obvious relationship between the severity of the illness and the causal organism, a fact also noted by Trimble (1957).

Of Gsell's (1953) three criteria for judging the therapeutic efficacy of antibiotics in the treatment of leptospirosis, one—the defervescence of fever before the seventh day of illness if treatment was started before the fourth day—appeared to have been achieved in the present series. While no claim could be made that this was of particular benefit to the individual patients it remains a simple objective sign used in assessing the severity of an infectious illness. The second—the presence of a normal cerebrospinal fluid on or after the seventh day of illness—was not sought, as routine lumbar punctures on patients not warranting them clinically were not performed. Although the number of patients developing a stiff neck was much smaller among those treated with penicillin—and then it developed on or before the sixth day of their illness—no claim could be made that abnormal cerebrospinal fluid was not present in the others, nor that it was necessarily abnormal in those with neck stiffness. The third criterion—the absence of a secondary rise of temperature on or after the seventh day of illness, if, as is thought (Edwards and Domm, 1960), due to an allergic reaction between the developing antibodies and the organisms or their products—may not have been affected by the administration of antibiotics once the disease became manifest.

It was thought that in the present series the renal involvement was better manifested by microscopy of the urine than by determinations of blood urea, which is a function as much of urine formation as of fluid intake and non-renal loss—factors very much in evidence in nauseated pyrexial patients under jungle-warfare conditions. As shown in Tables II and III, both renal and hepatic complications developed less commonly, and when they did develop they occurred within 48 hours of the starting of therapy in the penicillin-treated group. However, the final incidence of cases complicated by at least one of the four manifestations considered was of the order of 80% in both groups, and the difference, if any, in the final number of these complications per patient was marginal.

Summary

The course of leptospirosis in 28 cases treated with penicillin has been compared with that in 33 cases treated symptomatically. Penicillin significantly reduced the duration of pyrexia both in cases treated within four days of onset of illness and in those treated later. Penicillin possibly reduced the incidence of jaundice, renal involvement, and neck stiffness, apparently by preventing these from developing after more than 48 hours from the onset of treatment. The difficulties of clinical trials in leptospirosis are stressed. It is concluded that, while sufficient evidence exists at present for penicillin to be used in the treatment of the condition, further investigations are still warranted, but these should be most rigorously planned and conducted by physicians alert to the possibility of leptospirosis being a cause of pyrexia in cases that do not conform to the classical description of Weil's disease.

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REFERENCES

- Clein, L. (1956). *Lancet*, **1**, 289.
 Cook, A. T. (1959). *Ibid.*, **2**, 81.
 Doherty, R. L. (1960). *Ibid.*, **1**, 58.
 Edwards, G. A., and Domm, B. M. (1960). *Medicine (Baltimore)*, **39**, 117.
 Fairburn, A. C., and Semple, S. J. G. (1956). *Lancet*, **1**, 13.
 — (1960). *Ibid.*, **1**, 58.
 Gsell, O. (1953). In *Symposium on the Leptospiroses*, Medical Science Publication, No. 1. U.S. Government Printing Office, Washington, D.C.
 Mackay-Dick, J., and Robinson, J. F. (1957). *J. roy. Army Med. Cps*, **103**, 186.
 — (1959). *Lancet*, **1**, 100.
 Russell, R. W. R. (1958). *Ibid.*, **2**, 1143.
 Semple, S. J. G. (1959). *Ibid.*, **2**, 289.
 Trimble, A. P. (1957). *Proc. roy. Soc. Med.*, **50**, 125.
 Turner, L. H., Elisberg, B. L., Gordon Smith, C. E., and Broom, J. C. (1959). *Med. J. Malaya*, **2**, 83.

Preliminary Communications

Cardiopulmonary Bypass in Neonates

Severe congenital cyanotic heart disease has a high mortality within the first few weeks of life. Conditions producing right-to-left shunts and associated with obstruction of the right ventricle (due to infundibular stenosis) have until recently been treated by me with varieties of shunt procedure (classical Blalock's operation, Potts-Smith operation, or a shunt operation in which a synthetic graft or homograft is sutured between the pulmonary artery and aorta). However, such operations are not always successful, although the operative mortality is low. A direct attack on the obstruction, if technically possible, is obviously to be preferred. Operations attempted with conventional hypothermia have carried a high mortality, and the alternative possibility of obtaining partial correction of such conditions as the tetralogy of Fallot with the aid of cardiopulmonary bypass has always been kept in mind. The purpose of the present communication is to show what was attempted in two babies and to indicate the technical problems involved and possible methods of overcoming them.

CASE 1

A boy aged 2 days, birth weight 6 lb. 14 oz. (3,120 g.), was admitted to hospital because of cyanosis since birth. He was dyspnoeic, but apart from scattered moist sounds in the lungs, together with slight hepatomegaly, nothing abnormal was found on clinical examination. Chest radiography showed scattered opacities in both lung fields, possibly due to patchy atelectasis or total anomalous pulmonary venous drainage. He was nursed in an oxygen tent and given broad-spectrum antibiotic therapy, but in spite of medical treatment his heart failure grew progressively worse and on the tenth day of life operative correction of the anomaly was attempted.

In view of the baby's poor condition it was decided to support the circulation by instituting partial cardiopulmonary bypass without first opening the chest, and the left external iliac vein and the left common femoral artery were cannulated for this purpose. Partial bypass was begun, using a flow of 125 ml./min. The chest was then opened through a bilateral trans-sternal anterior thoracotomy and the heart was inspected. The right atrium

and ventricle were large and the pulmonary artery was twice the size of the aorta. The pulmonary veins joined behind the heart to form a common venous trunk which passed upwards to the left innominate vein. The left atrium and ventricle were small and the aorta was of normal size with normal coronary arteries. A 5/32-in. (4-mm.)-bore right atrial polyvinyl chloride (P.V.C.) catheter was inserted through the auricle and the venous drainage was switched to this from the external iliac catheter to obtain a bigger venous return to the oxygenator. The perfusion was then increased to 320 ml./min., and by use of a heat exchanger inserted in the arterial line cooling was begun. At a temperature of 29° C. cardiac arrest occurred and at 22° C. oesophageal temperature the pump was stopped. The venae cavae were clamped. The heart was rotated upwards and an anastomosis made between the common pulmonary venous trunk and the left atrium. The connexion to the left innominate vein was not divided and the atrial septal defect was not closed. The caval clamps were removed, partial bypass was restarted, and the patient was rewarmed. At a temperature of 36° C. the right atrial catheter was removed. The heart began to beat quite well at a temperature of 30° C.

Repeated small transfusions were given via the arterial cannula until the mean venous pressure had been raised to 10 mm. Hg; the chest was then closed, with drainage.

On the first post-operative day the baby's condition was encouraging, but on the second day laryngeal obstruction due to oedema necessitated tracheostomy. A descending infection of the respiratory tract proved impossible to control and the baby died after an apnoeic attack on the fifth post-operative day. Post-mortem examination showed that the surgical repair was satisfactory and that death had resulted from an acute infective tracheobronchitis causing areas of collapse with consolidation and obstructive emphysema in both lungs.

CASE 2

A girl aged 6 weeks, weighing 8 lb. 3 oz. (3,715 g.), was admitted to hospital in cardiac failure, with severe cyanosis and dyspnoea. She had been blue since birth, and on admission showed marked central cyanosis and hepatomegaly but no oedema. On auscultation there was a single second sound at the base, with a grade 2-3 systolic murmur at the left sternal edge. An electrocardiogram showed a mean manifest QRS axis of +130°, with right atrial and right ventricular hypertrophy. Chest radiography revealed that the heart was not enlarged but the apex was raised. The pulmonary segment was concave and the aorta right arching. Poor pulmonary vascularity was present and the diagnosis of tetralogy of Fallot was made. The baby was digitalized and given chlorothiazide, but by the second day after admission her condition had greatly deteriorated; her colour was a greyish blue and the respirations were Cheyne-Stokes in type. It was decided to attempt an emergency infundibular resection.

Under nitrous oxide and oxygen endotracheal anaesthesia, with a relaxant, both groins were incised. The right external iliac artery was prepared for perfusion cannulation and the left superficial femoral artery was cannulated for monitoring arterial pressure. The heart was exposed through a median sternotomy. Meantime a disposable, sterile regional perfusion oxygenator had been primed with A.C.D. blood to which heparin and calcium chloride had been added and a heat exchanger was incorporated in the circuit.

On inspection the venae cavae were normal, the right atrium was moderately hypertrophied and the right ventricle grossly so. The pulmonary artery was 3 mm. in diameter and showed no post-stenotic dilatation. The pulmonary venous drainage was normal and the left atrium and left ventricle were also normal. The aorta was one and a half times the normal diameter, apparently dextroposed, and gave origin to normal coursing through large coronary arteries.

The baby was given heparin and the external iliac artery was cannulated with a 1.5-mm. Bentall cannula. The right atrium was cannulated through the auricle with one 5/32-in. (4-mm.)-bore P.V.C. catheter and partial bypass was instituted with a flow of 60 ml./min. Cooling was begun and the flow increased to 360 ml./min. At an oesophageal temperature of 30° C. the heart became arrested and the right ventricle was decompressed through an intracardiac sucker. Cooling was maintained until a temperature of 18.6° C. was reached, when the venae cavae were clamped, the aorta was cross-clamped, and the pump was stopped. The right ventriculotomy was extended up to but not across the pulmonary valve ring. There was gross hypertrophy of the infundibular muscle, which crossed the outflow tract as numerous coarse trabeculae. There was no pulmonary valve stenosis, though the valve ring was somewhat narrowed. To avoid unnecessary trauma the ventricular septal defect was deliberately not visualized. The hypertrophied muscle was resected and the ventriculotomy sutured in its upper half. The intracardiac sucker was introduced through the lower half of the ventriculotomy and partial bypass recommenced with rewarming, the flow gradually being increased to 500 ml./min. As rewarming proceeded the right atrial catheter was manipulated through the tricuspid valve so as to decompress the ventricles, and the right ventriculotomy closure was completed, the intracardiac sucker being removed. The heart was reluctant to beat but responded to repeated small injections of 10% calcium chloride solution and two 0.25-mg. injections of adrenaline together with gentle massage. At a temperature of 37° C. the bypass was discontinued and the atrial catheter was removed. Hexadimethrine bromide ("polybrene") was given and repeated small arterial transfusions from the pump were required to restore the central arterial pressure to 135/75 mm. Hg. The arterial cannulae were then removed. The pericardium was left wide open and a window made between the anterior mediastinum and the right pleural cavity. The right pleural cavity and the anterior mediastinum were drained by separate tubes and the chest was closed.

Post-operatively the baby's colour had improved dramatically and she was quite pink. Her respirations were quiet and not laboured. Convalescence was uneventful.

DISCUSSION

It is an accepted principle that correction of a congenital defect and restoration of function to normal should be achieved at the earliest possible opportunity. Hitherto, for two main reasons open heart operations on the neonate have not been performed. Firstly, there is the technical difficulty of cannulating the small vessels at this age. Secondly, the size of the heart has discouraged attempts to correct intracardiac defects, again because of the difficulty of manipulating the sutures, etc., within the small cavities involved. However, it must be accepted that some patients will not survive the first few weeks of life unless at least partial relief of the disability is obtained.

In order to cope with the first problem it is evident that cannulations must be reduced to a minimum. The Drew technique (Drew and Anderson, 1959) of inducing profound hypothermia would therefore seem too complicated and the left atrial cannulation particularly difficult. Moreover, as in Case 1, it may be thought desirable in a bad-risk patient to establish partial bypass before opening the chest, and this inevitably entails the use of an oxygenator. However, by using a pump oxygenator with a heat exchanger, partial bypass and cooling can be achieved with one right atrial venous catheter and one perfusion arterial cannula. As the heart fails, the result of hypothermia, the lungs must be

protected by appropriate decompression, using intra-cardiac suction.

Certain criteria must be laid down with regard to the extracorporeal circuit. The pump should be capable of fine variation in flow from zero to 1 litre/minute and is preferably of the DeBakey type. That used at the Children's Hospital, Birmingham, has been constructed in the workshop of the Surgical Research Unit at the Queen Elizabeth Hospital.

Whatever oxygenator is used it should preferably have a low priming volume, and close estimation of variations of the volume of blood within the extracorporeal system should be possible, so that the baby is not bled into the pump circuit or, alternatively, over-transfused. As no suitable screen or disk oxygenator is commercially available in this country for such small infants, a bubble oxygenator was used in the two cases recorded. In the first this was a modified small Lillehei-De Wall oxygenator. For the second baby a regional perfusion oxygenator was used; such an oxygenator is convenient, is disposable, and is supplied sterilized.

In Case 1 the heat exchanger was a simple helix of P.V.C. tubing immersed in a water-tank the temperature of which was varied by adding ice or warm water as required. Better control of cooling and rewarming was obtained in Case 2 by using the small N.E.P. heat exchanger; the water-jacket was surrounded by water pumped from a reservoir through a Leonard mixing-valve. This latter arrangement gives a much finer control of the perfusion temperature.

A high-flow perfusion is used, the volume depending on the adequacy of venous return to the oxygenator. Thus, if partial bypass is established prior to opening the chest as in Case 1 a lower flow must be used owing to the smallness of the venous catheter inserted via an iliac vein. The right atrial catheter should be the largest that can be introduced through the right auricle, and a perfusion of 100-120 ml./kg./min. should be possible.

In an attempt to avoid loss of platelets and fibrinogen during perfusion, heparin is used in a dose of 5 mg./kg. body weight. Neutralization of the heparin is obtained by using hexadimethrine in a dose of 1½:1 of heparin. The hexadimethrine is not given until rewarming has raised the oesophageal temperature to 37° C. By this means the clotting mechanism is restored quickly to normal and troublesome post-operative bleeding is avoided.

It is important to rewarm the infant to 37° C. oesophageal temperature by means of the extracorporeal circulation and to prevent heat-loss thereafter by placing the infant on a water-heated rewarming blanket. If this is not done disastrous falls of temperature can occur during the period of decannulation and chest closure.

The second problem of open heart procedures in infancy is one of size of the heart. The difficulties can easily be met by the use of small retractors and fine needleholders with atraumatic sutures mounted on small needles.

If certain heart conditions in the neonatal period are regarded as constituting surgical emergencies it is a prerequisite that the extracorporeal circulation should be assembled without undue delay. It is usually not possible to call up blood donors at very short notice so that fresh heparinized or ethylenediaminetetra-acetic

acid (E.D.T.A.) blood can be obtained. Acid-citrate-dextrose (A.C.D.) blood taken within five days of operation is usually available at regional blood-transfusion centres. The quantity required is not large, and the use of fresh blood (with added heparin and calcium chloride) is perfectly satisfactory with the technique described (Foote *et al.*, 1961).

It may not always be possible to obtain a complete correction of the cardiac abnormality within the first few weeks of life. It is important to keep operation time and surgical trauma to the minimum necessary. Thus total correction of the tetralogy of Fallot should probably not be attempted as the heart is small, but surgical treatment must be directed to relief of the mechanical obstruction. However, in conditions such as ventricular septal defects, where the heart is large, it should be possible to obtain adequate visualization for a repair.

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REFERENCES

- Drew, C. E., and Anderson, I. M. (1959). *Lancet*, 1, 748.
Foote, A. V., Trede, M., and Maloney, J. V. (1961). *J. thorac. Surg.*, 42, 93.

Medical Memoranda

Acute Epididymo-orchitis and Teratoma of Testis

Acute non-specific epididymo-orchitis has a varied aetiology, the commonest predisposing factors being urinary infection, virus diseases, and trauma. The response to antibiotics is often indifferent and the swelling slow to subside. It is the absence of any obvious aetiological factor and the persistent enlargement that gives rise to the suspicion of underlying neoplasm.

Several writers have drawn attention to the masquerading of testicular neoplasm as epididymo-orchitis. Rose (1960) describes a case presenting with symptoms and signs indistinguishable from acute viral epididymo-orchitis. Patton *et al.* (1959), in a review of 510 cases of testicular neoplasm, state that epididymitis was the initial diagnosis in 16.3% of cases. Parker and Holyoke (1960) found that non-specific inflammation of the testis and epididymis was the most frequent diagnostic error in cases subsequently proved to be neoplastic. In a survey of 178 cases by Thompson *et al.* (1961) 19 patients were initially thought to have epididymo-orchitis. Cohen and Tomskey (1961) noted that the most frequent finding in teratocarcinoma and embryonal carcinoma was a history of treatment for epididymitis which did not resolve.

Two cases of teratocarcinoma of the testis have been seen at this hospital over the past six years. They illustrate the above presentation and the clinical difficulty of the inflammatory swelling that is slow to subside.