SKIN HISTAMINE IN RABBITS IN NEONATAL LIFE

By

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The histamine content of the rabbit skin is high at birth in comparison to adult values. A further sudden rise occurs 4 days after birth, and there is a sharp decline by 6th day, when values are nearly the same as at birth. Thereafter values approach adult levels in 2-3 weeks time. The probable causes of this sudden rise and fall have been discussed.

It is usually believed that foetal tissues contain very little histamine, and that an increase in the contents occur with age (Feldberg and Schilf, 1930). Such an increase has been observed in the lung of man, cow and cat, and in the liver of cow and skin of cat (Feldberg and Kellaway, 1937; Riley and West, 1953). However, this phenomenon is not universal, and a decrease in the histamine content of the skin with age has been noticed in the rabbit (Rocha e Silva, 1940) and in the man (Harris, 1927). During the last few years, Kahlson and his co-workers (1958) have demonstrated a tremendously augmented biosynthesis of histamine in foetal liver, a fact which accounts for increased urinary excretion of histamine during pregnancy. It was of interest to study if the same capacity is present in neonatal life, and if the sudden post natal change in environmental conditions causes any change in histamine metabolism.

METHODS

Animals.— Albino rabbits, bred in this laboratory were used. Only litters from healthy animals were used for the experiments. New born animals from individual litters were killed at varying time intervals (5 hrs, 2 days, 4 days, 6 days, 9 days, 12 days, and 15 days) for purposes of extraction and assay of histamine. Experiments were repeated with different litters, so that values obtained at different intervals are of equitably distributed litter mates.

Extraction and assay of histamine.—The method followed was that of Sanyal (1958). Briefly the tissue was extracted with 5 volumes of 10 per cent aqueous solution of trichloracetic acid, for 2 hours at room temperature, and then overnight in the refrigerator. The trichloracetic acid was removed by shaking with 4 volumes of ether. The ether layer containing the acid was

pipetted off. The procedure was repeated at least 4 times in order to get rid of all traces of acid, even a minute fraction of which may have deleterious action on the assay organ. Traces of ether were removed by gentle warming. The extract was then assayed against standard doses of histamine by matching at 2 or more dose levels on the atropinized guinea-pig ileum. When such a procedure is adopted the results are fairly accurate and any difference greater than 10 per cent may be considered significant.

RESULTS

In initial experiments, histamine contents of skin, lungs and spleen were determined. There was little difference in the values obtained in the lungs or spleen, as compared with adult values, and as such these organs were not studied any further.

The histamine content of the skin at various time intervals after birth is shown in Table I. It will be seen that values at birth are higher than adult levels, and the same values persist for about 48 hrs. A few estimations were done in between 5 hrs and 48 hrs period and values were in a similar range. However a sudden rise occurs in 4 days time and surprisingly values return to neonatal levels at 6 days. From this period, there is a gradual decline, till adult values are approached in 2-3 weeks time.

TABLE I

Changes in histamine content (μg/gm.) of rabbit's skin during the neonatal period

No. of observation	5 hrs	2 days	4 days	6 days	9 days	12 days	15 days	Adults
1.	40·0	24·0	94·0	32·0	20·0	18·0	12·5	10·7
2.	32·0	24·0	80·0	22·0	20·0	20·0	14·0	7·5
3.	20·0	20·0	72·0	40·0	27·0	17·0	15·0	12·0
4.	20·0	28·0	80·0	28·0	22·0	18·0	11·0	10·0
5.	26·0	26·0	84·0	28·0	18·0	22·0	12·0	—
6.	28·0	26·0	80·0	20·0	18·0	20·0	10·0	—
Mean:	27·6	24·6	81·6	28·3	20·8	19·1	12·4	10·0
S.D.	7·63	2·73	7·20	2·28	1·63	1·83	2·14	1·59
S.E.	3·11	1·11	2·93	2·94	1·37	0·76	0·87	0·59

DISCUSSION

The dramatic rise in skin histamine 4 days after birth in rabbits, and a still more interesting come back, by the 6th day raises several interesting possibilities. The sources of tissue histamine (Sanyal and Mishra, 1960) could be (a) histamine from the diet, (b) histidine decarboxylated by intestinal bacteria, (c) synthesis in the tissues. The first possibility can be ruled out, as during this period, the diet consists of mother's milk only, and as milk contains little histamine, this could not account for the rise.

Intestinal decarboxylation of histidine by bacterial fermentation is unlikely, in as much as at this stage of life, the intestines contain few, if any coliform organism which may decarboxylate histidine, the main inhabitant of the area during breast feeding, being various forms of lactobacillus (Cruick Shank, 1925; Snyder, 1940 and Paton, 1955).

The third alternative is more likely to be the factor involved, and further experimentation is necessary to prove this point. The facts which require explanation are (i) skin histamine at birth is higher than in adults, (ii) skin histamine shows a great rise 4 days after birth, (iii) the raised values persist for a short time only.

The power of foetal tissues to form histamine at an augmented rate (Kahlson, Rosengren and White, 1960) has already been demonstrated, and this fact may account for the initial raised values at birth. It is possible that a sharp increase in decarboxylation occurs 4 days after birth. It has been noted that decarboxylase enzymes are under the control of supra renal cortical hormones (Hicks and West, 1958) and that a reduction in adrenal tissue leads to raised histamine values (Marshall, 1943; Rose and Browne, 1941), and further that foetal adrenal tissue degenerates at birth and is gradually replaced by adult tissues (Benner, 1949). Thus an adrenal deficiency may account for high values at birth, and as there is further degeneration of foetal adrenal tissue, a sudden rise may be expected in histamine content, which will decrease as adult adrenal tissue is formed.

The changes can be explained in forms of stress phenomenon as well. It has been shown that after injury or after burn, there is a sharp rise in skin histamine (Bhatt and Sanyal, 1963a; Sanyal 1962), and as the skin comes in contact with the external environment, it is subjected to rough handling and there is a corresponding rise in skin histamine. In view of recent studies indicating that raised histamine content augments defense functions of skin (Kahlson, 1960; Bhatt and Sanyal, 1963b) this rise may be of physiological importance.

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