

The Effect of the Implantation of *Spirometra mansonioides* Spargana in the Growing Rat (35952)

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Mueller and Reed (1) have reported that the implantation of *S. mansonioides* spargana in normally growing rats did not enhance body weight gain. This was in contrast to their findings of marked weight gain in normal mice, hamsters, and hypothyroid and hypophysectomized rats implanted with spargana. Steelman *et al.* (2) have shown that the adult plateaued female rat responds to spargana implants with a body weight increase similar to that produced by growth hormone.

Due to the close similarities of the biological profiles of growth hormone and sparganum growth factor (SGF), it was of interest to conduct a more detailed examination of the effects of spargana implants in intact growing male and female rats. Preliminary experiments suggested that endogenous growth hormone secretion may be modified in spargana-implanted animals.

Methods. Groups of male and female rats (Carworth Farms), whose average body weights were from 100 to 160 g, were employed in the studies. In any one experiment, animals were allocated into groups on the basis of fasted body weight in such a manner that the average group body weights were the same and the standard errors of the mean body weights were comparable. All animals were fed standard laboratory chow pellets and tap water *ad libitum*, and were maintained in individual cages under constant temperature and lighting conditions.

Clipped scolices (approx 1 cm in length) of spargana were used for implantation (2) and were suspended in physiological saline and injected subcutaneously into the dorsal side of the neck using a syringe with an 18 gauge needle. Ten scolices were implanted in

each animal. The control animals received no implants.

In the initial study, groups of 15 male and female rats were implanted with spargana and were maintained for 14 days. On day 15, after an overnight fast, each animal was weighed and sacrificed. At autopsy a variety of endocrine and nonendocrine tissues were removed and weighed on a Roller-Smith balance.

In the next study, a comparison of *S. mansonioides* spargana and a mixture of Asian strains (Malay and Taiwan) of *Spirometra spargana* was conducted in male rats using groups of 10 animals. The treated animals received 10 scolices/rat for 14 days (2).

To ascertain the effect of *S. mansonioides* spargana implants on the pituitary as a function of time, male and female rats (Carworth Farms) in groups of 10 were sacrificed at intervals of 10, 20, 30, 40, and 50 days following implantation. Body and pituitary weights were obtained from the animals at autopsy. Epididymal fat pad weights were obtained from the study conducted with male rats.

A study with *S. mansonioides* spargana implants was conducted for the purpose of ascertaining the effect on plasma growth hormone levels. Groups of female rats were sacrificed at 0, 10, and 37 days following implantation. Blood was withdrawn from the abdominal aorta in heparinized syringes and pools were made from each group. The determinations of the plasma growth hormone levels were kindly carried out in the laboratories of Dr. A. V. Schally using standard radioimmune methods for rat growth hormone.

Results. Table I shows that many of the biological parameters measured were signifi-

TABLE I. The Effect of *S. mansonoides* Spargana Implants on Various Biological Parameters in Normal Male and Female Rats 14 Days After Implantation.^a

Index	Male		Female	
	Control	Implanted	Control	Implanted
Body wt change (g)	+58.6 ± 3.0	+52.1 ± 2.9	+37.6 ± 2	+37.5 ± 2
Testes (g)	2.67 ± 0.04	2.54 ± 0.05		
Seminal vesicle (mg)	112 ± 6	84 ± 4 ^b		
Ventral prostate (mg)	149 ± 9	112 ± 5 ^b		
Thymus (mg)	504 ± 22	343 ± 21 ^b	431 ± 23	331 ± 15 ^b
Adrenal (mg)	38 ± 1	39 ± 1	46 ± 2	40 ± 2 ^b
Liver (g)	5.96 ± 0.12	5.55 ± 0.11 ^b	5.52 ± 0.1	5.53 ± 0.1
Kidney (g)	1.45 ± 0.03	1.23 ± 0.03 ^b	1.31 ± 0.03	1.19 ± 0.02 ^b
Thyroids (mg)	10.5 ± 0.3	8.6 ± 0.3 ^b	13.2 ± 0.5	11.1 ± 0.4 ^b
Epididymal fat pad (mg)	1010 ± 40	1583 ± 118 ^b		
Pituitary (mg)	7.3 ± 0.2	4.5 ± 0.3 ^b	7.7 ± 0.3	4.8 ± 0.3 ^b
Ovaries (mg)			53 ± 3	40 ± 3 ^b
Uterus (mg)			261 ± 16	185 ± 15 ^b

^a Values ± standard error of the mean; 15 animals/group.

^b *p* value vs control, < 0.01.

cantly affected; whereas the body weights of the control and experimental animals were virtually identical. Most striking, was the marked decrease (37%) in pituitary weight. A concomitant increase (57%) in fat pad weights was seen in the implanted male rats. Adrenal weights were unchanged, but thyroid weights were significantly decreased. Although testes weights were unaffected, a significant decrease in accessory sex tissue weights was observed. Liver, kidney, and thymus weights were lower in the implanted animals.

The data obtained from the implanted fe-

male rats (Table I) essentially confirms that seen in the males. Once again, a pituitary weight decrease (38%) was observed which was virtually identical with that of males. A decrease in thyroid, ovary, and uterine weights was seen. Although liver and adrenal weights were unchanged, decreased weights were noted for both thymus and kidney.

A comparison (Table II) of the effects of *S. mansonoides* spargana with those of Asian origin vs unimplanted animals revealed that only the *S. mansonoides* spargana produced the dramatic effect on the pituitary and epididymal fat pad weights. Other indices were

TABLE II. Comparison of the Biological Effects of the Implantation of *S. mansonoides* Spargana and Asian *Spirometra* Spargana in Normal Male Rats 14 Days After Implantation.^a

Index	Control	<i>Spirometra mansonoides</i>	Asian <i>Spirometra</i>
Body wt change (g)	+75.9 ± 1.8	+71.4 ± 3.7	+85.1 ± 2.9 ^b
Testes (g)	3.22 ± 0.04	3.20 ± 0.05	3.20 ± 0.07
Seminal vesicles (mg)	258 ± 11	204 ± 8 ^c	218 ± 10 ^c
Ventral prostate (mg)	307 ± 11	229 ± 13 ^c	278 ± 14
Thymus (mg)	536 ± 21	465 ± 30 ^c	596 ± 33
Adrenal (mg)	42 ± 2	44 ± 1	39 ± 2
Liver (g)	7.61 ± 0.15	6.95 ± 0.20 ^b	7.94 ± 0.25
Kidney (g)	2.10 ± 0.05	1.72 ± 0.06 ^c	2.00 ± 0.05
Epididymal fat pad (mg)	1.84 ± 0.06	2.42 ± 0.12 ^c	2.12 ± 0.11 ^b
Thyroid (mg)	17.0 ± 1.1	12.9 ± 0.6 ^c	13.5 ± 0.6 ^b
Pituitary (mg)	9.3 ± 0.4	6.6 ± 0.4 ^c	9.5 ± 0.4

^a Ten animals/group; average initial body weight, 155-160 g.

^b *p* values vs control: < .05; ^c < .01.

TABLE III. The Effect of *S. mansonioides* Spargana Implants on Normal Male and Female Rats at Varying Time Intervals.^a

Post-implantation (days)	Body wt change (g)		Pituitary wt (mg)		Epididymal fat pad wt (g)	
	Control	Implanted	Control	Implanted	Control	Implanted
Males						
10	+46 ± 2	+31 ± 2 ^b	6.9 ± 0.3	3.8 ± 0.2 ^c	0.80 ± 0.05	0.91 ± 0.05
20	+127 ± 4	+104 ± 4 ^b	8.8 ± 0.3	6.0 ± 0.4 ^c	1.97 ± 0.14	2.84 ± 0.15 ^c
30	+177 ± 8	+171 ± 6	8.5 ± 0.4	6.1 ± 0.5 ^c	2.88 ± 0.18	3.48 ± 0.43 ^c
40	+209 ± 11	+218 ± 8	9.7 ± 0.5	8.2 ± 0.3 ^b	3.60 ± 0.33	4.31 ± 0.27
Females						
10	+21 ± 2	+25 ± 1	6.3 ± 0.3	6.0 ± 0.6		
20	+40 ± 1	+60 ± 3 ^c	9.2 ± 0.6	7.2 ± 0.2 ^c		
30	+52 ± 2	+68 ± 2 ^c	9.3 ± 0.3	6.9 ± 0.2 ^c		
40	+53 ± 2	+82 ± 4 ^c	10.9 ± 0.6	7.6 ± 0.3 ^c		
50	+73 ± 4	+78 ± 4	11.7 ± 0.4	7.7 ± 0.2 ^c		

^a ± Standard error of mean; 10 animals/group; initial weight of males, 115–120 g; initial weight of females, 135–145 g.

^b *p* value vs control: < .05; ^c < .01.

largely unaffected by the spargana of Asiatic origin. The animals receiving *S. mansonioides* implants responded in a fashion similar to those in Table I.

The depression of pituitary weights persists for as long as 50 days (Table III), although the maximum depression appears to occur between 10 and 20 days. In the males, as noted previously, the fat pad weights of implanted animals increased substantially. With regard to the body weight changes in the male, it is of interest to note that initially the implanted animals have a lower average body weight. Whereas in the female, a significant increase in body weight was noted through day 40. However by day 50 the average weights of the animals were comparable. As has been noted previously (2) in hypophysectomized rats, the major stimulation of growth occurs by day 30.

The plasma growth hormone levels in unimplanted female rats, together with those from animals implanted for 10 days and 37 days, are shown in Table IV. It is apparent that the drop in plasma growth hormone level measured by radioimmune assay at 10 days is related also to the decreased pituitary weight. The markedly elevated level seen at 37 days suggests a rebound in growth hormone secretion.

Discussion. The data presented show that,

although transient changes in body weights were seen, final body weights were not markedly affected by spargana implants. However, many tissues of the implanted animals were altered significantly. Of particular interest was the change in weight of the pituitaries. The decrease noted indicates an interference with pituitary growth and perhaps its ability to secrete one or more hormones. In the male rats a marked increase in fat pad weight was seen. This is similar to that previously reported in hypophysectomized rats. Steelman *et al.* (2) have shown that, unlike growth hormone, SGF does not increase lipolysis and mobilize lipids.

The decrease in weight of many of the tissues (Table I) suggests an interference with synthesis or secretion of pituitary hormones or an altered end organ response. The observed decrease in pituitary weight would

TABLE IV. The Effect of *S. mansonioides* Spargana Implants on the Plasma Growth Hormone Level.^a

Postimplantation (days)	Plasma growth hormone conc (ng/ml)
Unimplanted	26, 28
10	nd, 9
37	94, 101

^a Samples were prepared by pooling plasma from groups of 10 animals.

tend to favor the former explanation. It is of interest to note that some of the tissues (liver, kidney, thymus) exhibiting a decreased size in the normal rat show the opposite in the hypophysectomized rat (3). All of these tissues are known to be affected by pituitary growth hormone. If SGF were an incomplete growth hormone which caused a decrease in growth hormone secretion, and if SGF were the dominant growth stimulant, the various effects noted could possibly be explained.

Mueller (4) has reported that three other strains of *Spirometra spargana* are less effective growth stimulants than *S. mansonoides* in both the normal mouse and hypophysectomized rat. Through the courtesy of Dr. Mueller, a supply of two Asian strains was obtained. Due to the number of spargana available, the two strains were mixed and are here described as Asian strains. Table II shows that the Asian strains were less effective than *S. mansonoides* spargana in all parameters evaluated. Although the pituitary weights of animals with the Asian implants were not decreased, the body weights were significantly increased. This suggested a failure of the Asian implants to inhibit endogenous growth hormone and, indeed produced an increase in the normal growth response. The increase in thymus weight would confirm this. The higher liver weight was not quite statistically significant. It is, however, clear that the Asian strains have significant biological activity.

Since the decrease in pituitary weight was striking, it was of interest to determine whether this effect was transitory (Table III). Studies at various time intervals in male and female rats show a consistent effect on the pituitary but not on body weights. In the male there was an initial decrease of the rate of growth. This disappeared after 30 days. The maximum depression of pituitary weight occurred in 10 days followed by a partial recovery.

In the female rats (Table III) there was a stimulation of body weight which persisted for 40 days. The maximum depression of pituitary weights in the female occurred between 20 and 30 days.

The explanation of the difference in growth

response between males and females is not readily apparent. The fact that the female rat has a slower rate of growth than the male may be a factor. The adult female rat, in contrast to the male, reaches a stable weight between 250 and 350 g. This adult female rat will respond to exogenous growth hormone with an increase in body weight. It is extremely difficult to demonstrate an effect of exogenous growth hormone on the intact growing male rat.

The data cited above strongly suggested that there was an impairment of production and/or secretion of growth hormone in the spargana implanted intact rat. Measurements of plasma growth hormone levels (Table IV) have confirmed this hypothesis. The changes in plasma growth hormone appears to confirm the data in Tables I and III. The marked depression in pituitary weight is accompanied by a decrease in plasma level. After 37 days, when the animal has become increasingly resistant (2) to SGF, there is a rebound in the level of plasma growth hormone to compensate for the loss of activity of SGF.

From the data presented, it may be concluded that SGF has biological activities in growing male and female rats. The effects noted strongly suggest a suppression of endogenous growth hormone by the incomplete growth hormone-like SGF produced by spargana.

The authors are indebted to Dr. J. F. Mueller for supplying the Asian strains of *Spirometra spargana* and for the original stock of *Spirometra mansonoides* spargana. Members of the Endocrinology Department kindly carried out many of the experimental studies. Dr. D. A. Ostlind and members of the Merck Institute Department of Parasitology kindly provided additional spargana.

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