Quantitative evaluation of renal function in healthy Beagle puppies and mature dogs

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Abstract

Daily urinary collection and assessment of glomerular filtration rate (GFR) and effective renal plasma flow were performed in ten 2-month-old Beagle puppies and ten 6–9 year-old Beagle dogs to identify age-associated differences in renal function. The most striking differences in puppies compared to mature dogs were a higher daily urinary volume (+65%), GFR (+87%), free water reabsorption (+159%), a lower daily protein excretion (−88%), and fractional excretion of phosphorus (−35%). Renal function in Beagle puppies, but not mature dogs, was also quite different compared to data published in younger adult dogs.

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1. Introduction

Renal function in dogs is generally assessed in routine practice using indirect plasma and urine markers. More quantitative and sensitive methods, such as assessment of glomerular filtration rate (GFR), and fractional excretion, are also performed in clinical referral centers and under experimental conditions.

Nevertheless, few data on the influence of age on canine renal function have been published. In contrast to young adult animals, kidney physiology in puppies and mature dogs is poorly documented, whereas these represent two populations of interest in nephrology. For example, chronic renal failure (CRF) is observed not only in mature dogs but also in young animals with congenital renal disease. Few studies have documented renal function in healthy puppies. Most of these have involved measurements of a limited number of renal variables (GFR (Horster and Valtin, 1971; Goldsmith et al., 1979; Russo and Nash, 1980; Goldsmith et al., 1986; Lane et al., 2000), renal blood flow (Horster and Valtin, 1971; Jose et al., 1971; Aschinberg et al., 1975; Goldsmith et al., 1979), fractional excretion (Goldsmith et al., 1979; Russo and Nash, 1980; Lane et al., 2000) and protein excretion (Lane et al., 2000) at a given time of postnatal development, between day 2 (Horster and Valtin, 1971) and week 27 (Lane et al., 2000). Moreover, some relevant variables (urine specific gravity (USG)(Horster and Valtin, 1971; Lane et al., 2000), or protein excretion (Lane et al., 2000)) have rarely or, in the case of daily urine volume, never been published in puppies.

Extensive assessment of renal function under physiological conditions has paradoxically never been done in middle-aged dogs, while it is generally assumed empirically that renal function decreases with age in adult
dogs, as in humans. Moreover, we are unaware of a comparison of renal function between two canine populations with quite different ages.

The aim of this study was to extensively assess renal function in Beagle puppies and mature dogs using the same procedures.

2. Materials and methods

2.1. Animals

Ten male Beagle pups aged 65–68 days and weighing 3.0 ± 0.63 kg, and ten adult female Beagle dogs, which were previously reproductive females, aged between 6 and 9 years and weighing 13.6 ± 2.50 kg, were used.

Each dog was housed individually in facilities in accordance with animal care and use guidelines. Animals were fed once daily with specific commercial pet-food (mature dogs: 400 g/day (Harlan Teklad Dog Breeder Diet, Harlan Gannat, France); pups: 150 g/day (Medium Breed Puppy, Royal Canin, Aimargue, France). On the day of iohexol/PAH kinetics, dogs were fed after the final blood sample had been taken. Tap water was given ad libitum.

All the animals were considered clinically healthy based on physical examination, plasma biochemistry, urinary dipstick and USG. Blood pressure was not measured. All the measurements were performed in anoestrus.

2.2. Urine collection

After acclimation, dogs were placed for 4 days in metabolism cages for 24-h urine collection. Only urine taken on the last 2 days was used for analysis. All urine voided was collected at least twice daily and stored at 4 °C. Each morning after urine collection, the weight of the 24-h pooled urine was measured and USG was determined. Two aliquots (4 mL) of urine were centrifuged. Five milliliters of blood were sampled from the jugular vein before and after the 24-h urine collection for plasma biochemistry. Samples were stored at −20 °C until assay.

2.3. Pharmacokinetic studies

A pharmacokinetic study of iohexol and p-aminophippuric acid (PAH) was performed, as previously described (Laroute et al., 1999), within 3–7 days after the last 24-h urine collection. The nominal doses for iohexol (Omnipaque 300, Nycomed Imaging AS, Oslo, Norway) and PAH were 64.7 and 10 mg/kg, respectively. The PAH solution (100 mg/mL) was prepared immediately before administration by dissolving PAH (Sigma, Saint Quentin Fallavier, France) in sterile 0.9% NaCl. Iohexol and PAH were administered successively within 20 s via a catheter inserted into the cephalic vein. One-mL blood samples were obtained from the jugular vein at 0 (just before administration), 2, 5, 10, 20, and 30 min, and 1, 1.5, 2, 3.5, and 6 h in adult dogs, and 0, 2, 10, 30 min, and 1, 2, and 3 h in puppies. Blood was placed in a heparinised tube and centrifuged (1000g, 10 min, 4 °C). Two aliquots of plasma were stored at −20 °C until assays.

2.4. Urine and plasma biochemical assays

The following urine and plasma variables were determined using routine procedures: creatinine, phosphorus, sodium, potassium, chlorides, calcium, and osmolality.

Proteinuria was determined according to a modified Bio-Rad Protein method. Ten microlitres of urine was placed in 96-well plates with 250 µL of diluted dye reagent (Bio-Rad Protein Assay, Bio-Rad Laboratories, GmbH, München, Germany). The spectrophotometric determination of the dye-protein complex was assayed with a microplate reader (μQuant, Bio-Tek Instruments, Winooski, VT, USA) at 595 nm after 5 min incubation at room temperature. The quantitation limit of the assay was 50 µg/mL and within and between-day precision was lower than 10%.

2.5. Iohexol and PAH assays

Plasma concentrations of PAH and iohexol were simultaneously determined by high-performance liquid chromatography (Laroute et al., 1999). The within-day and between-day precisions were determined. Quality control samples were assayed in replicates of six on three separate days of assay at three different nominal fortification levels for each test article. The mean and standard deviation were calculated for each concentration on each day of assay. The within-day and between-day precisions were expressed by the relative standard deviation (coefficient of variation), as explained previously (Lynch, 1998).

Accuracy was determined from the between-day precision test and expressed by the difference between the mean of the results and the nominal concentration of the quality control samples (Lynch, 1998; Findlay et al., 2000).

2.6. Calculation of renal parameters

The following parameters were determined for all biochemical variables (x):

Quantity excreted \( (Q_x) = \) urinary concentration \( \times \) urine volume \( (V) \),

Urinary clearance \( (Cl_x) = Q_x / \) mean plasma concentration.
The mean plasma concentration was the mean of the values obtained at the beginning and the end of the collection period.

The fractional excretion (FE) of a substance was calculated by dividing the clearance of that substance by the measured urinary clearance of endogenous creatinine.

Moreover, the free water reabsorption (FWR) was calculated as follows:

\[
FWR = \frac{Cl_{osm} - V}{V}
\]

with \( Cl_{osm} \), the osmolar clearance.

The effective renal plasma flow (ERPF) and the glomerular filtration rate (GFR) were determined from the plasma clearance of PAH and iohexol, using a non-compartmental approach (Laroute et al., 1999). Plasma clearance (\( Cl, \) mL/kg/min) was determined as follows:

\[
Cl = \frac{\text{Dose}}{\text{AUC}}
\]

with dose (\( \mu g/kg \)), the exact dose of iohexol or PAH administered by intravenous route, and \( \text{AUC}\) (\( \mu g \text{ min/mL} \)), the area under the plasma concentration of iohexol or PAH vs. time curve. The filtration fraction (FF) was calculated by dividing the GFR value by the ERPF value.

The within- and between-day precisions of assays were lower than 6% for PAH and less than 13% for iohexol. The accuracy values for PAH and exo-iohexol were 106.3% and 101.3%, respectively. For both kinetics (Figs. 1 and 2), the extrapolated area was less than 15% of the total AUC. GFR was assessed by the plasma clearance of iohexol. Two stereoisomers, endo-iohexol and exo-iohexol, were identified, but their clearance values were very close (data not shown), as previously described (Laroute et al., 1999). Exo-iohexol, the most important stereoisomer (90% of the total iohexol concentration), was therefore used as a marker of GFR. GFR, FF, and ECFV were higher in puppies.

3. Results

Puppies had lower values \( (P < 0.001) \) of plasma sodium \( (140 \pm 1.3 \text{ vs. } 145 \pm 1.3 \text{ mmol/L}) \), creatinine \( (39 \pm 2.2 \text{ vs. } 55 \pm 5.6 \mu \text{mol/L}) \), and osmolality \( (288 \pm 6.7 \text{ vs. } 303 \pm 4.6 \text{ mOsm/kg}) \), and higher values \( (P < 0.001) \) of plasma potassium \( (5.1 \pm 0.36 \text{ vs. } 4.4 \pm 0.15 \text{ mmol/L}) \), calcium \( (2.9 \pm 0.06 \text{ vs. } 2.4 \pm 0.11 \text{ mmol/L}) \), and phosphorus \( (2.8 \pm 0.21 \text{ vs. } 1.1 \pm 0.20 \text{ mmol/L}) \). Plasma chloride concentration was similar in both groups \( (108 \pm 1.9 \text{ vs. } 108 \pm 1.8 \text{ mmol/L}) \).

The urinary volume \( (P < 0.001) \), USG \( (P < 0.05) \) and urine osmolality \( (P < 0.01) \) were significantly higher in puppies \( (28 \pm 4.9 \text{ mL/kg/day}, \ 1.042 \pm 0.007 \text{ and } 1572 \pm 400.0 \text{ mOsm/L}, \text{ respectively}) \) compared to values observed in mature dogs \( (17 \pm 9.2 \text{ mL/kg/day}, \ 1.035 \pm 0.008 \text{ and } 1241 \pm 338.4 \text{ mOsm/L}, \text{ respectively}) \). The total daily amount of proteins excreted in urine \( (Q_{proteins}) \) was higher \( (P < 0.05) \) in mature dogs \( (48 \pm 68.4 \text{ mg/kg of body weight}) \) than in puppies \( (6 \pm 1.9 \text{ mg/kg of body weight}) \). The mean value of urinary protein concentration in 24-h urine was 160 ± 82 and 3260 ± 4201 mg/L in puppies and mature dogs, respectively. \( Q_{proteins} \) showed large interindividual variations in mature dogs \( \text{range: } [2.2, 201.9] \) compared to puppies \( \text{range: } [3.8, 8.8] \). The between-day coefficient of variation was 24% and 35% in puppies and mature dogs, respectively.

The within- and between-day precision of assays were lower than 6% for PAH and less than 13% for iohexol. The accuracy values for PAH and exo-iohexol were 106.3% and 101.3%, respectively. For both kinetics (Figs. 1 and 2), the extrapolated area was less than 15% of the total AUC. GFR was assessed by the plasma clearance of iohexol. Two stereoisomers, endo-iohexol and exo-iohexol, were identified, but their clearance values were very close (data not shown), as previously described (Laroute et al., 1999). Exo-iohexol, the most important stereoisomer (90% of the total iohexol concentration), was therefore used as a marker of GFR. GFR, FF, and ECFV were higher in puppies.
Calcium 0.24 ± 0.149 a 0.099 ± 0.060
Chloride 0.033 ± 0.00664 b 0.011 ± 0.00552

Urinary clearance (mean ± SD, mL/kg/min) and fractional excretion (mean ± SD, %) of electrolytes in puppies and old dogs

<table>
<thead>
<tr>
<th>Electrolyte</th>
<th>Puppies</th>
<th>Old dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>0.0085 ± 0.00454</td>
<td>0.0067 ± 0.00351</td>
</tr>
<tr>
<td>Potassium</td>
<td>0.48 ± 0.0906 a</td>
<td>0.33 ± 0.168</td>
</tr>
<tr>
<td>Chloride</td>
<td>0.033 ± 0.00664 b</td>
<td>0.011 ± 0.00552</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.014 ± 0.00842 a</td>
<td>0.0039 ± 0.00208</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>0.73 ± 0.145</td>
<td>0.75 ± 0.310</td>
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</tbody>
</table>

Fractional excretion

<table>
<thead>
<tr>
<th>Electrolyte</th>
<th>Puppies</th>
<th>Old dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>0.14 ± 0.077</td>
<td>0.17 ± 0.082</td>
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<tr>
<td>Potassium</td>
<td>7.9 ± 1.60</td>
<td>8.1 ± 3.83</td>
</tr>
<tr>
<td>Chloride</td>
<td>0.54 ± 0.118 b</td>
<td>0.26 ± 0.127</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.24 ± 0.149 a</td>
<td>0.099 ± 0.060</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>12.0 ± 2.94 a</td>
<td>18.4 ± 7.01</td>
</tr>
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</table>

4. Discussion

Our results demonstrate that renal function in puppies and mature adult dogs differed considerably for most variables. Some drawbacks in our study design need to be discussed. First, repeated assessment of renal variables between birth and advanced age in the same subjects would have been more relevant but is unrealistic in species with a long life expectancy, like dogs. Secondly, the gender of the groups was not the same. We first assessed renal function in male puppies because some were earmarked for a separate study (Chetboul et al., 2001). Unfortunately, mature male Beagle dogs are more difficult to obtain compared to reproductive females in experimental Beagle colonies. The sex difference is potentially a serious limit in our experimental design. To our knowledge however, the only difference which is mentioned in the literature is that urine osmolality in female dogs is about 17% lower than in male dogs (Izzard and Rosborough, 1989).

In the same study, no significant difference was observed between adult male and female dogs for GFR values or for plasma creatinine, electrolytes and osmolality. Moreover there is no previous report of a gender difference for the fractional excretion of electrolytes. The age of our female dogs was representative of the age (about 6.5–7 years (Polzin et al., 1989)) of canine patients which are likely to be brought to clinicians for suspected CRF. A third limit is the difference in diet between each group, fed according to usual recommendations. Although it might have been more appropriate to give the same diet to all dogs, the nutritional requirements of puppies are quite different from those of mature dogs. The amount of food given was based on the manufacturer’s recommendations. The most important differences between the diets for mature dogs and puppies were apparent for calcium (1.6% and 1.0%), phosphorus (1.15% and 0.8%), and protein (25% and 32%) contents. Na intake may influence water intake and extracellular fluid volume. The dietary sodium contents were quite similar (0.47% and 0.35% for mature dogs and puppies, respectively), and the usual values for commercial diets. The corresponding average Na intakes, based on food consumption, were 6 and 8 mmol/kg/day respectively. This difference may also explain the observed differences in renal function, as sodium intake may affect total water intake and ECFV. Nevertheless, renal function remained unchanged in adult dogs with moderate renal impairment and fed either a low-sodium diet (0.18%) or a high-sodium diet (1.3%) (Greco et al., 1994).

Urine volume and USG were higher in puppies than in mature dogs. Urine volume in mature dogs seems relatively lower than what would have been expected from established values, i.e. about 20–40 mL/kg/day, but is similar to those previously determined in adult dogs, i.e. 12 ± 5.5 mL/kg/min (DiBartola et al., 1980). Ideally, the urinary bladder should have been completely emptied at the beginning and the end of the collection period. Nevertheless, such a procedure is very difficult in puppies (Lane et al., 2000). The extended time of collection moreover reduced this potential error in estimation of urine volume. The first 2 days were not taken into account because micturition was erratic on the first day and animals became accustomed to the metabolic cage after 1–2 days. USG values were within the
reference range. However, the ratio of urine to plasma osmolality, an indicator of renal concentrating capacity, was about six in puppies and four in mature dogs. This value rises from 2 to 7 between the age of 2 and 77 days after birth (Horster and Valtin, 1971). In adult dogs, it is about 6 (DiBartola et al., 1980), i.e. higher than in our mature dogs, which may indicate a lower ability of the kidney to concentrate urine in older dogs. 

\[ Q_{\text{proteins}} \] was about 8-fold higher in mature dogs than in puppies. \[ Q_{\text{proteins}} \] in puppies (6 ± 1.9 mg/kg/day) was similar to that determined previously in 11-week-old puppies (5 ± 2.2 mg/kg/day) (Lane et al., 2000), but lower than that observed in adult dogs (14 ± 7.7 mg/kg/day) (DiBartola et al., 1980). This difference may result from an increase in glomerular capillary pore density and surface area with age (Goldsmith et al., 1986), leading to increased ultrafiltration of proteins, or from the lower plasma protein concentration in puppies compared to mature dogs, potentially explained by lower liver synthesis of proteins (Wolford et al., 1988). As previously shown in rats (Casadevall et al., 1995), \[ Q_{\text{proteins}} \] in mature dogs (48 ± 68.4 mg/kg/day) was much higher than in puppies, and than in younger adult dogs (DiBartola et al., 1980). It showed both a large interindividual, and also, to a lesser extent, intraindividual variability, especially in mature dogs. This has previously been reported in adult dogs for urinary protein concentrations (range: 200–2200 mg/L, mean ± SD: 1340 ± 625 mg/L) and excretion (range: 4.55–28.3 mg/kg/day, mean ± SD: 14 ± 7.7 mg/kg/day) (DiBartola et al., 1980). In our study, three mature dogs were abnormally proteinuric (mean values over 2 days: 99, 122 and 202 mg/kg/day), i.e. \[ Q_{\text{proteins}} > 20 \text{ mg/kg/day} \] (DiBartola, 2000). The functional consequence of this proteinuria is unclear as other renal variables, especially GFR, were similar to those of normally proteinuric animals. Another dog showed \[ Q_{\text{proteins}} \] only on 1 day (day 1: 45 mg/kg/day; day 2: 13 mg/kg/day), which illustrates the need to repeat measurements to confirm proteinuria. Higher proteinuria in the older dogs may reflect an increased incidence of glomerular pathology with aging. On the other hand, proteinuria can arise from non-renal causes and physiological protein excretion by the canine kidney has been poorly investigated. Further studies are therefore needed to see if mature dogs with proteinuria are more prone to develop renal disease. GFR was unaltered under our conditions which at least indicates that proteinuria was not associated with an abnormally low GFR value.

Whatever the marker, GFR (expressed in mL/kg/min) nevertheless was much higher in puppies than in mature dogs. Insulin and endogenous creatinine clearance have been shown to be similar in puppies (Bovee et al., 1984). The mean plasma iohexol clearance was 7% and 32% higher than the endogenous creatinine clearance in puppies and mature dogs, respectively. Such a discrepancy is difficult to explain here, as urinary insulin clearance (considered as the reference method) was not assessed. In contrast to human neonates, renal development continues beyond birth in puppies, probably up to 15 weeks (Goldsmith et al., 1986; Lane et al., 2000). The predominant factor determining the rise in GFR during development is the increase in the surface area and pore density of the glomerular capillaries (Goldsmith et al., 1986).

In agreement with our results, endogenous creatinine clearance values are higher than normal adult values in puppies (Lane et al., 2000) and kittens (Hoskins et al., 1991). Lane et al. (2000) hypothesize that endogenous creatinine clearance decrease is due to a progressive increase in serum creatinine during this time, itself explained by an increase in muscle mass. This suggests that creatinine clearance is dependent on the serum concentration of creatinine. However, this assumption is incorrect, as serum creatinine concentration is a hybrid parameter that depends on the production of creatinine, its distribution, and its elimination (Watson et al., 2002). Therefore, the 30%-lower concentration in plasma creatinine concentration in puppies compared to mature dogs may in fact be explained by the 87%-higher GFR value, as previously suggested for kittens (Hoskins et al., 1991). However the higher value of volume of distribution of ioxel (i.e. ECFV) in puppies also suggests a higher total body water volume (which corresponds approximately to the volume of distribution of creatinine (Watson et al., 2002)). The lower plasma creatinine concentration in puppies may therefore result from an increase in both filtration and volume of distribution. From a practical point of view, the reference intervals for plasma creatinine should be different in puppies and adult dogs.

GFR values in the mature group are similar to values in younger adult dogs (Heiene and Moe, 1998). The common clinical assumption to consider any geriatric dog as potentially renal-impaired with its associated consequences (specific diet, dosage regimen adjustment), should therefore be reconsidered. In the past, it has also been hypothesized that mature dogs may be more sensitive to renal injury than young adults. Nevertheless, a unique study has clearly shown that GFR remained unaltered in geriatric dogs over 4 years after uninephrectomy (Finco et al., 1994). The higher prevalence of CRF in the geriatric population may be explained by the fact that CRF has a slow progression and that clinical onset occurs only at advanced age.

Interpretation of GFR values (expressed in mL/kg/min) for early diagnosis of CRF should take into account the age of the patient (at least in puppies). Another potential consequence of GFR changes in puppies is alteration in exposure to drugs cleared by the kidney, because drug dosage regimens are generally established in young healthy adults, that is in dogs with
much lower GFR values. Underexposure, leading to therapeutic failure, may therefore occur in 3–4 months old puppies. Inversely, because of the very low value of GFR at birth, the risk of overexposure in canine neonates is probably high. A careful monitoring of drug response is therefore recommended. Inversely, such a risk appears very limited in middle-aged dogs.

One of the issues arising from our results is the most appropriate way to scale GFR because age and body size were confounded factors in this study. GFR/ECFV was slightly lower in puppies than in mature dogs. New concepts of indexation of GFR to body size have been recently published (for a review, see Peters, 2004). Body surface area has been proposed as the reference for indexing physiological variables. However, the abandoning of such an indexation for GFR has been recommended (Turner and Reilly, 1995) and the formulae used to estimate body surface area in dogs are probably inaccurate (Price and Frazier, 1998). Because of the major role of the kidney in body water regulation, an indexation to ECFV has been proposed (Gleathill et al., 1995; Peters, 2004). The difference between GFR and GFR/ECFV may be difficult to understand. First of all, GFR is a primary parameter whereas GFR/ECFV is a hybrid parameter and, from a pharmacokinetic point of view, inversely proportional to the mean residence time of the GFR marker. To illustrate this difference, let us consider a pump immersed in a well with a given volume of water available. GFR corresponds to the intrinsic performance of the pump (that is the maximal flow rate irrespective of the volume of water available) whereas GFR/ECFV is inversely proportional to the time required to empty the water from the well. The intrinsic performance of the pump remains the same whatever the volume of water available in the well, but the time required for emptying the well is dependent on both the performance of the pump and the volume of water in the well. From a physiological point of view, filtration efficiency, i.e. the amount of water filtered per min by the kidneys, depends on both the ECFV and GFR. However, the intrinsic ability of the kidney, that is its efficacy, may vary. During dehydration, for example, although the efficiency of the kidney is decreased because less water is available for the filtration process, its intrinsic ability may remain unchanged. Whether to assess the intrinsic efficacy of the kidney or evaluate its efficiency in the presence of a given volume of ECFV remains debatable in the field of nephrology. Such aspects should be documented in dogs with various diseased conditions when renal function and ECFV are changing simultaneously or independently.

In our study, ERPF was similar in each age group and similar to values obtained in younger adult Beagle dogs using the same assessment method (14.3 ± 3.6 mL/kg/min) (Laroute et al., 1999). PAH has been shown to be an adequate marker of ERPF in 12–16-week puppies, as in adult dogs (Horster and Valtin, 1971; Jose et al., 1971). Because of the difference in GFR values, FF was almost 70% higher in puppies than in mature dogs. ERPF, like GFR, increases very rapidly during the first months of life (Jose et al., 1971). In one study performed in 2.5-month-old puppies (Horster and Valtin, 1971), FF was lower (38%) than in our study, but the animals were anaesthetized, which may have affected renal hemodynamics.

Urinary clearance differed between puppies and mature dog for potassium, chloride and calcium. Cl osm was 4-fold higher in puppies, but very close to values in adult dogs (0.047 ± 0.022 mL/kg/min) (DiBartola et al., 1980). Mature dogs therefore seem to have a lower renal ability to excrete electrolytes. FE, i.e. the fraction of filtered materials that is not reabsorbed, however is more relevant because it is an indicator of tubular function. In the present study, FE of electrolytes in puppies and mature dogs were similar to values (%) considered normal, i.e. <1 for sodium and chloride, <20 for potassium, and <39 for phosphorus (DiBartola, 2000). FE of sodium and potassium was similar in both groups, whereas chloride and calcium excretion was about 108% and 142% higher in puppies. Inversely, the FE of phosphorus was 35% lower in puppies. The renal tubules in puppies therefore reabsorb more phosphorus and less calcium than in mature dogs. The plasma concentration of phosphorus in puppies, compared to mature dogs was 2.5-fold higher, whereas calcaemia was only 20% higher, as observed previously (Wolford et al., 1988). Higher calcaemia in puppies, associated with a higher FE of calcium, indicates that calcium availability is much higher in puppies. The 64% higher osmolar FE in puppies shows that more electrolytes escape reabsorption than in mature dogs. FWR was 160% higher in puppies than in mature dogs and about 2-fold higher than in adult dogs (0.039 ± 0.019 mL/kg/min) (DiBartola et al., 1980). Water balance in puppies seems quite different compared to mature dogs, as shown by the 70% higher extracellular fluid volume, assessed indirectly by the volume of distribution of exo-iohexol.

In conclusion, canine renal function is age-dependent, but changes are more marked in puppies than in mature dogs, compared to young adults. These results emphasize the need to define reference intervals for quantitative renal variables that are adapted to each category of age.

References


