rapidly increases during the 1st 2 weeks (olfactory bulb) or 3 weeks after birth (cerebral cortex). Thereafter the enzyme activity increases more slowly up to 35 days of age. NaF-induced stimulation is, at all ages, greater in olfactory bulb than in cerebral cortex. These changes could indicate increased numbers of catalytic units during development.

Increased activity with development may also be attributable to alteration of the cell membrane structure or composition[24], but activity increase during development is considerably stimulated in the presence of detergent. In olfactory bulb homogenate, adenylate cyclase activity does not increase proportionaly to the basal activity and the absolute increase in cyclic AMP formation remains relatively constant. In cerebral cortex homogenate, activity progressively increases as a function of age being 3-fold higher on the 21st day than in the absence of detergent; decrease in activity between 21 and 35 days of age is increased (30%). A similar evolution, with higher levels of activity, is observed in response to sodium fluoride in both structures.

The comparison between olfactory bulb and cerebral cortex maturation reveals striking differences and adenylate cyclase activity of cerebral cortex homogenate remains consistently higher (1.73–6.60-fold) than that noted in olfactory bulb homogenate throughout the experimental period and whatever the incubation conditions (figure 1). Qualitatively similar differences with smaller amplitude are observed when enzyme activity is expressed on a wet weight or on a protein basis. However, in figure 2, enzyme activity is expressed as percentage of maximal activities found over the developmental period; the same pattern of evolution in cellular activity can then be observed in the 2 structures.

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The effect of dimethyl sulfoxide on tissue distribution of gentamicin

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Summary. Dimethyl sulfoxide (DMSO) and gentamicin were administered to rats i.p. No significant differences in gentamicin tissue concentrations were found between rats receiving DMSO and gentamicin, and rats receiving gentamicin alone. DMSO does not increase the tissue concentrations of gentamicin.

Aminoglycosides are valuable agents in the therapy of various infections. Some therapeutic failures may be due to insufficient penetration of the agent into body compartments in which infections occur.

Dimethyl sulfoxide (DMSO) has been shown to cross various body membranes[1]. Shortly after administration by various routes DMSO can be detected in almost every body space[2]. In addition, DMSO has been shown to enhance the penetration of many compounds through the intact skin and urinary bladder[3–6] and to increase the brain concentration of various substances when administered i.p. to rats[7].

We have investigated whether the concomitant administration of DMSO and gentamicin to rats would result in higher tissue levels of gentamicin as compared to rats receiving gentamicin alone.

Materials and methods. Charles-River male rats were divided into 3 groups. 1 group of 6 animals received gentamicin 6 mg/kg/day i.p. divided into 2 injections given 12 h apart for 10 days. The other group of 6 animals received the same dosage of gentamicin dissolved in 50% DMSO. (DMSO 0.69 g/kg/day) administered i.p. The 3rd group of animals received the same dosage of DMSO given i.p. and served as a control group. On the 11th day: 9 h after the last injection, the animals were sacrificed. This time was chosen in order to amplify possible differences in gentamicin organ concentrations between the groups. Tissues from the killed animals were removed aseptically, weighed, washed 3 times with phosphate buffered saline incubated in 2.5% trypsin solution (Difco 0152-13) for 2 h at 37 °C and then homogenized. The assay of gentamicin was performed with Oxford-cups on Mueller-Hinton Agar using *B. subtilis* (ATCC 6633) as the test organism. Plates were incubated at 37 °C for 18 h. Standard curves were made by dissolving gentamicin laboratory standard in pooled rat serum. All readings were performed in quintuplicate and then averaged. Statistical analysis was performed according to the Wilcoxon rank-sum-test, between the 2 methods of treatment.

Results. Our results indicate that the animal group receiving DMSO alone had no antibacterial activity in their tissues (table).

In the group the received DMSO and gentamicin, tissue gentamicin concentrations were similar to those obtained in the group that received gentamicin only, except for the heart tissue which had increased drug concentrations (table).

Discussion. DMSO is a dipolar hygroscopic solvent. It crosses various biological barriers causing little or no tissue damage[1]. Pharmacokinetic studies in rats demonstrate rapid DMSO absorption and distribution regardless of the route of administration. Serum and tissue peak levels are reached at about 4 h following administration, and decline slowly afterwards. High DMSO concentrations are obtained in the soft tissues, particularly in the spleen, lung, brain, kidney, heart and the liver.

These pharmacokinetic data, together with the ability of DMSO to enhance the penetration of various chemicals through a number of biological membranes such as the bladder[3,8], the skin[3,5] and the blood-brain barrier[7] led us to try and increase the tissue penetration of gentamicin.

Our data indicate that in the rat model, when both DMSO and gentamicin are administered i.p., DMSO fails to enhance the tissue penetration of gentamicin into the brain, lung, liver, spleen, bone and the testicular tissues. A somewhat higher concentration of gentamicin was found in the heart tissue of the animals treated with DMSO and gentamicin. It is doubtful, however, whether this difference is of biological importance. Since the tissue specimens were taken 9 h after the last drug administration it is possible that DMSO facilitated the exit of gentamicin from the tissues. However, the tissues of all the animals still contained the unmistakeable odor of DMSO even after being frozen for several days. Furthermore, previous studies detected appreciable amounts of DMSO 8 h following administration[2].

Gentamicin concentrations in tissues of rats

Organs	Gentamicin (n=6)	DMSO+ gentamicin (n=6)	Statistical significance
	Concentration in μg/ml ± SE		
Brain	0.28±0.07	0.8 ±0.21	$p>0.1$
Heart	0.24±0.09	0.87±0.22	$p<0.01$
Lung	0.66±0.12	0.46±0.12	$p>0.1$
Liver	0.62±0.11	0.27±0.12	$p>0.1$
Spleen	0.30±0.05	0.24±0.09	$p>0.1$
Testes	0.33±0.06	0.1*	
Bone	0.15±0.01	0.13±0.04	$p>0.1$
Muscle	1.1 ±0.01	0.43±0.12	$p>0.1$
Kidney	6.01±2.4	4.13±2.1	$p>0.1$

* Only 3 specimen assayed.

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Increased rate of melanization in hemolymph of American cockroaches *(Periplaneta americana)* and house crickets *(Acheta domesticus)* intoxicated by insecticides

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Summary. Treatment of house crickets and American cockroaches with any one of a variety of insecticides increased the rate of melanization in hemolymph incubated with diphenol substrates.

The darkening of insect hemolymph in vitro has commonly been attributed to phenoloxidase (tyrosinase) formation of melanin[1-4]. Hemolymph melanization commonly accompanies pathological conditions[5] and parasitism[4]. Hurst[6] reported increased hemolymph phenoloxidase activity, as measured by in vivo melanization, in *Tenebrio molitor* and *Musca domestica* treated with pyrethrins or DDT. Shorey[7] observed that a topically applied carbamate insecticide (Zectran) caused darkening of cabbage loopers and beet armyworms. We report here the observation that several insecticides (TEPP, dicrotophos, DDVP and DDT) cause an increased rate of melanization in insect hemolymph diphenol solutions.

Each of the following dosages was applied topically to the ventral abdomen of crickets in 2 μl of acetone: TEPP 4 μg, dicrotophos 10 μg, and DDT 50 μg. 30 min after knockdown hemolymph was collected by cutting off the hind legs and collection into 20 μl capillary tubes with gentle squeezing of the abdomen. When sufficient hemolymph was obtained for a test, 2 vol. of Narahashi saline[8] were added. The mixture was sonicated for a period just sufficient to break up the clots and to mix the saline with the hemolymph. The mixture was incubated on spot plates with an equal volume (20 μl) of a 1% solution (w/v) of catechol in Narahashi saline. Control hemolymph from untreated crickets was spotted on the same plate in the same manner. Spot plates were held in closed containers containing damp paper towel to prevent desication. Hemolymph from intoxicated crickets darkened the catechol solution at a much faster rate than control hemolymph. The effect was most obvious at 1-2 h of incubation. Intoxication of American cockroaches with 100 μg of DDT in 2 μl of acetone or with DDVP vapours and collection of their hemolymph by light centrifugation[9] produced similar results when incubated with diphenols (figure).