

## Originalien

# Nitrogen Loss in Normal and Obese Subjects During Total Fast

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### *Stickstoffverluste bei normalen und fettsüchtigen Personen während vollständigem Fasten.*

**Zusammenfassung.** Idealgewichtige, gesunde Versuchspersonen (12 Männer und 12 Frauen) wurden während 6tägigen Fastens und adipöse, aber im übrigen gesunde Personen (20 Männer, 28 Frauen) während 6–28tägigen Fastens untersucht. Bei allen Gruppen fand sich während der ersten 3 Fastentage ein signifikanter Anstieg des Stickstoffverlustes im Urin, gefolgt von einem kontinuierlichen Abfall. Der Anstieg der Stickstoffausscheidung erfolgte gleichzeitig mit einem Anstieg des Plasmaglukagons, was für einen Zusammenhang des letzteren mit vermehrter Gluconeogenese aus Aminosäuren spricht.

Bei gleichem Körpergewicht waren die Stickstoffverluste der männlichen Probanden größer als bei den weiblichen, sowohl bei normalgewichtigen wie auch bei übergewichtigen Personen. Andererseits war der Stickstoffverlust der adipösen Gruppen trotz viel höherem Körpergewicht und höherer Energieausgabe nicht größer als jener der normalgewichtigen. Der mittlere Stickstoffverlust pro Tag variierte zwischen 14,5 g (normal- und übergewichtige Männer während der ersten Fastentage) und 3,0 g (adipöse Frauen nach 4wöchigem Fasten).

Durch Berechnung der aus Protein freigesetzten Kalorienmenge (Urinstickstoff  $\times 6,25 \times 4,1$ ) und Entnahme der Gesamtenergieausgabe aus Stoffwechself Tabellen wurde ein Anteil des Proteins an der Gesamtkalorienausgabe von 15% (normalgewichtige Männer bei 6tägigem Fasten) bis 5% (adipöse Frauen nach 4 Fastenwochen) ermittelt. Die klinische Bedeutung des Stickstoffverlustes bei Null-Diät wird diskutiert.

**Schlüsselwörter:** Vollständiges Fasten, Stickstoff, Glukagon, Blutglucose.

**Summary.** Healthy volunteers of ideal weight (12 men and 12 women) were fasted for 6 days, and obese but otherwise healthy subjects (20 men, 28 women) for 6–28 days. In all groups studied a significant increase in urinary nitrogen loss from day 1 to day 3 of fasting was followed by a steady decrease. The early rise in urinary nitrogen excretion coincided with a rise in plasma glucagon levels, suggesting a relation of the latter to increased gluconeogenesis from amino acids.

At equal weight greater nitrogen losses were found in men than in women, in both normal and obese subjects. In spite of much higher weight and larger energy expenditure the nitrogen loss in obese subjects however was not higher than in normal ones. Mean daily nitrogen losses varied from 14.5 g (normal and obese men early in starvation) to 3.0 g (obese women after a 4-weeks fast).

Calculating the amount of calories derived from body protein (urinary nitrogen  $\times 6.25 \times 4.1$ ) and taking total energy expenditure from tabular metabolic values, the contribution of protein to total calorie output was found to vary from 15% (normal men 6 day fast) to 5% (obese women, 4th week of fasting). The clinical significance of nitrogen loss during therapeutic fasting is discussed.

**Key words:** Starvation, nitrogen, glucagon, blood glucose.

### Introduction

Protein loss in starvation, which is reflected by urinary nitrogen excretion [4, 10, 24, 26] presents several interesting aspects. From a biological point of view the ability of fasting man to conserve body protein is remarkable [4, 22, 23]. Nevertheless, there has been much discussion on whether nitrogen and lean tissue losses observed during therapeutic fasting are tolerable [2, 3, 11, 14, 30]. Clinical implications are, however, not limited to the treatment of obesity. Surgeons have pointed out that information on protein breakdown occurring in starvation is needed for the understanding of metabolic and nutritional problems met in their patients [17, 18, 21].

Extensive studies on the nitrogen balance were carried out in the fasting obese [2, 10, 11, 22, 23, 25, 29] but little information is available on nitrogen loss in normal subjects fasted for 6 or more days [1, 4], and we are unaware of reports concerning normal women fasted for a comparable length of time. Therefore a study was undertaken to establish the magnitude of nitrogen loss in fasting normal men and women and to enable comparison of obese and normal subjects of both sexes. Plasma glucagon levels were determined since this hormone has been implicated in the gluconeogenesis from amino acids in early starvation (Marliss *et al.*, 1970). Furthermore the contribution of protein breakdown to calorie output during starvation was calculated.

### Methods

The following groups of subjects were studied (Table 1): 1. 12 normal men and 2. 12 obese men matched for age and height and fasted for 6 days; 3. 12 normal women and 4. 12 obese women treated as groups 1 and 2; 5. 6 normal men and 6. 6 normal women taken from groups 1 and 2 and matched for age and weight to study sex difference of nitrogen loss in normal subjects; 7. 6 obese men and 8. 6 obese women taken from groups 2 and 4 and matched for age and weight to study sex difference of N-loss within the obese; 9. 8 obese men fasted for 3 weeks; 10. 8 obese women fasted for 4 weeks; 11. 8 obese women fasted twice for 2 weeks with interposition of 4 days on 600 calories/24 hour (composed of 52 g of protein, 58 g of carbohydrate and 18 g of fat).

Table 1. Clinical data of subjects studied during total fasting (mean and range)

Group	<i>n</i> <sup>a</sup>	Age Years	Height cm	weight (kg)		Deviation of initial from ideal weight <sup>b</sup> %	Duration of fast days
				initial	final		
1. Normal men	12	23.6 (20–27)	175.5 (163–185)	66.3 (55.3–77.9)	61.0 (51.4–71.8)	–	6
2. Obese men	12	24.5 (19–30)	175.6 (165–186)	110.5 (95.4–136.5)	104.6 (89.8–129.6)	52 (30–69)	6
3. Normal women	12	22.8 (20–28)	166.5 (161–173)	57.4 (49.5–64.2)	52.6 (45.3–58.5)	–	6
4. Obese women	12	23.7 (19–29)	166.3 (160–173)	92.0 (79.0–104.1)	86.4 (73.0–97.6)	49 (37–65)	6
5. Light weight normal men	6	23.8 (21–26)	171.8 (163–176)	60.7 (55.3–64.5)	56.0 (51.4–59.2)	–	6
6. Matched normal women	6	22.6 (20–27)	170.0 (163–174)	60.8 (56.9–64.2)	55.9 (52.9–58.5)	–	6
7. “Leight weight” obese men	6	25.0 (19–29)	173.1 (165–178)	99.2 (95.4–104.1)	93.5 (89.8–97.2)	41 (30–46)	6
8. Matched obese women	6	24.1 (20–29)	167.0 (160–173)	99.9 (92.1–104.1)	94.1 (86.1–98.8)	53 (44–56)	6
9. Obese men	8	35.8 (25–48)	177.8 (170–188)	115.5 (96.6–136.5)	101.4 (84.4–120.5)	55 (30–85)	21
10. Obese women	8	37.8 (25–59)	161.7 (155–169)	97.8 (82.4–124.0)	84.3 (69.6–110.6)	61 (40–99)	28
11. Obese women <sup>c</sup>	8	38.2 (25–58)	163.7 (152–172)	90.1 (70.7–125.0)	81.6 (62.9–114.2)	45 (25–103)	14
				83.0 (65.2–112.7)	77.6 (60.2–107.6)	34 (10–85)	14

<sup>a</sup> *n* = number of subjects.

<sup>b</sup> According to Metropolitan Life Insurance tables, 1959.

<sup>c</sup> Group 11 was fasted twice for 2 weeks with interposition of 4 days on 600 Cal/24 hr during which mean weight increased from 81.6 to 83.0 kg.

Healthy volunteers of strictly ideal weight were selected among medical students and obese but otherwise healthy subjects from the nutrition clinic. All subjects studied had normal values of serum creatinine and urea and normal glucose tolerance and hepatic screening tests. Prior to the study all subjects were instructed to maintain their body weight for 2–3 weeks before the beginning of the fast on a isocaloric diet consisting of approximately 15% protein, 35% fat and 50% carbohydrate. After admission to the metabolic ward the same diet was continued for 2 days. During the following starvation only tap water and weak tea with artificial sweeteners were allowed. No mineral or vitamin supplements or other medications were given. Adherence to total fasting was checked by quantitative estimation of 24 hr urine ketones (Göschke, 1970). To prevent the known negative effect of physical inactivity on nitrogen balance (Deitrick, 1948), all subjects were ambulant in order to maintain a rather low and uniform level of physical activity.

Estimation of nitrogen loss was limited to nitrogen excretion in 24 hr urine which during total fasting is representative of total nitrogen loss [4, 24, 26]. Urinary nitrogen was determined by the micro-Kjeldahl method and the result multiplied by 6.25 to obtain protein breakdown. Total calorie consumption and its composition were estimated according to Krizek (1969): Total calorie output was taken from tabular basal metabolism values [27] plus 33% to allow for the limited and controllable amount of physical activity.

This calculation was based on the mean weight of the fasting period. Muscle glycogen stores at onset of fasting were assumed to be 120 g in normals and 160 g in the obese (Cahill *et al.*, 1968). Liver glycogen, since almost depleted after an overnight fast (Hultman, 1971), was neglected. By subtracting the calories provided by protein and glycogen from total energy expenditure, the amount of calories derived from body fat breakdown was obtained (Krizek, 1969).

Venous blood glucose was estimated by the Technicon Autoanalyzer ferricyanide method. Plasma pancreatic glucagon was determined using a specific antiserum excluding nonpancreatic glucagon-like immunoreactivity and devoiding non specific reaction with plasma protein (Stahl, 1973, Stahl *et al.*, 1974). Bloods were drawn at 8–9 a.m., the first sample being taken after an overnight fast.

## Results

The urinary nitrogen excretion determined in normal and obese subjects during a *six day fast* is summarized in Table 2. A highly significant rise from the first to the third day was found which was followed by a steady decrease (Table 3). From Fig. 1 it can be seen that in a group of 7 normal men the increase in nitrogen

Table 2. Nitrogen and protein losses ( $m \pm \text{SEM}$ ) during complete starvation

Group	$n^a$	Duration of fast days	Nitrogen loss (g)		Protein loss (g)	
			total	per day	total	per day
1. Normal men	12	6	73.5 $\pm$ 2.6	12.2 $\pm$ 0.4	459 $\pm$ 16	76.3 $\pm$ 2.7
2. Obese men	12	6	72.7 $\pm$ 2.9	12.1 $\pm$ 0.5	454 $\pm$ 18	75.7 $\pm$ 3.0
3. Normal women	12	6	50.2 $\pm$ 0.9	8.3 $\pm$ 0.2	314 $\pm$ 5	52.3 $\pm$ 1.0
4. Obese women	12	6	53.6 $\pm$ 1.5	8.9 $\pm$ 0.3	335 $\pm$ 9	55.8 $\pm$ 1.5
5. Light weight normal men	6	6	70.7 $\pm$ 4.7	11.8 $\pm$ 0.8	442 $\pm$ 29	73.6 $\pm$ 4.9
6. Matched normal women	6	6	50.4 $\pm$ 1.0	8.4 $\pm$ 0.2	315 $\pm$ 6	52.3 $\pm$ 1.0
7. "Light weight" obese men	6	6	68.0 $\pm$ 3.2	11.3 $\pm$ 0.5	425 $\pm$ 20	70.8 $\pm$ 3.4
8. Matched obese women	6	6	55.6 $\pm$ 2.5	9.3 $\pm$ 0.4	348 $\pm$ 6	57.9 $\pm$ 2.7
9. Obese men	8	21	198.5 $\pm$ 10.5	9.5 $\pm$ 0.5	1242 $\pm$ 65	59.3 $\pm$ 3.1
10. Obese women	8	28	162.7 $\pm$ 9.9	5.8 $\pm$ 0.4	1017 $\pm$ 62	36.2 $\pm$ 2.2
11. Obese women <sup>b</sup>	8	14	103.8 $\pm$ 7.7	7.4 $\pm$ 0.2	649 $\pm$ 48	46.4 $\pm$ 3.4
		14	54.9 $\pm$ 3.4	3.9 $\pm$ 0.2	343 $\pm$ 22	24.5 $\pm$ 1.6

<sup>a</sup>  $n$  = number of subjects.<sup>b</sup> Fasted twice for 2 weeks (see Table 1).Table 3. Urinary nitrogen excretion during 6 days of total fasting in normal and obese subjects. The increase in nitrogen loss from day 1 to day 3 was highly significant by the paired *t*-test as was the ensuing decrease from day 3 to day 6

Group	$n^a$	Grams of nitrogen/24 hr ( $m \pm \text{SEM}$ )							Significance of variations in N-loss	
		Day preceeding fast	Days of fasting						Day 1 vs. 3 <i>p</i> -values	Day 3 vs. 6 <i>p</i> -values
			1	2	3	4	5	6		
1. Normal men	12	13.4 $\pm$ 0.6	10.7 $\pm$ 0.4	13.5 $\pm$ 0.5	14.5 $\pm$ 0.7	12.2 $\pm$ 0.6	11.5 $\pm$ 0.6	11.1 $\pm$ 0.5	0.001	0.001
2. Obese men	12	14.4 $\pm$ 1.0	10.7 $\pm$ 0.7	12.3 $\pm$ 0.6	14.0 $\pm$ 0.8	12.6 $\pm$ 0.5	12.1 $\pm$ 0.7	10.8 $\pm$ 0.4	0.01	0.001
3. Normal women	12	8.2 $\pm$ 0.3	6.6 $\pm$ 0.3	9.1 $\pm$ 0.5	9.6 $\pm$ 0.3	8.9 $\pm$ 0.3	8.4 $\pm$ 0.2	7.4 $\pm$ 0.2	0.001	0.001
4. Obese women	12	11.7 $\pm$ 1.0	7.8 $\pm$ 0.5	9.0 $\pm$ 0.5	9.9 $\pm$ 0.4	9.5 $\pm$ 0.3	8.8 $\pm$ 0.3	8.5 $\pm$ 0.4	0.001	0.01

<sup>a</sup>  $n$  = number of subjects.

Table 4. Mean composition of daily energy expenditure during total fasting

Group	$n^a$	Duration of fast days	Total		Protein		Fat		Glycogen	
			Cal	%	Cal	%	Cal	%	Cal	%
Normal men	12	6	2200	100	315	14	1810	82	80	4
Obese men	12	6	2960	100	310	10	2540	86	110	4
Normal women	12	6	1820	100	210	12	1530	84	80	4
Obese women	12	6	2260	100	230	10	1920	85	110	5
Obese men	8	21	2920	100	240	8	2650	91	30	1
Obese women	8	28	2180	100	150	7	2010	92	20	1
Obese women <sup>b</sup>	8	14	2120	100	190	9	1885	89	45	2
		14	2050	100	100	5	1905	93	45	2

<sup>a</sup>  $n$  = number of subjects.<sup>b</sup> Fasted twice for 2 weeks (see Table 1).

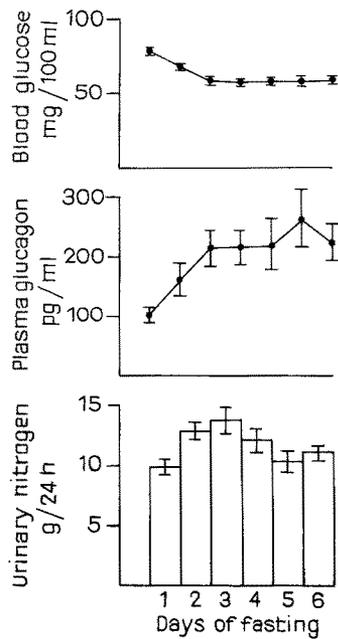


Fig. 1. Concentrations of blood glucose and plasma glucagon, and urinary nitrogen excretion in 7 normal males during total fasting ( $m \pm$  S.E.M.). A significant increase of urinary nitrogen excretion from day 1 to day 2 ( $p < 0.01$ ) and day 3 ( $p < 0.01$ ) of fasting coincided with a significant rise of plasma glucagon from overnight fasting level to values found after 1 day ( $p < 0.05$ ), 2 days ( $p < 0.01$ ) and 3 days ( $p < 0.01$ ) of complete starvation (paired t-test)

excretion early in fasting coincided with a rise in plasma glucagon level and the blood glucose fall known to occur in early starvation [4, 20, 24].

Nitrogen losses in the normal and the obese groups matched according to sex, age and height (groups 1 and 2, and groups 3 and 4, respectively) were of the same order in spite of large weight differences (Table 2). Normal men lost significantly more nitrogen ( $p < 0.01$ ) than normal women of comparable weight (Table 2, groups 5 and 6); a similar sex difference was found between the obese groups 7 and 8 ( $p < 0.02$ ). Total breakdown of body protein within 6 days of fasting varied from 314 to 459 g.

Nitrogen excretion in obese subjects during *prolonged fasting* is shown in Table 2 and Fig. 2. Of special interest is group 11 which was fasted intermittently. Following 14 days of starvation nitrogen excretion increased only little on 600 calories and 52 g of protein per day. Fecal and cutaneous nitrogen losses were not determined; but even assuming a mean fecal loss of 1.28 g (Reifenstein *et al.*, 1945) and a cutaneous loss of 0.25–0.5 g per day (Darke, 1960) which apply to regular diets, the nitrogen balance would have been positive in spite of the small protein and calorie intake. At the end of the second fortnight of fasting the mean nitrogen loss fell to 3 g per day.

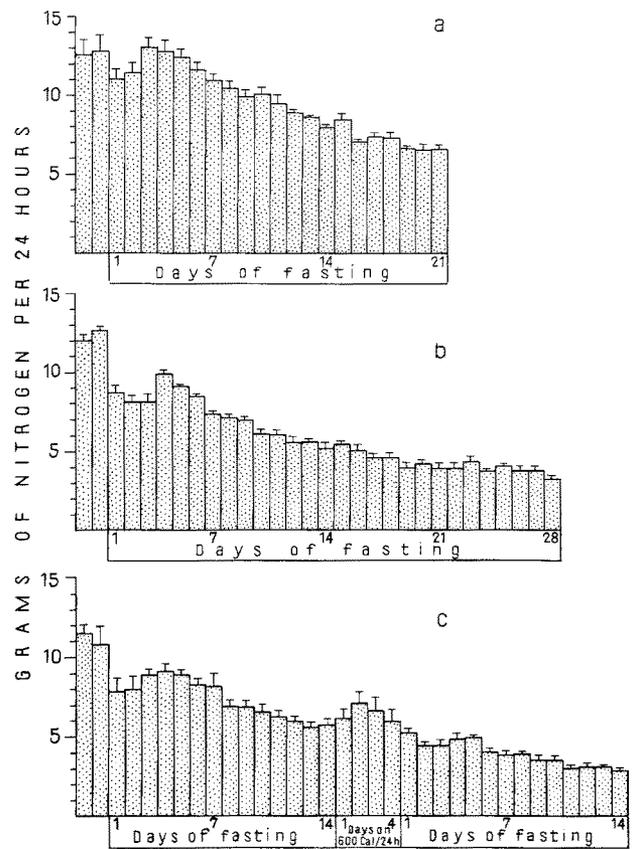


Fig. 2a–c. Daily urinary nitrogen excretion ( $m \pm$  S.E.M.) during 2 days prefast on isocaloric diet and during ensuing prolonged starvation. (a) 8 obese men, 3-weeks fast (group 9, Table 1). (b) 8 obese women, 4-weeks fast (group 10). (c) 8 obese women, fasted twice for two weeks and given 600 Cal/24 hr on 4 days in between (group 11)

From Table 4 it can be seen that during a six day fast about 80% of calorie output was provided by fat, 4–5% by glycogen and 10–15% by protein, the latter being highest in normal men and lowest in obese women. During prolonged fasting the mean contribution of body protein to total energy expenditure was from 5–8%. During the last week of fasting in groups 10 and 11 the contribution of protein approximated 5% and the one of fat 95%.

## Discussion

The data obtained during a 6 day fast reveal that nitrogen loss in men is significantly higher than in women, even if closely matched for age and weight. This sex difference in protein mobilization was demonstrated both in normal and obese subjects. Several factors might contribute to this finding: Differences in endocrine regulation of metabolism, the known

higher proportion of lean tissue and protein in total body mass (Forbes *et al.*, 1970) and the somewhat higher basal metabolism [27] in men.

In view of the higher energy expenditure and the larger protein stores of the obese (Cahill *et al.*, 1968), the finding that our obese subjects mobilized no more protein during fasting than lean ones was rather unexpected. However, in a study by Adibi (1971) massively obese patients (102–203 kg body weight) excreted even somewhat, although not significantly, less nitrogen during a 6 day fast than normal subjects. The normal group studied by Adibi was composed of 4 women and 2 men; mean daily nitrogen losses ranged from 9–10.5 g during the 6 day fast; no separate results for men and women were given.

In spite of differences in magnitude of nitrogen excretion, its pattern during a 6 day fast was strikingly uniform in that all groups studied showed a transient increase. This pattern was more pronounced in the young groups 1–4 (Table 3, Fig. 1) than in the somewhat older groups 9–11 (Fig. 2). A similar transient rise in urinary nitrogen excretion was described by Cahill *et al.* (1966) in 6 normal men fasted for 7 days. Since liver glycogen is almost depleted after one day of fasting, later on glucose concentrations have to be maintained largely by gluconeogenesis from amino acids (Hultman *et al.*, 1971; Cahill, 1971) which is paralleled by urinary nitrogen excretion (Owen *et al.*, 1969; Ditschuneit *et al.*, 1970). Hence the nitrogen loss early in starvation was interpreted by Cahill (1970) as a mechanism for providing glucose until brain adapts to keto-acid utilization. In obese subjects it has been shown that increased gluconeogenesis early in starvation corresponded to a rise in plasma glucagon. Since this hormone may promote increased extraction of gluconeogenic amino acids by the liver, glucagon has been implicated in the transient acceleration of gluconeogenesis (Marliss *et al.*, 1970). As can be seen from Fig. 1 a similar coincidence of increased gluconeogenesis from amino acids (as evidenced by urinary nitrogen excretion) and plasma glucagon rise was found in this group of normal subjects. That gluconeogenesis declined after day 3 of fasting in spite of continuous elevation of plasma glucagon (Fig. 1) may be due to progressive diminution of peripheral amino acid release (Cahill, 1971). The control of peripheral release of gluconeogenic amino acids during starvation has so far not been fully clarified.

It is recognized that the method used to estimate the composition of calorie consumption (Krizek *et al.*, 1969) affords only an approximation to the true state of affairs. However, another current method, combination of urinary nitrogen measurement and indirect calorimetry at the basal state (Cahill *et al.*,

1966) would not determine the amount and origin of calories expended at higher levels of physical activity. In this study the caloric output derived from protein was determined by urinary nitrogen measurement; that derived from glycogen at any rate is quite small, especially for longer periods of starvation. Figures given for total calorie expenditure are within the range found by others [10, 15], but even allowing for an error of  $\pm 10$ –20% it may be concluded that during a 6 day fast protein breakdown accounted for 10–17% of caloric output in normals, for 8–15% in the obese, and for about 5% in obese women during the fourth week of starvation.

Protein and lean body mass (LBM) losses found during prolonged fasting were of considerable magnitude. In the obese men fasted for 3 weeks the mean protein loss was 1240 g (Table 2) which corresponds to a LBM loss of 6.2 kg [10, 19, 26]. In the groups of women fasted for either 4 weeks or intermittently for twice 2 weeks protein and LBM losses approximated 1000 g and 5 kg, respectively. However, since in the obese not only fat but also protein stores are increased (Cahill *et al.*, 1968) and since starvation is followed by anabolism [11, 25, 29], a negative nitrogen balance is not considered a major disadvantage of therapeutic fasting. In view of the great decline of protein and LBM losses during weeks 1–3 of fasting, longer periods of starvation appear to have a more desirable effect on body composition of obese patients.

## References

1. Adibi, S.A.: Alteration in the urinary excretion rate of amino acids and nitrogen by dietary means in obese and normal human subjects. *J. Lab. Clin. Med.* **77**, 278 (1971)
2. Barnard, D.L., Ford, J., Garnett, E.S., Mardell, R.J., Whyman, A.E.: Changes in body composition produced by prolonged total starvation and refeeding. *Metabolism* **18**, 564 (1969)
3. Bortz, W.M.: Editorial comment. *Metabolism* **17**, 391 (1968)
4. Cahill, G.F., Jr., Herrera, M.G., Morgan, A.P., Soeldner, J.S., Steinke, J., Levy, P.L., Reichard, G.A., Jr., Kipnis, D.M.: Hormone-fuel interrelationships during fasting. *J. Clin. Invest.* **45**, 1751 (1966)
5. Cahill, G.F., Jr., Owen, O.E., Morgan, A.P.: The consumption of fuels during prolonged starvation. *Adv. Enzyme Regul.* **6**, 143 (1968)
6. Cahill, G.F., Jr.: Starvation in man. *N. Eng. J. Med.* **282**, 668 (1970)
7. Cahill, G.F., Jr.: Physiology of insulin in man. *Diabetes* **12**, 799 (1971)
8. Darke, S.J.: The cutaneous loss of nitrogen compounds in African adults. *Brit. J. Nutr.* **14**, 115 (1960)
9. Deitrick, J.E., Whedon, G.D., Shorr, E.: Effects of immobilization upon various metabolic and physiologic functions of normal men. *Amer. J. Med.* **4**, 3 (1948)
10. Ditschuneit, H., Faulhaber, J.-D., Beil, I., Pfeiffer, E.F.: Veränderungen des Stoffwechsels bei Null-Diät. *Internist* **11**, 176 (1970)

11. Drenick, E.J., Hunt, I.F., Swendseid, M.E.: Influence of fasting and refeeding on body composition. *Am. J. Publ. Health* **58**, 477 (1968)
12. Forbes, G.F., Reina, J.C.: Adult lean body mass declines with age: Some longitudinal observations. *Metabolism* **9**, 653 (1970)
13. Göschke, H.: Estimation of ketone bodies in blood, cerebrospinal fluid and urine. *Clin. Chim. Acta* **28**, 359 (1970)
14. Göschke, H.: Zur Behandlung der Adipositas mit prolongiertem Fasten. *Schweiz. med. Wschr.* **101**, 940 (1971)
15. Grande, F.: Energetics and weight reduction. *Amer. J. Clin. Nutr.* **4**, 305 (1968)
16. Hultman, E., Nilsson, L.H.: Liver glycogen in man. Effect of different diets and muscular exercise. *Adv. Exp. Med. Biol.* **11**, 143 (1971)
17. Jarret, F.: Intravenous Hyperalimentation. *Progress in Surgery* **13**, 138 (1974)
18. Kinney, J.M., Long, C.L., Duke, J.M.: In: Energy metabolism in trauma, page 103. R. Porter and J. Knight, eds. Ciba Foundation Symposium, London 1970
19. Krizek, V., Stepanek, P., Sadilek, L.: Starvation and anabolic steroids. *Metabolism* **7**, 585 (1969)
20. Marliss, E.B., Aoki, Th.T., Unger, R.H., Soeldner, J.St., Cahill, G.F., Jr.: Glucagon Levels and metabolic effects in fasting man. *J. Clin. Invest.* **49**, 2256 (1970)
21. Morgan, A., Filler, R.M., Moore, F.D.: Surgical Nutrition. *Med. Clin. N.A.* **54**, 1367 (1970)
22. Owen, O.E., Morgan, A.P., Kemp, H.G., Sullivan, J.M., Herrera, M.G., Cahill, G.F., Jr.: Brain metabolism during fasting. *J. Clin. Invest.* **46**, 1589 (1967)
23. Owen, O.E., Felig, Ph., Morgan, A.P., Wahren, J., Cahill, G.F., Jr.: Liver and kidney metabolism during prolonged starvation. *J. Clin. Invest.* **48**, 574 (1969)
24. Owen, O.E., Cahill, G.F., Jr.: Metabolic effects of exogenous glucocorticoids in fasted man. *J. Clin. Invest.* **52**, 2596 (1973)
25. Rath, R., Masek, J.: Changes in the nitrogen metabolism in obese women after fasting and refeeding. *Metabolism* **15**, 4 (1966)
26. Reifenshtein, E.C., Jr., Albright, F., Wells, Sh.L.: The accumulation, interpretation, and presentation of data pertaining to metabolic balances, notably those of calcium, phosphorus and nitrogen. *J. Clin. Endocrin.* **5**, 367 (1945)
27. Sandoz, Basel: Nomogramme für Grundumsatz-Bestimmung
28. Stahl, M., Girard, J., Rutishauser, M., Nars, P.P., Zuppiger, K.: Endocrine function of the pancreas in cystic fibrosis: Evidence for an impaired glucagon and insulin response following arginine infusion. *J. Pediat.* **84**, 821 (1974)
- 28a. Stahl, M.: Probleme und Bedeutung der quantitativen Glucagonbestimmung im Kindesalter. Habilitationsschrift 1973, Universität Basel
29. Van Riet, H.G., Schwarz, F., Der Kinderen, P.J.: Metabolic Observations during the treatment of obese patients by periods of total starvation. *Metabolism* **13**, 291 (1964)
30. Wauters, J.P., Busset, R., Dayer, A., Favre, H.: Effets de divers traitements amaigrissants sur la composition corporelle dans l'obésité simple. *Schweiz. med. Wschr.* **100**, 1272 (1970)

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