levels after SD, indicate that the cortical tissue in the U and DU groups was in a state of higher neuronal excitability than that of the control animals; this was more evident in the DU group. A possible explanation for the higher propagation rate of SD in undernourished animals could be, as suggested[4], the impairment of myelination caused by undernutrition[11]. Cellular[12-14] as well as neurochemical[3,15] alterations observed during undernutrition may also have contributed to the increased cortical excitability reported here. In addition, epileptiform activity associated with higher SD propagation rate and higher incidence of 'spontaneous' SD has been described in adult rabbits submitted to an acute alteration of the extracellular ionic environment[10]. Clinical[16] and experimental[17,18] evidence shows that the metabolism of water and electrolytes is disturbed during undernutrition. It is thus possible that dehydration, when associated with undernutrition, has a physiopathological significance different from that observed in the well-nourished condition. This possibility, specifically concerning brain excitability, seems to be supported by the present results. In conclusion, the present results show that dehydration early in life makes adult rats, undernourished after weaning, more susceptible to cortical SD, the opposite effect being observed in well-nourished animals. Since dehydration was performed early in life, and the effects on SD were observed in the adult animals, it is clear that a long-lasting change must have occurred in the brain. Additional studies are clearly warranted to reveal the underlying mechanisms, the effects of which have been observed in the present study. The experimental model described here may be useful for that purpose. It would also interesting to investigate the association between undernutrition and disturbances in body water and electrolyte contents observed in children[19,20], in order to detect any possible effect of such an association on brain excitability.

1 This work was supported by the Brazilian agencies CNPq and CAPES and by the Federal University of Pernambuco. The suggestions of Dr T.P. Hicks, which contributed to improve the English text, are very much appreciated.
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Relationship between glucose absorption and villus height in ageing

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Summary. There is a diminution of D-glucose absorption in the aged rat which is partly due to the decrease of the length of the villi.

The role of ageing in sugar absorption from the intestine has already been discussed by numerous authors[1-5]. However, there are discrepancies because of the different indices used. According to the literature, the number of villi does not change with age[6-11]. Therefore we decided to study whether the height of the villi changes during senescence and if so, in how far these changes influence their functional role, i.e. glucose absorption.

We used a low sugar concentration (4 mM), firstly to limit passive diffusion, and secondly because hardly any data are available on the absorption of this relatively low luminal sugar concentration. We also wanted to simulate the conditions in the aged small intestine, where lower intraluminal glucose concentrations may occur owing to reduced disaccharidase efficiencies[5].

Materials and methods. Young (6-month-old), adult (12-month-old) and aged (24-month-old) female Wistar rats were used. The animals were fasted overnight before the experiment. After Nembutal® anaesthesia the abdominal cavity was opened and the Musacchia[12] method applied. The small intestine was washed with Krebs-Henseleit bicarbonate saline and 6 cm segments prepared from the duodenum (D), jejunum (J) and ileum (I). 1.5 ml 4 mM D-glucose solution was introduced into each of the segments and the cavity clamped. Special care was taken to maintain the appropriate ambient temperature during the experiment. After 20 min the loops were emptied, the luminal content collected and centrifuged, and the glucose concentration determined according to Hultman[13], Hyvärinen and Nikkilä[14]. The sugar absorbed was related to the wet intestinal weight (segment-length in cm and 20 min). The wet weight/segment-length ratio was found to be constant during ageing, i.e. it does not alter the rate of absorption itself. A Carl Zeiss microprojecting device was used for the microscopical evaluation of the length of the villi.

Results. Figure 1 shows that glucose absorption was highest in the jejunum of young rats while it was less high in the duodenum and ileum. Identical findings were recorded in adults, and similar values were found in the duodenum and jejunum in the old rat. Less absorption was observed in the

old ileum. With the advance of age, absorption rate decreases in both the jejunum (J_{young}-J_{adult}: $p<0.01$; J_{young}-J_{old}: $p<0.01$), and the ileum (I_{young}-I_{old}: $0.02>p>0.01$). No changes were recorded in the duodenum. Changes in villus length are seen in figure 2. There was a decrease of villus length from the beginning of the duodenum to the end of the ileum. There was also a significant age-related reduction in villus height. This reduction differed however in the young and old ($p<0.01$) as well as the adult and old ($p<0.01$) duodenum. Similar values were established in the young and old jejunum ($p<0.01$) and adult and old jejunum ($p<0.01$) as well as in the ileum of the young and old rats ($p<0.01$) and for the young and adult ileum ($0.05>p>0.02$) and adult and old ileum ($p<0.01$). Figure 3 illustrates the relationship between absorption rate and villus height. Regression equations show that there is a clear-cut correlation ($r=1.00$) between absorption from the ileum and the height of the villi and it appears that a similar relationship ($r=0.87$) exists between jejunal absorption and villus length. No such relationship could be shown in the duodenum.

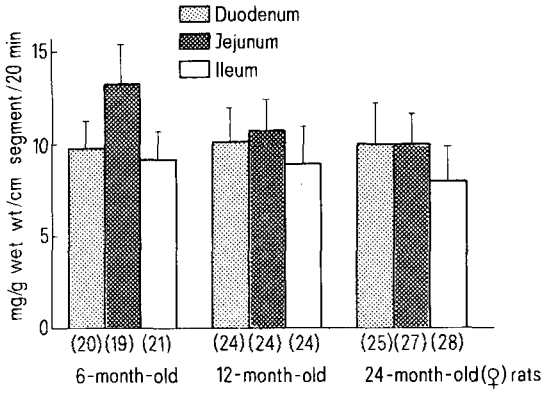

Fig. 1. Absorption of D-glucose from the duodenum, jejunum and ileum.
Verticals represent SD values. Number of animals in parentheses.

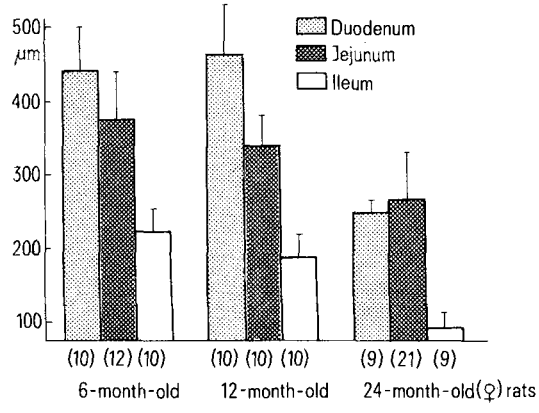

Fig. 2. Changes in villus height in the duodenum, jejunum and ileum.
Verticals represent SD values. Number of animals in parentheses.

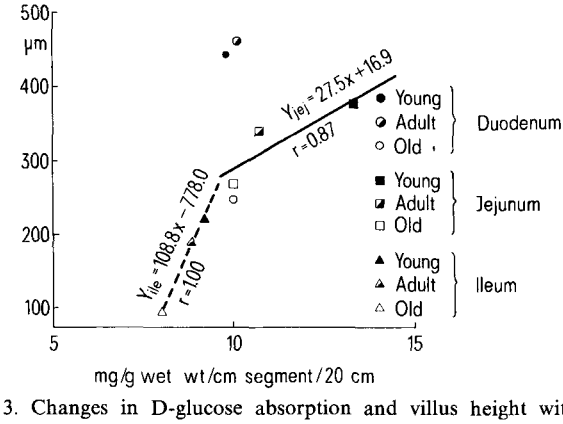

Fig. 3. Changes in D-glucose absorption and villus height with ageing.

Discussion. Our findings permitted the conclusion that the height of the villi decreases with age and might be one of the reasons for decreased sugar absorption. Reductions in villus length were most conspicuous in the duodenum and ileum, and less striking in the jejunum. In general, our observations are similar to those published by other authors; however, there are some differences. Clarke[15] reported that villus height decreases in the proximal intestine in ageing (about 1-year-old) male rats. Höhn et al.[16] using male rats, emphasized that the mucosal atrophy manifests itself mainly in a considerable reduction of the height of the villi in the proximal regions of the small intestine, while no such changes could be detected in the distal small intestine. The difference concerning the distal regions could be related to sex. One aspect of these intriguing phenomena might be the changes in absorption. There are some indications in the recent literature that sex may possibly modify the absorption of some metals. According to Dupuis et al.[17], increased calcium absorption occurs in the ileum of the female adult rat as compared to the male. This is based on the prolongation of Ca absorption. Our rats were females and this might partly explain the discrepancy, i.e. reduced villus height in the distal part as compared to the other regions of the small intestine.

With respect to the relationship between absorption and villus height, it should be mentioned that a similar tendency was observed by Menge et al.[18] who found a correlation ($r=0.83$) between jejunal glucose absorption and villus height. There was, however, no relationship between tryptophan absorption and the height of the villi in control animals and rats with excluded jejunal loops. It is hard to explain in the present study why no correlation was observed in the duodenum, in fact, there are no available data which refer to this proximal region of the entire small intestine. In our previous study[19] using a kinetic approach, we found that the absorption of D-glucose from the intestinal lumen at small (initial) concentrations (< 10 mM) takes place at a higher rate in the young rat than it does in advanced age. The present data, based on a 4 mM initial luminal concentration, seem to confirm these findings. It appears logical to believe that these changes during senescence are related not only to the length of the villi but, in general, to the absorption capacity of the small intestine as well. Nevertheless, the possible role of the age-dependent changes of the intestinal glucose carriers cannot be ruled out.

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Quercetin enhances water transport in toad bladder

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Summary. A highly significant enhancement of the hydrosmotic actions both of vasopressin and of exogenous cAMP was seen in the presence of quercetin. The hypothesis is advanced that quercetin affects the intracellular coupling between Ca^{++} and cAMP.

Work from this laboratory has shown that some inhibitors of (Na+K)ATPase, e.g. harmaline and vanadate, affect water transport across amphibian epithelia[2-4]. This property, which is not shared by the classical Na pump inhibitor, ouabain, can be used to analyze fundamental aspects of epithelial transport, such as the coupling of Na and water flows, and the mechanism of the modulation of cell permeability by hormonal signals[2-4]. Along this line, we investigated the effects of the flavonoid quercetin, another inhibitor of (Na+K)ATPase[5]. We report here that quercetin quickly and reproducibly enhanced the transepithelial water flow (J_w), induced by vasopressin or by exogenous cAMP, in toad bladder.

Materials and methods. Tropical toads *(Bufo marinus)* were obtained from Charles P. Chase Co., Miami, Florida, USA, and kept in a terrarium with free access to water. The urinary bladders were exposed to a standard osmotic gradient of approximately 200 mosm/kg H_2O. The composition of the Ringer solution was (in mM): NaCl, 112; $MgSO_4$, 1; KH_2PO_4, 1.2; $KHCO_3$, 2; $CaCl_2$, 1; osmolality, 220 mosm/kg H_2O; pH was adjusted to 7.8. The serosal side of the bladder was bathed by full-strength Ringer and the mucosal side by the same solution diluted 10-fold. Transepithelial water fluxes were continuously monitored with automatic, volumetric techniques previously described[2,6,7]. The drugs used were: vasopressin (Pitressin, Parke-Davis), cyclic AMP (Sigma) and quercetin (Sigma). The latter was dissolved in dimethylsulfoxide (DMSO), so that the concentration of DMSO was 0.05% (v/v) for 10^{-4} M quercetin in the Ringer solution. Where applicable, results were expressed as mean ± SEM and the p-values obtained by means of the Student's t-test for paired data.

Results. Quercetin can induce by itself a hydrosmotic effect across toad bladder. Although this action was not seen in every experiment, the increase in J_w was quite conspicuous and sustained in some bladders, as shown in figure 1. In a series of 12 consecutive experiments J_w went from 0.02 ± 0.01 to 0.30 ± 0.12 $\mu l \cdot min^{-1} \cdot cm^{-2}$ ($p < 0.05$), on addition of 0.1 mM quercetin to the serosal medium. Regardless of whether the drug stimulated J_w or not, the subsequent addition of vasopressin revealed that the hormonal effect was not only present (fig. 1) but even appeared to be enhanced by quercetin. To test this point, a series of paired studies was carried out in quarter-bladders of the same animal. Quercetin did potentiate the action of vasopressin (fig. 2) as can be easily seen by inspection of the peak values of J_w and of the cumulative J_w-values shown at the right hand side of the same figure.

As a step towards localizing the site of action of quercetin, we studied next the interaction between the flavonoid and exogenous cAMP. The results are summarized on figure 3 and clearly show that quercetin also enhanced the hydrosmotic action of cAMP. Finally, we looked at the action of quercetin in bladders in which J_w had been previously stimulated by vasopressin or cAMP. The drug produced a further increase in J_w, the onset of which was very rapid (within 1 min, see left part of figure 3, lower recording). Comparison of the cumulative J_w-values during 30-min periods before and after the addition of quercetin gave the following results: a) 35.8 and 72.0 $\mu l \cdot cm^{-2}$, respectively, in bladders preexposed to supramaximal concentration of vasopressin (50 $mU \cdot ml^{-1}$, $N = 9$, $p < 0.01$); b) 15.7 and 52.2 $\mu l \cdot cm^{-2}$, respectively, in bladders pre-exposed to cAMP (5 mM, $N = 6$, $p < 0.01$).

Discussion. The hitherto unreported effects of quercetin on water transport appear to be unique. Most drugs known to interfere with vasopressin-induced water flow in toad blad-

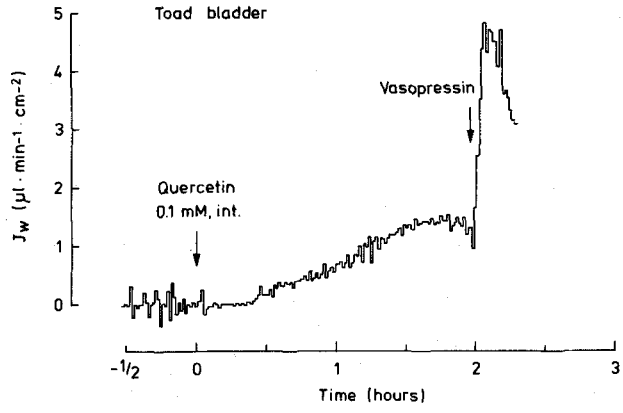

Figure 1. Stimulation of transepithelial osmosis (J_w) by quercetin added to the serosal (int.) medium bathing toad bladder. The presence of quercetin did not prevent a further increase in J_w by vasopressin (50 $mU \cdot ml^{-1}$).