and haemoglobin determinations were carried out on the daily samples of the oxalated blood. Tests for Rh antibodies were made on the serum of all mothers found to be Rh-negative.

Results

The cases were divided into two categories depending on whether the A-B-O group and the Rh types were compatible or incompatible with those of the mother, and the results are summarized in Tables I and II. As will be seen, the average icterus index of the cord serum for the group with compatible blood types was 10.8 units, as compared with the average of 9.2 units for the group with incompatible blood types. In most babies of both groups the icterus index rose immediately after birth, and at the highest point in the compatible group the average icterus index was 36.8 units, in comparison with an average at the highest point of 30.9 for the incompatible group.

These results indicate that the high icterus index of the cord serum and the rise which occurs in the neonatal period are not ascribable to any incompatibility involving the A-B-O groups or Rh types. In accordance with the previous observations (Weech, 1947) the values of the blood counts and haemoglobin determinations remained constant from day to day, indicating that the rise in icterus index was not due to haemolysis.

Comment

Inadequacy of the excretory function of the liver has been shown to be one of the phenomena associated with physiological icterus. The cause for this malfunction has not been determined, though most workers in the field have ascribed it to "immaturity" (Weech, 1947). Because erythroblastosis foetalis is also attended by a marked diminution in the excretory capacity of the liver, Wiener (1951) has postulated a pathogenesis for physiological icterus on an analogous basis. Examination of women at term demonstrates the constant presence in their serum of auto-antibodies in tests carried out at ice-box temperature, especially when enzyme-treated test cells are used. Almost invariably the antibodies are of the univalent variety, so they are presumably capable of traversing the placental barrier and coating the foetal red blood cells. As in the case of mild Rh sensitization, the auto-antibodies derived from the maternal circulation are only occasionally demonstrable free in the cord serum, but the practically universal occurrence of hyperbilirubinaemia in the newborn infant could be explained by the universal occurrence of auto-antibodies in the maternal blood.

One of us (A. S. W.) has further postulated that, since the antibodies are of the cold variety, the cooling of the baby's skin that attends his birth brings about clumping of the coated red cells and acts as the trigger mechanism that sets off the explosion that is physiological icterus. The high incidence of icterus in premature infants, with their poor temperature control, may have a similar explanation, although here developmental immaturity also has great plausibility.

We have recently encountered a case in which an expectant mother was found on antenatal testing to possess cold antibodies in her serum with a titre approximately three times as high as the upper limit found in other mothers. The baby born to this mother developed mild jaundice and anaemia, the haemoglobin dropping to 65% by the time the baby was 3 weeks old.

No other cause for the anaemia could be demonstrated. As the titre of cold antibodies has been shown to be elevated in cases of atypical pneumonia and infectious mononucleosis, a search is being made for cases in which pregnant women had these ailments shortly before term.

Summary

Studies of the A-B-O groups and Rh-Hr types revealed no relationship between these blood factors and the occurrence of physiological icterus in the newborn infant. The average icterus index of the cord serum in babies with compatible and incompatible blood types did not differ, being 10.8 and 9.2 units respectively. At the peak of the hyperbilirubinaemia the values were 36.8 and 30.9 units respectively. There was no fall in red blood cell count or haemoglobin concentration accompanying the rise of icterus index. The possible relationship of auto-antibodies to the syndrome of physiological icterus is discussed.

We wish to express our appreciation to Mrs. Elaine Rieders and Miss Barbara Didio for the performance of the blood counts and the icterus index determinations.

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ANGIOCARDIOGRAPHY IN CONGENITAL HEART DISEASE

ANAESTHESIA AND TECHNIQUE

BY

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Kreutzer *et al.* (1950) state that "angiocardiology is simple and harmless so far as our experience shows." The results from a series of 172 cases of angiocardiology performed for congenital heart disease at Guy's Hospital make it impossible to agree with this statement.

Literature

Forssmann (1929) was the first to introduce a catheter into the heart (his own) and also to inject a dye (iodoxyl B.P., "uroselectan" 35-50%), but it was not until 1937 that the first *clear* view of the right side of the heart and pulmonary arteries in man was shown by Castellanos *et al.* (1938a). They were unable to show the left side of the heart and aorta, because of the poor contrast medium used. In the following year Robb and Steinberg (1939), using "diodrast" 70% (diodone; the diethanolamine salt of 3,5-diiodo-4-pyridone-N-acetic acid, containing 49.8% iodine), showed the left side of the heart and aorta as well. Their technique, or some modification of it, is the one most commonly used to-day. In these investigations general anaesthesia seems to have been used very infrequently.

Kreutzer and his colleagues carried out their investigations entirely on infants and children without any form of general anaesthesia. They used diodone 75% as the contrast medium in doses of 10 ml. for the

newborn, 12 ml. up to 3 months, 15 ml. up to 1 year, and then 1.5 ml. per kg. of body weight for any child over 1 year. The injection was made intravenously through a procaine weal without exposing the vein. In performing angiocardiology in over 400 cases they had only one death—in an infant with complete transposition of the great vessels. The infant died with high temperature and convulsions 12 hours after injection of the contrast medium.

Castellanos *et al.* (1938b) also carried out their investigations on infants and children. They did not use general anaesthesia, but they realized that complete immobilization of the infant was necessary in order to obtain good angiocardigrams. At first prevention of movement was carried out by manual restraint, but it had the disadvantage that many assistants were required. In order to overcome this, they constructed a device called an "immobilizer," which was made in two sizes—for infants and older children. The contrast medium was injected through a cannula after exposing the vein under local analgesia.

Robb and Steinberg (1939) carried out 238 injections on 127 patients aged between 16 and 74 years. No general anaesthetic was administered, but in cases of "extreme nervousness" the patients were premedicated with a barbiturate. The only other pre-operative measure was to ensure that the stomach was empty. With the patient in the sitting position, the diodone (25–45 ml.) was given with the arm abducted.

Since that time Dotter and Steinberg (1949) have performed angiocardiology in over 1,000 patients without a fatality. Most of these were carried out according to the original technique described by Robb and Steinberg, except that in the last 448 injections, "neoiopax" 75% (sodium iodomethamate) was used as the contrast medium.

Under local analgesia Chavez *et al.* (1947) exposed the external jugular vein, and introduced a rubber catheter (size 12–14) into the right atrium or ventricle. They used 50–90 ml. of diodone as the contrast medium. They report only one death, which occurred after their paper was written.

Anstruther Smith (1950) seems to have been the first to report a series of cases (40) in which general anaesthesia was used. He considers that a general anaesthetic is essential for all children under 5 years and probably up to the age of 12. In his series, cardiac catheterization was performed first, and the contrast medium injected through the catheter after the latter had been withdrawn so that only a few inches remained in the vein. His patients were premedicated with pentobarbitone ("nembutal"), 0.6 gr. per stone (6 mg. per kg.) body weight, and atropine, 1/150 gr. (0.43 mg.), 45 minutes pre-operatively. Anaesthesia was induced with thiopentone and maintained with intermittent injections of the same drug. In a few of his cases angiocardiology alone was performed. These children received the same premedication as above, and anaesthesia was induced and maintained with "trilene" (trichlorethylene) and oxygen through a Boyle machine.

Lee (1950) advises the use of nitrous oxide, oxygen, and trilene for angiocardiology.

Present Investigation

In this series of 172 patients most have suffered from cyanotic congenital heart disease, though a few have been acyanotic. In 115 cases angiocardiology was

performed under general anaesthesia and in the remaining 57 under local analgesia with adequate premedication. The ages of these patients ranged from 3 to 37 years. Most children under the age of 12 received general anaesthesia, but the older patients did not require it. In this series three patients died on the table—two while under general anaesthesia and one who received local analgesia only. A fourth patient died immediately on arrival in the ward. A further patient—a child aged 3—developed signs of cerebral anoxia, but finally recovered sufficiently to return home. Angiocardiology was performed by Mr. I. M. Hill in 121 cases. In the remaining 51 cases it was carried out by Mr. Lawrence Whytehead.

Technique

The conscious patient is placed in the recumbent position on a special x-ray table designed by Hills (1948). On this table 10 exposures are taken in 10 seconds. The surface of the table is 5 ft. (152 cm.) above ground-level, and this tends to make induction of anaesthesia inconvenient; the younger patients therefore are anaesthetized on an ordinary theatre trolley and then transferred to the table.

Originally the young patients were premedicated with pentobarbitone, 0.5 gr. per stone (5 mg. per kg.) of body weight orally 1½ hours pre-operatively and atropine 1/100 gr. (0.65 mg.) 30 minutes pre-operatively. This method of sedation proved unsatisfactory, as cases occurred in which the children were awake on arrival in the x-ray department, and it was felt that the small children should not be alarmed in any way. The premedication was therefore changed to rectal thiopentone in a dosage of 1 g. per 50 lb. (22.7 kg.) body weight and atropine 1/100 gr. (0.65 mg.) half an hour pre-operatively. Rectal thiopentone in this dosage was not found to be too depressing even to the younger and more ill patients, and it was much more constant in action. The conscious patient is premedicated with pentobarbitone and atropine on the same scale of dosage as for children, with a maximum of 4.5 gr. (29 mg.) of pentobarbitone.

More recently, all patients have received a test dose of quinidine, 1½ gr. (0.1 g.), and, provided no reaction—for example, nausea, headache, or tinnitus—occurs, quinidine 3–5 gr. (0.2–0.32 g.) is given pre-operatively as a prophylactic against arrhythmias. It is administered either as a divided dose four hours and again two hours pre-operatively, or as a single dose two hours before operation. The dosage, and whether it is given once or twice pre-operatively, depend upon the age, weight, and size of the child. A test dose of diodone in the form of a tablet is given to all patients the day before operation. If no stomatitis develops the patient is considered to be not sensitive; transient urticarial rashes occur very occasionally, but, so far, sensitivity to this drug has not been observed.

In the early cases in the series anaesthesia was maintained with nitrous oxide, oxygen, and trilene through a Boyle machine. But this method was discontinued after the death of a girl aged 12 immediately on her return to the ward. It was realized that a large number of these children were extremely grave anaesthetic risks, and that the slightest degree of anoxia must not be allowed to occur. The patients therefore were induced with cyclopropane and oxygen, and also maintained with the same drug through a Coxeter-Mushin

absorber. This method gave a smooth induction with no trace of anoxia. After further experience it was observed that in a number of cases coughing or breath-holding occurred within 2-10 seconds of the introduction of the contrast medium. At times this was undoubtedly due to bronchospasm, because it was impossible to inflate the lungs, though there was no laryngeal spasm (confirmed by direct laryngoscopy). The coughing and breath-holding could not be prevented by increasing the depth of anaesthesia with cyclopropane, so ether is now added after induction with cyclopropane. Provided the level of anaesthesia was carried to that of deep second plane or early third plane with ether, these immediate respiratory complications became much less frequent.

Although cyclopropane and ether are both explosive mixtures, it was felt safe to use them in an x-ray department for the following reasons: (1) The gases are administered in a closed circuit. (2) If leakage of explosive mixtures should occur the relative absence of naked flames or sparks in a modern x-ray department is unlikely to give rise to an explosion. (3) The anaesthetic apparatus is placed next to the extraction grille of the air-conditioning plant, so that any gases that may have escaped will be removed from the room.

The patient, having been adequately anaesthetized with cyclopropane and ether, is transferred to the special x-ray table and the arm is abducted about 30 degrees from the side. A suitable vein is selected, and skin and subcutaneous tissues are infiltrated with procaine 2% in an endeavour to prevent venous spasm. The vein having been exposed, a large cannula of 0.224-mm. internal diameter is inserted. In the very young patients a smaller cannula of 0.148-mm. bore may have to be used. The cannula is connected to a 100-ml. transfusion syringe with a three-way tap. The syringe contains a "perspex" disk valve which enables normal saline to be separated from the contrast medium. The advantage of this arrangement lies in the fact that after the diodone has been given it is immediately washed through with about 20 ml. of saline. When the syringe has been connected to the cannula, having been partially filled with normal saline, 10-20 ml. of saline is injected to ensure that there is a free flow. The required quantity of diodone 70% is drawn into the syringe and, with the arm abducted to about 90-100 degrees, the injection is made as quickly as possible. The quantity of diodone used was calculated on the aggregation of several factors—for example, weight, size, age, physical development, and general condition of the child (I. M. Hill, 1950, personal communication). But more recently Whytehead has calculated the diodone requirements on a basis of 1.2 ml. per kg. of body weight. He has also introduced various modifications to the technique previously employed.

As soon as the cannula had been inserted a solution of procaine 0.2% in dextrose 5% is given by the drip method in order to reduce myocardial irritability and bronchial secretions. While the procaine is flowing at a rate of 10-20 mg. a minute (depending upon the weight of the patient) blood-pressure recordings are taken at one-minute intervals for four or five minutes. A fall of blood pressure amounting to 10-20 mm. Hg may be expected, but at the end of four or five minutes it is usually found to be steady at this lower level. It is now considered safe to inject the diodone solution provided the E.C.G. tracing is satisfactory. If, however, the blood pressure should continue to fall or a gross

drop of blood pressure should occur immediately and no improvement take place on slowing the rate of flow of procaine, then the angiogram ought to be abandoned. So far we have not had to resort to this in any of our cases.

The contrast medium having been injected, blood-pressure recordings are still taken at intervals of a minute. An immediate marked fall in blood pressure usually occurs, but within one to two minutes it starts to rise and in five to eight minutes is usually slightly above the reading taken immediately before the injection of diodone. Continuous blood-pressure records were taken by Howarth (1950), who found a similar fall in blood pressure in all her cases. If, however, the rise in blood pressure does not start within two minutes resuscitative measures should be introduced. Oxygen 100% is given and methylamphetamine hydrochloride (methedrine) 5-10 mg., intravenously. If there is no improvement preparations should be made for cardiac puncture and cardiac massage, a stop-watch being used to time events. Intracardiac injections of procaine 5% for ventricular arrhythmias and calcium chloride 1% to improve myocardial tone may have to be given. Immediately after the injection of diodone, procaine 0.2% is given in the same dosage as above until the blood-pressure recordings are satisfactory. E.C.G. tracings are taken throughout the investigation, starting immediately after induction of anaesthesia.

In only one case out of 90 in which E.C.G. tracings have been recorded has angiocardiology been abandoned, and this was due to a 2 to 1 heart-block, which persisted in spite of removal of cyclopropane from the anaesthetic mixture, the administration of intravenous procaine, and atropine. Nodal rhythm is often seen before the diodone injection, and after the injection S-T depression and abnormalities of conduction leading to incomplete heart-block are revealed. These appear to be expressions of coronary insufficiency. The patient, with oxygen through a B.L.B. mask, is then returned to the ward under the care of the anaesthetist and is placed in an oxygen tent for the next three to twelve hours.

Complications

Secretions in the tracheo-bronchial tree are not always inhibited satisfactorily by atropine. Their presence greatly enhances the danger of laryngeal spasm, which on this type of patient may produce sufficient anoxia to endanger life. Either angiocardiology must be abandoned or a further dose of atropine 1/100 gr. (0.65 mg.), must be injected intravenously by the anaesthetist before giving the anaesthetic. A sucker should always be available during angiocardiology.

Breath-holding due to bronchospasm or laryngospasm may occur when the diodone enters the pulmonary vessels; liability to this can be reduced to a marked degree by adequate depth of anaesthesia with ether, which is, of course, a bronchodilator. Intravenous procaine may also play some part in preventing bronchospasm. If the apnoea is due to bronchospasm, oxygen 100% must be administered, while the spasm itself might be relieved by an antihistamine drug, such as "benadryl" (diphenhydramine hydrochloride) or "anthisan" (mepyramine maleate), given intravenously. Up to this time we have had no experience of the use of the antihistamine drugs. If laryngeal spasm has occurred a gum-elastic catheter should be pushed gently through the vocal cords and oxygen given immediately. The delay in waiting for the laryngeal spasm to pass may

give rise to such a degree of anoxia that permanent cerebral damage occurs. Laryngeal spasm may also result from reflex vomiting during return to consciousness; the patient must therefore be kept under the observation of the anaesthetist until consciousness is regained.

Vomiting may continue for 24 hours after angiocardiology. This is probably due to the diodone, as it occurs in patients who have not been given a general anaesthetic.

Discussion

Statements have often been made which suggest that investigation by angiocardiology is without danger to the patient. There are two reasons for these statements. First, if investigations are carried out on comparatively fit patients the mortality rate is extremely low. Secondly, there is no doubt that, however well a general anaesthetic is administered, danger to the patients is greatly increased if they are "poor risk" subjects. Therefore in these extremely ill children suffering from congenital heart disease it is best to avoid a general anaesthetic if possible. This can be done in a co-operative well-premedicated child of about 9 years; but below this age the child tends to be uncooperative if it is sufficiently premedicated to remove all apprehension. Also, the sensation of heat, headache, and vomiting or nausea after injection of diodone may make the young child move while the x-ray films are being taken. Normal respiration in the anaesthetized child does not interfere with the films, but the conscious subjects are asked to hold their breath following injection.

A sign of grave prognostic significance is a history of cyanotic attacks or attacks of unconsciousness. All the four children that died had suffered from these attacks, as did the small child of 3 who suffered from cerebral anoxia. Four seconds after the injection of diodone this child developed bronchospasm, which lasted about 60 seconds. Spontaneous respirations then started, but after a few breaths apnoea occurred again. Artificial respiration with oxygen 100% was begun, and after about five minutes spontaneous respirations which were slow and shallow returned; this type of respiration continued for the next few hours while the patient was in an oxygen tent. The child remained in a semi-conscious state for 36 hours and was unable to swallow for 48 hours after angiocardiology.

All patients should be kept in the x-ray department for at least 15 minutes after the operation—as the danger period seems to be 30 seconds to 10 minutes after the injection of diodone. In the four fatal cases collapse occurred within this period. The child operated on under local analgesia vomited very shortly after the injection, became unconscious at the same time, and died within 10–15 minutes.

Of the remaining three patients two died early in the series before E.C.G. tracings were routine, but the third case was interesting in that the first sign of any upset was the presence of E.C.G. changes. Six seconds after the injection the child held its breath for about four seconds, but spontaneous respiration then started and the child's colour and pulse were good. Two minutes after the injection the child hyperventilated for 12 breaths; respirations then ceased and the pulse became impalpable. Cardiac massage was started five minutes later, but was of no avail. The E.C.G. tracings were suggestive of a posterior infarct at 30 seconds after the injection; this was followed by disorganized rhythm and finally ventricular fibrillation (G. L. L. Reynolds, 1950, personal communication). The interesting fact

about this patient was the presence of marked E.C.G. changes about one and a half minutes before any clinically detectable deterioration occurred.

Since even the slightest degrees of anoxia are probably the gravest dangers that these patients have to face, every effort should be made to prevent the occurrence of oxygen lack. This can be aided by full atropinization (1/100 gr. half an hour pre-operatively to any patient over the age of 1 year), so that secretions from the tracheo-bronchial tree are absent. Although intubation has not been done in any of these cases it seems that this ought to be carried out in order to maintain a perfect airway throughout.

Cardiac catheterization is usually performed some days or weeks before angiocardiology. The complete injection of diodone through our catheters cannot be carried out in 1.5–2 seconds, and therefore it is preferred to inject through a larger cannula. If, however, a particular heart defect or chamber is to be shown the catheter can be placed in that chamber and a small quantity of contrast medium injected satisfactorily.

Conclusions

A large number of these cases of congenital heart disease are serious anaesthetic risks. Angiocardiology should therefore be carried out in an x-ray theatre with full surgical and anaesthetic equipment to deal with any emergency. Pre-operative cyanotic attacks are of bad prognostic significance. The older patients should be premedicated with pentobarbitone and atropine, the younger with rectal thiopentone and atropine. Quinidine and a test dose of diodone should also be given pre-operatively. Cyclopropane, ether, and oxygen, through a cuffed endotracheal tube, form the anaesthetic of choice. Intravenous procaine, both before and after the injection of diodone, should be given through a large cannula inserted into the vein under direct vision. Serial blood pressures and E.C.G. tracings ought to be recorded. The patient must be carefully watched for 15 minutes after the injection; must be under the care of the anaesthetist until consciousness is regained; and must spend the first three to twelve hours post-operatively in an oxygen tent.

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Hampstead Health Institute (see *British Medical Journal*, January 20, p. 111; and May 5, p. 1024) is probably being bought by the London County Council for £10,000 and will be used when the clinic services in the area are increased.