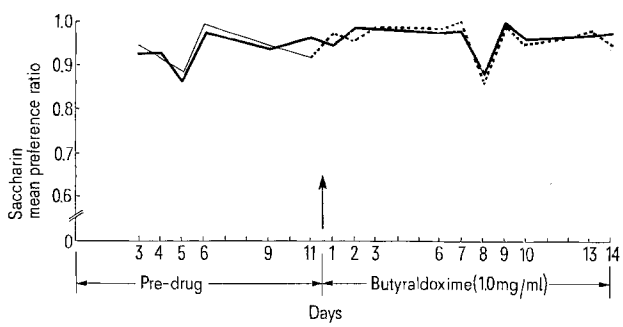
not on their specific effects with relation to alcohol, but rather on their character as noxious agents'[4].

Although the experimental procedure in the study of NACHMAN et al.[4] was quite different from ours[1,2], to clarify this point we conducted a saccharin preference experiment in C57BL mice following the same protocol used in our previous ethanol selection studies[1,2]. Salient features of our experimental design are: 1. the mice experienced, in a choice situation, the test solution for at least 11 days prior to introduction of butyraldoxime; such previous experience can significantly reduce any nonspecific conditioned aversion effects[5]. 2. Unlike the usual nonspecific conditioned aversion paradigm, our protocol included placing butyraldoxime in both drinking fluids – the water and the test solution –, so that mice received butyraldoxime regardless of which drinking cylinder they selected; this would further weaken any discrimination learning based upon a nonspecific aversion effect. It seems reasonable to assume that in an interpretation involving a nonspecific noxious agent, mice would experience noxious effects no matter which solution they drank, thereby making discrimination learning more difficult.

Twenty-four individually caged C57BL male mice were given continuous access to 2 drinking cylinders, one containing distilled water and the other a sodium saccharin solution (0.25 g per 100 ml). The left-right position of these cylinders was alternated every 1 to 3 days. The amount the mouse drank from each cylinder was recorded to the nearest ml and a preference ratio (volume of saccharin solution consumed/volume of saccharin solution consumed + volume of water consumed) was calculated. After 11 days, and for the next 14 days[6] butyraldoxime (1 mg/ml) was dissolved in both the water and saccharin drinking fluids for half the animals. The other 12 mice served as controls and were continued as before.

Both groups of mice showed a relatively stable mean preference ratio of 0.9 for the saccharin solution (Figure). Introduction of butyraldoxime (the dotted line) failed to produce any alteration in the mean preference ratio during the 14 days of butyraldoxime treatment. The lack of effect of the latter on saccharin preference is not unexpected, since no obvious metabolic interaction of butyraldoxime and saccharin is predicted. The present finding is consistent with our explanation that the pronounced decrease in ethanol preference on chronic ingestion of butyraldoxime is derived from the interaction of butyraldoxime + ethanol in vivo rather than from a nonspecific aversion effect produced by butyraldoxime alone.



Mean preference ratio of C57BL/Cum mice for a 0.25% saccharin solution as a function of time. The mean preference ratio for each group was calculated from observations made on the days indicated by number. The control group (solid line) received no drug throughout the duration of the experiment (25 days). Butyraldoxime was introduced (indicated by arrow) to the experimental group (dotted line) after the 11th day and continued for 14 days. Each group consisted of 12 mice.

Zusammenfassung. Butyraldoxim, das in C57BL-Mäusen bevorzugtes Alkoholtrinken vermindert, wurde im 2-Wahl-Vorzugsversuch in Wasser oder Saccharinlösung verabreicht und führte zu keiner konditionierten Aversion. Das Ergebnis bestätigt die Hypothese, der Butyraldoxim-Effekt beruhe auf spezifisch metabolischer Wechselwirkung mit Alkohol.

S. S. TENEN and B. K. KOE

Department of Pharmacology, Pfizer Inc., Groton (Connecticut 06340, USA), 27 March 1972.

[5] J. A. FARLEY, W. A. MCLAURIN, B. B. SCARBOROUGH and T. D. RAWLINGS, Psychol. Rep. *14*, 491 (1964).

[6] Butyraldoxime was also administered for 14 days in the ethanol studies[1,2]. In those studies a concentration of only 0.6 mg/ml was able to produce an alteration in ethanol preference. In the present saccharin study we increased the drug concentration in order to insure obtaining any possible conditioned aversive effects.

Behavioural Effects of an Antigonadotropin, of Sexual Hormones, and of Psychopharmaka in the Pumpkinseed Sunfish, *Lepomis gibbosus* (Centrarchidae)

A description of the behaviour of several species of *Lepomis* has been given by MILLER[1], further details and a quantitative behavioural analysis on *L. gibbosus* can be found in KRAMER[2,4–6]. The i.m. injection (3×0.2 mg/g body weight after 2 days delay, respectively) of the antigonadotropin Methallibure (I.C.I. 33828, a *bis*-thiourea derivative) decreased the sexual and suppressed the nest-building tendencies in 9 males significantly (i.e. $p < 0.01$) after 5 and 3 days p.i., respectively. Two motor patterns indicating a conflict between the aggressive and the sexual tendencies, viz. opercular spreads and leading ('Jagen', KRAMER[2]) diminished significantly after 5 days and after 1 day p.i., respectively. The effects lasted at least for a period of 11 to 16 days. 4 to 5 days p.i., although not having spawned, the animals performed fanning (parental care behaviour) for 4–5 days, indicating that the gondadotropin-inhibiting effect of Methallibure is accompanied by an increase of prolactin secretion. (The stimulating effect of prolactin on parental care behaviour has been shown elsewhere: Fiedler[3]; Kramer[2]). These various effects were not observed in the 5 control males, which had been injected with the vehicle. In the testes of males perorally treated with Methallibure for 4 weeks (0.65 mg/g body wt. × day), the process of gametogenesis was suspended. The diameter of the testis tubules decreased

[1] H. C. MILLER, Behaviour *22*, 88 (1964).

[2] B. KRAMER, Z. Tierpsychol. *28*, 351 (1971).

[3] K. FIEDLER, Zool. Jb., Physiol. *62*, 609 (1962).

[4] B. KRAMER, Diss. nat. Fak., J. W. Goethe-Universität, Frankfurt (1971).

[5] B. KRAMER, Z. Tierpshychol., in press.

[6] B. KRAMER, W. MOLENDA and K. FIEDLER, Gen. comp. Endocr. *13*, 515 (1969).

and the number of spermatozoa diminished. The tissue consisted almost entirely of spermatogonia. In 4 males intramuscularly pretreated with Methallibure, the i.m. injection of 0.06 mg/g body wt. 17-α-methyl-testosterone stimulated the intensity of aggressive behaviour significantly to 55% above the value before this injection, and the frequency of opercular spreads (+ 40%, difference significant) within 2–3 days p.i. In another 4 males pretreated with Methallibure, the i.m. injection of mammalian luteinizing hormone (NIH; 0.05 mg/g body wt.) increased the frequency of sexual (+222%) and aggressive (+283%) motor patterns as well as the frequency of opercular spreads (all at least $p < 0.05$). The i.m. injection of reserpine (0.0005 mg/g body wt.), which depletes the intraneuronal storage granules of catecholamines (especially norepinephrine), stimulated the aggressivity of 10 males significantly within 6 h. p.i. for a period of several days, whereas leading, a motor pattern which is performed by sexually highly excited animals, significantly diminished. Even a 2-, a 4- and an 8-fold dose of reserpine resulted in elevated aggressivity already 1 h p.i. and did not produce sedation. Chlorpromazine (0.125 mg/l dissolved in the aquarium water), which inhibits the action of released norepinephrine, depressed the aggressivity of 5 males significantly, as well as the nest building behaviour and the opercular spreads ($p < 0.05$). The sexual tendency remained high. The last mentioned observations support the hypothesis that the actual control of the aggressive and the nest-building tendencies may be mediated by norepinephrine. It is suggested that there is a long term (LH, testosterone) and an additional short term (catecholamines) control of reproductive behaviour in *L. gibbosus*.

Zusammenfassung. Ein synthetisches Antigonadotropin (Methallibur, I.C.I) hemmt das Sexual- und Nestbauverhalten von Sonnenbarsch-Männchen (*Lepomis gibbosus*). Testosteron hingegen steigert die Aggressivität, und Säuger-LH zudem noch die Sexualtendenz. Reserpin erhöht die Kampfstimmung; Chlorpromazin hemmt dagegen die Kampf- und Nestbaustimmung, nicht aber die Sexualtendenz.

B. KRAMER[7]

Zoologisches Institut der Universität, Siesmayerstrasse 70, D–6 Frankfurt a. M. (Germany), 13 April 1972.

[7] Present address: Groupe de Laboratoires du C.N.R.S., Laboratoire de Neurophysiologie Sensorielle Comparée, F-91 Gif-sur-Yvette (France).

Effect of Phenobarbital on Hepatocyte Proliferation in Rats Following Partial Hepatectomy

Administration of phenobarbital to experimental animals produces enlargement of the liver[1]. Hepatomegaly in mice following phenobarbital and other drugs has been ascribed to hepatocyte hypertrophy[2–4] or chiefly hyperplasia[5–8]. PAULINI et al.[9,10] showed that phenobarbital in young rats produced both hepatocyte hypertrophy and hyperplasia. The present study examines the effect of phenobarbital on hepatocyte proliferation in partially hepatectomized rats, measuring thymidine incorporation and the mitotic index.

Method. 36 male 10-week-old OFA (Lyon) rats, weight 260 to 377 g, were used. They were caged singly, allowed free access to food (Altromin®) and water, and randomly allocated to 4 treatment groups: Group 1: Controls, 2 rats/time interval, no treatment. Group 2: Phenobarbital alone, 2 rats/time interval; phenobarbital 80 mg/kg i.m. daily for 2 days prior to time zero (time of hepatectomy), 40 mg/kg i.m. at time zero. Group 3: Hepatectomy alone, 4 rats/time interval; 2/3 hepatectomy (HIGGINS[11]) under ether narcosis at time zero. Group 4: Hepatectomy plus phenobarbital, 4 rats/time interval; phenobarbital 80 mg/kg i.m. daily for 2 days prior to time zero, 40 mg/kg i.m. at time zero.

Sacrifice of rats was done at 16, 24 and 39 h after time zero. The time of hepatectomy was arranged so that all rats were sacrificed between 09.00 and 10.00 h. ^{3}H-thymidine, 3 mC/kg, was given i.p. 60 min before sacrifice. Liver tissue following sacrifice was prepared histologically for mitotic counts. Paraffin sections were coated with Ilford-G-5 emulsion, exposed for 14 days, and then stained with hematoxylin and eosin. Thymidine-labelled hepatocyte nuclei and hepatocyte mitoses (metaphase, anaphase and telophase) were counted in 200 consecutive microscopic fields for each rat. In every 10th field (i.e. 20 fields per rat)

[1] H. REMMER and H. J. MERKER, Klin. Wschr. *41*, 276 (1963).
[2] W. KUNZ, G. SCHAUDE, W. SCHMID and M. SIESS, Naunyn-Schmiedebergs Arch. Pharmak. exp. Path. *254*, 470 (1966).
[3] W. KUNZ, G. SCHAUDE, W. SCHMID and M. SIESS, Proc. Europ. Soc. Drug Tox. *7*, 113 (1966).
[4] Ch. PREISS, G. SCHAUDE and M. SIESS, Naunyn-Schmiedebergs Arch. Pharmak. exp. Path. *254*, 489 (1966).
[5] A. H. C. CONNEY and A. G. GILMAN, J. biol. Chem. *238*, 3682 (1963).
[6] P. B. HERDSON, M. S. GARVIN and R. B. JENNINGS, Lab. Invest. *13*, 1032 (1964).
[7] P. L. BURGER and P. B. HERDSON, Am. J. Path. *48*, 793 (1966).
[8] R. SCHULTE-HERMANN, R. THOM, I. SCHLICHT and W. KORANSKY, Naunyn-Schmiedebergs Arch. Pharmak. exp. Path. *261*, 42 (1968).
[9] K. PAULINI and G. BENEKE, 54. Verh. dt. Ges. Path., Vortrag 82 (1970).
[10] K. PAULINI, G. BENEKE and R. KULKA, Beitr. Path. *141*, 327 (1970).
[11] G. M. HIGGINS and R. M. ANDERSON, Arch. Path. *12*, 186 (1931).

Table I. ^{3}H-thymidine index of rat hepatocyte nuclei after partial hepatectomy and/or phenobarbital pre-treatment

Time after hepatectomy (h)	^{3}H-thymidine index ± S.D. (%)			
	Controls (no treatment) ($n = 2$)	Phenobarbital ($n = 2$)	Partial hepatectomy alone ($n = 4$)	Phenobarbital + partial hepatectomy ($n = 4$)
16	0.042 ± 0.059	2.059 ± 2.718	0.268 ± 0.344	12.365[a] ± 7.572
24	0.254 ± 0.308	1.631 ± 2.032	19.615 ± 9.274	30.291 ± 15.466
39	0.144 ± 0.108	0.293 ± 0.175	16.884 ± 8.466	22.980 ± 8.282

[a] $p < 0.01$ (vs. hepatectomy alone). Student t-test.