

# The effects of maternal intake and gestational age on materno-fetal transport of vitamin C in the guinea-pig

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The effects of maternal intake and gestational age on materno-fetal transport of vitamin C were investigated in female Dunkin-Hartley guinea-pigs. Twenty-four time-mated dams were fed on either a moderate-vitamin C (group A) or a high-vitamin C (group B) diet, throughout pregnancy. At days 49, 63 and 66 of gestation, and at term, three animals from each group were killed and fetuses removed by hysterectomy. Plasma, liver, kidney, lungs, heart, placenta and amniotic fluid were collected from dams and fetuses and subsequently analysed for vitamin C. Fetal plasma and amniotic fluid concentrations showed negative associations with gestational age for both dietary groups, independent of an effect of dam ( $P < 0.001$ ). A similar, though not significant, effect of gestational age was observed on placental vitamin C and group A fetal tissue concentrations. Fetal plasma, placental and amniotic fluid vitamin C concentrations were significantly higher in group B than group A ( $P < 0.001$ ), suggesting the influence of maternal diet. Although the level of maternal vitamin C intake can influence the circulating concentration in the fetus, there is a decrease associated with increasing gestational age, independent of the maternal diet. The gestational age-dependent change in the fetal accumulation of vitamin C may reflect changes in the rate of placental transfer.

## Vitamin C: Materno-fetal transport: Guinea-pig

Babies born preterm have a higher circulating concentration of vitamin C than babies born at term (Silvers *et al.* 1994; Berger *et al.* 1996). In view of the evidence that free radicals play a role in the pathophysiology of certain diseases of prematurity (Kelly & Lubec, 1995; Saugstad, 1996), a high plasma concentration of vitamin C, a known antioxidant, might be expected to confer some benefit. There is, however, interest in the possibility that at high concentration in the plasma of premature babies, vitamin C may act as a pro-oxidant. A large longitudinal study in premature babies has suggested that a high concentration of plasma vitamin C in the neonatal period is associated with poor outcome (Silvers *et al.* 1998). At concentrations measured in the plasma of premature babies vitamin C inhibits the antioxidant activity of caeruloplasmin (Gutteridge, 1991; Powers *et al.* 1995). Low concentrations of transferrin and caeruloplasmin (Lindeman *et al.* 1989, 1992, 1995; Silvers *et al.* 1994), and the presence of catalytic Fe in the plasma of premature babies (Kime *et al.* 1996) increase the likelihood that vitamin C may act pro-oxidatively in this group.

Plasma vitamin C concentrations at birth may be partly a function of gestational age (Silvers *et al.* 1994) but may also be influenced by maternal vitamin C intake during pregnancy (Pate *et al.* 1996). A study was undertaken to explore this.

## Materials and methods

### Reagents

Metaphosphoric acid (MPA) was obtained from BDH laboratory supplies, Poole, Dorset, UK. Hypnorm was obtained from Janssen Animal Health, Janssen Pharmaceuticals Ltd., Grove, Oxon., UK and sodium pentobarbitone from J. M. Loveridge plc, Southampton, Hants., UK. Ascorbic acid oxidase (EC 1.10.3.3), ascorbic acid, phenylenediamine and sodium acetate trihydrate were obtained from Sigma Chemical Co., Poole, Dorset, UK.

### Animals and diets

As the purpose of the study was to understand determinants of high plasma concentrations of vitamin C in the neonate, it was planned to place pregnant guinea-pigs on a diet either containing adequate vitamin C or supplemented to give a high vitamin C content. Due to problems encountered with a commercial diet the basal diets used were not the same (Table 1). All nutrients were considered adequate for normal breeding purposes.

Diet A was a commercial pelleted guinea-pig breeding diet containing 300 mg ascorbic acid/kg diet (SDS, Witham,

**Abbreviations:** (M-P), transport of vitamin C from the mother to the placenta; MPA, metaphosphoric acid; (P-F), transport of vitamin C from the placenta to the fetus.

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**Table 1.** Compositions of the diets used in the present study

Nutrients	Diet A	Diet B
Crude fat (g/kg)	48	45
Crude protein (g/kg)	189	160
Crude fibre (g/kg)	129	130
Ash (g/kg)	90	84
Gross energy (MJ/kg)	14.2	14.5
Minerals and trace elements (mg/kg diet)		
Iron	212	173
Copper	12	18
Manganese	86	85
Zinc	124	80
Cobalt	0.40	0.62
Iodine	0.992	1.740
Selenium	0.256	0.300
Fluorine	0.019	–
Vitamins (mg/kg diet)		
Retinol	3.636	7.500
Cholecalciferol	0.021	0.050
dl- $\alpha$ -Tocopherol	82	142
Thiamin hydrochloride	17.5	21.0
Riboflavin	23.4	25.0
Pyridoxine hydrochloride	18.1	18.0
Cyanocobalamin	0.18	0.04
Ascorbyl polyphosphate	300	5050
Menadione sodium bisulfite	114	35
Pteroylmonoglutamic acid	6.4	11.0
Nicotinic acid	78.4	80.0
Pantothenic acid	28.4	30.0
Choline	1187	1142
Inositol	1582	1580
Biotin	0.236	0.298
Salts (g/kg diet)		
Calcium	12	13
Phosphorus	7.5	5.0
Sodium	3.0	1.6
Chlorine	4.6	3.6
Magnesium	4.8	3.0

Essex, UK). Diet B consisted of a powdered basal diet (B&K Universal Ltd., Grimston, Aldborough, Hull, UK) containing only 50 mg ascorbic acid/kg diet, supplemented with 5000 mg ascorbic acid/kg diet. This was added dry to the powdered diet, which was then mixed and vegetable oil added (about 20 ml/kg) to make it palatable to the guinea-pigs. This diet was made up fresh every 2–3 d and stored at 4° whilst not in use. The concentration of vitamin C was 17-fold higher in diet B than diet A. There were differences in the concentrations of fat-soluble vitamins between the two diets but there is no basis for believing that this would influence vitamin C metabolism. Tap water containing 100 mg ascorbic acid/l for diet A and 1 g ascorbic acid/l for diet B was made available for the animals to drink *ad libitum*. Both groups also received dried autoclaved hay, fresh every 2–3 d. The ascorbic acid content of both diets was confirmed early in the experiment by extraction into MPA (50 g/l) and analysis as for tissue samples.

Twenty-four time-mated Dunkin-Hartley guinea-pigs were obtained from David Hall (Darley Oaks Farm, Newchurch, Nr Burton on Trent, Staffs., UK), and were randomly allocated to group A or group B. From 2–3 d after time-mating the animals were housed in two large floor pens in a room maintained at a temperature of 22° with a 12 h light–dark cycle. All the animals were fed *ad libitum*.

Time-mating permitted study of the dams and fetuses at specific points in gestation.

### Protocol

The guinea-pig has an average gestation of 72 d. Guinea-pig fetuses were removed on days 49, 63 and 66 of gestation. Day 49 was considered to be the earliest time point at which efficient fetal blood sampling could be guaranteed; gestation for 63 and 66 d represented prematurity (Kelly *et al.* 1991*a,b*). Fetuses were to be removed from three dams at each of these gestational ages from both groups A and B. Pups from the three remaining dams in each diet group were to be delivered naturally at term.

On the day of delivery dams were anaesthetized by subcutaneous administration of 800  $\mu$ l hypnorm–diazepam (50:50, v/v). Fatal intravenous injection of 500  $\mu$ l sodium pentobarbitone was then given to the animal approximately 20 min afterwards while the animal was fully anaesthetized. Cardiac puncture was then performed followed by exsanguination. The blood was collected into vials containing lithium heparin and immediately stored on ice. The following maternal organs were collected, washed in isotonic saline (9 g NaCl/l), and weighed: heart, liver, lungs and kidney. A small slice of each of these tissues was removed and stored with an equal amount by volume of 50 g/l MPA, to stabilize vitamin C. Samples were immediately placed on solid CO<sub>2</sub>, and stored at –70° until analysis of vitamin C content. The tissue handling procedure was carried out for all tissues collected throughout the experiment. Following collection of the required maternal organs the fetuses were removed by hysterectomy. Where possible, amniotic fluid was collected from each pup and frozen at –70° with an equal volume of 50 g/l MPA for later analysis of vitamin C concentration. Cardiac puncture was performed on each of the fetuses, the blood collected into lithium heparin and stored immediately on ice. This was done within approximately 10 min of initial administration of the fatal sodium pentobarbitone dose to the dam. The heart, liver, lungs, kidneys and placenta were collected from each pup and treated in the same manner as described previously for the dam's tissues. Blood was centrifuged at 13 000 g for 5 min at 4°, and the plasma placed into nine volumes of 50 g/l MPA and stored at –70°.

After thawing, all samples were kept at 4° during any subsequent processing to minimize oxidation of vitamin C.

### Vitamin C analysis

Vitamin C concentration was measured in MPA extracts of all the plasma and tissue samples collected. Tissue extracts were prepared by homogenizing (Ultra-Turrax homogenizer, Janke and Kunkel KG, Ikwawerke, Straufen I Breigau, Germany) each frozen tissue sample with nine volumes of 50 g/l MPA, followed by centrifugation at 13 000 g for 5 min at 4°, and the supernatant fractions were collected. Vitamin C analysis was performed by the method of Vuillemier & Keck (1989) on the Cobas Bio centrifugal analyser (Roche Products Ltd., Welwyn Garden City, Herts., UK). This method relies on the oxidation of ascorbic

acid to dehydroascorbic acid by ascorbic acid oxidase. The dehydroascorbic acid is then coupled to 1,2-phenylenediamine to produce a fluorescent product which is measured at an excitation wavelength of 350 nm and an emission wavelength of 430 nm. An internal quality control was prepared from human plasma, stored at  $-70^{\circ}$  and included in each sample run. The within-batch CV for this measurement was 1.6%, the between-batch CV, 2.8%.

### Statistical methods

All the data were stored on Excel 5.0 (Microsoft Ltd., Wokingham, Berks., UK) and analysed using SPSS for Windows, release 6.0 (SPSS UK Ltd., Woking, Surrey, UK). Two-way ANOVA was used to determine the effects of diet and gestational age on vitamin C concentrations in plasma and tissues. Post-hoc analysis was carried out using the Scheffé test. Associations between variables were explored using regression analysis. Where data for pups were included, a multiple regression analysis was performed in which dam was included in the analysis as a blocking factor.

### Results

Table 2 summarizes the number of animals used in the experiment. One of the dams fell sick and was humanely killed; two were found not to have conceived. The number of pups born to each dam ranged between one and eight, with a median of four. The size of a litter did not determine the plasma ascorbic acid level in the pups.

#### *The influence of gestational age on plasma vitamin C concentrations*

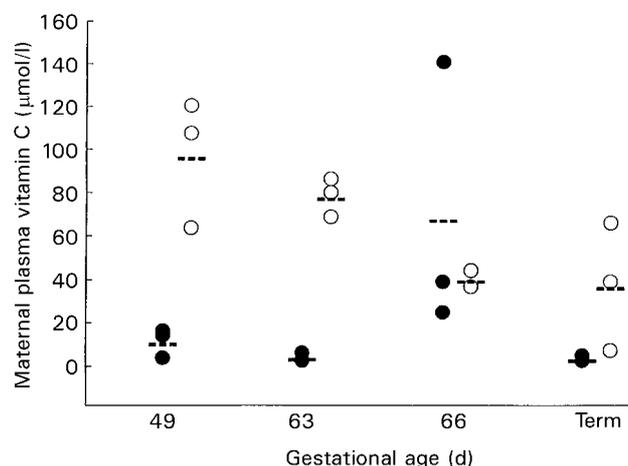
Fig. 1 shows the effect of gestational age on dam plasma vitamin C concentrations. There was a significant negative association between dam plasma vitamin C concentration and gestational age for group B ( $P=0.0089$ ) but not for group A.

In both dietary groups fetal plasma vitamin C concentrations at 49 d were several times greater than at any other time point in either the fetuses or the dams (Fig. 2). With increasing gestational age there was a decrease in plasma vitamin C concentration in both dietary groups. Group A fetuses showed an initial decline of 83% between day 49 and day 63 and relatively little variation thereafter. In group B fetuses, after correcting for the effect of dam, this association was linear and was statistically significant ( $P<0.001$ ).

**Table 2.** Numbers of dams and their fetuses completing the study\*

Gestational age	Group A		Group B	
	Dams	Fetuses	Dams	Fetuses
49 d	3	4, 6, 8	3	4, 5, 6
63 d	2	4, 3	3	6, 5, 4
66 d	3	3, 1, 6	2	2, 4
Term	2	2, 3	3	8, 3, 3

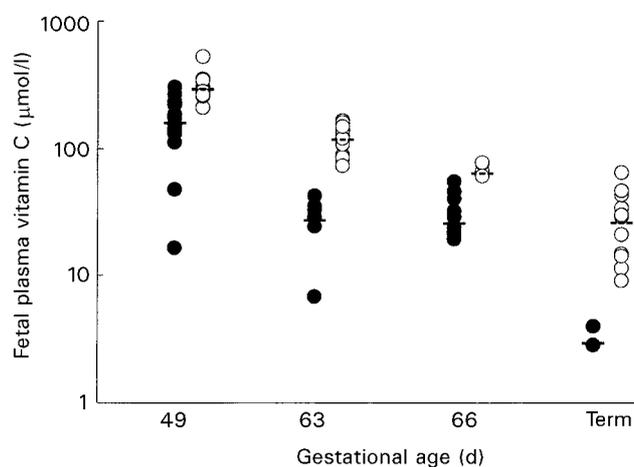
\* For details of diets and procedures, see Table 1 and pp. 485–487.



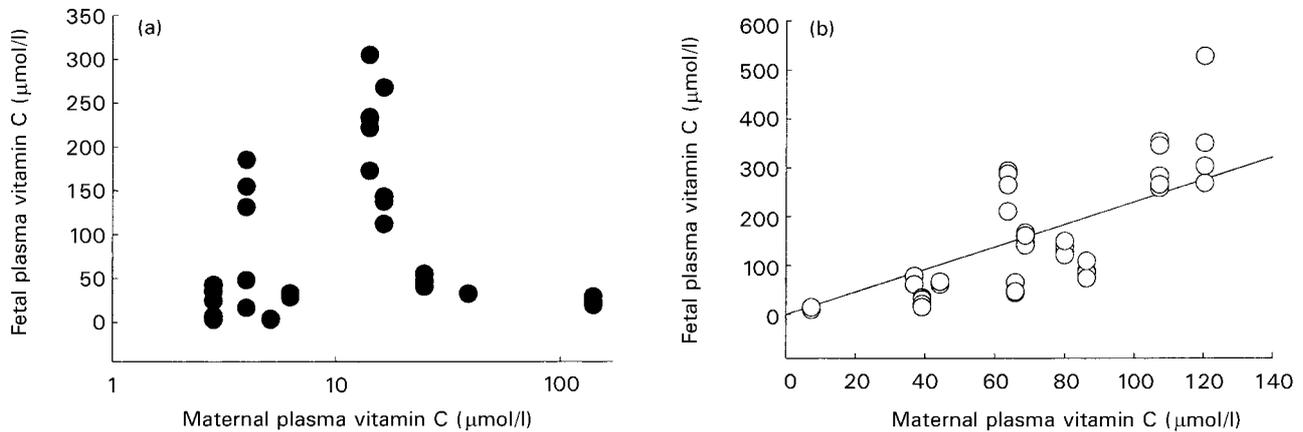
**Fig. 1.** Plasma vitamin C concentrations throughout gestation measured in guinea-pig dams fed on either a moderate- (group A, ●) or high- (group B, ○) vitamin C diet. Values are for individual guinea-pigs, with medians indicated by a broken line. Group B dams had higher vitamin C concentrations than group A dams at all time points ( $P<0.001$ ). For details of diets and procedures see Table 1 and pp. 485–487.

#### *The effect of maternal vitamin C intake on plasma vitamin C concentrations in dams and fetuses*

At 49 d, 63 d and at term, all the group A dams had lower plasma vitamin C concentrations than all group B dams (Fig. 1). One of the three dams killed at 66 d had unexpectedly high concentrations of plasma vitamin C for which we have no explanation. Results for the pups of this dam were not outliers. There was a clear effect of maternal diet on maternal plasma vitamin C concentration, but the few data points precluded statistical analysis. This effect of maternal diet was also seen in the fetuses (Fig. 2). The concentration of plasma vitamin C in fetuses from group A was significantly lower than in fetuses from group B at all points in



**Fig. 2.** Plasma vitamin C levels at different points in gestation in fetuses of dams fed on either a moderate- (group A, ●) or high- (group B, ○) vitamin C diet. Values are plotted on a logarithmic scale. Values for fetuses from group B were higher than those for group A at all time points ( $P<0.001$ ). For details of diets and procedures see Table 1 and pp. 485–487.



**Fig. 3.** Relationship between maternal plasma and fetal plasma vitamin C concentrations in guinea-pigs on (a) a moderate (group A, ●) or (b) a high (group B, ○) vitamin C intake. Group A values are plotted on a logarithmic scale. This association was significant for the high-intake group, independent of dam number ( $P = 0.0065$ ). For details of diets and procedures see Table 1 and pp. 485–487.

gestation ( $P < 0.001$ ). Throughout gestation all the fetuses maintained higher plasma vitamin C concentrations than their respective dams. For group B there was a significant positive association between fetal and dam plasma vitamin C concentrations, independent of dam, which is shown in Fig. 3(b) ( $P = 0.0065$ ). This association was not evident for group A.

Fig. 4 shows the ratio fetal : maternal vitamin C concentrations throughout gestation in both groups. The ratios in both groups showed a significant negative correlation with gestational age, independent of dam (group A,  $P = 0.0005$ ; group B,  $P = 0.0003$ ). There was also an effect of maternal vitamin C intake; the fetal : maternal ratio was significantly higher in group A than group B at 49 and 63 d gestation ( $P < 0.001$ ). These group differences had disappeared by 66 d.

#### *The influence of gestational age and diet on tissue vitamin C concentrations*

Dam tissue vitamin C concentrations are shown in Table 3. Median values were higher for vitamin C concentrations in the liver and lung than the kidney and heart regardless of diet. There were no striking differences in tissue vitamin C concentrations between the two dietary groups at any time point. Median concentrations of vitamin C in tissues from dams receiving a moderate-vitamin C diet were lower at term than earlier in gestation.

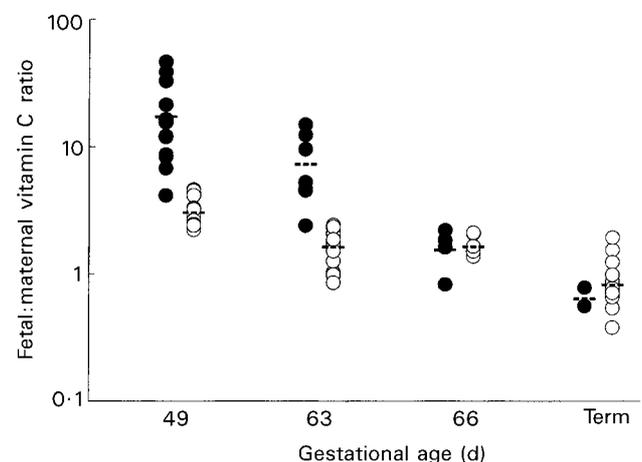
Vitamin C concentrations in tissues from fetuses at different stages in gestation are shown in Table 4. Maternal diet did not appear to exert any consistent effect on fetal tissue concentrations. One-way ANOVA, followed by the Scheffé test, showed that in group A fetuses the tissue concentrations of vitamin C were higher at 49 d gestation than all other time points ( $P < 0.05$ ). In fetuses from dams receiving a high vitamin C intake, this pattern was only evident for the liver. In contrast, in this group there was an increase in mean tissue vitamin C from 66 d to term in all tissues. This was significant for liver and lung ( $P < 0.05$ ).

#### *The influence of diet and gestational age on vitamin C concentrations in amniotic fluid*

Figs. 5(a) and 5(b) show amniotic fluid vitamin C concentrations throughout gestation in groups A and B respectively (notice the different scales for the y axes). There was a strong negative correlation between vitamin C concentration and gestational age for both groups ( $P < 0.001$ ) independent of dam. Amniotic fluid from group B had a significantly higher vitamin C concentration than that from group A at all time points ( $P < 0.001$ ).

#### *The influence of diet and gestational age on vitamin C concentrations in placenta*

The placenta showed some of the highest vitamin C concentrations measured in any of the fetal tissues. Fig. 6 shows that maternal vitamin C intake influenced concentrations in



**Fig. 4.** Fetal : maternal vitamin C concentrations throughout gestation in guinea-pigs fed on either a moderate- (group A, ●) or high- (group B, ○) vitamin C diet. Values are plotted on a logarithmic scale. Values are for individual guinea-pigs, with means indicated by a broken line. Two-way ANOVA showed a significant effect of diet and gestational age ( $P < 0.001$ ). For details of diets and procedures see Table 1 and pp. 485–487.

**Table 3.** Concentration of vitamin C in tissues of dams given different amounts of vitamin C during pregnancy\*  
(Median values for two or three guinea-pigs, with ranges in parentheses)

Diet	Gestational age	Vitamin C concentration ( $\mu\text{mol/g}$ wet wt)			
		Liver	Kidney	Lung	Heart
Moderate vitamin C (A)	49 d	1269 (1109–1698)	365 (362–1192)	1367 (1270–1439)	589 (266–2537)
	63 d	1037 (1030–1044)	300 (284–316)	1099 (1024–1174)	223 (214–231)
	66 d	1626 (1026–1664)	548 (403–1198)	1361 (1174–1464)	365 (255–623)
	Term	772 (717–864)	225 (271–325)	792 (715–915)	214 (181–211)
High vitamin C (B)	49 d	1776 (1578–1877)	631 (488–1712)	501 (366–1686)	229 (123–376)
	63 d	2184 (1686–2211)	530 (455–533)	2075 (1900–2090)	489 (484–750)
	66 d	2080 (1547–2613)	565 (480–650)	949 (851–1047)	288 (235–341)
	Term	1425 (1018–1661)	532 (209–747)	1559 (972–2188)	435 (375–518)

\* For details of diets and procedures, see Table 1 and pp. 485–487.

the placenta. Although for both groups, there was a trend towards a fall in vitamin C as gestation progressed, after correcting for dam the associations failed to reach significance. Placentas from fetuses in group B had significantly higher vitamin C concentrations than those from group A at each point in gestation ( $P < 0.001$ ).

### Discussion

#### *Differences in plasma, amniotic fluid and tissue vitamin C concentrations attributable to gestational age*

Irrespective of maternal vitamin C intake, concentrations of vitamin C in fetal plasma and tissues showed a similar pattern. The concentration of vitamin C was higher at 49 d than at later points in gestation. The fall was greatest between 49 d and 63 d for plasma and all tissues. For group A fetuses the concentration of vitamin C in all tissues was significantly greater than at all subsequent time points. A fall in fetal tissue concentration might be expected if the rate of transport to each fetus was unable to increase in response to increasing fetal mass. The fall in fetal plasma vitamin C concentration towards term would explain the higher concentration of plasma vitamin C in babies born preterm compared with babies born at term. The gestation-related fall in tissue vitamin C was curiously reversed at about term in pups born to mothers receiving the high-vitamin C

diet, among whom there was a consistent increase in tissue vitamin C between day 66 and term. The mechanism for this is unclear, but as plasma vitamin C continued to fall in this group it is not likely to have arisen from simple diffusion. From data from this group in particular it would be difficult to argue that high plasma vitamin C in babies born prematurely was due to impaired tissue uptake of this vitamin.

A similar gestation-related decline in vitamin C concentration was shown for amniotic fluid, the composition of which is determined by excretory activity of the developing kidney and lungs. Between 49 and 63 d the excretion of vitamin C into amniotic fluid showed a substantial drop, suggesting that placental transport of vitamin C was no longer providing vitamin C in excess of fetal requirements. For fetuses in group A the excretion of vitamin C into amniotic fluid was so low by day 63 as to suggest that materno-fetal transport was barely sufficient to meet requirements. This is surprising in view of the high concentration of vitamin C in placenta relative to other tissues, even in late gestation.

#### *Effects of maternal vitamin C intake on plasma and tissue concentrations*

Dietary intake of vitamin C by dams was also a determinant of fetal plasma and tissue vitamin C concentrations.

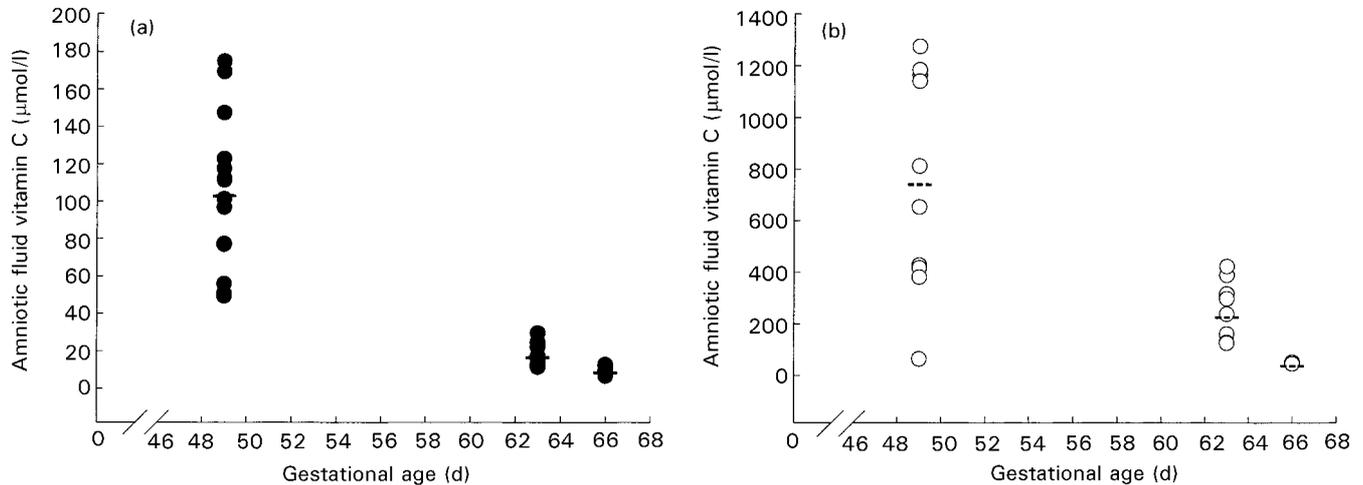
**Table 4.** Concentration of vitamin C in tissues of fetuses and pups from mothers given different amounts of vitamin C during pregnancy‡  
(Mean values and standard deviations for the numbers of fetuses specified in Table 2)

Diet	Gestational age	Vitamin C ( $\mu\text{mol/g}$ wet wt)							
		Liver		Kidney		Lung		Heart	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Moderate vitamin C (A)	49 d	1502*	310	1078*	174	1280*	192	711*	36
	63 d	468	24	703	132	467	3	540	22
	66 d	376	305	457	285	445	259	350	284
	Term	571	72	389	54	485	105	244	30
High vitamin C (B)	49 d	1154	154	993	64	804	400	695	151
	63 d	603	314	887	225	675	165	777	68
	66 d	490	314	514	252	342	158	368	262
	Term	1046†	44	762	261	828†	62	475	137

Mean values were significantly different from all later time points within the group, \* $P < 0.05$ .

Mean values were significantly different from those for day 66 within the group, † $P < 0.05$ .

‡ For details of diets and procedures, see Table 1 and pp. 485–487.

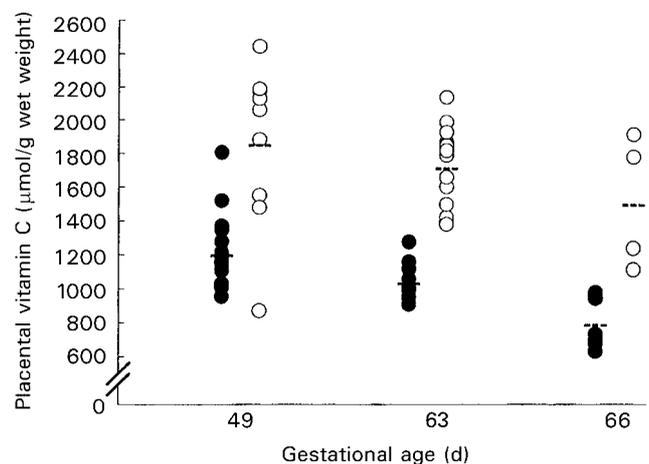


**Fig. 5.** Effect of gestational age on vitamin C concentrations in amniotic fluid in guinea-pigs fed on either a moderate- (group A, ●) or a high- (group B, ○) vitamin C diet. Values are for individual guinea-pigs, with means indicated by a broken line. Multiple regression analysis showed a significant negative association between amniotic fluid vitamin C concentration and gestational age for both groups ( $P < 0.001$ ). For details of diets and procedures see Table 1 and pp. 485–487.

Throughout gestation, dam concentrations of vitamin C were higher in the group fed on the high-vitamin C diet, and this pattern was repeated for the fetuses. The association between fetal and maternal vitamin C was stronger for the high-vitamin C group, probably because the range of values was much greater than for the moderate-vitamin C group. This relationship between dam and fetus is compatible with transport of vitamin C across the placenta by facilitated diffusion (Choi & Rose, 1989). High intakes of vitamin C by the mother during pregnancy could therefore increase plasma vitamin C levels in the newborn and might exacerbate effects of preterm delivery on plasma vitamin C. However, the ratio fetal : maternal plasma vitamin C fell towards term and showed less of an influence of maternal diet from 66 d. This suggests that the overriding determinant of plasma vitamin C at birth will be gestational age; shorter gestation would be expected to lead to high plasma vitamin C levels. This is borne out by the reported inverse relationship between plasma vitamin C measured within 2 h of birth and gestational age at delivery (Silvers *et al.* 1998). It must also be noted that during early gestation, values for the ratio fetal : maternal plasma vitamin C were much higher in the moderate-vitamin C intake group than in the high-vitamin C group. This occurred despite low maternal plasma vitamin C levels in this group, at times falling below the average for non-pregnant guinea-pigs (Habibzadeh *et al.* 1986). This suggests that during early gestation there is a drive towards maintaining high fetal plasma vitamin C concentrations which could occur even at the risk of depleting maternal vitamin C. For this group, which was fed on a commonly-used breeding diet, both maternal and fetal plasma vitamin C levels at term were lower than the average for non-pregnant guinea-pigs, raising the question of whether the recommended vitamin C concentrations for such diets are adequate. There is relatively little information regarding plasma vitamin C concentration during normal pregnancy in human subjects but there is some evidence to suggest a fall as pregnancy proceeds (Baker *et al.* 1975). A study by

Habibzadeh *et al.* (1986) suggested that a short-term deficiency of vitamin C during early pregnancy may affect reproductive performance. There may be other associated effects on maternal or fetal outcome.

Placental vitamin C levels were less sensitive to differences in maternal intake than were fetal plasma levels. This tissue may regulate the transfer of vitamin C from mother to placenta differently from the transfer from placenta to fetus. It is curious that the placenta retains such a high concentration of vitamin C under circumstances of relative fetal deprivation. Transport of vitamin C across the placenta can be considered as two functions; transport from the mother to the placenta (M–P) and transport from the placenta to fetus (P–F). The rate of (M–P) is evidently



**Fig. 6.** Placental vitamin C concentrations at different stages in gestation in dams fed on either a moderate- (group A, ●) or a high- (group B, ○) vitamin C diet, during pregnancy. Values are for individual guinea-pigs, with means indicated by a broken line. Group B placentas had significantly higher vitamin C concentrations than group A at all time points ( $P < 0.001$ ). For details of diets and procedures see Table 1 and pp. 485–487.

higher than (P-F), as reflected by the high concentrations of vitamin C found in the placenta. The modest gestational age-related fall in vitamin C concentrations in the placenta could be due to either a fall in (M-P) or a rise in (P-F). Our data support the former, because a gestation-related fall in fetal plasma and amniotic fluid vitamin C concentrations was detected, which might not be expected had there been a rise in (P-F) in later gestation.

Evidently, although gestational age is a key determinant of plasma and tissue concentrations of vitamin C in the developing fetus, maternal vitamin C intake is also a contributing factor.

The gestation-related decline in plasma and tissue concentrations of vitamin C is not characteristic of all other vitamins. Fat-soluble vitamins A and E show a greater fetal accumulation in the last trimester of pregnancy (Zachman, 1989; Dison *et al.* 1993). Folate, which appears to behave more like vitamin C in that there is a rapid fetal accumulation early in pregnancy, nevertheless shows an increased rate of transfer during the last weeks of pregnancy (Ek & Magnus, 1982). The decline in fetal vitamin C late in gestation occurs despite very high placental concentrations, supporting a regulatory role for the placenta. Rapid fetal development early in gestation is likely to create high demand for synthesis of collagen (Myllyla *et al.* 1978), which is a component of most tissues of the body including skin, tendon, bone, cartilage, blood vessels and teeth and is responsible for providing cell structure and shape. Collagen synthesis is vitamin C-dependent.

In conclusion, high plasma vitamin C concentrations in premature babies at birth are almost certainly due, primarily, to a fall in plasma and tissue vitamin C concentration that occurs in the fetus towards term. High intakes of vitamin C by the mother during pregnancy could contribute to this, but in practice this is of doubtful significance.

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# The Nutrition of the Rabbit

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Rabbit production systems are important providers of meat in many parts of the world. The species has many advantages, including rapid growth rate and good reproductive performance. It is adaptable in that it may be reared under intensive conditions, but is also successful under small scale production systems, which are of considerable value in the economics of emerging countries. Although not a ruminant, its digestive system allows it to thrive on high fibre raw materials. The meat has a comparatively healthy low fat image, which is increasingly important to consumers and there appear to be few impediments, such as religious considerations, to rabbit meat consumption. However, the science of rabbit production has received relatively little attention, although there are recognised rabbit research groups worldwide and a wealth of data exists in a scattered form in the literature. This book brings together that expertise under one cover. It covers a range of topics, from digestive physiology and nutrient/energy allowances to feed formulation and production. The information provided will be an invaluable asset to those involved in rabbit rearing, whether as companion animals or for meat production, and will also provide data of considerable interest to animal nutritionists and zoologists working on rabbits and related mammals.

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