fanilamide for rats by intravenous injection is indicated by the survival of the drug controls.

Eight additional animals were inoculated intraperitoneally with approximately 500,000 *Trypanosoma equiperdum;* 2 untreated controls died on the fifth day after inoculation. The remaining 6 animals were given capsules of sulfanilamide powder in dose of 0.2 to 0.5 g per kilo 24, 30, 48, 72, and 78 hours after inoculation (Table II). All succumbed to trypanosomiasis in 5 to 6 days after inoculation, the doses corresponding to as much as 12.0 to 30.0 g per kilo of weight.

Summary. Sulfanilamide by intravenous and oral administration was ineffective in the treatment of *Trypanosoma equiperdum* infections of rats.

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Estrus-Inhibiting Effects of Inanition

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The effects of complete and partial starvation upon the estrous cycle of adult female rats were studied. Smears from the vaginal mucosa were taken for at least 2 weeks before any experimental procedures were instituted. Seven groups of 5 rats each were used. One group was kept as control; 2 groups received no food or water, and another only water at the onset of starvation; the fifth group was starved intermittently so that the loss of weight was more gradual. The remaining 2 groups were starved completely without water until they died. Each animal was weighed daily. The water and food consumption of the groups fed was recorded daily. It was found that the animals in all the starved groups eventually showed complete inhibition of the estrous cycle, and that the inhibition was roughly related to the loss in body weight, as shown in the table. When the inhibition of the estrous cycle was complete, all but 2 groups were fed again, with resulting return to the normal cyclical changes in the vaginal mucosa.

Experiments to Determine the Factors Involved. In analyzing the estrus-inhibiting effects of starvation, one must distinguish between

TABLE I.
Estrus-Inhibiting Properties of Starvation Inanition.

Rat Group	Procedure instituted	Resulting anestrus in—days	Loss in Weight		Subsequent treatment	Effect on vaginal mucosa	Weight loss at end of experiment	
			%	Days			%	Days
St-25	Complete starvation	1-4	30	6	Continued starvation plus estrogen	Estrus in 3 days	40	11
St-26-7	Complete starvation	1-3	30	6	Continued starvation	Continued anestrus	42	11
St-19	Complete starvation	1-5	33	7	Refed	Estrus in 7 to 13 days	None	21
St-28	Complete starvation	2-4	25	5	Continued starvation plus Follutein	Estrus in 3 days	33	8
St-21	Complete starvation plus water	1-5	30	7	Refed	Estrus in 4 to 9 days	None	16
St-22	Chronic inanition	3-6	15	7	Refed	Estrus in 3 to 6 days	None	
St-20	Control	None	—	—	—	—	Gained 13	21

an inability of the vaginal mucosa to respond to estrogenic hormone; and the possibility that the ovaries have ceased to produce the hormone during the period of inanition. If the latter be true, one must further distinguish between a primary failure of the ovary, and a failure of the pituitary gland to produce the gonadotropic hormone. It is conceivable that any or all of these factors may be involved.

1. *The effect of estradiol monobenzoate upon the inanition anestrus.* Two groups of 10 rats were starved completely for 6 days. On the day starvation was begun 4 of the 10 animals were in estrus; 3 were just entering the diestrous phase; 2 were in diestrus; and 1 was in proestrus. The 4 in estrus completed their cycles and then entered permanent diestrus or anestrus. The 3 which were entering diestrus remained in anestrus throughout. Of the 2 rats in diestrus, 1 remained so, the other went as far as the nucleated epithelial stage on the second and third day of starvation and then developed anestrus. The animals in proestrus showed a normal cycle which ended in anestrus. These 10 rats were then divided into 2 groups on the sixth day of starvation. At this time, most of them had been in the anestrus for 4 days. One group was kept as an untreated control, while the rats of the other group were injected daily with 3 R.U. of estradiol monobenzoate (Progynon-B)* subcutaneously. The 5 untreated control rats continued in complete anestrus to the 11th day of starvation, when they were autopsied. The gonads were weighed and fixed for sectioning, as were the other glands of internal secretion. The 5 rats which received estrogen remained in anestrus for 24 hours, but on the 2nd day showed nucleated epithelial cells. On the 3rd day of injection and on the 9th day of starvation, all were in typical estrus and continued so until autopsy on the 11th day.

Two groups of 5 rats each were starved acutely except that one received drinking water. Their estrous behavior resembled that of the rats analyzed above. They were refed on the 7th day of starvation, when the percentage of body weight lost averaged 33, and all the rats had been in anestrus for 1 to 5 days. Five to 8 days following refeeding, when the animals had regained the loss in weight, a return to normal estrous cycles was evidenced. Two weeks after refeeding was begun, and all the rats were showing normal cycles, daily injections of 2 R.U. of estrogen were begun. Eleven days later the rats were starved as before, but due to the daily injections

* We are indebted to Drs. Gregory Stragnell and Erwin Schwenk of the Schering Corporation for their supply of Progynon-B.

of estrogen they continued to have cycles as though no starvation had been instituted. The control group of rats showed normal estrous cycles during these experiments.

Another group was underfed by allowing food freely for 24 hours after 48 hours of fasting. On the 8th day, when the rats had lost an average of 15% of their body weight, they were in anestrus for from 3 to 6 days. Upon being refed all rats continued anestrous from 3 to 6 days, when they resumed their normal cycles. This experiment was repeated 2 weeks later. This time the rats received daily injections of 2 R.U. of estrogen. The results confirm the impression gained from the above experiments. Animals that are acutely starved or chronically underfed will cease to have estrus when the body weight has dropped but some 15%. These rats may be made to have estrus again by the subcutaneous injection of estrogen even when 40% of the body weight has been lost. The presence of estrogen in the body prevents the appearance of this "inanition anestrus."

2. *The effect of gonadotropic hormone upon inanition anestrus.* A group of 5 rats was examined and then starved acutely. After 5 days of starvation with ensuing anestrus, the rats were injected with 3 to 4 R.U. of gonadotropic hormone (Follutein)† daily for 3 days. Forty-eight hours after the first injection the vaginal smear of 1 of the rats showed nucleated epithelial cells. In 72 hours (8th day of starvation) all 5 animals were in full estrus.

The lack of estrogen in the animal in sufficient quantities to activate the vaginal mucosa during the course of inanition is evidently due to diminished production of gonadotropic hormone, rather than to any inability of the ovary to respond to the hormone. No quantitative data are as yet available to warrant a statement as to any altered sensitivity of the ovary.

Discussion. It has been found that such diverse factors as double adrenalectomy,[1-5] dietary deficiencies,[6, 7] especially B_1-avitaminosis,[8]

† We are indebted to Drs. G. A. Harrop and John Anderson of E. R. Squibb & Sons for their supply of pituitary-like hormone.

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poisoning with dinitrophenol, thyroid extract[9-13] result in the loss of estrous cycles in rats. Analysis of these data indicated an underlying common factor, namely, the loss in weight in all of these experimental animals. Corroborative evidence against the assumption of some more specific cause of the anestrus was furnished by the fact that estrous activity was resumed when the weight lost had been regained. On the other hand, insulin injections,[14] manganese-free diets,[15] morphine,[16] and nicotine[17] poisonings in rats, procedures which resulted in no disturbance of nutrition in no way affected the estrous cycle. Our own experiments support the conclusion that in the investigations alluded to above, the loss of estrus was either wholly or at least in part due to the concomitant inanition. The inanition appears to produce anestrus through changes induced in the hypophysis.

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Progesterone Will Maintain Adrenalectomized Rats.*

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Certain observations suggest the possibility that progesterone is capable of maintaining the adrenalectomized animal. (a) There is a chemical similarity in the structure of progesterone and certain of the hormones found in the adrenal cortex.[1, 2] (b) 21-hydroxyprogesterone (desoxycorticosterone) will maintain the adrenalecto-

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