Glucose Reabsorption in the Newborn Dog Kidney[1] (37100)

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(Introduced by E. C. Foulkes)

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Renal tubular function, as measured by maximum glucose reabsorption (1, 2) and para-aminohippurate (PAH) secretion (3), is less efficient in the newborn than in the adult. Glomerular filtration rate (GFR) is also lower in all newborn animals studied (4). In the newborn human, maximum glucose transport (T_{m_G}) is less developed than GFR, since the ratio T_{m_G}/GFR is lower in the newborn than in the adult. As part of our ongoing studies of renal maturation in the newborn dog, the present experiments were carried out to determine if such a relationship of relative glomerular preponderance exists in this species of newborn animal as well.

Fetterman *et al.* (5) have presented evidence that the newborn human has greater anatomical glomerulotubular nephron heterogeneity than does the adult. Since the degree of splay during glucose titration is a manifestation of glomerular tubular nephron heterogeneity (6) such titration was performed on newborn dogs to determine whether these animals exhibit functional nephron heterogeneity during the neonatal period.

Materials and Methods. Glucose transport experiments were performed on 22 mongrel puppies, 1–36 days of age, and on 9 adult dogs. In addition, splay analyses were successfully performed on 16 of these puppies and on 2 adults. Each animal was anesthetized with 20–30 mg/kg sodium pentobarbital iv. Polyethylene catheters were placed in the right jugular vein for glucose infusions, the right femoral vein for replacement fluids, the left femoral vein for inulin infusion, the femoral artery for blood pressure measurement and blood sampling, and in the right and left ureters for urine collection from the individual kidneys. Esophageal temperature was maintained at 38 ± 0.5°, using a thermistor-telethermometer-heat-ray tube feedback system. Fluid balance was maintained by replacing urinary salt and water losses with a solution containing (mEq/liter): 124 Na; 10 K; 110 Cl and 24 HCO_3.

In the glucose titration experiments, plasma glucose (P_G) was maintained at steady levels by infusing 50% glucose solution at a constant rate for 40–50 min. Plasma glucose levels were then changed by increasing or decreasing the infusion rate for subsequent determinations. During the last 10–20 min of each infusion, renal clearance studies were performed on each kidney. Six to eight such clearances at different plasma glucose levels were performed on each animal. Of the 16 splay analyses, 13 were obtained during progressively increasing glucose infusion rates, and 3 obtained during progressively decreasing infusion rates. Blood samples were taken at midpoint of each clearance period, centrifuged, and the plasma then was diluted and precipitated with 0.33 *N* perchloric acid. Urine samples collected during each clearance period were treated in the same manner as plasma. Samples were then frozen, and analyzed for glucose immediately after the experiment, in duplicate, by the glucose oxidase method, using a Beckman glucose analyzer. Inulin clearance (GFR) was measured using techniques described previously (15).

Results. A plot of glucose load (GFR × P_G) *vs* glucose transport (glucose load — excreted glucose) (Fig. 1A) failed to reveal a constant maximum glucose transport at high

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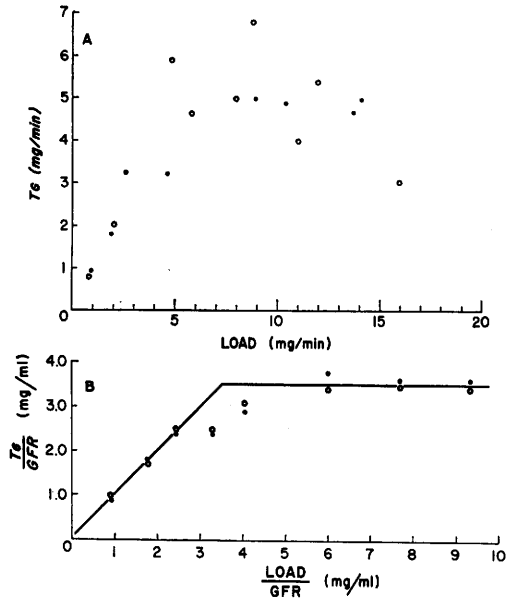

FIG. 1A. Glucose reabsorption as a function of load in a puppy titrated by progressively raising plasma glucose. (B) Glucose transport per milliliter of filtrate (T_G/GFR) plotted as a function of plasma glucose (load/GFR) in the same puppy shown in (A). The function drawn is a line of identity followed by a horizontal line based on visual inspection of the data (●) Right kidney, (○) left kidney.

filtered loads in experiments in which plasma glucose was progressively increased or progressively decreased. However, when both glucose transport (T_G) and glucose load were factored by the GFR during any clearance period, typical glucose titration curves were produced for each animal, resulting in a constant maximum ratio of T_G/GFR at high glucose loads (Fig. 1B). This maximum T_G/GFR will hereafter be designated $(T_G/\text{GFR})_M$. Since an insufficient number of points were obtained from each animal to detect splay, a mass plot of T_G/GFR *vs* load/GFR for all animals was made (Fig. 2). Since T_G/GFR varied from animal to animal, results of T_G/GFR are expressed as a fraction of $(T_G/\text{GFR})_M$ for each animal. Inspection of such a plot reveals that puppies less than 2 wk of age exhibit greater splay than do older puppies and adults. Glucose threshold in those animals having greater splay was much lower than in older dogs. In addition, a greater glucose load/GFR was necessary to reach saturation in animals exhibiting greater splay.

Glucose transport, at saturating loads, varied directly with GFR (Fig. 3). In Fig. 3A, T_G is plotted as a function of GFR for 2 puppies of the same age. Tubular load was at least 1.5 times greater than T_G, for each point. There was excellent correlation between T_G and GFR in these 2 puppies ($r = 0.96$). In Fig. 3B, T_G is plotted as a function of GFR for all animals in the study, where each point represents glucose transport at loads at least 1.5 times greater than T_G. There was excellent correlation between T_G and GFR for all puppies ($r = 0.77$) and for adults ($r = 0.88$).

The mean value of $(T_G/\text{GFR})_M$ for the

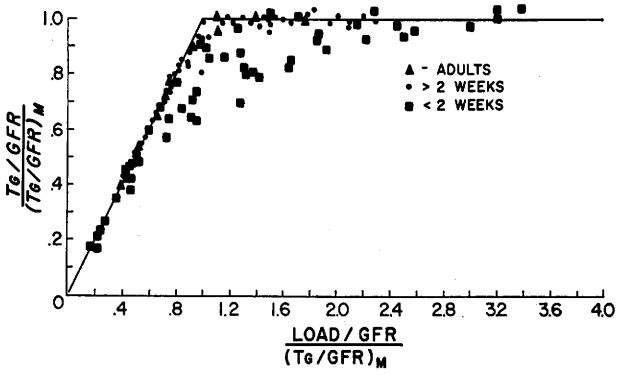

FIG. 2. Mass plot of T_G/GFR and load/GFR factored by $(T_G/\text{GFR})_M$ showing greater splay for puppies less than 2 wk (■) than for older puppies (●) and adults (▲). The function drawn is a line of identity followed by a horizontal line with a value of 1.

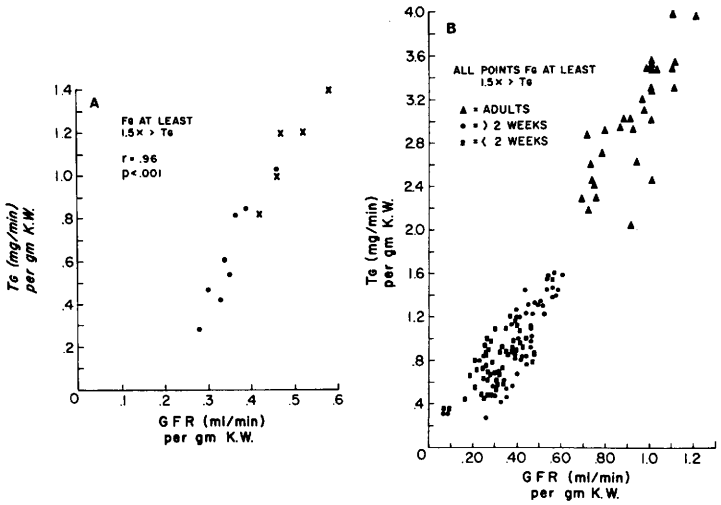

FIG. 3A. Maximum T_G as a function of GFR in 2 puppies of the same age. (B) Maximum T_G as a function of GFR in all animals studied. All values in both figures are factored by wet kidney weight.

puppy was significantly lower ($p < .01$) than for the adult (Table I). There was no difference of $(T_G/GFR)_M$ between the puppies younger and older than 2 wk, nor between the adult dogs of the present experiments and those calculated from the data of Bradley *et al.* (7). It is worth noting that there was no difference in $(T_G/GFR)_M$ between those puppies titrated by progressively increasing or decreasing the glucose load.

Discussion. Puppies less than 2 wk of age exhibit greater glucose titration splay than do older puppies and adult dogs. The degree of splay found in our adult dogs is similar to that found by Bradley *et al.* (7) for adult dogs. The splay found in puppies is consistent with a large degree of glomerulotubular nephron heterogeneity. The diminution of splay in the puppy coincides with completion of nephrogenesis in this species at 2 wk of age (8).

Variation of maximum glucose transport with GFR has been well documented for adult rats (9–11) and dogs (12, 13). Our data show that the newborn dog also is subject to changes in maximum glucose transport with changes in GFR. Tune and Burg (14) suggested that this dependence of maximum T_G on GFR may be due to deterioration of the animal over the time of the experimental procedure. In our experiments, animals titrated by progressively raising P_G, had $(T_G/GFR)_M$ measurements performed relatively late in the experiments, whereas animals titrated by progressively lowering P_G had $(T_G/GFR)_M$ measurements performed relatively early in the experiment. The observation that $(T_G/GFR)_M$ was the same for animals titrated by progressively increasing or decreasing glucose load, suggests that deterioration of the animal was not an explanation for the relationship seen between T_G and GFR. This dependence of maximum T_G on GFR precludes any valid comparison between two groups of animals unless there is correction for the value of the GFR determined at the time of measurement of the maximum T_G.

TABLE I. $(T_G/GFR)_M$ for Puppies and Adult Dogs[a]

Group	No. Animals	Values	$(T_G/GFR)_M$ (mean ± SE; mg/ml)
Puppies <2 wk	13	59	2.65 ± 0.10
>2 wk	9	46	2.60 ± 0.12
Adults	9	31	3.43 ± 0.10
Adults from Bradley et al. (7)	3	3	3.30 ± 0.40

[a] All values of filtered load exceeding 1.5 × T_G were included.

GFR per gram of wet kidney weight is lower in puppies than adults (15, 16). However, $(T_G/\text{GFR})_M$ is lower in all puppies less than 36 days of age than in the adult. Therefore, tubular function appears to be even more depressed than GFR in the newborn puppy, similar to the situation found in the newborn human (1, 2).

Summary. Newborn puppies have greater glucose titration splay than do older dogs, with a resultant lower plasma glucose threshold. The greater splay coincides with continuing nephrogenesis in the newborn puppy and may be explained by increased glomerulotubular nephron heterogeneity. A linear relationship between T_G and GFR at saturating loads applies to the newborn as well as to the adult dog. Tubular function appears to be more depressed than glomerular function in the young puppy.

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