BRITISH MEDICAL JOURNAL

LONDON SATURDAY JANUARY 9 1943

THE PREMATURE INFANT: MANAGEMENT AND PROGNOSIS

BY

W. R. F. COLLIS, M.D., F.R.C.P., F.R.C.P.I., D.P.H.

Physician to the National Children's Hospital; Paediatrician to the Rotunda Hospital

AND

M. A. MAJEKODUNMI, M.D., D.C.H., L.M.

Assistant to the Paediatric Department, Rotunda Hospital

There has been widespread discussion, with grave disagreement, between observers in various countries concerning the correct definition of prematurity. The obstetrical conception of prematurity is unacceptable from the paediatric point of view, because the dates given by pregnant women are notoriously inaccurate. Also, debilitating diseases in the mother have such a profound influence on the birth weight and vitality of the infant that a baby born under such conditions, even when it reaches term or sometimes goes past it, must be regarded as immature, as it tends to be under-developed and incapable of carrying on independent extra-uterine existence without special measures to help it.

The definition of prematurity now widely accepted is that recommended by the International Committee at Geneva in 1937, and agreed to by the British Paediatric Association in 1938; this gave the higher limit of viable prematurity as a birth weight of 5½ lb. and the lower limit as the 28th week of pregnancy, irrespective of the weight at birth. This standard has been found satisfactory in the Rotunda Hospital, where a special department has recently been established for the management of premature and weakly infants.

We are of the opinion that the question of the premature infant has not received the attention it deserves from the medical profession in general. A study of the public health reports of most of the thickly populated areas of Great Britain and Ireland reveals a considerable reduction in the infant mortality rate during the past ten years—i.e., from about 100 to 60 per 1,000 births. On the other hand there has been no appreciable reduction in the neonatal death rate, which still remains at about 32. This means that 50% of the infant mortality during the first year of life occurs within the first month. For a more detailed analysis of the neonatal death rate one must turn to the maternity hospital reports. The latest report of the Rotunda Hospital records 39 neonatal deaths from a total of 3,194 live births; of these 39 infants 25 (60%) were premature. In the National Maternity Hospital, Dublin, out of a total of 133 neonatal deaths 67 (50%) occurred among premature infants; and in the Royal Edinburgh Maternity Hospital in 1938 the proportion was over 50%. These figures show that the greatest single cause of death in the neonatal period is prematurity. Hence, if any appreciable reduction is to be made in neonatal mortality attention must be focused upon the management of premature infants and the causes of their death.

The Outlook for the Premature Infant

Before advocating the difficult and expensive measures necessary, however, it is wise to find out whether the saving of this group of infants is biologically sound. Opinions certainly differ as to the outlook for the premature infant. Capper (1928) maintains that it as often as not becomes the backward school child or a candidate for a home for imbeciles. On the other hand Wallich and Fruhinsholz (J. H. Hess, 1923)

record that Newton, Rousseau, Voltaire, Couvier, Victor Hugo, Lamartine, and Renan were all premature-born. As late as Dec., 1940, we find Robert Hutchison, then President of the Royal College of Physicians and ex-President of the British Paediatric Association, when writing of premature babies saying: "I have a strong suspicion that, of those who survive, a large proportion turn out defective, either physically or mentally, or both."

To help to clear up the matter we have recently made a follow-up study of a group of premature infants which had passed through the paediatric department of the Rotunda Hospital within the last seven years. We were able to trace 45 of these. Seven had died—two within the first month of discharge from hospital, four during the first year, and one at the age of 2 years from bronchopneumonia following an attack of measles. The death rate in this group is only slightly higher than the infant mortality rate in the city of Dublin as a whole.

Of the 38 survivors nine can be said to have some slight abnormality—e.g., three of the children, all of whom are under 5 years of age, have not yet learnt to control the bladder. We feel confident, however, that they will eventually overcome this handicap, as some of the 7-year-olds whom we examined did not learn bladder control until they were 6 years of age. Four of the children have some speech defect (three stutter slightly and one has idioglossia). Those also, we believe, will overcome their handicap if carefully trained during development. One of the remainder has a right-sided hemiplegia: the right hand shows a choreiform movement together with a typical dinner-fork deformity. The lesion in this case would appear to be in the region of the basal ganglia. The child is at present 7 years old, and is able to walk almost perfectly in her special boots. Briefly, the clinical history is as follows:

Weight at birth: 4 lb. 13 oz.
How much premature: 6 weeks
Place in family: 8th
Mother's health in pregnancy: Severe albuminuria
Remarks: Baby very jaundiced at birth; was treated for icterus gravis

The other has Little's diplegia; this is an only child, and her mother is very intelligent and co-operative. Through her patient training the child has now learned to walk, and continues to progress as well as might be expected. She is now 3 years old. A brief summary of her hospital chart shows the following:

Weight at birth: 3 lb. 1 oz.
Nature of labour: Rather difficult delivery with version and manipulations
How much premature: 9 weeks
Place in family: 1st
Remarks: Crown of head appeared bruised. Child was 10 weeks in hospital, and was discharged weighing 6 lb. 3 oz.

To sum up, we found that out of the 38 surviving children 29 (76%) were perfectly developed and equal in weight and height to the average full-term infant for their age; of the remaining 9 only two were found to have severe defects, and in neither case could the result be attributed to their prematurity. The series is small, but we are justified in allowing these figures to support our previous belief, founded upon individual

observation, that premature infants, if without congenital stigmata and given special care, will generally grow up normally.

The Rotunda Paediatric Department

Some 15 years ago the Rotunda Hospital contained no paediatric department, intern or extern. There were no temperature charts for babies, and few notes were kept regarding their progress. It is stated that some 60% of all premature and sickly babies born in the hospital died before discharge. A paediatric department was then founded, and has since gradually developed into the following organization. Special nurseries with 31 cots have been set aside for the management of all premature infants and those suffering from other neonatal disorders. These nurseries are under the control of a paediatrician and managed by a paediatrically trained nursing staff. The normal babies are still managed in the general puerperal wards with their mothers, though each baby now has its own chart, on which its daily weight and temperatures, together with other clinical observations, are noted. A large extern clinic for babies born in the hospital or in its district has also been instituted. The method in the Rotunda Hospital differs from that in some other well-known maternity hospitals in the way normal and abnormal babies are managed in different departments. It has been adopted for two reasons. First, if a sister is given charge of all infants, normal and abnormal, the latter do not receive the same attention as if she has all her time to concentrate on them. Secondly, by leaving the normal babies with their mothers and their midwives in the wards both the latter are taught to manage the babies by ordinary simple methods which can be carried on in the home. It must be admitted that this exposes the normal babies to some degree of infection from visitors; but we believe the system is in accordance with the movement of medical opinion, for we visualize a time when every mother going into a maternity hospital will be provided by society with a room, or at least a cubicle, for herself and her baby during the few days she must spend within its walls. This will entail some modification of present arrangements in the puerperal wards, but the necessity for a nursery for the special cases will still exist.

The result of these measures is seen in the last report of the Rotunda Hospital, quoted above, the premature death rate having fallen from 60% to the present figure of 16%. The measures which are responsible for this very large reduction are discussed below under four headings: (1) maintenance of body temperature; (2) feeding; (3) nursing technique; (4) prevention of infection.

Body Temperature

In the premature infant the heat-regulating mechanism is imperfectly developed at the time of birth, and unless the infant is kept warm by the application of external heat the body temperature quickly falls. This inability to regulate and to maintain a normal body temperature is attributed to incomplete balance between loss and production of heat. The premature infant, if left unattended, rapidly cools down to the temperature of the surrounding air, and among the factors which favour such a rapid lowering of the body temperature are: (a) the relatively great area of heat-eliminating surface—i.e., the skin as compared with body weight; (b) the absence of subcutaneous fat, which increases the escape of heat from the body (Blackfan and Yaglou, 1933); (c) the very low production of heat; and (d) the failure to increase this by crying, kicking, and other activities when the environmental temperature falls below normal.

On the other hand, hyperthermia is very easily induced in these infants, as the heat-eliminating mechanism is equally imperfectly developed: the sweat glands do not function as freely as in full-term infants, and sometimes they fail to act at all. Incubators are now available for the maintenance of body temperature in premature infants; some modern ones are so constructed that the temperature and humidity of the air are automatically adjusted, and the infant can be fed, weighed, and the diapers changed without removing it from the incubator. Incubators are, however, very expensive, and in our opinion are too complicated for use in an institution that has a large number of infants to look after.

When one is confronted with the problem of a premature infant in the environment usually met with in practice the

quickest and cheapest way to maintain its body temperature is by the use of three hot-water bottles suitably covered with blankets or flannels, one being placed on each side of the infant and the third at the feet. The water is changed in rotation every few hours. In more favourable circumstances electric pads or electrically heated blankets may be used with advantage, provided they are closely watched to prevent overheating. For hospital purposes or in nursing homes some form of heated cot is most efficacious. In the Rotunda Hospital a simple incubator cot is used, which consists of a rectangular wooden box, divided into an upper and a lower compartment by a removable "mattress" formed of zinc strips criss-crossed on an oak frame. In the lower compartment are fitted two high-resistance electric bulbs, which keep the temperature of the cot between 80 and 85° F. The upper compartment, well cushioned, receives the infant. This incubator cot is a modification by one of us (W. R. F. C.) of the type introduced by Allen-of Belfast.

In addition to the use of the heated cot the temperature of the ward is maintained at 70 to 75° F. by central heating. Such a high temperature tends to dry the air, and premature infants do not thrive in a low relative humidity. To combat this difficulty a humidifier which keeps the relative humidity of the ward between 60 and 65% has been installed in the premature ward. Conditioned air is of course the ideal, but for financial reasons we have not yet been able to install the apparatus in the Rotunda nurseries. All infants weighing less than 5 lb. at birth are nursed in this specially heated ward of high relative humidity. When they are 5 lb. in weight they are transferred to a cooler ward with a temperature of 60 to 65° F. and a relative humidity of from 40 to 45%. It has been our experience that larger premature infants of 5 to 5½ lb. do not gain weight as readily when nursed in the heated and humid ward as when kept in the cool ward. In the private house the relative humidity can be maintained by the use of a steam kettle or by spraying the room frequently with warm water, or, if the floor material is suitable, by mopping the latter with a wet towel. The premature infant becomes dehydrated if the relative humidity of the room is allowed to fall below 30%, and this very quickly takes place if electric heaters are used in a badly ventilated room.

The use of suprarenal cortical hormone (both synthetic and/or the extract of the gland cortex) for the treatment of dehydration and for stimulating growth in premature infants has recently been reported upon favourably by some observers. We have used this substance in some cases, both to treat dehydration and to prevent it, but we have not found it of general benefit. It has proved of great value, however, in some cases of birth shock and in certain cases of dehydration, possibly those associated with a ketosis.

In spite of the use of the heated cots for external application of heat the temperature of premature infants fluctuates considerably in the first few days of life, and some of them cool down to an alarming degree within half an hour of birth. It is often very difficult to restore the temperature to normal by employment of the incubator cot alone, so recourse has to be had to some means of stimulating the infant's production of heat. The method we now use as a routine at the Rotunda Hospital is the administration of thyroid, which has proved most successful. The infant is given 1/4 gr. of thyroid (B & W) on admission, and 1/10 gr. twice daily for the next three to four weeks. We have found this hormone extremely useful in maintaining the body temperature and stimulating growth in premature infants.

Feeding

The digestive apparatus, even in the smallest premature infant, is reasonably well developed: most of the digestive ferments are present as early as the fourth foetal month, increasing gradually until the adult level is reached when the baby is 3 months old (Hess, 1923). The ideal food is breast milk, and every effort should be made to secure this. The mothers of such infants seldom, however, have enough milk until about the third or fourth day. In such circumstances, if possible, pooled breast milk should be obtained or a wet-nurse be engaged. In a great many cases it will be found impossible to obtain an adequate supply of breast milk, and artificial feeding will have to be resorted to.

At the Rotunda Hospital the smaller premature infants are usually fed two-hourly by day and three-hourly by night,

making a total of ten feeds in the twenty-four hours; the larger infants are fed three-hourly. Immediately on admission to the nursery the infants are given water 1/2 oz., glucose 1/2 drachm, and thyroid gr. 1/4. Feeding is started two hours later, except in the case of cyanosed infants and infants born of toxæmic mothers, who are kept on glucose-water for the first 12 hours. For the first three or four feeds the infants are given a weak mixture of milk and water (e.g., 1 part of milk and 2 parts of water), gradually increasing to a stronger mixture in two to three days. Breast milk is used when available, and by the end of the first week the infants are able to take this undiluted. When breast milk is not available, however, humanized dried milk or peptonized milk is substituted: these preparations are almost impossible to obtain at present, and we are now using half-cream "Cow & Gate," dried acid milk, or boiled cows' milk with equal success. Because of the low food value of weak milk mixtures they have to be reinforced by the addition of sugar (1 drachm to 2 oz. of the mixture). It is well known that premature infants take sugar with avidity during the early days of life, and it has been suggested that hypoglycaemia may be the cause of death in some of them, especially those weighing less than 3 lb. at birth. We have found, however, that they do not tolerate such a high percentage of sugar after two or three weeks, and the earliest clinical indication of carbohydrate intolerance is when the buttocks tend to get red. When this occurs sugar is cut down to about 1 drachm in 3 oz. of the mixture, and the protein content is correspondingly increased: this increase must, however, be very gradual, otherwise the infant will develop protein dyspepsia and start vomiting curds.

Our experience has been that infants weighing less than 4 lb. at birth or who have had a difficult delivery are seldom capable of sucking from the breast, and even when the milk is expressed are too weak to obtain an adequate supply from the bottle. Special teats, Breck feeders, pipettes, and spoon-feeding have been recommended for such infants; but these methods are unsatisfactory, as the feed tends to get into the larynx, causing coughing and choking. We now use gavage (tube feeding) for babies who are unable to suck easily. The pharyngeal reflex is imperfectly developed in these infants, so that the operation is carried out with the minimum of disturbance while they lie in their cots. When the infant starts to suck at the tube it is a sign that bottle-feeding may be gradually started. By this means we are able to avoid giving concentrated mixtures as advocated by some workers: these in our opinion are a potent cause of digestive disturbances. Instead of thickened feeds we give more feeds in the twenty-four hours—i.e., about 10 oz. to babies weighing 3 lb. or less, and about 15 oz. to babies over 4 lb. It is our experience that at this period of life the quantity of feeds is more important than the quality. By giving large quantities of fluid, in addition to keeping the infants in an optimum air condition, we have been able to reduce the initial weight loss to a considerable degree, and in some cases to eliminate it.

We have found it impossible to make an invariable rule for supplying the calorie requirements of our premature infants; some of them take as much as 45 to 50 calories per lb. body weight in the first twenty-four hours, while others will not; but none of these infants will gain weight after ten days on anything less than 60 calories per lb. body weight a day, and often we have to increase to 100 or more.

Vitamin Therapy.—Vitamin concentrates are administered to all our premature infants from a very early date. Vitamins A and D are added to the feeds in the form of adexolin from the second day of life. 3 minims daily is given at first, and this is gradually increased until 5 minims is being given by the end of the first month. Redoxon (vitamin C) 10 mg. daily is added to the feeds from the fourth week. Infants who have had a difficult delivery or who have haemorrhagic disease of the newborn are given vitamin K as a routine—0.5 to 1 c.cm. kapilon twice daily.

Nursing Technique

Of equal importance to feeding and other measures in the management of the premature infant is the nursing technique. In the Rotunda Hospital the following routine has been most successful. Immediately after birth the cord is ligatured and cut; the baby is cleansed with warm olive oil and wrapped

in a warmed gamgee jacket of known weight. Recently, since olive oil can no longer be obtained, we have refrained from washing them altogether, leaving the vernix to fall off gradually. On admission to the nursery the baby is weighed and the rectal temperature taken. A dry dressing is applied to the cord, strict precautions being taken to prevent sepsis; the dressing is kept in place by a flannel abdominal binder. If the infant weighs under 4½ lb. its limbs are wrapped in cotton-wool; if under 4 lb. the head is also wrapped in cotton-wool. Glucose-water and thyroid gr. 1/4 are now given as already outlined; the baby's colour is most carefully observed and the rectal temperature taken again after two hours. If the general condition is not now satisfactory—i.e., if the baby is cyanosed or has birth shock—some form of stimulant is administered, such as nikethamide (coramine), rectal coffee-saline, or brandy. If the condition is satisfactory two-hourly feeding is begun. The baby is subsequently cleansed with olive oil once a day; the diapers are changed five times daily, when the baby is stimulated to induce crying in order to prevent atelectasis: at these times the genitals are cleansed with sterile water and the buttocks rubbed with a cream containing castor oil, zinc oxide, and tinct. benzoini co. The baby is turned on its side every four hours to prevent congestion of the lungs. A bi-daily temperature chart is kept and the baby weighed three times a week.

Infection

Infection is one of the commonest causes of death in the neonatal period. Newborn infants as a rule, and premature ones in particular, have but little power of resistance, and succumb very readily when infected. In an analysis of the causes of death of 101 premature infants in Edinburgh Maternity Hospital it was found that 43 of the deaths were due to infection (McNeil, 1940). Such a finding, however, is not confined to Edinburgh. It has been our experience on more than one occasion, and that of all other maternity hospitals of our acquaintance. The sources of these infections are as a rule:

(a) *Fingers of Attendants.*—Organisms are conveyed to the fingers from septic spots on the face or other parts of the body or from masks which have become infected; if the hands are not properly washed, contact with the premature infants implants the organisms on their delicate skin and gives rise to infection.

(b) *Improperly Sterilized Feeds and Teats.*—During the early days of life the contents of infants' intestines are sterile, and if their feeds are not thoroughly sterilized they tend to contract a sudden heavy infection with coliform organisms. These are absorbed not uncommonly into the circulation and are later excreted by the kidneys, giving rise to pyelitis and secondary enteritis in both male and female infants.

(c) *Droplet Infection.*—This is caused by attendants or visitors, with or without obvious respiratory infection, breathing over the infants; the commonest organisms thus spread are pneumococci, streptococci, and staphylococci.

Infection has been found our greatest difficulty in the Rotunda Hospital nurseries. Again and again it has appeared in spite of the most stringent regulations. During the present year we have had a persistent outbreak of enteritis. As well as enforcing the most stringent regulations regarding the sterilizing of feeds, bottles, etc., and washing of the nurses' hands, we do not now allow admissions from outside the hospital or infected cases from the puerperal wards even to the isolation wards in the nursery. No visitors or students are permitted entry to any of the infant wards. The nurses' nasopharynxes are periodically examined and swabbed, and sterile masks are supplied in sufficient quantities to avoid their being worn when permeated by saliva, and the nurses are instructed never to touch them with their fingers once they are adjusted.

Discussion

There is no doubt that the measures necessary to reduce the death rate of premature infants are elaborate and complicated, but the results that may be obtained are so remarkable as to make them well worth while. In the past far too much publicity has been devoted to the maternal complications of obstetrics and far too little to those of the child. If the neonatal death rate is to be reduced, as can so easily be done, a new attitude to the whole subject is essential. A proper paediatric unit must be developed in every maternity hospital. There should be a maternity hospital in every region. For babies born outside the maternity hospitals, units of a similar nature

should be set up in all children's hospitals. It can be said that attempting to manage premature babies in the general wards of children's hospitals is almost waste of time, as they will tend to become infected and die.

We have dealt here with the management of the premature baby exclusively, and so far have said nothing in regard to the prevention of the condition. This is largely a social matter that can no longer be ignored. The maternity centre in New York has been able, by pre-natal care, to reduce the percentage of premature births by one-third. In a certain home for unmarried women in Oslo the proportion has been reduced to 2%, compared with 32% still prevailing among women of the same class attending the ordinary obstetrical clinic. Nutrition, sufficient rest, and relief from strain are the most important predisposing factors. In this connexion it is well to mention that cerebral haemorrhage is a common cause of death among premature babies, and recent work suggests that one of the reasons for this is lack of vitamin K in the mother's diet. Women suffering from even mild types of the toxæmias of pregnancy are usually placed upon deficiency diets. In the past obstetricians have often failed to recognize the importance of adding vitamin concentrates to these diets. In all such cases it is wise to give special injections of vitamin K.

Finally, we may sum up the position in regard to prematurity by saying that when a combined effort is made by the obstetrician and the paediatrician a considerable reduction will occur in its incidence and its death rate, and as a result we may expect a general improvement in the whole neonatal mortality.

REFERENCES

- Blackfan, K. D., and Yaglou, C. P. (1933). *Amer. J. Dis. Child.*, **46**, 1175.
Capper, Aaron (1928). *Ibid.*, **35**, 263, 443.
Hess, J. H. (1923). *Premature and Congenitally Diseased Infants*, J. and A. Churchill, London.
Hutchison, Robert (1940). *Lancet*, **2**, 799.
McNeil, Charles (1940). *Ibid.*, **1**, 819.
Wallich and Fruhinsholz: Quoted by Hess (loc. cit.).

TREATMENT OF WOUNDS AND INFLAMMATION BY X RAYS AND RADIUM RAYS

BY

N. S. FINZI, M.B., D.M.R.E.

Director, X-ray Department, St. Bartholomew's Hospital

AND

F. FREUND, M.D.Vienna, M.R.C.S., L.R.C.P., D.M.R.E.

Radiologist, E.M.S.

The use of x rays and other radiations in the treatment of wounds and inflammations has been much neglected. Dr. Leopold Freund of Vienna, who was the first to employ x rays for any form of therapy, used them for inflammations more than 40 years ago. One of us treated such cases as long as 36 years ago, and the other has done experimental research work on the basic principles underlying this treatment. The causes of this neglect are various. First, the indications for the treatment were so universal that it came to be looked at askance by the profession, who feared that it was a semi-quack treatment. Secondly, the discovery of the value of x rays and radium γ rays in malignant disease overshadowed their other uses. Thirdly, incorrect dosage was used in the earlier days. It was not until 1928 that it came to be universally realized that the doses previously given were too large and either produced inferior results or caused the late development of telangiectases and atrophy of the skin. Fourthly, it has been found that the action of ultra-violet and sunlight increases the liability to these late changes if larger doses have to be given, as in keloid. Finally, in the earlier days of the use of x rays the penetration, in treating deep-seated conditions, was much too low, so that the surface received an overdose and the deep part an underdose. Also, in those days accurate measurement of the dose, except that administered to the surface, was impossible.

With the very small doses now employed by some radiologists it is possible to carry on treatment, if necessary, for very long periods without the slightest risk of after-effects: this necessity, of course, arises only in the most chronic inflammations. Success has been obtained by ray therapy in such diverse conditions as carbuncle, erysipelas, suppurative parotitis, tuberculous glands, tuberculous peritonitis, actinomycosis, chilblains, whitlow, gas gangrene, osteomyelitis, and many others.

Basis of Treatment

In wounds there are two purposes to which irradiation can be put. One is the acceleration of the healing of clean wounds and the prevention of keloid; the other is to check the local inflammatory reaction, if there is no foreign body or sequestrum present. It does not matter whether the infection is acute, subacute, or chronic, except that one tends to use even smaller doses in acute cases. Experimental research work was done on the mode of action of small doses of x rays at the Holzknecht Institute in Vienna by one of us and by Shuichi Fukase. This gave the following results:

(1) Under treatment with small doses of x rays polymorphonuclear leucocytes in exudates break down more quickly than they usually do. Some think that this increased breakdown of polymorphs may be combined with the liberation of immune bodies and that the acceleration of healing is achieved by this means. (2) Wounds of the skin and of the cornea of animals heal sooner in the part treated locally by x rays. On the shaved skin of rabbits incisions were made about 12 cm.

FIG. 1.—Cut in back of a rabbit 5 days after Section A had been irradiated. This section is firmly united, while Section B is still ununited.

long down to the superficial fascia. One half of the incision was covered with lead and the other half was treated by x rays immediately after the wound was inflicted. The wounds were left open and the animals kept in their usual surroundings. In that part treated by x rays hardly any exudate or other sign of cellular reaction occurred either as to the naked-eye or the microscopical appearance. The treated part of the wound was healed in 8 days as if it had been sewn up. The untreated part became infected and healed slowly by granulation. (Figs. 1 and 2.) Wounds of the cornea healed without surrounding inflammation on the side treated by x rays, but with marked infiltration on the side not treated. (3) Experimentally produced fractures of both fibulae of rabbits heal more quickly on the side treated with x rays. The callus on the irradiated side is less in quantity, is formed earlier, and is more heavily calcified. (4) After the inunction of tuberculin into the skin no reaction takes place in the part of the skin treated by x rays soon after the inunction. This shows the local effect of x-ray