Tab. II. Body weight, adrenal weight and adrenal corticosterone content in *ovariectomized female rats*, killed 1, 2, 4, and 8 months after gonadectomy

		1 month	2 months	4 months	8 months
Body weight (g)	C	206 ± 4.5[a]	221 ± 5.5	226.6 ± 7.1	266.0 ± 9.4
	G	231.8 ± 8.5	268.8 ± 8.7	270.0 ± 12.0	319.0 ± 16.0
Δ C%		+ 13[d]	+ 22[c]	+ 19[d]	+ 20[d]
Adrenal weight (mg)	C	23.1 ± 0.9	17.3 ± 1.0	20.5 ± 0.7	20.3 ± 0.8
	G	19.6 ± 0.73	16.1 ± 0.27	15.4 ± 0.6	16.9 ± 0.4
Δ C%		− 15[d]	− 7 n.s.	− 25[b]	− 17[c]
Adrenal weight (mg)/body weight (g)	C	112.0 ± 3.2	78.0 ± 4.1	90.4 ± 2.4	76.6 ± 2.9
	G	84.0 ± 3.1	60.2 ± 1.7	56.8 ± 1.9	53.4 ± 1.3
Δ C%		− 25[b]	− 23[c]	− 37[b]	− 30[b]
Adrenal corticosterone per whole gland (μg)	C	1.35 ± 0.16	2.20 ± 0.20	2.16 ± 0.26	2.90 ± 0.30
	G	0.72 ± 0.09	0.86 ± 0.12	0.96 ± 0.16	0.82 ± 0.13
Δ C%		− 47[c]	− 61[b]	− 56[c]	− 72[b]
Adrenal corticosterone (μg)/adrenal weight (g)	C	59.5 ± 4.2	129.7 ± 11.4	103.5 ± 10.6	145.0 ± 13
	G	39.4 ± 6.2	52.5 ± 7.3	65.3 ± 7.3	48.0 ± 7.5
Δ C%		− 34[d]	− 59[c]	− 37[d]	− 60[b]
Adrenal corticosterone (μg)/body weight (kg)	C	6.5 ± 0.6	10.0 ± 0.8	9.5 ± 1.1	10.3 ± 1.3
	G	3.1 ± 0.3	3.2 ± 0.6	3.8 ± 0.3	2.6 ± 0.3
Δ C%		− 52[b]	− 68[b]	− 60[b]	− 75[b]

For explanation of symbols and abbreviations, see Table I.

HALBERG found decreased hormone storage in ovariectomized mice[11], this diminution being, however, far smaller than the one observed in Wistar rats of the present experiment.

According to the results obtained, there is some evidence for a dissociation between the weight-modifying and corticosterone-content-decreasing factors in adrenals of gonadectomized rats. Contrary to the results observed in chronic experiments under the influence of other different factors[7,12], gonadectomy modifies the corticosterone content to a much higher extent than the weight of the gland.

The authors' attention was drawn to the high corticosterone content of the adrenal in control animals. To outrule the possibility of an increased output due to stress previous to death, an additional experiment was performed, in which the effect of Nembutal *versus* decapitation was compared. Results obtained when Nembutal was used were significantly lower ($0.02 > P > 0.01$).

With the analytical method used, only corticosterone and cortisol were determined, the latter steroid giving readings 3 times lower than corticosterone[8]. The results obtained show, therefore, a clear decrease in corticosterone content, but do not rule out the possibility of the formation or increased production of other corticoids.

Even an augmented secretion of cortisol, at the expense of corticosterone, would give lower readings in the fluorometer, which this method would assign to a reduction in total corticoids. Further experiments, employing different analytical techniques, would be necessary and are being carried out to obtain better understanding of this aspect of the problem.

Zusammenfassung. Ein bedeutender Rückgang des Corticosterongehaltes in den Nebennieren wurde bei weiblichen und männlichen Wistar-Ratten nach Kastration beobachtet. Die Verminderung ist aber besonders bei den männlichen Kastraten überraschend, da sich bei diesen nach der Gonadektomie das Drüsengewicht nicht ändert. Bei den Weibchen hingegen ist die Hormongehaltverminderung bedeutend stärker als der entsprechende Rückgang des Drüsengewichts. Nach diesen Resultaten dürfte eine Dissoziation zwischen Gewichts- und Corticosterongehalt-vermindernden Faktoren bei kastrierten Ratten angenommen werden.

A. A. NICOLA, C. P. LANTOS, and J. H. TRAMEZZANI

Instituto de Biología y Medicina Experimental, Laboratorio de Neurobiología, Buenos Aires (Argentine), June 12, 1962.

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The Comparative Enhancement of the Depressant Action of Alcohol by Eight Representative Ataractic and Analgesic Drugs[1]

The continued extensive use of tranquilizers emphasize the importance of a possible synergistic action of these drugs with alcoholic beverages. The enhancement of the effects of centrally depressant drugs including alcohol by tranquilizers has been reported[2–6]. In contrast, these drugs have been used successfully in the treatment of alcoholism[7,8]. The evaluation of a synergistic action in humans is difficult and time consuming. A rapid pharma-

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cologic procedure for studying the potentiating action of tranquilizers on alcohol is described.

Experimental. Eight drugs were tested for possible synergistic action with ethanol. These were phenaglycodol meprobamate, hydroxyzine, chlorpromazine, reserpine, *d*-propoxyphene, codeine and morphine. All of the test drugs were administered by stomach tube as a homogenate in 2% gelatin. The ethanol was diluted with saline and injected intraperitoneally. The volume of each dose administered was 0.5 ml per 20 g of mouse. The ethanol and the drugs were given as nearly simultaneously as possible, with the exception of reserpine which was administered 1 h before the alcohol. In preliminary tests, maximal observable symptoms appeared within 30 min after the administration of each of the test drugs except reserpine. After reserpine maximal symptoms appeared in slightly over 1 h.

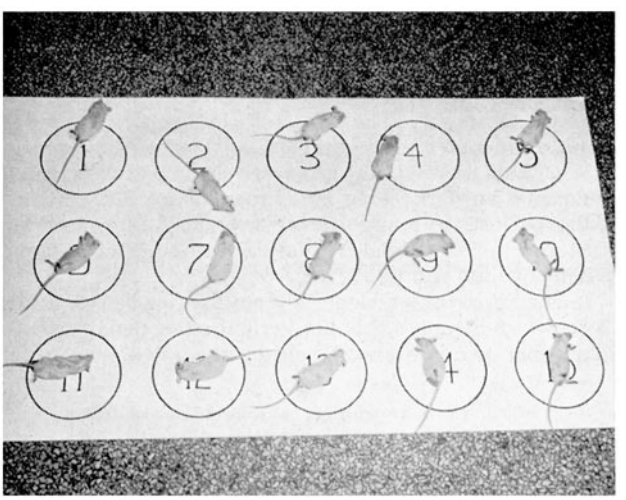
Many tranquilizers will potentiate barbiturates. A typical procedure employs 'sleeping time' induced by hexobarbital with and without tranquilizers[9]. The end-point in such a test is reproducible in that a return of righting reflex is considered to be the end of the sleeping period. An animal so arousing does not usually relapse. However, with alcohol no easily measurable end-point is present. Awakening from ethanol-narcosis is a gradual process. We have observed that mice will roll over or right themselves and then relapse. However, when they can move a short distance, they seldom return to a state of narcosis or sleep.

After the alcohol was injected and the mice were comatose, they were placed in the center of a circle with a six inch diameter (Figure). A return to 'mobility' was recorded as the number of minutes required, after receiving the ethanol, for the mouse to move beyond the border of the circle. Separate control animals receiving only alcohol, were used for each test drug.

Comparison of prolongation of 'Immobility Time' in mice. All animals received 5 mg/kg of ethanol i.p. Drugs were administered *per os* immediately prior to alcohol except reserpine which was given 1 h before alcohol

Drug	Dose mg/kg	Time-min Loss of mobility	*P* Value (vs control)
Phenaglycodol	00.0	92.6	—
	40.0	150.2	<0.001
	20.0	122.3	<0.01
	10.0	110.7	<0.01
	5.0	85.1	non significant
Meprobamate	00.0	86.6	—
	55.0	145.3	<0.001
	27.5	113.1	<0.001
	13.7	103.0	<0.01
	6.8	96.6	non significant
	3.4	95.4	non significant
Hydroxyzine	00.0	91.3	—
	96.0	135.9	<0.001
	48.0	115.9	<0.001
	24.0	102.0	<0.05
	12.0	95.7	non significant
Chlorpromazine	0.0	89.9	—
	6.0	301.8	<0.001
	3.0	167.9	<0.001
	1.5	121.7	<0.01
	0.75	91.1	non significant
Reserpine	0.0	89.5	—
	2.0	148.9	<0.001
	1.0	128.9	<0.001
	0.5	112.7	<0.001
	0.25	102.7	<0.001
	0.125	99.6	<0.01
	0.065	94.3	non significant
Dextro-Propoxyphene HCl	0.0	91.4	—
	200.0[a]	92.1	non significant
	100.0	89.5	non significant
	50.0	90.6	non significant
	25.0	87.7	non significant
	12.5	90.6	non significant
Codeine HCl	0.0	92.0	—
	300.0	89.6	non significant
	200.0	92.4	non significant
	100.0	90.8	non significant
	50.0	92.9	non significant
	25.0	90.7	non significant
	12.5	89.3	non significant
Morphine SO_4	0.0	92.0	—
	200.0	154.4	<0.001
	100.0	121.3	<0.001
	50.0	103.8	non significant
	25.0	99.3	non significant
	12.5	94.2	non significant

[a] The highest dose of *d*-propoxyphene (200 mg/kg) plus ethanol caused deaths of eight of ten animals. Immobility time of survivors not lengthened.



Measurement of 'Immobility Time' after alcohol-narcosis.

Results and Discussion. The Table compares the potentiating properties of the drugs. The minimal potentiating dosages for the tranquilizers were: reserpine 0.125 mg/kg, chlorpromazine 1.5 mg/kg, phenaglycodol 10 mg/kg, meprobamate 13.7 mg/kg, and hydroxyzine 24 mg/kg. Three analgesic drugs were used, morphine, codeine, and *d*-propoxyphene. Only morphine significantly potentiated the alcohol by our measurement and this was in a dosage of 100 mg/kg. Neither of the other two analgesics potentiated ethanol-narcosis. Such dissimilarities of action of morphine and codeine have been recently reported. Weiss and Rossi[10] have reported that a trifluorinated phenothiazine selectively potentiated the acute toxicity of morphine but not of codeine.

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The described procedure is simple, inexpensive and reproducible. It can be used to explore not only the duration of action of ethanol but also the modification of activity of ethanol by other drugs. Our data indicate that the order of potentiating properties of the drugs used were reserpine >, chlorpromazine >, phenaglycodol >, meprobamate >, hydroxyzine >, morphine >, *d*-propoxyphene and codeine. The latter two drugs failed to potentiate ethanol-narcosis.

Studies of the possible potentiating action of tranquilizers and other drugs on alcohol depression is becoming increasingly important because of the increase in therapeutic usage of tranquilizers and continued social usage of alcohol.

Zusammenfassung. Eine Methode zur Messung der Potenzierung von Tranquilizern und Analgetika auf Äthanoldepression wird beschrieben. Unbeweglichkeit von Mäusen wird als Kriterium der Depression genommen. Die fünf Tranquilizer, die gebraucht wurden, haben Äthanol in verschiedenen Graden potenziert. Von den drei analgetischen Drogen hat Morphin, nicht aber *d*-Propoxyphen und Codein, Äthanolnarkose potenziert.

R. B. FORNEY, H. R. HULPIEU, and F. W. HUGHES

Department of Pharmacology, Indiana University School of Medicine, Indianapolis (U.S.A.), July 2, 1962.

PRO EXPERIMENTIS

Zunahme der tödlichen Dosis von g-Strophanthin beim Meerschweinchen in Abhängigkeit von der infundierten Flüssigkeitsmenge

Bei Meerschweinchen in Urethannarkose wurde die tödliche Dosis von g-Strophanthin durch Dauerinfusion mit Geschwindigkeiten von 10 und 1,5 µg/kg/min bestimmt. Dabei wurde die Konzentration der Lösungen und dementsprechend die infundierten ml/min so verändert, dass die letale Menge bei beiden Geschwindigkeiten einmal in 2 ml, zum anderen in rund 15 ml/Tier enthalten war. In der Tabelle sind die geometrischen Mittelwerte aus Versuchen an je 6 Tieren zusammengefasst. Die mittlere tödliche Dosis war unabhängig von der Infusionsdauer, stieg aber in Abhängigkeit von der infundierten Flüssigkeitsmenge um rund 20% an.

In der Literatur ist wiederholt ein Anstieg der tödlichen Dosis von g-Strophanthin bei Verlängerung der Infusions*dauer* über 30 min hinaus beschrieben worden (FROMHERZ und BÄCHTHOLD[1]; HOFFMANN und LENDLE[2]; KRAUPP, OBENAUS, PILLAT und STUMPF[3]). Es ist wahrscheinlich, wenn auch nicht mehr im einzelnen nachprüfbar, dass bei einer Versuchsdauer von mehr als 2 h grössere Flüssigkeitsmengen gegeben wurden und der Anstieg des Titers hierauf und nicht auf eine Elimination von g-Strophanthin zurückzuführen ist. Da Meerschweinchen in Urethannarkose kaum Harn absondern, kommt eine Ausscheidung durch die Nieren nicht in Frage. Wahrscheinlich wird das g-Strophanthin zusammen mit der infundierten Flüssigkeit in der Peripherie abgelagert.

Die praktische Konsequenz aus diesen Ergebnissen ist offensichtlich. Auf eine theoretische Folgerung soll aber noch hingewiesen werden: Wenn sich im akuten Versuch nicht einmal die Elimination des kurz wirkenden g-Strophanthins einwandfrei feststellen lässt, so ist das bei kumulierenden Glykosiden erst recht aussichtslos.

Tödliche Dosen von g-Strophanthin bei Dauerinfusion unter verschiedenen Versuchsbedingungen

g-Strophanthin, µg/kg/min	10	1,5	10	1,5
Verbrauchte ml/Tier	2,0	2,0	14,5	>16,0
Infusionsdauer, min	12	131	25	>160[a]
Mittlere tödliche Dosis, µg/kg	196 (185–208)	196 (186–207)	244 (221–269)	>235 (213–259)

[a] 2 Tiere überlebten länger als 200 min.

Summary. The LD_{50} of ouabain in guinea-pigs rose in correlation with the infused volume but not with increasing duration of infusion.

W. SCHAUMANN

Pharmakologisches Laboratorium der Fa. C. F. Boehringer & Söhne GmbH, Mannheim-Waldhof (Deutschland), 3. Juli 1962.

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CONGRESSUS

France

Symposium of the European Biology Section of the International Association of Gerontology

Paris, April 2–4, 1962

The symposium was held at the Department of Physiology of the Faculté de Médecine and attended by 42 research workers actively engaged in basic research on the ageing processes.

The various original contributions presented to this meeting will later be published in full in various journals and in their original language, but it has been felt that a comprehensive English summary of the various papers might be useful both for experimental gerontologists and for biologists interested in the modern trends of research on ageing.

Three main topics were discussed in this meeting: (1) The phenomenon of 'differential ageing' in Man; (2) Biochemistry of ageing; and (3) The action of some external factors on the rate of ageing. The discussion leaders for these three main themes were, respectively, Professor F. BOURLIÈRE (Paris), Professor F. VERZÁR (Basel) and Dr. P. ALEXANDER (London). A final session, devoted to various specific problems was chaired by Dr. T. GEIL (Kjobenhavn).