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Role of Atrial Natriuretic Peptide in the Response to Blood Volume Expansion in the Weanling Rat[1]

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ABSTRACT. After acute blood volume expansion (BVE) in the rat, diuresis and natriuresis are reported to be minimal in rats 20 to 30 d of age, but increase to mature levels by 40 d of age. To evaluate the role of atrial natriuretic peptide (ANP) and its renal action in BVE, anesthetized Sprague-Dawley rats were studied at 25 to 30 (group I) and 45 to 50 d of age (group II). Hematocrit, mean arterial pressure, glomerular filtration rate, urine flow rate, urine sodium excretion, urine cyclic GMP excretion, and plasma ANP concentration ([ANP]) were measured before and after infusion of donor littermate whole blood, 2.5% body wt (BVE), and in time controls (no BVE) in each group. Baseline hematocrit, mean arterial pressure, and glomerular filtration rate were greater in group II than group I, but urine flow rate, urine sodium excretion, urine cyclic GMP excretion, and [ANP] did not differ. BVE caused a prompt increase in urine flow rate, urine sodium excretion, and [ANP], but not urine cyclic GMP excretion, in both groups, but there was no difference in the response between groups. Additional groups of rats of the same ages as groups I and II studied using a protocol similar to that of a previous report also showed the "mature" diuretic and natriuretic response even in the younger animals. We conclude that there is no further maturation of the renal response to acute BVE in the euvolemic rat after 25 d of age. The increase in [ANP] after acute BVE in the immature weanling rat is consistent with a role for ANP in mediation of the renal response. (*Pediatr Res* 27: 396–400, 1990)

Abbreviations

ANP, atrial natriuretic peptide
cGMP, guanosine 3′·5′-cyclic monophosphate
FE_{Na}, fractional excretion of sodium
MAP, mean arterial pressure

Compared to the adult, the immature kidney responds to acute volume expansion with attenuated diuresis and natriuresis (1–4). Since the discovery of ANP, there has been considerable interest in defining the role of ANP in volume regulation during development (5). We have recently shown (6) that the reduced diuresis and natriuresis after acute saline volume expansion in the preweaning compared to the postweaning rat is associated with a smaller increase in plasma ANP concentration and in urinary excretion of cGMP, the putative second messenger for ANP (7). We also found that experimental increase in the hematocrit by isovolemic exchange transfusion further reduced diuresis and cGMP excretion after saline expansion in preweaning rats 15 to 20 d of age (6).

Bengele and Solomon (1) reported that acute blood volume expansion in postweaning Wistar rats resulted in little diuretic and natriuretic response until 30 to 35 d of age, with achievement of the adult efficient pattern of renal response by 45 to 50 d of age (1). These authors concluded that the renal response to blood volume expansion in the rat matures relatively late when compared to the development of other renal functions previously investigated, and raised the possibility that developmental changes in a natriuretic hormone may be responsible.

Our study was designed to test the hypothesis that alterations in circulating ANP levels and/or in the renal response to ANP are responsible for the changing renal response to acute blood volume expansion during postweaning development in the rat. The ages chosen for study were 25 to 30 d and 45 to 50 d of age, as these ranges represent the immature and adult renal responses to blood volume expansion as described previously (1).

MATERIALS AND METHODS

Experiments were performed in 71 male and female Sprague-Dawley rats. All studies were performed with the highest standards of humane care, to minimize discomfort to the experimental animals. The male/female ratio was 0.92 and did not differ significantly between groups. Litter size was reduced when necessary to a maximum of 12 pups to minimize interanimal variation in body size. Rats were kept with their mothers until weaning at 21 d of age, after which they were fed standard Rat Chow (Purina 5012, Ralston-Purina, St. Louis, MO). Animals were studied at 25 to 30 d (group I; C = time control, E = volume expanded) or at 45 to 50 d of age (Group II C and E). On the night before the experiment, animals were fasted but were allowed access to water. The rat was anesthetized with sodium pentobarbital (Abbott Laboratories, North Chicago, IL), 50 mg/kg injected intraperitoneally, and was placed on a thermostatically controlled heating table to maintain body temperature 37 to 38°C. Additional doses of pentobarbital (1 mg) were infused i.v. as needed during the experiment to maintain adequate anesthesia. A tracheostomy was performed, and a carotid artery was cannulated for blood withdrawal and monitoring of MAP using a Statham 23ID transducer coupled to a recorder (Hewlett-Packard 2544, Hewlett-Packard Co., Palo Alto, CA). A jugular vein was cannulated for infusion of 0.85% saline con-

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taining [^{3}H]inulin (New England Nuclear, Boston, MA), 10 μCi/mL, at 12 mL/kg/h. The left ureter was exposed through a midabdominal incision, and was cannulated for collection of urine in weighed cups.

After a 60-min equilibration period, five 20-min urine collections were obtained, with 300 μL of blood being drawn from the carotid catheter in the middle of each urine collection. All blood withdrawn was replaced with an equal volume of littermate whole blood. Groups IC and IIC served as time controls. In groups IE and IIE, immediately after starting the third urine collection, donor littermate whole blood collected in 0.5 M EDTA was infused i.v. over 2 min (vol = 2.5% body wt). Blood donors were the same sex as recipients. After the last urine collection period, 1 mL blood was drawn for plasma ANP concentration, the rat was killed by i.v. infusion of saturated KCl solution, and the kidneys were removed and weighed.

Four additional groups of rats were treated identically except that at the end of the first urine collection period, 1 mL blood was withdrawn for measurement of plasma ANP concentration, and was replaced with an equal volume of donor littermate whole blood. Three min after completing the second urine collection (*i.e.* 1 min after completion of blood volume expansion in groups IE and IIE), a second 1-mL blood sample was withdrawn for plasma ANP assay. After this, the animal was killed as above.

Unlike the results of Bengele and Solomon (1), our study failed to show a difference in the renal response to acute blood volume expansion between 25 and 50 d of age (see Results). To determine whether differences in experimental protocol account for the discrepancy, two additional groups of rats were studied. Group III consisted of five rats 25 to 30 d of age, whereas group IV was comprised of five rats 45 to 50 d of age. Each animal was fasted with access to water the night before the experiment, and was anesthetized with sodium pentobarbital as described for groups I and II. The animal was placed on a thermostatically controlled heating table, a tracheotomy was performed, and a jugular vein was cannulated for infusion of saline (0.85%) containing [^{3}H] inulin, 10 μCi/mL, at 0.5 mL/h in animals of group III and at 1.0 mL/h in group IV. A carotid artery was cannulated for monitoring MAP as above, and for blood sampling. The bladder was cannulated through a small suprapubic incision, and the majority of the bladder dome was tied off to reduce dead space. After a 2-h equilibration period, three 20-min urine collections were obtained, after which littermate donor blood (vol equal to 2.3% body wt) was infused over 2 to 3 min through the carotid artery catheter. Three additional 20-min urine collections were obtained. Blood samples (300 μL) were obtained midpoint in each of the six urine collections and were replaced with equal volumes of blood donor, as described above. After the experiment, each animal was killed as described above.

Assays. ANP. Plasma ANP concentration was determined by RIA as previously described by this laboratory (8). Briefly, plasma samples were acid extracted over octyldecylsilane cartridges (Sep-Pak, Waters Assoc., Milford, MA) and the assay was performed using rabbit anti-rat ANP antibody (Peninsula Laboratories, Belmont, CA). Intraassay variation was 4.6%, whereas interassay variation was 9.7% (8).

Sodium. Urine sodium concentration was measured by flame photometer (Corning Model 435, Corning Glass Works, Medfield, MA), with lithium as the internal standard.

Urine cGMP. Urine cGMP concentration was determined by RIA as described previously (8).

[^{3}H]inulin activity. Radioactivity was measured in aliquots of plasma and urine using a β-scintillation counter (Beckman Instruments, Irvine, CA). Inulin clearance was calculated as the product of urine flow and the urine-to-plasma radioactivity ratio.

Statistical Analysis. Urine collection data were factored by kidney wt to control for changes due to growth alone. Comparison between periods in groups I and II were performed by analysis of variance for repeated measures, whereas comparisons between groups for each period were performed by 2-way analysis of variance, with age and blood vol expansion as determinants. Comparisons between the four groups (Table 2) were performed by one-way analysis of variance. The significance of change in variables resulting from volume expansion (Table 2) was measured by the *t* population test compared to zero. The efficiency of the diuretic response to acute blood volume expansion in each group was calculated as the fraction of infused volume excreted in the 60 min after the start of infusion (1). Statistical significance was defined as $p < 0.05$.

RESULTS

The characteristics of rats used in the experimental studies are shown in Table 1. There was no difference in age, body wt, or kidney wt between the experimental protocols within either age group. Body wt and kidney wt increased approximately 2-fold between the age ranges studied. As shown in Table 2 and Figure 1, hematocrit at the beginning of the experiment was approximately 43 vol % in group I and 48% in group II. There was no change in hematocrit during the experiment in the time controls for either group, but there was a 4 to 7% increase as a result of blood volume expansion in each group. As shown in Table 2 and Figure 2, MAP was higher in group II than group I, and increased gradually as a result of blood volume expansion in both groups. GFR (factored for kidney wt) was initially higher in group II than group I, and did not change significantly during the experiment in either group (Fig. 3).

As shown in Figure 4, urine flow rate (factored for kidney wt) was not different between groups during the initial two control periods, and increased 4-fold as a result of blood volume expansion in each group. There was no effect of age on the diuretic response to blood volume expansion. A similar response to blood volume expansion was found for sodium excretion (Fig. 5). As with urine flow, there was no difference in the natriuretic response to blood volume expansion between between rats of groups I and II. Although urinary cGMP excretion tended to increase with time in each group, there was no significant change during the experiment in control or volume expanded groups, and no effect of age (Fig. 6). Baseline plasma ANP concentration was 116 ± 13 pg/mL in group I and 121 ± 20 pg/mL in group II. These values are similar to those in the adult rat (99 ± 21 pg/mL) (9). Plasma levels of ANP did not change in time control groups and increased to 614 ± 161 pg/mL in rats of group I and to 484 ± 91 pg/mL in animals of group II 1 minute after completion of vol expansion (Fig. 7). There was no difference between groups in peak ANP levels. Sixty min after blood volume expansion, plasma ANP concentration had decreased nearly to control levels (Fig. 7).

Shown in Table 2 are the results of experiments in groups III and IV. For each of the variables measured, there were no

Table 1. *Characteristics of rats**

Group, treatment	No. of animals	Age (d)	Body wt	L kidney wt
			(kg × 10^3)	
IC C	11	27.3 ± 0.5	65.3 ± 4.0	0.39 ± 0.03
IC A	10	27.9 ± 0.5	69.4 ± 3.9	0.38 ± 0.02
IE C	8	27.4 ± 0.5	71.2 ± 2.7	0.44 ± 0.02
IE A	6	27.5 ± 0.6	70.7 ± 1.4	0.45 ± 0.02
IIC C	6	46.7 ± 0.6	163.8 ± 11.4	0.80 ± 0.10
IIC A	5	45.5 ± 1.2	176.6 ± 9.7	0.87 ± 0.06
IIE C	9	47.0 ± 0.4	174.9 ± 9.1	0.89 ± 0.06
IIE A	6	46.3 ± 0.2	165.1 ± 15.6	0.80 ± 0.08
IIIE C	5	27.4 ± 0.5	70.6 ± 5.1	0.49 ± 0.03
IVE C	5	46.4 ± 0.2	159.2 ± 8.4	0.92 ± 0.05

* C C, time control clearance study; C A, time control ANP measurement; E C, volume expanded clearance study; E A, volume expanded ANP measurement.

Table 2. *Physiologic measurements**

Groups	IE	*p*	IIE	III	*p*	IV
Hematocrit control (%)	43.2 ± 0.9	<0.005	48.2 ± 0.9	42.6 ± 1.1	<0.005	47.5 ± 0.5
Hematocrit change (%)	4.8 ± 1.5†	NS	7.1 ± 0.3†	7.6 ± 0.4†	NS	4.0 ± 0.6†
MAP control (kPa)	12.7 ± 0.4	<0.001	16.9 ± 0.3	14.3 ± 0.5	NS	15.8 ± 0.5
MAP change (kPa)	1.4 ± 0.4	NS	0.1 ± 0.5	0.9 ± 0.5	NS	−0.1 ± 0.5
GFR control (mL/min/g KW)	0.65 ± 0.11	NS	1.01 ± 0.09	0.93 ± 0.11	NS	0.71 ± 0.05
GFR change (mL/min/g KW)	0.11 ± 0.13	NS	0.06 ± 0.09	0.38 ± 0.13†	NS	0.19 ± 0.13
UV control (μL/min/g KW)	13.8 ± 3.2	NS	11.2 ± 2.1	8.1 ± 1.6	NS	7.9 ± 1.9
UV control (% of saline vol infused)	81 ± 16	NS	56 ± 9	97 ± 22	NS	95 ± 19
UV change (% of blood vol infused)	117 ± 16	NS	106 ± 10	141 ± 13	NS	91 ± 23
FE_{Na} control (%)	NA		NA	1.04 ± 0.24	NS	0.96 ± 0.42
FE_{Na} change (%)	NA		NA	5.09 ± 0.64†	NS	4.79 ± 0.81†

* Control = mean of preexpansion periods (1 and 2, groups I and II; 1 to 3, groups III and IV); expanded = mean of postexpansion periods (3 to 5, groups I and II; 4 to 6, groups III and IV); change = difference between expanded and control periods. NA, plasma Na not available; KW, kidney wt.

† Change different from zero ($p < 0.05$).

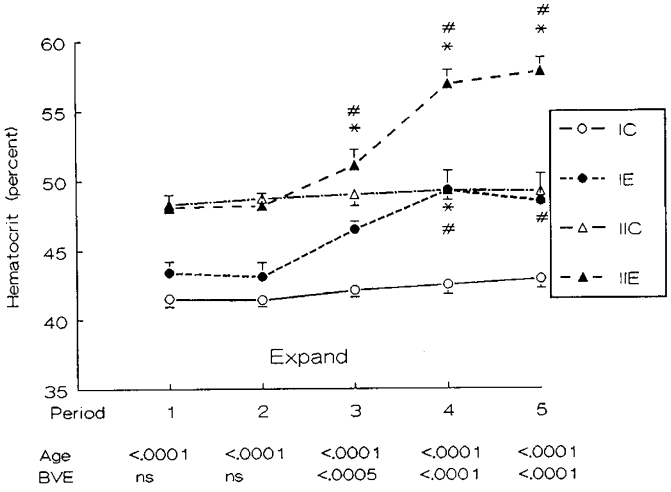

Fig. 1. Hematocrit during each of the urine collection periods for each group. In this and subsequent figures, values are mean ± SEM: * $p < 0.05$ *versus* same group, period 1; * $p < 0.05$ *versus* same group, period 2. *p* values (derived from two-way analysis of variance) at the bottom of the graph indicate differences between groups for each period as a function of each variable. There was no significant difference between groups for the interaction of both variables. Number of rats in each group: IC 11; IE eight; IIC six; IIE nine.

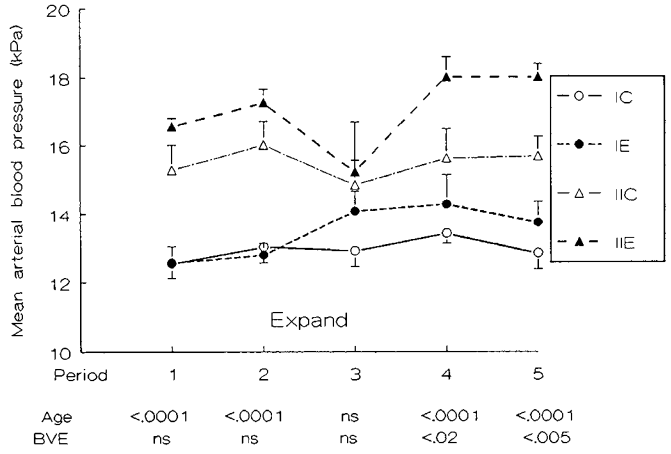

Fig. 2. Mean arterial blood pressure. Number of rats in each group: IC 11; IE eight; IIC six; IIE nine.

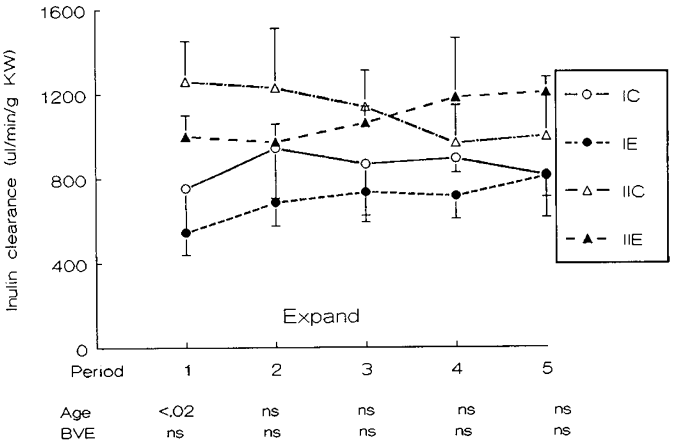

Fig. 3. Inulin clearance factored for kidney wt (*KW*). Number of rats in each group: IC five; IE six; IIC five; IIE five.

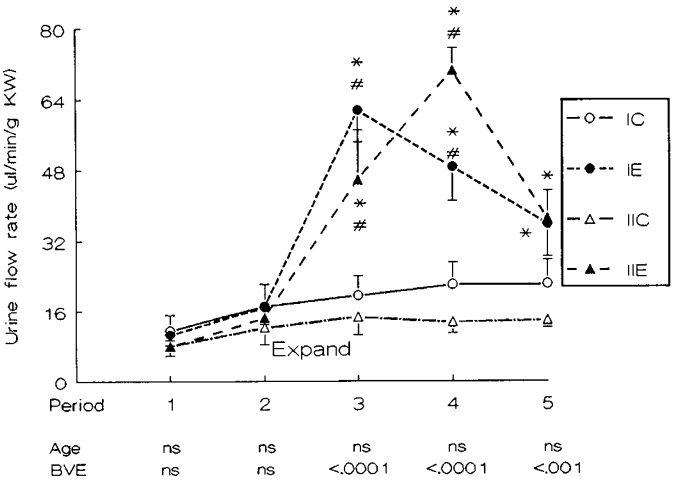

Fig. 4. Urine flow rate factored for kidney wt (*KW*). Number of rats in each group: IC 11; IE eight; IIC six; IIE nine.

significant differences between groups I and III or between groups II and IV. As for groups I and II, initial hematocrit was 5% lower in group III than in group IV, and the increase in hematocrit due to blood volume expansion was not different between groups III and IV. There was no significant difference between groups III and IV in MAP or in GFR. Control urine flow rate was not different between groups III and IV, and the fraction of volume infused excreted during the initial three control periods was not

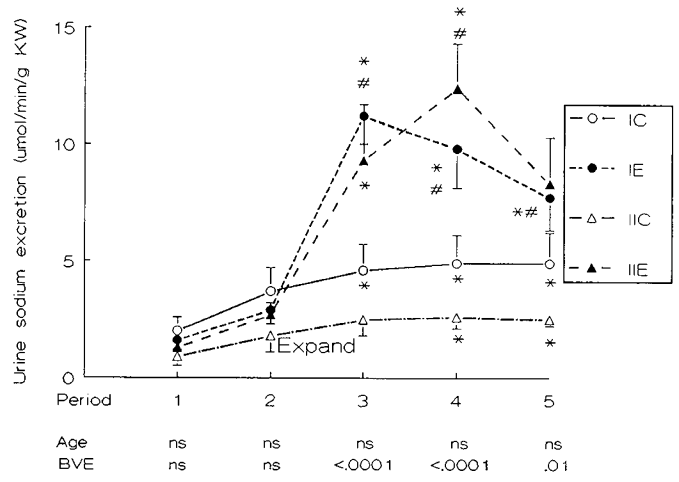

Fig. 5. Urine sodium excretion factored for kidney weight (*KW*). Number of rats in each group: IC 11; IE eight; IIC six; IIE nine.

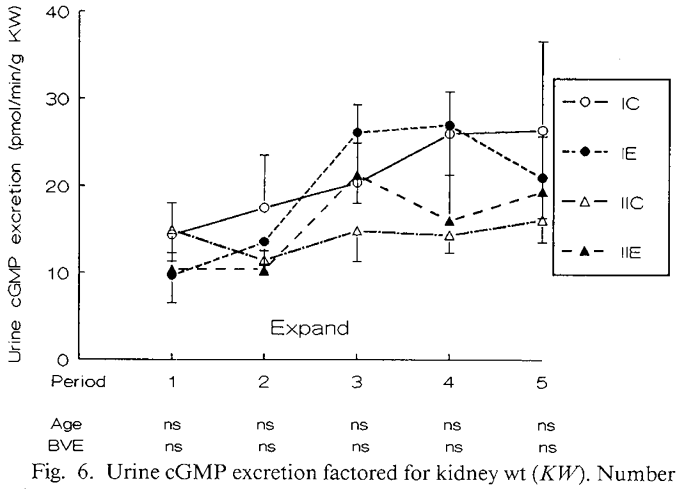

Fig. 6. Urine cGMP excretion factored for kidney wt (*KW*). Number of rats in each group: IC eight; IE six; IIC five; IIE eight.

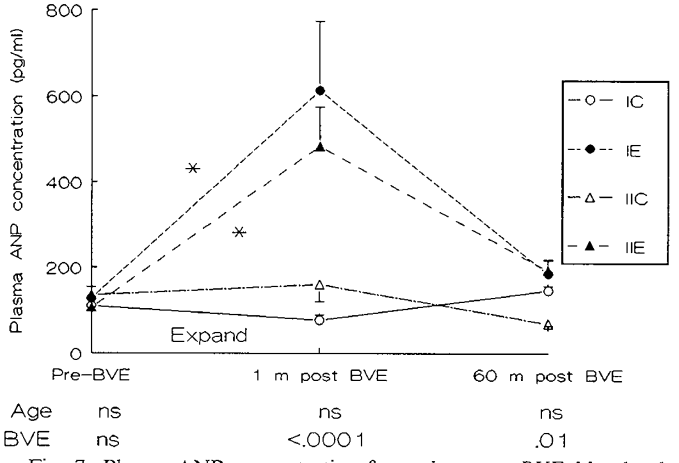

Fig. 7. Plasma ANP concentration for each group. *BVE*, blood volume expansion; $^{*}p < 0.05$ within group (paired *t* test).

different from 100% in either group. Control fractional sodium excretion also did not differ between groups III and IV, suggesting that the initial volume state was similar in the two age groups. Most importantly, the fraction of blood volume infused excreted as urine in the three periods after expansion, as well as the increase in fractional FE_{Na}, were not different between the two age groups.

DISCUSSION

The results of our study show that acute blood volume expansion in the immature rat 25 to 50 d of age resulted in a prompt increase in urine flow and sodium excretion. The diuresis and natriuresis were associated with a marked increase in plasma ANP concentration, consistent with a role of ANP in mediation of the effects. Inasmuch as the renal response to acute blood volume expansion in the adult rat can be largely inhibited by prior injection of MAb against ANP (10), it is likely that ANP release and the renal response to blood volume expansion are similar in the postweaning rats. It should be noted that both the present study and that of Hirth *et al.* (10) were performed in anesthetized rats, because others have shown that rats made autoimmune to ANP have blunted diuresis and natriuresis after acute saline volume expansion when anesthetized, but not when conscious (11). These authors postulated that ANP may have a role in volume homeostasis only in pathophysiologic states, and that the renal response to acute volume expansion in conscious animals may be mediated by other factors (11). Even in anesthetized animals, the contribution of ANP to the renal response to acute blood volume expansion may account for less than 50% of the diuretic and natriuretic response (12). Moreover, the early natriuretic response (occurring in the first 45 min after volume expansion) may be only minimally dependent on ANP levels (12). However, others have concluded that the renal response to acute blood volume expansion without hemodilution is primarily mediated by ANP because additional ANP infusion did not result in any synergistic increase in diuresis or natriuresis (9).

The lack of increase in GFR after acute blood volume expansion in our study suggests that the renal response is mediated by tubular rather than hemodynamic changes. Others have also failed to show an increase in GFR after acute blood volume expansion in the adult rat (9), whereas subsequent ANP infusion raised inulin clearance without further increasing natriuresis or diuresis (9). We found previously that ANP infusion in euvolemic rats increased GFR in adults but not in animals 34 to 37 d of age (8). However, the relationship between urine sodium excretion or cGMP excretion and plasma ANP concentration were not different from adults (8). It is possible that acute blood volume expansion causes subtle changes in renal hemodynamics or GFR that were not detected in our study, such that their potential contribution to the observed renal response should not be discounted.

In the conscious adult rat, urinary cGMP excretion correlates well with natriuresis resulting from infusion of ANP, and is therefore thought to be a reliable marker of the renal response to circulating ANP (7). However, in our study, despite a 5- to 6-fold increase in plasma ANP levels after acute blood volume expansion in the young rat, there was no significant increase in urinary cGMP excretion. It is unlikely that our assay lacks sufficient sensitivity to detect an increase in urinary cGMP excretion, because we have found that acute saline expansion in the immature rat results in a significant change (6). The mechanism underlying this dissociation is unclear, but may relate to a transfusion-induced reduction in other stimuli for guanylate cyclase activation (such as endothelial-derived relaxant factor), increased cGMP-phosphodiesterase activity, or altered transport of cGMP into the tubular lumen. A recent study has also shown that dopamine enhances the diuretic and natriuretic action of ANP independent of urine cGMP excretion (13). It is therefore possible that the renal response to ANP released by blood volume expansion is mediated (or modulated) by dopamine (14) rather than by a guanylate cyclase-dependent mechanism.

In view of the study of Bengele and Solomon (1) using Wistar rats, the lack of change in the diuretic and natriuretic response to blood volume expansion from 30 to 45 d of age in Sprague-Dawley rats of our study was unexpected. There was a tendency for urine flow and sodium excretion to peak earlier (at 20 min after expansion) in rats of group I than in those of group II (40

min after expansion), although differences were not significant. Inasmuch as in the experimental clearance studies there were eight rats in group I and nine in group II, it is unlikely that lack of differences resulted from type II statistical error. There do not appear to be any significant differences in control MAP and GFR between comparably aged animals in groups I and II of our study and those of Bengele and Solomon (1). Differences in the experimental protocol between groups I and II of our study and the previous study include a lower baseline saline infusion rate, use of a bladder rather than a ureteral catheter, and a longer preexpansion control period in the latter (1).

To determine whether these differences could account for the discrepant findings, we studied two additional groups (III and IV) in which urine was collected by bladder catheter, and saline infusion rate and timing of experimental periods were identical to those of Bengele and Solomon (1). Fluid balance was achieved during the control period, and the "mature" pattern of diuresis was again demonstrated for both groups. In group III, control MAP and GFR tended to be higher than in younger rats of the previous study (1). Most notable is the difference in control fractional sodium excretion between group III (1.04%) and 24- to 31-d-old rats of the previous study (<0.3%), compared to the similarity of that of group IV (0.96%) and 44- to 51-d-old rats of the previous study (0.7–0.8%) (1). The increasing control FE_{Na} with age of animals in the former study (1), suggests that younger rats were more volume contracted than older animals. The change in FE_{Na} with volume expansion in groups III and IV (4.79–5.09%) compared to 0.154 to 1.896% in 24- to 51-d-old rats of the previous study (1) indicates that animals in the previous study were more volume contracted even after blood volume expansion. It therefore appears that differences in intravascular volume most likely account for the discrepant results between the two studies. Although it is possible that the altitude at which the previous study was performed (5000 feet) may have affected the results, no mention is made of blood replacement for that withdrawn for sampling (1). It is more likely that failure to replace blood withdrawn during the experiment caused a proportionately greater volume depletion in the younger rats and resulted in the apparent limited renal response in smaller animals as well as a smaller magnitude of response at all ages. The outcome of a subsequent study by these investigators in which somatic growth was accelerated by reducing the size of litters at birth (15) is consistent with this conclusion. Thus, acceleration of the development of the "mature" response to blood volume expansion in fast growing rats indicates an association of the response with body size rather than with the chronologic age of the animal (1). This conclusion is consistent with the anatomic development of the kidney, which is complete by approximately 25 d, but is not affected by alteration in the time of weaning (16, 17). Thus, maturation of the renal response to acute volume expansion in the rat may involve changes in the release (18) or renal action of ANP (19) during the preweaning period. In euvolemic animals, there does not appear to be a further development of the response after weaning at 21 d.

In summary, acute blood volume expansion in the immature rat 25 to 50 d of age resulted in a prompt increase in plasma ANP concentration, urine flow, and sodium excretion. Despite a 5- to 6-fold increase in plasma ANP concentration with expansion, there was no significant increase in urine cGMP excretion. The dissociation of cGMP excretion from sodium excretion may be due to the action of ANP at a step independent of (or distal to) guanylate cyclase. In rats ranging in age from 25 to 50 d of age, there was no developmental change in ANP concentration or in the diuretic or natriuretic response to acute blood volume expansion. It is likely that these findings differ from those of a previous report in which younger postweaning rats had a limited renal response to blood volume expansion as a result of proportionately greater volume contraction of the younger rats in that study (1). The difficulties inherent in the investigation of renal functional development require caution in interpretation and comparison of experiments in immature animals. Additional studies will be required to further elucidate the potential role for ANP in mediation of volume homeostasis in early development.

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REFERENCES

1. Bengele HH, Solomon S 1974 Development of renal response to blood volume expansion in the rat. Am J Physiol 227:364–368
2. Dean RFA, McCance RA 1949 The renal responses of infants and adults to the administration of hypertonic solutions of sodium chloride and urea. J Physiol (Lond) 109:81–97
3. Kleinman LI, Reuter JH 1974 Renal response of the new-born dog to a saline load: the role of intrarenal blood flow distribution. J Physiol (Lond) 239:225–236
4. Misanko BS, Evan AP, Bengele HH, Solomon S 1979 Renal response to Ringer expansion in developing rats. Biol Neonate 35:52–59
5. Smith FG, Sato T, Varille VA, Robillard JE 1989 Atrial natriuretic factor during fetal and postnatal life: a review. J Dev Physiol (in press)
6. Chevalier RL, Thornhill BA, Peach MJ, Carey RM 1990 Hematocrit modulates the response of ANP to volume expansion in the immature rat. Am J Physiol (in press)
7. Wong KR, Xie MH, Shi LB, Liu FY, Huang CL, Gardner DG, Cogan MG 1988 Urinary cGMP as biological marker of the renal activity of atrial natriuretic factor. Am J Physiol 255:F1220–F1224
8. Chevalier RL, Gomez RA, Carey RM, Peach MJ, Linden JM 1988 Renal effects of atrial natriuretic peptide infusion in young and adult rats. Pediatr Res 24:333–337
9. Paul RV, Ferguson T, Navar LG 1988 ANF secretion and renal responses to volume expansion with equilibrated blood. Am J Physiol 255:F936–F943
10. Hirth C, Stasch JP, John A, Kazda S, Morich F, Neuser D, Wohlfeil S 1986 The renal response to acute hypervolemia is caused by atrial natriuretic peptides. J Cardiovasc Pharmacol 8:268–275
11. Skata M, Greenwald JE, Needleman P 1988 Paradoxical relationship between atriopeptin plasma levels and diuresis-natriuresis induced by acute volume expansion. Proc Natl Acad Sci USA 85:3155–3159
12. Barbee RW, Trippodo NC 1987 The contribution of atrial natriuretic factor to acute volume natriuresis in rats. Am J Physiol 253:F1129–F1135
13. Katoh T, Sophasan S, Kurakawa K 1989 Permissive role of dopamine in renal action of ANP in volume-expanded rats. Am J Physiol 257:F300–F309
14. Hegde SS, Jadhav AL, Lokhandwala MF 1989 Role of kidney dopamine in the natriuretic response to volume expansion in rats. Hypertension 13:828–834
15. Bengele HH, Solomon S 1976 Development of the renal response to blood volume expansion in normal and fast-growing rats. Am J Physiol 231:832–836
16. Speller AM, Moffat DB 1977 Tubulo-vascular relationships in the developing kidney. J Anat 123:487–500
17. Boss JMN, Dlouha H, Kraus M, Krecek J 1963 The structure of the kidney in relation to age and diet in white rats during the weaning period. J Physiol 168:196–204.
18. Pollock DM, Banks RO 1985 Lower atrial natriuretic activity in the newborn versus adult rat. Min Elect Metab 11:41–44
19. Braunlich H, Solomon S 1987 Renal effects of atrial natriuretic factor in the rats of different ages. Physiol Bohemoslov 36:119–124