administration of methandrostenolone, showing that no alteration had occurred in the metabolism of phenylbutazone. Equilibrium dialysis experiments indicated competition between phenylbutazone and oxyphenbutazone, and that the former has a relatively greater affinity for albumin. These findings suggest that phenylbutazone masks the influence of methadrostenolone on plasma levels of oxyphenbutazone, presumably by displacing oxyphenbutazone from plasma protein binding sites. Comparable *in vitro* studies with phenobarbital and *p*-hydroxyphenobarbital indicate the absence of significant competition for albumin binding sites.

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Effect of Pralidoxime on Electrical Activity of the Cat Brain* (33339)

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Pralidoxime (pyridine-2-aldoxime methiodide, 2-PAM) is an ionic compound of a type that is not expected to penetrate the blood-brain barrier easily. However, the evidence on this point is conflicting (1). Rutland (2) found that 2-PAM reactivated blood cholinesterase but not brain cholines-

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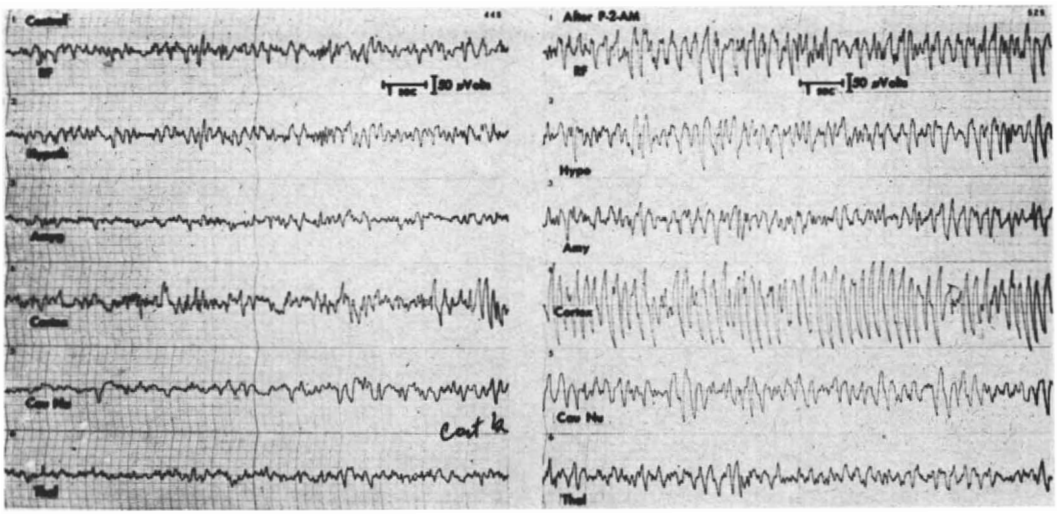

FIG. 1. Effect of 2-PAM on EEG of cat brain. Left, control, right, 30 min after administration of 50 mg/kg 2-PAM i.p. Mesencephalic reticular formation (RF) anterior hypothalamus (Hypoth) basal nucleus of amygdala (Amgy) median suprasylvian gyrus (Cortex) head of caudate nucleus (Cau Nu) posterior ventrolateral nucleus of thalamus (Thal).

terase in rats poisoned by sarin but Firemark *et al.* (3) demonstrated concentrations of 10^{-6}–$10^{-5}M$ of 2-PAM-^{14}C in rat brains perfused for 10 min. Rosenberg (4) showed that 2-PAM raised the brain cholinesterase levels of rabbits poisoned with paraoxon. Longo *et al.* (5) found that 30–50 mg/kg of 2-PAM did not alter the EEG of rabbits but antagonized the desynchronization and electrical grand mal pattern produced by sarin. The present study demonstrates that 2-PAM in intraperitoneal doses of 30–75 mg/kg apparently attains concentrations in cat brain sufficient to produce sedation and EEG patterns characteristic of CNS depression. These doses also prevented convulsions and electrical signs of preconvulsive or convulsive activity when the animals were given pentylenetetrazol.

Methods. Six adult 2.5–3.0-kg male and female cats with electrodes chronically implanted in their brains were used in these studies. Electrodes were placed by standard stereotaxic techniques and a Baltimore stereotaxic instrument using the coordinates of Snider and Neimer (6). Sites implanted were the mesencephalic reticular formation, the basal nucleus of the amygdala, the posterior ventrolateral nucleus of the thalamus, the anterior hypothalamus, the head of the caudate nucleus, and the median suprasylvian gyrus. Electrodes were 34 SWG stainless-steel wire insulated with Diamel. Ground leads were attached to screws fixed in the skull. Recording was begun 2 weeks after electrode implantation. Drugs were administered to each cat 1–15 times at intervals of at least 5 days. The cats were restrained in canvas bags and recording was done in a grounded, shielded cage using a Grass model 5 polygraph with model 5-P5-C EEG preamplifiers. Predrug recording was continued until both alert and sleep patterns were obtained after which drugs were administered intraperitoneally. Behavior was observed continuously and correlated with EEG activity.

Electrode positions were verified by standard histological techniques using coronal sections prepared from brains fixed in 10% formalin.

Results. After doses of 10–30 mg/kg of pralidoxime i.p. EEG patterns from cortical and deep electrodes did not differ from those obtained from unmedicated dozing or relaxed cats. EEG's of both control and medicated animals exhibited intermittent high amplitude, low frequency spindles. Behaviorally, the animals that received 2-PAM were relaxed and showed a tendency to sleep.

Larger doses (30–75 mg/kg) of 2-PAM

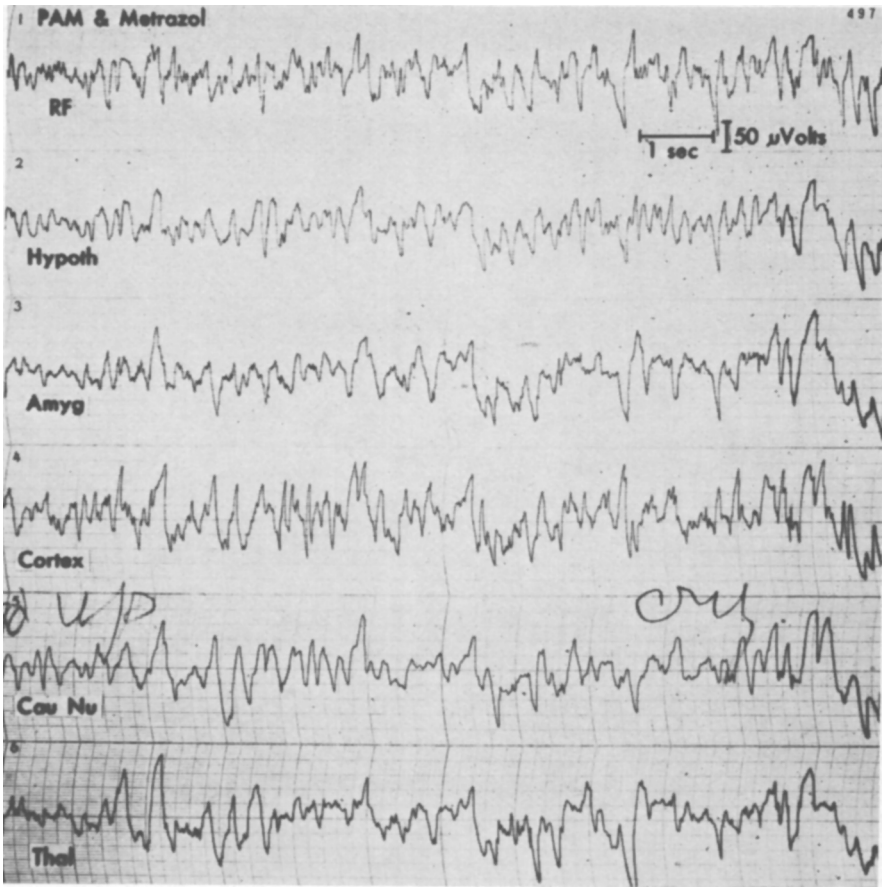

FIG. 2. Effect of pentylenetetrazol 35 mg/kg i.p. on EEG of cat premedicated with pralidoxime, 50 mg/kg i.p. No spiking activity characteristic of convulsions occurred. Tracing taken 5 min after injection of pentylenetetrazol.

produced the EEG pattern shown in Fig. 1, which emerged from a pattern similar to that produced by sleep. High-amplitude 4–5 cps waves appeared in all areas monitored; most prominently in the cortex. This pattern appeared about 20 min after drug administration, reached a maximum in about 30 min, and persisted for about 40 min. Behaviorally, the animals were sedated and indifferent to auditory and visual stimuli but able to react to noxious stimuli.

Anticonvulsant activity of 2-PAM was demonstrated in 3 cats that were given 25–45 mg/kg of pentylenetetrazol 30 min after i.p. injections of 2-PAM, 50 mg/kg. The CD_{50} for pentylenetetrazol in cats was estimated to be 25 mg/kg by Tuttle and Elliott (unpublished results). As shown in Fig. 2 no electrical activity characteristic of the preconvulsive state appeared and none of the animals convulsed. However, after injection of the convulsant the animals became restless and vocal for a brief period with concomitant descynchronization of the EEG. These doses of pentylenetetrazol produced EEG spiking and behavioral convulsions in cats premedicated with anticholinergic doses of methantheline bromide.

Further evidence of anticonvulsant activity was obtained from administration of 0.7–2.0 mg/kg of physostigmine after 30–75 mg/kg of 2-PAM. Physostigmine in this dose range was shown to be a convulsant by Bokums and Elliott (7). 2-PAM effectively blocked the peripheral cholinergic effects and the production of seizures but not the desynchroni-

zation of the EEG, development of hypersynchronous activity in the amygdala, and restless, violent behavior attributed by Bokums and Elliott (7) to physostigmine.

Discussion. We have shown that 2-PAM in doses up to 30 mg/kg i.p. does not alter the EEG of cats but that 30–75 mg/kg produce an EEG characteristic of central nervous system depressants that is accompanied by behavioral sedation or tranquilization not progressing to anesthesia within the dose range studied. The depressant action has an anticonvulsant component since 50 mg/kg of 2-PAM prevented induction of convulsions by pentylenetetrazol and 30–75 mg/kg blocked the convulsant action of physostigmine.

The brain of the cat differs from that of the rabbit in its reaction to 2-PAM since Longo *et al.* (5) using doses in the same range as ours found no effect of 2-PAM on the EEG of the normal rabbit brain. In both species, however, these doses antagonized centrally acting cholinergic agents; sarin in the rabbit and physostigmine in the cat. It appears that 2-PAM crosses the blood-brain barrier in cats and rabbits and can achieve concentrations sufficient to antagonize some of the effects of cholinergic and other central nervous stimulants.

Summary. In cats, pralidoxime in doses of 30–75 mg/kg produces sedation and an EEG pattern like that seen after administration of CNS depressants. These doses also prevent convulsions induced by pentylenetetrazol or physostigmine. Apparently significant amounts of pralidoxime cross the blood-brain barrier in cats.

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Spermatozoan Decapacitation Factor (DF) in Human Seminal Plasma* (33340)

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Decapacitation Factor (DF) is a substance demonstrated to be present in the seminal plasma of the rabbit, bull, boar, stallion, monkey, and ram by its ability to prevent fertilization of rabbit ova (1–3). DF, as its name implies, functionally reverses sperm capacitation, the process normally occurring in the female reproductive tract that enables sperm to penetrate ova, a property sperm do not possess at the time of initial deposition in the female (4–7).

The seminal plasmas of the bull and rabbit are potent sources of DF and the sperm of these species require capacitation (4, 5, 7). It appears, therefore, that the presence of DF in seminal plasma is an indication that capacitation occurs in that species. The present paper offers unequivocal evidence that DF occurs in human seminal plasma. Two earlier reports suggested that DF was present in human seminal plasma but fertility was not completely inhibited (1, 2). Brief, prelimi-

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