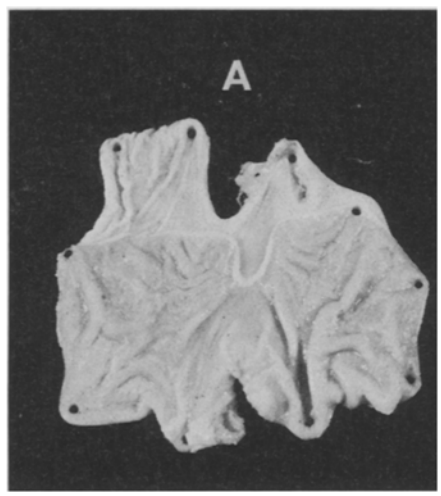

Fig. A) Stomach of a control rat. The animal was fed 1 h/day and kept in standard laboratory cage for 2 weeks.

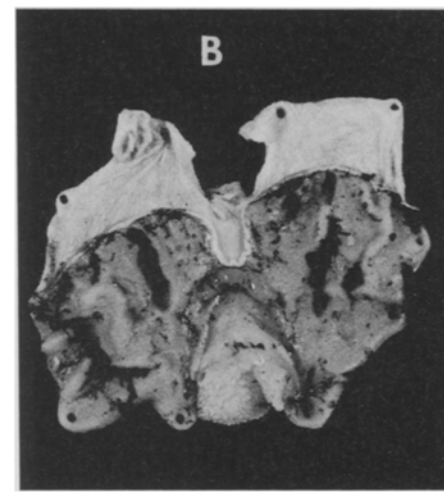

Fig. B) Stomach of an 'active' rat. The animal was fed 1 h/day and kept in an activity wheel for 2 weeks. The antral area and body of the stomach show confluent ulceration.

Most of the animals with exertion ulcers survive the procedure while in 'self-starvation' conditions, especially if the laboratory chow diet is used as the food, the majority of the animals die within 2 weeks[5]. The possible role of the composition of the diet in the 'self-starvation' phenomenon is also suggested by the observation that an isocaloric substitution of the laboratory chow diet by a high fat diet protected animals against death[5].

The pathogenesis of the gastric lesions observed in the 'self-starved' rats is not clear at this time. However, morphologically they resemble the picture of 'stress' ulcers or an acute hemorrhagic gastritis, which are at this time believed to be due to a damaged gastric mucosal barrier and increased back diffusion of hydrogen ions[10].

The results of the present study indicate that early death in 'self-starved' animals is probably a result of extensive gastric lesions and associated blood loss. Furthermore, our data suggest that gastric ulcers may be produced in rats without the use of force or drugs[11].

Zusammenfassung. Nachweis von Magenulzerationen und Magenerosionen bei Albinoratten nach bestimmter Fütterung und nachherigem Laufkäfig-Aufenthalt. Problem der Stressulzeration und die Rolle der Diät werden erörtert.

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Compartmental Analysis of Efflux of Extracellular Space Markers in Rabbit Detrusor Muscle

In a previous study[1] the volume of the extracellular space in isolated rabbit detrusor muscle was examined using [^{14}C]-labelled mannitol, sucrose, inulin and dextran. The uptake of mannitol and sucrose reached equilibrium at a volume of about 60 ml/100 g wet wt after 1–2 h whereas the uptake of inulin and dextran was not only slower, equilibration being reached after about 2 h, but also was smaller, the equilibration volume being about 43 ml/100 g wet wt. Graphical analysis of efflux data showed that the efflux of mannitol, sucrose and inulin was incomplete even after 6 h and was multicompartmental in nature. In the present study, the efflux of [^{14}C]-labelled mannitol, sucrose and inulin has been analyzed further using a computer programme, written for the APL/360 System[2], so as to obtain data on the number and sizes of compartments and their rate constants and half times.

Materials and methods. Pieces of rabbit detrusor muscle were prepared and subsequently labelled with tracer concentrations of [^{14}C]-labelled mannitol, sucrose or inulin as described previously[1]. At the end of this period tissues were removed, blotted, rinsed rapidly and transferred to a series of tubes containing tracer-free Krebs solution. Efflux was then followed for 6 h. The [^{14}C]-content of tissues and of all efflux material was determined by

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liquid scintillation spectrometry as described previously[1].

It was assumed that the [^{14}C] tracer was released from a number of compartments exponentially. The dpm/min in the tissue at time t [$f(t)$] will thus be given by the equation:

$$f(t) = \sum_{i=1}^{n} A_i \exp^{-K_i t} + D$$

where A_i represents the compartment size; K_i is the efflux rate constant; n is the number of compartments; and D represents a bound fraction from which there is no appreciable efflux during the duration of the experiment.

Values for these parameters were determined using the computer programme described by COOK and TAYLOR[2] based on the model developed by DANIEL and ROBINSON[3]. The size of the bound fraction (D) was determined using the method of DICK and LEA[4]. The method proposed by HUXLEY[5] was used to correct for the interaction between compartments on the assumption that they were in series.

Results. In all experiments, plots of rates of efflux versus tissue radioactivity[4] revealed positive intercepts of tissue radioactivity at zero efflux. After subtraction of this value, the final slopes in log – log plots of efflux rate versus tissue radioactivity became close to one. Hence a bound (or very slowly exchangeable) fraction (D) must be postulated for all three compounds. After subtraction of this bound fraction, computer analysis showed that 3 exchangeable fractions could best account for the observed efflux of mannitol, sucrose and inulin in rabbit detrusor muscle, thus confirming the previous graphical analysis[1]. Since 3 exponential terms were required to fit the data, efflux may be defined as:

$$Y = \text{tissue radioactivity,}$$
$$= A \exp(-K_1 t) + B \exp(-K_2 t) + C \exp(-K_3 t) + D$$

Values for these parameters, corrected by the method of HUXLEY[5], are given in the Table. It can be seen that the efflux of mannitol and sucrose could be described by compartments with essentially similar sizes, rate constants and half times. However, the size of the fast compartment (A) of efflux of mannitol and sucrose was approximately equal to the total space occupied by inulin.

Discussion. Many authors[2,3,6–8] have pointed out that the analysis of efflux curves as sums of exponential curves is subject to many difficulties. In the method[2] used in this study, the standard error of the observed points from those obtained by peeling the curve using every possible combination, is computed. The arrangement providing the smallest standard error will thus provide the parameters which describe the observed curve most accurately. However, any of the exponential terms may contain further terms representing efflux from different physical compartments with similar rate constants.

About 5% of [^{60}Co]-EDTA and of [^{14}C]-sorbitol taken up by guinea-pig *Taenia coli*[9] exhibited slow efflux kinetics. Similar findings for the efflux of other extracellular space markers have been reported for myometrium[3,10] frog stomach muscle[11] and guinea-pig ileum[12].

From the Table it can be seen that the size of the fast compartment (A) for both mannitol and sucrose was equal to the total space (compartments A + B + C) occupied by inulin. If compartments B and C for mannitol and sucrose are intracellular in location, then the total inulin space may be an approximate measure of the extracellular space in this tissue. Further work is required however to determine whether this is indeed the case. Evidence that sucrose and mannitol do indeed enter the intracellular compartment(s) in this tissue, has been provided by calculations of the intracellular Na^+ concentrations using the total spaces occupied by mannitol and sucrose as measures of the extracellular space[1].

Compartmental analysis of efflux of extracellular space markers in rabbit detrusor muscle

Parameters	Extracellular space marker		
	Inulin	Mannitol	Sucrose
A	19.2 ± 1.8	43.6 ± 7.2	38.4 ± 3.9
t	3.8 ± 1.2	5.7 ± 2.7	4.5 ± 1.2
K_1	0.2379 ± 0.0636	0.2208 ± 0.0838	0.1883 ± 0.0464
B	10.4 ± 3.6	12.9 ± 5.6	11.7 ± 3.9
t	28.4 ± 8.5	20.7 ± 7.7	17.4 ± 2.5
K_2	0.0315 ± 0.0076	0.0445 ± 0.0101	0.0419 ± 0.0051
C	11.5 ± 1.7	2.5 ± 0.42	3.2 ± 0.48
t	60.0 ± 8.1	98.6 ± 13.9	96.7 ± 12.6
K_3	0.0127 ± 0.0014	0.0074 ± 0.0009	0.0075 ± 0.0008
D	0.8 ± 0.08	1.4 ± 0.14	3.3 ± 0.29

A, B, C and D are in ml/100 g wet weight; t are in min; K_1, K_2 and K_3 are in min^{-1}; Mean ± S.E. of the mean of 4 observations.

Zusammenfassung. Mit Hilfe des Computers wurde die Abgabe von [^{14}C]-markiertem Mannit, Succrose und Inulin aus isoliertem Kaninchen-Detrusormuskel analysiert. Alle drei Verbindungen werden aus mindestens drei Abschnitten abgegeben und aus einer gebundenen Fraktion gelöst. Die Grösse des am raschesten von Mannit und Succrose beanspruchten Abschnittes entspricht derjenigen des Inulins.

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