

perature (average Q_{10} , 0.46; S.E.M., ± 0.14 ; range, 0.22 to 0.90). In Fig. 1B, as temperature was raised slightly from 36°C, activity fell to about one-third and remained constant as temperature was maintained at 38°C. Activity increased fivefold upon subsequent cooling to 28°C and then decreased in similar fashion as the brain was again warmed.

Thirty-one neurons (39 percent) showed no change in their discharge rate over the temperature range studied, and in six neurons variations in discharge rate were independent of temperature. Four cells, which maintained the same discharge rate at both high and low temperatures, showed a transient acceleration during temperature change.

Although these 80 neurons were not definitely identified, the majority are almost certainly pyramidal tract cells with a relatively well-understood function in the control of movement. Since we were changing the temperature of all of the brain supplied by the carotid, it is clear that alterations in the intensity of synaptic bombardment may contribute to the temperature dependency of spontaneous discharge. However, it is possible that the effects observed result from a temperature dependence of the ionic and metabolic processes of the cell since even adjacent neurons from a reasonably homogeneous population frequently showed very different responses to a given temperature change. In some invertebrates all neurons show changes in excitability with temperature (5). The variety of responses on warming in these neurons results from the interaction between the hyperpolarizing force of an electrogenic Na^+ pump and the depolarizing tendency resulting from the greater temperature dependence of the Na^+ than of the K^+ resting membrane conductance (6).

There is other evidence to support the view that many neurons not directly concerned with temperature information have temperature-dependent processes governing their excitability. For example, spinal motoneurons become spontaneously active on cooling (7), as do tongue mechanoreceptors (8) and muscle spindle afferent fibers (9). Gartside and Lippold (10) have studied responses of neurons of sensory cortex of the rat to local temperature changes. They found that 65 percent of preparations showed an increased activity on cooling, whereas 20 percent showed decreased activity and 15 percent showed no change. The differ-

ences between these and our results may be due to the species, the area of cortex studied, or the method of cooling. Their results are, however, in agreement with the thesis that neurons in the central nervous system may exhibit a nonspecific thermosensitivity.

We have shown that the discharge rates of 48 percent of neurons studied in the sensorimotor cortex of the cat are significantly affected by changes in brain temperature. These results strongly suggest that thermosensitivity of a neuron does not necessarily indicate a role for that neuron in transmission of thermal information or in thermoregulation, as has been implied in previous studies (1, 2).

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Strontium-90: Effects of Chronic Ingestion on Farrowing Performance of Miniature Swine

Abstract. *In experiments involving the ingestion of strontium-90 by nearly 800 female miniature swine and extending over three generations, no significant differences in litter size, percentage of stillborn, or birth weight were observed between controls and animals ingesting up to 625 microcuries of strontium-90 per day. At 625 microcuries per day, these animals were ingesting more than a million times the peak value of strontium-90 ever reported in the American diet. Animals on 3100 microcuries per day did not survive the gestation period. From these studies, it is evident that feeding levels of strontium-90 high enough to affect fetal or neonatal mortality in this species will not permit maternal survival long enough for the bearing of young.*

Effects of the daily ingestion of ^{90}Sr have been studied in our laboratory since 1958. Miniature swine are used in these studies because they are omnivores with a mature weight, dietary requirement, gastrointestinal tract, and

bone mass similar to man (1). The original design and early results of this experiment were reviewed previously (2, 3).

During the course of this study, 773 female Pitman-Moore miniature swine,

Table 1. Strontium-90 concentrations and radiation dose rates in swine bones.

Feeding level ($\mu\text{C}/\text{day}$)	^{90}Sr concentration in bone (microcuries per gram of ash) *		Dose rates to bone (rad/day)		
	Original dams	F_1 and F_2 generation adults	Original dams*	F_1 and F_2 generations	
				In utero†	Adults*
1	0.0032	0.0036	0.064	0.004	0.072
5	.016	.018	.32	.02	.36
25	.08	.09	1.6	.1	1.8
125	.4	.53	8	.5	11
625	2		40	2.5	

* At ^{90}Sr skeletal equilibrium (live bone averaged 40 percent ash).
during second half of gestation.

† Average to fetal skeleton

representing three generations, were exposed to feeding levels of ^{90}Sr ranging from 1 to 3100 $\mu\text{C}/\text{day}$. There were 194 untreated female littermate controls. Currently, 173 experimental swine with 8 to 11 years of exposure and 67 controls are being maintained for lifetime observation and study. Original dams were started on the experiment at 9 months of age, fed ^{90}Sr daily, and bred at apparent ^{90}Sr skeletal equilibrium to unexposed males; their female offspring were gradually raised, commensurate with growth and food intake, to the same ^{90}Sr feeding level as the dam by 6 months of age. These F_1 animals were then bred to provide the F_2 generation, which was exposed in the same manner as the F_1 . Attained ^{90}Sr body burdens in these swine, determined by skeletal and soft tissue radioanalysis, reached approximately 10 times the daily intake of ^{90}Sr for the F_1 and F_2 generations and 7.5 times that for the original dams.

Radioanalysis results were utilized to calculate average radiation dose rates to bone for the original dams and the adult F_1 and F_2 offspring at ^{90}Sr equilibrium, and for the F_1 and F_2 fetuses in utero, by methods detailed elsewhere (4). Table 1 lists the average concentrations of ^{90}Sr measured in the bone ash of the animals on the various ^{90}Sr feeding levels and the resulting radiation dose rates to bones. As ^{90}Sr is predominantly a bone-seeking radionuclide, less than 1 percent of the body burden is found in the soft tissues, giving radiation dose rates $\sim 1/1000$ of those to bone. The gonadal dose is of the same magnitude as the dose to other soft tissues since the range of the β -particles from skeletal ^{90}Sr - ^{90}Y is not sufficient to contribute direct β -radiation to the gonads. In studies with thermoluminescent dosimeters implanted in 55- to 110-day term fetuses, we have observed no significant maternal contribution to the radiation dose to critical fetal tissues. Essentially all fetal radiation is derived from the ^{90}Sr deposited in their own tissues.

Table 2 shows the farrowing performance, one litter per sow, of the original dams that ingested ^{90}Sr from 9 months of age. There were no significant differences in litter size, percentage of stillborn, or birth weight between controls and animals ingesting up to 625 μC of ^{90}Sr per day. Animals ingesting 3100 $\mu\text{C}/\text{day}$ did not survive the gestation period. The difference observed in weaning weights of offspring of sows that received 625 μC was attributed to the fact that these dams were

Table 2. Farrowing performance of original dams that had ingested ^{90}Sr since 9 months of age.*

Feeding level ($\mu\text{C}/\text{day}$)	No. of litters†	Litter size	Percentage of stillborn	Birth weight (g)	Percentage weaned‡	Weaning weight (kg)
625	6	6.0 $\pm$ 1.5	5.5	615 $\pm$ 143	89 $\pm$ 19	4.7 $\pm$ 1.1§
125	12	5.8 $\pm$ 1.4	0	675 $\pm$ 28	95 $\pm$ 6	5.8 $\pm$ 0.3
25	17	6.4 $\pm$ 1.0	0.9	729 $\pm$ 56	90 $\pm$ 9	5.3 $\pm$ 0.6
5	8	5.6 $\pm$ 1.2	4.8	799 $\pm$ 76	84 $\pm$ 18	6.1 $\pm$ 0.8
1	22	5.8 $\pm$ 0.8	1.6	696 $\pm$ 48	81 $\pm$ 13	5.1 $\pm$ 0.5
0	49	5.3 $\pm$ 0.5	1.9	707 $\pm$ 43	87 $\pm$ 6	6.0 $\pm$ 0.4

* All values expressed with 95 percent confidence intervals, except those for the percentage of stillborn, for which, with the use of binomial distribution tables, no significant differences were noted from control values. † One litter per sow.

‡ Percentage weaned = $\frac{\text{Litter size} - (\text{stillborn} + \text{No. died before weaning})}{\text{Litter size}} \times 100$.

§ Significantly different ($P < .05$) from controls (attributed to radiation effects on milk output of dam).

suffering severe hematopoietic effects and were not supplying milk in quantities equivalent to those of the control or of the sows receiving a lower feeding level.

The farrowing performance, one litter per sow, of F_1 dams exposed to ^{90}Sr from conception (F_1 generation) is given in Table 3. Again, there were no significant differences in the percentage of stillborn, birth weight, or weaning weight between controls and animals at all levels of ^{90}Sr feeding, from 0 through 125 $\mu\text{C}/\text{day}$, except in the case of the animals that received 25 $\mu\text{C}/\text{day}$, which showed a significant increase in litter size as compared to the control animals—an observation that is unexplained at this time. The F_1 animals receiving in excess of 125 $\mu\text{C}/\text{day}$ did not survive to produce offspring.

To place these swine data in some perspective relative to human exposures, in Table 4 we compare the ^{90}Sr feeding levels and attained body burdens in this study to those that are recommended as permissible limits for occupational exposure by the International Commission on Radiological Protection (ICRP) (5) and to the peak dietary level of ^{90}Sr ever reported in American diets, about 3×10^{-5} μC per gram of dietary calcium (6). Farrowing performance in these animals was not shown to be affected by continuous intake levels a million times higher than the highest reported levels in American diets, nor by ^{90}Sr body burdens 2350 times higher than ICRP limits.

We wish to emphasize that significant radiation effects have, indeed, been observed in the animals of this study.

Table 3. Farrowing performance of F_1 dams exposed to ^{90}Sr since conception.*

Feeding level ($\mu\text{C}/\text{day}$)	No. of litters†	Litter size	Percentage of stillborn	Birth weight (g)	Percentage weaned‡	Weaning weight (kg)
125	3	4.0 $\pm$ 2.5	0	718 $\pm$ 260	100	4.7 $\pm$ 1.4
25	13	6.7 $\pm$ 0.7§	0	711 $\pm$ 64	92 $\pm$ 6	5.5 $\pm$ 0.8
5	11	4.8 $\pm$ 0.4	1.9	725 $\pm$ 69	89 $\pm$ 9	5.4 $\pm$ 0.4
1	14	4.9 $\pm$ 0.6	0	719 $\pm$ 53	95 $\pm$ 7	5.4 $\pm$ 0.6
0	49	5.3 $\pm$ 0.5	1.9	707 $\pm$ 43	87 $\pm$ 6	6.0 $\pm$ 0.4

* Same as in Table 2. † Same as in Table 2. ‡ Same as in Table 2. § Significantly different ($P < .05$) from controls.

Table 4. Relation of swine study to human parameters.

Original dams or adult F_1 and F_2 swine			Factor by which swine study exceeds	
Feeding level		Attained body burden* (microcuries of ^{90}Sr)	ICRP permissible body burden of 2 μC of ^{90}Sr †	Peak ^{90}Sr in American diets ($< 3 \times 10^{-5}$ μC per gram of Ca in food)‡
Microcuries of ^{90}Sr per day	Microcuries of ^{90}Sr per gram of Ca in feed			
625	37.5	4700§	2350	1250 $\times 10^3$
125	7.5	1250	625	250 $\times 10^3$
25	1.5	250	125	50 $\times 10^3$
5	0.3	50	25	10 $\times 10^3$
1	0.06	10	5	2 $\times 10^3$

* Average live weight of swine skeleton is 6.3 kg. † International Commission on Radiological Protection limits for continuous occupational exposure (5). ‡ As reported to the United Nations Scientific Committee on the Effects of Atomic Radiation (6). § Original dams; other values for F_1 and F_2 adults.

None of the second generation swine on 625 $\mu\text{C}/\text{day}$ survived to produce a third generation. There have been 69 cases of hematopoietic disorders in swine ingesting ^{90}Sr —55 in the F_1 and F_2 animals and 14 in the original dams; there were two such disorders in the original control dams. Bone tumors have been seen in seven animals of those groups that received 125 and 625 $\mu\text{C}/\text{day}$. Progress reports on these facets of the experiment have been published previously (7, 8).

Our purpose in this report is to emphasize the fact that, despite the high levels of ^{90}Sr fed and the abundant evidence of hematopoietic and carcinogenic effects, we have seen no evidence of an effect on fetal or neonatal mortality. From these studies we would infer that effects on fetal or neonatal mortality are not to be anticipated in human populations when mothers are exposed to ^{90}Sr , because ^{90}Sr intake levels high enough to affect fetal or neonatal mortality would not permit maternal survival long enough for the bearing of young. Since ^{90}Sr is a predominantly bone-seeking radionuclide, the effects will be manifest in bone and hematopoietic tissue in later life and will not affect fetal or neonatal mortality.

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Gibberellic Acid: A Growth Factor in the Unicellular Alga *Gymnodinium breve*

Abstract. *Gibberellic acid stimulates growth in the unicellular alga Gymnodinium breve (dinoflagellate). The maximum effect was obtained with 10^{-7} molar gibberellic acid, whereas concentrations greater than 5×10^{-7} mole per liter were inhibitory. The effect of the compound is observed as a marked shortening of the lag period, which is normally 6 to 8 days after inoculation.*

Gibberellic acid (GA) is a plant hormone which influences the activity of almost any plant tissue or organ. Responses include changes in growth rates and development of excised embryo, coleoptile, or primary leaf (1). The ex-

cised endosperm of cereals respond very quickly (1 day) to small quantities of GA. As little as 3×10^{-10} mole of GA per liter can cause release of reducing sugars from barley endosperm resulting from increased formation and secretion of α -amylase by aleurone cells surrounding the endosperm (2). At least part of the increased α -amylase activity is the result of de novo synthesis of the enzyme molecule (3). This synthesis is associated with synthesis of RNA after the addition of GA (4).

There is little information on the effect of GA on either multicellular or unicellular algae. The cell size of *Euglena* is increased when GA is added at a concentration of 1000 mg/liter (5). In *Ulothrix subtilissima* 0.05 mg/liter gives a sevenfold increase in growth, whereas higher concentrations are inhibitory (6). In *Trichomonas foetus* 910 mg of GA per liter has an inhibitory effect, whereas lower concentrations have no effects (7).

We have found that GA has a marked effect on the growth of *Gymnodinium breve*, a toxigenic marine dinoflagellate. Periodically this organism increases in number and discolors coastal waters mainly along the eastern coast of the United States and the Gulf of Mexico (8), resulting in the phenomenon popularly known as Red Tide. There is ample evidence that an active compound produced by this organism is responsible for catastrophic mortalities of various marine animals (9), presumably through a neurotoxic effect (10).

While looking for optimum conditions for the growth of this organism, we found that GA (11) in low quantities induces rapid growth in axenic cultures. We used a synthetic medium containing inorganic salts, trace elements, and thiamin-HCl (1 mg/liter), biotin (0.5 $\mu\text{g}/\text{liter}$), and vitamin B_{12} (1 $\mu\text{g}/\text{liter}$). The cultures were grown at 18°C under continuous illumination.

The growth curve (Fig. 1) of this organism is normally characterized by a lag period of 6 to 8 days; in many instances cell numbers are even reduced

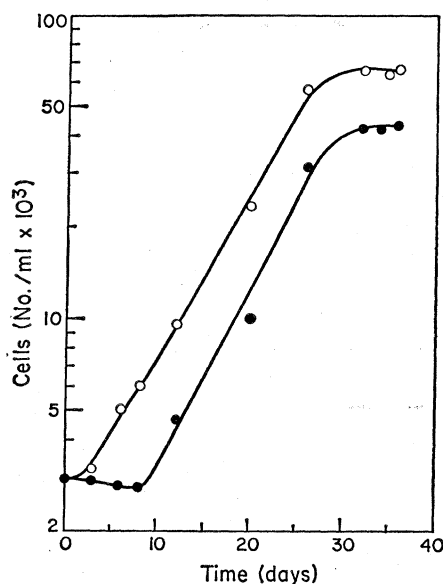


Fig. 1. Growth curves of *Gymnodinium breve* without GA (●) and with $10^{-7}M$ GA (○).

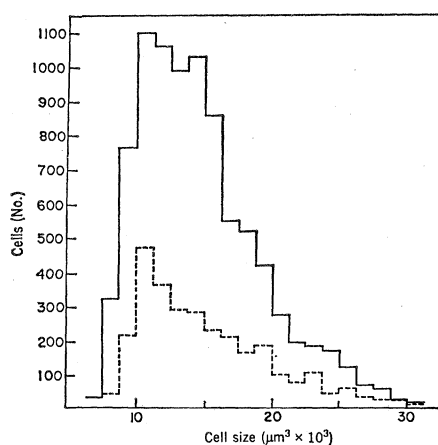


Fig. 2. Distribution of cell sizes of *Gymnodinium breve* recorded and plotted with automatic particle size distribution analyzer model J (Coulter Electronics Inc.). (Solid line) With $10^{-7}M$ GA; (dashed line) control. Histogram was plotted from cell sample after 28 days of growth.