

ADAPTIVE RESPONSES TO FEEDING IN BURMESE PYTHONS: PAY BEFORE PUMPING

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Summary

Burmese pythons normally consume large meals after long intervals. We measured gut contents, O₂ consumption rates, small intestinal brush-border uptake rates of amino acids and glucose, organ masses and blood chemistry in pythons during the 30 days following ingestion of meals equivalent to 25% of their body mass. Within 1–3 days after ingestion, O₂ consumption rates, intestinal nutrient uptake rates and uptake capacities peaked at 17, 6–26 and 11–24 times fasting levels, respectively. Small intestinal mass doubled, and other organs also increased in mass. Changes in blood chemistry included a 78% decline in P_{O₂} and a large ‘alkaline tide’ associated with gastric acid secretion (i.e. a rise in blood pH and HCO₃[−] concentrations and a fall in Cl[−] concentration). All of these values

returned to fasting levels by the time of defecation at 8–14 days. The response of O₂ consumption (referred to as specific dynamic action, SDA) is the largest, and the up-regulation of intestinal nutrient transporters the second largest, response reported for any vertebrate upon feeding. The SDA is as large as the factorial rise in O₂ consumption measured in mammalian sprinters and is sustained for much longer. The extra energy expended for digestion is equivalent to 32% of the meal’s energy yield, with much of it being measured before the prey energy was absorbed.

Key words: blood chemistry, digestive adaptation, nutrient transport, specific dynamic action, *Python molurus*.

Introduction

Many animal species feed and digest at intervals. Numerous features of gastrointestinal physiology and anatomy adapt to and are regulated by the resulting fluctuations in nutrient delivery to the gut (Karasov and Diamond, 1983a). Such typical responses to feeding include intestinal hypertrophy and up-regulation of intestinal nutrient transporters and hydrolytic enzymes (Karasov and Diamond, 1987; Toloza *et al.* 1991). However, in most species studied to date these responses are modest in scope and accordingly difficult to study, exhibiting at most a twofold range of activities or tissue masses. These limited scopes may be related to the fact that the usual model species, such as laboratory mice and rats, consume relatively small meals at frequent intervals, so that the intestine is not normally at rest for long periods.

If this interpretation of limited regulatory scope is correct, then animal species that normally feed after long intervals on relatively large meals might be expected to exhibit larger feeding responses. Natural meal intervals and meal sizes reach an extreme in sit-and-wait foraging boid, pythonid and viperid snakes. In the wild these snakes feed approximately every 1–2 months when active, can fast for up to 18 months, and consume huge meals equivalent to 50–160% of their own body mass (Pope, 1961; Slip and Shine, 1988; Martin, 1992; Greene, 1992; Secor and Nagy, 1994).

To test this expectation, we previously measured the feeding response of a sit-and-wait foraging viperid snake, the sidewinder rattlesnake *Crotalus cerastes*, which feeds on average every 1–1.5 months in the wild (Secor and Nagy, 1994). We found that, within 24 h after consuming a meal equivalent to 26% of its body mass, a previously fasted *C. cerastes* undergoes a sevenfold increase in metabolic rate, five- to eightfold increases in intestinal nutrient transporter activities, and a more than twofold increase in small intestinal mass (Secor *et al.* 1994). Following completion of digestion, metabolic rates return to basal levels, nutrient transporters are down-regulated, and the small intestine atrophies. We hypothesize for *C. cerastes* that this feeding response is an adaptation to conserve energy during digestive quiescence, since the intestine is an expensive organ to maintain, and that the rapid physiological and morphological responses observed following ingestion are required for the snake to be able to digest the meal efficiently. The high energy cost of initiating digestion would thus be more than offset by the energy savings resulting from not maintaining the gut during the period of quiescence.

The present paper extends these observations to the Burmese python (*Python molurus*), a snake species selected for two reasons. First, the very large feeding responses that we observed in *C. cerastes* (much larger than in the usual

laboratory rodent models) would have made it a highly advantageous species for studying intestinal regulation, except for two serious drawbacks: sidewinders are venomous and are not widely available for study. In contrast, Burmese pythons are docile and non-venomous, bred in captivity and readily available. Second, our previous study of a single snake species did not establish that its large feeding response is actually an adaptation to infrequent feeding; perhaps it is instead a peculiarity of viperids, or just of *C. cerastes*. The generality of our interpretation could be tested on *P. molurus* which, like *C. cerastes*, is a sit-and-wait forager consuming large meals and capable of fasting for many months (Pope, 1961), but which belongs instead to the family Pythonidae, phylogenetically distant from viperids (McDowell, 1987).

Hence, the present paper examines metabolic, physiological and morphological responses to feeding in *P. molurus*. To facilitate direct comparison with *C. cerastes*, we repeated on *P. molurus* the following measurements that we had made on *C. cerastes*: meal passage rate, O₂ consumption following feeding, small intestinal brush-border uptake rates of the sugars L- and D-glucose and the neutral amino acids L-leucine and L-proline, and changes in wet masses of the intestine and other organs. We also added the following measurements not performed in our previous study: small intestinal brush-border uptake rates of the acidic amino acid L-aspartate and the basic amino acid L-lysine, nutrient uptake rates in the cecum and large intestine, changes in organ dry masses and blood chemistry.

Materials and methods

Animals, maintenance and sampling

Burmese pythons (*Python molurus* Linnaeus) are native to the Indo-Chinese subregion and are among the largest snake species, reaching lengths of 6 m and weighing over 100 kg (Pope, 1961). From a commercial breeder (Captive Bred Reptiles, Oklahoma City, OK) we purchased 76 newly hatched *P. molurus* originating from three clutches (32, 40 and 4 hatchlings from clutches A, B and C, respectively). The snakes were housed in individual plastic cages with water available *ad libitum*, in a room maintained at 28–30 °C with a 14h:10h light:dark cycle. Every 2 weeks we offered each snake one or several laboratory mice or rats to eat such that the combined mass of the meal averaged 25 % of the snake's body mass.

Prior to the start of each experiment, we withheld food from snakes for 1 month to ensure that they became post-digestive. We then fed each snake two or three young rats such that the total mass of the meal equalled 25.0±0.4 % (mean ± S.E.M.) of the snake's body mass. We used 29 snakes for this study (19 females and 10 males, mean mass 737±28 g, mean age 47±3 weeks), with 8, 19 and 2 individuals from clutches A, B and C, respectively. For all parameters measured, we tested for sex-related and clutch-related differences and found none.

Of the 29 snakes, 8 were used for repeated measurements of O₂ consumption (see below). The other 21 snakes (mean mass 738±34 g) were killed for morphological and *in vitro*

physiological studies by severing the spinal cord immediately posterior to the skull. Three snakes each were killed at 6 h, 12 h and 1, 3, 6, 14 and 30 days after feeding. For each of five time periods (12 h to 14 days post-feeding), the three individual snakes sampled for that time period were killed on a single day, whereas for the other two time periods (6 h and 30 days) the three individuals were killed on different days. Since we observed our pythons to defecate at 8–14 days (mean 10.4±0.7 days, *N*=20) after feeding, our measurements at 6 h to 6 days were on digesting snakes, while those at 14 and 30 days were on snakes that had just completed digestion and on post-absorptive snakes, respectively. Mean body masses of snakes did not differ significantly ($F_{6,14}=0.24$, $P=0.955$) among the seven sampling periods.

Metabolic response

We used closed-system respirometry (see Vleck, 1987; Secor *et al.* 1994, for experimental details) to measure the metabolic response to digestion in eight pythons (mean mass 735±49 g), maintained at 30 °C. Air samples were drawn for analysis from the respirometry chambers at the beginning and end of a 0.2–1 h period, O₂ concentrations were measured with an Applied Electrochemistry S-3A O₂ analyzer, and O₂ consumption (\dot{V}_{O_2} , corrected for standard temperature and pressure) was calculated as ml O₂ g⁻¹ h⁻¹. We measured \dot{V}_{O_2} of each snake daily from 3 days before to 15 days after feeding.

Rate of digestion

We determined the extent of digestion and the rate of meal passage by taking X-ray photographs of four snakes during digestion and by examining the gut contents of all 21 killed snakes. From killed snakes, we removed and weighed the stomach and small intestine, flushed them of their contents, and then re-weighed them. The difference in organ masses before and after flushing was taken as the wet mass of the organ contents and was compared with the wet mass of the ingested meal. X-ray photographs, taken daily for 1 week after feeding, revealed the breakdown of the ingested rodent skeletons within the snake's stomach.

Nutrient uptake measurements

We measured the rates of nutrient uptake across the brush-border membrane of the small intestine by methods already described in detail by Karasov and Diamond (1983b) and Secor *et al.* (1994). Briefly, the intestine was quickly removed, washed out with ice-cold Ringer's solution, everted and cut into 1 cm sleeves, which were mounted on grooved glass rods. Sleeves were first preincubated for 5 min in Ringer's solution at 30 °C and then incubated for 2 min at 30 °C in a Ringer's solution containing a radiolabelled nutrient plus an adherent fluid marker with a different radiolabel. We measured uptake rates of the amino acids L-aspartate, L-leucine, L-lysine and L-proline (each at 50 mmol l⁻¹ and labelled with ³H) and the sugars L-glucose (at trace concentrations and labelled with ³H) and D-glucose (at 20 mmol l⁻¹ and labelled with ¹⁴C). We selected the four amino acids because each is transported predominantly by a different

one of the following major intestinal amino acid transporters (Stevens *et al.* 1982): the acidic, neutral, basic and imino acid transporters, respectively. To correct for the amounts of these transported nutrients in the fluid adherent to the sleeve, we used [¹⁴C]polyethylene glycol for the [³H]amino acids and for L-[³H]glucose, and L-[³H]glucose for D-[¹⁴C]glucose. These pairs of transported solutes and adherent fluid markers yield total uptake (carrier-mediated plus passive diffusional) for each amino acid, passive uptake of L-glucose and carrier-mediated uptake of D-glucose. Uptake rates were expressed as nmoles per minute per milligram of sleeve wet mass.

We also measured Na⁺-independent uptake of L-proline and L-leucine by preincubating and incubating sleeves in Na⁺-free Ringer's solutions in which all NaCl had been isosmotically replaced with choline chloride. We calculated Na⁺-dependent uptake of these two amino acids by subtracting their Na⁺-independent uptake from their total uptake measured in normal (Na⁺-containing) Ringer. Our choices of incubation time and temperature, solute concentrations and solution composition are explained in Secor *et al.* (1994).

We measured uptake rates of L-leucine, L-proline and D-glucose in five regions of the intestinal tract: three regions of the small intestine cut into equal-length parts (proximal, middle and distal), cecum and the proximal half of the large intestine. We measured uptake of L-aspartate and L-lysine only in the three small intestinal segments. In contrast to sidewinder intestine (Secor *et al.* 1994), python small intestine exhibited no obvious abrupt change in appearance from one end to the other; there was merely a gradual decline in intestinal diameter towards the distal end, such that the mass of the distal small intestinal segment averaged 66±3% of the mass of the proximal or middle segments. The cecum, a structure of unknown function in snakes and present in many primitive snakes (Cundall *et al.* 1993), is a blind diverticulum that extends proximally for several centimeters from the junction of the small and large intestines and that is attached to the most distal part of the small intestine by connective tissue. The total uptake capacity of the whole length of the small intestine for each nutrient was obtained by calculating, for each small intestinal region, the product of its uptake rate (nmol min⁻¹ mg⁻¹) times its mass, then summing the products of the three regions.

Blood chemistry

At all seven sampling intervals except 14 days after feeding, we drew 1–2 ml of blood directly from the snake's heart just prior to killing it. Whole blood with sodium heparin added as an anticoagulant was centrifuged for 10 min at 4000 revs min⁻¹ at 4 °C. The plasma was analyzed (model 747 Hitachi Blood Analyzer) for concentrations of Na⁺, K⁺, Cl⁻, Ca²⁺, phosphorus, CO₂, glucose, cholesterol, creatinine, total protein, albumin and alkaline phosphatase. We drew a second set of blood samples from four fasting snakes and again at 1, 2 and 5 days after those snakes had fed. Whole blood of this second set of samples was analyzed (model 168 Corning pH/blood gas analyzer) for pH, P_{CO₂}, P_{O₂} and HCO₃⁻.

Morphological responses

To quantify feeding responses of intestinal morphology, we measured the total small intestinal wet mass, plus the wet masses of scrapable mucosa and residual serosa (Diamond and Karasov, 1984) of one sleeve from each small intestinal region of each killed snake. Since some other organs besides the small intestine hypertrophy and atrophy in response to hyperphagia and fasting in other vertebrate species (e.g. Toloza *et al.* 1991), we also measured the wet masses and dry masses (dried to constant mass at 60 °C) of the following organs: paired lungs, heart, liver, empty stomach, full gallbladder, pancreas, large intestine, paired kidneys and paired abdominal fat bodies.

Statistical analyses

We carried out three statistical analyses on most dependent variables: analysis of variance (ANOVA), to test for an effect of sampling time (days after feeding); analysis of covariance (ANCOVA), to test whether body mass was a significant covariate and whether sampling time still had an effect when body mass was included as a covariate; and a second ANCOVA, to test for a significant interaction between the effects of body mass and of sampling time (Zar, 1974). We report the ANOVA results for variables for which body mass proved not to be a significant covariate (uptake rates, uptake capacities and blood chemistry). We report the results for the first ANCOVA for variables for which body mass did prove to be a significant covariate but without a significant interaction between the effects of body mass and of sampling time (organ, intestinal, mucosal and serosal masses). For wet and dry masses of fat bodies there did prove to be such a significant interaction; hence, we report only the results of the ANOVA. To test for effects of pre- and post-feeding day on metabolic response, and to test for effects of intestinal position on uptake rates, we used a repeated-measure design ANOVA. In conjunction with ANOVAs or ANCOVAs, we made pairwise mean comparisons between sampling days. In the text, we report the results of ANOVAs and ANCOVAs in terms of their *F* and *P* values, and we state *P* values of significant pairwise comparisons. Statistical significance is taken as the *P* ≤ 0.05 level. We present our results as means ± 1 S.E.M., or else as mass-adjusted means (least-squares means from ANCOVA) ± 1 S.E.M. Sample sizes are the number of snakes given in this Materials and methods section for each sampling time or type of measurement and will not be repeated throughout the text. All statistical analyses were carried out using the microcomputer version of SAS (PC-SAS, SAS Institute, Inc. 1988).

Results

Metabolic response

Minimum rates of O₂ consumption (\dot{V}_{O_2}) in eight fasted snakes averaged 0.034±0.003 ml O₂ g⁻¹ h⁻¹. For these eight individuals, \dot{V}_{O_2} did not vary significantly with body mass, probably because of their narrow range of masses (572–951 g). Following the snakes' ingestion of food, \dot{V}_{O_2} rose significantly

by 12 h to 5.7 times the fasting rate, and peaked at 24 h at $0.58 \pm 0.06 \text{ ml O}_2 \text{ g}^{-1} \text{ h}^{-1}$, 17 times the fasting rate (Fig. 1). At 36 h, \dot{V}_{O_2} was not significantly different from this peak value. At day 2, \dot{V}_{O_2} had declined significantly ($P < 0.001$) and declined further ($P < 0.02$) at days 3, 4 and 6, though values still remained significantly higher than the fasting rate. By day 8 and subsequently, \dot{V}_{O_2} did not differ significantly from the fasting rate.

Digestion rate

From dissections and from X-ray photographs, we observed that rats were swallowed head-first and were aligned in series in the snake's stomach, the tail of each rat close to the head of the next-swallowed rat. At 1 day post-feeding, pythons had reduced the mass of the ingested meal within the stomach by $27 \pm 2\%$ (Fig. 2); much of the musculature of the head and pectoral girdle of the first ingested rat was removed, while the rat's skull was still intact. By day 2, X-ray photographs revealed that the anterior half of the first rat's skeleton had been completely digested within the snake's stomach and that the posterior half had begun to disarticulate. At day 3, only $27 \pm 7\%$ of the ingested meal mass remained within the stomach, the first and second (if three were consumed) rats were completely digested, and the last rat was missing much of its head and shoulders. At this time, the intestinal contents peaked at $5.3 \pm 1.7\%$ of the ingested mass. X-ray photographs at days 4 and 5 showed the final disintegration of the rats' skeletons within the snakes' stomachs. By day 6, the stomach contained only large mats of hair, which were eventually (by day 14) passed to the large intestine. At days 14 and 30, both the stomach and small intestine were completely empty. At day 14, only one of the three killed snakes still had fecal matter

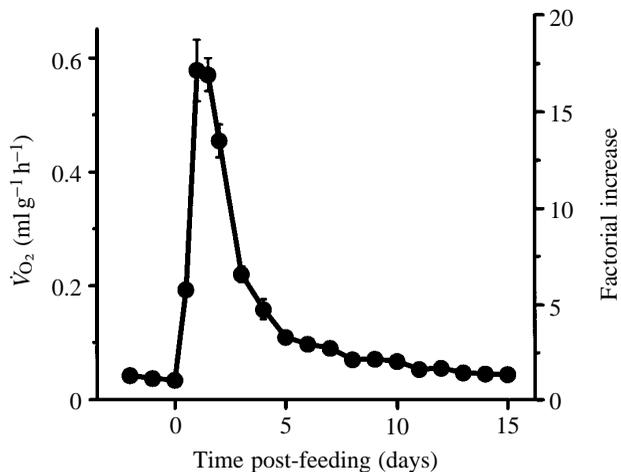


Fig. 1. Mean O_2 consumption rates of Burmese pythons ($N=8$) for 3 days before and 15 days after consuming a rat meal equivalent in mass to approximately 25% of the snake's body mass. The right-hand axis shows the factorial increases in \dot{V}_{O_2} above pre-feeding values. In this and subsequent figures, vertical bars represent ± 1 S.E.M. or least-squares mean, but bars are omitted if they are smaller than the symbol for the mean value. Note that \dot{V}_{O_2} peaks at day 1 post-feeding, at a value 17 times that before feeding.

within its large intestine, while at day 30 the large intestine was completely empty for all three killed snakes. Most pythons in our colony defecated 8–14 days after consuming meals, equalling 25% of their body mass, but individuals occasionally did not defecate for more than 3 weeks after feeding.

Nutrient transport

Positional effects

Transport rates of each solute during most sampling periods differed significantly with intestinal position. For almost all sampling periods and solutes, transport rates by the proximal and middle small intestine were equal to each other and often significantly greater than transport by the distal small intestine. We therefore averaged uptake measurements from the proximal and middle segments and henceforth refer to those two combined segments as the anterior segment ($N=3$ for each sampling period). Uptake rates of L-leucine, L-proline and D-glucose by the cecum and large intestine were significantly less than their uptake by the small intestine for most sampling times but were statistically indistinguishable from each other; hence, we averaged their values in a similar way and refer to these regions jointly as the large intestine ($N=3$ for each sampling period).

Uptake rates

In the anterior small intestine (Fig. 3), uptake rates differed significantly among sampling times for all five solutes studied (L-aspartate, $F_{6,12}=4.62$, $P=0.01$; L-leucine, $F_{6,14}=12.6$, $P \leq 0.0001$; L-lysine, $F_{6,14}=11.0$, $P \leq 0.0001$; L-proline, $F_{6,14}=7.14$, $P=0.001$; D-glucose, $F_{6,14}=20.4$, $P \leq 0.0001$). Rates had increased significantly ($P < 0.05$) above fasting values (taking snakes killed 30 days after feeding as representative of fasted snakes) by 6 h after feeding for L-leucine, L-lysine and L-proline, by 12 h for D-glucose, and by 3 days for L-aspartate. These rates peaked at day 1 for L-leucine, L-lysine and L-proline, and at day 3 for L-aspartate and D-glucose, at values

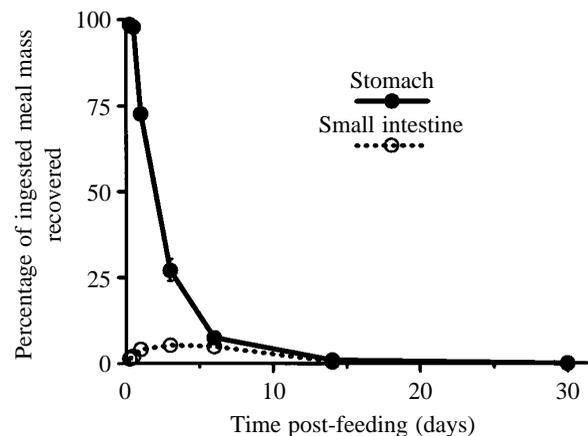


Fig. 2. Percentage of the ingested meal mass recovered from the stomach and small intestine, as a function of number of days post-feeding. In this and all subsequent figures (except Fig. 8), $N=3$ for each sampling period. Note that food mass in the stomach decreases rapidly as it is being broken down and passed into the small intestine.

6.4, 7.6, 7.3, 15.7 and 16.5 times the fasting values, respectively. At day 6, uptake rates of L-aspartate, L-leucine and L-proline had declined significantly ($P < 0.005$) below these peak values and remained statistically unchanged through days 14 and 30. Uptake rates of L-lysine and D-glucose had declined significantly ($P < 0.002$) below peak values by day 14, to values statistically equivalent to fasting values.

In the distal small intestine (Fig. 3), uptake rates differed significantly among sampling times for L-leucine ($F_{6,14}=10.4$, $P=0.0002$) and L-proline ($F_{6,14}=3.08$, $P=0.039$), but not for L-aspartate ($F_{6,12}=0.47$, $P=0.82$), L-lysine ($F_{6,14}=2.64$, $P=0.06$) or D-glucose ($F_{6,14}=1.45$, $P=0.26$). Rates had increased significantly above fasting values by 6 h for L-leucine ($P=0.03$) and by 12 h for L-lysine ($P=0.004$) and L-proline ($P=0.03$), but not until 6 days for D-glucose ($P=0.04$). Uptake rates then declined and did not differ between days 6 and 30 for L-leucine and L-proline and between days 14 and 30 for L-lysine and D-glucose. The large intestine (including the cecum) exhibited no significant change with time in uptake rates of any solutes

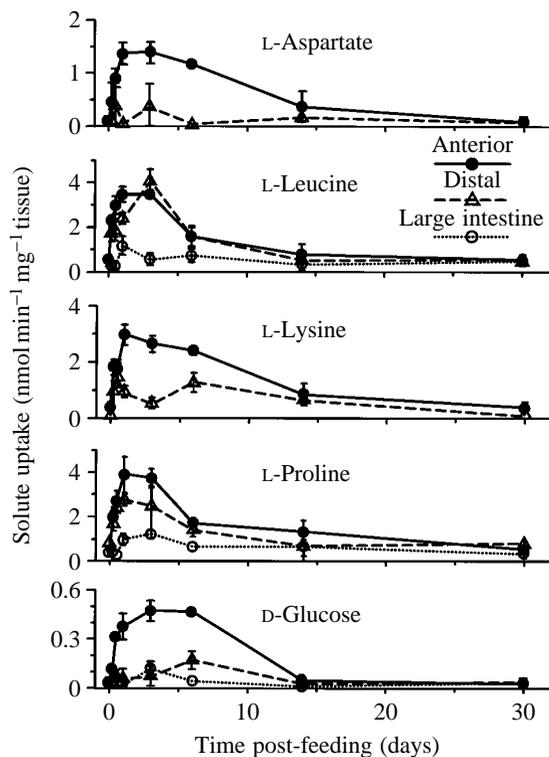


Fig. 3. Intestinal brush-border uptake rates of the amino acids L-aspartate, L-leucine, L-lysine and L-proline and the sugar D-glucose, as a function of days post-feeding. All solutes were measured in both the anterior and distal regions of the small intestine, while leucine, proline and glucose uptakes were also measured in the large intestine (including the cecum). In this and subsequent figures, values at day 0 (immediately before feeding) are taken as the day-30 post-feeding value. Note that anterior uptake rates are generally highest and peak steeply 1–3 days post-feeding, that distal rates are generally lower and respond less to feeding, and that large intestinal rates are generally lowest and do not respond.

studied (L-leucine, $F_{6,14}=1.55$, $P=0.24$; L-proline, $F_{6,14}=1.49$, $P=0.25$; D-glucose, $F_{6,14}=1.37$, $P=0.30$) (Fig. 3).

The passive permeability coefficient of glucose (K_p) was calculated from the L-glucose uptake rate, measured only in the anterior small intestine at 12 h and on days 3, 6 and 14. K_p averaged $0.0046 \pm 0.0017 \mu\text{l min}^{-1} \text{mg}^{-1}$ and differed significantly ($F_{3,8}=4.36$, $P=0.04$) among those sampling days. At day 3 ($0.012 \pm 0.004 \mu\text{l min}^{-1} \text{mg}^{-1}$), K_p was significantly greater ($P < 0.03$) than at days 6 ($0.002 \pm 0.002 \mu\text{l min}^{-1} \text{mg}^{-1}$) and 14 ($0.0 \pm 0.0 \mu\text{l min}^{-1} \text{mg}^{-1}$). The percentage of total D-glucose uptake that was passive was significantly higher ($P < 0.05$) at 12 h ($31 \pm 6\%$) and day 3 ($31 \pm 11\%$) than at day 6 ($6 \pm 6\%$) or day 14 ($0 \pm 0\%$).

Uptake ratios

Being adapted to a diet high in protein and low in carbohydrate, most carnivorous animal species possess ratios of small intestinal brush-border amino acid uptake to D-glucose uptake greater than 1.0, while ratios for most herbivorous species are less than 1.0 (Karasov and Diamond, 1988). In python anterior small intestine, the ratios of L-leucine, L-lysine and L-proline uptake to D-glucose uptake significantly exceeded 1.0 for all sampling periods, while the ratio for L-aspartate to D-glucose significantly exceeded 1.0 between 12 h and 6 days post-feeding (Fig. 4). Although amino acid uptake rates rose during digestion, these ratios were nevertheless highest in fasting snakes because D-glucose uptake rates were then so low. The ratios declined from 12 h to 6 days because D-glucose uptake rose even more steeply than did amino acid uptake.

Na^+ -independent and Na^+ -dependent uptake

In the anterior small intestine, the Na^+ -independent uptakes of L-leucine ($F_{6,14}=3.49$, $P=0.03$) and L-proline ($F_{6,14}=22.4$, $P \leq 0.0001$) differed significantly among sampling times (Fig. 5). Uptake rates had increased significantly above fasting levels (taken as values 30 days after feeding) by 12 h for L-leucine ($P=0.01$) and by day 1 for L-proline ($P \leq 0.0001$). Na^+ -independent uptake of L-leucine peaked at day 1 at 4.5 times

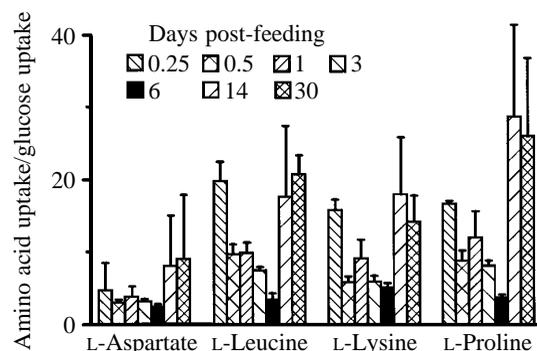


Fig. 4. Ratios of amino acid uptakes (L-aspartate, L-leucine, L-lysine or L-proline) to D-glucose uptake of the anterior small intestine for each sampling period. Note that ratios decline from 6 h to day 6 post-feeding, a period when amino acid and glucose uptakes both increase, because glucose uptake rises more steeply.

fasting levels, then declined significantly ($P=0.004$) by day 6 and significantly further ($P=0.045$) by day 14, to remain unchanged at day 30, while Na^+ -independent uptake of L-proline peaked at day 3 at 9.1 times fasting levels and then decreased significantly ($P\leq 0.0001$) by day 6 and again ($P=0.01$) by day 30. For neither L-leucine ($F_{6,14}=1.29$, $P=0.32$) nor L-proline ($F_{6,14}=2.7$, $P=0.06$) did the ANOVA detect significant variation in Na^+ -dependent uptake with sampling time, but pairwise comparisons demonstrated a 26-fold increase for L-leucine at day 3 ($P=0.05$) and a 22-fold increase for L-proline at 12 h ($P=0.008$) compared with fasting levels. These are the largest factorial increases that we observed in transport for any substrate. The Na^+ -independent component accounted for 74–100% and 49–100% of total uptake of L-leucine and L-proline, respectively, depending on the sampling day; the percentage was highest ($87\pm 7\%$ and $92\pm 4\%$ for these two amino acids, respectively) during days 1–6.

In the distal small intestine, the ANOVA detected no significant variation among sampling days in either the Na^+ -independent or Na^+ -dependent uptake of L-leucine ($F_{6,12}=1.56$, $P=0.24$ and $F_{6,12}=1.73$, $P=0.20$, respectively) and L-proline ($F_{6,13}=1.64$, $P=0.21$ and $F_{6,13}=1.41$, $P=0.28$, respectively). Pairwise comparisons revealed greater ($P=0.04$) Na^+ -independent uptake of L-proline on day 1 than on day 6, and greater ($P<0.04$) Na^+ -dependent uptake of L-leucine on day 3 than on days 6, 14 and 30. As in the anterior small intestine, most uptake ($84\pm 9\%$ for L-leucine, $59\pm 8\%$ for L-proline) in the distal intestine during days 1–6 was Na^+ -independent.

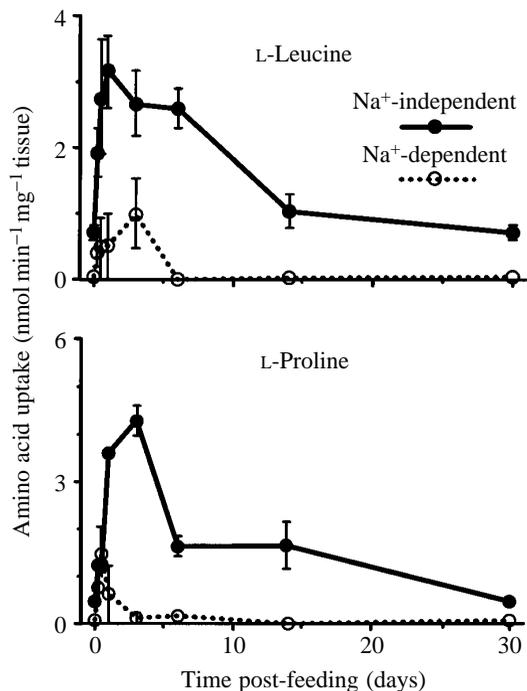


Fig. 5. Na^+ -independent and Na^+ -dependent components of L-leucine and L-proline uptakes by the anterior small intestine, as a function of days post-feeding. Note that Na^+ -independent uptake predominates and responds to feeding for both of these amino acids.

Uptake capacity

As described above (see Materials and methods), we calculated nutrient uptake capacities of the whole length of the small intestine as the sum of regional products of uptake rate times intestinal mass (Fig. 6). The uptake rates of all nutrients in the anterior small intestine increased steeply after feeding, and intestinal mass also increases after feeding (see below). Hence, uptake capacities also varied significantly among sampling times for all five nutrients (L-aspartate, $F_{6,12}=8.47$, $P=0.001$; L-leucine, $F_{6,14}=17.5$, $P\leq 0.0001$; L-lysine, $F_{6,14}=27.6$, $P\leq 0.0001$; L-proline, $F_{6,14}=17.5$, $P\leq 0.0001$; and D-glucose, $F_{6,14}=9.61$, $P=0.0003$). Uptake capacities had risen significantly above ($P<0.04$) fasting values by 6 h for L-aspartate and L-leucine and by 12 h for L-lysine, L-proline and D-glucose. Peak capacity was attained at day 1 for L-lysine and at day 3 for L-aspartate, L-leucine, L-proline and D-glucose, at 16, 24, 14, 11 and 24 times fasting values, respectively. These increases in uptake capacity are due primarily to transporter up-regulation (increases in uptake rates by up to 6- to 17-fold) and secondarily to increases in intestinal mass (by up to twofold). All uptake capacities had declined significantly ($P<0.05$) by day 14 and remained unchanged at day 30.

Blood chemistry

Plasma of fasted snakes (30 days after feeding) was clear,

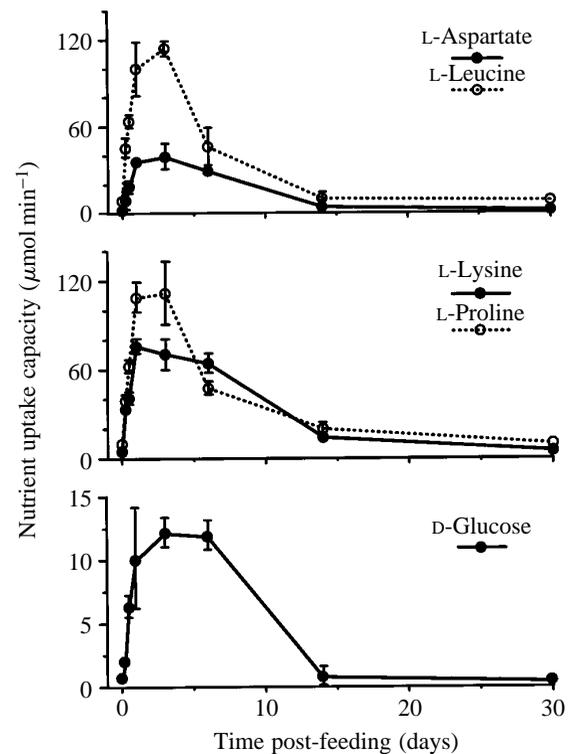


Fig. 6. Uptake capacities of the whole length of the small intestine for L-aspartate, L-leucine, L-lysine, L-proline and D-glucose, as a function of days post-feeding. Uptake capacity was calculated as the sum of regional products of uptake rate \times intestinal mass, and the rapid rises in uptake capacity result from a combination of rises in both uptake rates (Fig. 3) and intestinal mass (Fig. 9).

with a greenish tint due to its high riboflavin content (Vilella and Thein, 1967), whereas plasma of digesting snakes was noticeably turbid due to its high lipid content (D. L. Puppione, S. M. Secor and J. Diamond, unpublished data). Solutes whose plasma concentrations did not vary significantly among sampling times were K^+ ($F_{5,12}=2.23$, $P=0.12$), Ca^{2+} ($F_{5,12}=2.46$, $P=0.09$), glucose ($F_{5,12}=1.92$, $P=0.16$), cholesterol ($F_{5,12}=0.94$, $P=0.49$), total protein ($F_{5,12}=1.18$, $P=0.37$) and albumin ($F_{5,12}=0.58$, $P=0.71$) (Fig. 7). Cl^- was the only measured constituent whose plasma concentration decreased after feeding ($F_{5,12}=3.97$, $P=0.02$): at 6 h it was unchanged from fasting levels (128 ± 2 mmol l $^{-1}$) but then declined significantly ($P=0.01$) by 12 h (114 ± 3 mmol l $^{-1}$) and reached a minimum value of 110 ± 4 mmol l $^{-1}$ at 3 days (Fig. 7).

Plasma concentrations of all other solutes studied increased after feeding (Na^+ , $F_{5,12}=5.68$, $P=0.007$; HCO_3^- , $F_{3,12}=7.15$, $P=0.005$; phosphorus, $F_{5,12}=6.35$, $P=0.004$; CO_2 , $F_{5,12}=5.58$, $P=0.007$; creatinine, $F_{5,12}=4.00$, $P=0.03$; alkaline phosphatase, $F_{5,12}=4.81$, $P=0.01$) (Figs 7, 8). Na^+ concentration increased significantly ($P=0.002$) from fasting values (157 ± 0 mmol l $^{-1}$) to peak at 6 h at 170 ± 2 mmol l $^{-1}$, and then declined significantly ($P=0.01$) by 12 h (160 ± 2 mmol l $^{-1}$). Phosphorus concentration increased ($P=0.03$) from fasting levels of 6.7 ± 0.3 mg dl $^{-1}$ within 24 h and peaked at 11.4 ± 0.7 mg dl $^{-1}$ at 3 days. CO_2 concentration peaked at 6 h at almost twice its fasting value (20.0 ± 1.5 versus 11 ± 0.6 mmol l $^{-1}$) and remained

significantly elevated between 1 and 6 days. Between 6 h and 1 day, creatinine levels (0.37 ± 0.03 mg dl $^{-1}$) were significantly increased ($P=0.005$) above the fasting level of 0.23 ± 0.03 mg dl $^{-1}$. Alkaline phosphatase increased ($P=0.002$) from a fasting level of 53 ± 7 units l $^{-1}$ to 81 ± 7 units l $^{-1}$ at 6 h and then declined significantly by day 3.

Measurements on whole blood revealed significant feeding responses of blood pH ($F_{3,12}=4.25$, $P=0.03$), P_{CO_2} ($F_{3,12}=11.3$, $P=0.001$) and P_{O_2} ($F_{3,12}=13.5$, $P=0.0004$) (Fig. 8). Blood pH and P_{CO_2} rose, and P_{O_2} dropped, after feeding. Blood pH was highest at day 1 (7.49 ± 0.01), significantly greater ($P=0.005$) than at day 5 (7.19 ± 0.11). P_{CO_2} more than doubled from resting levels at day 1 and remained significantly elevated at days 2 and 5, while P_{O_2} declined significantly ($P=0.04$) at day 1 and plunged to 22% of fasting levels at day 2.

Morphological responses

Small intestine

The mass of the anterior small intestine increased significantly by 40% over fasting levels within 6 h of feeding, peaked at day 3 at a twofold increase, remained elevated at day 6, and declined to fasting levels by day 14 (Fig. 9). The ANOVA detected no significant change in distal small intestinal mass ($F_{6,14}=1.05$, $P=0.43$) among sampling times, although pairwise comparisons showed that the mass at day 1 was significantly heavier ($P=0.02$) than fasting values by a factor of 1.7.

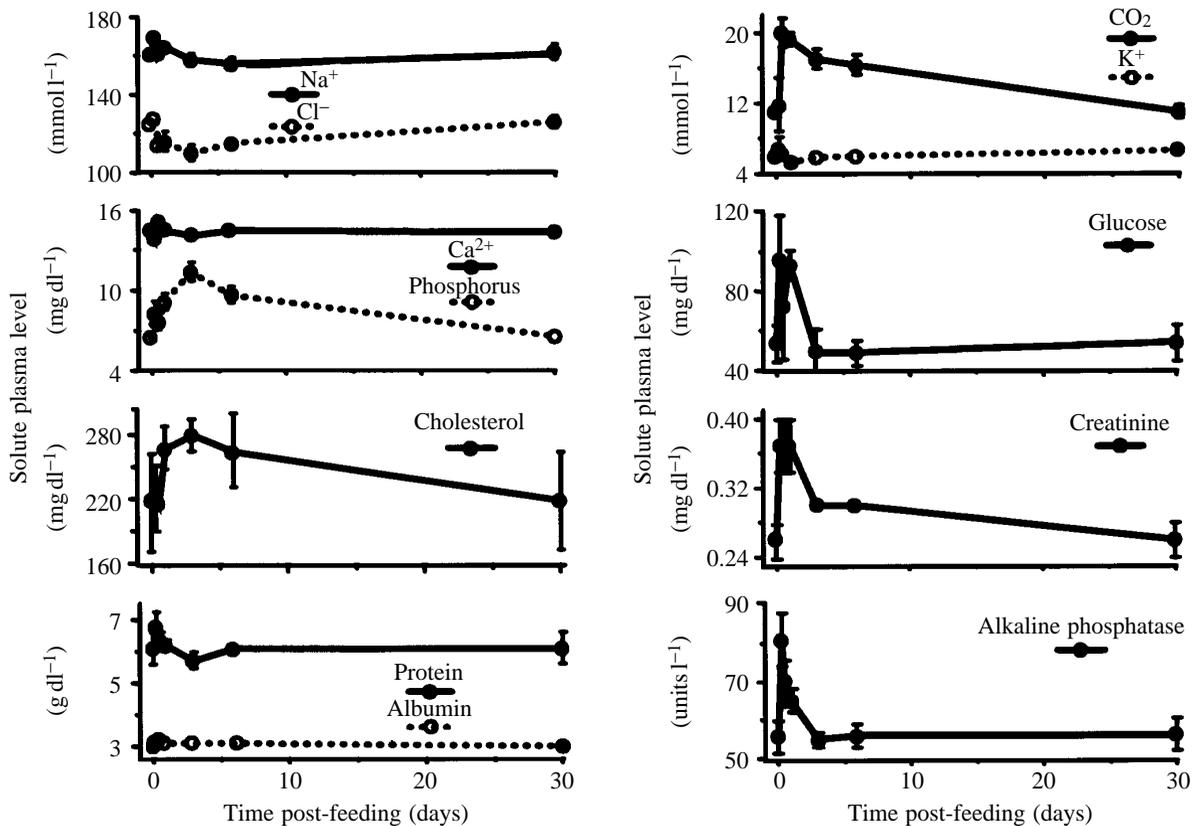


Fig. 7. Solute plasma levels, as a function of days post-feeding. Note the post-feeding decrease in Cl^- and rises in CO_2 , phosphorus, creatinine and alkaline phosphatase levels. Alkaline phosphatase activity is measured in international units.

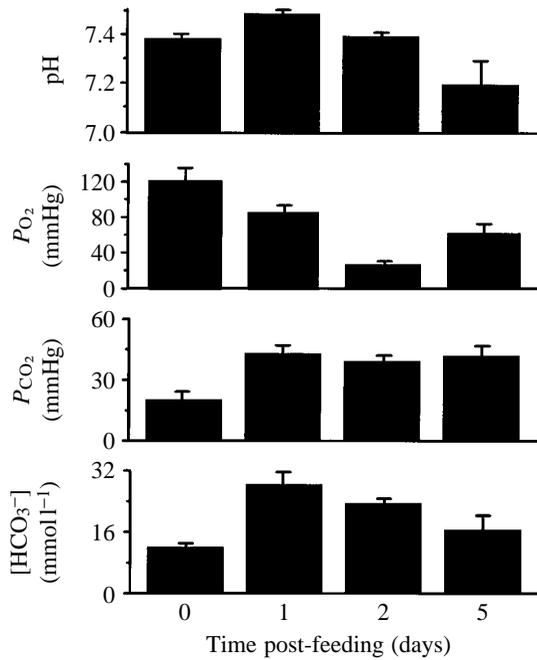


Fig. 8. Mean pH, P_{CO_2} , P_{O_2} and HCO_3^- concentrations of blood samples drawn sequentially from the same four snakes while fasting and at days 1, 2 and 5 post-feeding. Note that pH, P_{CO_2} and HCO_3^- concentrations rise and P_{O_2} falls after feeding (1 mmHg=133.3 kPa).

Most of the increase in anterior small intestinal mass resulted from the mass increase of its mucosal layer (by 2.7 times at day 3, $P \leq 0.0001$). The ANOVA detected no variation of anterior small intestinal serosal mass among sampling days, although serosal mass at day 1 exceeded fasting levels in a pairwise comparison ($P=0.03$). Both the mucosal and serosal masses of the distal small intestine were independent of sampling time ($F_{6,14}=1.04$, $P=0.44$ and $F_{6,14}=0.70$, $P=0.66$, respectively).

Other organs

Wet masses of the lungs ($F_{6,13}=7.32$, $P=0.001$), heart ($F_{6,13}=8.31$, $P=0.001$), liver ($F_{6,13}=4.39$, $P=0.01$), empty stomach ($F_{6,13}=3.76$, $P=0.02$), full gallbladder ($F_{6,13}=4.80$, $P=0.009$) and kidneys ($F_{6,13}=3.34$, $P=0.03$) differed significantly among sampling times, but wet masses of the pancreas ($F_{6,13}=2.24$, $P=0.11$), large intestine ($F_{6,13}=1.01$, $P=0.46$) and abdominal fat bodies ($F_{6,13}=1.14$, $P=0.44$) did not (Fig. 10). Dry mass measurements yielded the same conclusions, except that variation in liver and stomach masses was now no longer significant.

Most of these organ feeding responses involved increases rather than decreases in mass. Stomach wet mass peaked at 26% above fasting levels by 6 h; kidney wet mass increased by 45% by day 1; liver wet mass increased by 53% at day 3; and lung wet mass almost doubled by day 14. The response was opposite for the full gallbladder, where wet and dry masses following feeding declined by 64% and 69%, respectively, because of emptying of bile.

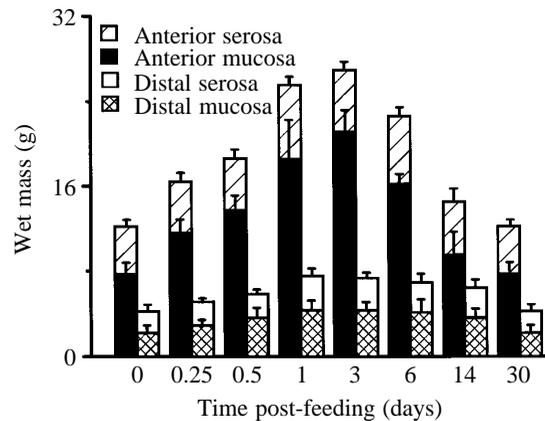


Fig. 9. Wet masses of the serosal and mucosal layers of the anterior and distal small intestine, as a function of days post-feeding. Note that anterior mucosal mass almost triples upon feeding, while the masses of the other layers remain unchanged.

Discussion

Metabolic response

In mammals and fish, the metabolic response to digestion (commonly referred to as specific dynamic action) involves an increase in oxygen consumption by approximately 25–50% (Brody, 1945) and 60–160% (Jobling, 1981), respectively. These responses are trivial compared with the 17-fold response of pythons described here (Table 1). Benedict (1932), one of the first authors to measure metabolic responses to digestion in snakes, obtained metabolic responses of 1.7–7 for *Python molurus*, *Boa constrictor* and *Pituophis melanoleucus* consuming meals equivalent to 3–22% of their body mass. Our 17-fold increases were for *P. molurus* consuming larger meals (25% of their body mass). We have subsequently found that response magnitude in *P. molurus* scales with meal size, increasing to a 45-fold response for snakes consuming a meal equivalent to 100% of body mass, which is not at all an unnaturally large meal: wild snakes consuming relatively much larger meals have been recorded (Greene, 1992).

These metabolic responses of digesting pythons are comparable to or larger than the responses of mammals running at maximum speed during a brief sprint. Some values of the ratio of maximal \dot{V}_{O_2} to basal metabolic rate for mammalian sprinters are 16 for dogs (Young *et al.* 1959), 18 for human athletes (Benedict, 1914; Margaria *et al.* 1963), 21 for foxes (Irving *et al.* 1955; Weibel *et al.* 1983), 21 for steers (Jones *et al.* 1989), 21 for draft horses (Brody, 1945; Birlenbach and Leith, 1994) and 45 for racehorses (Brody, 1945; Birlenbach and Leith, 1994). However, mammalian sprinters can sustain those metabolic responses only briefly, while pythons can do so while lying at rest for several days. Interestingly, the oxygen consumption rate that we have measured for fasting pythons during a 'sprint' (snakes that we induced to move rapidly, by snake standards, at 0.5 km h⁻¹) is only 0.20±0.04 ml O₂ g⁻¹ h⁻¹ ($N=3$), less than half the value for digesting pythons.

There is an extensive literature on the metabolic response to

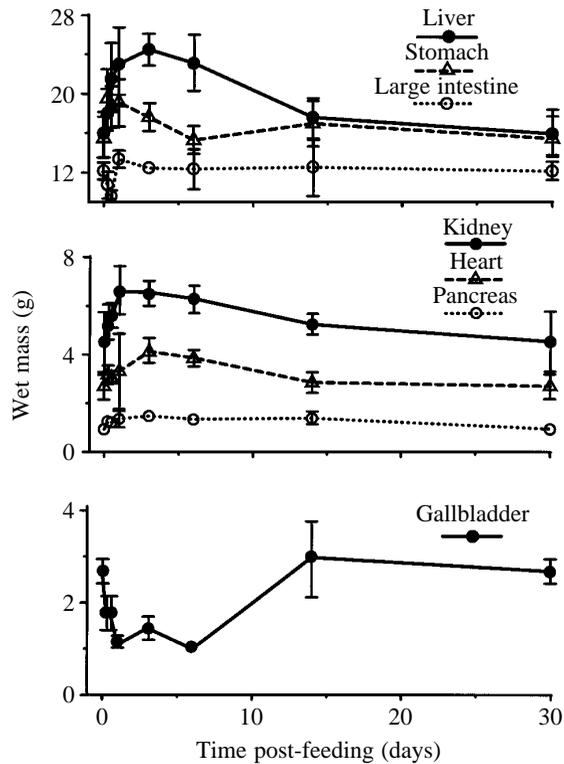


Fig. 10. Wet masses of seven organs, as a function of days post-feeding. Gallbladder mass decreases significantly upon feeding as a result of gallbladder emptying, while the masses of the other organs (except for the pancreas and large intestine) increase significantly.

feeding in other species (see Brody, 1945; Jobling, 1981; Rothwell and Stock, 1983; Blaxter, 1989, for reviews). Proposed contributing mechanisms include both pre-absorptive and post-absorptive mechanisms. Examples of pre-absorptive mechanisms include the energetic costs of gastric, pancreatic, biliary and intestinal secretion, the costs of transporter and enzyme up-regulation and the costs of growth of the intestine and other tissues. Examples of post-absorptive mechanisms include costs of biochemical transformations involved in intermediary metabolism. Both pre-absorptive and post-absorptive mechanisms are believed to be important in other animal species, because intravenous infusion of nutrients also yields increased metabolic rates, but by smaller factors than observed for oral consumption of energetically equivalent intact meals (Borsook, 1936; Coulson and Hernandez, 1983). We assume that both pre-absorptive and post-absorptive mechanisms are also important in pythons, because much of the pythons' increase in metabolic rate is measured within 12 or 24 h of feeding (Fig. 1), at a time when most of the meal is still unabsorbed within the snake's stomach, and because much of the increase is also measured later during the post-absorptive phase of digestion (Fig. 1). Three factors combine to make the metabolic response to feeding so large in pythons compared with that in mammals: the pythons' much larger meal size; their gut atrophy during their long fasts, requiring a high investment in rebuilding the atrophied gut; and their much

Table 1. Comparisons between three obligate carnivorous species of similar body mass, with respect to body and intestinal masses, intestinal brush-border nutrient uptake rates, intestinal brush-border nutrient uptake capacities and other metabolic measurements

	Trout	Burmese python	Mink
Mass			
Body mass, BM (g)	400	740	690
Intestinal mass (g)	7.9	32	39
Intestinal mass/BM	0.020	0.043	0.057
Uptake rates (nmol min⁻¹ mg⁻¹)			
L-Aspartate	0.4	1.1	1.3
L-Leucine	1.2	3.7	2.3
L-Lysine	0.8	2.0	2.0
L-Proline	1.1	3.3	2.7
D-Glucose	0.1	0.3	0.9
Uptake capacity (μmol min⁻¹ body mass^{-0.75})			
L-Aspartate	0.04	0.27	0.37
L-Leucine	0.15	0.80	0.74
L-Lysine	0.09	0.50	0.41
L-Proline	0.09	0.78	1.19
D-Glucose	0.01	0.08	0.37
Metabolic rate, MR			
SMR or BMR (ml O ₂ g ⁻¹ h ⁻¹)	0.11	0.034	0.73
Peak digesting MR (ml O ₂ g ⁻¹ h ⁻¹)	0.21	0.58	0.88
Peak locomotion MR (ml O ₂ g ⁻¹ h ⁻¹)	0.76	0.20	6.4
Metabolic scope for digestion	2.0	17.0	1.2
Metabolic scope for locomotion	6.9	6.0	8.8

The three species compared are the ectothermic rainbow trout *Salmo gairdneri* (Buddington and Diamond, 1987; LeGrow and Beamish, 1986; Rao, 1968), the endothermic mink *Mustela vison* (Buddington *et al.* 1991; Farrell and Wood, 1968; Williams, 1983), and the Burmese python (*Python molurus*) 3 days post-feeding.

For measurements of nutrient uptake rates and capacities, solute incubation concentrations in each species (20–50 mmol l⁻¹) were chosen to be above K_m values and to yield approximations of V_{max} values.

Basal metabolic rates (BMR) of mink are much higher than the standard metabolic rates (SMR) of trout or python, as expected.

All three species at their peak locomotory performance (trout swimming at 3.2 km h⁻¹, mink running at 4.5 km h⁻¹, pythons crawling at 0.5 km h⁻¹) display similar metabolic scope (ratio of peak locomotory metabolic rate to BMR or SMR). However, in other respects, i.e., with their relatively high intestinal masses, high nutrient uptake rates and normalized uptake capacities and metabolic rates, pythons at the peak of digestion are more like endotherms than ectotherms. The metabolic scope of digesting pythons, 1 day post-feeding, is much higher than that of the other species during digestion or even during locomotion.

Intestinal brush border nutrient uptake capacities are normalized to metabolic live mass:body mass^{-0.75}.

lower basal metabolic rates, constituting the low baseline from which oxygen consumption rises during digestion.

One can estimate the total energy that our pythons expend on the total nutritive process (from ingestion to growth), as the

product of two factors: the O₂ consumption above fasting rates during the 7 days of significantly elevated O₂ consumption (the area under the curve of Fig. 1); and an assumed factor of 18.3 J of energy expended per ml O₂ consumed (Nagy, 1983). This calculation yields an estimate of 411±39 kJ as the energy of digestion. This value equals 32±1% of the metabolizable energy content of the ingested rats, assuming an 85% assimilation efficiency for pythons and 8 kJ g⁻¹ wet mass of rat (S. M. Secor and J. Diamond, unpublished measurements). This relative cost of digestion for pythons (i.e. digestive cost expressed as a percentage of the metabolizable energy of a meal) is greater than those values (10–23%) calculated for other vertebrates (Jobling, 1981; Costa and Kooyman, 1984). The fact that pythons experience increased relative, as well as absolute, costs of digestion suggests that some digestive processes are disproportionately important in pythons (and in other sit-and-wait foraging snakes: see below) compared with other species. Those disproportionately important processes may especially include the costs of tissue growth and transporter and enzyme up-regulation following the atrophy and down-regulation that occur during the long fasting periods of sit-and-wait foraging species.

Much of this energy of digestion is expended within the first day or two, when most of the meal is still within the snakes' stomach. Evidently, much or most of the energy of digestion does not come from the absorbed energy content of the prey currently being digested, but from the snakes' stored energy reserves. In support of this interpretation, we have found evidence of post-feeding fat mobilization in the form of a 60-fold rise of plasma triglyceride levels within 24 h of feeding (Secor and Diamond, 1994a). Thus, digesting pythons operate on the principle of self-service gasoline stations: pay before pumping.

Digestion rates

The time to defecation (8–14 days) for *Python molurus* ranging in body mass from 125 to 1400 g (467±85 g) is similar to that for the sidewinder rattlesnake *C. cerastes* [11–14 days, body mass 70–200 g (124±13 g): Secor *et al.* 1994], but is twice as long as that for the colubrid snakes *Elaphe guttata* (3–4 days, mean body mass 300 g: Greenwald and Kanter, 1979) and *Natrix natrix* (4–5 days, body mass 80–100 g: Skoczlas, 1970). These differences are probably not due to differences in body mass, since pythons and sidewinders exhibit no significant variation ($P>0.21$) in time to defecation related to variation in body mass, and since the body mass of the colubrid *Elaphe guttata* is intermediate between that of pythons and sidewinders.

Pythons digested all skeletal elements of their meal within 6 days, whereas stomachs of sidewinders occasionally still contained skeletal elements 10 days after eating. Mats of detached hair were the last items to leave the python's stomach, suggesting that pythons control the sequence in which portions of their meals leave the stomach. Hair, the first item loosened from the rat's carcass in the python's stomach, is difficult to digest and constitutes the main component of python feces.

Evidently, the more digestible portions of the prey, muscle, viscera and bone, pass first into the small intestine, leaving the non-digestible hair to pass through last.

Differences in digestion rates among snake species are probably related to factors such as the natural interval between meals, and consequently the degree of atrophy between meals, and basal metabolic rate. The two colubrid snake species (*E. guttata* and *N. natrix*) presumably have more frequent natural meals than do pythons or sidewinders, and therefore undergo relatively less intestinal atrophy, so that the intestine is ready for digestion much sooner after the prey has been consumed (Secor and Diamond, 1994b). Pythons and sidewinders share long meal intervals and high levels of intestinal atrophy, but sidewinders have lower mass-specific basal metabolic rates, which are likely to be reflected in slower rates of biosynthesis.

Nutrient transport

A proximal-to-distal gradient of nutrient transport activity along the small intestine characterizes many vertebrate species (Buddington *et al.* 1991; Dykstra and Karasov, 1992; Secor *et al.* 1994). In our pythons, this gradient was more pronounced in digesting snakes than in fasting snakes, because of greater up-regulation of transporters proximally than distally in digesting snakes.

The factorial increases in intestinal brush-border nutrient transporter rates of pythons upon feeding (6–17) are similar to those of sidewinders (Secor *et al.* 1994) and far exceed those of other vertebrate species under physiological conditions. The only higher factor known to us is for the intestinal glucose transporter in weaned sheep receiving intestinally perfused sugars to bypass the rumen (Shirazi-Beechey *et al.* 1991). Those increases in python transporter rates make the largest contribution to pythons' observed increases in whole intestine transporter uptake capacities; the increase in intestinal mass (by up to twofold) makes a smaller contribution. In contrast, in response to a change in diet or arousal from hibernation, rodents regulate their sugar and amino acid transporters over a span of only twofold (Ferraris and Diamond, 1989; Carey and Sills, 1992).

It may initially appear surprising that both pythons and sidewinders up-regulate their glucose transporter activity by factors at least as large as for their amino acid transporters. The diets of these carnivores yield far more amino acids than glucose, and one might therefore have expected little response of the glucose transporter to feeding if its sole function were to absorb ingested glucose. However, glucose is still a major energy currency in the plasma of these snakes. Hence, the function of glucose transporter regulation may instead be to recover glucose diffusing down the concentration gradient from plasma into the intestinal lumen (Secor *et al.* 1994).

Like the overall speed of digestion, the speed of transporter up-regulation is somewhat faster in pythons than in sidewinders. Up-regulated transporter capacities are still undetectable in sidewinders at 12 h after feeding and are not apparent until 24 h, whereas they are detectable in pythons by 6 or 12 h. In pythons, the various nutrient transporters are up-

and down-regulated with similar but not identical time courses (Fig. 3), while in sidewinders the up-regulated glucose transporter activity returns to baseline values much more rapidly than do the amino acid transporter activities. Sidewinders (Secor *et al.* 1994) and pythons up-regulate both the Na⁺-dependent and Na⁺-independent mechanisms of amino acid transport (Fig. 5). While some of the Na⁺-independent uptake may be due to passive diffusion, at least part of it (and probably all of the Na⁺-dependent uptake) is carrier-mediated, as shown by its saturation kinetics and competition among different amino acids (Stevens *et al.* 1982; Karasov *et al.* 1986; Secor *et al.* 1994). As in sidewinders (Secor *et al.* 1994) and most other vertebrate species (Karasov *et al.* 1985b), passive uptake accounts for only a small percentage (0–31%) of glucose uptake in pythons.

Endothermic vertebrate species generally possess intestinal nutrient uptake capacities (summed over the whole length of the small intestine) many times greater than those of ectotherms of similar body mass and dietary habits (Karasov *et al.* 1985a,b). We have shown previously that capacities of digesting sidewinders are similar to or higher than those of endothermic carnivores (Secor *et al.* 1994), and we now find the same to be true for digesting pythons. Amino acid transport rates and capacities of digesting pythons are close to those of a similar-sized mammalian carnivore, the mink, and greater than those of a similar-sized ectothermic carnivore, the rainbow trout (Table 1).

In pythons, as in most other vertebrates (Karasov *et al.* 1985b), nutrient transporter activities are much lower in the large intestine than in the small intestine. Uptake rates in python proximal large intestine are only 5–38% of those in python anterior small intestine. If the rates that we measured in the proximal part of the large intestine are maintained throughout the distal part, which we did not study, then total large intestinal uptake capacity would be equivalent to only 10, 12 and 10% of small intestinal uptake capacity for L-leucine, L-proline and D-glucose, respectively. Python large intestine may play a limited role in mopping up nutrients that have passed unabsorbed through the small intestine and a larger role in absorbing salts and water plus trace nutrients synthesized by intestinal microbes.

Blood chemistry

The plasma and blood solute concentrations that we measured in fasting pythons fall within the range of values reported from many species of fasting snakes (Dessauer, 1970). The largest changes accompanying feeding are a 2.5-fold increase in plasma HCO₃⁻ concentration and a 70% drop in blood P_O₂ (Figs 7 and 8). The rise in plasma HCO₃⁻ concentration, and the associated rise in blood pH and drop in plasma Cl⁻ concentration, constitute the temporary alkalosis or so-called 'alkaline tide' due to massive gastric secretion of HCl by a transport mechanism that exchanges blood Cl⁻ for HCO₃⁻. A large alkaline tide has also been described in fed alligators (Coulson *et al.* 1950). The big drop in blood O₂ and increase in CO₂ concentrations presumably arise from the big

increase in O₂ consumption and metabolic rate that we measured (Fig. 1). The rise in phosphorus and alkaline phosphatase levels may reflect phosphate release or mobilization, while the rise in creatinine level (an end-product of nitrogen metabolism) may reflect utilization of body protein stores for rebuilding the gut.

Morphological responses

The large metabolic response of fed pythons requires rapid growth of many organs that have atrophied during the fasting period of low metabolic activity. The first organs to respond with significant increases in wet mass (within 6 h of the snake's consuming a meal) are the stomach and small intestine, the organs most immediately involved in digesting the meal. The later mass increases of the lungs, heart, liver and kidneys serve to support the increased rates of gas exchange, to process and circulate the absorbed nutrients and to excrete the resulting wastes. In the case of the small intestine, we documented the growth response by increases not only in intestinal mass but also in mucosal mass, length of mucosal folds, enterocyte size and microvillus length (S. M. Secor and J. Diamond, unpublished observations). We previously observed increases in intestinal mass, mucosal mass and enterocyte size in fed sidewinders (Secor *et al.* 1994). Carey (1990) found that ground squirrels (*Spermophilus tridecemlineatus*) increase intestinal wet mass 3.5-fold within several months after arousal from hibernation.

Comparison of pythons with sidewinders, and adaptive significance

We can now summarize our comparison of the digestive responses of pythons, described in this paper, with those of the sidewinders that we studied previously (Secor *et al.* 1994). Both species increase their metabolic rate upon feeding, but the factorial increase is larger in pythons than in sidewinders fed the same relative size meal (17-fold *versus* 7-fold, respectively). Pythons complete digestion more rapidly. Both species up-regulate nutrient transport rates, but pythons do so more rapidly (within 6 h *versus* within 24 h, respectively). Sidewinders and pythons up-regulate both the Na⁺-dependent and the Na⁺-independent components of amino acid uptake. Both species rapidly increase their small intestinal mass. We have established the existence of post-feeding increases in mass for several other organs of pythons, but we did not establish such increases in sidewinders.

Despite these differences of detail, the main conclusion is that these two species, which are phylogenetically distant but ecologically similar in being sit-and-wait foragers taking large meals at long intervals, resemble each other in their massive physiological and anatomical responses to feeding. In contrast, we observed much smaller responses in snake species that feed relatively frequently under natural conditions (Secor and Diamond, 1994b). These results support our interpretation that large feeding responses are not a phylogenetic peculiarity of rattlesnakes but are an evolved adaptation to large infrequent meals. *Python molurus* in the wild waits in ambush to prey

predominantly on large mammals (as large as deer, jackals and leopards) and experiences long intervals between natural feeding bouts (Wall, 1912; Pope, 1961). Female pythons normally do not eat during the 4 or 5 months required for gestation and incubation of the eggs, and captive individuals survive fasts of over a year (Wall, 1912; de Vosjoli, 1991). The metabolic cost of the pythons' feeding response is large and amounts to 32% of the energy payoff of the ingested meal. Nevertheless, in return for this expenditure, pythons spare themselves the heavy energy burden that maintenance of the intestine would otherwise require during the expected long fasts.

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