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# The Role of the Protein Contents of Food on Shay Ulceration in Rats

by

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With 3 figures

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In our former experiments we stated that duodenal souring induced simultaneously with the SHAY operation (1) assured the total intactness of the gastric mucosa (2). In such cases neither ulceration nor erosion develops. According to the examinations of MOLNÁR, SOMOGYI and CSALAY, the SHAY-ulcer manifests itself more readily in animals kept on a tryptophan or methionine-deficient diet than in controls fed under normal conditions (3).

According to these data we raised the question whether in SHAY rats kept on a protein-deficient diet duodenal souring was able to activate the intestinal parahormones and thereby to prevent ulceration, or whether the protective effect fails to take place. In the latter case, the duodenal protective mechanism stopped may be made responsible for the increased inclination of ulcer development in animals kept on a protein-deficient diet.

## Method

Our examinations were carried out in white male rats weighting 120 to 140 g. They were divided into 3 groups one receiving for 1 month a normal, the sceond one a methionine- and the third one a tryptophan-deficient diet (4). The SHAY operation was effected under slight ether anaesthesia after 48 hours of preliminary fasting. The operation consisted of median laparotomy, of clamping off the pylorus, and of pyloric ligation. Simultaneously with the operation the animals were given and intraduodenal injection of 0,9% NaCl and 0,4% HCl solution, respectively, at amounts of 2 ml/100 g body weight (5). 14 hours after the operation the animals were sacrificed, and the gastric contents were collected for chemical analysis. The amount of secretion was measured in a graduated test tube. Following the pH determination the gastric content was titrated with 0,1 n NaOH solution in the presence of phenolphthaleine indicator and the total acidity was expressed in clinical units — 1 ml 0,1 n NaOH litre of gastric fluid. From the changes of the gastric mucosa the index of ulceration was calculated as shown in the following scheme:

| | |
|---|---|
| lesion smaller than 1 mm | 1 point |
| lesion between 1 mm and 2 mms | 2 points |
| lesion between 2 mms and 5 mms | 5 points |
| lesion between 5 mms and 10 mms | 10 points |
| lesion and perforation, resp., exceeding 10 mms | 20 points |

The points showing the changes in each group were added and divided with the number of animals in the group. Thus the value of the index of ulceration was obtained.

## Results

18 animals kept on normal, 18 given a methionine-deficient and 18 animals fed a tryptophan-deficient diet belonged to experimental group 1, 2 and 3, respectively. Corresponding to the state of deficiency, the weight-curve of the latter animals showed a decreasing tendency (Fig. 1).

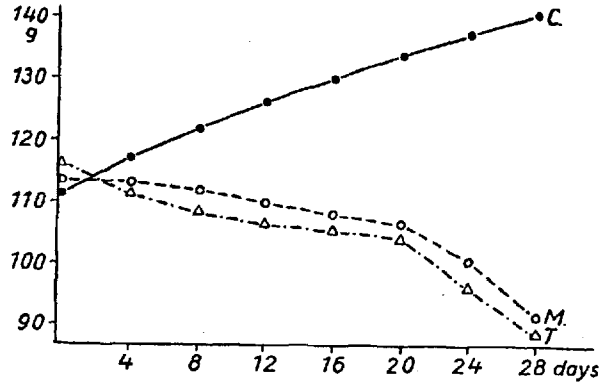


Fig. 1. Weight curve of rats. (C) controls, (M) given a methionine-deficient, and (T) a tryptophan-deficient diet.

After 1 month of the above regime the animals belonging to all 3 groups were subjected to the SHAY operation. They were fasted for 48 hours previously but given drink-water ad libitum. Simultaneously with the operation the animals were injected intraduodenally. 9 animals of each group received a 0,9% NaCl solution and the other 9 a 0,4% HCl solution, at an amount of 2 ml/100 g body weight. Dilution of the hydrochloric acid from a concentrated solution was affected using physiologic saline. The gastric mucosa of the animals sacrificed 14 hours after the operation showed the following results (Fig. 2).

Severe lesions were stated in the mucous membrane of the control animals treated with physiological saline. The index of ulceration was 17. The mucous membrane was completely intact in controls treated with HCl. In 2 cases a definite vascularization was observed but also that in the glandular portion of the stomach and not in the rumen, although SHAY's operation causes changes primarily in the rumen.

The animals given a methionine-deficient diet and physiologic saline at operation showed extremely severe changes in their gastric mucosa. The index of ulceration was 47. There was not even the slightest intact area on the gastric mucosa and not only the rumen but also the secretion portion showed significant lesion. HCl treatment, though markedly moderating the changes, was unable to prevent them completely. The index of ulceration was 21.

In animals fed a tryptophan-deficient diet the conditions were similar to those found in the former group. The animals treated with physiological saline suffered markedly more severe changes after the SHAY operation than the controls. Index of ulceration: 42. Intraduodenal HCl injection only decreased also in this case the number and graveness of ulcerations but was unable to provide complete protection for the gastric mucosa. The index of ulceration was 19.

The result of examinations carried out in the gastric fluid are summarized in Fig. 3.

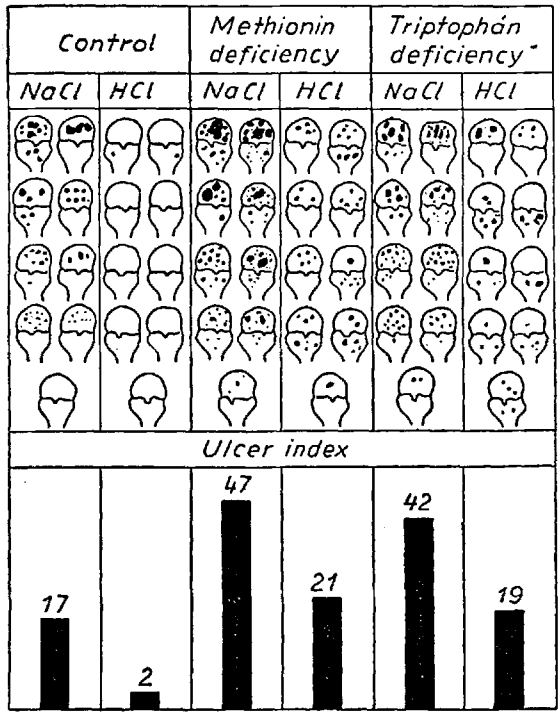


Fig. 2. Schematic appearance of the gastric mucosa and index of ulceration in Shay rats. Controls, animals given a methionine- and tryptophan-deficient diet, respectively, and intraduodenally injected 2 ml/100 g body weight of 0,9% NaCl and 0,4% HCl solution, respectively.

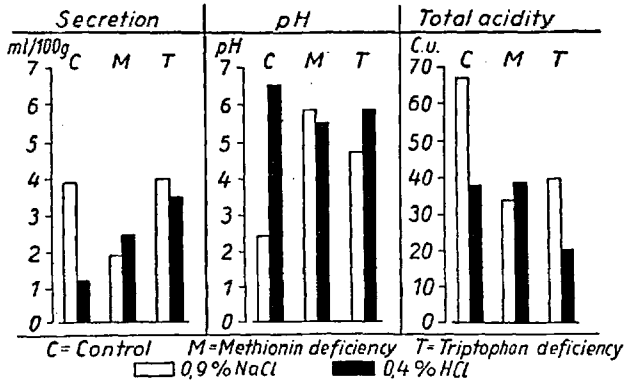


Fig. 3. Values of the amount of gastric secretion, pH of gastric content and total acidity in Shay rats. Controls, animals given a methionine- and tryptophan-deficient diet, respectively and, simultaneously with the pyloric igation, intraduodenally injected 2 ml/100 g body weight of 0,9% NaCl and 0,4% HCl solution, respectively.

In contrast to physiological saline, in the control animals HCl treatment decreased the amount of secretion, caused a shift toward the alkaline direction in the pH value and, correspondigly, the total acidity showed also a decrease.

In animals fed a methionine-deficient diet HCl treatment had a rather slight influence, as compared to the physiologic saline solution. It is remarkable that the amount of secretion, the pH, and total acidity value did not express that significant difference which did exist between the index of ulceration of animals both treated with HCl but differently, belonging to the control or the methionine-deficient group; moreover, the changes are of a reverse direction. Neither the ulcer-index moderating effect of HCl treatment is reflected in the results of the chemical analysises.

The group fed a tryptophan-deficient and the other a normal diet but likewise treated with NaCl failed to show the significant difference in secretion amount, in pH and in total acidity value which had been characteristic for the index of ulceration of the two other groups. HCl treatment, on the other hand, significantly decreased the amount of secretion in this group, and also the change in pH, and in total acidity corresponds to the anti-ulcerogen effect.

## Discussion

The role of diet, as an aetiological factor in the development of ulcera has not yet been elucidated in a satisfactory manner. SINGER (6) described hyperplastic ulceration in the fore-stomach of rats kept on a diet of bread and sawdust, that is, in a calory- and protein-deficient state. FIBIGER (7) gave his rats only white bread. He observed ulceration in the stomach of his animals and considered the phenomenon to be due to the action of parasites. According to the opinion of PAPPENHEIM and LARIMORE (8) the lesions in the experiments were caused by the deficient diet but these authors could give neither explanation of the nature of the mechanism nor of the deficiency. They assumed the animals to swallow hairs on the deficient diet and that ulceration developed due to the irritative effect of these hairs. WEECH and PAIGE (9) observed ulceration in one third of his dogs given a protein-poor diet. Also LIKÉS and FREEMAN (10) supported the results of these examinations and contributed with the statement that reduction of the fat contents of the diet further increased the ulcerogenous effect of protein deficiency. CHEN (11) prevented the ulcer demonstrating itself on a protein-deficient diet using the mixture of agar-agar and glycose, and this way he verified the aetiological role of inefficient diet. HOELZEL and DA COSTA (12) found ulcera in one third of their rats fed a protein-deficient diet. The lesions extended both to the fore-stomach and to the glandular portion of the stomach. ORTEN (13) likewise observed ulceration in young and adult rats given a protein-deficient diet. SHARPLES (14) explained his similar observation by assuming that the lack of different amino acids and vitamins alike may cause ulceration. He induced hyperplasia and ulceration by a diet poor of cystine, riboflavine, pyridoxine and choline, respectively. He demonstrated that, while giving the same amount of acid and pepsin to the animals, the lesions were more extended in those kept on the diet. Since he could prevent the development of ulcera also by the administration of cystine, he assumed that the lack of sulphurous amino acids would have been most responsible for the development of lesions. WEISS and ARON (15) studied the amino acids with respect to the protective effect of histidine and tryptophan on the MANN-ulcer (16). They considered histidine to be more important whereas FÜRTH and SCHOLL (17) stressed the importance of tryptophan. According to BERG (18), through alteration

of the vessels in the mucous membrane, fasting results in a reduction of the mucosal protective effect. Also after SHAY's operation the seriousness of ulceration depends on the time of preliminary fasting, longer time being more favourable. SÓS, KEMÉNY, VÉGHELYI, NAGY, ERDÉLYI and TÓTH (19) gave silica powder to rats kept on a methionine-deficient diet and observed the reactivity of the mucosa to definitely increase. The gastric mucosa became hyperplastic. CSALAY, HORVÁTH and SÓS (20) demonstrated by their experiments that animals fed a methionine-deficient diet were resistant to histamine ulcera, but this resistance against histamine was a specific phenomenon. By the way, histamine has an ulcerogenous effect only under special conditions. MOLNÁR, SOMOGYI and CSALAY (3) observed the methionine-deficient diet to have a SHAY-ulcer aggravating effect. Their experiments were carried out in animals fasted for 24 hours and not given even water, and this explains the low index of ulceration in the control animals. Most recently HAHN, BAUGH and FOSTER (21) sanguinated animals and kept them on a low-protein diet. Under such conditions perforating ulcers developed in a great number.

In agreement with the above facts also our own examinations unanimously supported the significant role of protein deficiency in ulceration. Our former experiments allow to suppose that following duodenal souring a functional vasodilation manifests itself in the splanchnic region (22). The phenomenon is of hormonal nature since it was demonstrable also in couples of dogs with a crossed circulation (23). Duodenal souring improves this way the blood supply of the gastric mucosa and because of the existing functional vasodilation vascular spasms disturbing the oxygen supply cannot come into being. This explains why the SHAY-ulcer does not develop in animals given a normal diet but treated with HCl. The outfall of the protective effect in the case of deficiently fed animals may be experienced either because, due to the ineffective protein synthesis duodenal souring is able to activate only little tissue hormone, or, because the peripheral vascular region does not react to this, although the activation had taken place. The likelihood of the former supposition is further supported by the fact that, according to our experiments just being carried out, in animals fed a protein-deficient diet duodenal souring increases only very slightly the urinary uropancreosymin level (24). From our examinations also the conclusion can be drawn that no strict parallelity between the degree of ulceration and secretion amount, pH and total acidity exists.

*Summary*

Duodenal souring induced simultaneously with SHAY's operation totally prevents the development of ulcers. In animals previously fed a tryptophan- ormethionine-deficient diet, respectively, this antiulcerogen effect showed a considerable decrease. In control animals the protective effect of duodenal souring is associated with the effect of activated tissue hormones inhibiting the gastric secretion and improving the blood supply of the stomach whereas the absence of this protective effect in animals fed a deficient diet may be explained by the disturbance in parahormone synthesis due to protein-deficiency. According to our opinion protein-deficient diet predisposes to ulceration on the one side, because it produces a disturbance in the synthesis of intestinal parahormones.

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# Aktivierung der ATP-Spaltung im Warm- und Kaltblütermuskel durch Gefrieren und mechanische Verletzung

Von W. PARTMANN

Mit 15 Abbildungen und 4 Tabellen

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Während des Auftauens von Warmblütermuskulatur, die unmittelbar nach dem Tode eingefroren wurde, kommt es häufig zu einer Taukontraktur. Sie wird auch als Taurigor bezeichnet. BENDALL und MARSH haben zuerst darauf hingewiesen, daß diese Kontraktur durch die relativ rasche Spaltung von ATP beim Auftauen bedingt ist. Durch das Gefrieren des Gewebes unmittelbar nach dem Tode werden die glykolytischen Prozesse verlangsamt und bei genügend großer Temperatursenkung praktisch fixiert. Das hierbei noch vorhandene ATP bleibt erhalten und wird erst durch die Temperaturerhöhung beim Auftauen unter Entfaltung seiner physiologischen Kontraktionswirkung vollständig gespalten (1). Im Warmblütermuskel, speziell beim