completely curative with negative lymph node transfers. The same results were observed when 0.5 mg bismuth salicylate per kg of weight was given every 3 days for 5 doses (totalling 2.5 mg) by intramuscular injection. Similar results were observed with terramycin hydrochloride administered intramuscularly. Thus the administration of 2.5 mg per kg once daily for 15 doses (totalling 37.5 mg) was without detectable therapeutic activity. But when administered along with 0.3 mg Mapharsen per kg by intravenous injection every 3 days for 5 doses (totalling 1.5 mg), this dosage of terramycin hydrochloride was completely curative with negative lymph node transfers. The same results were observed when bismuth salicylate was administered intramuscularly every 3 days for 5 injections in dose of 0.5 mg per kg (totalling 2.5 mg). Since both Mapharsen and bismuth salicylate alone in these doses per kg of weight were not completely curative with positive lymph node transfers, it is apparent that both compounds act synergistically or additively with terramycin hydrochloride in the treatment of experimental syphilis of rabbits, as has been observed with penicillin(4-6).

Summary. (1) Terramycin hydrochloride by oral administration in single doses of 50 to 250 mg per kg of weight were not completely curative in the treatment of acute syphilitic orchitis of rabbits. (2) When administered orally twice daily for 15 days in succession the total minimal curative dose was 150 to 300 mg per kg of weight. (3) By intramuscular injection the single minimal curative dose was 75 to 100 mg per kg of weight. When administered once daily for 15 days in succession the total minimal curative dose was 75 to 150 mg per kg by this route of administration. (4) Mapharsen by intravenous injection and bismuth salicylate by intramuscular injection yielded pronounced synergistic or additive therapeutic effects when given along with terramycin hydrochloride by oral and intramuscular administration.

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Received December 11, 1951. P.S.E.B.M., 1952, v79.

Hibernation in the Alligator. (19302)

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In common with several other species of reptiles the reaction of the alligator to various types of stimuli is slow enough to allow the observer much more time than would be the case if warm blooded animals had been employed(1,2). Unfortunately the concentration of various blood constituents is not constant but is subject to certain seasonal changes. McIlhenny(3) commented on the fact that the alligator does not eat for several months in the winter either in his native habitat or in the confines of a heated zoological garden. This loss of the desire to eat constituted almost the sole experimental evidence that the alligator is an animal which hibernates in the winter. In the course of over 3 years of research we have been able to collect a considerable amount of data on the effect of season on the alligator and on the caiman, a closely related tropical species.

Effect of temperature and light on blood glucose and growth rate. About 200 alligators and 35 South American caimans were observed under laboratory conditions. Pre-

TABLE I. Effect of Length of Day on Growth Rate and Fasting Blood Glucose.

Hr light	Nov. 19	Dec. 20	Jan. 17	Feb. 21	Mar. 23	Apr. 20	June 10	July 5	Aug. 8	Sept. 12	Oct. 18	Nov. 8	Dec. 5
						Glucose, mg %*							
10	73	75	109	128	123	121	118	94	136	114	48	66	60
14	75	81	110	133	118	107	119	89	143	121	40	39	52
						Body wt in g*							
10	40	40	37	41	51	59	66	74	81	81	—	—	79
14	44	43	39	45	59	68	79	82	86	83	—	—	80

* Each number represents avg of 12 alligators.

liminary studies on the alligator revealed that hypoglycemia and anorexia were coincident with the approach of winter regardless of the temperature of the animal's habitat. To determine the exact effect of temperature and light on hibernation 24 three-month-old alligators were selected and divided into 2 groups of 12. Both groups were placed in a constant temperature room which had no windows but which was lighted by fluorescent lights. One group was exposed to the artificial light for 10 hours a day and the other group to the same light for 14 hours a day for a period of over a year. The room temperature was 28°C, which is the average temperature of New Orleans on June 21. The longest days in the locality are 14 hours in June and the shortest are 10 hours in December. Under these conditions both groups were kept at the summer temperature; one group was exposed to "December light" and the other group to "June light". The animals were weighed and measured at approximately monthly intervals and glucose was determined by the Folin-Wu method using 0.1 ml of blood from the tip of the tail. Skinned white rats were fed to both groups. From Table I, which presents the average body weights and blood glucose values for each group, it would appear that hypoglycemia began in both groups in October and ended in late January. Differences between the two groups are probably not significant. It is curious that animals maintained under these constant conditions should still exhibit the usual seasonal hypoglycemia. Whatever mechanism is involved it seems to be independent of light or temperature. Both during the course of the light experiment and for the next 2 years blood glucose was determined on scores of other alligators at all seasons of the year. The results confirmed the observation that the glucose level drops in October or November and rises again in February or March. Blood glucose analyses were also performed each month on 30 caimans (*C. latirostris*). There is some doubt as to the exact point of origin of these animals although it is known that they came from somewhere in South America. No significant variation in monthly blood glucose has been observed in the eight months they have been kept in the laboratory; the highest blood glucose was 94 mg % and the lowest was 76 mg %. There is no reason to believe that the caimans, which are tropical reptiles, hibernate in the winter months since their blood glucose level seems to be reasonably constant and since they ate as well in January as they did in July.

Effect of semi-starvation on seasonal blood glucose. Nine 2-year-old alligators were fasted from Dec. 19 to May 9 and frequent glucose analyses were conducted to see if semi-starvation would prevent the rise in blood glucose in the spring. The average blood glucose did not rise as long as the animals were fasted although the alligators showed obvious signs of hunger when any food was placed near them. It would seem that the anorexia is not necessarily associated with hypoglycemia although the two occur at the same time in the normal seasonal cycle. In spite of the fact that the animals were seriously emaciated on May 9, the last day of the fast, the glucose rose to the normal seasonal level after 2 weeks of feeding and the alligators quickly regained their lost weight.

Effect of hormones on fasting blood glucose. Thirty small alligators were divided into 3 equal groups in December. One group re-

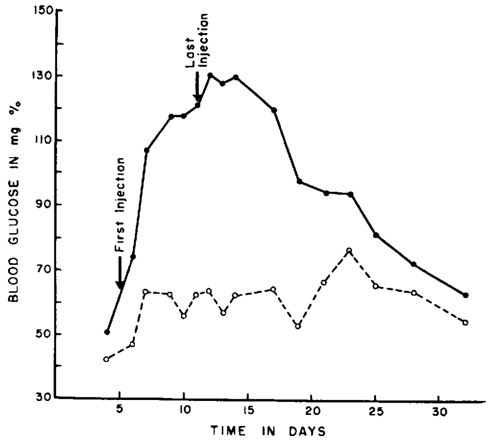

FIG. 1. The effect of whole sheep pituitary powder (Armour) on the fasting blood glucose of the alligator (December). Solid line represents avg of 5 experimentals injected daily with .3 mg/100 g body wt; the broken line represents avg of 4 controls.

ceived 0.1 mg desiccated thyroid per 100 g body weight intraperitoneally every other day; another group received 5 mg/100 g body weight of whole sheep pituitary powder (Armour) every other day, and the third group served as controls. After 2 weeks of these injections the average glucose level of the thyroid series was 35 mg %, the average of the 6 survivors of the pituitary injections was 90 mg %, and the average of the controls was 33 mg %. The pituitary series was discontinued and although the thyroid series was continued for an additional 3 weeks the blood glucose level at the end of that time was still no higher than that of the control group. Further studies of the action of crude pituitary powder were conducted in January on nine 18 inch alligators. Five of these animals received 0.3 mg whole pituitary powder per 100 g of body weight each day for 6 days while the other 4 served as controls. The results are recorded in Fig. 1. Successive injections of powdered desiccated liver or brain suspensions had no effect on the level of glucose of the controls. Although it would appear that the alligator is quite sensitive to very small amounts of whole pituitary powder it is by no means certain that the variations in the output of a "glycotropic" factor from the animal's own hypophysis are responsible for the seasonal rise and fall in blood glucose.

Effect of season on oxygen consumption and metabolic rate. It was considered possible that the failure of the alligators to eat for a large part of the year could be due to a hormone which controls metabolism and which directly or indirectly controls the desire to eat. Experiments were devised to measure the oxygen consumption in both winter and summer and to attempt to relate it to the metabolism. The measurement of oxygen consumption was accomplished by the relatively simple method of measuring the decline in pressure of the air in a calibrated vacuum desiccator which contained the alligator and wet soda lime to absorb the CO_2. All measurements were performed at the average summer temperature for New Orleans (28°C) by submerging the desiccator in a water bath or by placing it in a large temperature controlled incubator. All animals were allowed to equilibrate with the temperature at 28° for several hours and to accustom themselves to their temporary surroundings before measurements were taken. The smallest animals were allowed to remain in the desiccators for periods of about a day for each run. At the close of each experiment the air in the desiccator was flushed out by use of a water pump, the alligator was again equilibrated, and another run was begun. Three runs were performed on each small animal. The procedure was the same for larger alligators (up to 3 kg) except that the high rate of oxygen consumption necessitated a shorter test period which varied from about 1 hour for the very largest animals to 10 hours for some of 300 g size. In most cases 5 or 6 separate oxygen consumption tests were run on the larger animals. Since it is never possible to eliminate entirely the increase in oxygen consumption occasioned by movement of the test animal it was decided to use only the run in which the animal consumed the least oxygen in a given time. In most cases the first run gave results which were considerably higher than the second while the second and third runs usually checked to within about 10%. It must be emphasized that none of the results obtained were considered to be indicative of

TABLE II. Effect of Season on Oxygen Consumption by 19 Alligators and 17 Caimans.

	Alligator avg		Caiman avg	
	Winter	Summer	Winter	Summer
Body wt	49.7	87.7	116	161
Ml, O_2/g/day	1.92 ± .07*	1.77 ± .06	1.69 ± .08	1.53 ± .07

$$* \text{ P.E.} = .6745 \sqrt{\frac{(v)^2}{n(n-1)}}.$$

"basal metabolism" since that state would be difficult to define in a crocodilian. Under the conditions of these experiments the animals usually remained very quiet and in the majority of cases hours would pass without the slightest sign of motion. The winter series of experiments was conducted in December and January and the summer series in June and July. All animals were fasted for at least 3 days prior to the run which was finally recorded. Since an increase in body weight between the winter and summer experiments led to an increase in surface area of unknown magnitude it seems reasonable to equate the oxygen consumption in terms of ml O_2/g/24 hours. It was possible to demonstrate that the largest animals (3 kg) used about 0.5 ml O_2/g/day while the smallest (about 50 g) consumed about 2 ml/g/day.

The results of seasonal metabolic studies on one group of small alligators and on one group of caimans appear in Table II. It can be seen that the oxygen consumption per unit weight is slightly less in summer than in winter in both alligators and caimans. This probably does not indicate a lower "absolute" metabolic rate but rather a decrease in apparent metabolic rate due to decreased surface area per unit body weight. It is perhaps natural to expect closely related species such as the alligator and caiman to have the same metabolic rate and all evidence points to this as being correct.

Effect of hormones on metabolic rate. Since hypoglycemia is the most marked feature of hibernation in the alligator it was decided to determine the effect on metabolism of various substances which might change the blood glucose concentration. Five fasting alligators with an average weight of about 100 g were selected for study. Each animal was placed in a desiccator and control runs were performed on each for 3 successive days. The animals were then removed from the desiccators and placed in a tank of water for several hours to repair any effects of dehydration. Each was then injected intramuscularly with regular insulin (5 units/kg) and again placed in his respective desiccator. Since insulin does not produce any hypoglycemia for about 7 hours (unpublished observations) the animals were allowed to equilibrate for about 5 hours before the desiccators were sealed. In view of the fact that insulin in the dose used in this experiment exerts an effect for about 48 hours, only 2 separate 24-hour runs were conducted. Following the disappearance of the insulin from the blood each animal received 500 mg/kilo of glucose intraperitoneally and the oxygen consumption was measured on each of the next 2 days. After the disappearance of the glucose each animal was again removed, given water to drink, and then injected with 5 mg/100 g of crude whole pituitary powder (Armour). Twenty-four hours later each was again injected with 10 mg/100 g and oxygen consumption was measured on each of the next 2 days. The results are presented in Table III. Pituitary powder produced a slight but possibly significant increase in the rate of oxygen consumption whereas glucose and insulin seemed to have no effect. Since the significance of the results of the short term injections of pituitary powder on metabolism was questionable, 25 other alligators were selected for experiments to determine the effect of prolonged injections of desiccated thyroid and pituitary powder. Ten animals received 0.1 mg of desiccated thyroid every other day for 3 weeks, 10 received 5 mg of whole pituitary powder every other day for 2 weeks and 5 animals served

TABLE III. Influence of Insulin, Glucose, and Pituitary Powder on Oxygen Consumption (ml/g/day) on 5 Alligators.

	Body wt, g	Control	Insulin	Glucose	Pituitary powder
	114	1.08	1.29	1.32	1.33
	107	.96	1.11	1.18	1.24
	170	1.49	1.31	.94	1.22
	92	1.37	1.41	1.38	1.54
	73	1.90	1.88	1.97	2.56
Avg	111	1.36	1.40	1.36	1.58

TABLE IV. Influence of Prolonged Administration of Desiccated Thyroid and Pituitary Powder on Oxygen Consumption.

	No. alligators	Avg body wt	Ml O_2/g/day, avg and range
Control	5	42	1.73 (1.26–2.00)
Thyroid	10	42	1.83 (1.06–2.38)
Pit. powder	5	45	2.20 (1.83–2.70)

as controls. Unfortunately the pituitary powder was toxic enough to kill 5 of the 10 in that series before the oxygen studies were conducted. At the conclusion of the periods of injection oxygen consumption was measured on each of the alligators for 3 successive days. To make the experiment more nearly comparable to the one presented in Table III the lowest oxygen consumption of the first 2 runs was used to compute the averages shown in Table IV. Again it appears that pituitary powder produces an increase in metabolism in the alligator. It is questionable whether thyroid powder in the quantity injected is instrumental in producing much change in the metabolic rate in spite of the fact that the dosage employed is several times that required to produce an effect in a mammal.

Summary. Although alligators are quite active in the winter if the temperature is high they have a pronounced hypoglycemia and no appetite. There is no seasonal change in metabolic rate in either the alligator or caiman. The caiman does not hibernate. Pituitary powder produces prolonged hyperglycemia and increases the metabolic rate. Desiccated thyroid powder has no effect on blood sugar. Neither glucose nor insulin had any effect on metabolic rate.

The authors wish to express their gratitude to Dr. F. G. Brazda for his helpful suggestions and to H. C. Dessauer, Lucy Gremillion, and J. K. Williams for their technical aid.

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Received December 11, 1951. P.S.E.B.M., 1952, v79.

Effect of Parahydroxypropiophenone on Experimental Ovarian Tumors in Rats.* (19303)

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Experimental gonadal tumors have been developed in this laboratory by transplantation of a gonad into the spleen of castrated animals(1,2). Since it is postulated that the pituitary of such an animal is subjected to decreased gonadotrophin inhibition, it would follow that excessive or uninhibited pituitary gonadotrophin production is probably a factor of prime importance in the formation of these tumors. The fact that exogenous gonadotrophins will accelerate such tumor formation(3), lends credence to the validity of this hypothesis.

The present work was undertaken to investigate the property of non-estrogenic pituitary inhibition(4,5) attributed to parahydroxypro-

* This investigation was supported in part by the Damon Runyon Memorial Fund.