the peak of activity occurred between R_F 0.6 and 0.9, but there was considerably more activity in the sap from treated plants. The difference between treatments was highly significant. In terms of kinetin equivalents, sap from untreated plants contained 3 μg of kinetin per liter; from treated plants, 30 μg of kinetin per liter. Similar results were obtained with earlier collections of sap from the same plants.

The experiments were repeated with "Cabernet Sauvignon" vines (20 plants per treatment) grown in nutrient culture solutions containing CCC. Again, cytokinin activity at R_F 0.6 to 0.9 was significantly higher ($P = 0.01$) in the sap from treated plants than in that from controls. In this case up to 20-fold differences in activity at R_F 0.6 to 0.9 were recorded.

It is considered that CCC in the sap did not affect the response of the soybean callus to cytokinins in the active fractions. In the solvent system used, CCC migrated to R_F 0.22 to 0.37, as revealed by Dragendorff's reagent (*6*), that is, well behind the active fractions in the sap extracts. Furthermore, CCC at levels up to 500 mg/liter had no significant effect on the growth of callus exposed to 0.5 mg of kinetin per liter.

Further work is needed to establish whether this effect of CCC is directly related to cytokinin synthesis by the root, or whether it is a reflection of greater net cytokinin synthesis by the larger root meristem. The findings might have implications in relation to the known effects of CCC and cytokinins on fruit set in grapes.

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Snake Food Preference: Innate Intraspecific Geographic Variation

Abstract. *Compared to Florida individuals, a smaller percentage of Massachusetts* Thamnophis sirtalis sirtalis *will accept fish. Both experienced adults and isolated newborn snakes respond similarly; the behavior is innate and correlated with habitat differences between the two localities. Although food preference in* Natrix sipedon *is also innate, geographic variation is not as clearcut.*

A particular snake's preference in food is the result of genetic determination and subsequent environmental modification. Although many isolated studies of the food habits of individual snake species exist, these have mostly been made on the basis of stomach contents in preserved specimens (*1*), or on the food preferences of animals from one locality (*2*). My study, part of an extensive survey of the feeding behavior of American Colubridae (*3*), concerns differences in food preferences between northern and southern *Thamnophis sirtalis sirtalis* and *Natrix sipedon.* Both species occur sympatrically over a wide geographical range (*4*) and were obtained for observation from similar habitats, the swampy margins of streams and periodic marshes. This difference in food preference is present both in adults and inexperienced snakes, and is apparently innate. The fact that this innate preference shows geographic variation is significant and has not previously been demonstrated in vertebrates..

Adult *Thamnophis sirtalis* and *Natrix sipedon,* obtained from the localities given in Table 1, were tested with earthworms, pieces of smelt (*Osmerus mordax*), *Rana pipiens* (tadpoles and adults), *Anolis carolinensis,* miscellaneous small snakes, and newborn mice. Litters subsequently obtained from these snakes were separated from the adults and also tested. After capture or birth the snakes were kept in 20-gallon aquaria lined with paper towels and containing one water dish. The adults were maintained in groups of six, and one litter of offspring was kept in each cage. All animals were without food for 1 to 2 weeks before testing commenced. Food was only brought into the room immediately before feeding. Groups were then offered one food item at a time. If this was not accepted within 5 minutes, another item was substituted. The order of presentation was random. Only if the snakes fed regularly (that is, not less than nine out of ten trials) on an item when tested at weekly intervals (ten repetitions) was this considered a positive response. The juveniles accepting fish have survived for over 2 years in the laboratory.

No snakes accepted lizards or snakes. Five adult *Thamnophis sirtalis* (20 percent) from Massachusetts accepted newborn mice, but snakes from other localities did not do so. As Table 1 shows for both *Natrix sipedon* and *Thamnophis sirtalis* from Florida there was no difference between the responses of experienced adults, captured in the wild, and their newborn offspring, reared in captivity and in isolation from their parents, in preference for fish (χ^2 for *Natrix* adults compared with young = 0.019; $.8 < P < .9$. χ^2 for *Thamnophis* adults compared with young = 0.045; $.8 < P < .9$). Thus the innate choice of newborn snakes parallels the choice of experienced adults.

In Florida these two species differ in their preference for fish (adults $\chi_c^2 = 16.7$; $P < .001$; juveniles $\chi_c^2 = 49.9$; $P < .001$). Except for *Natrix* from Potomac, Maryland, all individuals of both species accepted *Rana pipiens.*

The northern individuals of *Thamnophis sirtalis* show a marked trend away from fish preference (juveniles $\chi_c^2 = 31.2$; $P < .001$; adults $\chi_c^2 = 11.7$; $P < .001$). In *Natrix sipedon*

Table 1. Geographic variation in food preference in *Thamnophis sirtalis* and *Natrix sipedon.* A, adult; NB, newborn.

Locality	Snakes (No.)		Accepting test food (No.)					
			Worms		Fish		Frogs or tadpoles	
	A	NB	A	NB	A	NB	A	NB
			Thamnophis sirtalis					
Everglades, S. Florida	16	64	0	64	15	59	16	64
Potomac, Maryland	2		2		0		2	
Wayland, Massachusetts	4	15	0	15	1	3	4	15
			Natrix sipedon					
Everglades, S. Florida	86	168	0	0	30	57	86	168
Potomac, Maryland	7	20	0	0	4	16	3	20
Great Swamp, New Jersey	1	18	0	0	1	7	1	18

the picture is more complicated. Although there is no significant difference between the New Jersey and South Florida juveniles ($\chi_c^2 = 0.18$; $.75 > P < .5$), the Potomac, Maryland, individuals responded differently ($\chi_c^2 = 14.9$; d.f. $= 2$; $P < .001$) and showed a greater preference for fish (80 percent compared to 34 and 39 percent).

Thamnophis sirtalis has the greatest geographical range of any North American snake (*4*). Fitch (*1*) while allowing the possibility of geographical variation in feeding habits, suggested that "throughout the widespread area of its occurrence the species seems to be remarkably stable in its (feeding) habits." My results indicate that this species does show geographic variation, and that this difference is innate. This phenomenon may be associated with habitat differences between the areas. Although *Natrix sipedon* is an aquatic snake always closely associated with fresh water, in *Thamnophis sirtalis* the association tends to decrease as one moves northward. In Florida there is a marked seasonal drying of the Everglade ponds, and a resultant concentration of fish in small water bodies. This coincides with the production of large numbers of offspring in both *Thamnophis* and *Natrix* and may be a significant factor controlling selection of preference for fish in these snakes.

At times any species faces adverse changes in its environment. Snakes must adjust quickly to any change in abundance of prey. Intraspecifically, they show geographic variation in food preference, and furthermore, in any local population snakes show innate polymorphism in food preference; a small percentage of the population will accept prey not accepted by most of the population (Table 1). This provides flexibility and a potentiality for invading new habitats and meeting long-term environmental and climatic changes.

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Genetic Control of Drug Levels in Man: Phenylbutazone

Abstract. *Phenylbutazone was administered to seven pairs of identical (monozygotic) twins and to seven pairs of fraternal (dizygotic) twins. Individual half-lives ranged from 1.2 to 7.3 days. Subjects with identical genotypes (monozygotic twins) exhibited very similar phenylbutazone half-lives; significantly greater differences in half-life occurred in dizygotic twins. The previously established large variations among individuals in phenylbutazone metabolism appear to be genetically, rather than environmentally, determined.*

Increasing evidence indicates intraspecies variations in the metabolism of many drugs. Humans exhibit particularly large differences in the half-lives of phenylbutazone (*1*) and dicumarol (*2*), but it remains to be established whether such differences are due primarily to environmental or genetic causes. Multiple environmental factors are known to alter the rates of drug metabolism in experimental animals (*3*): for example, phenylbutazone and other drugs enhance their own metabolism in dogs (*4*).

In man several polymorphisms involving drugs have been described. Those with the highest frequency concern glucose-6-phosphate dehydrogenase deficiency and isoniazid acetylation; neither involves the liver microsomal enzymes that oxidize phenylbutazone, dicumarol, and many other drugs.

Individual differences in phenylbutazone metabolism have therapeutic implications. Toxicity may develop primarily in subjects having long half-lives in plasma, whereas those having short half-lives may not attain sufficient or sufficiently sustained levels to benefit from the drug.

This study was designed to determine whether the wide variability in phenylbutazone metabolism was due primarily to genetic or environmental factors. We employed 14 pairs of volunteer twins from the Washington, D.C., area; seven were identical and seven were fraternal. All subjects were Caucasian, over 21 years of age, and in good health. None took drugs for at least 1 month before administration of phenylbutazone. Each volunteer was typed for approximately 30 blood groups to document the nature of the twinship; the results confirmed the twins' views of whether they were identical or fraternal.

At 0800 hours each subject received a single oral dose of phenylbutazone (about 6 mg/kg) (*5*); since only 100-mg tablets were available, dosages were adjusted to the closest 50 mg. Because the dose was not always exactly 6 mg/kg, the initial levels of plasma phenylbutazone (Fig. 1) varied. However, in this study absolute plasma levels were not critical because, within the levels attained, they did not affect the values for phenylbutazone half-lives. Twenty-four (in some cases, 48) hours after administration of phenylbutazone, blood was drawn in tubes containing oxalate, and the plasma was assayed for phenylbutazone by the method of Burns *et al.* (*1*); subsequent specimens were drawn at regular intervals. To determine whether administration of a single dose of phenylbutazone changed the rate of elimination of a subsequent dose, two sets of identical twins received a second similar dose of phenylbutazone 9 days later.

Figure 1 shows the decay of phenylbutazone in plasma of three sets of identical and three sets of fraternal

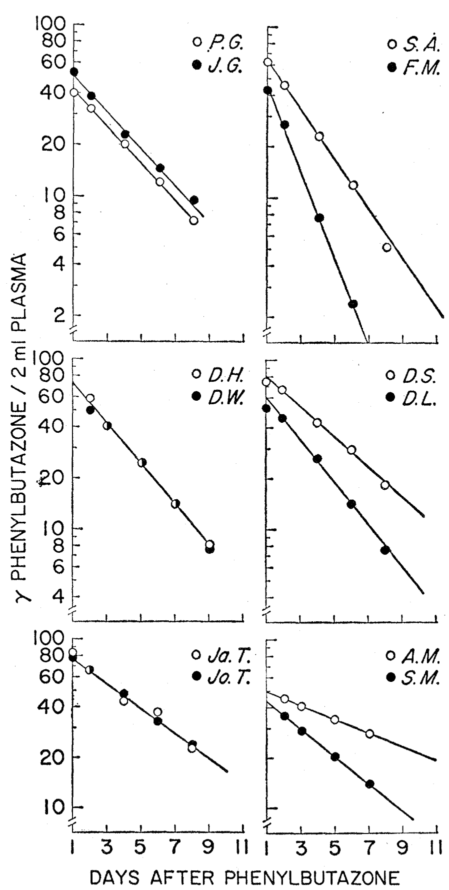

Fig. 1. Decline of phenylbutazone in the plasma of three sets of identical twins (left) and three sets of fraternal twins (right). The log of the phenylbutazone concentration in 2 ml of plasma is shown at intervals after a single oral dose (6 mg/kg).