and the last culture, in cell morphology or in the size of nuclei or sex chromatin.

In early transfers of both the human mammary tumor and the rabbit kidney cell lines, counts correspond, respectively, to the incidence of sex chromatin in somatic human tissue (*7, 11*) and in explants and primary cultures of cells of rat (*3*), dog, and cat (*12*). Although sex chromatin incidence in early transfers was higher in the human tumor than in the rabbit cells, in both cell lines it dropped with subculturing to 2 to 9 percent (Fig. 1).

Both cell lines also retained the insensitivity of their source material to certain viruses. In contrast to such established human cell lines as HeLa and H.Ep.No.1 (*13*), the human tumor cultures did not support the virus of infectious bovine rhinotracheitis. In contrast to an established rabbit-kidney cell line obtained from Drew (*14*) and propagated further in this laboratory, preliminary studies with our rabbit kidney cultures indicate that, up to the current passage, they fail to support poliovirus.

Culturing of the rabbit kidney cells continues for the purpose of investigating any relationship between a possible complete loss of sex chromatin and concomitant changes in morphology and viral sensitivity (*15*).

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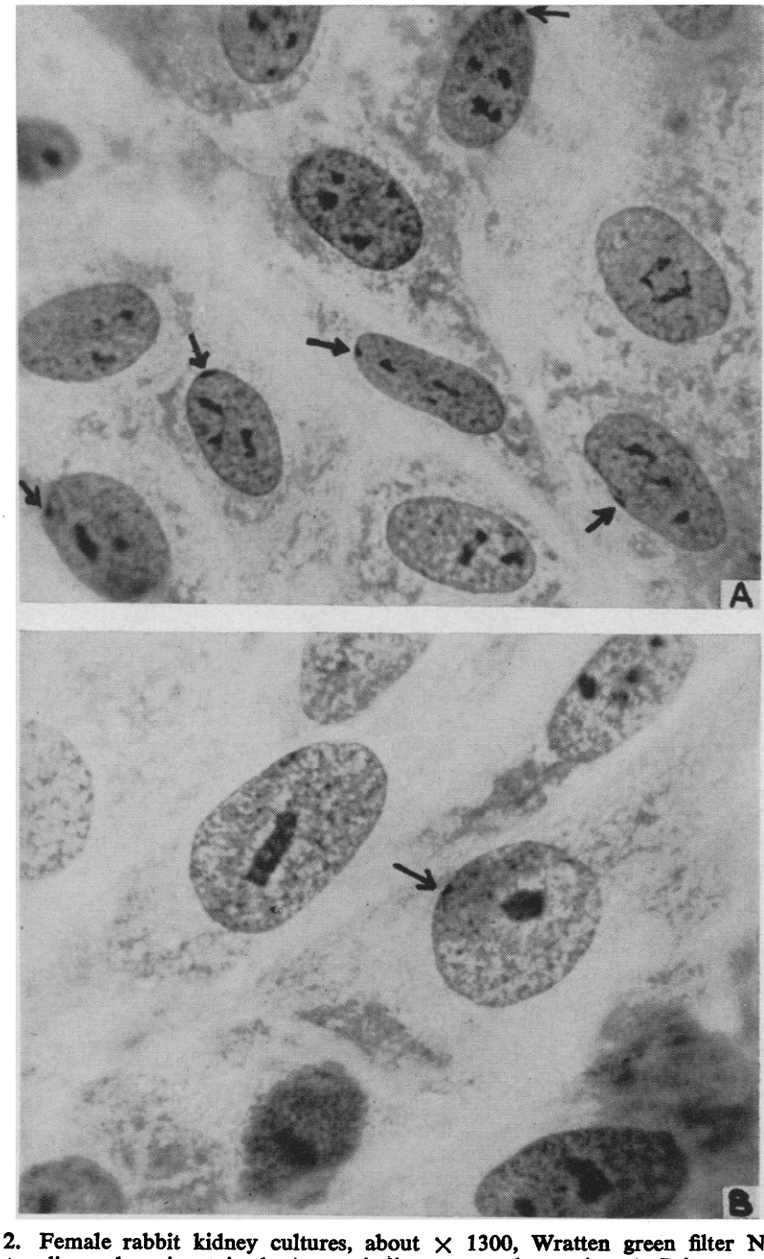


Fig. 2. Female rabbit kidney cultures, about × 1300, Wratten green filter No. 11, hemotoxylin and eosin stained. Arrow indicates sex chromatin. *A*. Primary culture, sex chromatin 35 percent. Width of nuclei average is 14 μ, range 8 to 24 μ. Average size of sex chromatin: width 1.2 μ, length 1.6 μ. *B*. 38th week, 20th transfer, sex chromatin 6 percent. Width of nuclei average is 14 μ, range 8 to 28 μ. Average size of sex chromatin: width 1.1 μ, length 1.8 μ. Culture retains whorl-like arrangement of cells and oval nuclei and elongated cytoplasm of earlier transfers. Note typical wedge-shaped chromatin mass larger than nearby fine chromatin granules.

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## Excessive Stimulation of Salivary Gland Growth by Isoproterenol

*Abstract.* In the rat, chronic treatment with isoproterenol can cause a selective growth of the salivary glands to approximately five times their normal size within 17 days. This enlargement is principally due to mitotic proliferation and hypertrophy of the parenchymatous cells.

It was recently observed that chronic treatment with very large doses of isoproterenol is tolerated by the rat if the compound is administered intraperitoneally. By this procedure, certain otherwise undetectable actions of this catecholamine became evident (for example, production of aortic aneurisms and nephrocalcinosis). In the course of this work it was incidentally

noted that rats chronically treated with isoproterenol secrete an extraordinarily large amount of very viscous saliva, with the result that the fur over most of the body surface is constantly moist (*1*).

The data reported here show that this excessive salivation is due to a true sialadenotrophic action of isoproterenol; the compound is not merely a sialagogue but a potent and selective stimulator of salivary gland growth.

Thirty female rats of the Holtzman strain, with a mean initial body weight of 134 g (range, 130 to 140 g), were subdivided into two equal groups. Group 1 was treated with 50 mg of isoproterenol in 0.2 ml of water, twice daily, intraperitoneally, while group 2 acted as untreated controls. Six animals of group 1 died during the course of the experiment, showing obvious enlargement of the salivary glands; the rest were killed, together with the controls, after 17 days of treatment. The salivary glands of all the sacrificed animals were fixed (in SUSA solution saturated with picric acid) for subsequent weighing and histologic [Periodic Acid Schiff (PAS), hematoxylin-phloxine] study. In the treated rats, the enlargement of the salivary glands (Fig. 1) was so pronounced that it could easily be recognized during life by mere inspection and palpation of the neck region. The weight range of the control glands was 333 to 516 mg, as compared with 2531 to 2574 mg after treatment.

Histologic study revealed that the enlargement of the salivary glands is almost entirely due to intense mitotic proliferation of the serous, mucous, and duct cells; it is accompanied by microscopic evidence of increased secretory activity. The stroma showed only a moderate degree of edema, and imbibition with slightly PAS-positive material. The parotid, submaxillary, and sublingual glands were enlarged to approximately the same degree, whereas the external lacrimal gland remained essentially unaffected.

The true parenchymatous growth of salivary gland tissue thus induced experimentally bears little resemblance to the various types of clinical sialadenitis (for example, postoperative parotitis, uveoparotitis), the latter being essentially inflammatory lesions. However, the changes produced by isoproterenol are structurally similar to the "idiopathic," true hypertrophies and hyperplasias of the human salivary glands that have been described as "sialadenoses" in patients suffering from various endocrine and nervous diseases (see *2*). A similar selective parenchymatous growth of the salivary glands has also often been reported to occur in man as a result of malnutrition and psychic stress. During World War II this condition apparently assumed epidemic proportions among the inmates of the ghetto of Warsaw (*3*) and the concentration camp of Terezin (Theresienstadt); indeed, this type of salivary gland enlargement has even been referred to in the literature as the "symptom of Terezin" (*4*).

It remains to be seen, however, whether these clinical salivary gland enlargements are pathogenetically related to that produced experimentally by isoproterenol, and whether natural catecholamines, when elaborated in excess by chromaffin or nervous tissue, can exert similar effects under certain conditions (*5*).

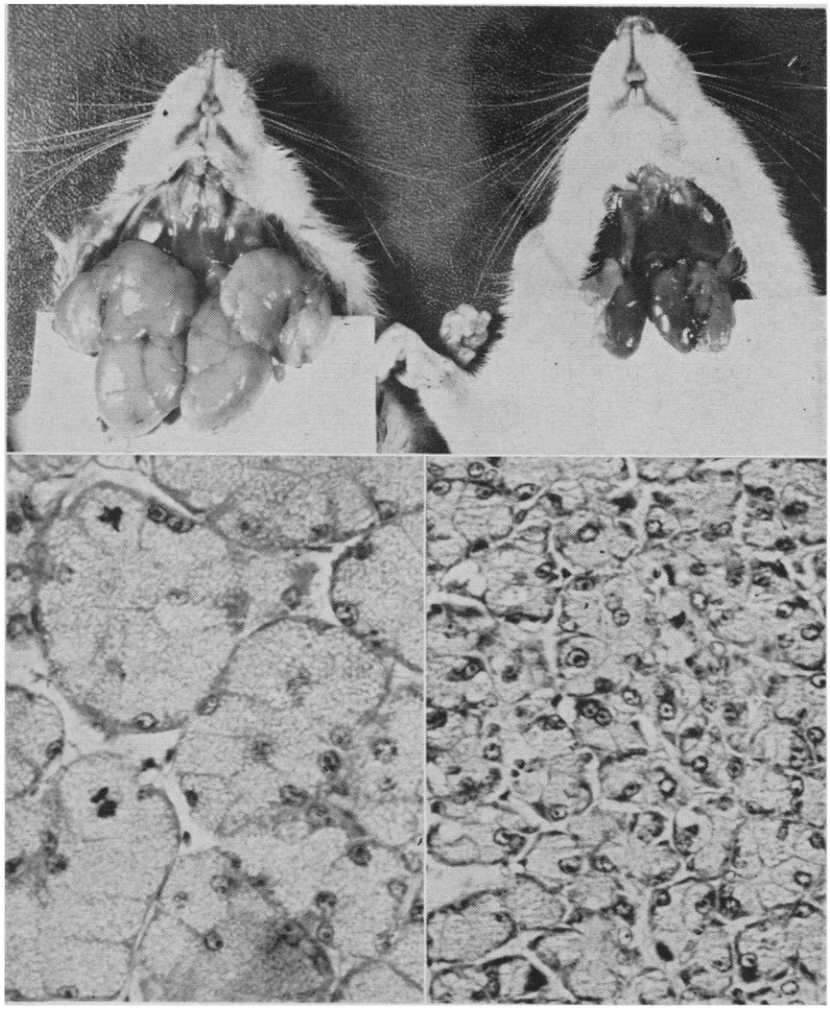

Fig. 1. (Top) Greatly enlarged salivary glands of an isoproterenol-treated rat (left) in comparison with salivary glands of an untreated control. (Bottom, left) Mitotic proliferation and cellular hypertrophy in the parotid gland of an isoproterenol-treated rat, in comparison with (right) cells in an untreated control (× 420).

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