

The premature infant

by

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When one considers the premature infant, immediately one realises 2 problems, viz. the concept, and the definition. The concept is simple, in that the premature infant is one who is 'pushed' out into the cruel world before he is ripe for it, *i.e.* he is an 'unripe' or 'immature' baby, before he has had time and opportunities for all his systems to be fully developed. But when one comes down to the practical definition as to which particular infant is premature or not then difficulties arise. The criteria suggested and the inherent difficulties in each is shown in the following table:—

Criterion	Comment
Gestation period	Calculation unreliable
Birth weight	Easily measurable and can be uniformly compared but racial differences and the large diabetic immature infant are exceptions.
Length, head and thorax measurements	Cumbersome and difficult to be accurate.
Radiological maturity	Impractical

There have been many other criteria suggested but finally for practicability and simplicity, it is internationally agreed that a premature infant is one whose birth weight is 2,500 grams or less, *i.e.* approximately 5½ pounds or less. However, in K.K. Hospital, we have chosen the figure of 5 pounds or less as being a more realistic birth weight both from the point of view of racial difference in birth weight among

the local babies who are generally smaller than European babies and from the point of view of facilities available in the Hospital for premature infant care. Generally, this standard has worked fairly well with regard to the care of these prematures.

Incidence

Using 5 lb. and under as the criterion, the incidence of prematurity in K.K. Hospital is seen in the following table:—

Year	Total No. Live Births	Premature Births	
		No.	Per cent
1962	37,770	1872	5.0
1963	38,148	1799	4.7
1964	42,927	2036	4.7
Total:	118,845	5707	4.8

Some representative figures using 5½ lb. and less birth weight are as follows:—

Finland	32,283 live births	4.9%	prematures
Ireland	3,627 „ „	8.7%	„
Japan	1,951 „ „	9.9%	„
Scotland	3,156 „ „	11.0%	„
Singapore	118,845 „ „	4.8%	„

(5 lb. & less)

In an effort to estimate the incidence of prematurity in K.K. in regard to the 3 different races, the percentages of live births racially is compared to the racial premature incidence as follows:—

Race	% of total live births	% of prematures
Chinese	74	78
Malays	17	14
Indians	9	8

In K.K. at least, there does not seem to be any racial difference. One has to realise the limitation of Hospital figures and applying it in general to the whole population of Singapore. But since approximately 60% of births in Singapore occur in K.K. Hospital, the figures given here may be taken as fairly representative of Singapore itself.

Causes

There is no single clear-cut cause of prematurity but there may be several predisposing factors and in each particular case there may be a combination of several factors. Many of these factors are not overwhelmingly significant but the following are usually accepted as contributory factors:—

A. Foetus

1. *Multiple pregnancy*: The incidence of low birth weight is greater in multiple births than in singletons.
2. *Congenital deformities*: Gross deformities often predispose to premature labour.
3. *Foetal diseases*: Intra-uterine infection and Rh-isoimmunisation may result in premature delivery.

B. Mother

1. *Age*: Generally infants tend to be smaller at the extremes of maternal age.

2. *Birth order*: In some surveys first-borns are more prone to prematurity.
3. *Birth spacing*: Very close and very wide spacing have generally been found to predispose to premature births.
4. *Maternal complications*: Statistically, approximately 30-50% of all prematures have been found to be associated with complications in the mother. The complications include toxæmias, antepartum haemorrhage, hydramnios, infections, acute and chronic maternal disease, premature rupture of membranes and induction of labour for obstetric complications.
5. *Habitual prematurity*: For some still unknown reason some mothers consistently produce premature babies.

C. Socio-economic

The following socio-economic circumstances have been found to be associated with a higher incidence of prematurity.

1. *Poor diet*
2. *Inadequate antenatal care*
3. *Employment* in latter half of pregnancy

Pathophysiology

All the pathophysiological handicaps exhibited by the premature infant are due essentially to the immature development of the various systems of the body. In other words, the premature infant's systems are still not developed to the extent that would enable him to survive independently of the mother. It is the present purpose only to enumerate the more important deficits in order to understand the measures to be taken to sustain these "unripe" infants till time is given them for fuller development.

1. Tendency to intracranial haemorrhage

Many factors contribute to this very common complication, not the least of which is the fragile skull which is therefore subjected to undue compression and relaxation during birth and secondarily stretching the poorly developed

intracranial vessels with consequent bleeding. The situation is made worse by the increased capillary permeability both inherent and acquired by attendant anoxia. Once small petechial haemorrhages occur, the leak is not sealed because of the poorly developed clotting factors. In the same way, bleeding elsewhere can also occur with equally disastrous results, *e.g.* pulmonary or adrenal haemorrhage.

2. Poor respiration

Respiratory failure is as common or even more common than intracranial haemorrhage as a cause of death in prematures. Respiratory effort itself is reduced due to immature development of the respiratory centre or due to intracranial haemorrhage, accentuated by poor development of the thoracic cage and muscles of respiration. Even if, perchance, the respiratory excursions are adequate, gaseous diffusion in the lungs may be inadequate for survival. This later disadvantage is due to the inadequate development of the lung alveoli, the immature cuboidal epithelium in contrast to the fully developed squamous epithelium impedes gaseous exchange. Enzyme systems for reduction of surface tension are deficient so that expansion of lung alveoli cannot take place. Furthermore, the tendency to haemorrhage is equally seen in the lung capillaries, so that it is no wonder that at autopsy the premature infant's lung is often solid, non-expanded, and histologically haemorrhages may be seen with hyaline membrane formation. Finally, the defensive cough reflex is almost non-existent and the premature will allow mucus, milk, etc. to trickle down into his aveoli and drown himself.

3. Inadequate feeding apparatus

The sucking and swallowing reflex may not be developed so that spontaneous active feeding is precluded. Coupled with a poor laryngeal reflex, fluids given orally find their way into the lungs instead of into the stomach. Peristaltic activity is reduced and constipation may result and because of the immaturity, the simple complication may result in intestinal obstruction and death. The stomach is of small capacity and coupled with a poor cardiac sphincter, food tends to be regurgitated up and this sets in motion again opportunities for aspiration pneu-

monia. Even if milk is able to be ingested and held back, digestion, absorption and metabolism will be below par. There is no doubt that the liver is unable to carry out its manifold metabolic functions at the same degree of efficiency as the non-premature infant.

4. Tendency to kernicterus

The immaturity of the glucuronyl-transferase enzyme system of liver renders prematures incapable of conjugating the toxic indirect bilirubin to the non-toxic bilirubin glucuronide, with attendant severe jaundice and then possible brain damage. This is especially important in this country where it has been shown that even full-term infants are especially prone to hyperbilirubinaemia and kernicterus due to erythrocytic glucose-6-phosphate dehydrogenase deficiency and so-called liver immaturity.

5. Poor resistance to infection

This is obvious in the premature as its non-specific and specific defence mechanisms are not fully developed. He has a poor level of humoral antibodies, so that he is especially prone to infections. Severely infected prematures, because of their inherent inanition and lethargy, may not show the usual responses to infection that normal babies do, and which allow the paediatrician to recognise the fact that such babies are indeed infected. However, the premature infant with a severe infection, *e.g.* a septic meningitis, may have no fever, no neck rigidity, no tense fontanelle, no fits, etc, and may only fail to feed well, a symptom which seems to be shown by many non-infected prematures anyway. And yet, at autopsy, the meninges are filled with pus.

6. Poor haemopoiesis

Because of the inadequate iron stores and the immaturity of the bone marrow, all premature infants are prone to anaemia, not at birth but subsequently. Hb. F of the cord blood is higher than that of full-term infants and has been suggested as one of the criteria for prematurity.

7. Poor temperature regulation

The premature baby find difficulty in adjust-

ing its temperature because of immature apparatus for heat production and heat loss. Poor heat production is due to hypometabolism, lack of movement and poor shivering reflex. Heat loss is increased because of the relative large surface area and a small amount of insulating tissue, *viz.* the thinness of the skin and subcutaneous tissue. Heat loss adjustment is also poor because of the poor sweating mechanism. Finally, the central temperature regulating mechanism in the brain is immature.

8. Inadequate renal function

There is an overall immaturity of renal function especially with reference to clearance of metabolic substances, water excretion, electrolyte balance and acid-base balance, so that oedema and acidosis are common.

Clinical Profile

Many of the clinical features of a premature infant are the consequence of the above handicaps, so that the premature besides being small is lethargic, cold, often cyanosed, has irregular respiration, oedema, ineffectual cry, etc. At the same time, the head is relatively large with soft skull and wide open sutures. The abdomen is relatively large because of the relatively large liver and the thin abdominal wall often allows one to see the coils of gut underneath. The skin is fine and glossy especially over the palms and soles. The male genitalia are small and the testes often undescended. The female infant has a relatively large clitoris but small labia majora so that the labia minora appear large by contrast. There is abundant lanugo hair but soft nails. As with any clinical description, no amount of words can describe adequately what a premature infant looks like but once seen, the premature infant can be easily recognised.

Management

The principles of the care of a premature infant are based on prevention of premature births which is actually the province of the obstetrician, and the actual care when the infant is born. With regard to the latter, all the efforts are channelled towards providing an environment approximating as closely as pos-

sible what the foetus had been experiencing in utero, and yet recognising the hazards which may arise consequent on such efforts, for the ideal of an artificial placenta or mother, has still not been attained. In another context, is iatrogenic pathology so easily produced by the doctor as in the well-intentioned efforts made on behalf of the premature baby, so much so that the concept of "masterly inactivity" has much to commend itself.

Care in the labour and delivery of a premature baby may influence the prognosis considerably. Analgesia and anesthesia should be reduced to the minimum and constant attention paid to the maintenance of maximum maternal oxygenation. No undue delay in the second stage of labour and an ample episiotomy assist considerably in the survival of prematures. The subsequent management of premature infants in a hospital will depend on the facilities available together with the number of trained staff which can be spared for such specialised care.

Once the baby is delivered, in K.K. Hospital, the routine is as follows. Mucus and secretions are sucked out from the mouth and nose, the baby is weighed and then wrapped in a blanket and placed on the side, with the head of the specially provided cot slightly lowered to prevent aspiration. Every effort is made to keep the baby warm with well-protected hot water bottles and the baby handled as little as possible. The baby is then transferred to the Premature Nursery.

Depending on the birth weight and the general condition and availability of incubators, the baby is either put into a Premature Nursery cot or an incubator, the latter being reserved for the smaller and more feeble prematures. The prepared incubator is heated up to 95°F and the relative humidity at 95-100%, and oxygen as necessary. Inj. Vit. K 1 mg. is given as this is sufficient as a prophylactic against haemorrhagic disease of the newborn and yet unable to cause hyperbilirubinaemia. During the first 48 hours, the infants are watched very carefully for untoward signs, and the side postures are changed alternately.

Barrier nursing is practised for each infant who has individual lockers for thermometers, nurses gowns, oil, swabs, etc. Temperatures are taken rectally twice daily and when the infant is

well settled, oil swabbed twice a week. No chemotherapy is routinely given and antibiotics exhibited only if there are indications for prevention of likely infection or in the treatment of infection itself.

If all goes well, the problem of feeding is then tackled. Delay in feeding is still practised here although other workers have suggested that early feeding may not be harmful and may indeed be beneficial if there are sufficient well-trained staff.

a) Initiation of feeds

Generally speaking, feeding is started late when the birth weight is less, e.g.

Birth weight	Time of feeding
Under 3 lb.	After 48 hr.
3-4 lb.	„ 36 „
4-5 lb.	„ 24 „

These are just guides and each baby has to be individualised.

b) Routes and mode of feeding

If the baby cannot suck or swallow, then tube feeds are instituted. If the infant can suck and swallow, a premature bottle is used. I/V fluids through the umbilicus or via scalp vein are used if the infant is dehydrated.

c) Type of feeds

Expressed breast milk is the ideal food. Substitutes include the various forms of cow's milk preparations, but due to the economic status of the majority of mothers here, unmodified cow's milk powder is used in various dilutions to suit each baby with additions of

sugar. The first few feeds offered is boiled water in case aspiration should occur.

d) Intervals and strengths

Once milk feeds are initiated all infants under 4 lb. are offered feeds 2 hourly by day and 3 hourly by night making a total of 10 feeds in the 24 hours. One drachm is offered at each feed for the first day and approximately increased by one drachm per feed each day. EBM needs to be in $\frac{1}{2}$ strength for the first day and full strength (F.S.) subsequently. For milk powder, $\frac{1}{4}$ strength is offered till the infant has graduated to 1 ounce per feed when $\frac{1}{2}$ strength can be given, and $\frac{2}{3}$ strength when 2 ounces have been reached. When $\frac{1}{2}$ strength and 1 oz. per feed are reached, the times of feeding are reduced to 3 Hourly. making 8 feeds in 24 hr. When $\frac{2}{3}$ strength and 2 oz. per feed are reached, the infant can be given 7 feeds in 24 hr. and when the infant reaches 4 lb. in weight and taking $2\frac{1}{2}$ ounces of $\frac{2}{3}$ strength, the baby is prepared for discharge after the mother has learned how to make the feeds and feed the infant.

A word or two is needed about the daily drachm increments. If the baby is taking orally, the daily drachm increments can be carried out smoothly if while on $\frac{1}{4}$ strength feeds, he takes less than 10 minutes for each feed; the $\frac{1}{2}$ strength feeds when he takes less than 15 minutes for each feed and the $\frac{2}{3}$ strength feeds when he takes less than 20 minutes per feed. Increments when the infant takes too long for his feeds leads to vomiting and possible aspiration. When the infant is tube fed, the useful criterion for the time taken for each feed and hence the sign of readiness or otherwise to increase the feed is absent, and such infants should be carefully watched to see if the increments are justified. In summary, then, the following schedule for oral feeds can be used as a guide:—

Strength	No. feeds/24 hr.	Duration of feed	Drachm increment till
$\frac{1}{4}$	10	10 minutes	1 ounce
$\frac{1}{2}$	8	15 „	2 „
$\frac{2}{3}$	7	20 „	As infant can take

e) Dietary supplements

From the age of 2 weeks, vitamins and iron are given in the following preparations:—

Concentrated Vit. A & D drops 1 minim
b.d. (1 min = 3,000 I.U. of A & 300 I.U.
of D.)

Ascorbic acid 5 mg. t.d.s.

Mist. FAC gr. 1 t.d.s.

In conclusion then it is seen that the above procedure carried out in K.K. Hospital are guiding principles which have been formulated to the needs and facilities available in Singapore. These principles have to be modified as and when circumstances arise as all premature infants do not behave similarly. It is also seen that the procedures are in great part nursing procedures, and it is true to say that the survival or otherwise of premature infants depends a great deal on the efficiency of the nursing per-

sonnel. Once the baby is discharged from the nursery, letters are sent to the nearest Infant Welfare Clinic so that the staff of these clinics may carry on the further management of these infants. They are also followed up in the K.K. Premature follow-up clinics for observation of progress and specialist advice. It is impossible to teach doctors and nurses to take care of premature infants by instructions alone. They will have to practise these under supervision.

Complications

Obviously, premature infants are more prone to complications than mature infants. The relative importance of these complications can be gauged from the following figures on autopsy of prematures dying in 1962, 1963 and 1964 in K.K. Hospital. These figures may be taken as giving a fairly reliable picture because approximately 80% of prematures dying in K.K. are autopsied.

Complication 3 yr: 1962-1964	Number 3 yr: 1962-1964
Intracranial haemorrhage	337
Pulmonary distress syndrome	334
Prematurity (no obvious cause)	246
Broncho pneumonia	206
Gastro-enteritis	34
Septic meningitis	26
Congenital heart disease	21
Kernicterus	5
Miscellaneous	77

From this it can be seen that the main problems which loom large in causing death among prematures in K.K. Hospital are intracranial haemorrhage, pulmonary complications, combination of factors in immaturity of the various systems and infections.

Intracranial haemorrhage, even if it did not cause the death of the infant, would be responsible in a great degree to the mental and physical sequelae of the survivors. There is no effective treatment for this complication, and

therefore prevention of intracranial haemorrhage is of major importance.

Pulmonary ventilatory failure may be due to hyaline membrane disease, atelectasis, pulmonary haemorrhage or aspiration pneumonia. By far, the commonest is hyaline membrane disease, the management of which is still not very effective. There are as many methods and regimes of treatment as there are theories about the cause of the disease.

By prematurity itself, is meant that there is

no obvious pathological cause for the death but that the immaturity of the organ systems themselves militate against survival, and include many of the very small prematures.

Infection as a complication is of great importance to the paediatrician because it should be preventable and treatable. Very often, evidence of infection is afforded by the presence of septic spots in the skin, which are small and red about the diameter of $\frac{1}{2}$ to 1 mm. These then become papular, and then pustular. The macular stage should be recognised and antibiotics given (often a combination of penicillin and streptomycin in the first instance). Another infective syndrome needing emphasis is septic meningitis as it is very silent in the premature in that the only symptomatology may be difficulty in feeding, a symptom shared by many normal prematures. There may be no fever, no neck stiffness, no Kernig's sign and no fits and yet a lumbar puncture will reveal a purulent CSF. Gastroenteritis is the other tricky infection because once it occurs, it often spreads like wildfire and the only effective means of eradication of an outbreak is to close the nurseries for some period of time. The commonest organism cultured from the stools are pathogenic B. Coli.

Kernicterus due to prematurity is much less common, now that prophylactic injections of Vit. K are limited 2 mg. at the most, and serum bilirubins estimated in those with hyperbilirubinaemia so that prophylactic exchange transfusions can be carried out.

Survival Rates

Survival rates are difficult of comparison between different centres especially in areas where the pounds and ounces weight scales are used, as the more developed countries now use the metric system of weights. In such comparisons one has to realise that the major factor is the availability of bed space, adequate premature nurseries and trained staff. By such recognised standards, K.K. Hospital is, of course, rather inadequate. However, the following table summarises the average mortality rates for 4 years in England and Wales (Born and nursed in hospitals. Report of Ministry of

Health (1957), H.M. Stationery Office, London) and in K.K. Hospital for 3 years in the different weight categories:—

Birth weight Gm.	England & Wales %	K.K.H. %
1001-1500	68.1	77.9
1501-2000	19.1	25.8
2001-2250	7.5	4.5

The better figures in K.K. Hospital for the bigger birth weight category is probably due to the greater degree of maturity for comparable birth weights because of the inherently smaller average birth weight of our local infants.

Prognosis of Survivals

Whether all the time, energy and money expended on the care of prematures by methods currently used is worthwhile will depend not only on the saving of premature lives, but also whether the survivals will grow up into individuals without much mental and physical sequelae. To obtain such figures which are valid needs a longitudinal study of large numbers of prematures followed up for several years with adequate controls. One such study has just been completed by Drillien, who found that prematures with a birth weight of 3 lb. or less followed up for periods of 4 years or more, that 50% of them are ineducable in a normal school due to mental or severe physical crippling, and that 25% needed special educational facilities because they were mentally backward. Only 25% had I.Q.'s in the low average, average or superior ranges. 75% had behaviour disorders and more than half had physical defects. Regarding height and weight, 25% were below the 5th percentile. However, for those with a birth weight of more than 4½ lb. the I.Q. was normal. What was also disturbing was the fact that in the centres in Edinburgh, those prematures born in 1953-1954 had more sequelae than those born during 1948-1950, probably because of a greater number of survivals in the later period.