MITOSES OCCURRING IN THE ACANTHOSIS PRODUCED BY HORMONES

E. UEHLINGER, W. JADASSOHN AND H. E. FIERZ*

(Received for publication April 30, 1941)

A short time ago we called attention to the fact that dropping a very small amount of estrone on the mammilla of the guinea pig elicited a considerable acanthosis of the mammillary epithelium. This acanthosis appears soon after the application of estrone; within 5 days we find that the epithelium is 4–5 times its former width; and on examination after 30 days, it is 6–8 times its original width.

It is, therefore, striking, that, despite this violent epithelial activity (travail épithelial) scarcely a mitosis is to be seen.

It has often been pointed out that it is astonishing that so few mitoses are to be seen in normal skin, and in the enormous acanthosis which is produced by Estrone the lack of numerous mitoses is even more astonishing.

Even the fact that there are so few mitoses in normal skin has frequently led observers to the assumption that "there is, in addition to mitotic division, an amitotic, so-called direct division of the nuclei" (Pinkus (2)). However, the occurrence of such an amitotic division is not proven, and Pinkus himself believes "it probable that mitotic division of the basal cells is the only normal reproductive form of the basal cells"; and Pinkus states this to be of his opinion despite the insignificant number of mitoses to be found in normal epidermis, despite the occurrence of cells with two nuclei, and despite certain findings in tissue cultures.

Dustin (3) and his collaborators have discovered a method which succeeds in demonstrating mitotic nuclear division in tissues in which mitotic figures are not otherwise found. These authors

* From the Pathological Institute, St. Gaul, Switzerland, and the Federal Technische Hochschule, Zurich, Switzerland.

injected colchicin into guinea pigs (25 μ of Colchicin were injected per 30 grams of guinea pig); and sacrificed the animals $9\frac{1}{2}$ hours later. With this procedure one finds many more mitoses than are discoverable without the administration of colchicin.

According to Bastenie and Zilberscag (4) this effect of colchicin can be interpreted as follows: (1) the entry into the mitotic phase of all those cells which are capable of karyokinesis, but which normally would have entered this phase only slowly and suc-

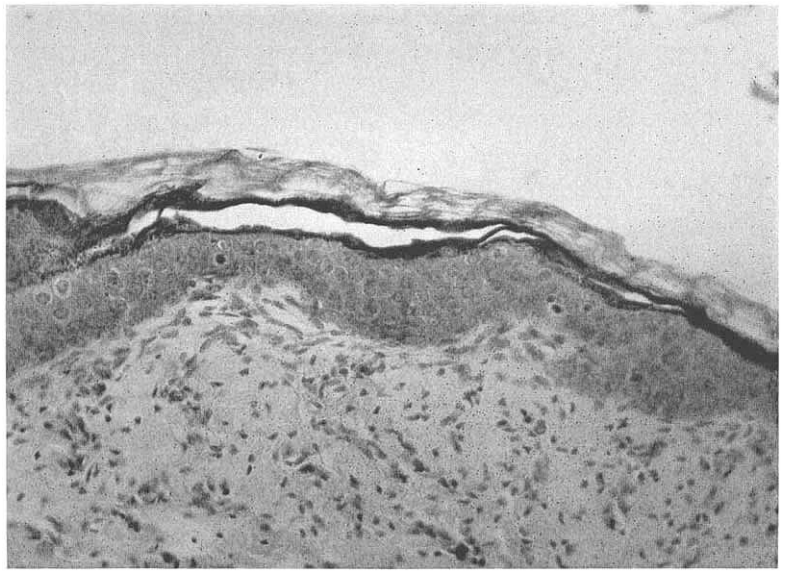

FIG. 1. EPITHELIUM OF THE NIPPLE OF A MALE GUINEA PIG; UNTREATED Excision $9\frac{1}{2}$ hours after injection of colchicin (25μ per 30 gr. of guinea pig). Magnification 1:260.

cessively: "(1) entree en mitose de toutes les cellules aptes a la cinese mais qui normalement ne s'y seraient engagees que lentement et successivement. (2) The arrest and accumulation in the metaphase of all the mitoses abruptly elicited: "(2) Arret et accumulation, au stade de metaphase, de toutes les mitoses brutalement declenchées)."

A large number of striking histologic pictures have been published, showing the huge numbers of mitoses which have been elicited by the application of the "colchicin method" of Dustin.

Among these pictures there are some showing the uterus of animals in which female sex hormone had been injected. To these published histologic pictures we would now like to add those of the acanthosis of the mammillary epithelium which is produced by the local effect of dropping on of estrone (fig. 1, 2 and 3).

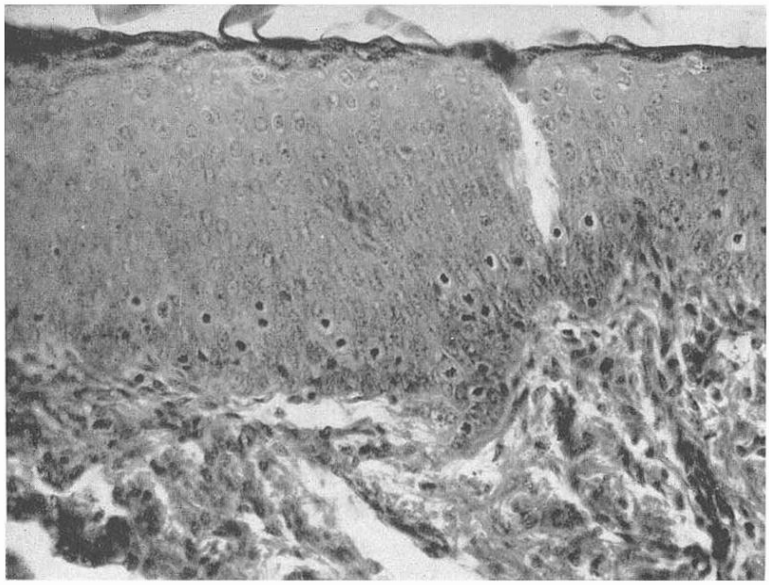

FIG. 2. EPITHELIUM OF THE NIPPLE OF A MALE GUINEA PIG
One drop of estrone solution (1μ per cc.) was applied daily to the nipple. Excision on the 5th day after four applications. 9½ hours after injection of colchicin (25μ per 30 gr. of guinea pig). Magnification 1:260 (same as fig. 1).

We were able to observe the following:

1. In normal epidermis there are relatively few mitoses even after injection of colchicin, although the mitoses are definitely more numerous than when no colchicin has been given; and there are even occasional sites with quite numerous mitotic figures.

2. The mitoses in the normal epidermis are by no means confined to the basal cell layer, but are occasionally seen in the stratum Malpighii.

3. In the acanthosis of mammillary epithelium which has been

produced by estrone there are great numbers of mitoses even after few applications of the hormone.

4. These mitoses are present in the basal cell layer and in the stratum Malpighii, but only in the lower third of the latter.

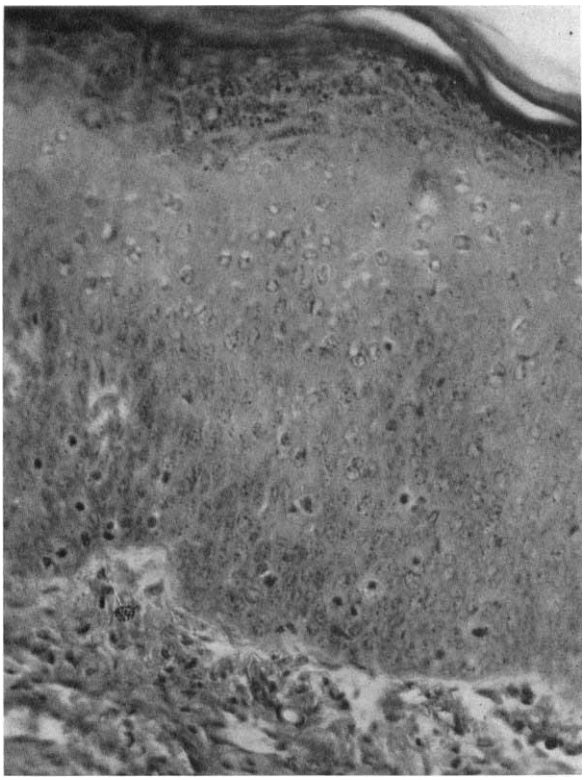

FIG. 3. EPITHELIUM OF THE NIPPLE OF A MALE GUINEA PIG

One drop of estrone solution (1μ per cc.) was applied daily to the nipple. Excision on 31st day, after 30 applications. 9½ hours after injection of colchicin (25μ per 30 gr. of guinea pig). Magnification 1:260 (same as two preceding figures).

5. All our attempts to make mitoses visible through the percutaneous application of colchicin were unsuccessful.

6. The addition of colchicin to the solution of estrone which is dropped on the mammilla does not reduce the effect of the estrone on the epithelial growth; nor is this estrone effect reduced by the injection of small amounts of colchicin.

Our experiments indicate that the fact that no mitoses can be seen without colchicin does not constitute grounds for the assumption that no mitotic nuclear division takes place in extreme, rapidly developing acanthosis. For the colchicin method demonstrates that even extremely numerous mitoses may be present, but not be demonstrable without colchicin.

Mitoses are not confined to the basal cell layer, but are found also in the lower parts of the stratum Malpighii. It is therefore correct not to identify the stratum germinativum with the basal cell layer, as was formerly done. The stratum germinativum must today be considered to include both basal cell layer and stratum Malpighii.

BIBLIOGRAPHY

(1) JADASSOHN, UEHLINGER AND FIERZ: Schweiz. med. Wschr., **1**: 6, 1941.
(2) PINKUS: Hdb. d. Haut- und Geschlechtskrankheiten, **1**: 1, p. 89, 1927.
(3) DUSTIN: Vol. Jubilaire J. Demoor, 170, 1937.
(4) BASTENIE AND ZYLBERSZAC: Arch. Internat. de Med. exp., **13**: 183, 1938.