THE INFLUENCE OF PREGNANCY AND LACTATION ON
THE MORPHOLOGY AND ABSORPTIVE CAPACITY OF
THE RAT SMALL INTESTINE

I. L. CRAFT

Institute of Obstetrics and Gynaecology, Chelsea Hospital for Women,
London, S.W.3

(Received 7 July 1969)

SUMMARY

1. A study of the length, total weight and weight per cm of the small intestine
of virgin, pregnant and lactating rats has provided evidence for an increase in
intestinal surface area in pregnancy and lactation.

2. Because of such alterations in morphology of the gut the absorption, in vivo,
of the substrates studied, glucose and glycine, has been expressed in terms of amount
transferred per loop and also per g dry weight of intestine.

3. Using these parameters the results show that pregnancy does not alter the
ability of the upper jejunum to absorb glucose and glycine. In lactation there is a
significant decrease in the transfer of these substances when expressed per g dry
weight of intestine, but not in absolute terms.

INTRODUCTION

It is known that hormonal states may modify intestinal absorption (Levin & Smyth, 1963;
Levin, Newey & Smyth, 1965; London & Segal, 1967). However, little is known of the effect
of pregnancy and lactation on this function. Penzes & Simon (1968) reported increased in vivo
absorption of DL-methionine in lactating rats but no significant change in pregnancy. Absorp-
tion was expressed as the lumen disappearance of methionine from the whole small intestine
over a given absorptive period. In the only other work on the effect of pregnancy Larralde,
Fernandez-Otero & Gonzalez (1966) reported increased in vivo absorption of glucose, and
Larralde & Fernandez-Otero (1968) reported increased in vitro absorption of glucose and
glycine in rats. In the first investigation absorption was expressed per cm length of intestine
perfused and in the second per everted gut sac. The interpretation of these results depends on
whether or not there is an alteration in mucosal surface area per unit length of intestine.

There is conflicting evidence as to the effect of pregnancy on the weight of the small intestine.
Abramson (1934) described an increase in rats, but Souders & Morgan (1957), who related
intestinal weight to corrected body weight (i.e. total body weight less that of the uterus and

Correspondence: Dr I. L. Craft, Department of Obstetrics and Gynaecology, Queen Mary's Hospital,

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contents), found no significant increase. However, no attempt has been made to relate intestinal weight to length in pregnancy. In lactation, hypertrophy of the gut wall and increase in intestinal length and weight have been described (Fell, Smith & Campbell, 1963) and these changes have been considered to be secondary to hyperphagia (Campbell & Fell, 1964). As an increased intake of food also occurs in pregnancy (Cole & Hart, 1938), similar changes are likely to result.

Whilst a net increase in absorption is to be expected in both conditions, it is of interest to know whether the absorptive capacity of a given area of mucosa is altered. If there is an increase in weight per unit length of intestine in these states, this suggests there may be an increase in mucosal surface area, and results of absorption studies might be more accurately assessed if expressed in absolute terms and also per unit weight of intestine, as suggested by Levin & Smith (1963). This study was therefore undertaken to evaluate the effect of pregnancy and lactation on the weight and length of the small intestine and on the absorption in vivo of glucose and glycine.

METHODS

Experimental procedure

The experiments were carried out on virgin female, pregnant and lactating white Wistar rats supplied by A. Tuck and Son, Rayleigh, Essex, and maintained on a cube diet (Oxoid No. 41B). Food and water were freely available. Pregnant animals were primiparae and 18–20 days pregnant at the time experiments were performed. Lactating rats were supplied at the time of weaning 21 days after delivery. Those used for the study concerned with the weight and length of the small intestine were from stock animals of the same age and mean initial body weight (range 190–200 g). Those used for the absorption study were from a more mature group of animals whose mean final body weights were: virgin 264 g ± SEM 4, n = 64; pregnant 312 g ± 8, n = 31; lactating 277 g ± 7, n = 21.

In preparation for measurement of the relative weights and lengths of the small intestine, food was withdrawn 18–24 hr before experiments, to reduce the lumen food content. Animals were killed by fracture-dislocating the cervical spine under ether anaesthesia and the abdomen opened in the midline. The small intestine from the pylorus to the caecum was removed, freed of its mesentery and its length measured immediately by holding vertically against a ruler. The lumen was then washed out with 0.9% saline and the intestine cut into shorter lengths, opened, gently blotted and weighed in a tared container to give the total wet weight. Dry weight was determined after drying at 120° for 24 hr.

The in vivo absorption study was undertaken using a closed loop method (Matthews et al., 1968). Animals were anaesthetized with ether and a loop of approximately 15 cm of proximal jejunum was made between ligatures starting at the duodeno-jejunal junction. This part of the intestine was used because of the ease of locating a comparable segment in different animals. 1.0 ml of the solution studied was introduced into the lumen through a fine needle (No. 21) attached to a tuberculin syringe. This volume caused moderate distension of each loop. (The exact volume introduced by each syringe was checked by weighing.) After an absorptive period of 5 min, the loop was removed and the animal killed. The contents were recovered by draining and their volume measured.

Glucose 10 m-mole/l and 20 m-mole/l, and glycine 10 m-mole/l, 20 m-mole/l and 50 m-mole/l solutions were used. In some experiments on virgin animals phloridzin (10 mg/100 ml) was
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added to glucose solutions. All solutions were made up in Krebs-Ringer bicarbonate saline, pH 7.4, and injected at room temperature. Radioactive tracer doses of $[^{14}C]$-labelled glucose and glycine were added to respective solutions before use. $[^{14}C]$-glycine (U) (specific activity 7-0 mCi/m-mole) and $[^{14}C]$-D-glucose (U) (specific activity 2-9 mCi/mmole) were supplied

| Table 1. Relationships between body weight, length, and wet and dry weights of the small intestine in virgin and lactating white rats (mean ± SEM) |
|---|---|---|---|---|---|
| No. of animals | Body weight (g) | Intestinal length (cm) | Wet weight (g) | Dry weight (g) | Water content (g) |
| Virgin | 15 | 218±1.5 | 107.4±1.6 | 3.74±0.09 | 1.00±0.04 | 2.74±0.05 |
| Lactating | 12 | 229±3.5 | 125.6±2.1 | 7.43±0.15 | 1.70±0.03 | 5.73±0.14 |
| $t$ | 2.930 | 6.805 | 20.968 | 12.209 | 20.703 |
| $P$ | < 0.01 | < 0.001 | < 0.001 | < 0.001 | < 0.001 |

| Table 2. Wet and dry weights of the small intestine expressed per cm length in virgin and lactating white rats (mean ± SEM) |
|---|---|---|---|---|
| No. of animals | Wet weight (mg/cm) | Dry weight (mg/cm) | Water content (mg/cm) |
| Virgin | 15 | 34.90±0.85 | 8.65±0.67 | 26.25±0.58 |
| Lactating | 12 | 59.22±1.91 | 13.52±0.24 | 45.70±1.14 |
| $t$ | 15.550 | 6.032 | 16.012 |
| $P$ | < 0.001 | < 0.001 | < 0.001 |

| Table 3. Relationships between body weight, length, and wet and dry weights of the small intestine in virgin and pregnant white rats (mean ± SEM) |
|---|---|---|---|---|---|
| No. of animals | Body weight (g) | Corrected body weight (g) | Intestinal length (cm) | Wet weight (g) | Dry weight (g) | Water content (g) |
| Virgin | 25 | 212±1.7 | 107.1±1.3 | 3.75±0.10 | 1.00±0.03 | 2.75±0.07 |
| Pregnant | 25 | 261±3.1 | 220±2.7 | 4.49±0.13 | 1.20±0.04 | 3.29±0.10 |
| $t$ | 13.460 | 2.475 | 4.383 | 3.969 | 4.308 |
| $P$ | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 |

freeze dried by the Radiochemical Centre (Amersham, Bucks). 50 mCi of each were made up in 5 ml 0.9% saline and 0.5 ml aliquots of each added to 100 ml of the appropriate solutions. 0.1 ml samples of the initial solution introduced into the lumen and the final solution recovered at the end of the absorptive period were assayed for radioactivity in a Nuclear-Chicago Model 6860 (Mark 1) liquid scintillation counter. The scintillation fluid was Nuclear Enterprises
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(Edinburgh) NE240 containing a dioxane base, plus 4% cab-o-sil used to form a gel to retain any solid particles in suspension. The counting efficiency of each sample was determined by reference to a calibration curve which was plotted from a set of quenched standards using an external $^{133}$Ba source and a channels ratio method.

<table>
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<tr>
<th>No. of animals</th>
<th>Wet weight (mg/cm)</th>
<th>Dry weight (mg/cm)</th>
<th>Water content (mg/cm)</th>
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</thead>
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<td>Virgin</td>
<td>25</td>
<td>35·15±1·13</td>
<td>9·34±0·36</td>
</tr>
<tr>
<td>Pregnant</td>
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<td>42·00±1·32</td>
<td>11·23±0·39</td>
</tr>
<tr>
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<td>3·869</td>
<td>3·480</td>
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<tr>
<td>$P$</td>
<td></td>
<td>&lt;0·001</td>
<td>&lt;0·01</td>
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</table>

Statistical methods

The significance of differences between mean values was assessed by the $t$ test, and values of $P = 0·02$ or less considered significant.

RESULTS

In the comparison of absorption in different physiological states the parameters used should, ideally, have the same significance. If results are expressed only in relation to the length of intestine across which transfer is occurring, then intestinal weight should be the same per unit length.

The results of this study show that lactation induces a significant increase in total length of the small intestine, in its total wet and dry weights, and in wet and dry weight per unit length (Tables 1 and 2). Table 3 shows that the length of the small intestine of pregnant animals is the same as that in virgin animals. However, there is a significant increase in total wet and dry weight and in wet and dry weight per cm length (Tables 3 and 4). Histological examination of sections of intestine taken from comparable sites in each of these groups of animals showed that lactation causes hypertrophy of all layers of the gut wall, including the villi, and suggested that this also occurred to a lesser degree in pregnancy.

Because of this evidence for an alteration in mucosal surface area per unit length of intestine in pregnancy and lactation, absorption has been expressed as absolute amounts of glucose and glycine absorbed per loop, and also per g dry weight of intestine. Fig. 1 shows that in virgin animals the relationship between initial lumen glucose concentration and the amount absorbed is linear over the concentration range studied. In the presence of phloridzin, absorption was markedly depressed to 24% of control values at 10 m-mole/l (1·63 mg±SEM 0·2 g dry wt$^{-1}$ 5 min$^{-1}$, $n = 5$, compared with 6·83±0·45, $n = 5$, in the control group); and to 58% at 20 m-mole/l (8·11±0·93, $n = 5$, compared with 14·11±0·58, $n = 12$). This inhibition is significant at both concentrations ($P < 0·001$) and suggests that in spite of the linear relationship between glucose concentration and absorption rate, specific mechanisms play a large part in glucose absorption under the experimental conditions used.
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FIG. 1. Relationship between initial concentration of glucose in intestinal lumen in virgin rats and amount absorbed per g dry wt intestine, with and without added phloridzin. The number of experiments at each concentration is shown in parentheses.

FIG. 2. Relationship between initial concentration of glucose in virgin (○), pregnant (●) and lactating (△) rats and amount absorbed per g dry wt intestine.
Fig. 3. Relationship between initial concentration of glucose in virgin (○), pregnant (●) and lactating (Δ) rats and absolute amount absorbed per loop.

Fig. 4. Relationship between initial concentration of glycine in virgin (○), pregnant (●) and lactating (Δ) rats and amount absorbed per g dry wt intestine.
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In Fig. 2 the relationship between concentration of glucose introduced into the lumen and the amount absorbed per g dry weight over 5 min is shown for virgin, pregnant and lactating rats. Fig. 3 shows the data expressed on a different basis with the absolute amount of glucose absorbed per loop plotted against concentration. There is no difference in the absolute transfer of glucose in these states. However, when expressed per g dry weight, there is a significant decrease in lactation. (Glucose 10 m-mole/l: absorption 6·83 mg±SEM 0·40 g dry weight⁻¹ 5 min⁻¹, n = 5; in lactating rats, 4·87±0·38, n = 4, P < 0·02. Glucose 20 m-mole/l: absorption in virgin rats 14·1 ± 0·58, n = 12; in lactating rats, 8·60±0·65, n = 8, P < 0·001.)

![Graph](image)

**Fig. 5. Relationship between initial concentration of glycine in virgin (○), pregnant (●) and lactating (△) rats and absolute amount absorbed per loop.**

The results for glycine are shown in Figs. 4 and 5, and, as with glucose, there is no significant difference in the absolute amount of glycine transferred, but when expressed in relation to intestinal weight there is a significant decrease in lactation. (Glycine 10 m-mole/l: absorption in virgin rats 2·95 mg±0·18 g dry wt⁻¹ 5 min⁻¹, n = 5; in lactating rats, 1·32±0·15, n = 4, P < 0·001. Glycine 50 m-mole/l: absorption in virgin rats 10·7 ± 0·86, n = 10; in lactating rats, 6·92±0·65, n = 5, P < 0·02).

**DISCUSSION**

Evidence for an increase in mucosal area of the small bowel in pregnancy has not been previously described, whilst that occurring in lactation is well documented. Fell, Smith & Campbell (1963) reported increases in weight and nitrogen content of the small gut in lactating rats and described an increase in length although no measurements were recorded. The increases in weight and length found in this study in lactation are highly significant, whilst the length of intestine found in virgin and pregnant animals (mean 107 cm) is very similar to that found for male animals of the same strain and body weight range (111 cm) by Fisher & Parsons.
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(1950). More detailed evidence for an increased mucosal surface area in the lactating rat has been reported by Boyne, Fell & Robb (1966) who calculated this from measurements of photographs of histological sections of intestine using a formula given by Warren (1939). Similar hypertrophy accompanying lactation has been described in sheep (Fell, Campbell & Boyne, 1964) and in the mouse (Campbell & Fell, 1964). Whether such changes occur in the human is not known. The hypertrophic changes found in lactation in rats are maximal at the time of weaning when food intake is greatest, and Campbell & Fell (1964) considered this rather than hormonal mechanisms to be the immediate cause, as the changes were greatest in animals fed ad libitum and could be partially or completely reduced by restricting the dietary intake. They failed to demonstrate similar changes in newly parous mice injected with lactogenic hormone and Fell, Smith & Campbell (1963) showed the failure of parturition alone to bring about these changes in the absence of lactation. Other conditions in which hyperphagia occurs also produce hypertrophy of the small intestine (Dowling, 1967). In pregnancy, although it is probable the increased intake of food is responsible for the changes, a contributory effect of hormonal changes has not been ruled out.

Though it has been suggested that a relationship exists between intestinal hypertrophy and absorptive capacity, this is not invariably the case. Levin, Newey & Smyth (1965) reported decreased transfer of sugars and glycine in short-term starvation, a condition reported to result in shortening of the gut and mucosal atrophy. However, Kershaw, Neame & Wiseman (1960) reported significant increases of glucose and L-histidine absorption in the same condition. Dowling & Booth (1967) found there was not only a relationship between enhanced in vivo glucose absorption and small bowel hypertrophy in rats following gut resection, but also a correlation between villous height and the amount of glucose absorbed. There is no evidence that such a state of affairs exists in pregnancy or lactation, for there was no significant increase in absolute absorption of either substrate per intestinal loop. Indeed, when the results were expressed on a weight basis, absorption was reduced. A similar reduction might have been expected in pregnancy since the intestinal dry weight increases slightly in this state. However, the reductions in absorption were not statistically significant.

Since absolute absorption is unchanged and there is increased dietary intake in pregnancy and lactation, an overall increase in absorption is to be expected, and indeed Campbell & Fell (1964) have shown that this is the case in lactation, for the coefficient of digestibility of protein remains unchanged despite the increased food intake. The results found in lactation in this study suggest a decreased absorptive ability per unit mucosal area. Why this should occur in the presence of villous hypertrophy is difficult to understand unless the latter is a compensatory mechanism. However, the interpretation of results expressed on a weight basis must be treated with caution in conditions associated with changes in gut morphology. It is possible that dry weight may not bear a direct relation to mucosal surface area, for there may be a greater increase in the weight of muscle layers compared with mucosa, per unit length of intestine. If this is the case, absorption, expressed on a weight basis, will be misleadingly low.

The results found in pregnancy, whilst in agreement with those of Penzes & Simon (1968), conflict with those of Larralde et al. (1966) and Larralde & Fernandez-Otero (1968). The latter authors suggested that increased absorption occurred in pregnancy due to some change in the intestinal mucosa, rather than possible variations in motility, blood flow, etc. However, they did not relate absorption to intestinal weight, nor take account of possible changes in mucosal surface area per unit length of intestine. There is little information concerning the effect of sex
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hormones on absorption. Semen (1968) reported that oestrogens and progestogens have opposing effects on the in vitro absorption of glucose in the dog, oestradiol promoting an increase and progesterone a decrease.

ACKNOWLEDGMENT

This work was supported by an Exchequer Grant from the Ministry of Health.

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