death occurs. If this value of 10 mm Hg for oxygen is subtracted from 50 mm Hg, the lowest barometric pressure at which gasping was found to occur in an atmosphere of pure oxygen, 40 mm Hg remain for the partial pressures of carbon dioxide and water vapor. It is evident that these pressures must fall considerably below the values given by Armstrong. The fall in the partial pressure of carbon dioxide is due, as is well known, to the hyperventilation occurring during anoxia and the fall in water vapor tension is probably the result of two factors: (a) lowering of body temperature as a result of anoxia[5] and (b) the lack of equilibrium between alveolar air and blood as a result of the increased ventilation.[2]

Summary. Two groups of male rats were subjected to a progressive reduction in barometric pressure while in an atmosphere of pure oxygen in order to discover the pressure at which respiratory failure occurred. The first group gave an average value of 65 mm Hg with variations between 60 and 75 mm Hg, and the second group, allowed to hyperventilate for an additional 20 minutes, gave an average value of 60 mm Hg with variations between 50 and 70 mm Hg. The difference between the two groups shows that the additional hyperventilation had a slight effect on reducing the atmospheric pressure at which respiratory failure occurred in this experiment. These results indicate that the partial pressures of carbon dioxide and water vapor fall lower than previously assumed and therefore life is possible at a higher altitude in the presence of pure oxygen than heretofore believed.

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Effects of Yeast Extracts and Phenylmercuric Nitrate on Yeast Respiration and Growth.

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In earlier papers it has been pointed out that yeast extracts having the property of increasing respiration are able to offset the toxicity of phenylmercuric nitrate and of *n*-butyl-*p*-hydroxybenzoate for molds[1] and to overcome the depressant effects of phenylmercuric nitrate on skin respiration without loss of inhibitory power for *S. aureus* in the concentrations employed.[2] We had also found that, with certain fractions from yeast, ability to stimulate the oxygen uptake of yeast paralleled ability to increase yeast proliferation.[3]

In continuation of our studies on respiration depression as an index of toxicity and on the relation between respiration and growth we have investigated the effects of phenylmercuric nitrate on the growth and respiration of yeast and the ability of yeast extracts to modify those effects.

Respiration experiments were carried out at 37.5°C by the previously described Warburg manometric technic,[4,5] using a suspension containing 1.56 mg (dry weight) of Fleischmann's bakers' yeast in Ringer-phosphate-glucose (0.02% glucose, pH 7.2). Aqueous-alcoholic yeast extracts were pre-

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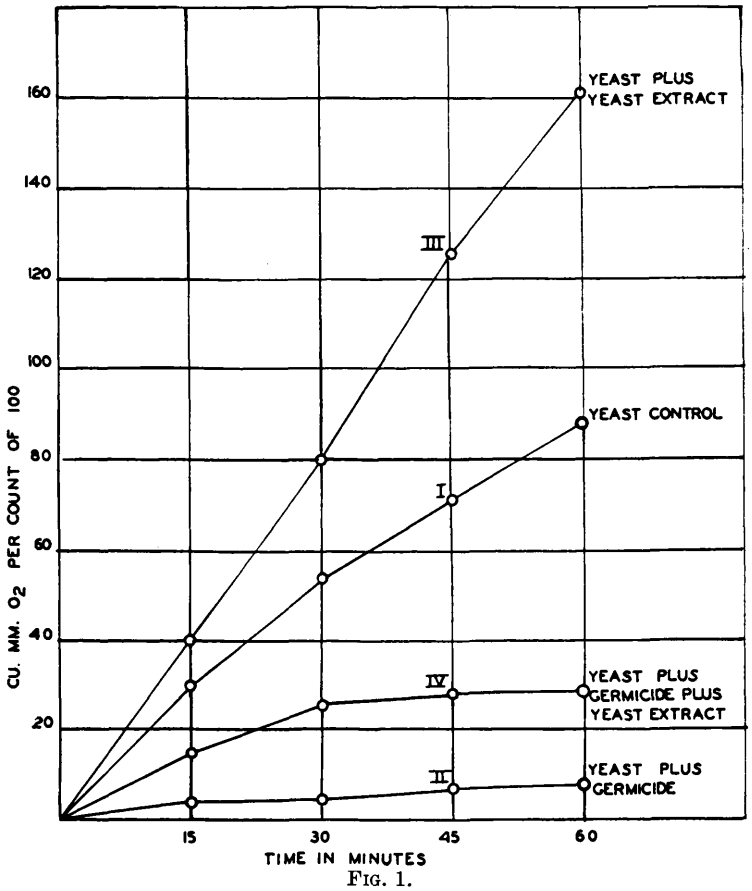

FIG. 1.
Effects of Phenylmercuric Nitrate and Yeast Extract on Yeast Respiration.

pared as described previously[4] from Fleischmann's bakers' yeast and corresponded to crude Fraction A of the earlier work.[4]

Fig. 1 shows the result of a typical experiment on the effects of phenylmercuric nitrate and yeast extract on the respiration of bakers' yeast. Each point represents the average of duplicate determinations which agreed within 5% or better. Curve I represents the normal respiration of the yeast suspension. In Curve II, phenylmercuric nitrate sufficient to give a concentration of 1:100,000 was tipped in from the side arm immediately after the equilibrium period. Very little oxygen uptake was observed and the cells were completely killed at the end of the hour experimental period as determined by methylene blue staining. In Curve III, yeast extract to give a final concentration of 1 mg per cc was tipped in and gave an immediate increase in oxygen consumption amounting to 86% at the end of the hour. All cells were living at this time. Curve IV shows the result of adding a mixture of phenylmercuric nitrate and yeast extract to give the same final concentrations. The respiration, while considerably depressed, continued for 45 minutes, after which further oxygen uptake ceased. Protection was afforded by the extract.

In other sets of experiments, the phenylmercuric nitrate was added at the beginning of the experiment and the extract was tipped in after 30 minutes; or the extract was added at the beginning of the experiment and the germicide after 30 minutes. In the former case, the extract exerted no protective action detectable either by respiratory or methylene blue criteria. In the latter case, the respiration, which was initially increased above the control, fell below it upon addition of the

germicide and steadily decreased in rate until respiration had almost ceased after 45 minutes, although no cells were dead by the methylene blue method. Again, protection is indicated. As a further check on the viability of the cells at the end of the experiment, a loop-full was taken from each respirometer flask and was plated out on sterile Sabouraud's medium and incubated at 30°C over night. Suspensions to which the germicide had been added after prior exposure to the extract gave as good growth as the controls, whereas the suspensions which were first exposed to the phenylmercuric nitrate gave no growth.

During the preparation of the yeast extracts, certain fractions were obtained which were without effect on the oxygen uptake of yeast or which had only an extremely slight effect (20% stimulation after 1 hour). These extracts were ineffective in offsetting the toxic action of the phenylmercuric nitrate as shown by respiration, methylene blue and plating criteria.

The effects of the yeast extract in counteracting the inhibitory action of phenylmercuric nitrate on the growth of yeast was demonstrated as follows. Petri plates were prepared containing solid Sabouraud's medium with different concentrations of phenylmercuric nitrate. In half of the plates the medium also contained 1% of yeast extract. Each plate was inoculated in the center with a loopful of a 72-hour culture of a pure strain of *Saccharomyces cerevisiae* isolated from Fleischmann's bakers' yeast. After 3 days of incubation at room temperature, the area of the yeast growth was measured with a planimeter. Results of a typical experiment are given in Table I.

TABLE I.
Effect of Phenylmercuric Nitrate and Yeast Extract on Growth of *S. cerevisiæ*.

Dilution of phenylmercuric nitrate	Colony area in in²	
	No extract	1% extract
1:10,000	.001	.003
1:20,000	.001	.003
1:30,000	.005	
1:40,000	.004	.008
1:50,000	.004	.008
1:100,000		.020
1:200,000	.008	.033
No phenylmercuric nitrate	.020	.047

Discussion. The results reported demonstrate that an aqueous-alcoholic yeast extract will protect bakers' yeast from the toxic action of phenylmercuric nitrate. This protection may be evaluated by respiration measurements, thus confirming earlier findings with regard to respiration as an index of toxicity.[1,2,6] However, after the respiration rate has fallen to zero, the yeast cells, under the conditions of the experiments, are still viable, as indicated by the methylene blue and plating experiments. Greig and Hoogerheide[6] have pointed out that bacteriostasis may occur without alteration of metabolic rate. We have found that yeast extracts not only increase oxygen uptake but also increase fermentation of yeast suspensions, and that "wound hormone" preparations from yeast, while very active in increasing yeast proliferation, have relatively little effect on yeast respiration.[7] It is well known that certain growth factors for yeast, such an pantothenic acid[8] and biotin,[9] markedly influence the metabolism of yeasts deficient in these substances. On the other hand, we have found the respiration of unstarved bakers' yeast and of the pure strain of *S. cerevisiae* derived therefrom to be relatively little affected by most of the bios components.[5,7,10]

[6] Adams, P. D., *Arch. Dermatol. and Syphilol.*, 1936, **36**, 606; Cook, E. S., *Chem. Products*, 1939, **1**, 65, and 1939, **2**, 89; Amersbach, J. C., Nutini, L. G., and Cook, E. S., *Arch. Dermatol. and Syphilol.*, 1941, **43**, 948; Manifold, M. D., *Proc. Roy. Soc. Med.*, 1940, **33**, 12; Bronfenbrenner, J., Hershey, A. D., and Doubly, J., *J. Bact.*, 1939, **37**, 583; Ely, J. D., *ibid.*, 1939, **38**, 391; Greig, M. E., and Hoogerheide, J. C., *ibid.*, 1941, **41**, 549, 557; Baker, Z., Harrison, R. W., and Miller, B. F., *J. Exp. Med.*, 1941, **73**, 249.

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[9] Burk, D., Winzler, R. J., and du Vigneaud, V., *J. Biol. Chem.*, 1941, **140**, xxi.

[10] Cook, E. S., Walter, E. M., Rack, F. J., Eilert, M. R., and Sawyer, M. A., *Studies Inst. Divi Thomae*, 1941, **3**, 147.

Summary. Phenylmercuric nitrate in a dilution of 1:100,000 is toxic to suspensions of bakers' yeast as shown by respiration measurements, methylene blue staining, and plating. One per cent of an aqueous-alcoholic yeast extract protects yeast to some extent from this germicidal action. Respiration may cease after introduction of yeast extract and phenylmercuric nitrate, but the yeast is still viable as shown by methylene blue staining and plating tests. The importance of respiratory depression in the mechanism of phenylmercuric nitrate toxicity is supported, but caution must be exercised in the use of respiratory depression as a sole criterion of toxicity for yeast. The yeast extract overcomes the growth-depressant effects of phenylmercuric nitrate on yeast.

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Comparison of Effects of Cobra Venom and Morphine on Unanesthetized Cat.

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The effect of morphine on cats and other felines differs radically from that which it exerts on man and other higher animals in two respects. (1) Instead of depressing the brain and neuromuscular activity, it produces excitation and delirium. (2) Instead of causing myosis, morphine dilates the pupil. Since cobra venom is employed clinically as an analgesic[1-4] it was desirable to compare its effects with those of morphine on unanesthetized cats because all previous studies on cats had been made under general anesthesia. In the present paper a comparison was made of (1) behavior and neuromuscular activity and (2) the pupils of unanesthetized cats after administration of the respective drugs.

Twenty cats were employed in this research. Inasmuch as the same animals were used repeatedly after complete recovery from successive injections, over 70 experiments were performed. The cobra venom employed was that made in these laboratories, free from hemotoxic and cytotoxic principles as well as proteins and virtually a solution of cobra neurotoxin. This solution, assayed on mice, was injected intramuscularly in doses ranging from 5 to 20 m. u. per kilo of cat. Morphine was used in the form of sulfate.

Behavior. While morphine induces in cats an excitement which increases with size of the dose and lasts for 18 hours or more, cobra venom has an exactly opposite action. Doses of 5 to 10 m. u. per kilo of cobra venom had little or no effect on cats. Occasionally they effected a mild euphoria causing the cats to roll pleasurably on their backs in the same way in which they react to catnip. Larger doses of cobra venom (10 to 20 m. u.) were sedative. The animals lay quietly and drowsed but roused to a touch. Very large doses (40 m. u. per kilo) of cobra venom were more depressant and caused unsteadiness of gait and tremor. The behavior of cats injected with cobra venom is apparently the reverse of their reaction to morphine, which induced excitement corresponding to size of the dose. The mild primary stimulation supervening an hour after injection of cobra venom was followed by a sedation proportional to size of the dose and lasting over 18 hours.

Eyes. In all experiments on cat's pupils constant illumination was maintained and there was no abrupt exposure to direct light.

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