Zeitschrift für Ernährungswissenschaft

Journal of Nutritional Sciences · Journal des Sciences de la Nutrition

Band 11 Heft 1 März 1972

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The effect of total starvation and low calorie diet on components of weight loss and other metabolic changes in patients with regulatory obesity

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With 5 figures

(Received September 26, 1970)

During recent years intermittent or periodic starvation has been recognized as powerful therapeutic tool in the treatment of obesity. This slimming procedure has been of considerable value in those cases especially, that resist to other forms of dietary treatment (7, 8, 11, 14, 21). Some authors even thought that prolonged fasting could be able to eliminate metabolic disturbances resulting from a state of persistent overweight and to shift deranged metabolism to normal one (7, 19).

It has been known that during starvation may appear some side-effects like ketonuria, hypotension or anemia, but in general the feeling of hunger disappears and patients tolerate this method of treatment quite well (30). There is not so far any adequate explanation as to the mechanism of this phenomenon. Also possible alteration of abnormal metabolism of obese which might be induced by starvation are still obscure.

The purpose of the present study has been to find out on the basis of balance studies and determinations of some biochemical parameters whether during starvation it could appear any changes having been able to elucidate beneficial effect of this method of treatment. Moreover, it has been attempted to compare the influence of prolonged fasting and low calorie diet on components of weight loss and other metabolic changes in the same obese patients.

Material and methods

The studies were done on 19 female patients with regulatory obesity aged between 18 and 51 years in whom the onset of obesity occurred 8 until 25 years ago. The degree of obesity

ranged from 130 to 220 per cent, on average 167 per cent. There was no diabetes family history and glucose tolerance in all patients was nearly normal.

For 5 days, before the study began, all patients were kept on low calorie diet that consisted of 14 calories/kg of ideal body weight/day, 1.2 g/kg/day of protein, 0.5 g/kg/day of fat. This preliminary period was applied in order to adjust patients to new conditions of hospital ward and changing food habits. Then a 6 days metabolic periods started, during which all balance studies were carried out. Patients were fed the same low calorie diet as before. Afterwards, 14 days period of total starvation was applied, during which patients did not eat any food, drinking only 1.5 l. of mineral water per day. Complementary treatment consisted of 1.0 g of sodium chloride, 1.5 g of potassium chloride, vitamin A+E, C and complex of B, in amounts covering daily requirement, as well as some sedatives. After starvation, 6 days refeeding period followed. Patients were fed in this period a low calorie diet, containing 7 cal/kg/day, 0.75 g/kg/day of protein, 0.2 g/kg/day of fat.

Nitrogen, sodium and potassium balances were done and calculated from every day analysis of consumed food and all excreta. At the beginnig and at the end of each metabolic period were made the determinations of serum amino-N (29), FFA (10), glucose (18) and insulin – like activity (4) by the method of Ball and Merill, based on the measurement of CO_2 produced during glucose utilization in the presence of insulin, by fat tissue taken from epidydymal pad of the rat, total body water as antipyrine space, total extracellular water as thiocyanate space. Also assessment of acid-base balance was made in all patients. From the obtained data of nitrogen, sodium and potassium balances changes of fat free tissue (lean body mass), total extracellular water and total intracellular water as well as fat tissue were calculated with the method of Reifenstein and al. (25).

Results and discussion

The example of typical balance study done in one case of obesity is presented in fig. 1.

During the first 6 days period of low calorie diet there was a small weight reduction accompanied by nitrogen and potassium loss. Sodium balance was slightly positive. The effect of starvation on weight loss was in this case considerable. The patient lost 7 kg of body weight during 14 days fast.

Nitrogen balance in this period was strongly negative, but nitrogen loss was the greatest in the first week of starvation then tended to diminish. The same concerns potassium balance, which in the second week of starvation become even positive. It is worthwhile to mention that during starvation concentration of blood ketone bodies rose to 37 mg/100 ml. During refeeding period, when low calorie diet was applied (350–450 calories per day) nitrogen balance become positive despite rather low protein intake (0.75 g/kg of ideal body weight). Sodium and potassium balance were also positive. Weight reduction stopped, but there was no weight gain.

These findings are in keeping with some reports which revealed that nitrogen and potassium balance had been strongly negative in the first period of starvation (1, 5, 8, 11, 24). However absolute losses of N and K decreased if starvation prolonged over several weeks (6, 23) or sharply stopped during refeeding period even with low-calorie diet.

BIRKENHÄGER (6) observed that during starvation the ratio of the total loss of K to the total loss of N had been similar to the value for the ratio of the concentrations of these elements in the fat free protoplasm. To elucidate significance of these data it was interesting to estimate the influence of starvation and low calorie diet upon the components of weight losses.

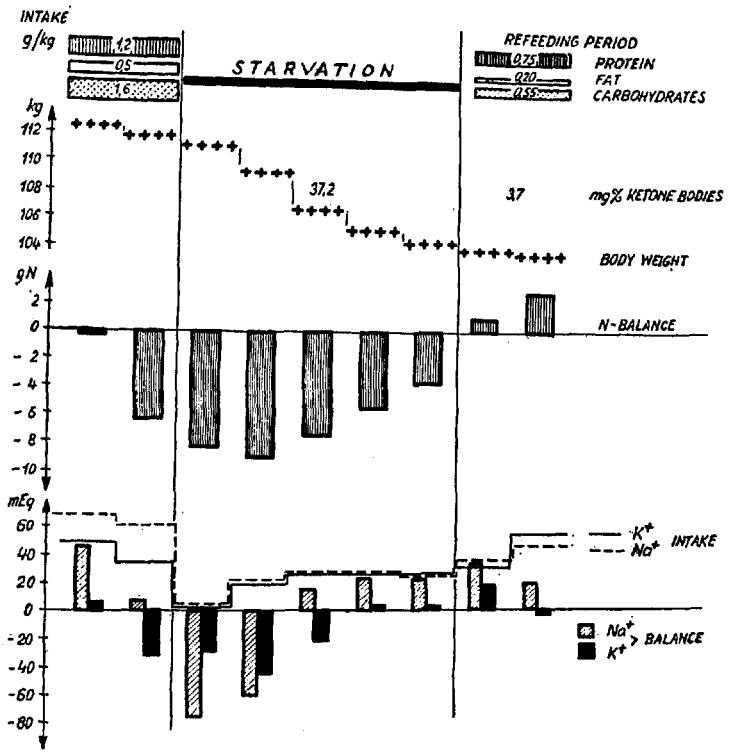

Fig. 1. Nitrogen and electrolytes balance (Na^+ and K^+) in regulatory obesity treated by starvation (♀ M. W.).

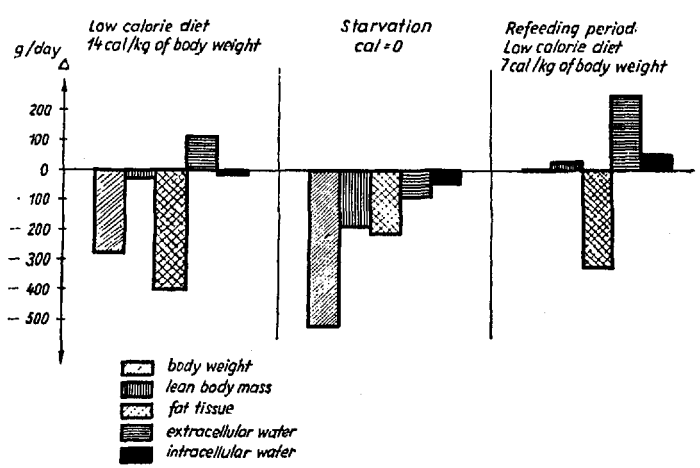

Fig. 2. Metabolic changes in obese patients.

Fig. 2 demonstrates the effect of treatment with low calorie diet and starvation upon the components of weight loss, calculated from the balance studies and partly compared with the results of antipyrine and thiocyanate space measurements. During the first period of study while patients were on low-calorie diet, weight reduction was much lesser than during starvation. However this loss was to a greater extent, caused by fat tissue reduction than those which had been observed during prolonged fasting. Also in starvation period was noted more considerable loss of fatless tissue and slight reduction of water compartments. There did not appear further loss of weight, while low calorie diet had been applied once more in refeeding period. It is interesting, however, that despite the failure to get weight fall in this period, the reduction of fat tissue was still going on. We also revealed in refeeding period by means of balance techniques as well as antipyrine and thiocyanate space measurements gain of extracellular body water, slight increase of fatless tissue (fat free protoplasm) and intracellular body water. These data throws some light why it is difficult to achieve further weight loss while starvation period comes to an end – the phenomenon which has been recently reported (8, 17, 24). Thus, in refeeding period takes place a very good utilization of ingested protein resulting in gain of fat free protoplasm as well as it occurs the retention of water which was lost during starvation. It is difficult to interpret mechanism of the reduction of water compartments during starvation. The negative balance for sodium was persistent in all studied cases in the initial phase of fast. This may account for the decrease of extracellular water. Some authors suggested possible effect of carbohydrate deprivation upon the increase of natriuresis (9, 15, 20). During refeeding period, while carbohydrates were consumed, we also observed that natriuresis had stopped and sodium started to conserve. It is not possible however to consider carbohydrates intake as the unique factor responsible for sodium and water conservation in refeeding period. Recent reports revealed that prolonged fast may give rise to the enhancement of aldosterone production and secretion of antidiuretic hormone (16, 27). This problem rquires further investigations.

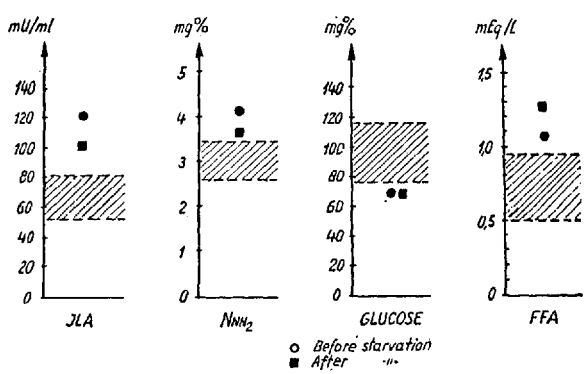

Fig. 3. Mean values of some blood compounds in patients with regulatory obesity treated by starvation (fasting values).

Fig. 3 shows the effect of starvation on some biochemical parameters determined in blood serum.

Concentrations of FFA were elevated above the normal level in obese patients before starvation. During the fast these values increased still on and at the end of this period on average amounted to 1.3 mEqu/l but when refeeding had started fell down immediately even below initial levels. It is hardly possible to explain the findings because at present even the causes of high levels of serum FFA in obesity are not well elucidated. Perhaps, this is a result of impaired mechanism of lipolysis caused by disorders of hormonal regulation (3).

The rise of serum FFA level during starvation may be a consequence of increased fatty acid mobilisation. However KROTKIEWSKI et al. got evidence that during fast had existed certain degree of inactivity in lipids mobilisation (22). In view of this findings we are able to consider poorer utilization of fatty acids by tissue to be more decisive factor.

Fasting values of serum amino-N, and ILA shown on this figure were also elevated in all cases, but they decreased nearly to the normal values after starvation. Serum glucose concentrations were below normal values but despite this there did not appear any clinical symptoms of hypoglycemia.

High values of serum ILA in obese subject were only poorly correlated with blood glucose concentration and did not correlate too with free fatty acids levels. This evidence support hypothesis about insensitivity of adipocytes to insulin on obesity (2, 23).

All above mentioned data may suggest that starvation is able to change some not clearly understood control mechanism in obese. But it is a matter for discussion whether this change could be thought of as advantageous or harmful. To answer this question, we did studies of the effect of ingestion of protein meal, composed of specially produced defatted cottage cheese in the amount 0.4 g/kg of protein, on the serum insulin-like activity, amino-N, glucose and FFA response. The results are presented in the fig. 4.

The most striking were the changes of serum ILA after protein loading. There was an increase of ILA in healthy lean persons with the peak appearing after 90 min. and gradual decline up to 270 min. Serum ILA in obese patients rose more slowly achieving its maximum after 2 to 3 hours. The degree of the increase was much lesser than healthy persons. The effect of starvation upon insulin response to amino acids loading was very considerable. We did not observe increment of ILA but rather transitory decrease below fasting values.

Since the studies of. FLOYD et al (12) it has been known that ingestion of mixture of amino acids or protein meal are strong stimulus for insulin secretion. This response may be altered in diabetes so that the peak of insulin secretion is nearly half that of normal or even less (13, 28). Very similar hanges we observed in obese after treatment with total fast. Therefore it is possible to draw conclusion that starvation impairs insulin response to protein loading shifting it to more diabetes-like. It is worthwhile to mention that in the same patients we also observed impairment of glucose tolerance.

Amino-N changes after ingestion of protein meal were also influenced by starvation. The increase of amino-N after meal was delayed and reached its maximum after 3 hours. This phenomenon also suggests deterioration of the regulatory mechanism which governs amino acid utilization in tissues by long lasting starvation in obese. There were any statistically significant alterations of glucose and FFA concentrations after protein loading.

The changes of acid-base balance during the studies are presented in the fig. 5. Blood pH did not decrease very much being rather within normal level. Nevertheless,

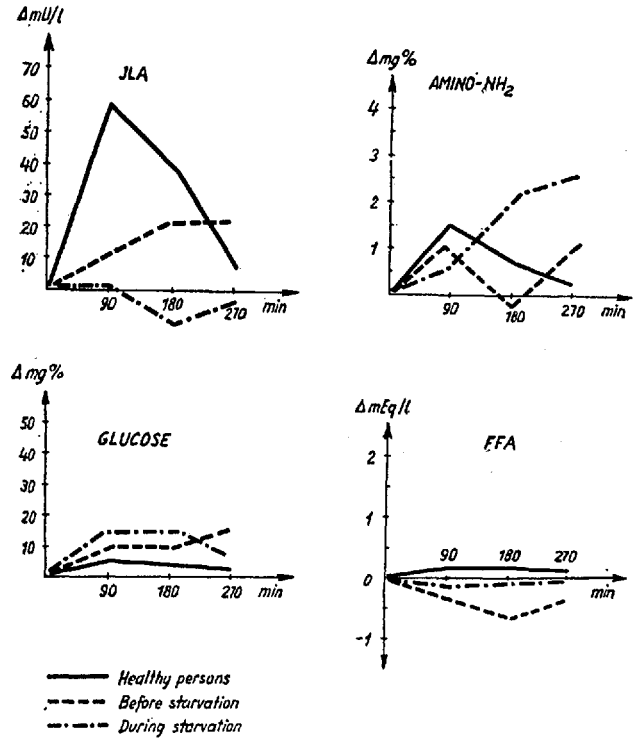

Fig. 4. The effect of ingestion of protein (0.4 g/kg of body weight) upon changes of some blood compounds incases of regulatory obesity treated by starvation (mean values).

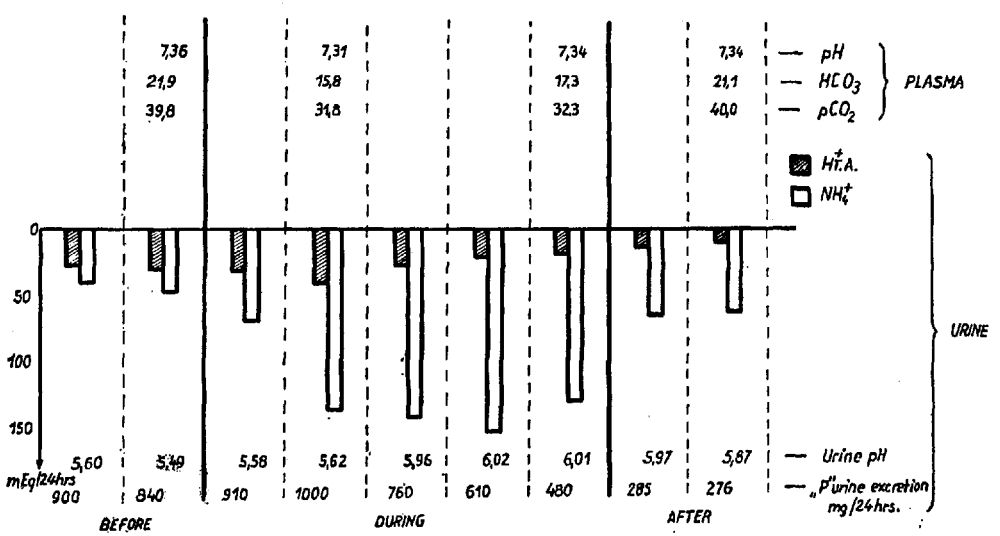

Fig. 5. Parameters of hydrogen ion metabolism in patients with regulatory obesity treated by starvation (mean values).

during starvation metabolic acidosis developed in all observed cases due to the increase of ketone bodies. This metabolic acidosis was compensated by respiratory mechanism. We observed a fall of plasma p-CO_2 and HCO_3^+ concentration. These changes levelled off in refeeding period. Starvation slightly increased pH of the urine, chiefly due to the rise of ammonium ion excretion but without increase of H^+ ion excretion (T. A.: titration acidity). Urine osmolality increased in first week of fasting due to decrease of urine output, then diminished while diuresis had arisen. Phosphorus excretion also rose in first week of starvation and this change correlated with the increment of nitrogen loss. Then, phosphorus excretion was reduced, in particular in refeeding period. These findings brought evidence that despite considerable rise of ketone bodies acidosis was well compensated by respiratory and buffer mechanisms. Nevertheless, metabolic acidosis is rather common feature of starvation. Some authors even concluded that failure to develop acidosis or its sudden improvement might be a good indication of surreptitious eating by the patients (26).

All above data can be summarized as follows: weight loss was more considerable during starvation than while patients were on low calorie diet, but stopped in refeeding period in spite of the application of very low calorie diet. Reduction of fat tissue was maintained throughout all periods of study but was not at all the greatest during starvation. Nitrogen and potassium balances were strongly negative during fasting and swiftly became positive in refeeding period. These two balances were in good correlation. Sodium balance was negative during starvation and in the same time total body water also was reduced. These losses were made up in refeeding period by quick retention of sodium as well as extracellular water. This water gain may account for failure of further weight loss despite application of very low calorie diet after starvation. Metabolic acidosis developped during starvation but was well compensated by respiratory mechanism.

Whatever the final explanation with regard to precise pathophysiologic mechanism involved it seems reasonable to conclude that all these data do not give strong evidence that starvation is able to change completely deranged metabolism in obese. On the contrary the findings pointed out that there could be a possibility of further impairment of certain metabolic responses i. e. insulin response. It is necessary to remind too, that highest loss of fat tissue was not obtained during starvation. So, chief advantages of this method of treatment of obesity lay rather on psychologic than on metabolic side because it offer a real chance for definite weight loss in most resistant cases. Nevertheless we would bear in mind that recently prognosis for fully satisfactory dietary treatment of extreme obesity is still rather bad.

Summary

The effect of total starvation and low caloric diet on components of weight loss was investigated in 19 women with regulatory obesity by means of nitrogen, sodium and potassium balance studies, as well as thiocyanate and antipyrine space measurements.

Determinations of serum insulin – like activity, amino-N, FFA, glucose and acid-base balance estimation were also carried out in each metabolic period. It was concluded that the most considerable weight loss in obese patients was obtained during starvation but this was caused by the reduction of fat and fat free tissue in equal parts. Weight loss induced by low calorie diet was nearly entirely due to the loss of fat tissue. Failure to obtain further weight loss after starvation while low calorie diet was applied in refeeding period, might be accounted for by considerable gain of extracellular water that exceeded in mass the reduction of fat tissue. Starvation in obese subjects gave rise to the development of metabolic acidosis with

the increase of ketonemia. Metabolic acidosis was well compensated by respiratory and buffer mechanisms. Prolonged fasting brought about some impairment of insulin response to protein test meal as well as caused disturbances of amino acids utilization. The authors recommend starvation as a method of treatment of obese only in most resistant cases which did not respond to low calorie diet.

Zusammenfassung

Bei 19 Frauen mit Fettsucht wurde der Einfluß der vollen Hungertherapie und niederkalorischen Diät auf die Bestandteile des Körpergewichts untersucht. Als Methode wurde die Stickstoff-Natrium-Kalium-Bilanz-Untersuchung sowie die Thiocyanat- und Antipyrin-Berechnung angewandt.

Während jeder Stoffwechselperiode wurden Seruminsulinbestimmungen (Aktivität, Amino-Stickstoff, Fettstoff-Glukose, Säure-Basen-Gleichgewicht) ausgeführt. Aus diesen Untersuchungen war zu schließen, daß bei fettsüchtigen Patienten der stärkste Gewichtsverlust während der Hungerperiode eintritt, doch wurde dies verursacht durch die Fettreduktion und die Verminderung fettfreien Bindegewebes in vergleichbaren Körperpartien. Der Gewichtsverlust bei niederkalorischer Diät ist fast ausschließlich auf die Verminderung des Fettgewebes zurückzuführen. Ein Ausbleiben weiterer Gewichtsverluste nach der Hungerperiode bei Zuführung niederkalorischer Diät während der nachfolgenden Ernährungsaufbauphase mag auf eine bemerkenswerte Zunahme an extrazellulärem Wasser zurückzuführen sein, welches mengenmäßig die Reduktion des Fettgewebes überstieg. Die Hungertherapie bei Fettsüchtigen begünstigte die Entwicklung einer stoffwechselbedingten Azidose mit verstärkter Ketonämie. Die stoffwechselbedingte Azidose konnte durch Atmungs- und Puffer-Mechanismen gut kompensiert werden. Verlängertes Fasten verschlechterte die Insulinausscheidung nach Protein-Test-Diät und verursachte Störungen im Aminosäureverbrauch. Die Verfasser empfehlen daher die Hungertherapie nur in solchen Fällen von Fettsucht, die auf eine niederkalorische Diät nicht ansprechen.

References

1. Apfelbaum, M., Equilibre du bilan azoté au cours de la diète protèique. Abstracts of papers of 8th International Congress of Nutrition. (Prague, A—23 (1969). — 2. Bagdade, J. D., Lancet, **1968**/II, 630. — 3. Balasse, E., Diabetologia **4**, 20 (1968). — 4. Ball, E. G., M. A. Merill, Endocrinology **69**, 596 (1961). — 5. Ball, M. R., L. H. Kyle, J. J. Canary, J. Clin. Endocrin. **27**, 273 (1967). — 6. Birkenhäger I. C., A. Haak, I. G. Ackers, Metabolism **17**, 391 (1968). — 7. Bloom, W. L. Metabolism **8** 214 (1959). — 8. Bolinger, R. E. B. P. Lukert, R. W. Brown, L. Guevara, R. Steiberg, Arch. Intern. Med. **118**, 3 (1966). — 9. Bortz, W. M., P. Howat, W. L. Holmes, Amer. J. Clin. Nutr. **21**, 1291 (1968). — 10. Dole, V. P., J. Clin. Invest. **35** 150 (1956). — 11. Drenick, E. I. W. H. M. E. Swenseid, Blond. S. Tuttle. J. Amer. Med. Ass. **187** 100 (1964). — 12. Floyd, I. C. Ir., S. S. Fajans, R. F. Knopf, I. W. Conn, J. Rull, Clin. Res. **13**, 322 (1965). — 13. Floyd, I. C. Ir., S. S. Fajans, C. Thiffault, R. F. Knopf, E. Guntsche, I. E. Conn, Clin. Res. **14**, 280 (1966). — 14. Gibiński, K., Pol. Tyg. Lek. **24**, 951 (1969). — 15. Hamvi, G. I., M. C. Mitchell, R. G. Wieland, F. A. Kruger, Amer. J. Clin. Nutr. **20**, 897 (1967). — 16. Hermann, L. S., N. C. Hansen, P. Groenback, M. Iversen, Ugeskr. Loeger **131**, 192 (1969). — 17. Hermann, L. S., E. Nathan, M. Iversen, P. Grönback, Ugeskr. Loeger **131**, 188 (1969). — 18. Hyvarrinen, A., E. A. Nikillä, Clin. Chim. Acta **7**, 140 (1962). — 19. Jackson, J. M. D., M. T. McKiddie, K. D. Buchanan, Lancet **1969**/I, 285. — 20. Katz, A. I., D. R. Hollingworth, F. H. Epstein, J. Lab. Clin. Med. **72**, 93 (1968). — 21. Krebs, W., Pol. Arch. Med. Wewn. **42**, 421 (1969). — 22. Krotkiewski, M., K. Roszkowska, Pol. Arch. Med. Wewn. **42**, 433 (1969). 23. Mancini, M., Poriete, C. O. Moro, R. Cerqua, M. Cuzzupoli, S. Matarese, L. A. Cioffi. Changes in plasma lipid concentration in obese patients during total

fasting and very low calorie intake. Abstracts of the 8th International Congress of Nutrition (Prague 1969). — 24. RATH, R., J. MASEK, Metabolism **15**, 1 (1966). — 25. REIFENSTEIN, E. C. IR., E. ALBRIGHT, J. Clin. Endocrin. **5**, 367 (1945). — 26. ROSS, S. K., A. MACLEOD, I. T. IRELAND, W. S. T. THOMSON, Brit. Med. J. **1969**/I, 380. — 27. SCHMIDT, H., I. JANIK, K. D. VOIGT, Dtsch. Med. Woch. **94**, 78 (1969). — 28. SPARKS, L. K., G. COPINSCHI, C. L. DONALDSON, A. S. BLUM, P. H. FORSHAM, Diabetes **16**, 268 (1967). — 29. STEIN, W. H., S. MOORE, J. biol. Chem. **211**, 915 (1954). — 30. THOMSON, T., J. RUNCIE, W. MILLER, Lancet **1966**/II, 992.

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