

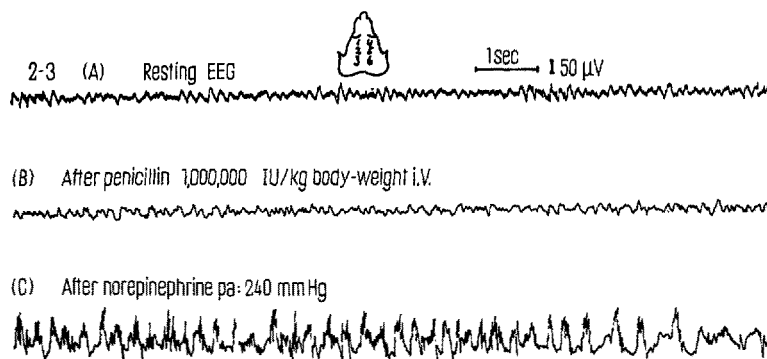


Fig. 2

festations. We have observed clinical correlates to the experimental findings in certain cases with generalized epileptic fits, following periods of reduced perfusion pressure during penicilline administration, where the seizures ceased after cessation of the penicilline administration.

**Résumé.** En expérimentant sur le chien, l'on peut produire des lésions de la barrière hémato-encéphalique aussi bien en diminuant qu'en élevant la pression de perfusion cérébrale. Ainsi l'administration d'un produit épi-

leptogène tel que la Pénicilline déclenche des crises comitiales alors que celle-ci est normalement arrêtée par la barrière hémato-encéphalique lorsque cette dernière est intacte. En clinique, des cas d'épilepsie de même mécanisme ont été démontrés.

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### Effect of Selenium and Type of Diet on the Pattern of Food and Water Intake in the Rat

The results of several studies, reviewed elsewhere<sup>1,2</sup>, have indicated that the trace element selenium is capable of enhancing the susceptibility to dental caries particularly when consumed during the developmental period of the teeth. For a better understanding of this relationship, it was thought advisable to investigate the effect of selenium and type of caries-producing diet consumed on the pattern of feeding and drinking habits of rats. No such studies have been reported previously.

**Materials and methods.** Male, weanling albino rats of the Sprague-Dawley-strain were used. They were housed individually in metal cages with raised screen bottoms. The animals were maintained on 2 caries-producing diets, designated as diet (A) and diet (B), commonly used in experimental caries research<sup>3,4</sup>. The % composition of the diets was as follows: diet (A) sucrose 66, dried skim milk powder 32, liver substance 2; diet (B) ground corn 64, powdered whole milk 32, alfalfa meal 4.8, sodium chloride 1, irradiated yeast 0.2.

A total of 19 rats were assigned to each of the 2 diets. Of those, 10 animals were placed in the experimental group and 9 served as controls. The study lasted for 21 days and 3 rats did not finish the experimental period. Selenium, as sodium selenite, in the amount of 3 ppm was added to the drinking water of the animals assigned to the experimental group of each diet. The controls consumed tap water. Food and water were provided ad libitum. The daily consumption of food and water was measured accurately by methods described in previous works<sup>5,6</sup>.

**Results and discussion.** The findings of the study appear in Table I. Normal control rats fed diet (B) gained more

weight than their counterparts on diet (A), although animals in both diets ate the same amount of food. As was anticipated, the mean weight gain of the animals ingesting selenium in both diets was significantly less, as determined by the *t* test, than that of their controls. The food and water intake of rats ingesting selenium was considerably reduced compared with their controls. The differences in food and water consumption between the control and selenium group of rats fed diets (A) and (B) were analyzed by the *t* test and were found to be statistically significant.

The data regarding the ratio of food to water intake shown in Table I revealed that in the normal control rats fed diet (A) the physiological relation of food to water consumption has been reversed, that is, more food than water was consumed. Such an observation has not been reported previously. For the selenium group of rats given the same diet the ratio of food to water remained similar to that of the controls. However, administration of selenium to rats consuming diet (B) resulted in a ratio of food to water lower than that of the controls. The proportion of food to water ingested by the control rats fed diet (B) was in the order of 1:1.53 which is appreciably

<sup>1</sup> D. M. HADJIMARKOS, *Archs envir. Hlth* 10, 983 (1965).

<sup>2</sup> D. M. HADJIMARKOS, *Borden's Rev. Nutr. Res.* 27, 1 (July-Sept. 1966).

<sup>3</sup> R. S. STEPHEN and M. R. HARRIS, *Advances in Experimental Caries Research* (Ed. R. F. SOGNAES; Am. Ass. Adv. Sci. Washington, D.C. 1955), p. 47.

<sup>4</sup> J. C. MUHLER and H. G. DAY, *J. Am. dent. Ass.* 41, 528 (1950).

<sup>5</sup> D. M. HADJIMARKOS, *Experientia* 22, 117 (1966).

<sup>6</sup> D. M. HADJIMARKOS, *Archs envir. Hlth* 14, 881 (1967).

Table I. Effect of selenium in the drinking water of rats on weight gain, daily food and water intake, and ratio of food to water consumption

| Item specified          | Diet (A)              |                         | Diet (B)    |                         |
|-------------------------|-----------------------|-------------------------|-------------|-------------------------|
|                         | Control               | Se                      | Control     | Se                      |
| No. of animals          | 8                     | 10                      | 8           | 9                       |
| Mean initial weight (g) | 44.1                  | 44.4                    | 43.0        | 43.6                    |
| Mean weight gain (g)    | 76.6 ± 4 <sup>a</sup> | 58.1 ± 4 <sup>b</sup>   | 93.6 ± 6    | 76.8 ± 3 <sup>c</sup>   |
| Mean food intake (g)    | 10.3 ± 0.50           | 8.7 ± 0.34 <sup>d</sup> | 10.3 ± 0.56 | 8.7 ± 0.21 <sup>d</sup> |
| Mean water intake (ml)  | 9.3 ± 0.23            | 7.1 ± 0.31 <sup>e</sup> | 15.8 ± 1.40 | 9.7 ± 0.20 <sup>e</sup> |
| Ratio of food/water     | 1:0.90                | 1:0.82                  | 1:1.53      | 1:1.11                  |

<sup>a</sup> Standard error. <sup>b</sup> Significantly different from the control,  $P < 0.01$ . <sup>c</sup> Significantly different from the control,  $P < 0.05$ . <sup>d</sup> Significantly different from the mean food intake of the control,  $P < 0.05$ . <sup>e</sup> Significantly different from the mean water intake of the control,  $P < 0.01$ .

below that of about 1 part of food to 2 parts of water seen in normal rats fed Purina laboratory chow<sup>5,7,8</sup>.

Pronounced disturbances in the ratio of food to water intake may have a decisive influence in determining the degree of cariogenicity of a diet. It was reported recently<sup>9</sup> that weanling rats fed a diet containing 67% sucrose and 29% skim milk powder, resembling diet (A) of the present study, developed significantly more caries than those receiving similar diets in which the skim milk powder was replaced by an equal amount of either casein or simulated skim milk powder, the latter having a protein content similar to that of the natural skim milk powder. On the basis of the results with diet (A) of the present work, it is proposed that the unexplained increase in caries activity observed in rats fed a diet containing sucrose and skim milk powder<sup>9</sup> was brought about by the pronounced depression in water consumption. Such a reduction in the intake of water may have increased the caries-producing capacity of the diet by enhancing the retention of food particles on the surfaces of the teeth and thus increasing the length of time food remained in the mouth of the animals. The proposed explanation is supported by the results of previous studies showing that rats receiving a sucrose diet in fluid form developed less caries compared with animals ingesting the same diet in dry form<sup>10,11</sup>.

Administration of selenium to rats consuming diet (A) resulted in a ratio of food to water intake similar to that of the controls. This was an unexpected finding since a previous work demonstrated that in rats fed Purina laboratory chow ingestion of selenium reduced the intake of water significantly more than that of food<sup>6</sup>. It seems that when normal rats eat a type of diet which reverses the physiological relation of food to water intake and more food than water is consumed, as in the case of diet (A), ingestion of selenium does not produce any further substantial reduction in water intake.

In contrast to diet (A), it was shown that administration of selenium to rats on diet (B) decreased the intake of water more than that of food thus lowering considerably the food to water ratio as compared with controls. This finding corroborates the results of a recent study<sup>6</sup>, and suggests that ingestion of selenium after the development of the teeth may produce some increase in caries in rats by impairing the oral clearance of food particles as a result of a reduction in water intake which is considerably higher than that of food.

Calculations of the amount of food and water consumed by weekly intervals, presented in Table II, disclosed that rats fed diets (A) and (B) responded differently to the ingestion of selenium. Animals on diet (A) consumed progressively less food and water than their controls. On

Table II. Mean daily intake of food and water in rats by weekly intervals

| Time interval | Food intake (g/day) |      |        | Water intake (ml/day) |      |        |
|---------------|---------------------|------|--------|-----------------------|------|--------|
|               | Control             | Se   | % dif. | Control               | Se   | % dif. |
| Diet (A)      |                     |      |        |                       |      |        |
| First week    | 6.7                 | 6.3  | 6.0    | 6.4                   | 5.9  | 7.9    |
| Second week   | 10.5                | 9.4  | 10.5   | 9.3                   | 7.4  | 20.5   |
| Third week    | 13.7                | 10.3 | 24.9   | 11.9                  | 7.8  | 34.5   |
| Total         | 10.3                | 8.7  | 15.6   | 9.3                   | 7.1  | 23.7   |
| Diet (B)      |                     |      |        |                       |      |        |
| First week    | 7.4                 | 6.2  | 16.3   | 11.1                  | 7.4  | 33.3   |
| Second week   | 10.7                | 9.3  | 13.1   | 15.9                  | 10.2 | 35.9   |
| Third week    | 13.3                | 11.2 | 15.8   | 20.7                  | 12.1 | 41.6   |
| Total         | 10.3                | 8.7  | 15.6   | 15.8                  | 9.7  | 38.7   |

the other hand, rats fed diet (B) showed some increase in food consumption, after an initial decrease, as the experimental period advanced but a continuous and pronounced decline in water intake in comparison with the control group. These differences in eating and drinking habits resulting from administration of selenium to rats given different caries-producing diets cannot be explained at present, but they may play a role in determining the degree of cariogenicity of a diet.

In conclusion, the findings of the present study suggest that disturbances in the regulation of food to water intake resulting either from the physical or nutritional characteristics of the diet or in response to an agent, such as selenium, may be a new and heretofore unsuspected factor which influences the degree of cariogenicity of a diet. A substantial voluntary reduction in water intake may increase the caries-potential of the diet by enhancing the adhesiveness of food particles on the surfaces of the teeth and thus delaying oral clearance.

<sup>7</sup> J. L. STROMINGER, Yale J. Biol. Med. 19, 279 (1947).

<sup>8</sup> M. J. FREGLY and R. E. TAYLOR, *Thirst* (Ed. M. J. WAYNER; The Macmillan Co., New York 1964), p. 139.

<sup>9</sup> R. M. GREEN, *Helv. odont. Acta* 17, 32 (1967).

<sup>10</sup> E. P. ANDERSON, J. K. SMITH, C. A. ELVEHJEM and P. H. PHILLIPS, *J. Nutr.* 35, 371 (1948).

<sup>11</sup> J. HALDI, W. WYNN, J. H. SHAW and R. F. SOGNAES, *J. Nutr.* 49, 295 (1953).

**Zusammenfassung.** Erhielten junge, normale Ratten eine Grunddiät von Rohrzucker oder Mais, so war das physiologische Verhältnis zwischen Futter- und Wasserverbrauch gestört. Die Beigabe von Selen verminderte Futter- und Wasserverbrauch, das letztere in höherem Grade. Das Ergebnis weist darauf hin, dass in der Störung der normalen Regelung von Futter- und Wasserverbrauch

möglicherweise ein neuer Faktor vorliegt, der die Intensität der Zahnkaries in Ratten beeinflusst.

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## Gereizte und ungereizte Rattenzwerchfelle in einer Kaliumtyrodelösung von 137 mM

Nach der Iontentheorie der Erregung ist ein Muskel nach längerer vollständiger Depolarisation unerregbar, d.h. auch zu keiner Kontraktion mehr fähig<sup>1</sup>. Messungen des Membranpotentials, nach schlagartigem Badwechsel von normaler in eine Kaliumtyrodelösung, ergaben am Meerschweinchenvorhof eine Halbwertszeit des Potentialabfalls von 12 sec<sup>2</sup>. Es wurde jedoch in der Literatur über mechanische Aktivität bei hoher K<sup>+</sup>-Konzentration berichtet, eine Situation, in der die Membran völlig unerregbar sein müsste<sup>3</sup>. Die Reizschwellenverschiebung bei einer Depolarisation durch verschiedene [Ca]<sub>e</sub> ist ebenfalls bekannt<sup>4</sup>.

In der vorliegenden Untersuchung soll am Zwerchfell der Ratte eine K<sup>+</sup>-Kontraktur erzeugt werden und bei verschiedenen [Ca<sup>++</sup>] und Reizarten die Erregbarkeit unter diesen Bedingungen beschrieben werden.

**Methodik.** Von 100–150 g schweren Ratten wurde das Zwerchfell herauspräpariert und in Tyrodelösung von jedem Zwerchfell ein Streifen von ca. 5 mm Breite in Faserlängsrichtung abgeschnitten und in einem Organbad in isometrischer Anordnung aufgehängt. Einzelheiten der Versuchsanordnung siehe <sup>5</sup>. In der Kaliumlösung wurde das gesamte NaCl der Tyrodelösung durch KCl ersetzt (137 mM).

Die Potentiale wurden extrazellulär mit einer Saug-elektrode abgeleitet<sup>6</sup>. Die direkte und indirekte Reizung erfolgte supramaximal.

**Ergebnisse.** Zwischen den geprüften Gruppen auf Figur 1 bestehen signifikante Unterschiede. (< 1% Irrtumswahrscheinlichkeit, Ausnahme Gruppe 1: 10 msec bei 7,2 mM CaCl<sub>2</sub>.)

- 1 H. REICHEL, *Muskelpysiologie* (Springer Verlag, Berlin, Göttingen, Heidelberg 1960).
- 2 U. WOLLERT, *Pflügers Arch. ges. Physiol.* 289, 191 (1966).
- 3 K. BRECHT, K. BARBEY, W. KUTSCHA und P. PAUSCHINGER, *Pflügers Arch. ges. Physiol.* 273, 130 (1961).
- 4 K. BRECHT, P. PAUSCHINGER und W. KUTSCHA, *Pflügers Arch. ges. Physiol.* 277, 178 (1963).
- 5 W. KLAUS, H. LÜLLMANN und E. MUSCHOLL, *Pflügers Arch. ges. Physiol.* 272, 316 (1961).
- 6 B. F. HOFFMANN, P. F. CRANFIELD, E. LEPESCHKIN, B. SURAWICZ und H. C. HERRLICH, *Am. J. Physiol.* 196, 1297 (1964).

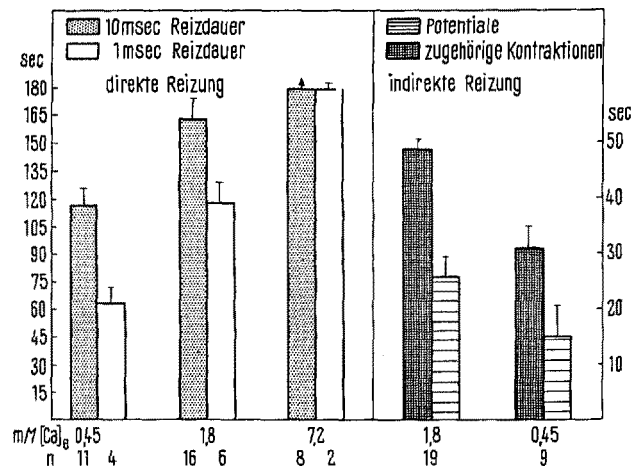


Fig. 1. Zeitpunkte (in sec) des Verschwindens der extrazellulär abgeleiteten Potentiale sowie der Kontraktionen nach raschem Einbringen der Präparate in Kaliumtyrodelösung.

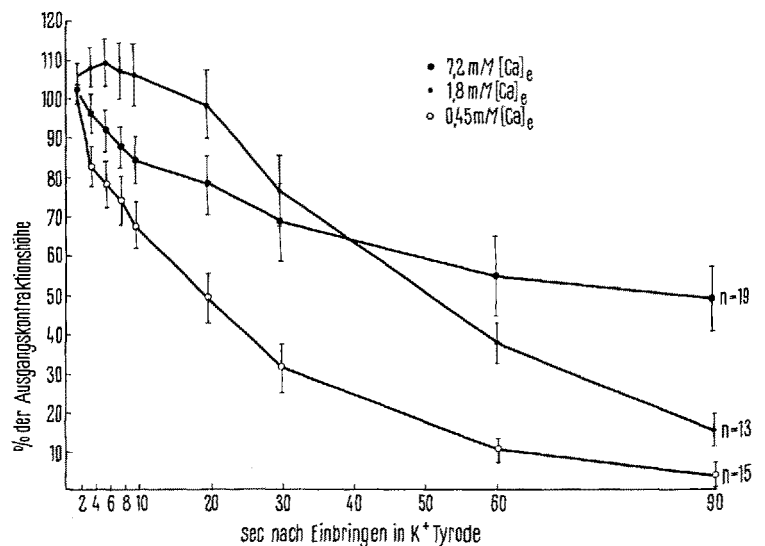


Fig. 2. Relative Veränderungen der Einzelkontraktionshöhe von Zwerchfelstreifen nach Einbringen in Kaliumlösung bei verschiedenen Kalziumkonzentrationen. Die Kontraktionshöhe in normaler Tyrode ist gleich 100% gesetzt. Direkte Reizung: supramaximal, 10 msec.