Upper Respiratory Obstruction and Cot Death

In this country cot death or sudden unexpected death in infancy is the commonest cause of infant death outside the neonatal period. Any theory of its cause must take into account the established facts: it is a condition that occurs most frequently during the winter months—76% of cases occur between October and March, i.e. in 50% of the year, and it also occurs most frequently in babies from the first to the fourth month of life (Froggatt, Lynas, and Marshall, 1968; Ministry of Health (1965). Though the theory of cow's milk anaphylaxis will account for a proportion of cases, it does not seem adequate for many of those that have been appropriately investigated, nor does it explain the seasonal occurrence of the disease. Signs of respiratory infection were present in 68% of cot death cases, and in 32% of controls (Ministry of Health, 1965, 1970).

We suggest that a common march of events may be as follows. First, there is a mild nasal infection in a baby who is an obligate nose breather. Babies react differently from adults to upper airway obstruction, for the baby can show a diminished tidal volume with no increase in respiratory frequency, in the face of increasing upper airway obstruction. Second, this is particularly dangerous during the winter months, for in a cool environment the demand for oxygen is increased even in a baby who is dressed and in a cot (Hey and O'Connell, 1970). Thus with a simultaneous increase in oxygen requirement and decrease in ventilation, lethal hypoxia could develop insidiously but rapidly. We also suggest that the infant of 1 to 4 months is particularly at risk, because during this period he has not learnt to mouth breathe, and is emerging from the relative isolation of the neonate to meet more sources of infection, and he is being encouraged to sleep through the night without waking for a feed.

Shaw (1968, 1970) has similarly suggested nasal infection and obstruction as the cause of sudden death. Shaw's suggestion arose from close and astute clinical observation, while our proposal is based on experimental findings incidental to work on lung mechanics (Lewis, 1969). In the course

of this work for which the parent's permission was obtained in each case, the baby was placed in a trunk plethysmograph (Cross, 1949). Ventilation is estimated in this instrument by measuring the amount the body swells with each breath. This is achieved by sealing the infant into the plethysmograph in airtight fashion with a rubber cuff encircling the face. This cuff passes along the jaw line, up in front of the ears and across the vertex of the skull; when inflated its outer circumference makes contact with an appropriate opening in the lid of the trunk plethysmograph. Thus the baby's face is open to the outside air. For the calculation of lung mechanics the oesophageal pressure is measured with a latex balloon fixed to a feeding tube and passed through the mouth into the oesophagus. Under normal circumstances inflation of the cuff around the baby's face makes no difference to the pressure excursion observed in the oesophagus. In certain cases, however, a very different state of affairs has been revealed (see Fig. 1), where with the cuff inflated the oesophageal pressure swings are of the order of 12·5 cm water, but as the cuff

FIG. 1.—Record of plethysmograph pressure and oesophageal pressure as cuff is deflated. Note that plethysmograph ceases to record as air seal is broken, but more importantly the normal oesophageal pressure swing is shown to be only about 4 cm water. The baby remains asleep throughout.

FIG. 2.—Sections of trace where the cuff was again causing upper airway obstruction. In the 2nd and 4th section one sees increasing oesophageal pressure swings with decreasing tidal volume.

is deflated the oesophageal pressure swings become less and less, revealing that the cuff has caused an upper airway obstruction. The regularity of the respiration shows that the baby's sleep is in no way disturbed by this obstruction. Fig. 2 illustrates a finding even more sinister in this context. With a temporary and deliberately high cuff pressure we find not only an increasing oesophageal pressure swing, but an actual diminution of tidal volume. Our first reaction to this finding was that it revealed a potential difficulty in the use of the trunk plethysmograph, but it was also apparent that the baby was reacting—or failing to react—to upper airway obstruction in a manner we would not have expected.

As these findings were incidental to the main study, we responded by always monitoring the oesophageal pressure before and during the positioning of the cuff and only accepted the results as normal if the oesophageal pressure swing remained unchanged with the baby at rest. Thus we have only a small amount of further information on the nature and site of the obstruction. We could, of course, observe the anterior nares at all times and there was certainly no blockage at this level. We could see through the perspex lid of the plethysmograph that when the cuff was in a 'bad position' it did not press against the front of the throat of the infant. The obstruction seemed to occur either if the jaw was pushed backwards or if the floor of the mouth was raised when the cuff was under the jaw. Ardran and Kemp (1970) have published radiographs showing the normal airway of the neonate running above the hard and soft

palates with apposition of the tongue and soft palate obliterating the cavity of the mouth. We have, with Dr. Peter Armstrong of King's College Hospital, demonstrated the obliteration of this airway (in lateral view) above the soft palate in a baby when we deliberately inflated the cuff in a 'bad position'.

The inappropriate response of some infants to nasal obstruction is illustrated in the condition of choanal atresia. Eichenwald and McCracken (1969) describe two patterns of behaviour in babies with posterior choanal atresia (obstruction of the posterior nares). Either the baby makes increasingly vigorous inspiratory efforts after delivery, becomes cyanotic, and may die; or, being cyanotic at rest with the mouth closed, returns to a normal colour when he cries. A pattern of behaviour is described which is unthinkable in an adult suddenly faced with total nasal obstruction, to whom mouth breathing represents no difficulty whatsoever. It is of interest to note that in addition to being in many instances an obligate nose breather the baby is peculiarly well adapted to nose breathing. This is necessary of course if he is to suck, and Polgar and Kong (1965) have found that in the normal human infant the nose contributes a smaller proportion of airway resistance than it does in the adult.

We suggest further that obstruction of the nose may well have been present but undetected in cases of cot death because the normal necropsy extends from the soft palate to the anus and does not include any examination of the upper airways. In the single case which has so far been examined

(with this thought in mind) by our colleagues in Forensic Pathology at The London Hospital, they have indeed found the posterior nares blocked with mucus in a case of cot death.

We are continuing to investigate upper airway obstruction in the infant. If this theory of causation is correct it may be that the incidence of cot deaths could be reduced by vigorous treatment of 'minor' nasal infection in those infants who are particularly at risk.

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Decreased Duodenal Monoamine Oxidase Activity in Coeliac Disease

The enzyme monoamine oxidase (MAO; EC 1.4.3.4.) has been extensively studied in recent years (Davison, 1958; Sandler, Collins, and Youdim, 1971). Its activity varies widely from tissue to tissue and from species to species. In the human (Levine and Sjoerdsma, 1962), unlike some other animals (Penttilä, 1968), the small intestinal mucosa possesses one of the highest levels of activity in the body. While the precise function of MAO remains a matter of some dispute, it seems likely that the

mucosal enzyme of the normal gut forms a first line of defence against an excess of exogenous (dietary) amines such as tyramine (Sandler *et al.*, 1971). It may also be concerned in the inactivation of endogenous amines, notably 5-hydroxytryptamine. This amine is present in relatively high concentrations in the mammalian gastrointestinal tract (Erspamer, 1966).

The status of gut mucosal MAO in disease has so far received scant attention. In malabsorption syndromes there may be an overproduction of certain monamines within the gut (Haverback, Dyce, and Thomas, 1960). There are also histochemical data on record (Spiro *et al.*, 1964; Riecken *et al.*, 1966) to indicate that gastrointestinal MAO activity is reduced. Thus any toxic effect the amines may exert on the whole organism is likely to be magnified.

It, therefore, seemed important to confirm by quantitative means these histochemical impressions and to investigate further the nature of the enzyme defect.

Subjects and Methods

The 16 children selected for this study were aged between 1 and 9 years. Coeliac disease was considered a possible diagnosis as they were failing to thrive and were passing frequent offensive stools. In those children in whom coeliac disease was confirmed histologically, the faecal fat excretion exceeded 5 g/day and the clinical condition improved rapidly following a gluten-free diet.

Collection of biopsies. Patients were starved of solid food for 12 hours and then sedated with pethidine and promethazine half an hour before biopsy. A Watson intestinal biopsy capsule (port size 5 mm) was passed into the third or fourth part of the duodenum and its precise position identified radiologically. Once obtained, the tissue was rapidly divided into two pieces, one being preserved in 10% formol saline for histological examination and the other placed in a glass bottle and stored at -20°C before quantitative assay of MAO activity.

Histological examination. Tissues were sectioned, stained with haematoxylin and eosin, and examined microscopically.

Quantitative MAO assay. Biopsy specimens were homogenized in a small amount of distilled water (approx. 1 ml) using an all-glass tissue grinder; duplicate portions (0.1 ml) of the homogenate were assayed according to the microfluorimetric method of Kraml (1965) using kynuramine as substrate.

All values of MAO activity are expressed as microgrammes of 4-hydroxyquinoline (4HQ) formed per mg protein per 30 min incubation at 37°C . Protein was determined by the method of Lowry *et al.* (1951) using crystalline bovine serum albumin as standard.