(21); undecylate, 0.15 (25); sodium chloride controls, 0.19 (70).

Methyl esters of the fatty acids were found to be somewhat toxic. Experiments are in progress to demonstrate the comparative ketogenic effect of the ethyl esters of palmitic and stearic acids with that of acetoacetate when administered in much smaller doses.

8745 P

Initiation of Lactation in the Hypophysectomized Guinea Pig.

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The anterior pituitary secretes a hormone concerned in the initiation of lactation. Male or immature female guinea pigs whose mammary glands are developed under the influence of ovarian grafts or oestrin injections lactate when the source of oestrin is removed, but will not do so if the pituitary is simultaneously removed.[1] The following experiments indicate that the adrenal cortex, as well as the pituitary, may be involved in the initiation of lactation in the guinea pig.

Series I. Fourteen guinea pigs were prepared for lactation by prolonged oestrin injections or, in some of the males, by functional ovarian grafts. At the time the ovarian grafts were removed or oestrin injections discontinued hypophysectomy was performed. Injections of a purified preparation of lactogenic hormone* were begun immediately. This treatment in no instance initiated lactation, although continued from 5 to 15 days. In 3 partially hypophysectomized animals lactation was initiated.

Series II. Nine animals similarly prepared for lactation were hypophysectomized and treated with a crude alkaline extract of sheep pituitaries.* This extract contains, in addition to the lactogenic hormone, most if not all of the other known pituitary hormones.

The crude extract, in contrast to the purified lactogenic preparations initiated lactation in the hypophysectomized guinea pigs in every case. Six animals from Group I, failing to lactate on puri-

1 Nelson, W. O., PROC. SOC. EXP. BIOL. AND MED., 1935, **33**, 222.

* For the crude pituitary extract, Theelin, and purified lactogenic hormone used here the authors are indebted to Dr. Oliver Kamm of Parke, Davis & Co.

fied lactogenic material, were subsequently treated with crude pituitary extract and lactation was then initiated in every case.

Since the hormonic requirements for the initiation of lactation in the guinea pig after hypophysectomy were not met by the hypophyseal lactogenic hormone alone, a second factor was sought for. A possible explanation was suggested by the observations of lactation deficiencies in adrenalectomized animals,[2, 3] and by the fact that large amounts of the adrenal cortical hormone are necessary for normal lactation in adrenalectomized rats.[3] With this in mind the following experiments were carried out.

Series III. Seven immature males or females were treated for at least 3 weeks with a minimum of 40 R.U. of Theelin* or Amniotin† per day. At the time treatment was stopped hypophysectomy was performed and daily injections of 10 mg. (0.5 rabbit unit) of purified lactogenic hormone plus 2 cc. of adrenal cortical hormone were begun. (The adrenal cortical extracts used here were generously furnished by Dr. W. W. Swingle of Princeton University.) This treatment initiated lactation in every case, and by continued treatment milk could be kept flowing for about 5 days.

Series IV. Three pregnant females were hypophysectomized within 3 days of expected delivery. These animals did not lactate following parturition even when treated with a purified lactogenic hormone. In 2 similar cases, however, in which cortical hormone was added to the lactogenic hormone lactation occurred.

In one case hypophysectomy was performed after lactation had been initiated following parturition. Lactation stopped within 2 days. It was reinitiated after 2 days' treatment with adrenal cortical and purified lactogenic hormones.

Series V. Three animals prepared as in Group III were allowed to go untreated for 4 days after hypophysectomy. After this interval lactation could still be induced by purified lactogenic hormone plus adrenal cortical hormone.

Series VI. Lactation could not be initiated in 3 normal, adult, female guinea pigs treated during and following oestrus with 5 daily injections of 2 cc. of cortical hormone alone. Purified lactogenic hormone is known to induce lactation in such animals.

Lactation once initiated by cortical and lactogenic hormones could

2 Brownell, K. A., Lockwood, J. E., and Hartman, F. A., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 783

3 Gaunt, R., and Tobin, C. E., *Am. J. Phys.*, 1936, **115**, 588.

† The Amniotin was kindly supplied by Dr. J. A. Morrell of E. R. Squibb & Sons.

not be maintained by cortical hormone alone in the one hypophysectomized animal thus treated from Series III.

Series VII. Lactation could not be maintained (as judged by the death of suckling litters) in 3 hypophysectomized, lactating rats treated with cortical and purified lactogenic hormones. This result was expected in view of the fact that even with crude pituitary extracts we could not maintain lactation in 12 such rats.

Summary. A purified lactogenic hormone, unlike crude pituitary extracts, has failed to initiate lactation in hypophysectomized guinea pigs. Lactogenic hormone plus the adrenal cortical hormone (Swingle-Pfiffner extract) has initiated lactation in such animals in every case.‡

8746 C

Production of Shwartzman Reaction in Rabbits with Purified Fraction of *B. coli* Filtrate.

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Previous publications[1, 2] from this laboratory described a method for the separation and concentration of the factor in *B. coli* filtrates which produces hemorrhage in mouse tumors. Since *B. coli* filtrates are known to produce the Shwartzman reaction in rabbits, it was of interest to ascertain whether the purest fraction of the tumor-affecting agent obtained thus far[2] was also capable of eliciting hemorrhage in prepared sites in the skin of rabbits. It was also desirable to make quantitative comparisons between the original filtrate and the purified fraction as to their ability to produce hemorrhage in tumors of mice as well as the Shwartzman reaction in the rabbit.

Equivalent tumor-affecting doses were determined by performing

‡ Judging by gross observation at autopsy, anterior lobe removal was complete in all of these cases. To verify this, however, sections of the sella turcica contents have been made in most cases, although not yet complete in a few cases. We have omitted in this account those animals, a considerable number, that failed to survive the operation long enough to allow for the necessary observations.

1 Shear, M. J., and Andervont, H. B., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 323.

2 Shear, M. J., *ibid.*, 1936, **34**, 325.