greater P_{32} uptake by tumor nuclei should therefore be attributed to mitotic activity.

There are 14.8×10^{-10} mg P/liver nucleus and 12.8×10^{-10} mg P/tumor nucleus. From the nuclear phosphorus composition and the nuclear P_{32} content at 48 hours, the specific activity of tumor nuclei is found to be more than four times that of liver nuclei. Calculating from the daily P_{31} retention[3] and the per cent. P_{32} uptake, each nucleus will incorporate a quantity of P_{31} equal to 8.9 per cent. of its P_{31} content in five hours. It will thus take 56 hours for the nucleus to synthesize a quantity of P_{31} equal to the amount it originally contained. This should be the time required to synthesize a new nucleus. This value agrees approximately with the observed rate of growth of the tumor which doubles in size in about two days at this phase of its growth curve.[4] It is interesting, though it may be purely a coincidence, that approximately the same time is obtained for the duration of the mitotic cycle in root tips by analysis of effects of x-rays and neutrons.[5]

A detailed account of these experiments will be presented elsewhere.

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MODE OF ACTION OF ESTROGENS ON THE MAMMARY GLAND

FOLLOWING the demonstration by Lyons and Pencharz[1] in 1936 of the failure of estrogenic hormone to produce growth of the mammary glands of hypophysectomized guinea pigs, a sisable literature has appeared in confirmation of this work, which has been extended to include the rat, mouse, cat, rabbit and ground squirrel.[2] These observations emphasized the importance of the pituitary to the mammary gland and gave rise to the theory that injected estrogens exert their effects through the mediation of the pituitary, which was postulated to produce a specific mammogenic hormone.[3]

The specificity of the relationship between the pituitary and mammary growth has, however, been called into serious question by the demonstration[4] that in intact rats which were restricted to a diet comparable to that consumed by hypophysectomized litter-mates, the glands likewise failed to respond to administered estrogen. It has been shown,[5] further, that when hypophysectomized rats were treated with growth complex, growth of the mammary gland could be elicited by estradiol benzoate, and that the degree of stimulation could be correlated with the weight gain of the animals.

Recent experiments permit of a new approach to the problem of the mode of action of estrogenic substances on the mammary gland. By the direct application of the hormone to the nipple area it is possible to obtain a local effect on the nipple and mammary gland. In this manner one can observe the effects of the test substance in the intact animal, thereby obviating the complication of nutritional disturbances produced by hypophysectomy.

Immature male rhesus monkeys were used. The left nipple of each animal was painted daily with a solution of estrone in 95 per cent. alcohol, 0.05 mgm per cc. To the right nipple alcohol alone was similarly applied. Two animals were so treated for a period of 75 days. The entire glands were then removed. A third animal was treated in this manner for 50 days, and the breasts were removed 105 days later. The mammary glands were then fixed, dissected, stained and cleared, and studied as whole mounts.

In all cases the left mammary gland was distinctly larger and more developed than the right one (see Fig. 1). This difference in size exceeded, in each instance, the minor variations between right and left glands occasionally encountered in a study of more than 200 pairs of control monkey mammaries, including the breasts of 30 males.

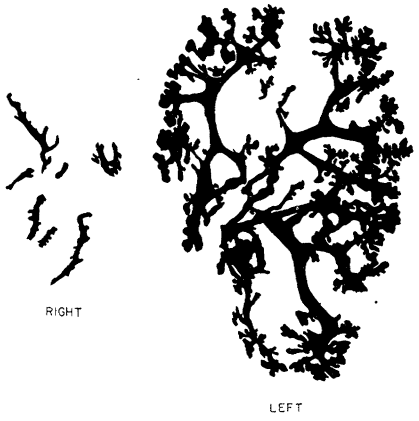

FIG. 1. Right and left mammary glands of prepubertal male monkey after daily application of alcoholic solution of estrone to left nipple for 75 days. Silhouette tracings from photographs of actual specimens.

These observations are regarded as evidence for the direct action of percutaneously administered estrogen on the mammary gland. While not controverting the possible existence of pituitary mammogenic hormones,

[3] L. W. Tuttle, personal communication.

[4] Growth curves obtained from I. L. Chaikoff and H. B. Jones, unpublished.

[5] A. Marshak, *Proc. Nat. Acad. Sci.*, 25: 502–510, 1939.

[6] Fellow of the John Simon Guggenheim Memorial Foundation.

[1] W. R. Lyons and R. I. Pencharz, *Proc. Soc. Exp. Biol. and Med.*, 33: 589, 1936.

[2] E. T. Gomez and C. W. Turner, *Mo. Agr. Exp. Sta. Res. Bul.* 259, 1937.

[3] A. A. Lewis and C. W. Turner, *Mo. Agr. Exp. Sta. Res. Bul.* 310, 1939.

[4] E. B. Astwood, C. F. Geschickter and E. O. Rausch, *Am. Jour. Anat.*, 61: 373, 1937.

[5] I. T. Nathanson, D. T. Shaw and C. C. Franseen, *Proc. Soc. Exp. Biol. and Med.*, 42: 652, 1939.

or even the possibility of estrogenic stimulation of the production of mammogenic hormones by the pituitary, the present experiments offer no support for the view that administered estrogens necessarily stimulate mammary growth through the mediation of the pituitary. For if such were the case, a similar growth response would be expected in both glands, rather than the local, unilateral effect observed.

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THE CONTROL OF PROTOPLASMIC STREAMING

PROTOPLASMIC streaming owes its existence to a motive force the magnitude of which has heretofore not been measured. In order that this might be done the technique here described has been developed.

The slime mold, *Physarum polycephalum,* served as material. Protoplasmic streaming in slime molds is extraordinarily active and exhibits a rhythmic reversal in direction of flow.

Small bits of plasmodia placed on cover-glasses coated with agar soon spread into thin sheets, which later develop protoplasmic strands. Among such cultures there are forms which can be changed so that there are two protoplasmic bodies connected by a single strand. A plasmodium thus shaped is inverted over a chamber which is divided into two compartments (A and B, Fig. 1) by an agar block (C, Fig. 1).

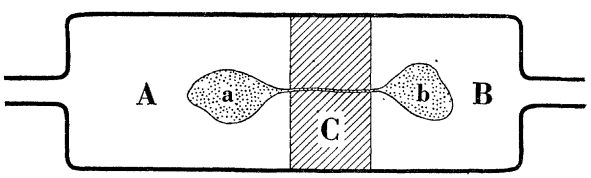

FIG. 1. Schematic representation of the chamber.

The construction is such that the two compartments may be kept airtight without the wall separating them blocking protoplasmic flow in the connecting strand. One of the two compartments is kept at constant atmospheric pressure, whereas the pressure in the other compartment is under control.

When there is no pressure difference between the two compartments, the shuttle movement of the protoplasm goes on normally, causing a corresponding change in the volume of the two protoplasmic masses (A and B, Fig. 1). When, however, a difference in air pressure is established between the two compartments, the movement of the protoplasm in the connecting strand is strikingly affected. If a slightly lower pressure (weak vacuum) is applied to one of the compartments, the flow of the protoplasm in the connecting strand into that compartment is accelerated. When a slightly higher pressure is applied to the same compartment, the flow of the protoplasm along the connecting strand into that compartment is retarded. If the pressure applied is stronger than the motive force developed in the plasmodium, then the forward-moving protoplasm is forced backwards. The direction and velocity of the protoplasmic movement in the connecting strand can thus be accurately controlled. Artificial control of protoplasmic streaming in this manner does not cause any observable damage. Flow continues normally after the applied pressure is released.

By this method it is possible to ascertain the precise degree of pressure necessary to hold the protoplasm at a standstill. The pressure at this point, which is regarded as equal in absolute value to the motive force responsible for the protoplasmic streaming, may be termed the balance-pressure. The range of the balance-pressure is usually between $\pm$ 20 cm of water. The maximum absolute value thus far encountered is 28 cm of water. So sensitive is the movement of the protoplasm that the slightest deviation (less than 0.2 cm of water) from the point of balance-pressure will induce movement in an 8 mm connecting strand.

As the motive force changes spontaneously, the balance-pressure must be adjusted accordingly, if the protoplasm is to be kept immobile. In order to determine in what manner and to what extent the motive force changes in relation to time, the instantaneous values of the balance-pressures (*i.e.,* the values taken at any given instant) are recorded at five-second intervals. By plotting a series of these values as ordinates against time as abscissas, undulating curves are obtained which faithfully portray the distinguishing features of the changes which the motive force undergoes during the rhythmic succession of vital processes. The graphs thus obtained give a complete view of the rhythm in protoplasmic activity. All characteristics of rhythm such as wave form, frequency, polarity and amplitude are portrayed by the graphical representation.

The study of many examples of wave trains mapped in this way leads to the conclusion that the characteristic change in amplitude and in form of wave is, in all probability, due to the interference of different rhythms. This concept necessarily implies the co-existence, in one and the same plasmodium, of different frequencies of the mechanism responsible for the motive force. In other words, a plasmodium is a polyrhythmic system.

In this brief note I am not in a position to go into further details of description and discussion of my experiments, except to say that in addition to an analysis of protoplasmic rhythm the method here touched upon is a means for attacking such problems as that of the relative influence of motive force and viscosity in protoplasmic flow. The procedure outlined above also suggests a new method for measuring protoplasmic viscosity by applying the principle of