rate. Even after twelve hours the delay of clotting is still adequate when judged by the criterion previously stated.

The problem of long-term anticoagulant therapy with intramuscular heparin was also studied in the same way.

Fig. 3 shows the dosage of heparin and the delay in clotting times in one patient over a period of four days. An initial dose of 37,500 units of heparin was given intramuscularly, followed by injections of 25,000 units (1 ml. of solution) twelve-hourly. The delay of clotting was satisfactory

FIG. 3.—Long-term anticoagulant therapy with intramuscular heparin.

throughout and there was some indication that the dosage of heparin could be decreased after the initial stages. This was shown by the increase in the delay of clotting after the first two or three days. It therefore seems probable that either the dosage of heparin may be decreased after this time or the time interval between injections may be increased.

Discussion

There are some disadvantages to the intramuscular injection of heparin. It was at first found that the injection was attended in some patients by local pain. This, however, was satisfactorily overcome by the simultaneous injection of procaine: 1–1.5 ml. of a 1% solution of procaine should be given in the same syringe as the heparin. This has no effect on the action of the drug and considerably diminishes the pain.

The discomfort of the injection may also be ameliorated by injecting into the vastus lateralis muscle, and not into the buttock upon which the patient has to lie.

Very occasionally a haematoma may develop at the site of injection. This is not a common complication, and was encountered only twice during the course of this work. Bauer *et al.* (1950) reported five significant haematomata in a series of 41 patients treated with intramuscular heparin. These workers used large needles for the injection, presumably because of the consistence of their heparin solution. The heparin solution used in the present work was aqueous, and so this disadvantage was overcome. Indeed, a fine needle, 18–20 gauge, should be used, and not the ordinary intramuscular needle. In this way the possibility of trauma is reduced to a minimum, and haematomata can usually be avoided. Elaborate precautions are unnecessary when making the injection, but care should always be exercised.

Hitherto, treatment with anticoagulant drugs has almost invariably demanded admission of the patient to an institution. This has been rendered necessary by the numerous intravenous injections required for heparin therapy, and

by the frequent laboratory tests which must always be done to control dicoumarol dosage. Neither of these factors need be considered when heparin is given intramuscularly. The clotting time is never grossly prolonged, and the risk of haemorrhage is extremely slight. The results obtained in this investigation indicate that the treatment may be conveniently and safely carried out in the home. If this conclusion is confirmed by subsequent work, the use of an anticoagulant in domiciliary practice would constitute a significant advance for both patient and doctor.

Summary and Conclusions

The possibility of giving heparin by intramuscular injection has been studied in 20 patients. A concentrated aqueous solution of heparin of strength 25,000 units per ml. was used. Results indicate that this is a satisfactory method for short-term or long-term anticoagulant therapy.

An initial dose of 1.5 ml. of this solution followed by 1 ml. twice daily is recommended as a scheme of dosage.

Local pain and occasional haematomata which may result are discussed, and the way in which these disadvantages may be prevented or minimized is indicated.

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ANAESTHESIA IN THE NEWBORN*

BY

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The newborn infant differs so greatly from the adult in his anatomy and physiology that the approach to anaesthesia in the two groups must be quite different. In the past there has been a tendency to adapt to infants those methods of anaesthesia which have proved to be of value in adults. The time has come to consider the problem of anaesthetizing the newborn in relation to their peculiar physiology.

During early life the ribs of an infant are disposed almost horizontally when the infant is in the erect position. Movements of the ribs can therefore produce only insignificant effects on the capacity of the thoracic cage, and costal respiration is practically impossible.

The Neonatal Lung

In addition to the relatively poor mechanism for its ventilation, the neonatal lung itself is a comparatively rudimentary structure. The area available for respiratory exchange is small in comparison with that of the adult lung: the amount per cubic centimetre of lung volume is half that of adult lung tissue, and the respiratory surface of the lungs per kilogram of body weight is about one-third that of the adult (Engel, 1947). To compensate for these deficiencies, as well as for the high oxygen consumption per kilogram of body weight, the infant has a rapid respiratory rate.

The infantile tracheo-bronchial tree is to some extent adapted to function in these circumstances, and the area of

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the cross-section of the trachea of the newborn infant per unit of lung volume is twice that at 12 months. The sagittal diameter of the trachea of the neonatal infant is variously quoted as 3.6 to 5.7 mm. and of the adult as 15 to 20 mm. The diameter of the adult trachea is four to five times greater than that of the infant. If the forces governing the rate of flow of gases through the trachea follow Poiseuille's law, it would follow that an increase in the rate of flow in the child's trachea would produce an effect on the resistance to respiration 4^4 times greater than the increase in resistance produced by the same increase in the rate of flow through the adult trachea. In other words, if an increase in the rate of flow through an adult trachea increases the resistance to respiration by, say, x , the same increase in the flow rate through an infant's trachea would increase the resistance by $256x$.

On theoretical grounds, then, it is desirable that any technique employed for anaesthetizing young babies should not tend to increase the respiratory volume per minute, and should, if possible, reduce the amount of mechanical energy required for pulmonary respiration.

In addition to these mechanical differences between adult and neonatal respiratory systems, there seem to be certain differences in the sensitivity of the respiratory centre. The experiments in which Snyder and Rosenfeld (1937) observed the activity of the respiratory centres of post-mature foetal rabbits showed that smaller reductions in blood carbon-dioxide levels were required to produce acapnia in the young animals than in the maternal animals.

The immature state of the neuromuscular system in the newborn eliminates some of the problems which are met with in adult anaesthesia. The adult type of reaction to the irritation of an endotracheal tube under light anaesthesia is not seen in infants. The so-called "bucking" is impossible in children under 3 months of age, because until this time the cervical muscles are not capable of raising the head from the pillow. The only sign of irritation of the trachea under light levels of anaesthesia is a disturbance in the rhythm of respiration.

Similarly, deep levels of anaesthesia or heavy curarization are not necessary to produce muscular relaxation, because muscle tone is virtually non-existent in the newborn. During abdominal operations on young infants, intrusion of the abdominal contents into the operative field is sometimes very troublesome, but factors other than muscle tone appear to be mainly responsible for this. The infant at birth has an abdomen adapted to accommodate an alimentary tract which is devoid of gas, and thereafter the intestines acquire their gaseous content. It would seem inevitable that this, combined with the purely diaphragmatic type of respiration, would produce protrusion of the gut through the wound on opening the child's abdomen soon after birth.

The relative absence of muscle tone in infants can easily be demonstrated by artificial ventilation of the lungs under light anaesthesia; in small babies it is possible to inflate the lungs by the application of surprisingly low pressures, in sharp contrast with the resistance to inflation which the adult patient exhibits under similar conditions.

This ease with which the neonatal lungs can be inflated, combined with the small reduction in blood CO_2 required to produce acapnia, permits easy control of the respiration in young infants. In this respect the behaviour of the lightly anaesthetized infant bears a striking resemblance to the curarized and anaesthetized adult. Control of the respiration is extremely desirable in infants because it relieves the respiratory muscles of their whole load, and

in abdominal surgery does much to prevent the pushing out of the abdominal contents. There is one theoretical objection to this procedure—there must be a shift of the oxygen dissociation curve of the blood to the left, thus reducing the peripheral oxygen tension. Barcroft (1946), however, showed that in newborn mammals the arterial oxygen saturation is only 75%, because the permeability of the pulmonary alveolar walls to oxygen is lowered, and that high oxygen atmospheres are able to raise the saturation level. In neonatal anaesthetic practice, then, a high oxygen atmosphere would more than compensate for the shift in the dissociation curve produced by artificial hyperventilation.

Use of Muscle Relaxants

In the light of these observations it is necessary to consider the use of muscle relaxants in the newborn. In anaesthetic practice generally these drugs can be used to reduce the dose of anaesthetic agent required for the production of good operating conditions because: (1) they reduce respiratory movements and enable adequate ventilation of the lungs to be carried out by the intermittent application of positive intrapulmonary pressures, without the use of excessive pressures; (2) they produce muscular relaxation in the surgical field; and (3) they reduce the effects of irritation by endotracheal tubes.

In the newborn, as has already been shown, control of the respiration is easily obtained at light levels of anaesthesia without the use of relaxants: muscle relaxation does not appear to be of major importance in the production of good operating conditions, and the usual untoward effects of endotracheal-tube induction are not seen. On these grounds it can be said that the use of relaxant drugs in anaesthesia is contraindicated in the newborn patient, and I have abandoned these drugs in such cases.

In view of the desirability of keeping the patient's respiratory activity at minimal levels and the relative absence of muscle tone, cyclopropane would seem to be an ideal anaesthetic drug for neonatal patients. The type of respiration which it produces would minimize the pushing out of the abdominal contents by the movements of the diaphragm, and the lack of muscle-relaxing properties would not be disadvantageous. There are, however, certain other effects which, I feel, render it undesirable. During surgical operations there is undoubtedly a greater loss of blood from those patients who are anaesthetized with cyclopropane, and this becomes a point of major importance in choosing an anaesthetic agent for a patient whose total blood volume is 300–400 ml. Prolonged administration of this drug to very small infants seems to produce in the early post-operative period a shock picture comparable to that often seen after its use in adults. For these reasons I consider that cyclopropane has little value in anaesthesia for the newborn, and that diethyl ether is the principal anaesthetic agent of choice, provided that the respiratory effect is reduced by controlled respiration produced by hyperventilation.

Operative Risk

The operative risk in newborn infants at term is slight, but it increases rapidly during the first week of life. This is in part due to the fact that the continuance of the abnormal state which the operation is designed to rectify increases the risk in some cases, but there is evidence to show that the resistance of all newborn mammals to physiological abuse becomes reduced during early extrauterine life. Glass *et al.* (1944), in a series of experiments on rabbits, estimated their survival time when they were subjected to

complete anoxia at term and at various days after term, and found that if the survival time in minutes was plotted graphically against the age of the animal the curve showed a regular decline from 30 minutes at term to 2 minutes at 20 days.

In those cases in which there is obstruction at some level of the alimentary tract the impairment of respiratory function by the aspiration of regurgitated fluid increases with time, and reflects on the operative risk; but this can be minimized by continuous aspiration of the pharynx in the pre-operative period.

In general, it can be said that the optimum time to operate is during the first 24 hours of life, or at the earliest period at which the blood urea and the urinary chlorides can be brought to normal levels.

Premedication

Some authorities have recently recommended that premedication of very young infants with morphine should be done. Leigh and Belton (1948) suggest a dose of 1/400 gr. (0.16 mg.) of morphine for 7-lb. (3.2-kg.) babies. This treatment appears to facilitate the smooth maintenance of anaesthesia, and would seem desirable if respiration is not to be aided or controlled. It does, however, make the induction of anaesthesia by inhalation agents—a tedious process at best—a very prolonged procedure.

Atropine should be given in all cases, and a dose which can be used on all newborn cases is 1/200 gr. (0.32 mg.).

Endotracheal Intubation

There are certain anatomical differences between the largest of newborn infants and adults that produce greater technical difficulties in the former. The infant larynx occupies a higher position in the neck in relation to the vertebrae, and the axis of its lumen tends to pass forwards as well as downwards. With the descent of the larynx which takes place in later life the forward angulation disappears (Tucker, 1932).

The complication of endotracheal intubation in young children that is most to be feared is subglottic oedema, the danger of which following instrumentation was first pointed out by Chevalier Jackson. Gillespie (1939) says that this oedema is the result of streptococcal invasion of abrasions produced by trauma during laryngoscopy, and that if care is taken during inhalation the risk is negligible. In his own published series of 70 cases of children under 18 months he does not report one instance of this complication. I have not met any case of respiratory stridor, nor have I seen any evidence of laryngeal oedema at post-mortem examination, following endotracheal intubation of neonatal infants. On the other hand, necropsy has revealed varying degrees of tracheitis, including one case in which there was on the anterior wall of the trachea a small circular ulcer similar to those reported recently by Dwyer *et al.* (1949). These lesions do not seem to have contributed towards the fatal outcome in these cases.

The advantages to be derived from intubation are very great, in that the tube ensures a reliable airway and enables the lungs to be readily inflated, and is an invaluable insurance against the dangers of gastric regurgitation, which is very common in the obstructive group of cases.

Apparatus

If CO₂-absorption apparatus is used on the newborn the only suitable standard equipment is the ¼-lb. (114-g.) Waters type of absorber described by Cope (1947). This has certain inherent disadvantages which greatly impair its

value. Despite the fact that it is designed to reduce dead space, those parts of the apparatus which lie between the patient's respiratory tract and the soda lime have a considerable internal capacity. When the absorber is connected to an endotracheal tube its positioning is difficult if a considerable length of tubing is not used between the endotracheal tube and the absorber.

During the operation the Ayre's T-piece is very much easier to handle than the Cope absorber, and the internal capacity between the gas inlet and the patient is very small, so that with adequate flows of gas rebreathing is minimal. Artificial ventilation may be carried out by attaching a double-ended bag (B.L.B. type) to the exhaust tube, the open end of which is fitted with a vulcanite tap. This tap can be adjusted so that the intermittent pressure applied to the bag expels the amount of gas required to maintain the equilibrium of the system.

Thoracic and Abdominal Operations

I have now adopted a routine technique based on the views set out in this paper for anaesthetizing newborn infants for thoracic and abdominal operations.

The child is brought to the theatre dressed in a gamgee jacket and bonnet, and with the limbs bound in cotton-wool. An intravenous drip is run into one leg, and in cases in which there is alimentary obstruction a tube is passed into the stomach or, when there is oesophageal atresia, to the site of the obstruction. The thoracic cases that are cyanosed are brought up in an oxygen tent, and are transferred to the operating table only when the induction of anaesthesia is about to begin. The child lies on an electric pad on the table.

Induction of anaesthesia is effected by leading gases from a continuous-flow machine to beneath a Schimmelbusch mask covered by a thick layer of gauze, and separated from the patient's face by a thick layer of gamgee tissue.

Initially the gas flow is at the rate of 2 litres of oxygen a minute, maintained for one minute. At the end of this time 100 ml. of CO₂ a minute is added, and, finally, ether vapour to the limit of the patient's tolerance.

When the child breathes the full vapour concentration of ether regularly, the largest possible endotracheal tube is inserted, and this is connected by the shortest possible length of rubber tubing to an Ayre's T-piece.

The gas flow is adjusted to give a 50% O₂ and N₂O mixture flowing at a total rate of 3–4 litres a minute, and the ether vapour is turned off until the child shows movement of the limbs. In the meantime the mouth is packed with sterile ribbon gauze and the endotracheal tube is fixed. Ether is added to the mixture in concentrations just high enough to prevent movement.

The patient is now placed in the correct position for the operation, and a double-ended bag is fitted to the exhaust limb of the Ayre's T-piece. When the incision is made the respiration is brought under control by intermittent positive pressure applied by squeezing the bag, and the child is kept from spontaneous breathing throughout the operation.

Anaesthesia is maintained at the lightest possible level, and in view of the difficulty of eliciting and interpreting the signs of anaesthesia in these cases the ether vapour is turned off at intervals of 20 minutes for a period long enough to allow a return of some movements of the limbs. In this way rapid recovery after operation is ensured.

The method has proved to be extremely satisfactory, and the babies appear to be in much better condition post-operatively than those in whom spontaneous respiration was allowed to continue throughout the operation, or in

whom deeper levels of anaesthesia were attained. There seems to be rather less bleeding, and the surgeon is unhampered by respiratory activity.

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OBSTETRIC ANALGESIA AND PLACENTAL INSUFFICIENCY

BY

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For the relief of pain in labour the combination of general medication and intermittent inhalation analgesia can be very effective and is suitable for all types of labour. Relief from pain is effectively obtained by careful antenatal preparation, by careful supervision during labour, by the judicious use of analgesic drugs such as pethidine, and by inhalation of a mixture that provides analgesia within 15 seconds. Success depends largely on the quality of the psychological management. The mother will be satisfied only if she appreciates the rationale of the method—that she will be aware of uterine contractions and will feel the baby delivered, but will not feel pain.

I closely supervised pain relief in a series of 200 labours, including 141 primiparae, selected at random but with every prospect of normal delivery. The patients had received no antenatal preparation for analgesia. Supervision and reassurance during labour were therefore exacting, but 89% admitted that analgesia was adequate. Subsequent experience has emphasized the well-known fact that antenatal preparation makes supervision in labour easier and more effective. Failure to obtain adequate analgesia has been due to lack of co-operation (or inadequate preparation for labour), to continuous backache at the end of the first stage of labour (needing higher dosage of analgesic drug), and to labour being well advanced on arrival in hospital.

In the 200 cases the inhaled mixture was either 0.5% trichlorethylene in air or 75% nitrous oxide with 25% oxygen, in both of which mixtures the oxygen content is at least as great as that of air. The commonly used 50% nitrous oxide with air provides only 10% oxygen: inhalation of such a mixture lowers the arterial oxygen tension to below 50 mm. Hg (McQuiston, Cullen, and Cook, 1943). This fall in tension is rapid. Examination with an oximeter (G. af. Geijerstam, 1949—personal communication) has shown that when a woman in labour inhales 4 litres of pure nitrous oxide in about 10 seconds the percentage saturation of her blood with oxygen falls from the normal 96% to 69% within 20 seconds, that is, to an oxygen tension of about 40 mm. Hg. The particular value of intermittent inhalation is to provide pain relief with negligible respiratory depression in the baby. It is important that the

analgesic should not contribute to oxygen lack, which is a potent and insidious depressant of nervous function. The following considerations suggest that even intermittent inhalation of an oxygen-deficient mixture may contribute to intrauterine asphyxia when placental function is impaired.

Oxygen Transfer to Foetus

It is generally agreed that the passage of oxygen from mother to foetus is a matter of diffusion across the placenta, and that there is an oxygen-tension gradient towards the baby. Eastman (1930) has calculated that the probable oxygen tension in the placenta available to umbilical-vein blood during labour is 40–50 mm. Hg, compared with the 90 mm. Hg of maternal arterial blood. Whatever the actual figures may be, transfer is facilitated by devices such as an arrangement of vessels in the placenta whereby the streams of maternal and foetal blood run parallel but in opposite directions, so that umbilical-vein blood has maximum exposure to maternal arterial blood (Spanner, 1935); by the large numbers of foetal blood cells for oxygen transport (Windle, 1941); and by a difference in the oxygen dissociation curves of the two bloods which promotes the passage of oxygen across the tissue barrier. With a maternal arterial oxygen tension of 50 mm. Hg or less, the oxygen-tension gradient across the placenta is considerably reduced and possibly abolished.

There is little doubt, too, that a progressive decline in the saturation of the blood reaching the foetus takes place towards the end of gestation, and the point at which labour occurs is variable. Windle (1945) points out that, so long as normal healthy conditions prevail in the placenta, a reservoir of oxygen in combination with haemoglobin is present to provide for the needs of the foetus. This constitutes a factor of safety equivalent to at least 40 ml. of oxygen in the human at term, and enables the foetus to survive severe oxygen lack in the mother for short periods of time. The safety margin may be reduced by ageing of the placenta, by partial separation of the placenta, and by conditions in the placenta involving deposition of fibrin and ischaemic necrosis of villi.

Intrauterine Asphyxia

It is commonly accepted that changes in the foetal heart rate afford evidence of intrauterine asphyxia. This change in rate is similar to that seen in asphyxia in the adult where there is a preliminary acceleration followed by bradycardia. The cardiac acceleration is thought to be due to reduced vagal restraint together with increased sympathetic drive. The acceleration is later converted to positive vagal slowing, due either to a rise in arterial blood pressure acting via the carotid and aortic nerves or to a central discharge (McDowall, 1938).

A similar effect is seen in asphyxia neonatorum: when a baby takes occasional gasps with a long pause between, the pulse becomes progressively slower between gasps, but rises to the normal rate within a few seconds after a gasp which introduces oxygen into the lungs. When regular respiration is established the rate remains at 120–140 a minute. This implies that the vascular reflexes concerned in asphyxia of the adult are well developed in the foetus at the end of pregnancy, though the tachycardia mechanism may not operate. Barcroft (1946) wrote that there is a good chance of there being some vagus control before birth in man, but that it is not necessarily always present. It has been demonstrated experimentally in the goat that clamping the umbilical cord causes foetal bradycardia (Helliwell and Hutton, 1950).