Pendant la deuxième phase, l'activité mitotique, sans être aussi élevée que lors de la phase de régénération, est loin d'être négligeable. A ce moment pourtant, les cellules semblent échapper aux mécanismes de régulation normale car le rythme circadien est perdu. D'autres recherches que nous avons réalisées chez des animaux traités par le DENA et soumis à une hépatectomie partielle confirment ce fait (BARBASON et al., sous presse). Des observations allant dans le même sens ont été réalisées récemment par RABES et al.[7].

Au cours de la deuxième phase de la période prénéoplastique se déroule un autre phénomène: l'augmentation des amas de cellules présentant des déficits enzymatiques et capables de retenir le glycogène. Du 30e au 60e jour de traitement, le volume relatif de ces amas est quintuplé. Le mécanisme exact de cet accroissement est peu connu. L'index mitotique n'est pas différent dans le parenchyme normal et dans les amas de cellules PAS positives après le jeûne. Il est difficile de tirer une conclusion sans une meilleure connaissance du cycle cellulaire dans ces deux localisations. Des recherches sont porsuivies dans ce sens.

Il n'est pas exclu pourtant que l'augmentation de volume des amas PAS positifs soit simplement due à l'apparition d'amas cellulaires nouveaux qui finissent par confluer.

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Mitotic Activity of Adrenal Medullary Cells in the Mouse at Different Ages and Following Unilateral Adrenalectomy

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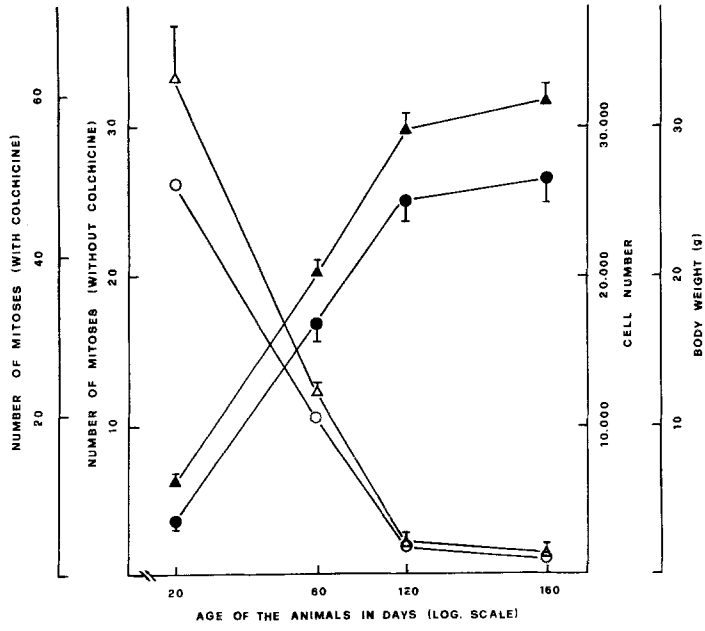
Summary. The number of mitoses as well as the number of the cells of the adrenal medulla was determined in the mouse at various ages and after unilateral adrenalectomy. It was found that a decrease in the mitoses and an increase in the cell number occurs up to 4 months. In 12-month-old rats, mitoses, although rare, are still present. No changes in the mitosis and cell number was observed after unilateral adrenalectomy.

Previous studies showed that chromaffin cells of the adrenal medulla of adult rat are able to undergo mitosis[1,2]. The aim of the present research was to determine the number of mitoses in the adrenal medullary cells of the mouse at various ages and following unilateral adrenalectomy, a condition of possible stimulation to proliferation. The number of mitoses was related to the number of the cells of the whole adrenal medulla to investigate whether the mitotic activity could be ascribed to the growth of the organ or to renewal processes of the chromaffin cells.

Gray mice of 'Snell' strain maintained on a complete semisynthetic diet (Zoofarm, Padua, Italy) were used. Unilateral adrenalectomy was performed through a dorsal incision in 4-month-old mice. The animals were allowed to drink 1% NaCl and were sacrificed 5, 10 or 15 days after the surgical operation. All the animals were killed at noon[3]. Some mice were injected i.p. with colchicine (in 8% ethanol solution) at the dose of 0.1 mg/100 g body wt., 3 h before sacrifice. Adrenal glands were fixed either in ethanol-chloroform-acetic acid mixture (6:3:1 v:v) for 3 h or in acetate buffer pH. 5.8 containing formol 10% and potassium bichromate 5% for 12 h. The latter procedure is commonly used for the chromaffin reaction. The whole gland was cut into serial sections (6 μm thick). The sections were stained with ematoxilin and eosin. Each section was examined under the microscope using a



Number of mitoses (with or without colchicine) and of cells per whole adrenal medulla and body weight of mice at various ages. ○—○, number of mitoses (with colchicine); △—△, number of mitoses (without colchicine); ●—●, cell number; ▲—▲, body weight. Vertical bars represents SEM.

magnification of ×1000, to detect the mitotic figures. The number of adrenal medullary cells was determined as follows: the sections were photographed and the negative films were projected on a paper sheet of uniform thickness; the pictures of the medulla were cut out and weighed. In 1 out of 6 sections the nuclei of the cells were counted with the microscope. The number of the cells per whole adrenal medulla was determined according to the following relation: $A:B = X:C$, where: A is the total number of cells counted in all the sections examined; B is the weight (in mg) of the paper pictures corresponding to the sections examined; C is the weight (in mg) of all the paper pictures; X is the number of the cells in the whole adrenal medulla. The data obtained were corrected using the equations reported by HAUG[4] to obviate the error due to the presence of the same cell in several contiguous sections.

As shown in the Figure, the number of mitoses in the adrenal medullary cell decreases in a linear fashion with the log of the age until 4 months, the reverse behaviour is shown by the number of chromaffin cells, as well as the body weight; both of these parameters, in fact, increase until 4 months and then reach a plateau. The ratio between the number of mitoses observed in the presence of colchicine and that observed in the absence of colchicine is almost costant (2.6–2.2).

Unilateral adrenalectomy in the adult rat does not result in a substantial increase of the number of either mitoses or cells per whole adrenal medulla (Table). This result is therefore in agreement with that reported by McKAY and McKAY[5], who showed no increase in the volume of the remaining medulla after unilateral adrenalectomy in the rat. The lack of hyperplasia in the remaining adrenal medulla could be explained by the presence of extramedullary chromaffin tissue.

The observation that mitotic activity occurs in the chromaffin cells of the adrenal medulla of the mouse is in agreement with analogous findings obtained in the rat[1,2,6,7], the golden hamster[8] and the rabbit[9]. These results therefore demonstrate that a proliferative ability persists in the chromaffin cells of the adrenal medulla during the postnatal life, although the adrenal medullary cells have been thought to be postmitotic cells[10], on the basis of their origin from sympatogonic cells. Since the mitotic activity is inversely related to the increase in the cell number, it appears that the only consequence of the observed mitotic activity is the postnatal growth of the organ. This seems to be particulary true in the first 4 months of the postnatal life, when a conspicuous variation in the number of both mitoses and cells occurs. The persisting mitotic activity in adult mice (4–12 months) is apparently associated with the slow increase in cell number and therefore could be responsible for additional growing processes (a continuous increase in body weight, although to a progressively reduced extent occurs in mice with aging); however, renewal processes, as acknowledged by some authors[8,9], cannot be excluded.

As shown by the presence of chromaffin reaction, mitoses occur in differentiated elements, thus excluding the possibility that immature cells remaining in the gland during the postnatal life are responsible for the observed mitotic activity[11].

Number of mitoses and of cells per whole adrenal medulla following unilateral adrenalectomy[a]

Days after unilateral adrenalectomy	No. of mitoses per whole adrenal medulla[b]	Cell number per whole adrenal medulla
5	2	24062
10	4	25200
15	3	23878

[a] 4 months old mice were used. [b] Mitoses were counted after colchicine treatment.

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Experimental Allergic Encephalomyelitis in T-Lymphocyte Deficient Rats

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Summary. Thymectomized, lethally irradiated rats reconstituted with syngeneic bone marrow were injected with rat brain in complete Freund adjuvant mixture. Both, they and sham-thymectomized, irradiated and bone marrow protected rats displayed a higher incidence of leg paralysis than normal non-irradiated animals. Thymectomy lowered the incidence of the disease.

The mechanism of experimental allergic encephalomyelitis (EAE) became rather obscured when it was found that the disease can be elicited without a mononuclear cell attack upon the neural tissue[2]. Recently it has also been shown that autoimmune thyroiditis developes in neonatally thymectomized rats given 3-methylcholanthrene[3]. This would suggest that the activity of circulating antibodies is at the bottom of at least these autoimmune

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