

These slightly different gradients are probably due to variations in blubber thickness. We could not be certain that the thermistor probe penetrated completely through the blubber layer; therefore we do not know whether our maximum readings represent a true deep body temperature. A rectal temperature of 33°C was obtained with a flexible tube-mounted thermistor inserted 18 inches. Readings of 30° to 33°C were obtained under the tongue with the same instrument. From previous experience (1), we feel that the whale was 1° or 2° cooler than would be expected. The general mechanism of thermal regulation appears to be the same as that found in live porpoises which are approximately 1/100 as large as this whale (2). The blubber is an insulating layer, and the preferred pathway of heat disposal is through the uninsulated extremities.

Electrocardiograms were taken on an instrument which one of us (A.S.) uses in his private medical practice. Because the whale was completely out of the water we were able to place leads in most of the positions analogous to those used on humans. Figure 1 shows a precordial lead record from the whale heart as contrasted to a normal human record. The pulse rate was about 27 beats per minute, compared with 70 in man and more than 600 in the smallest mammals. However, it was still nearly twice that recorded on a much smaller white whale (3). Since the beats closely follow one another we presume that this represents tachycardia and that a more normal rate would be 8 to 10. The high rate probably reflected the deteriorating condition of the animal. The time scale for the events in a single beat are much longer than any known previously. The PR interval, for instance, was about 0.68 second as compared to half this in the white whale and a maximum of 0.20 second in humans.

This cursory report is given to show that it is possible to obtain physiological information from a beached cetacean if one has the instruments ready to take advantage of the situation. A live whale in the water is an imposing experimental subject, but grounded animals are more manageable and fairly frequent. Unfortunately most people consider the great mass of potentially putrifying meat more of a potential health hazard than a scientific opportunity. We would appreciate immediate notification of similar live strandings anywhere in New England.

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### Inhibition of $\delta$ -Aminolevulinic Acid Dehydrase by $\delta$ -Oximinolevulinic Acid

**Abstract.**  $\delta$ -Oximinolevulinic acid competitively inhibits  $\delta$ -aminolevulinic acid dehydrase at low concentrations.

The enzyme  $\delta$ -aminolevulinic acid (ALA) dehydrase involved in the conversion of ALA to porphobilinogen has been studied by Gibson, Neuberger,

and Scott (1) and others (2). In studying analogues of ALA it was found that  $\delta$ -oximinolevulinic acid acted as a competitive inhibitor of ALA dehydrase, producing significant inhibition at low concentrations.

$\delta$ -Aminolevulinic acid and  $\beta$ -ketoacidipic acid were purchased from the Nutritional Biochemicals Corporation.  $\delta$ -Chlorolevulinic acid was synthesized by the method of Neuberger and Scott (3).  $\delta$ -Oximinolevulinic acid was synthesized by the method of Neuberger, Scott, and Shuster (4).  $\delta$ -Acetamidolevulinic acid was provided by Anthony Schrecker of the National Cancer Institute. 2-Amino-4-thiazolepropionic acid was prepared as described by Neuberger and Scott (3).

The homogenates were prepared from CAF<sub>1</sub> mouse livers as described by Gibson, Neuberger, and Scott (1). Each tube contained 1 ml of liver

Table 1. Inhibition of  $\delta$ -aminolevulinic acid dehydrase by various compounds.

Compound added	Concentration (M)		Volume of compound and ALA added (ml)	Ratio of compound to ALA	Inhibition (%)
	ALA added				
<i><math>\delta</math>-Chlorolevulinic acid</i>					
$7.5 \times 10^{-2}$	$7.5 \times 10^{-3}$		1.32	10:1	100
$7.5 \times 10^{-3}$	$7.5 \times 10^{-3}$		1.32	1:1	96
$7.5 \times 10^{-4}$	$7.5 \times 10^{-3}$		1.32	0.1:1	0
$7.5 \times 10^{-5}$	$7.5 \times 10^{-3}$		1.32	0.01:1	0
<i><math>\delta</math>-Acetamidolevulinic acid</i>					
$7.5 \times 10^{-2}$	$7.5 \times 10^{-3}$		1.32	10:1	37
$7.5 \times 10^{-3}$	$7.5 \times 10^{-3}$		1.32	1:1	0
$7.5 \times 10^{-4}$	$7.5 \times 10^{-3}$		1.32	0.1:1	0
$7.5 \times 10^{-5}$	$7.5 \times 10^{-3}$		1.32	0.01:1	0
<i><math>\beta</math>-Ketoacidipic acid</i>					
$7.5 \times 10^{-2}$	$7.5 \times 10^{-3}$		1.32	10:1	100
$7.5 \times 10^{-3}$	$7.5 \times 10^{-3}$		1.32	1:1	79
$7.5 \times 10^{-4}$	$7.5 \times 10^{-3}$		1.32	0.1:1	11
$7.5 \times 10^{-5}$	$7.5 \times 10^{-3}$		1.32	0.01:1	0
<i>2-Amino-4-thiazolepropionic acid</i>					
$7.5 \times 10^{-2}$	$7.5 \times 10^{-3}$		1.32	10:1	92
$7.5 \times 10^{-3}$	$7.5 \times 10^{-3}$		1.32	1:1	8
$7.5 \times 10^{-4}$	$7.5 \times 10^{-3}$		1.32	0.1:1	0
$7.5 \times 10^{-5}$	$7.5 \times 10^{-3}$		1.32	0.01:1	0
<i><math>\delta</math>-Oximinolevulinic acid</i>					
$7.5 \times 10^{-2}$	$7.5 \times 10^{-3}$		1.32	10:1	100
$7.5 \times 10^{-3}$	$7.5 \times 10^{-3}$		1.32	1:1	96
$7.5 \times 10^{-4}$	$7.5 \times 10^{-3}$		1.32	0.1:1	75
$7.5 \times 10^{-5}$	$7.5 \times 10^{-3}$		1.32	0.01:1	27
$7.5 \times 10^{-1}$	$5 \times 10^{-2}$		.33	10:1	95
$7.5 \times 10^{-2}$	$5 \times 10^{-2}$		.33	1:1	92
$7.5 \times 10^{-3}$	$5 \times 10^{-2}$		.33	0.1:1	72
$7.5 \times 10^{-4}$	$5 \times 10^{-2}$		.33	0.01:1	26

Table 2. Inhibition of  $\delta$ -aminolevulinic acid dehydrase by  $\delta$ -oximinolevulinic acid.

Tube	Concentration (M)		Volume of compound and ALA added (ml)	Ratio of compound to ALA	Inhibition (%)
	$\delta$ -Oximinolevulinic acid added	ALA added			
1	$7.5 \times 10^{-2}$	$7.5 \times 10^{-3}$	1.32	10:1	94
2	$7.5 \times 10^{-3}$	$7.5 \times 10^{-3}$	1.32	1:1	90
3	$7.5 \times 10^{-4}$	$7.5 \times 10^{-3}$	1.32	0.1:1	66
4	$7.5 \times 10^{-5}$	$7.5 \times 10^{-3}$	1.32	0.01:1	29
5	$7.5 \times 10^{-4}$	$9 \times 10^{-2}$	1.32	1:120	27
6	$7.5 \times 10^{-4}$	$6 \times 10^{-2}$	1.32	1:80	38
7	$7.5 \times 10^{-4}$	$3 \times 10^{-2}$	1.32	1:40	47
8	$7.5 \times 10^{-4}$	$7.5 \times 10^{-3}$	1.32	1:10	58

homogenate (1 part wet-weight CAF<sub>1</sub> liver homogenized in twice its weight of 0.15M KCl); 1 ml of 0.067M phosphate buffer at pH 6.8; 1 ml of 0.01M glutathione; and the volume of ALA and analog added as indicated in Tables 1 and 2. After evacuation of air, the mixture was activated at 37°C for 1 hour. In the experiments whose results are given in Table 1 and the lower half of Table 2 (tubes 5 to 8) the ALA was added 10 minutes after the analog. In the experiments in the upper half of Table 2 (tubes 1 to 4) the ALA and analog were added simultaneously. The incubation was continued for 1 hour and the amount of porphobilinogen was determined by use of Ehrlich's reagent after precipitation of protein as described by Gibson, Neuberger, and Scott (1). Pooled homogenates were used in the study of each compound. The percentage inhibition was calculated from the formula

$$100 [1 - (P_t/P_s)]$$

where  $P_t$  is the amount of porphobilinogen formed in 1 hour in the presence of inhibitor and substrate and  $P_s$  is the amount of porphobilinogen formed in 1 hour in the presence of substrate alone.

In Table 1 are presented the inhibitory effects of a group of compounds on ALA dehydrase. All the compounds produce inhibition of varying degrees at high concentrations, but only  $\delta$ -oximinolevulinic acid is inhibitory at low concentrations. Two different concentrations of ALA (using 1.32 ml of  $7.5 \times 10^{-3}M$  ALA and 0.33 ml of  $5 \times 10^{-2}M$  ALA) were studied with the same ratios of  $\delta$ -oximinolevulinic acid to ALA in both cases. The percentage inhibition is constant for a given ratio of inhibitor to analog at the different ALA concentrations. In these experiments the analog was added 10 minutes before ALA.

In the upper half of Table 2 (tubes 1 to 4) are presented the inhibitory effects of  $\delta$ -oximinolevulinic acid when it is added simultaneously with ALA in the same concentrations and ratios as in Table 1. The inhibition is the same as it is when the analog is added 10 minutes before ALA. In the lower half of Table 2 (tubes 5 to 8) are the data obtained by using a constant concentration of  $\delta$ -oximinolevulinic acid ( $7.5 \times 10^{-4}M$ ) with varying concentrations of ALA added 10 minutes after the analog. It is seen from both tables that increasing concentrations of ALA overcome the inhibition of  $\delta$ -oximinolevulinic acid, thus demonstrating the competitive nature of the inhibition. Also it is seen in both tables that at

various concentrations of ALA and  $\delta$ -oximinolevulinic acid the inhibition is relatively constant for a given ratio of analog to substrate.

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### A Genetic Constitution Frustrating the Sexual Drive in *Drosophila paulistorum*

*Abstract.* Hybrids obtained in the laboratory between two subspecies of *Drosophila paulistorum* possess a genetic constitution which is discordant enough so that the hybrid females repel the courtship of all males, and will mate with none. The hybrid males will court and will be rejected by almost all females, including their own hybrid siblings.

It has been shown (1) that the species *Drosophila paulistorum* actually represents a cluster of six subspecies, and that reproductive isolation of various sorts is being evolved between these incipient species, now in *statu nascendi*. Crosses between three (Centro-American, Amazonian, Andean-South Brazilian) of the six subspecies result in the production of fertile female and sterile male hybrids. The cause of the male sterility has been investigated (2) and found to depend upon the genotype of the mother involved. Any female which carries any mixture of the chromosomes of different subspecies deposits eggs giving rise to sterile male zygotes and to fertile female ones. (Intersubspecific insemination is accomplished more quickly here, and hybrid females can be tested for fertility by etherizing the females and immediately placing them with mature, unetherized males. The males will then approach and will often mount the females while they are still partly anesthetized. Subsequently, the females always produce offspring.) The male sterility is independent of the genotype of the male parents and the genotype of the sons themselves.

The mode of action of a reproductive isolating mechanism such as this seems to be unprecedented in genetic literature, but the same species-complex has evolved still another extraordinary isolating device: inter-subspecific hybrids have been obtained by crossing Amazonian males with Andean-South Brazilian females. Most crosses between these two subspecies fail because of the powerful sexual isolation barrier. However, after repeated and lengthy attempts, viable male and female hybrids were obtained. It should be emphasized that these were normal males and normal females as far as the external and internal anatomy were concerned. Yet the genic endowments contributed by the parents of these hybrids are so discordant, that the hybrids are virtually unable to perform, successfully, the mating rituals that are normal in this species.

A study of the behavior of living flies under a microscope in special observation chambers showed that the hybrid females (25 have been observed and dissected so far) will not accept any males which court them, regardless of how vigorous or persistent the courtship is. They have been observed to reject consistently the males of both parental subspecies, as well as their own hybrid males. They accomplish this by assuming the posture of rejection of the courtship which is characteristic of *D. paulistorum*: the female lowers her head and elevates the tip of her abdomen so that the vaginal orifice is inaccessible to an approaching male. Only twice have Andean-South Brazilian males been seen to rush in so quickly that they succeeded in mounting the hybrid females; however, in one case, it took the female 2 minutes to repel the male by shaking violently from side to side, and, in the second instance, it took only 1 minute and 47 seconds. [Copulation normally takes an average of 17 minutes and 12 seconds in this species (3).] Furthermore, dissection of the female reproductive tracts involved, in physiological saline, showed that no sperm was transferred to the females in these two instances.

The hybrid males (19 have been observed and dissected so far) are of less interest in this respect, because they are completely sterile. Even so, they are rarely successful in courting females, and they have been placed and observed with mature females of both parental subspecies, as well as with their own hybrid females. These males have been observed in a total of only seven copulae, whereas a normal *D. paulistorum* male will begin courting again immediately after dismounting one female, and may inseminate several females per day.