

In the presence of DNP, transport was depressed at all levels of intestine and, except for the persistence of a very slight decline along the ileum, the longitudinal gradient was abolished. The energy-independent transfer that remains after DNP poisoning could represent either passive or facilitated diffusion. The fact that essentially no gradation in activity persists in the presence of DNP indicates that the peak activity in segments 4-6 observed without DNP is not due to some morphological or mechanical factor or to some regular bias inherent in the procedure, but is due to a specific distribution of the active transport system along the intestine.

The Figure illustrates the point that in order to measure the maximum effect of an inhibitory agent on transport, in either absolute amounts or percentages, the site along the intestine capable of maximum transport should be chosen for study. This point has been illustrated previously for the effects of hypoxia, fluoride and bile salts on glucose transport^{2,13}.

Zusammenfassung. Der Transport des L-Methionins durch die Rattendarmwand wurde in vitro untersucht. Die Transportgeschwindigkeit im Verlaufe von 1 h ist am höchsten im unteren Jejunum und im oberen Ileum (Abschnitte 4, 5 und 6). DNP-verursachte Hemmung ist in diesen Darmabschnitten am stärksten, was das Verschwinden des Maximums bewirkt.

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¹³ A. S. NUNN, R. D. BAKER, and G. W. SEARLE, *Life Sci.* 9, 646 (1963).

Sex Difference in Liver Tryptophan Pyrrolase Activity of Starved Rats

Liver tryptophan pyrrolase (LTP) activity in female rabbits subjected to starvation has been characterized by ROSENTHAL et al.¹ as a bimodal response with peak values occurring within 18-36 h and between 7-11 days from commencement of starvation. CHIANCONE², however, obtained no significant alteration of LTP activity in male rats subjected to fasting for 8-13 days. It seemed pertinent therefore to investigate the influence of sex on the LTP activity of rats subjected to starvation.

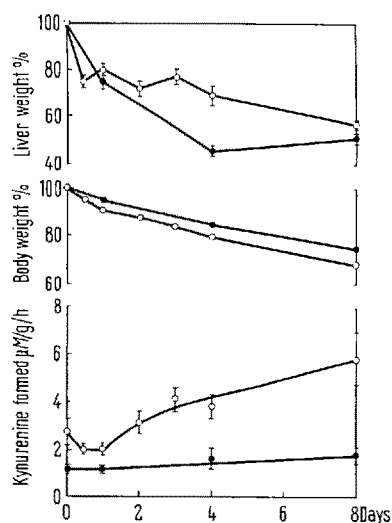
Adult Sprague-Dawley rats of both sexes were maintained ad libitum on commercial rat checkers before being used in the starvation experiments. Water was available to the animals at all times. The estimation of enzyme activity was identical to that of ROSENTHAL et al.¹ except that entire livers from one to three identically treated rats were pooled to yield a minimum of 7 g for homogenization. Although the data are presented on a fresh tissue weight basis, calculations on a protein basis yield essentially comparable results.

In male rats fed ad libitum, the LTP activity averaged $1.04 \mu\text{M}$ kynurenine formed/g/h which increased to $1.86 \mu\text{M/g/h}$ after 8 days' starvation, but this difference is of doubtful significance (Figure). In ad libitum fed female rats, however, the LTP activity ($2.70 \mu\text{M/g/h}$) was about three times higher than in ad libitum fed males. The value decreased to a minimum ($1.98 \mu\text{M/g/h}$) after 24 h starvation before again increasing to $5.75 \mu\text{M/g/h}$ after 8 days' starvation. For male and female rats, body and liver weight decreased in a regular fashion during the starvation period.

The variability and the high values of ad libitum fed female rats suggested the possibility that a bimodal response may occur very early and, because rats eat regularly between periods of 2-4 h, the ad libitum fed female rats may have been voluntarily starved for a short period of time. In order to test this hypothesis, and to stabilize the animals in a more constant physiological state, re-feeding techniques were initiated. Rats were initially starved for 24 h and then re-fed ad libitum for 48 h thus

giving assurance that the animals were well fed, as shown by a rapid regaining of body weight after refeeding (Table, Group C). The effect of short periods of starvation (4 and 24 h) on the LTP activity, liver weight and body weight of such *refed* rats, is presented in the Table.

In male rats, the LTP activity was not altered significantly by this procedure, but in female rats (Group C) the enzyme activity decreased to $1.06 \mu\text{M/g/h}$. It may be noted that the LTP activity of both male and female rats



Kynurenine formation, body weight and liver weight of male (—●—) and female (—○—) rats vs. days of starvation. Each point represents average data obtained for 6 to 9 determinations. The vertical bar represents 1 standard error.

¹ H. L. ROSENTHAL, B. M. BARACK, and I. HAESSLER, *Proc. Soc. exp. Biol. Med.* 117, 222 (1964).

² F. M. CHIANCONE, *Boll. Soc. ital. Biol. sper.* 31, 1310 (1955).

Liver tryptophan pyrrolase (LTP) activity of male and female rats

Group	Treatment ^a	No.	Body weight g	Liver weight g	LTP Activity ^b $\mu\text{M/g/h} \pm \text{S.E.}^c$	Total LTP Activity $\mu\text{M/h}$
Female						
A	Fed ad libitum	12	266	9.9	2.70 ± 0.63	26.7
B	Starved 24 h	11	242	7.8	1.98 ± 0.19	15.4
C	B + refed 48 h	6	269	10.5	1.06 ± 0.11	11.1
D	C + restarved 4 h	7	269	8.5	2.26 ± 0.34	19.2
E	C + restarved 24 h	7	253	7.2	1.06 ± 0.18	7.6
Male						
A	Fed ad libitum	7	452	15.9	1.04 ± 0.12	16.5
B	Starved 24 h	7	425	12.0	1.06 ± 0.12	12.7
C	B + refed 48 h	4	454	11.0	1.24 ± 0.40	13.5
D	C + restarved 4 h	4	453	10.8	1.36 ± 0.17	14.7

^a See text for experimental details. ^b Significance. Females: C vs. A, $P < 0.05 > 0.01$; C vs. B, $P < 0.01$; C vs. D, $P < 0.01$. Males: Groups A, B, and D not significantly different from C. ^c S.E. = Standard error.

(Group C) was similar following the starvation-refeeding regimen. The LTP activity in *refed* male rats subjected to 4 h starvation is unaffected, but in similarly treated female rats, the LTP activity increased from 1.06 to 2.26 $\mu\text{M/g/h}$ (Group D), a value not significantly different from that found in ad libitum fed untreated animals (Group A). In refed female rats starved for 24 h (Group E), the LTP activity again decreased to the refed values of Group C. The total LTP activity for both male and female animals reflect the changing enzyme activity comparable to that expressed on a concentration basis.

The present data confirm the report of CHIANCONE² that LTP activity of male rats is not significantly altered during starvation. However, the enzyme activity in female rats is markedly affected by the stress of starvation in accord with the responses found in female rabbits¹.

Female rats and rabbits subjected to the stress of fasting show a bimodal response of LTP activity which varies with the duration of starvation and the time interval for each response is dependent on the species. Although the starvation response occurs only in female animals, SCHOR and FRIEDEN³ obtained a bimodal response of LTP activity in male and female rats injected with alloxan. The induction of LTP activity following parenteral injections of L-tryptophan^{4,5} or cortisone⁶⁻⁸ also occurs in both male and female animals. OELKERS⁹ has recently demonstrated in vitro depression of tryptophan pyrrolase by free estrogens and estrone sulfate. It is conceivable that starvation of female animals may alter estrogenic activity.

Our data suggest that the difference in LTP response between male and female animals during starvation differs

from other inducing systems for LTP by a mechanism that is as yet ill defined and unknown¹⁰.

Zusammenfassung. Die Tryptophanpyrrolase (LTP) ausgewachsener weiblicher Ratten nimmt während 4-stündiger Hungerperiode von 1,06 μM Kynurenin auf 2,26 $\mu\text{M/g/h}$ zu. Sie erreicht nach 24 h wieder Normalwerte, um dann während einer 8-tägigen Hungerperiode auf 5,75 $\mu\text{M/g/h}$ anzusteigen. Die LTP männlicher Ratten zeigt nur unbedeutenden Anstieg während gleicher Hungerperioden.

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Zur zellulären Aminosäure-Inkorporation im in- und exkretorischen Pankreas unter experimentellen Bedingungen

In Anlehnung an Studien zum RNS-Stoffwechsel im Pankreas¹ nahmen wir an normalen und vorbehandelten Ratten (Versuchsbedingungen in der Tabelle) autoradiographische Untersuchungen der nuklearen und cyto-

plasmatischen Eiweiss-Synthese (EW-S) von Inselzellen vor. Ferner führten wir Aktivitätsmessungen (Methan-durchfluss) im exkretorischen Parenchym durch (2,0 mCi ³H-I-Phenylalanin; spezifische Aktivität 39,4 Ci/mM; i.p.; Tötung jeweils nach 1 h; Einzelheiten der Methodik siehe ¹). Um den experimentell induzierten Einfluss auf den Pool der freien Aminosäure ausgleichen zu können, wurden ausserdem Aktivitätsmessungen in Vergleichs-