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in dogs. Qualitatively, R-29764 is more closely related to haloperidol, pimozide and penfluridol than to chlorpromazine. The side-effect liability is expected to be very low when hypotensive, autonomic and undesirable neurological side-effects are concerned. 31 references. (Author abstract)

05 TOXICOLOGY AND SIDE EFFECTS

226848 Mendelson, Wallace B.; Cicero, Theodore J. Lab. of Clinical Psychopharmacology, NIMH, Bldg. 10, Room 3N224, Bethesda, MD 20014 **Possible role of the alpha-adrenergic system in narcotic withdrawal: toxic interaction between methadone and phenoxybenzamine. (Unpublished paper).** Bethesda, MD, NIMH, 1975. 6 p.

Possible toxic effects of phenoxybenzamine in methadone addicted rats were tested. Rats were divided into three groups: methadone - saline, phenoxybenzamine, and methadone - phenoxybensamine. The results show that there were significantly more frequent deaths in the methadone - phenoxybenzamine group than in either of the other two groups. Thus, although an earlier animal study suggested that phenoxybenzamine may block some signs of narcotic withdrawal, the toxic interaction observed in this study would seem to contraindicate the use of phenoxybenzamine in treating human addicts. 8 references.

226944 Lefkowitz, Stanely S.; Chian, Chinlee Yang. Department of Microbiology, Texas Tech University School of Medicine, Lubbock, TX 79409 **Effects of delta-9-tetrahydrocannabinol on mouse spleens.** Research Communications in Chemical Pathology and Pharmacology. 11(4):659-662, 1975.

The effects of delta9-tetrahydrocannabinol (THC) on the plaque forming cell response of mice immunized with sheep erythrocytes were examined. It was found that a marked suppression of plaque forming cells occurred concomitant with a general loss of spleen cellularity following administration of THC. These results suggest rather marked effects of this drug on antibody synthesis. 6 references. (Author abstract)

227391 Bourdois, P. S.; Junghani, J.; Perraud, J.; Reinert, H. Centre de Recherche Pfizer, 37400 Amboise, France **Transplacental effects of drugs on hearing, vision, and behaviour.** Toxicology and Applied Pharmacology. 33(1):196, 1975.

At the Fourteenth Annual Meeting of the Society of Toxicology, held at Williambsurg, Virginia, in March 1973, the transplacental effects of drugs on hearing, vision, and behavior in rats and cat were reported. The open field technique was used to measure two stereotype responses (ambulation and rearing) and emotion (defecation). Amphetamine, iproniazid chlorpromazine, pemoline, and monosodium glutamate were tested in 4-week-old rats. Preyer's reflex, elicited by audiometer generated sounds at threshold amplitude and different frequencies, was chosen to test hearing. Gentamicin, kanamycin, dihydrostreptomycin, and ethacrynic acid were examined in 25-day-old rats and guinea-pigs. Cats were used to test the effects on vestibular function. Vision was tested by recording stroboscope evoked cortical potentials. (Journal abstract modified)

228554 Yershova, V. P. Stavropol'skogo meditsinskogo instituta, Stavropol, U.S.S.R. **/The effect of chronic injections of chlorpromazine on oogenesis and progeny development in albino mice./** O vliyanii khronicheskikh in"yektsiy aminazina na oogenez i razvitiye potomstva zhivotnykh (belykh myshey). Farmakologiya i toksikologiya (Moskva). 38(4):473-476, 1975.

The effect of chlorpromazine on oogenesis and progeny development was investigated in albino mice subjected to chronic chlorpromazine injections during various stages of pregnancy. Chlorpromazine administration in doses of 16mg/kg prior to the onset of pregnancy was found to inhibit oogenesis, thus reducing the number of young mice in the litter. Chlorpromazine administration prior to pregnancy coupled with a single injection of the drug at the end of gestation was found to either interrupt the pregnancy or seriously disturb postnatal development of some of the offspring. Postnatal disturbances included: delayed growth and motor activity; lack of motion coordination; changes in skin; diarrhea; and underdevelopment of the organs and of their histological structures. 13 references. (Journal abstract modified)

228977 Roszell, D. K.; Horita, A. Riverview Hospital, Essondale, British Columbia **The effects of haloperidol and thioridazine on apomorphine- and LSD-induced hyperthermia in the rabbit.** Journal of Psychiatric Research (Oxford). 12(2):117-123, 1975.

The administration of LSD (100micrograms/kg) or apomorphine (4mg/kg) to male New Zealand rabbits resulted in a pronounced hyperthermic response accompanied by behavioral excitation and sympathetic activity. In addition, apomorphine exhibited several compulsive stereotyped responses, such as head turning and gnawing. Rabbits, which were pretreated with various doses of thioridazine or haloperidol, responded to LSD with slightly attenuated hyperthermia and behavioral excitation. The apomorphine induced responses were markedly attenuated or abolished with far smaller doses of the neuroleptics. The hyperthermic action of apomorphine was more sensitive to the actions of the antagonists than were the behavioral signs, total blockade being seen with 0.50mg/kg of thioridazine and 0.05mg/kg of haloperidol. The hyperthermic response to apomorphine thus represents a sensitive dopaminergic response, and may serve as a useful model in the evaluation of the antidopamine activity of the neuroleptic drugs. 15 references. (Author abstract)

231604 Sethi, N; Sethi, B. B. Central Drug Research Institute, Lucknow, India **A teratogenic study of haloperidol.** Indian Journal of Psychiatry (Madurai). 16(2):165-169, 1974.

The effects of administering haloperidol to pregnant rats on the offspring of those rats were examined to study the possibility of teratogenic side-effects. Pregnant female mice were divided into four treatment groups: the first three groups received haloperidol in doses of 2.5, 5, and 10mg/kg bodyweight respectively by gavage on gestation days 6 through 15 (the period of organogenesis). The fourth group served as control. All animals were delivered by caesarean section on the 20th day postcoitus. No visceral or skeletal deformities were found; but the implantation number was reduced and resorptions were high, reducing the litter size in drug treated animals. Litter size was markedly reduced in the highest dose group. Litter weight was significantly affected in the groups receiving 5 and 10mg/kg daily. It is concluded that haloperidol is embryotoxic and not teratogenic. 7 references.

06 METHODS DEVELOPMENT

227207 Simon, P.; Boissier, J. R. Paris **Evaluating potential anti-depressants in animals.** Journal of International Medical Research (Northampton). 3(Suppl. 3):14-17, 1975.

At the International Vivalan Symposium, held in London in November 1974, a paper was presented in which the process of evaluating potential antidepressants in animals was