Absence of Tooth Malformation in Offspring of Rats Treated with a Long-Acting Sulphonamide

Tooth alterations in rats born of mothers treated during pregnancy with a long-acting sulphonamide (2-sulphanilamide, 4-6-dimethoxy-pyrimidine = SDmP) have been reported[1,2]. These reports led us to consider if such malformation might occur also with 2-sulphanilamide, 3-methoxy-pyrazine (SmP)[3] recently studied in Farmitalia Research Laboratories[4-6].

Female albino rats (Sprague-Dawley strain), weighing from 200 to 300 g, were mated for 12 h and treated during gestation for different periods with SmP or SDmP.

Litters were left with mothers till weaning time (21 days) and dams were fed ad libitum with balanced diet and aqua fontis.

SmP and SDmP, used for comparison, were administered in the diet in different concentrations to provide the chosen doses.

The sulphonamide SDmP induces malformation of the incisors of weaned rats (Figure 1) with a frequency proportional to the dose (see Table), but these effects are conditioned by the period at which the treatment is carried out, since they take place only if the 14th day of gestation is included. As is known, the formation of tooth placode[7] occurs during this stage of foetal development.

SmP causes no alteration when administered in the sensitive period under the same conditions and also at higher doses, and the teeth of rats so treated are similar to those of controls (Figure 2).

The absence of malformations in the rats treated with SmP is not due to an incomplete absorption of the drug, as this sulphonamide is well absorbed in the rat[5].

We think that these data, which show the good tolerance of SmP, would be interesting also from the point of view of general experimental teratology.

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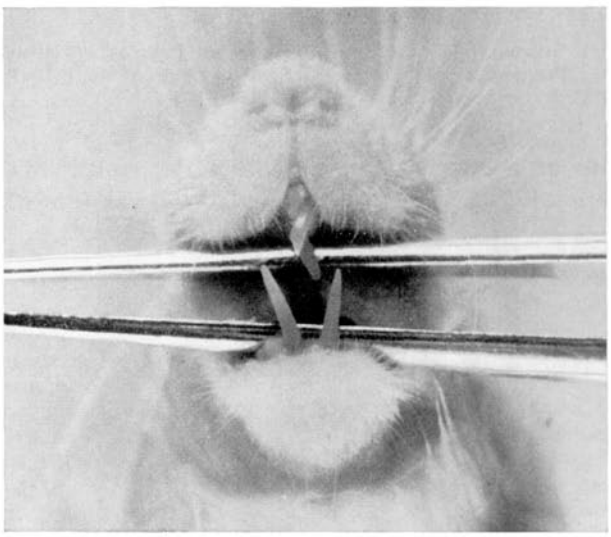

Fig. 1. Incisors of weaned rat, born of mother treated from the 11th to the 20th day of gestation with 75 mg/kg of SDmP, a long-acting sulphonamide.

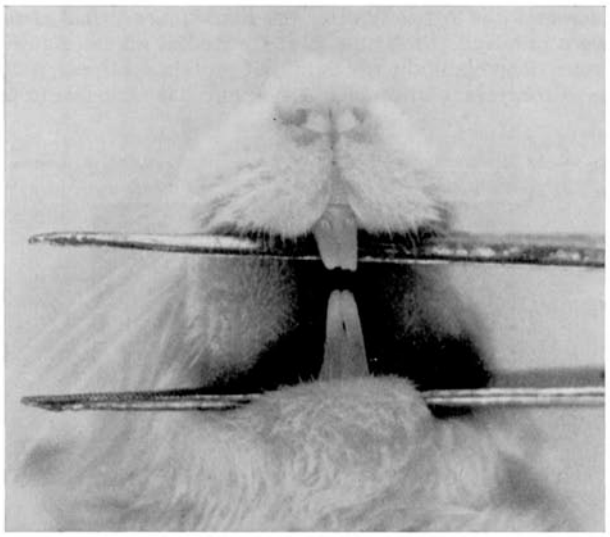

Fig. 2. Incisors of weaned rat, born of control mother.

Rat: malformations of incisors in the litter

Treatment	Groups	Dose mg/kg rat	Administration period in days of gestation	No. of gestations	No. of live foetuses	No. of abnormal rats at birth	No. of survivors at weaning	Rats with malocclusions of incisors No.	%
SDmP	a	50	2–20	26	327	0	159	28	17.6
	b	50	2–13	22	275	0	124	0	0
	c	50	11–20	24	263	0	121	15	12.4
	d	75	11–20	24	264	0	75	62	85
SmP	e	50	2–20	25	312	0	208	0	0
	f	75	11–20	26	298	0	185	0	0
	g	100	11–20	24	272	0	115	0	0
Controls	h	–	–	59	660	0	378	0	0

One must consider in fact the possibility of the appearance, after birth, of delayed teratogenic effects, such as those on the teeth, and the need to carry out the treatment during the whole gestation to show a crude teratogenic effect.

In fact, some ontogenetic moments may be easily missed using fractional treatment, especially in animals having relatively rapid gestations. On the other hand, if the determination of the precise moment of the pregnancy which is sensitive to the drug should be of interest, the fractional treatment may show it in further trials.

Riassunto. La 2-sulfanilamido, 3-metossi-pirazina, a differenza della 2-sulfanilamido,4-6-dimetossi-pirimidina, non induce malformazioni dentarie nella prole, qualora venga somministrata al ratto durante la gestazione.

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Uridine Incorporation into Pyramidal Nuclei of the Mouse Brain

Recent memory has been assigned to the hippocampal zone of the brain in mammals and longer-term memory to the neocortex (STEPIEN et al.[1]). Intracerebral injections of puromycin into the hippocampi have been found to cause loss of short-term memory, whereas longer-term memory was lost only after the remaining cortical areas were involved (FLEXNER et al.[2]). Studies on the significance of compounds, which inhibit protein synthesis, such as puromycin, and brain function also has rationale from the early work of HYDEN[3] who demonstrated a correlation between neuron function and nucleotide incorporation into pyramidal cells of the mouse brain.

A male C3H mouse received i.v. 5 μC of (H)^3-uridine 1.15 C/m*M*) per g of body weight and was sacrificed 2 h later. Tissues were fixed in Bouins solution and autoradiographs of slide material were made with Kodak NTB1

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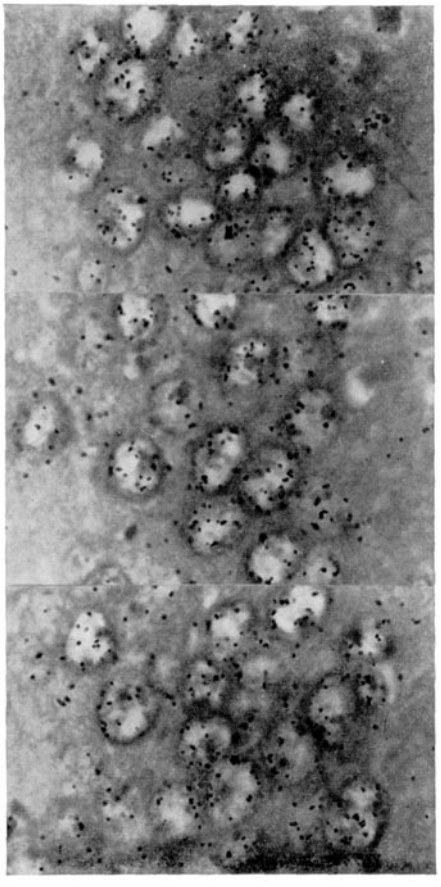

Fig. 1

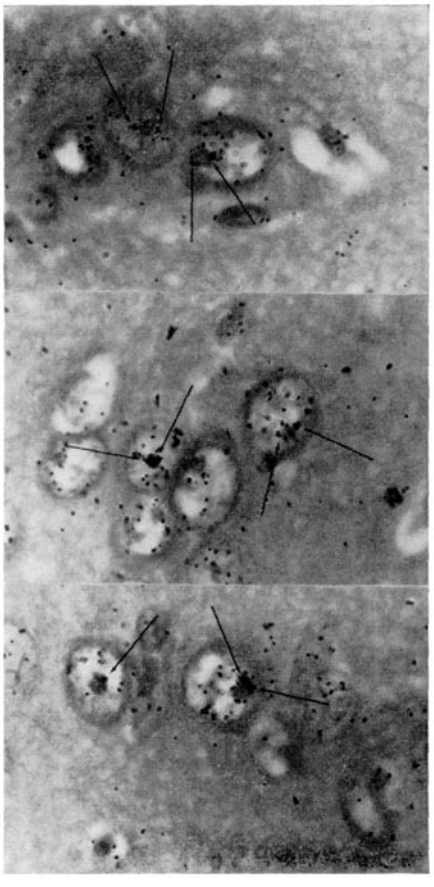

Fig. 2