Analysis of Segmental Phosphate Absorption in Intact Rats
A Compartmental Analysis Approach

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Abstract
Available information supports the dominance of the proximal intestine in inorganic phosphate (Pi) absorption. However, there is no strategy for analyzing segmental Pi absorption from a spontaneously propelled meal in an intact animal. We propose a solution using compartmental analysis. After intragastric administration of a 32P-labeled Pi liquid meal containing a nonabsorbable marker, [14C]polyethylene glycol (PEG), rats were killed at 2, 10, 20, 30, 60, 120, and 240 min. The gastrointestinal tract was removed and divided into seven segments, from which 32P and [14C]PEG were recovered. Data was expressed as a percentage of the dose fed, i.e., (32P/[14C]PEG) segment/ dose fed for each segment. A compartmental model was constructed and the rate constants for intersegmental transit and segmental absorption were estimated. The "goodness of fit" between the simulated model and the actual data indicates the estimated rate constants reflect in vivo events. The duodenum, with the highest transit and absorption rates, accounted for a third of the total absorption. However, the terminal ileum, with a lower absorption rate but a longer transit time, absorbed an equal amount of Pi. This approach allows the analysis of the mechanism and the regulation of Pi absorption under more authentic in vivo conditions. (J. Clin. Invest. 1993. 91:915–922.) Key words: distal intestine ・ gastrointestinal transit ・ liquid meal ・ proximal intestine

Introduction
In previous studies in rat intestinal segments, we have demonstrated the presence of active inorganic phosphate (Pi) absorption in jejunum even in vitamin D–deficient (–D) rats (1, 2). 1,25-Dihydroxyvitamin D (1,25D) repletion in these rats caused the induction of active Pi absorption in the duodenum and marked augmentation of active Pi absorption in the jejunum (1–3). Little or no active Pi absorption, in both –D and 1,25D-replete rats, was noted in the ileum (1) and the colon (4). These and similar findings by others (5) have led to the consensus that the bulk of Pi absorption is accomplished in the proximal intestine (6). However, all of these studies were based on measurements in isolated intestinal segments, bathed in or perfused with artificial solutions. The segmental contribution to Pi absorption in a living animal, however, can only be assessed in an intestine in which the natural physiological conditions and regulatory mechanisms are not altered and the forward progression of the meal is not impeded.

Although many studies have evaluated total intestinal Pi absorption in vivo (5, 7), only three have attempted to resolve this total Pi absorption into components contributed by different intestinal segments. In one study in the rat, the transit rate was measured in one group of animals and the absorptive rate for Pi was measured in ligated intestinal loops in a different group of animals (8). The failure to measure transit and absorption simultaneously in the same animal and the disruption of the anatomical and physiological continuity of the intestine cast doubt on the observations as truly reflecting in vivo events. In the other two studies in chicks (9) and laying hens (10), respectively, absorption was measured at only one time point, and the relationship of this time point to the meal was not clearly defined. These constraints raise difficulties in interpreting the data because Pi absorption in a given segment would be expected to vary with time after the administration of a meal.

In the current study we propose a new approach to the analysis of in vivo segmental Pi absorption. A compartmental model describing the transit and absorption of Pi was developed from the experimental data. This model was then used to estimate the rate of Pi absorption and the percentage of Pi absorbed by the different intestinal segments over time. The "goodness of fit" found between the experimental data and the curves generated by the simulated model suggests that compartmental analysis can be applied to the in vivo analysis of segmental Pi (or other nutrients) absorption from a food bolus advancing unhindered through the gastrointestinal tract.

Methods
Study design. 43 male Sprague-Dawley rats weighing 100–150 g and fed a diet that contained 1.2% and 0.8% of Ca and Pi, respectively, were used for all experiments. The liquid meal (0.85 ± 0.04 ml) was given by gastric gavage (5 Fr, 15-in. Pharmaseal tubing, Baxter Healthcare Corp., Valencia, CA) after an 18-h fast. Rats were fed between 10 and 11 a.m. each day in all experiments. After administration of the feeding solution the animals were deprived of food and water. Rats were anesthetized by intraperitoneal injection of sodium pentobarbital (50 mg/kg) at 2 (n = 4), 10 (n = 9), 20 (n = 7), 30 (n = 6), 60 (n = 8), 120 (n = 5), and 240 (n = 3) min after intragastric feeding. The number of rats used at each time point was determined by the variability of the observations at that time point. Immediately after anesthesia the abdomen was opened and the gastrointestinal tract exposed. The gastrointestinal tract was immediately clamped at the esophageal–gastric junction...
and above the anus. As shown in Fig. 1, the entire intestine was then removed and divided into seven segments: stomach, the duodenum (10 cm), four equal segments of the remaining small intestine (20–24 cm each—proximal segment 1, proximal segment 2, distal segment 1, and distal segment 2), and cecum/colon. The length of the small intestine for all the rats was 99.5 cm.

Although there is general agreement on the duodenum as the segment that extends from the pylorus to the ligament of Treitz, there is less consensus on the definition for the jejunum or the ileum. This is because there is not a distinct anatomical site that separates the two segments. In the human, the jejunum is generally defined as the first two-fifths of the intestine past the ligament of Treitz and the ileum as the last three-fifths of the small intestine (11). In the rat, however, the term “ileum” has been used to refer to only the last 10 cm (as in Using studies [12]) to as much as the entire second half of the small intestine past the ligament of Treitz in whole-animal studies (8). As a generalization, our proximal segments 1 and 2 would represent the conventionally defined jejunum, and our distal segments 1 and 2, the ileum.

Each segment was perfused with 35 ml of normal saline (0.9% NaCl). The amount of saline perfused was based on a previous report in the literature (13) and also on the amount determined in our laboratory to effectively remove the entire dose of [14C]polyethylene glycol [14C]-PEG. The perfusate was weighed and samples were analyzed for [32P] and [14C]-PEG.

Placement of the feeding tube. To determine the length required for intragastric feeding, three rats were anesthetized and dissected to expose the esophagus and stomach, and feeding tubes were advanced through the mouth into the stomach of each rat (14). A length of 9.4 cm was required to position the tip of the feeding tube in the stomach of all three rats. The position of the feeding tube was further confirmed by filling a feeding tube with 1 ml of barium sulfate and advancing the tube 9 cm in a fasted and anesthetized rat. X-ray films were taken before and after injection of 1 ml of barium sulfate. The pictures revealed the tip of the tube was in the fundus and the injected contrast was found only in the stomach.

Liquid meal. A liquid meal not containing other nutrients was used to allow comparison with other studies measuring mineral absorption (8, 15, 16). The liquid meal contained sodium phosphate (10 mg/ml), PEG (mol wt 4,000, 1 g/100 ml), 2 μCi [14C]-labeled PEG ([14C]-PEG, 60 mCi/mmol), and 1 μCi [32P] tracer (9,000 Ci/mmol). [32P] and [14C]-PEG were used as markers of P1 and PEG movement. PEG served as a nonabsorbable, liquid-phase marker (17, 18) to document movement of the meal through the intestinal tract and as a reference against which P1 absorption was measured.

The concentration of P1 used in the present study was based on previous studies conducted in rats (8, 15, 19) and humans (20). Studies have used concentrations that ranged from 0, i.e., tracer only (8, 15) to 240 mM (20). In the present study we decided to use a concentration of 83 mM. At this concentration we were giving the rats 2.19 mg P1.

Radioisotope analysis. To determine [32P] and [14C]-PEG activity in samples, aliquots were taken and counted in duplicate in a two-channel liquid scintillation counter (model LS 5801, Beckman Instruments, Inc., Palo Alto, CA) that automatically corrected for quench and spillover.

Calculations. In each rat, total recovery of [14C]PEG and [32P] was determined by summing the activities recovered in all individual segments. The total intestinal P1 absorption (in percent dose) was calculated as \[1 - \frac{(32P/14C)PEG_{\text{entire}}}{(32P/14C)PEG_{\text{entire}}} \times 100\]. The segmental recoveries of PEG and P1 at any time point were expressed as a percentage of the amount fed and were calculated as \([14C]PEG_{(\text{segment})}/[14C]PEG_{(\text{entire segment})} \times 14CPEG_{(\text{entire})} \times 100\), respectively.

The mean residence time of PEG, rate of P1 absorption, and percent P1 absorbed by each segment were estimated using compartmental analysis. The compartmental model shown in Fig. 2 was used for this purpose and represents transit and absorption of P1 assuming first-order kinetics. Fig. 1 summarizes the definitions of the seven intestinal segments, which are represented by the larger boxes in Fig. 2. The model shown in Fig. 2 depicts compartments as smaller boxes, transit rate constants as \(k_{12}, k_{23}, \ldots, k_{n-1,n}\) (where \(k_{ij}\) is the transition rate constant from segment \(i\) to \(j\)), and absorption rate constants as \(k_{12}, k_{23}, \ldots, k_{n-1,n}\) (where \(k_{ij}\) is the absorption rate constant from segment \(i\) into segment \(j\)). No detectable P1 absorption occurred from the stomach (compartment 1). Because of the significant transit delays occurring in the last three segments (distal segments 1 and 2, and cecum/colon), as evident from inspection of the segmental P1 and PEG data, it was not reasonable to model these segments as single homogeneous compartments. Instead, each of these segments was represented by a series of identical compartments with the same transit constant (\(k_{ij}\) or \(k_{ij}\)) and absorption (\(k_{12}, k_{23}, \ldots, k_{ij}\) ) rate constants. The numbering of the rate constants in distal segments 1 and 2 and cecum/colon reflects this assumption and refers to segment and not compartment numbers. The total number of compartments selected to represent each of these three segments was determined by a “goodness of fit” analysis of simulated models (see below). Administration of the liquid meal was modeled as a bolus injection into the stomach, compartment 1 in Fig. 2. The six shaded compartments (16 through 21), correspond to output from compartments 2, 3, and 4, the sum of the output from compartments 5 through 8, the sum of the output from compartments 9 through 13, and the sum of the output from compartments 14 and 15.

Compartment model rate constants were estimated using the nonlinear, ordinary least squares estimation capabilities of the ADAPT II pharmacokinetic modeling package (21). To estimate all the rate constants of the model shown in Fig. 2, the following two-step procedure was used. First, the compartment model was used to estimate seven PEG transit rate constants (\(k_{12}, k_{23}, k_{34}, k_{45}, k_{56}, k_{67}, k_{78}\)), assuming no PEG absorption (i.e., \(k_{12} = k_{23} = k_{34} = k_{45} = k_{56} = k_{67} = 0\)). Next the P1 data were used to estimate the six absorption rate constants, with the transit rate constants fixed at their least squares estimates obtained from the PEG data. This is based on the assumption that P1 and PEG transit through the gastrointestinal tract at the same rate. Based on the movement of the markers observed in this study, this assumption appeared valid (see results). Approximate values for the standard deviations of all rate constant estimates were also obtained (see Landow and DiStefano [22]). In order to arrive at the model shown in Fig. 2, the above two-step estimation procedure was implemented using candidate models with different numbers of compartments to represent distal segments 1 and 2 and cecum/colon. Adding more compartments than shown in Fig. 2 to represent the delays in these distal segments

![Figure 1. Definition of intestinal segments.](image-url)
produced <1% reduction in the overall sum of squares. It should be noted that all the measured data for each of the segments was used to define the least squares criterion for the PEG and P data. In both cases a total of 272 observations were used (32 for stomach, 36 for duodenum, 36 for proximal segment 1, 42 for proximal segment 2, 42 for distal segment 1, 42 for distal segment 2, and 42 for cecum/colon).

Using the least squares estimates of the rate constants, the compartment model of Fig. 2 was simulated to predict the percent P absorbed by duodenum, proximal segment 1, proximal segment 2, distal segment 1, and distal segment 2 (no absorption was reliably detected in cecum/colon, see below). These were estimated as the activities in compartments 16 through 21 at 10, 20, 30, 60, 120, and 240 min after administration of the liquid meal. The associated standard deviations for percent P absorbed by each segment were estimated with the Monte Carlo simulation option (n = 500) of ADAPT II (21), using the least squares estimates for the rate constants and their standard deviations to define a log-normal distribution for each parameter. Absorption rate profiles, i.e., the rate of P absorbed from the duodenum through the terminal ileum as a function of time, denoted as rabsduo(t), rabsproxseg1(t), rabsproxseg2(t), rabsdistseg1(t), and rabsdistseg2(t), were constructed from the model as follows: (1) rabsduo(t) = k02x2(t); (2) rabsproxseg1(t) = k03x3(t); (3) rabsproxseg2(t) = k04x4(t); (4) rabsdistseg1(t) = k05x5(t) + x6(t) + x7(t); (5) rabsdistseg2(t) = k06x6(t) + x7(t) + x8(t) + x9(t) + x10(t) + x11(t) + x12(t) + x13(t). Finally, the mean residence time (MRT) of PEG in each segment (MRTduo through MRTdistseg2) were calculated from the least squares estimates of the transit rate constants as follows: (1) MRTduo = 1/k21; (2) MRTproxseg1 = 1/k32; (3) MRTproxseg2 = 1/k43; (4) MRTdistseg1 = 3/k54; (5) MRTdistseg2 = 6/k65.

Values are presented as mean±SD, except where noted in the text.

**Results**

**Recovery of P and PEG.** Total recovery of PEG was 89±6%. Recovery of P was 90% at 2 min and then progressively decreased with time due to absorption.

**Intestinal transit of PEG and P.** The movement of PEG through the intestine over time is shown in Fig. 3. At 20 min ~ 80% of the recovered PEG was at or beyond proximal segment 2 and by 2 h virtually all of the recovered PEG had reached distal segment 2. An identical transit pattern was observed for P (not shown), suggesting that the two solutes advanced through the gastrointestinal tract at the same rate.

The least squares estimates for the transit rate constants obtained by fitting the compartment model (Fig. 2) to the collected PEG data are listed in Table I. The standard deviation obtained for k37 was >10 times higher than the estimate and therefore was not included in the analysis. The PEG activities predicted by this fitted model are shown in Fig. 3 along with the measured data (shown as mean±SD) for each of the seven measured segments (all of the data were used in the parameter estimation). The correlation coefficient (r) for the seven segments, stomach, duodenum, proximal segment 1, proximal segment 2, distal segment 1, distal segment 2, and cecum/colon, are 0.99, 0.81, 0.87, 0.80, 0.82, 0.93, and 0.98, respectively. The estimates of the MRT for PEG in each segment are as follows: stomach, 5.6±0.03 min; duodenum, 2.7±0.3 min; proximal segment 1, 5.8±0.5 min; proximal segment 2, 29.8±2.6 min; distal segment 1, 51.1±3.5 min; distal segment 2, 106.4±11.7 min. These results indicate that transit through the stomach, duodenum, and proximal segment 1 are comparable, whereas there is a progressive reduction in the transit rates through the more distal segments.

**P absorption.** Absorption of P, from the liquid meal over time is shown in Fig. 4. About 40% of the P fed was absorbed in the first 30 min and 91% was absorbed by 2 h.

Table II gives the least squares estimates for the absorption rate constants along with their standard deviations for each intestinal segment. The standard deviation for the estimate of k47 was >10 times higher than the estimated value suggesting the absence of absorption in cecum/colon in this study. Fig. 5 shows the model predictions for the percent P in each segment along with the measured data shown as the mean±SD. The r values for the stomach, duodenum, proximal segment 1, proximal segment 2, distal segment 1, distal segment 2, and cecum/colon were 0.98, 0.87, 0.80, 0.82, 0.93, and 0.98, respectively.
colon are 0.97, 0.90, 0.87, 0.82, 0.78, 0.74, 0.81, and 0.90, respectively. The estimated P, absorption rate profiles for the small intestine segments (see Methods) are displayed in Fig. 6. Inspection of these curves indicates that the maximal rate of P, absorption is substantially higher in the duodenum than in any other segment.

Table III shows the estimated values of percent P, absorbed (±SD) by the small intestine segments at five of the observation time points. The duodenum and distal segment 2 (terminal ileum) each absorbed one-third of the total P, dose with the remaining one-third absorbed by the rest of the intestine in between.

**Discussion**

In the current study we have developed a model for analyzing segmental solute P, absorption from a spontaneously propelled liquid meal in vivo. As discussed earlier, of the few studies published, none has satisfied the theoretical and experimental considerations associated with absorption from a continuously moving food bolus through an untampered gastrointestinal tract (8–10).

A more rigorous study design was used by Marcus and Lengemann in analyzing segmental calcium absorption in vivo (16, 23). Animals fed either a liquid or a solid diet containing 47Ca and a nonabsorbable isotopic marker, 89Y were killed in incremental time intervals after feeding. Based on the recovery of these isotopes in consecutive intestinal segments, a 47Ca curve and a 89Y curve were generated for each segment defining the amount of each isotope remaining in the segment over time. The area under the curve (AUC) for 47Ca was then subtracted from the AUC for 89Y for each segment and this difference in AUC was taken to represent the Ca absorption which had occurred up to a given segment. Based on such calculations, they concluded that the bulk of in vivo Ca absorption occurred in ileum. 89Y and 47Ca, however, did not move through the gastrointestinal tract at the same rate (16, 23). In addition, Fig. 7 attempts to examine the validity of equating the difference in AUCs to the absorption of Ca. Schematized 47Ca and 89Y curves are depicted in a proximal segment with a
Table I. Estimates of Transit Rate Constants

<table>
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<tr>
<th>Parameter</th>
<th>Estimate</th>
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<tr>
<td>(k_{21})</td>
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<tr>
<td>(k_{32})</td>
<td>0.373±0.040</td>
</tr>
<tr>
<td>(k_{43})</td>
<td>0.172±0.015</td>
</tr>
<tr>
<td>(k_{54})</td>
<td>0.034±0.003</td>
</tr>
<tr>
<td>(k_{65})</td>
<td>0.059±0.004</td>
</tr>
<tr>
<td>(k_{06})</td>
<td>0.056±0.006</td>
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</table>

Values are estimates of the transit rate constants±SD. The estimates are based on data from 100–150-g fasted rats (n = 42) after intragastric feeding of a liquid meal containing \([^{14}C]\)PEG, 10 mg of PEG, \(^{32}\)P, and 10 mg of sodium phosphate. At various time points rats were killed and the intestine was removed. The segments were perfused with saline and the perfusate counted for \([^{14}C]\)PEG and \(^{32}\)P. The percent PEG in each segment was determined for each rat. Estimates for \(k_{32}\), \(k_{43}\), \(k_{54}\), \(k_{65}\), and \(k_{06}\) were obtained by fitting the compartmental model (Fig. 1) with the absorption rate constants set at zero to the PEG data using the nonlinear least squares estimation procedure contained in ADAPT II (21). The associated covariance matrix was also calculated to determine the SD for each transit rate constant. See Fig. 2 for definitions of parameters.

Figure 4. Absorption of Pi, as a function of time after intragastric administration of \(^{32}\)P and \([^{14}C]\)PEG to fasting Sprague-Dawley rats (100–150 g). See Table I for methods. Percentage of fed Pi absorbed was calculated from the equation: 1-(\(^{32}\)P/\([^{14}C]\)PEG recovered from the rat)/(\(^{32}\)P/\([^{14}C]\)PEG fed)). Data are expressed as means±SE, n = 3–9.

Table II. Estimates of Pi, Absorption Rate Constants

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
</tr>
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<tbody>
<tr>
<td>(k_{02})</td>
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</tr>
<tr>
<td>(k_{03})</td>
<td>0.015±0.027</td>
</tr>
<tr>
<td>(k_{04})</td>
<td>0.007±0.008</td>
</tr>
<tr>
<td>(k_{05})</td>
<td>0.004±0.006</td>
</tr>
<tr>
<td>(k_{06})</td>
<td>0.035±0.010</td>
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</tbody>
</table>

Values are estimates±SD of the Pi absorption rate constants in the intestine based on data from 100–150-g fasted rats (n = 42) after intragastric feeding of a liquid meal containing \([^{14}C]\)PEG, 10 mg of PEG, \(^{32}\)P, and 10 mg of sodium phosphate. At various time points rats were killed and the intestine was removed. The segments were perfused with saline and the perfusate counted for \([^{14}C]\)PEG and \(^{32}\)P. The percent dose Pi, in each segment was determined for each rat. The absorption rate constants \(k_{02}\), \(k_{03}\), \(k_{04}\), \(k_{05}\), \(k_{06}\), and \(k_{07}\) were estimated by fitting the compartmental model (Fig. 2) to the Pi data using the nonlinear least squares estimation procedure contained in ADAPT II (21). The transit rate constants were set at values obtained in Table I. The associated covariance matrix was also calculated to determine the SDs for each absorption rate constant. See Fig. 2 for definitions of parameters.

We propose an approach using compartmental analysis, a technique frequently employed in pharmacokinetic studies. This form of analysis has been used to describe the dynamic disappearance rates of a drug from the circulation following its administration into different "compartment." We have adapted this principle to analyze the in vivo, dynamic absorption rate (disappearance rate) of a solute (drug) from the intestinal lumen (circulation) of different segments after the intragastric administration of a liquid meal.

The compartment model developed from the experimental data assumes that the fluxes of \(^{32}\)P and \([^{14}C]\)PEG are governed by first-order kinetics, are in the directions indicated by the arrows in Fig. 2, and that the distribution of \(^{32}\)P and \([^{14}C]\)PEG within each compartment is homogeneous. Because PEG is not absorbed, it is a reasonable approximation to consider its fluxes are governed by first-order kinetics. For Pi, given the level fed (83 mM), the passive process is dominant and can be described by first-order kinetics (7). Cramer (8) has previously demonstrated negligible secretion into the gastrointestinal tract of administered \(^{32}\)P 6 h after the dose. His study, therefore, indicates that the second assumption is valid. In order to account for the significant delays occurring in distal segments 1 and 2, and cecum/colon, each of these segments was modeled by a series of identical compartments (with the same transit and absorption rate constants). This approach satisfies the third assumption and seems reasonable in that we are only interested in the overall transit and absorption properties of these segments, and not in the kinetic inhomogeneities that may exist along the length of each of the segments. Given these assumptions, the model allows for the estimation in each segment of the mean residence time of the meal, the rate of Pi absorption, and percent Pi absorbed (Tables I–III). The plausibility of the model is supported by its ability to describe the experimental data (Figs. 3 and 5), and suggests that the model can be used to provide estimates of in vivo Pi transport and absorption kinetics in different intestinal segments.
Consistent with previous reports (8, 24, 25), we observed rapid gastric emptying of the liquid meal and rapid movement through the proximal small intestine. 90% of the administered meal left the stomach by 10 min. As early as 10–20 min after administration, the meal began to appear in the distal small intestine and almost all of the recovered dose reached the terminal ileum (distal segment 2) by 2 h. The transit rate of the meal, however, slowed dramatically as the meal moved down the intestine. The mean residence time of the liquid meal went from 6 min in the duodenum to 52 min in distal segment 1 and 116 min in the distal segment 2. Traditionally, the early appearance of an orally administered isotopic Pi in blood has been interpreted to reflect the contribution of absorption by the proximal intestine (5, 25). Our data, however, demonstrate that a liquid meal arrives in the distal small intestine as early as 10–20 min after its consumption. This raises the possibility that the early appearance of an enterally administered nutrient in the circulation may derive from the distal intestine as well.

Our choice of using a liquid meal (8, 16) and the Pi concentration (8, 19, 20) is based on the majority of published studies.
on the measurement of total Pi absorption from an experimental meal. The high percentage absorption (96%) may be attributed to the relatively small quantity of Pi fed after an overnight fast and the use of young growing rats. Pi absorption began within the first 10 min after feeding and was completed by 2 h (Fig. 4).

Pi absorption rate constant was highest in the duodenum, which exhibited a value 50 times greater than the lowest rate constant measured in distal segment 1 (Table II). Fig. 6, however, also illustrates that while the duodenum has the highest maximal rate of absorption, the rapid movement of the meal through this segment quickly lowered absorption to zero and limited total Pi absorption in the duodenum to only 34% of the dose (Table III). In contrast, distal segment 2 (terminal ileum), despite having a much lower absorption rate constant (Table II), continued absorbing Pi over a substantially longer period of time (Fig. 6) due to the slower movement of the liquid meal (Table I). The result was that distal segment 2 ended up absorbing as much Pi (33%, Table III) as the duodenum. The remaining one-third of the absorbed Pi was accomplished in the intervening small intestine with proximal segment 2 playing the major role (20%, Table II). Thus, the contribution to total Pi absorption was fairly evenly distributed between duodenum (35%), jejunum (25%, proximal segments 1 and 2), and ileum (40%, distal segments 1 and 2).

These observations highlight the limitations of studies using isolated intestinal segments in predicting the physiology of Pi absorption in an untampered intestinal tract. Our results suggest that in the intact intestine, the distal small intestine which is poorly adapted for Pi absorption when studied in isolation (7), absorbs as much Pi as the more proximal segments endowed with highly efficient Pi absorptive mechanisms(s). The longer mean residence time in the distal small intestine which translates into longer contact time for absorption is an important factor. In addition, it is possible that local luminal factors may increase the availability of Pi for absorption and/or activate additional transport mechanisms for Pi absorption, e.g., the presence of bile salts in the distal intestine in vivo can increase Pi transport through the intercellular pathway (27).

It should be pointed out that despite the differences in methodology used, our data are surprisingly similar to those of Cramer (8). Cramer reported that 38% of the Pi administered was absorbed in the ileum which he defined as the distal 42 cm. In our study the ileum (distal segments 1 and 2) representing the distal 40–45 cm absorbed 40% of the Pi dose. In addition, Cramer’s data also indicated substantial absorption in the proximal small intestine. The first 12 cm distal to the pylorus (equivalent to our duodenum) accounted for 29% and the middle 42 cm (proximal segments 1 and 2 in our study) accounted for 25% of total Pi absorption.

In conclusion, we have demonstrated that the technique of compartmental modeling can be used to analyze and integrate segmental absorptive events of Pi from a spontaneously propelled liquid meal along the intact intestinal tract of normal conscious rats. This opens up the exciting opportunity of reexamining many of the important mechanistic and regulatory mechanisms, established (virtually without exception) from experimental models that have been anatomically or physiologically altered. In our model, animals were anesthetized not to obtain postmortem events, but to obtain “snap-shot” information on premortem events, generated under completely unampered conditions. This new technique is also potentially applicable to the in vivo analysis of segmental absorption of other nutrients.
Acknowledgments

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