ducing acid with sucrose. The organism herein described does not. *C. ulcerogenes* was once isolated from ulcers of the skin in a man. It was non-pathogenic for animals. This is apparently the first time an organism with the characteristics given has been isolated from a brain abscess or a case of meningitis. It is of peculiar interest because of the low order of pathogenicity exhibited in the case described and in the laboratory animals, but yet possesses what was apparently the ability to cause an abscess and meningitis in a child.

Summary. An organism resembling *Corynebacterium ulcerogenes* was isolated repeatedly in pure culture from a brain abscess and spinal fluid of a 7-year-old child. The morphological and biochemical characteristics of the organism were determined, and found to be culturally identical to *C. ulcerogenes*. It was found to be resistant to penicillin, *in vitro*, but inhibited in growth by sulfanilamide, sulfamerazine, sulfasuxidine, and sulfaguanidine. Sulfamerazine was the most effective. The organism was non-pathogenic to guinea pigs, white mice, rabbits, and hamsters, irrespective of the route of inoculation.

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Fumaric Acid Salts as Hydrogogue Cathartics.*

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The alkali metal salts of certain organic acids, notably tartaric and citric acids, have been used for many years as cathartics and for certain other therapeutic purposes. Since the beginning of the present war, tartaric acid has become difficult to obtain and the supply of other commonly used organic acids has been somewhat curtailed. Hence, a search for satisfactory substitutes has been instituted and fumaric acid has been suggested as a likely possibility. It is similar in chemical structure to tartaric acid, is available in large amounts at a moderate cost, and is a "physiological" substance in the sense that it occurs naturally in animal tissues.[1]

The present study was undertaken to determine the laxative effects of fumarates and is a part of a larger study designed to determine the general effects of the administration of fumarates, in varying doses, to different species of animals. The only other extensive published data on the laxative effects of fumarates found in the literature are those of Gold and Zahm[2] who compared the laxative potency of fumarates, sodium tartrate, and magnesium acid citrate in constipated human subjects and showed that the laxative efficacies of the fumarates of sodium, calcium, and magnesium are approximately the same and that these 3 also possess approximately the same laxative potency as sodium tartrate and magnesium acid citrate, gram for gram.

Methods. The subjects chosen for this study were either ambulant or bed patients hospitalized for chronic disease at the Wayne County General Hospital. Many of them had hypertrophic or rheumatoid arthritis, heart disease, Parkinson's Disease, or other afflictions which required institutional care. All the patients volunteered for this study. Each patient had chronic constipation with a long history of dependence on some form of laxative. The patients were considered constipated after 3 or more days without a bowel movement.

The 4 preparations studied, magnesium fumarate, calcium fumarate, sodium fumarate, and Rochelle Salts, were administered by dis-

* Aided by a grant from Chas. Pfizer and Company, Inc., Brooklyn, New York.

[1] Annau, E., *et al., Z. f. physiol. Chem.*, 1935, **236**, 1; 1936, **244**, 105.

[2] Gold, H., and Zahm, W., *J. Am. Pharm. Assn.*, 1943, **32**, 173.

TABLE I.
Laxative Effect of Rochelle Salts and Fumarates.

	10 g doses 497 doses in 138 patients					15 g doses 105 doses in 32 patients				
		Satisfactory		Unsatisfactory			Satisfactory		Unsatisfactory	
Salts administered	No. of doses	No. of doses	%	No. of doses	%	No. of doses	No. of doses	%	No. of doses	%
Rochelle Salts	174	94	54	80	46	14	10	71	4	29
Sodium Fumarate	107	55	51	52	48	25	14	56	11	44
Magnesium Fumarate	73	36	49	37	51	39	24	61	15	39
Calcium Fumarate	143	82	57	61	43	26	11	42	15	58

solving the salt in a half glass of water using either 10 g or 15 g doses. Each salt was given to relieve 2 successive periods of constipation. Thus, an opportunity was afforded in the same patient to observe the effect of the same salt at least twice. Each patient received in succession all 4 salts or as many as the period of hospitalization and/or the extent of the constipation would permit. The sequence of administration of the 4 salts was not constant. In those patients who received both the 10 g and the 15 g doses the smaller dose preceded the larger.

A record was kept by the nurse of the date, the salt, the dose, the time the medication was given, the time of the bowel movement, and the type of stool (normal, soft, watery). The results were recorded as excellent, good, poor, or failure. A response was considered *excellent* if one or more loose watery stools resulted within 24 hours after the dose. A response was considered *good* if one or more soft stools resulted within 24 hours. The results were recorded *poor* if a hard stool occurred and a *failure* if no bowel movement followed the medication. Other methods, involving both objective and subjective approaches to evaluation of laxation, have been employed in similar investigations; after careful study, it was decided that the present criteria for estimating the efficacy of the cathartic employed, were best suited to the present experimental conditions.

Of the total of 143 patients studied, 111 patients received doses of 10 g each, 5 patients were given 15 g per dose, and 27 patients first were given doses of 10 g and later doses of 15 g each. The number of doses taken by the different patients varied greatly; some received only one dose while others took as many as 19 doses during a period of 6 months of observation. Seventy-one patients received only one drug, 27 patients received 2 drugs, 14 patients received 3 drugs, and 31 patients received 4 drugs. The average number of single doses per patient was 4.2. There were 497 single 10 g doses given and 105 single 15 g doses, thus making a total of 602.

Results. In Table I are summarized the results of the studies of the laxative effect of Rochelle Salts and the 3 fumarates with both the 10 g and the 15 g dose. For this analysis we have considered that a soft or a liquid stool was a "satisfactory" response. If a hard stool occurred or if no bowel movement followed the medication, the response was considered as "unsatisfactory." It will be observed that the average percentage of satisfactory response following the administration of the fumarates is only slightly less than that of Rochelle Salts, a commonly used hydrogogue cathartic. These data indicate that the laxative effects of the fumarates of sodium, magnesium and calcium are approximately the same. The percentage of satisfactory response is only slightly better with the 15 g dose of fumarates as compared with the 10 g dose of fumarates. From Table I, it appears that Rochelle Salts at the 15 g level are far more effective than any of the other salts or than this salt at the 10 g level. However, the total number of doses (15) seems too small to warrant a final conclusion on this point.

The length of time between the taking of the salt and the first bowel movement varied widely between patients and in the same patient with the same amount of the same medication. The average time elapsing be-

tween taking the fumarates and the first bowel movement was about 6 hours.

The 3 salts, magnesium fumarate, calcium fumarate, and sodium fumarate, are free from toxic effects in the doses which were used.

The data obtained in this study are strikingly similar to those reported by Gold and Zahm, and indicate that the fumarates provide a satisfactory substitute for the tartrates as laxative agents.

Summary. The laxative action of sodium, magnesium, and calcium fumarates has been compared with that of sodium potassium tartrate in 143 chronically constipated patients. The fumarates have been found as satisfactory as Rochelle Salts as a laxative agent.

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A Method for Consistent Induction of Chronic Hyperglycemia with Alloxan.

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The capacity of alloxan for inducing in the experimental animal a state resembling diabetes mellitus[1,2,3] has opened a new and promising approach to the study of the disease. One of the major problems involved in the use of alloxan lies in the inconstant and variable responses of experimental animals to its administration.[1,4,5] Large doses of alloxan frequently cause toxic deaths with hepatic or renal lesions, while smaller doses inconstantly produce chronic hyperglycemia. The experience of Lackey *et al.*[6] is a common one; they observed that 60% of rats injected intraabdominally with 200 mg of alloxan per kg of body weight developed moderate to severe diabetes, while 40% either died during the first 72 hours or failed to become diabetic.

In view of the manifest desirability of standardizing the experimental approach to the study of the chronic hyperglycemic state in rats, means were investigated whereby a high percentage of rats treated with alloxan would develop hyperglycemia, with relatively few deaths and with relatively little tendency to become comatose on ordinary laboratory diets. We have found, in substance, that withdrawal of all food from adult animals for periods of 48 to 60 hours will render them almost uniformly susceptible to the subsequent subcutaneous injection of 175 mg of alloxan per kg of body weight. The chronic hyperglycemia so produced leads to few fatalities in the rat and the tendency toward spontaneous recovery of normal blood sugar levels is greatly reduced as compared with animals made diabetic under other conditions.

The animals used were white rats of the Sprague-Dawley strain which were fed on ordinary pellet ration throughout except where otherwise indicated. The dose of alloxan was 175 mg per kg after correction for the molecule of water in alloxan monohydrate. Alloxan samples from two different commercial sources were used, with no discernible differences in their effects. The final solution used contained 19.9 mg of alloxan per ml and was always made just before use; one ml of this solution for each 100 g of body weight was then administered subcutaneously. In most of the experiments the animals used weighed 200-280 g, and dosages were measured to the

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[2] Brunschwig, A., Allen, J. G., Goldner, M. G., and Gomori, G., *J. A. M. A.*, 1943, **122**, 966.

[3] Bailey, C. C., and Bailey, O. T., *J. A. M. A.*, 1943, **122**, 1185.

[4] Gomori, G., and Goldner, M. G., PROC. SOC. EXP. BIOL. AND MED., 1943, **54**, 287.

[5] Bailey, C. C., Bailey, O. T., and Leech, R. S., *N. Eng. J. Med.*, 1944, **230**, 533.

[6] Lackey, R. W., Brinde, C. A., Gill, A. J., and Harris, L. C., PROC. SOC. EXP. BIOL. AND MED., 1944, **57**, 191.