CYANOTIC ATTACKS IN NEWBORN INFANTS

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By the term 'cyanotic attacks in newborn infants' I mean sudden attacks of cyanosis, lasting from a few moments up to half an hour, in children whose colour was previously normal, and whose colour returns to normal in atmospheric air after the attack. I do not include the sudden development of cyanosis in a baby who remains blue until death.

In an extensive search of the literature I was unable to find any paper on the subject, though a number of papers concerning cyanosis or other neonatal problems mention briefly the occurrence of short periods of cyanosis. I could not find the term 'cyanotic attacks' or 'blue attacks' in the index of any of 14 recent British and American text-books of paediatrics: yet every midwife and every paediatrician responsible for the care of newborn babies is fully conversant with the frequency and alarming nature of these attacks.

The most comprehensive statement about cyanotic attacks was that by Crosse and Young (1954). They wrote that the attacks

> 'may be due to intracranial birth injury, pulmonary atelectasis, hyaline membrane, congenital malformation of the respiratory tract, or of the diaphragm or of the heart, obstruction of the respiratory tract by aspiration, infection, over- or under-heating, too much handling, or to overfeeding which causes abdominal distension and hence respiratory embarrassment. The differential diagnosis of the cause of the attack is often difficult, but if there are no signs of developmental defects, it should be assumed that the attacks are functional in origin.'

Clein (1929) thought that intermittent cyanosis in premature babies was mainly due to cerebral haemorrhage. Capper (1936) wrote that 'an infant whose cyanosis is intermittent rather than continuous is usually suspected of suffering an intracranial injury'. Phillips (1936) wrote that 'frequent cyanotic attacks are the rule with premature babies. They occur without apparent cause. Respirations may cease for as long as one minute. An attack may come on following a feed, the full stomach interfering with the action of the diaphragm'. Bonar (1937) suggested that intermittent cyanosis is likely to be due to increased intracranial pressure, atelectasis, or obstruction of the air passages by mucus. Harris (1950) wrote that the commonest cause of respiratory obstruction in newborn babies was mucous plugs in the nares.

The Present Study

This study is based on 170 babies who had cyanotic attacks in the newborn period in the Jessop Hospital for Women at Sheffield in the eight-year period 1949 to 1956. In the last six years there was an average of 26 cases each year. The study includes babies born on district and admitted to the hospital. The average number of live-born babies delivered each year in the hospital during this period, or admitted from the district, was 1,680. During the latter part of the time we used a detailed proforma in each case.

Results

Birth Weight. One hundred and three of the babies (60%) were premature (Table 1). One baby was post-mature and died from cerebral haemorrhage. During this period 10% of the babies in the hospital were premature.

Day of Onset of Cyanotic Attacks. In 40% of the babies the attacks began in the first 24 hours, and in 72% in the first three days (Table 2). Six babies had their first cyanotic attack after the first week, the oldest baby (premature) having an attack on the 27th day after birth. There seemed to be no relationship between certain prenatal factors (to be discussed below) and the day of onset of the cyanotic attacks.

The Frequency of Attacks. Forty per cent. of the babies had only one known cyanotic attack, 32% had two to four attacks and 28% had five attacks or more.

Prenatal Factors. Table 3 shows the incidence of maternal illness. Toxaemia is defined as the

TABLE 1

BIRTH WEIGHT AND MORTALITY OF BABIES WITH CYANOTIC ATTACKS COMPARED WITH MORTALITY OF OTHER BABIES IN THE HOSPITAL

Birth Weight (lb. oz.)	Babies with Cyanotic Attacks*		Babies without Cyanotic Attacks, 1951-1955*	
	Total	Mortality (Percentage)	Total	Mortality (Percentage)
2 8 or less	19	84·2	35	74·3
2 9 to 3 8	27	66·6	86	26·7
3 9 to 4 8	29	68·9	184	12·5
4 9 to 5 8	26	61·6	474	2·9
Premature babies not weighed ..	2	—	—	—
Total premature babies ..	103	70·0	779	10·9
Total full-term babies	57	14·9	7,481	0·7

* Includes previable births (26 or 27 weeks' gestation), and all congenital anomalies, including anencephaly.

The figures include babies admitted to the hospital because of illness.

occurrence after the 26th week of any two of the following: (1) A blood pressure of over 140 mm. systolic or 90 mm. diastolic; (2) 50 mg. % or more of albumin in the urine; (3) non-dependent oedema.

Forty-six mothers (27%) had toxaemia, 18 (11%) had hypertension without toxaemia, and 25 others (15%) had antepartum haemorrhage (Table 3). In addition one mother was very ill with toxic hepatitis.

The Jessop Hospital at Sheffield is a teaching hospital and takes a large proportion of abnormal cases, but the high incidence of toxaemia, hypertension and antepartum haemorrhage is notable. It might be thought that the high incidence of toxaemia in mothers of infants with cyanotic attacks could be explained by the frequency with which toxaemia causes premature delivery (Table 4), but the incidence of prematurity (60%) in babies with cyanotic attacks was exactly the same whether their

TABLE 2

DAY OF ONSET OF CYANOTIC ATTACKS

Day of Life	Total Number	Percentage of Total
1	68	40
2	29	17
3	25	15
4	16	9
5	8	5
6	13	8
7	3	2
8 days or more	6	4

TABLE 3

PRENATAL FACTORS IN CYANOTIC ATTACKS RELATED TO ILLNESS DURING PREGNANCY

Illness	Number	Total
Toxaemia	39	
Toxaemia with antepartum haemorrhage	4	
Toxaemia with pyelonephritis, anaemia, diabetes	1 each	46 (27·1%)
Hypertension without toxaemia ..	12	
Hypertension with antepartum haemorrhage	2	
Hypertension with anaemia, hydramnios, hyperemesis, mitral stenosis ..	1 each	18 (10·6%)
Chronic nephritis	1	1
Antepartum haemorrhage (apart from above)	22	
Antepartum haemorrhage at 3 months, Antepartum haemorrhage at 3 months with pulmonary tuberculosis		
Antepartum haemorrhage at 5 months	1 each	25 (14·9%)
Hydramnios (apart from above) ..	4	4
Diabetes (apart from above)	3	3
Anaemia		
Anaemia with pyelonephritis, mitral stenosis	1 ezch	3
Mitral stenosis with hyperemesis, congenital heart disease, severe toxic hepatitis and pyelonephritis, pyelonephritis with disseminated sclerosis, syphilis, haemorrhage due to papilloma of bladder, bicornuate uterus	1 each	7

mothers had toxaemia or not. Analysis of a three-year period (1953-55) showed that of 597 babies born to mothers who had toxaemia, 22 (3·7%) had cyanotic attacks. During that period 4,471 non-toxaemic mothers gave birth to live-born babies, but only 61 (1·3%) had cyanotic attacks. Hence there is an association between toxaemia in the mother and cyanotic attacks in the baby, and this is unrelated to prematurity. There is the same association between cyanotic attacks in the baby and hypertension or antepartum haemorrhage, and the same arguments apply. For instance, during the same period, 203 mothers who had had antepartum haemorrhage (without toxaemia) gave birth to live-born babies: 6·1% of these had cyanotic attacks. During that period 4,865 mothers gave birth to live-born babies without having had antepartum haemorrhage, and of these 1·2% had cyanotic attacks.

There was no relationship between the day of

TABLE 4

RELATIONSHIP OF CERTAIN PRENATAL CONDITIONS WITH PREMATURITY IN BABIES HAVING CYANOTIC ATTACKS

Condition	Total	Premature	Full-term Babies
Toxaemia	46	28 (60·8%)	18
Nephritis, chronic ..	1	1	0
Hypertension	18	9 (50·0%)	9
Antepartum haemorrhage	24	18 (75·0%)	6
Other conditions ..	81	47 (58·0%)	34
Total	170	103 (60·6%)	67

onset of the cyanotic attacks and the prenatal factors above, or between the age of the mother and the incidence of cyanotic attacks.

Eighteen of the babies with cyanotic attacks were twins. In no case did both twins have cyanotic attacks.

One child had congenital stippled epiphyses and another had hydrocephalus. Six were notably oedematous at birth, three of these being born to mothers with toxaemia or hypertension.

Natal Factors. One hundred and thirty-four of the babies were vertex deliveries, 15 of them being delivered by forceps: 24 were delivered by caesarean section; 12 were breech presentations.

Forty-one (24%) of the babies had grade 2 or 3 asphyxia, using Flagg's classification. In 1955 and 1956, 4·6% of the babies born in the hospital had grade 2 or 3 asphyxia, and 16 of the 39 babies (41%) born in those years who had cyanotic attacks had grade 2 or 3 asphyxia.

Postnatal Conditions. Twitching or convulsions occurred in 27 of the babies. In only four of these children was there twitching at the time of a cyanotic attack, on one or two occasions only, and in all these children several cyanotic attacks occurred without twitching being observed. In all the others the twitching or convulsion bore no time relationship to the attacks of cyanosis.

Mortality and Findings at Necropsy. Eighty-two of the children died (48%), and necropsies were carried out on 72 of them. The principal finding at necropsy was severe atelectasis, with or without hyaline membrane, in 36% of the babies. For comparison, I studied the necropsy findings in 115 consecutive babies who had died without having cyanotic attacks, and of whom 67% were prematurely born: 29% of these showed atelectasis as the principal finding—a very similar figure.

The second commonest finding at necropsy was gross cerebral haemorrhage in 33% of the babies. This figure is precisely the same as that in the babies who died without cyanotic attacks.

Other findings consisted of marked cerebral oedema alone, tracheo-oesophageal fistula (two of which died after operation), gross pulmonary haemorrhage and infections. It was notable that only two babies had gross congenital heart disease whereas in the control group there were eight of these in the 115 babies.

TABLE 5
FINDINGS AT NECROPSY IN 72 BABIES SUFFERING FROM CYANOTIC ATTACKS

Necropsy Findings	Number	Total
Atelectasis with or without hyaline membrane	15	
Atelectasis with cerebral oedema	10	
Atelectasis with massive pulmonary haemorrhage	1	26 (36%)
Gross cerebral haemorrhage alone	19	
Gross cerebral haemorrhage with pulmonary haemorrhage	1	
Gross cerebral haemorrhage with atelectasis	4	24 (33%)
Infections:		
E. coli septicaemia	2	
E. coli meningitis	1	
Pneumococcal meningitis	1	
Bronchopneumonia	1	5
Cerebral oedema alone	3	
Cerebral oedema with liver haemorrhage	1	4
Anomalies of oesophagus	3	3
Pulmonary haemorrhage	2	2
Congenital heart disease	2	2
Kernikterus with atelectasis	1	1
Micrognathia with prematurity	1	1
Sclerema	1	1
Nil gross	3	3
Total	72	72
Percentage premature 84		

Prognostic Features. These can be related to weight at birth, day of onset, frequency of attacks, and twitching and convulsions.

WEIGHT AT BIRTH. The mortality in the prematurely born babies with cyanotic attacks was 70%, as compared with 15% in the full-term babies (Table 1). This corresponds with figures of 10·9% and 0·7% respectively in all other prematurely born and full-term babies born in the hospital or admitted because of illness from outside. In all cases previable babies and gross congenital anomalies, such as anencephaly, are included.

DAY OF ONSET. Of those who had the first cyanotic attack in the first three days after birth, 47% recovered: of those who had the first attack on the fourth day or later 61% recovered.

FREQUENCY OF ATTACKS. Of those who had one to four known attacks, 58% recovered as compared with 32% of those having five or more known attacks.

ASSOCIATION WITH TWITCHING OR CONVULSIONS. Of the 27 children with cyanotic attacks and convulsions, eight recovered and 19 died. Eight of the latter were found at necropsy to have cerebral haemorrhage, three had severe cerebral oedema, two had atelectasis, and two congenital heart disease. Two of these eight survivors have been followed up for five years and one is mentally defective.

Difficulties in the Diagnosis. It is almost certain that in many of the babies a cyanotic attack was due to obstruction of the respiratory passages by mucus, liquor, meconium, vomitus or milk. This was thought to be the only cause in 29 babies who

recovered. One cause of difficulty in this connexion is the fact that the newborn baby often fails to open his mouth to breathe when his nose becomes blocked. In 11 other babies the cyanotic attacks occurred during a feed, and it would be reasonable to suppose that the attack was due to the inhalation of milk, though this was not confirmed by aspiration. The majority, however, of the babies who had their first cyanotic attack in the first two days had not at the time begun to receive food by mouth (most of the babies being prematurely born), so that there could be no connexion between feeds and the attacks.

The fact that mucus or vomitus was aspirated from a baby in the attack, and that the baby recovered after such aspiration, by no means proved that the attacks were due to respiratory obstruction due to inhalation of those materials. In several babies one attack occurred during a feed, while other attacks in the same baby bore no time relation to feeds. For instance, a baby's first cyanotic attack occurred during a feed, and several further attacks were unrelated to feeds. At necropsy a massive cerebral haemorrhage was found. In several other babies a considerable amount of mucus was extracted during one cyanotic attack, while in other attacks little was obtained, and not enough to account for the attack. In one child the first attack occurred in a feed, and was ascribed to inhalation of food, while four further attacks appeared to be related to attacks of apnoea without respiratory obstruction. A premature baby had his first cyanotic attack at 30 hours, having been previously well, and much mucus was aspirated, after which he recovered. He died the same day from pneumococcal meningitis. A 2 lb. baby had an attack during a tube feed, having been previously well. He died the same day of *E. coli* septicaemia.

Many of the attacks were probably due to unexplained phases of apnoea. I saw one baby have repeated attacks of cyanosis due to apnoea without respiratory obstruction. He responded repeatedly to gentle stimulation and survived.

Discussion

The obvious difficulty of determining the cause of cyanotic attacks during life, together with a striking absence of literature on the subject, led me to determine some facts about the condition. I am aware, however, that many questions have been left unanswered. It is obvious that many attacks were simply due to temporary respiratory obstruction; it is equally clear that many were not. It is likely that many of the attacks were due to apnoea without respiratory obstruction, but the reason for the attacks of apnoea is not known. Phasic respiration is common in healthy premature babies, and in some the irregularity of respiratory rhythm is exaggerated. Miller (1957) in his paper on respiratory function in the newborn found that attacks of apnoea and cyanosis were almost confined to babies, premature or full-term, in whom there was a notable rise of respiratory rate after the first hour from the figure of about 40 found in healthy babies to a figure of 60 or so. When the respiratory rate remained fairly constant at about 40 per minute, no respiratory problems were encountered. All the attacks of apnoea and all the deaths occurred in babies whose respiratory rate rose to the region of 60 after the first hour. Miller regarded a progressive fall of the respiratory rate in those babies as a bad sign; he found that if the respiratory rate fell below 20 per minute in a small premature baby survival was unlikely.

It would be easy to confuse a cyanotic attack with a convulsion, but in our cases we found the association unusual. An occasional baby had both cyanotic attacks and convulsions, but more often than not it would have twitching without a cyanotic attack or a cyanotic attack without a convulsion. There was a high incidence of severe atelectasis or of gross cerebral haemorrhage at necropsy, but it is interesting to note that there was almost exactly the same incidence of these conditions in babies who did not have cyanotic attacks. It is commonly thought that congenital heart disease is a common cause of the attacks. Our findings show that it is a rare cause.

There seems to be a definite association between maternal toxaemia, hypertension and antepartum haemorrhage, but the reason for this is not clear. It may well be related in some way to foetal anoxia with consequent respiratory difficulties.

It may be concluded that the nature and origin of cyanotic attacks is a good subject for speculation. It is certainly a subject which will repay further observation and research.

Summary

The known facts about 170 newborn babies who had cyanotic attacks have been presented. The following are the principal findings:

(1) Sixty per cent. of the babies were premature.

(2) There was a significantly higher incidence of maternal toxaemia, hypertension and antepartum haemorrhage in mothers of babies who had cyanotic attacks than in controls. This relationship was not merely due to the higher incidence of prematurity in those conditions.

(3) Twenty-four per cent. of the babies had grade 2

or 3 asphyxia at birth as compared with an incidence of 6% in controls.

(4) Forty-eight per cent. of the babies died. In premature babies the figure was 70%, as compared with 15% in full-term babies.

(5) At necropsy 36% showed severe atelectasis, with or without hyaline membrane, and 33% showed gross cerebral haemorrhage. The corresponding figures in babies who died without cyanotic attacks were almost identical. Congenital heart disease was only a rare cause of the condition.

(6) The principal causes of cyanotic attacks were obstruction of the respiratory tract by mucus or other material, attacks of apnoea and convulsions. The reason for the attacks of apnoea is not understood.

(7) The difficulties of making a correct clinical diagnosis are emphasized, and the need for further research is indicated.

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