only in the RER fraction. The disturbances in the spectral interactions are also most prominent in this fraction. When, however, the drastic fall in Cyt. P-450 content of RER (72%) is taken into account, a significant qualitative effect of Pr can only be seen in the SER. Liver microsomes are known to contain multiple forms of Cyt. P-450. It is possible that the apparent increase in the binding capacity occurring in RER is due to an enrichment of a more active form in the remaining part (28%) of this cytochrome.

Our results indicate that light lanthanons do not cause changes in the spectral interactions only by decreasing the concentration of Cyt. P-450, but also cause a qualitative change in the Cyt. P-450 molecule or in this microenvironment. There are differences in the binding capacity between SER and RER subfractions. This may indicate that more than one kind of Cyt. P-450 molecule is reacting, or that some endogenous substrates may partly mask one or more binding sites of the cytochrome. The reaction of lanthanons with the lipid factor may, on the other hand, disturb the access of ligands to the cytochrome molecule[6,16].

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Chlorpromazine: A potential physiological teratogen

C. J. Sherry

Department of Biology, College of Science, Texas A & M University, College Station (Texas 77843, USA),
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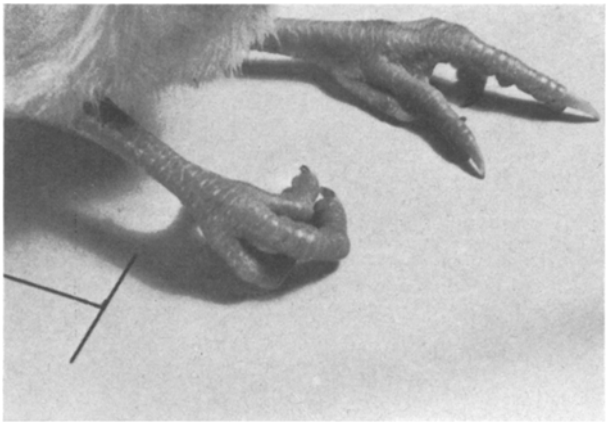
Summary. Chlorpromazine, a drug commonly administered as an antiemetic during pregnancy, when administered prenatally to chick embryos, was associated postnatally with a 'curled toe' anomaly (ED 50% of 88 µg/egg for the 4-day-embryo).

Chlorpromazine (CPZ) can and does cross the placental barrier in both animals and man[1-7]. It is routinely administered to human females during the first trimester of pregnancy to control nausea and vomiting (i.e. 25 mg/kg)[8]. It has been reported that administration of large doses (i.e. 50–150 mg/day to 8000 mg/10 days) to control maternal depression and/or psychotic behavior has no neonatal effects[9-12]. However, a number of extrapyramidal dysfunctions have been reported following prenatal human exposure to relatively large doses of CPZ[13-15]. In addition, in rodents, if CPZ is administered prior to gestation, no births take place[16]. If CPZ treatment is suspended prior to gestation, a few litters are born, but each litter has fewer pups than expected[16-19] and the pups that are born are small for dates[16]. This data suggest that it would be important to determine if CPZ is a physiological and/or anatomical teratogen. Since the developing chicken embryo responds to all known teratogens[20,21], it was decided to determine the effect of prenatal exposure to CPZ on the postnatal development of the chicken.

Methods. 120 eggs were obtained from the Colonial Poultry Farms and refrigerated prior to incubation to insure that they would be at the same developmental age[22]. Following the technique of Karnofsky[21], 6 groups



The 'curled toe' anomaly. Note that all of the phalanges on 1 limb and 2 sets of phalanges on the other are involved. The neck and upper limb muscle are not involved in the anomaly. In addition, cloacal evacuation is normal.

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of 20 eggs each were injected with 0, 1, 10, 100, 1000 or 10,000 µg/egg CPZ at 96 h of incubation. When hatched, the chicks were exposed to the following behavioral tests: imprinting (beginning at 3 days of age); open field (14 days of age); conditioned avoidance response to light onset (21 days of age); position habit in a T maze for a food reward (21 days of age). All chicks that survived to hatching were subjected to a standardized autopsy procedure[22,23].

Results. The lethal dose 50%, as determined by the exact probit method[24], was 4000 µg/egg. The groups treated with 1, 10, 100 µg CPZ took fewer trials to reach criterion on the T maze than the control group, while the 1000 and 10,000 µg groups took more trials (Kruskal-Wallis, 0.05 confidence level)[25]. While not statistically significant, the following observations also suggest long term alterations in behavior. The drug-treated chicks tended to have shorter latencies in an imprinting situation, less activity in an open field apparatus, and tended to require more trials to criterion in the conditioned avoidance problem. 17% of all of the drug-treated chicks that survived to hatching showed a 'curled toe' anomaly. The 'curled toe' could be relatively mild and involve 1 or 2 toes on 1 foot, or relatively severe, as shown in the figure, and involve all of the toes on 1 or both feet. The effective dose 50% for 'curled toes' is 88 µg/egg as determined by the exact probit method[24].

Discussion. The 'curled toe' anomaly was not reported by other investigators who exposed chick embryos to CPZ[26,27]. However, the 'curled toe' anomaly is quite similar to that reported for chicks born of riboflavin-deficient mothers[28]. It seems likely that the curled toe is a physiological rather than strictly an anatomical anomaly since the 'curled toe' released to some extent during Nembuthal anesthesia (1.0 mg/kg). While great caution should be exercised in extrapolating from animal studies to humans, it is clear that prenatal exposure to CPZ is associated with long term behavioral alterations[29–36]. It is also clear that prenatal exposure to CPZ can be associated with extrapyramidal dysfunction in humans[13–15]. Since the animals in this study also demonstrated behavioral as well as a potential neurological anomaly, it would be important to reconsider the administration of CPZ to human females of childbearing age and in particular, as an antiemetic during the critical first trimester of pregnancy.

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Toxicity of ouabain on Drosophila melanogaster

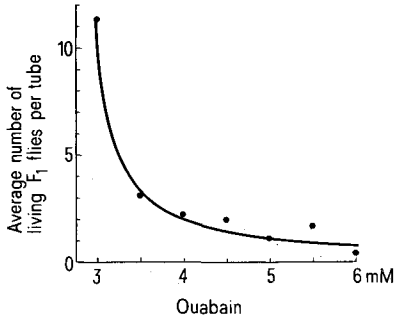
H. Beikirch

Zentrallaboratorium für Mutagenitätsprüfung der Deutschen Forschungsgemeinschaft, Breisacher Strasse 33, D-7800 Freiburg i. Br. (Federal Republic of Germany, BRD), 8 October 1976

Summary. Ouabain, also called g-strophantin, is an inhibitor of the Na^+/K^+-activated plasma membrane ATPase. Treatment of Drosophila melanogaster with 3–6 mM of this substance leads to a markedly reduced survival of the flies.

Recently, the use of ouabain as a selective agent in mammalian cell cultures has been described by some authors, and they were able to show that this compound can be applied in an in vitro system for mutagenicity testing[1–3]. In an attempt to use ouabain resistance as a selective system not only for cells in culture but also for whole animals, we tested the toxicity of the compound with adult Drosophila flies and the development of their progeny. The used strain was Berlin wild (+K). The animals were fed with a cornmeal-agar-syrup medium containing different concentrations of ouabain. For each concentration 10 test tubes were used. 3 pairs of flies were put into each tube. After a treatment period of 6 days at 28 °C (this temperature was chosen to shorten the usual generation time of 14 days at 26 °C), the parent flies were removed. After an additional treatment period of 6 days, the F_1 progeny was scored.

At a low concentration, the toxicity of ouabain increases with increasing concentration (table). At higher concentrations, a saturation effect is clearly demonstrated in the figure where the average number of living F_1 animals per tube is plotted against the ouabain concentration. An exact estimation of the dead flies in the tubes was not possible. With the results described, it is possible to test



Survival of the progeny after ouabain treatment.

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