terial was not purified, but the activated stock mix was dissolved in corn oil and given by stomach tube.

It is emphasized again that the dose of each preparation was 75 international antirachitic units per g of body weight. There was no standardization of toxic factors, if such exist.

The duration of life in each group is shown graphically in Fig. 1, each unit space representing one rat and each fall, therefore, represents the death of one animal.

In Group 1, the first rat was found dead on the 11th day, and the 8th on the 26th day; the 9th rat survived to the 67th day. This last survivor was a male, but ordinarily no distinction could be made between the two sexes in survival time. The average period of survival was 29.5 days and 15.4 days respectively.

In Group 2, the first rat, (m), died on the 23rd day, while the last (f) died on the 75th day. The average survival period for males was 43.3 days, for the females, 42.3 days.

In Group 3, the first rat (f) died on the 43rd day, the 10th (f) on the 94th day, and the 11th (m) on the 114th day. The mean survival time was 68.4 days for males, 71 for females.

Despite the small numbers of animals in each group it appears that the differences in toxic responses to the different preparations may be specific. Since the antirachitic dose of each preparation was the same, it must be concluded that the fatal outcome of toxication was conditioned, at least, by some other factor not expressed by antirachitic units. Post mortem examination did not reveal any differences of significance in the type of lesions.

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Effects of Various Chemical Agents on Survival of Primative Respiratory Mechanism.

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That young animals are much less susceptible to anoxia than are adults has been well established.[1-5] Selle and Witten[4] have shown that the respiratory center of rats, rabbits, cats and dogs is itself much more tenacious and viable in the young than in the adult, and that until approximately 6 weeks of age the survival of the respiratory mechanism of the rat is inversely proportional to age. Following decapitation or ligation of the cerebral vessels, the isolated ischemic head of a full grown rat gasps 5 to 8 times over a period of 10 or 20 sec and thereafter remains motionless; in a week old animal the phenomenon continues for 30 min or more.

Unlike adults, rats under 6 weeks of age display 2 periods of respiratory movements: an initial series which consists of 6 to 12 gasps and lasts 20 to 30 sec, and a second series which begins 30 to 50 sec after cessation of the initial or first series and lasts for a variable time depending upon the age. The total number of gasps in both series, as well as the total duration of gasping, is greater the younger the animal. The second series, which is influenced most by age, lasts 30 to 40 min in new-born animals. As age increases, the number of gasps, as well as duration of gasping, diminishes uniformly. Similar observations have been made on

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4 Selle, W. A., and Witten, G. A., PROC. SOC. EXP. BIOL. AND MED., 1941, **47**, 495.

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ischemic heads of rabbits, cats and dogs.

The present study was designed to determine the effectiveness of certain drugs on the activity of this primitive respiratory mechanism. Using a technique previously described[4] for determination of survival of this mechanism, a large number of chemical agents (67) varying widely in composition and action, were injected subcutaneously or intraperitoneally into 12 - 15-day-old rats (weight 18-26 g). Following an interval ranging from 5 min to several hours, or even days, depending upon the rapidity of action of the test material, the head was quickly isolated. The gasps resulting were mechanically recorded. In a few experiments the animals were given anesthetic gases, rather than hypodermic injections, prior to decapitation.

Control animals consisted of an equal number of 12 - 15-day-old litter mates weighing 18-25 g. Such animals show a uniform respiratory pattern of 23 to 30 gasps following onset of anoxia, there being a relatively constant number of gasps in the first series (8) and a variable number in the second series (15-22). The survival time is 3-6 min and is influenced, as is the number of gasps of the second series, by litter characteristics and by the nutritive condition and degree of hydration of the animals. Untreated litter mates subjected to identical conditions yield remarkably uniform results. In the present series the variation in survival time of the controls was about 8%, the variation in the number of gasps was 4.8%. The results for the test animals were compared with those of the litter mate controls which were given a similar volume of the vehicle (usually .9% NaCl) used in the experimental animals. Deviations from control values were expressed in per cent.

Most of the chemical agents tested had little or no effect on the nature or character of the gasping pattern or on the total duration of gasping unless given in toxic amounts, in which case the survival period was greatly decreased. In a number of instances, however, definite changes in the character and number of gasps, as well as the total duration of gasping, were observed with non-toxic doses. Table I gives the results for some of the more effective drugs tried, together with the dosage used and the time thereafter at which the effect of the drug was noted.

Outstanding among the agents which reduced the survival time and the number of gasps are iodoacetic acid, thyroxin, dinitrophenol, ether, chloroform and hypnotics of the barbituric acid series. Agents which have been found to increase the total number of gasps and the duration of gasping are morphine, alcohol, chloralose, urethane and cyclopropane. With exception of morphine, the latter increased the survival time by 150 to 280%, and the number of gasps of the second series by 100 to 280%. Morphine brought about increases of about 50%. The character of gasps in the second series was markedly altered by these drugs. In general,

TABLE I.
Influence of Various Chemical Agents on Survival of the Isolated Heads of 12-15-day-old Rats.

Chemical	Dose	Interval after drug given	No. of Animals	Respiratory activity based on avg control values: Total No. gasps %	Survival time %
1. Iodoacetic Acid	.05 cc 1%	8 min.	10	decreased 82	decreased 85
2. Ether	5% in air	5 "	11	" 77	" 80
3. Chloroform	2% " "	5 "	8	" 75	" 85
4. Nembutal	.1 cc 1%	8 "	16	" 64	" 65
5. Dinitrophenol	.3 cc 1%	30 "	17	" 58	" 68
6. Thyroxin	.05 mg daily	8 days	10	" 20	" 52
7. Morphine	2 mg	1 hr	12	increased 54	increased 49
8. Cyclopropane	25% in air	5 min	13	" 170	" 78
9. Alcohol	.5 cc 20%	15 "	15	" 265	" 156
10. Chloralose	.1 cc 1%	15 "	12	" 270	" 280
11. Urethane	.4 cc 4%	15 "	13	" 280	" 250

the strength or amplitude of the mandibular movements was somewhat reduced in the early phase of the second series. The duration of individual gasps was always shorter the greater the frequency of gasping.

Although the total expenditure of energy has not been accurately determined, it is apparent that morphine, alcohol, urethane, chloralose and cyclopropane definitely increase the over-all energy liberation. The mechanism involved in this additional energy liberation is being studied.

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Ejaculation Induced by a Uterine Drug (Gravitol)

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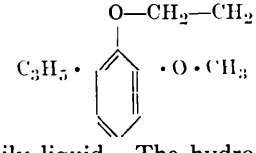
Gravitol is the di-ethyl-amino-ethyl-ether of 2-methoxy-6-allyl-phenol. The base itself



is a thin oily liquid. The hydrochloride is a crystalline water-soluble substance. For the purposes of this investigation the 1% aqueous solution of the hydrochloride was used. Gravitol, also on the market with the trade names Clavitol and Uterol, has been introduced as a uterine drug.[1] Significant stimulating as well as depressing actions upon uterus, intestine, blood vessels and blood pressure were previously described by Barkan and his associates.[2–6] Pharmacological observations were also reported by Anan[7] and Okazaki.[8] A discussion on the drug's action upon the heart went on between van Dongen and Bijlsma[9–11] on the one hand and de Boer[12,13] on the other. Regarding the action upon the heart Jackson[14] published extremely interesting observations. As far as the general toxicity is concerned[4] there is a definite combination and alternation of both central stimulation culminating in convulsions, and depression with motor paralysis. Following preliminary observations made in collaboration with E. Käer, it was found that among the signs of stimulation the most consistent action is the ejaculation induced by the drug in male guinea pigs.†

Procedure. Mature male guinea pigs varying in weight between about 500 and 900 g were kept on a mixed diet. After some days of acclimatisation they were used for the experiments. Subcutaneous injections with 1% Gravitol solution were made in 7 different doses, from 10 to 50 mg per

* Partially aided by The Rockefeller Foundation.

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† A preliminary report has been presented before The American Society for Pharmacology and Experimental Therapeutics, Boston Meeting, April, 1942.