15-Hydroxyprostaglandin dehydrogenase and hexokinase in spontaneously hypertensive rat kidney

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Summary. 15-Hydroxyprostaglandin dehydrogenase (PGDH) surged in hypertensive (SHR) and normotensive (WKY) rat kidney at 8 days of age, is greatest in SHR. Hexokinase fell in SHR at 17 days of age, but thereafter was similar to WKY. This suggests multisystem enzymatic abnormalities in SHR kidney during development of hypertension.
Key words. Rat; kidney; hypertensive; prostaglandin dehydrogenase; hexokinase.

15-Hydroxyprostaglandin dehydrogenase (PGDH) inactivates prostaglandins and exists as NAD-PGDH (type I) and NADP-PGDH (type II)[1,2]. Hexokinase (HK) catalyzes phosphorylation of glucose[3]. PGDH, but not HK, has been measured in homogenates of kidney from genetically hypertensive rats. These enzymes were examined utilizing assays developed in this laboratory and kidneys from our colony of Wistar-Okomoto normotensive (WKY) and hypertensive (SHR) rats in order further to define the temporal relationship between prostaglandin and carbohydrate metabolism.

Materials and methods. Kidneys were taken from 46–49th generation SHR rats, from a 45th generation male-female pair and from WKY age-matched controls. Rats were sacrificed by decapitation. Kidneys were stored at −80°C. Kidney, whole or divided into cortex (C) and medulla (M) at the outer M/inner C zone, was powdered while frozen and then homogenized[1]. HK was assayed at 25°C[3]. PGDH was measured by the macroassay procedure for 0.1–1 mg tissue utilizing PGE_1[1]. NAD-PGDH and NADP-PGDH were measured with 0.7 mM NAD or NADP, respectively. Systolic blood pressure was measured in 2- and 16-month-old rats by the tail cuff method[4]. Results are presented as mean ± SD: significance at $p \leqslant 0.05$ by Student's t-test.

Results and discussion. The blood pressures in 2- and 16-month-old SHR were 98 ± 3 and 165 ± 8 mm Hg, respectively; corresponding WKY values were 80 ± 4 and 92 ± 8 mm Hg. Heart weights from 2-month SHR were 0.53 ± 0.2 g. The SHR/WKY heart weight ratio was 1.14. The 16-month SHR hearts weighed 2.15 ± 0.08 g and SHR/WKY ratio was significantly elevated to 2.72. Therefore, the hypertension was accompanied by myocardial hypertrophy.

NAD-PGDH peaked significantly at 8–17 days of age in SHR and WKY kidney (fig. 1). Activity was significantly higher in SHR than in WKY at 8–30 days. NAD-PGDH returned to baseline in WKY by 1 month, but dit not decrease significantly before 2 months in SHR kidney.

NADP-PGDH was significantly elevated in SHR at 8–30 days, but only from 8 to 17 days in WKY kidneys (fig. 2). Both had a significant return to baseline by 2 months of age.

NAD-PGDH was significantly higher than NADP-PGDH in newborn through 1-month-old SHR kidneys, and in newborn through 17-day-old WKY specimens. The C/M ratios of both enzymes in SHR and WKY kidneys were near unity, although activity tended to be higher in C. NAD-PGDH in normal Sprague-Dawley rats in this laboratory has been noted to be higher in the inner C[5]. Other studies on fractionated homogenates of kidney have revealed a C/M ratio of greater than 1[6].

HK in newborn SHR was 444 ± 24 (n = 7) mmol/kg/h, significantly higher than the 290 ± 35 (n = 5) for WKY kidneys. However, there was a marked reversal by 17 days in which SHR at 187 ± 12 (n = 8) was significantly lower than the 463 ± 23 (n = 6) mmol/kg/h level in WKY specimens. By 2 months, the activities were increased and similar in both SHR and WKY. HK in renal cortex of SHR was 435 ± 54 (n = 12) and 655 ± 62 (n = 8) mmol/kg/h at 2 and 16 months, respectively. The C/M ratios were 0.60 and 0.97, respectively. The corresponding 2- and 16-month activities for cortical HK in WKY was 279 ± 193 (n = 8) and 549 ± 33 (n = 7) mmol/kg/h with C/M ratios of 0.40 and 0.65. These data on C/M ratios are similar to normal Sprague-Dawley rats[3]. However, the temporal change of a fall in SHR within the first month was not seen in WKY. A biphasic fall in outer M was previously noted for Sprague-Dawley rats[3,7]. The actual levels of HK activity in these SHR and WKY are lower than previous values in kidney[3,7]. This suggests that the SHR and WKY strains may be different from the Sprague-Dawley.

Temporal changes of PGDH with development have been previously examined with radioactive tracer assays and also reveal a peak activity within the first month of development[6–12]. SHR PGDH was less than WKY at 3 weeks (37 vs 48 mmol/kg/h) and fell to the 5–7 activity range by 6 weeks[8,11]. Similar levels were also noted elsewhere[9]. Other investigators have found PGDH activity much lower (0.08–0.55 mmol/kg/h), but with SHR less than WKY[6,12]. The actual level of peak PGDH in the present study and the prolonged surge in SHR relative to WKY has not been previously reported. Apparently, SHR kidneys have an elevated capacity for catabolism of the 15-OH

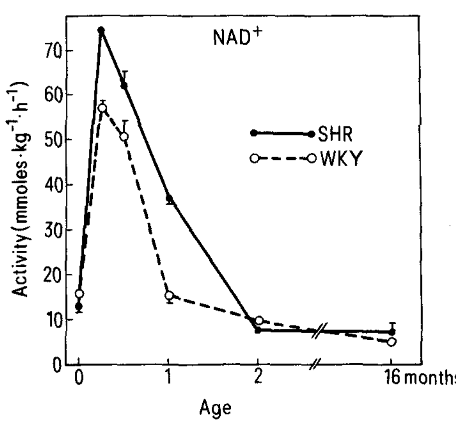

Figure 1. NAD-PGDH in kidney. The ages are newborn, 8 and 17 days, and 1, 2 and 16 months. Respective numbers of animals are as follows: SHR = 7,8,8,8,12 and 8; WKY = 5,5,6,9,8 and 7. Values are mean ± SD. Significant differences ($p \leqslant 0.05$) are given in the text.

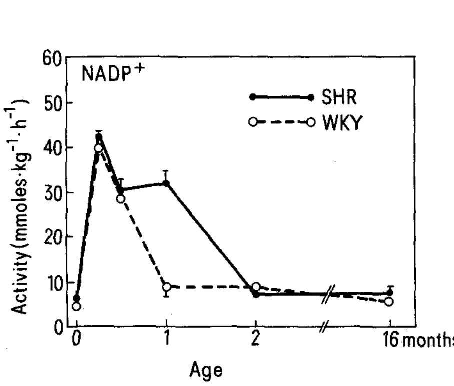

Figure 2. NADP-PGDH in kidney. See figure 1 for number of animals.

group early in development that lasts longer than in WKY. The potential significance of this discordance in the evoloving hypertension in SHR is further supported by studies of renovascular hypertension in which there is a transient surge in NAD-PGDH 10 days after initiation of hypertension[13]. Thereafter, the PGDH returns to normal despite maintenance of the hypertension.

The validity of the assay utilizing PGE_1 as substrate has been previously documented[1,5]. Endogenous NADH oxidase in kidney does not interfere with the assay and the conditions minimize reaction by other prostaglandin-degrading enzymes. The concentration of PGE_1 for half-maximal activity was less than 1 μM for NAD-PGDH and NADP-PGDH in these homogenates, even though a value of 1 μM was noted for purified rat kidney NAD-PGDH[5], and 153 μM for purified swine kidney NADP-PGDH[2]. The latter enzyme is a nonspecific dehydrogenase and exists in multiple enzymatic forms in crude tissue[2]. Purification of the enzymes may select certain forms or remove factors modifying activity.

In view of the known multifactorial nature of hypertension and the temporal patterns found in this study, it is concluded that changes in PGDH and HK in kidney during early development in SHR may reflect a primary etiological derangement in prostaglandin and carbohydrate metabolism that the expressed as elevated pressure in the latter stages of development.

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The significance of temperature and barometric pressure changes for the snow surface activity of *Isotoma hiemalis* (Collembola)[1]

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Summary. Temperature is limiting for the snow surface activity of *Isotoma hiemalis*: values below a threshold of −2.5° to −3 °C are avoided. Changing barometric pressure leads to increased surface activity, thus being responsible for mass appearances. These experiments provide the first evidence for sensitivity to and reaction to barometric pressure changes in insects.
Key words. Collembola; snow; activity; temperature; barometric pressure changes.

The emergence of Collembola from the snow has always attracted the interest of naturalists. Many detailed reports can be found in the older literature[2–5]. Even the few recent papers do not deal with all aspects of the phenomenon[6–10]. Experimental work has only been done in the field of cold hardiness (for a review see Sømme[11]). Unfortunately, the weather conditions accompanying the observations of mass appearances have not been considered sufficiently. However, in most cases changing weather seems to coincide with spectacular mass occurrences. It is evident that mild temperatures favor the activity on the snow surface[5,7,8], but the high relative humidity usually linked with such temperatures could also be of some importance[5]. Observations on other snow-insects, like *Boreus*[6,12] or *Chionea*[13–16], cannot shed further light on the question; nevertheless, these papers also indicate a relation to weather changes. Nadig[15] was able to show that relative humidity is a most important environmental factor for surface activity of *Chionea*.

There were always situations where the presence or absence of snow-insects on the snow cover could not be explained by the existing theories. The animals often showed a strikingly different appearance pattern on apparently equivalent consecutive days. Also, there was no answer to the question of how the animals can respond to favorable weather conditions on the surface when they have retreated deep into the snow or even into the soil. Macnamara[5] has already postulated 'some kind of tropism'. The often-adopted hypothesis that melting water seeping into the ground brings Collembola up onto the surface cannot be held in most cases as mass emergences can be observed throughout the winter and e.g. *I. hiemalis* of the *mucronata*-morph living in moist drains never appear on the surface during spring[17].

Light, temperature and relative humidity can be excluded as triggering factors for a mass emergence, as they remain almost constant within or below the snow cover. For foresters 'lots of snow fleas' are the infallible sign of an approaching weather change, mostly connected with precipitation. This fact was already known to the naturalists of the last century[5,18,19]. The coincidence of weather changes with increased surface activity suggests that atmospheric pressure changes may be involved in some way.

The present paper deals with the reaction of Collembola to snow temperature and barometric pressure changes.

Materials and methods. Field observations were carried out in our research area Gurnigel in the Bernese Prealps (for site description see Zettel and v. Allmen[20]).

For the pressure experiments, animals freshly caught on the snow surface were kept in a climatic chamber on fresh snow in exsiccators of 10 l content. One vessel was hermetically closed in order to maintain constant pressure conditions. Another