bacterial sensitivity. The results of the authors quoted are probably incorrect in that they have committed our initial error of studying the Schwartzschild factor during a period of decreasing sensitivity; an error, however, which we corrected by means of our controls.

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Observations on Administration of Chondroitin in Peptic Ulcers.

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The effectiveness of mucin in the treatment of peptic ulcer has usually been ascribed to a local coating effect by which it protects the mucous membrane, its acid combining power, or to an inhibition of peptic digestion. Because we observed beneficial effects from mucin in dogs with liver injury,[1] where the results could hardly be ascribed to a local action, we became interested in its possible systemic effects. Mucin is a glycoprotein, a combination of protein with a carbohydrate radical (the prosthetic group). Chondroitin sulphuric acid, the prosthetic group of chondromucoid, is very similar in composition to the mucoitin that is present in mucin and benefits animals with experimental liver injury as does mucin. Chondroitin and mucin both contain glucuronic acid, which is known to be used by the liver for the detoxification of phenol derivatives and other substances. We felt that a study of a group of patients with peptic ulcer treated with chondroitin might indicate whether any of the action of mucin could be ascribed to a systemic effect produced by the glucuronic acid that it contains. Determinations of the uronic acid content of various batches of commercial mucin by Link's modification of the Lefevre and Tollens method[2] gave results varying from 1.2 to 2.5% glucuronic acid. The theoretical glucuronic acid content of chondroitin is 37.6%; the chondroitin that we have used (at first prepared by us, later made for us by the courtesy of Chappel Bros. Inc.) varied from 95 to 98% pure. We have used 3 to 6 gm. of chondroitin per patient per day in divided

[1] Crandall, L. A., Roberts, G. M., and Gibbs, J. W., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 1082.

[2] Lefevre and Tollens, *J. Am. Chem. Soc.*, 1930, **52**, 775.

doses; this contains an amount of glucuronic acid equivalent to that in the usual daily dose of mucin. Chondroitin is not a gummy material, could hardly be expected to coat the mucous membrane, and was given in the form of the free acid; its action, therefore, cannot be attributed to any local effect.

Twenty-two patients with peptic ulcer have been observed over periods of 2 to 9 months. In 20 cases the ulcer was in the duodenum; one case had an ulcer of a gastro-enterostomy stoma, and one had both lesser curvature and duodenal ulcers. In all but 2 cases the ulcer was verified by X-ray, both of these cases presented the classic ulcer syndrome. The history of ulcer prior to chondroitin therapy varied from 1 to 18 years. All the patients had previously been on alkali treatment, which completely relieved the distress in 4 and gave partial relief in all but 4 during the most recent period of alkalinization.

Treatment was ambulatory in every case, and was carried out in the Dispensary of the Northwestern University Medical School and in the ulcer clinic of Dr. Singer at Cook County Hospital. We wish to express our appreciation to Drs. Snorf and Mahle of Northwestern and to Dr. Singer for their most helpful cooperation. In almost every case the patient was either already on a bland diet or was much restricted in choice of food by financial conditions. The plan we endeavored to follow was to make no change other than the administration of chondroitin, except that when the patient was taking alkaline powders these were gradually eliminated during the first 3 or 4 days of treatment. In most cases the patient was already on a modified diet or had voluntarily resumed a bland diet with reappearance of distress, so that only occasionally was any appreciable modification necessary. Such ambulatory treatment allowed less supervision of the patient than would have been possible had hospitalization been employed, but it was felt that maintaining all other factors as constant as possible permitted more accurate inferences as to the effectiveness of chondroitin.

Of the 22 patients, 10 were relieved. Relief is defined as a practically complete absence of ulcer symptoms during the period of treatment except for recrudescence of distress following major dietary indiscretions. Of the remaining 12 cases, 6 appeared to show some benefit. Six of the 10 cases that were relieved were subjected to withdrawal of chondroitin for a short period during the first two months of therapy and in all of them the typical ulcer distress returned, to disappear again when treatment was resumed. Four of the 10 cases that responded had not been completely relieved

by alkali therapy in the few months preceding chondroitin, although all 10 had shown remissions on alkali at some time during their ulcer history. The average time for disappearance of symptoms in 10 patients was 7 days. In those cases that were rechecked by X-ray, a decrease in spasm was noted. It is worthy of note that 5 of the patients complained of headache, which was usually more frequent and severe during those periods when ulcer distress was present. This headache was not related to previous alkali therapy. In these 5 cases the headaches promptly disappeared when chondroitin was administered, in fact the ulcer distress usually persisted longer than the headache.

It is our impression that the administration of chondroitin produced definite improvement in about 45% of our series of patients, who were in general under unfavorable conditions of diet. The fact that distress disappeared on therapy, reappeared when treatment was discontinued, and disappeared again when chondroitin was resumed is significant. Most of the patients also exhibited a gain in weight and improvement in general condition.

These results are obviously much inferior to those reported following the administration of neutral gastric mucin containing equivalent amounts of glucuronic acid. It appears probable that the systemic action of the prosthetic group of the mucin molecule (mucoitin) accounts for a part of the effectiveness of mucin in the treatment of gastric ulcers, perhaps by supplying building stones for the formation of mucus in the body of the patient. It is highly possible that the administration of large amounts of glucuronic acid, a substance of considerable biologic importance, may be beneficial in a manner not yet clearly understood. There is no evidence that the body finds any difficulty in producing galactosamine or glucosamine in amounts adequate to its needs; if this is correct glucuronic acid is the portion of the chondroitin molecule which might be expected to be physiologically active.

Our results also indicate that the local action of mucin is a factor in promoting the healing of peptic ulcer, but a definite statement on this point is impossible until the rôle of the various amino sugars can be determined.