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# PLASMA RENIN ACTIVITY, ALDOSTERONE and DOPAMINE β -HYDROXYLASE ACTIVITY AS A FUNCTION OF AGE IN NORMAL CHILDREN.

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## SUMMARY

In 149 children between 6 days and 15 years of age, plasma renin activity (PRA) and aldosterone (PA) were measured by radioimmunoassay and plasma dopamine β hydroxylase activity (DBH) by the method of Nagatsu. PRA and PA decreased with age from 496 ± 119 ng/l/min for PRA and 643 ± 158 pg/ml for PA in 6 to 30 day-old newborns to 37.8 ± 4.7 ng/l/min for PRA and 43.1 ± 8.3 pg/ml for PA in 9 to 15 year-old children. DBH increased with age from less than detection limit values (< 2 IU) in 6 day to 3 month-old newborns to 17.2 ± 5.1 IU in 9 to 15 year-old children. In addition a significant relationship was found between PRA and PA (log PA = 0.99 log PRA -0.058, r = 0.732, n = 104, p < 0.001) and PRA and DBH (log DBH = -0.41 log PRA +1.62, r = 0.404, n = 80, p < 0.001). These results demonstrate the opposite evolution of the Renin-Angiotensin-Aldosterone System and of the sympathoadrenal system during development.

## SPECULATION

The Renin-Angiotensin-Aldosterone-System (RAAS) is activated in the newborn. Possible reasons include a compensatory mechanism for an immature sympathoadrenal system since it was shown that from infancy to childhood, PRA and PA decrease while DBH increases. Thus the RAAS could well represent an important factor in the control of sodium balance and blood pressure at this time of the development.

## INTRODUCTION

The activity of the renin-angiotensin-aldosterone-system (RAAS) has been reported to be higher in newborns and infants than in adults. Concerning the significance of this hyperactivity, we hypothetized (15) that it could be a compensatory mechanism for an immature sympathetic nervous system.

In order to emphasize this point, we simultaneously followed the evolution of plasma renin activity (PRA), aldosterone (PA) and dopamine β hydroxylase activity (DBH) in normal subjects aged from 6 days to 15 years.

## MATERIAL AND METHODS

The 149 children included in this study, after informed parental consent, were hospitalized for a benign illness. All were normal with respect to body weight, height, cranial perimeter and bone age. None were premature infants. A standard clinical and biological examination allowed to exclude any history of cardiovascular, renal, digestive and endocrine diseases. For 15 days at least, none received drugs known to interfere with renin secretion and the sympathetic nervous system activity. Any other therapeutic administration was interrupted at least 5 days before the study. The subjects received a normal sodium diet for their age, estimated to be at 2 to 3 mEq of sodium/kg/24 h. In addition caffeine containing beverages were strictly avoided.

Blood samples (7 ml) were always drawn before 10 a.m. : 2 hours after feeding for the infants and for older children 2 hours after breakfast and after one hour of recumbency. Blood was maintained and centrifuged at + 4°C and the separated plasma was kept at -25°C until assay.

Radioimmunoassay were used for PRA (20) and PA (1) determinations. DBH was measured according to Nagatsu (14). After 1 hour of recumbency, our normal adult values were found at 35.9 ± 3.6 ng/l/min for PRA, 44.9 ± 5.2 pg/ml for PA and 24.1 ± 2.6 IU for DBH.

The results were expressed as mean ± SEM and analyzed by the Student "t" test.

## RESULTS

As shown in Table I, PRA and PA were markedly increased in infants and then decreased with advancing age, reaching normal adult values at 2 and 9 years of age for PA and PRA respectively. In spite of very carefully controlled conditions of sampling, the individual values observed before one year of age were highly variable. However a close inverse relationship was found between PRA and age (log PRA = -0.007 age months + 2.48, r = 0.728, n = 128, p < 0.001) and PA and age (log PA = -0.008 age months + 2.48, r = 0.662, n = 125, p < 0.001). In addition PRA and PA values were significantly related (log PA = 0.99 log PRA - 0.058, r = 0.732, n = 104, p < 0.001).

On the contrary, in the same subjects DBH exhibited an overall increase with age (log DBH = 0.05 age months + 0.52, r = 0.561, n = 89, p < 0.001). Even though DBH activity was under the detection limit of our method, i.e. 2 IU before 3 months of age, its values were no longer different from adult ones after the age of 2 years. A significant inverse relationship was found between PRA and DBH values (log DBH = -0.41 log PRA + 1.622, r = 0.404, n = 80, p < 0.001).

## DISCUSSION

The Renin-Angiotensin-Aldosterone (RAAS) and the sympathetic nervous systems are of major importance in the control of blood pressure and hydromineral metabolism. In order to evaluate their respective importance during the development PRA, PA and DBH were simultaneously measured in a large number of healthy subjects aged from 6 days to 15 years.

In carefully standardized conditions of sampling it was shown that the activity of the RAAS was more than 10 times greater in newborns than in adults. Afterwards, PRA and PA values rapidly declined until 1 year of age and then gradually reached adult values respectively in 2 and 9 year-old children. Such an enhanced activity in newborns and infants is in close agreement with the results that we (15) and others (7, 12, 18) have previously reported. Moreover the close relationship demonstrated between PRA and PA indicates that the renin remains, at all ages, a major stimulus for aldosterone secretion.

On the contrary, in accord with previous findings (11, 23), plasma DBH activity was indetectable before 3 months of age and afterwards it sharply increased to reach adult values between 2 and 5 years of age. Although the physiological meaning of plasma DBH remains to be fully clarified, it is generally accepted that it could be related to the unstimulated, genetically determined, level of the sympathetic nerves activity (16, 24).

Such a viewpoint is strengthened by the fact that the urinary excretion catecholamines and metabolites, which directly reflects the sympatho-adrenal activity, follows, during the development, the same evolution as do plasma DBH (3, 4, 5, 21).

Our results seem differ from the reports of elevated plasma catecholamin at birth (2, 13). However these high values could be due to the delivery induced stress as in young infants plasma DBH as well as urinary catecholamines are low.

Taken as a whole, the present study demonstrates a marked opposite influence of age on the basal activity of the RAAS and sympathetic nervous system, which play a major role in the control of blood pressure and sodium excretion (6).

It thus appears that :

i) during the first of life, when sodium balance is maintained in spite immature kidney functions (9, 10), the RAAS whose basal activity as well as responses to different stimuli are enhanced (8, 17, 19) might be of primary importance. ii) after that age, the sympathetic nervous system develops and influence of the RAAS declines. iii) the existence of a significant inverse relationship between PRA and plasma DBH values allows to support that the increased RAAS activity which characterize young infants could be, in part, compensatory for an immature sympathetic nervous system.

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| AGE | | 6 → 30 days | 1 → 3 months | 3 → 6 months | 6 → 12 months | 1 → 2 years | 2 → 5 years | 5 → 7 years | 7 → 9 years | 9 → 15 years | Adults |
|---|---|---|---|---|---|---|---|---|---|---|---|
| PRA ng/l/min | $\bar{x}$ | 496 | 374 | 334 | 333 | 271 | 110 | 94.6 | 87.9 | 37.8 | 35.9 |
| | ±SEM | ±119 | ±51 | ±38 | ±64 | ±34 | ±14 | ±12.8 | ±22.4 | ±4.7 | ±3.6 |
| | n | 16 | 20 | 14 | 15 | 20 | 15 | 9 | 9 | 9 | 36 |
| | | S | S | S | S | S | S | S | S | NS | |
| PA pg/ml | $\bar{x}$ | 643 | 490 | 414 | 429 | 314 | 74.8 | 59.8 | 34 | 43.1 | 44.9 |
| | ±SEM | ±158 | ±84.5 | ±122 | ±102 | ±46 | ±20 | ±14 | ±5.8 | ±8.3 | ±5.2 |
| | n | 14 | 25 | 11 | 12 | 18 | 12 | 8 | 10 | 11 | 14 |
| | | S | S | S | S | S | NS | NS | NS | NS | |
| DBH IU | $\bar{x}$ | < 2 | < 2 | 3.3 | 5.8 | 5.1 | 14.3 | 14.8 | 20.2 | 17.2 | 24.1 |
| | ±SEM | | | ±0.5 | ±1.1 | ±1.2 | ±4.1 | ±4.7 | ±3.6 | ±5.1 | ±2.6 |
| | n | 6 | 10 | 8 | 13 | 16 | 7 | 8 | 10 | 11 | 28 |
| | | | | S | S | S | NS | NS | NS | NS | |

Children values were significantly (S) or non significantly (NS) different compared to adult.
(S for $p < 0.05$ - NS for $p > 0.05$)


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