11. Physiological saline: 0.05 ml on days 0 to 7; 0.1 ml on days 8 to 30. Propylthiouracil (PTU): 0.05 ml of 0.2 percent PTU (in 1 percent carboxymethyl-cellulose) on days 0 to 10; 0.1 ml on days 11 to 20; 0.1 ml of 0.4 percent PTU on days 21 to 30. L-Thyroxine: 1 μg (in physiological saline) on days 0 to 7; 2 μg on days 8 to 14; 3 μg on days 15 to 21; 5 μg on days 22 to 30 (*16*). The extent of hypothyroidism caused by PTU was determined by histologically monitoring the thyroid for lack of colloid and hypoplastic follicular epithelium; PTU caused complete blockage as early as day 5.

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Salicylate: Action on Normal Body Temperature in Rats

Abstract. *Rats receiving intraperitoneal injections of sodium salicylate (30 to 300 milligrams per kilogram of body weight) showed a decline in rectal temperature of up to 5.5°C when placed in a 5°C environment. High dosages of salicylate lowered the rectal temperatures of rats kept in a 23°C environment. The finding that salicylate can lower nonfebrile body temperature suggests that this class of antipyretic agents does affect normal temperature regulation.*

It is generally believed that the effectiveness of salicylates is restricted to the lowering of body temperature previously elevated by pyrogens and that salicylates have little or no effect on afebrile subjects (*1*). I present here evidence which demonstrates that salicylate does lower the normal body temperature of rats, especially if the animals are in a cold environment.

Sixty-four female albino rats, weighing between 260 and 360 g each, were placed, in groups of four or five at a time, in individual metal cages in a cold chamber maintained at 5° ± 1°C. The fur of half of the rats was shaved. After 15 minutes in the cold, the rats received an intraperitoneal injection of either sodium salicylate (30, 60, 120, 180, 240, or 300 mg per kilogram of body weight) dissolved in 2 ml of isotonic saline or 2 ml of saline alone. Each rat was tested only once at a single dosage of sodium salicylate or saline. They remained in the cold chamber for 1 hour more and were then removed to an environment with a temperature of 23° ± 1°C. A thermistor probe which recorded rectal temperatures was connected to a telethermometer (Yellow Springs Instrument Company). At the sampling intervals, the thermistor probe was inserted 5 cm into the anus of each rat. Temperatures were taken immediately before the rats were placed in the cold, every 15 minutes during the 1-hour cold test, and for up to 4 hours after they had been returned to the 23°C environment. Four rats each in the shaved and unshaved groups were tested at each dosage of salicylate, and eight rats in each group were tested with saline. A group of 20 unshaved rats received intraperitoneal injections of either sodium salicylate dissolved in saline (30, 60, 120, 180, or 300 mg/kg, three rats per dosage) or saline alone (five rats) and were kept at an ambient temperature of 23°C for 4 hours, during which time their rectal temperatures were recorded periodically.

Figure 1 shows the effect of the low, medium, and high dosages of sodium salicylate on the body temperature of

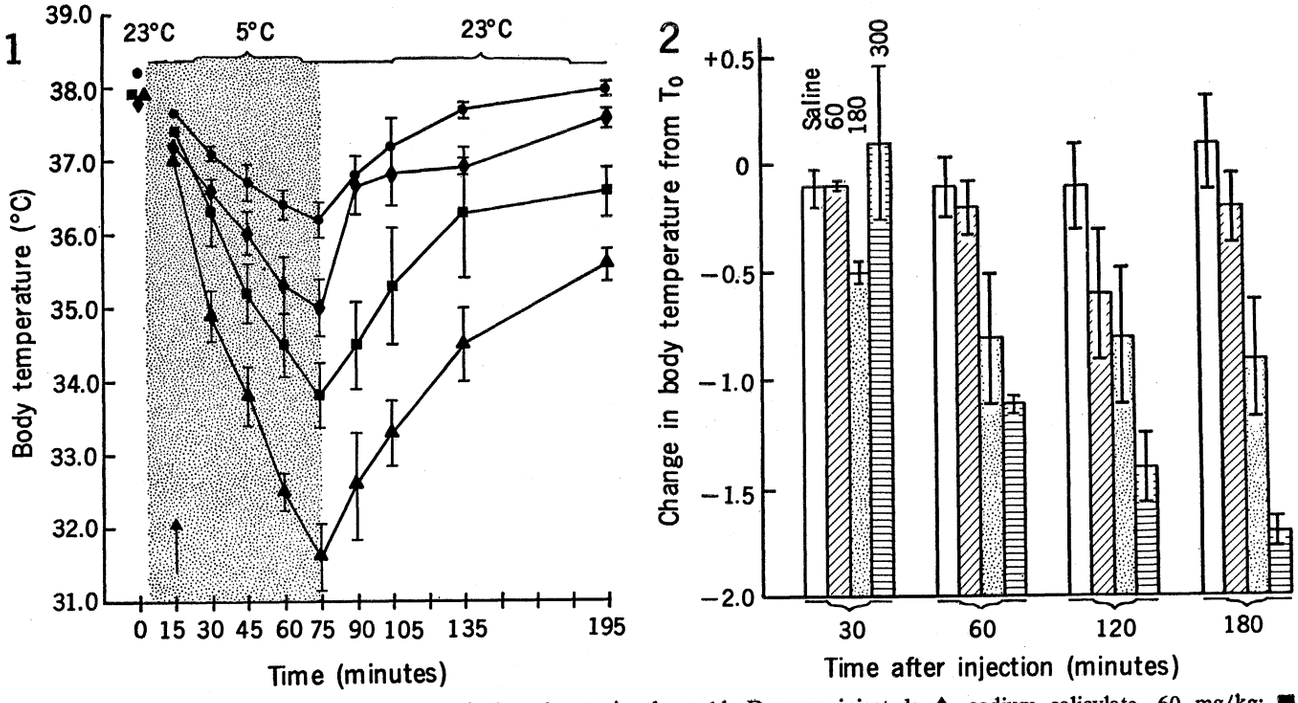

Fig. 1 (left). Change in body temperature of shaved rats in the cold. Dosages injected: ♦, sodium salicylate, 60 mg/kg; ■, sodium salicylate, 180 mg/kg; ▲, sodium salicylate, 300 mg/kg; ●, saline. The time of injection of sodium salicylate or saline is indicated by the arrow. Vertical lines indicate the standard error of the mean. Fig. 2 (right). Change in body temperature (body temperature before injection = T_0) of unshaved rats kept at 23°C for 30 to 180 minutes after the injection of sodium salicylate or saline. Numbers above bars indicate the dosages of sodium salicylate in milligrams per kilogram of body weight.

shaved rats in the cold and the course of return to normal temperature in the 23°C environment (the curves for 120 and 240 mg/kg, omitted for the sake of clarity, fall appropriately between their respective higher and lower dosages). The curve for rats given 30 mg of sodium salicylate per kilogram of body weight was significantly different from the curve for rats given saline. (The mean rectal temperature of the four rats after 15 minutes in the cold was 37.9°C. One-half hour after injection of sodium salicylate the mean rectal temperature was 36.0°C, and 1 hour after injection it was 35.3°C.) There was an orderly, progressive dose-dependent decrease in body temperature for all concentrations of salicylate tested. Within 30 minutes of drug administration there was no overlap in the standard errors of the means of each group except for the 30 and 60 mg/kg groups. The rectal temperatures of all the shaved rats were lower than those of the unshaved rats. Within 2 hours after removal from the cold, the body temperatures of all the rats except those given the two highest dosages of sodium salicylate had returned to those values that prevailed before the administration of the drug. The decline in the rectal temperatures of the unshaved rats was also dependent on the dosage of salicylate given. One hour after injection the rectal temperatures of the groups given saline or sodium salicylate (60, 180, or 300 mg/kg in saline) had declined, respectively, by 0.4°, 0.7°, 2.5°, and 3.6°C. Sodium salicylate in dosages of 180 and 300 mg/kg also lowered the body temperature of unshaved rats maintained at 23°C, although the decline was more gradual and not as great as for rats in the cold (Fig. 2). The body temperatures of all the animals returned to the values that prevailed before drug injection within 4 hours.

It is clear that the higher dosages of sodium salicylate lowered the normal body temperature of rats in a 23°C environment, and at all dosages tested sodium salicylate lowered the body temperature of rats in the cold. Salicylates have been thought to be effective in lowering only febrile temperatures. The data presented here demonstrate that they can lower normal, nonfebrile temperatures also.

Body temperature rises when either heat production is augmented or heat loss is lessened, or when both effects occur simultaneously. These changes are brought about when warm-sensitive neurons in the brain decrease or cold-sensitive neurons increase their respective firing rates (*2*). Bacterial pyrogen causes fever by affecting both types of thermoregulatory neurons (*2, 3*). Salicylates increase the sensitivity of pyrogen-suppressed neurons, and the body temperature declines (*3*). However, salicylates may also act directly on thermoregulatory neurons whose firing rates have not been changed by previous administration of pyrogen (*4*). Cold stress, like pyrogens, may act through some biochemical intermediary, possibly prostaglandins, to alter the firing rate of thermosensitive neurons and cause increased heat production and decreased heat loss. In the cold, however, this action would lead not to fever but rather to the maintenance of a normal body temperature or at best to a slight degree of hyperthermia, because of the increased loss of heat to the environment. If prostaglandins are released during cold stress as well as during fever, and if, as has already been demonstrated (*5*), salicylates inhibit the release of prostaglandins, then one should expect a decrease in body temperature in the cold, which is what the data presented here demonstrate.

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Polychlorinated Biphenyls and DDT Alter Species Composition in Mixed Cultures of Algae

Abstract. *Either DDT or polychlorinated biphenyls were added to mixed cultures containing a marine diatom and a marine green alga that were sensitive and resistant, respectively, to these organochlorine compounds. The diatom grew faster and was therefore dominant in control cultures, but its dominance diminished in treated cultures, even at concentrations of chlorinated hydrocarbons that had no apparent effect in pure cultures. Such stable pollutants could disrupt the species composition of phytoplankton communities, thereby affecting whole ecosystems.*

The impact of certain persistent chlorinated hydrocarbons on various higher nontarget organisms has been well documented (*1*), but effects on photosynthetic algae, the base of aquatic food webs, have not been extensively studied. Marine phytoplankton vary in sensitivity to chlorinated hydrocarbons, including DDT [1,1,1-trichloro-2,2-bis (*p*-chlorophenyl)ethane] and polychlorinated biphenyls (PCBs). Some species show effects at concentrations as low as a few parts per billion (ppb), whereas others are resistant to much higher concentrations (*2, 3*). Some of these chemicals, especially DDT and PCBs, are extremely widespread pollutants of the biosphere, and, because they are selectively toxic to certain sensitive algal species, it has been hypothesized that they could alter the species composition of phytoplankton communities (*2, 3*). Evidence for this hypothesis is lacking; we therefore investigated the effects of DDT and PCBs in mixed algal cultures containing a sensitive and a resistant species.

Two marine organisms were selected on the basis of their sensitivity to organochlorine compounds: growth of the diatom *Thalassiosira pseudonana* was inhibited by PCBs and DDT, whereas *Dunaliella tertiolecta*, a green alga, was not affected by these chemicals (*3*). Methods of culture and procedures for treatment have been described (*3*). Cultures contained a total of 10^4 exponentially growing cells per milliliter at zero time; mixed cultures contained the two species in a 1:1 ratio. Mixed and pure cultures were treated simultaneously. Cells in pure