asymmetry of the molecule. Hyaluronidase specifically reverses the action of hyaluronate on E.S.R. Intravenous injection of hyaluronate in guinea pig and rabbit leads to increased E.S.R. Intravenous injection of hyaluronidase promptly causes the increased rate to become normal.

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Effect of Wheat Germ on Creatinuria in Dermatomyositis and Progressive Muscular Dystrophy.*

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Milhorat, Weber, and Toscani[1] reported a decrease in the creatinuria of 2 patients with dermatomyositis who were given 125 g of fresh whole wheat germ daily. This effect was increased when the wheat germ was incubated *in vitro* with normal human gastric juice.

The present report presents some of the results of investigations carried out in an effort to identify the factor, or factors, in wheat germ having these effects. The subjects were 5 patients with dermatomyositis, and 3 patients with progressive muscular dystrophy. All subjects had extensive muscular wasting, and spontaneously excreted large amounts of creatine. The patients were given a creatine-creatinine-free diet and were maintained in a special metabolism ward where the diet and urinary collections could be rigorously supervised. After adequate periods of control the subjects were given various substances to test any possible effect on the creatinuria. Most of the substances were given daily to 4 or more of the subjects for periods of at least one week and usually for periods of 2 months. Briefly, the observations were as follows: only 3 of the patients with dermatomyositis (subjects A, B, and C), and one with progressive muscular dystrophy (subject D) were able to ingest as much as 125 g wheat germ daily. During the control periods the average daily levels of spontaneous creatinuria of the 3 patients with dermatomyositis were as follows: subject A, 0.450 g (maximum 0.524, minimum 0.405); subject B, 0.240 g (max. 0.275, min. 0.190); and subject C, 0.150 g (max. 0.240, min. 0.105). The average daily outputs of creatine were unchanged during the first 2 weeks of wheat germ administration, but during the third week they decreased to the following levels: subject A, 0.355 g (max. 0.406, min. 0.279); subject B, 0.082 g (max. 0.090, min. 0.078); and subject C, 0.080 g (max. 0.093, min. 0.072). Subject A was given wheat germ for a total period of 7 months. During the last 2 weeks of this period the average daily creatinuria was 0.310 g (max. 0.365, min. 0.256). Essentially similar results were observed in the patient with progressive muscular dystrophy (subject D). The average daily output of creatine of 0.350 g (max. 0.470, min. 0.338) gradually decreased during the third and fourth weeks of wheat germ feeding to levels of around 0.250 g (max. 0.266, min. 0.218). The excretion of creatine continued at these low levels for the next 2 weeks during which wheat germ was given, and for a period of 3 weeks after the administration had been stopped. The wheat germ given in this experiment had been vacuum packed at the mill and was kept in sealed cans until used. In a subsequent experiment wheat germ which had been stored and received in bulk was given to this patient in the same amounts as in the previous study. No effect on the creatine output was observed during

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1 Milhorat, A. T., Weber, F. C., and Toscani, V., PROC. SOC. EXP. BIOL. AND MED., 1940, **43**, 470.

the second period of feeding with this latter sample.

In all experiments the wheat germ was given in about 600 cc tomato juice daily, but neither 700 cc tomato juice nor 500 mg ascorbic acid daily affected the creatinuria. In 2 series of experiments in which wheat germ was incubated *in vitro* with normal human gastric juice at 37°C for 2 hours, 30 g of wheat germ daily had about the same effect as 125 g of the untreated material. Wheat germ incubated with brewers' yeast, extract of whole hog pancreas, or an extract of fresh beef liver had no more effect on the creatinuria than had fresh wheat germ.

Samples of wheat germ obtained from different sources varied considerably in their effects on creatinuria. Prolonged exposure of the wheat germ to air reduced the effects. Wheat germ defatted by continuous extraction with cold ethyl ether had definite effects, but these were less than those of the fresh product. These effects were not increased when the subjects received tocopherol by intramuscular injection. No effect on creatinuria was observed with wheat germ that had been defatted by extraction with ethylene dichloride. Water extracts of ether-defatted wheat germ were ineffective. The administration of large amounts of thiamin chloride, riboflavin, calcium pantothenate, para-amino benzoic acid, pyridoxine hydrochloride, nicotinic acid, nicotinamide, brewers' yeast, brewers' yeast concentrate, vitamin A, vitamin D, cottonseed oil (prime summer yellow grade), liver extract, soy bean phosphatides, bile salts, and hog pancreatin failed to affect the creatinuria. Wheat germ oil obtained by the cold-press method had doubtful effects when given in amounts of as much as 60 cc daily. A concentrate of tocopherols prepared by high vacuum molecular distillation from cold-pressed wheat germ oil was likewise ineffective.

The daily administration of 50 mg alpha-tocopherol by intramuscular injection for periods of as long as 6 months had no effect. The ingestion of yeast, ascorbic acid, pyridoxine, and other vitamin preparations during such periods did not affect the creatinuria. One patient with progressive muscular dystrophy (subject E) was given 20 g of soy bean lecithin daily. Aside from a slight increase there was no essential change in the urinary output of creatine during the first 10 days of administration. However, after the 15th day of lecithin ingestion the creatinuria dropped slowly to an average daily level of 0.150 g (max. 0.190, min. 0.110) from the previous control level of 0.270 g (max. 0.380, min. 0.240). When the administration of lecithin was discontinued the creatine output remained at the low level for about 6 days and then slowly rose to its previous level.

Summary. The administration of large amounts of fresh wheat germ which was vacuum packed and sealed reduced the creatinuria in 3 patients with dermatomyositis. Other samples of wheat germ, stored in bulk, were ineffective. In another subject with progressive muscular dystrophy the creatinuria was diminished in one experiment and unaffected during a second period of wheat germ feeding. Wheat germ incubated *in vitro* with normal human gastric juice had more effect on creatinuria than had the fresh product. Prolonged extraction with ethyl ether reduced but did not remove completely the factor or factors in wheat germ that lower the output of creatine. On the other hand, wheat germ defatted by extraction with ethylene dichloride was entirely without effect on the creatinuria. Of various vitamins and other substances investigated only soy bean lecithin reduced the creatinuria.

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(b) Soy bean lecithin and phosphatides (American Lecithin Company, Inc., Elmhurst, N.Y.).

(c) Wheat germ oil obtained by cold-press method (International Vitamin Corporation, New York, N.Y.).

(d) Ethylene dichloride-defatted wheat germ (Abbott Laboratories, North Chicago, Ill.).