of urine (due to the absence of ADH).

There are at least three possible sites of entrance for red blood cells into the urine. One possible region is the peritubular capillaries. Swann described these as being "leaky" and suggested that a free communication exists between these vessels and the interstitial space (5). Evidence for the existence of large pores in the peritubular capillaries is given by electron microscopy studies (6). However, a mechanism for getting the red cells into the urine from the interstitial space has not been proposed. Another possible entrance site for red blood cells is through the glomerular capillaries by virtue of an increased glomerular pressure, although it seems unlikely that venous pressure transmissions would be effective in increasing transmural pressure at the glomerular membrane (7). A factor opposing the glomeruli as the site of entrance is that renal venous pressure elevations are transmitted rapidly to the proximal tubules (7, 8), which would decrease the glomerular transmural pressure. The third and most plausible site is "pores" in the walls of blood vessels bordering the renal pelvis which could be temporarily opened, allowing for passage of red cells into the urine. The reverse phenomenon, pyelovenous backflow, has been produced by maintaining moderate intrapelvic pressure for a sustained period, or for a shorter period at higher pressures (9, 10). A direct, temporary communication can be established between the kidney pelvis and the large superficial pelvic veins by elevated intrapelvic pressure (9). The possibility of "veno-pelvic" flow merits further investigation.

As reported by Winton (2), oliguria was obtained following renal venous pressure elevation. At least two factors may contribute to the development of the oliguria: Partial ureteral obstruction, allowing more time for reabsorption of water from the tubules (11) and increased back pressure with decreased glomerular filtration rate (2, 12-14).

TABLE I

EFFECT OF INCREASED RENAL VENOUS PRESSURE ON THE KIDNEY*
HEART-LUNG-KIDNEY PREPARATION

Exp. No.	Hematuria	% RBC in Urine	Urine Flow (% of Control)	Renal LVP* (mm Hg)
1	+	1.5	10	63
2	+	0.9	69	61
3	+	0.1	87	25
4	+	1.0	17	58
5	+	1.8	86	55

INTACT DOG KIDNEY PREPARATION

1	+	0.5	7	68
2	+	0.5	42	43
3	+	0.6	44	62
4	+	1.0	43	38
5	+	0.1	39	60
6	+	0.2	37	63

*Minimal Increase in Large Vein Pressure Required to Elicit Hematuria

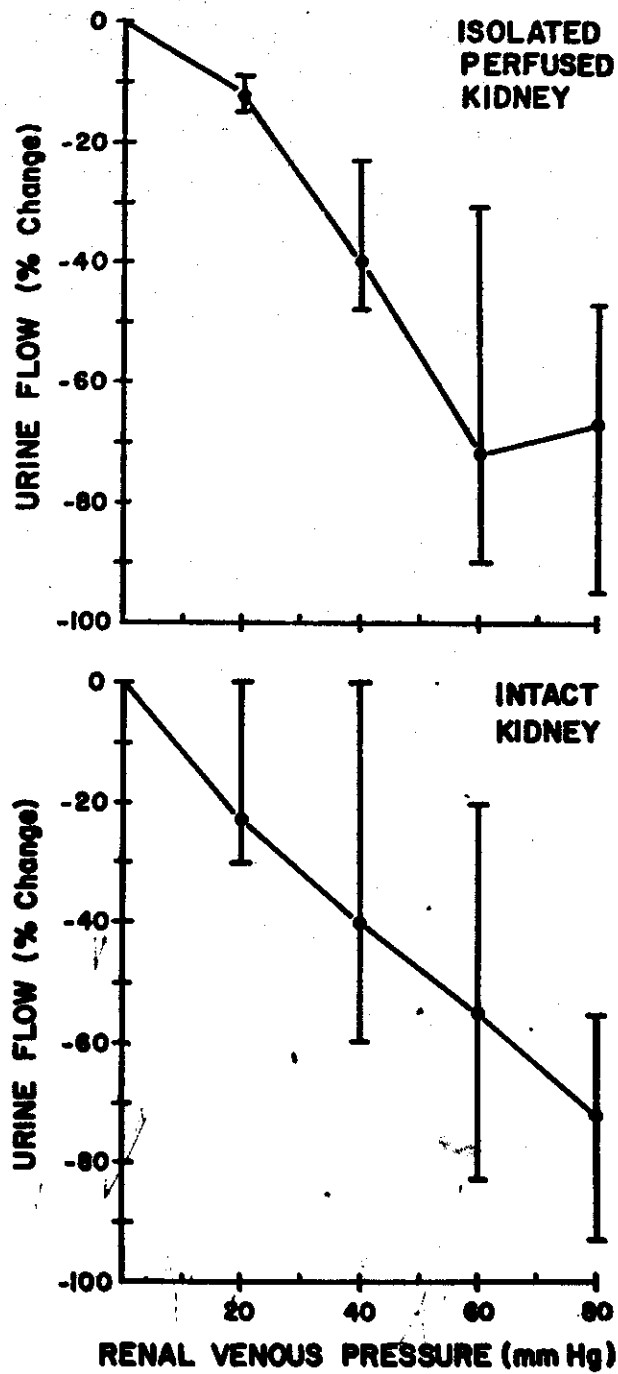


FIGURE 1. The effect of increasing renal venous pressure on the urine flow rate. The vertical lines indicate the total range at the various pressures.

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