

acids in plasma and urine were estimated by the photoelectric ninhydrin method of Moore and Stein (1954) with the use of an automatic Spinco Beckman Amino Acid Analyzer model 120B. Plasma was deproteinized with picric acid (Stein and Moore, 1954). Creatinine in plasma and urine was determined spectrophotometrically. After treatment with franconit KL suspension, the absorbance in the presence of picrate was measured at 500 nm (Gorter and De Graaff, 1955).

### Results

The concentrations of amino acids in plasma and urine and their tubular reabsorption before and after treatment are set out in the Table.

The Table makes it clear that on admission, before vitamin C, there was conspicuous decreased reabsorption of various amino acids, particularly of histidine, methionine, lysine, threonine, isoleucine, phenylalanine, tyrosine, glycine, serine, alanine, and asparagine + glutamine. There was only a slight decrease in reabsorption of arginine, valine, leucine, and glutamic acid. Small amounts of proline in free form were detectable in the urine.

Four weeks after the start of the vitamin C administration, tubular reabsorption of most of the amino acids had reached normal values (Table). That of histidine, threonine, glycine, phenylalanine, and tyrosine had not completely returned to normal.

### Discussion

It is clear from the results obtained on the present study that in vitamin C deficiency the tubular reabsorption of the aromatic amino acids, phenylalanine and tyrosine, is reduced, whereas in vitamin D deficiency it is not (Huisman, 1954). As in our earlier investigations it was found that it takes many weeks, even with ample vitamin C administration, before the tubular reabsorption of all amino acids reaches normal values.

### Summary

Tubular reabsorption of amino acids has been measured in a boy aged 8 months suffering from uncomplicated vitamin C deficiency, both before and after the administration of vitamin C.

Before treatment there was a decreased reabsorption of a number of amino acids, particularly of histidine, glycine, methionine, and also of tyrosine and phenylalanine.

Four weeks after the start of the treatment with 150 mg vitamin C per day, tubular reabsorption of most of the amino acids had reached normal values, but that of threonine, glycine, and tyrosine had not completely returned to normal.

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## Apnoeic attacks in the newborn treated with aminophylline

It has been postulated that a significant cause of brain damage in surviving premature babies is hypoxia secondary to recurrent apnoea (McDonald, 1963; Bacola *et al.*, 1966; Daily, Klaus, and Meyer, 1969). Present methods of managing such episodes consist of external stimulation, administration of oxygen, and assisted ventilation. However successful such measures are they do not prevent further apnoeic attacks which may be serious to the baby. It was this thought that suggested that aminophylline, by virtue of its direct action on the respiratory and vasomotor centres and on the myocardium, might be useful in the treatment and prevention of prolonged apnoeic attacks in the small baby.

The present preliminary paper describes clinical observations in 10 babies.

### Material and methods

Ten preterm babies suffering from idiopathic respiratory distress syndrome (RDS) were studied. Criteria for diagnosis were those of Reynolds, Robertson, and Wigglesworth (1968). An apnoeic attack was defined as a period of nonbreathing, usually lasting more than 30 seconds, during which cyanosis and slowing of the heart rate occurred. Hourly heart and respiratory rates were recorded. Routine care of babies consisted

TABLE  
*Details of 10 newborns with apnoeic attacks treated with aminophylline*

Case no.	Gestation (wk)	Birthweight (g)	Day of onset of attack	No. of attacks before aminophylline	No. of attacks on aminophylline	Outcome
1	26	860	3	8 (after feeds)	Occasional apnoea without cyanosis; less than 30 sec	Alive; satisfactory developmental progress at 15 mth
2	32	1940	2	5	None	Alive; satisfactory developmental progress at 13 mth
3	30	1350	6 hr	7	Occasional apnoea without cyanosis; less than 30 sec	Alive; satisfactory at 9 mth
4	32	1640	3	8	2	Died on 5th dy of hyaline membrane disease and massive pulmonary haemorrhage
5	29	1280	2	6	Occasional apnoea without cyanosis; less than 30 sec	Alive and well at 9 mth
6	34	2130	2	3	None	Alive and well at 8 mth
7	29	1040	3	4 (after feeds)	None	Alive and well at 10 mth
8	30	1410	2	2 (after feeds)	None	Twin I; alive and well at 12 mth
9	30	940	2	2 (after feeds)	Occasional apnoea without cyanosis; less than 30 sec	Twin II; alive and well at 12 mth
10	34	2200	6	5	None	Alive and well at 7 mth

of nursing on the 'apnoea alarm mattress' (Vickers), measuring the oxygen concentration with Beckman D25 analyser and blood gas tensions using capillary or venous samples, and management as outlined by Usher (1963) (with some modifications). Aminophylline suppositories 5 mg were given 6-hourly for 3 doses and then 6-hourly if indicated; and were used when one or more attacks occurred in spite of external stimulation (flicking baby's heels) and increasing ambient oxygen concentrations to 70% or more via mask.

### Results (Table)

In 5 babies aminophylline suppository was active within 7 minutes of administration as judged by a slight increase in heart and respiratory rates above the 'pre-aminophylline' levels. In the other 5 babies no significant effects on heart or respiratory rates were noted. Except for Case 4, cyanotic attacks were completely abolished, but 4 babies (Cases 1, 3, 5, and 9) continued to have very occasional apnoeic spells lasting less than 30 seconds and without cyanosis or slowing of the heart. These episodes were not considered pathological. 4 babies (Cases 1, 7, 8, and 9) had a total of 16 attacks after tube feeds before aminophylline was started but none after its use.

All babies could be effectively managed in ambient oxygen concentrations of 40% or less, i.e. at levels required to oxygenate the baby because of RDS. This suggests that aminophylline may also exert some beneficial effect on the course of RDS.

Side effects were not observed. It is unlikely that the death of one baby (Case 4) was associated with aminophylline administration, since none

had been given for 50 hours before the baby's sudden deterioration.

### Comment

The pathophysiological changes during cyanotic apnoeic attacks in premature babies have been described by Daily *et al.* (1969) and Girling (1972). It has been suggested that whatever the reason for the lack of efficient respiratory drive causing prolonged apnoea, many of the subsequent features are of hypoxic origin. It is clearly important, therefore, to maintain adequate respirations and cardiac output in the ill preterm baby if hypoxic brain damage is to be avoided. Aminophylline has been shown to be useful in this context and there is good pharmacological evidence that it should be so. It possesses direct stimulant actions on the respiratory and vasomotor centres in the medulla resulting in the increase of rate and depth of breathing, and acts directly on the myocardium causing increase in the force of contraction, cardiac output, and decrease of venous pressure (Ritchie, 1970).

Aminophylline suppositories were used because of the ease of administration and wide margin of safety. The dose of 5 mg remains empirical and it is likely that smaller doses and other routes of administration may be equally effective. Further studies are in progress.

### Summary

In 10 preterm babies with birthweights ranging from 860 to 2200 gm recurring apnoeic attacks ceased or became infrequent after administration of aminophylline 5 mg suppositories at 6-hourly intervals. 9 of the 10 babies survived.

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