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ASPHYXIA NEONATORUM TREATED BY ELECTRICAL STIMULATION OF THE PHRENIC NERVE

BY

K. W. CROSS, M.B., B.S., M.R.C.P.

AND

P. W. ROBERTS, B.Sc.

(From the Physiology Department and Physics Department,
St. Mary's Hospital Medical School, London)

Sarnoff and his colleagues (1948, 1950) have recently reintroduced an old method of artificial respiration by the electrical stimulation of the phrenic nerve in the neck through the intact skin. This method was first used as far back as 1783 by Hufeland, who discharged a series of condensers through the patient. The method was again tried after the discovery of electromagnetic induction, when the shocking coil was used. Israel (1927, 1928) reported the use of the shocking coil for the resuscitation of newborn infants, and was most impressed with the results obtained. With modern equipment it is possible to obtain a controlled and smoother contraction of the diaphragm than was previously possible.

Description of Apparatus

The electrical wave-form used to stimulate respiratory movements when applied to the phrenic nerve consists of negative-going rectangular pulses of $\frac{1}{4}$ millisecond

duration repeated at intervals of approximately 10 milliseconds. The pulses increase linearly in amplitude until they reach a maximum, when, after a further short period of stimulation, they cease. This complete cycle is repeated at a rate of 18 times a minute, the period of stimulation occupying two-thirds of the cycle and a rest period occupying the other one-third.

In our instrument all these qualities were made variable, but the values given here are those we have found most suitable in practice, and in any commercial instruments these could be pre-set. The output intensity can be controlled and, as can be seen from the diagram, currents as large as 110 mA peak were found necessary.

The apparatus is similar to that used in electrotherapy. It consists of a double triode valve connected as a multivibrator feeding the screen grid of a pentode output valve via a cathode follower. The control grid is fed with negative-going saw-tooth waves from a squegging oscillator. The output is obtained from the anode of the pentode via a large condenser, thus making the mean current zero and avoiding polarization within the tissues. The power for the apparatus is supplied from the 230 v. A.C. supply.

Technique of Treatment

The active electrode is a silver-plated probe, the end of which is covered with a single layer of lint soaked in saturated saline immediately before use. This electrode makes contact with an oval area of about 8 by 6 mm. on the baby's neck. The infant is placed supine, lying on the rectangular indifferent electrode (made of electrode metal), 14 by 5 cm. in area. This electrode is also covered by lint soaked in saline.

The position of the most readily accessible part of the phrenic nerve was carefully described by Duchenne de Boulogne in 1851, and is above Erb's point. With the head turned to the opposite side the phrenic nerve is found just behind the sternomastoid muscle at the junction of the middle and lower thirds of that muscle. With use of the electrodes described, muscles other than the ipsilateral diaphragm are often stimulated, and most commonly the arm was abducted from the side with each stimulation. We have not sought to confine stimulation to the phrenic nerve alone by using a smaller electrode, because this arm movement will assist expansion of the lungs. When the phrenic nerve is being stimulated the epigastrium is seen to protrude chiefly on the side being treated.

Additional evidence of diaphragmatic movement is obtained by hearing the inspiration, with or without the stethoscope, and when the Rotunda oxygen mask (referred to below) was being used one could on occasion see the rubber reservoir diminish in size. More effective inspirations can be caused by the bilateral stimulation of both phrenic nerves; this was attempted in a few cases, but it is more difficult for a single operator to apply and to maintain the electrodes in the correct position. When only one active electrode was being used it was our practice, in cases which required prolonged treatment, to change from time to time the side of stimulation.

A peak current of 3–5 mA through the electrodes described is sufficient to provide adequate ventilation in the adult. When we tried to resuscitate babies we soon realized that larger currents were necessary. For this reason, and in order to obtain quantitative data, a second stimulator was constructed which contained a peak-reading voltmeter consisting of a calibrated

cathode-ray tube and an ohmmeter. When the right instrument was available—for both were in use—and there was time to make observations, readings of potential difference and resistance were noted when "adequate movement of the diaphragm" occurred. From these two readings the peak current was calculated, but this figure can be regarded only as an approximation, as the current wave-form will not be identical with the voltage wave-form; also the resistance between the electrodes may not be the same when pulses are applied as when a direct current meter reading is taken.

Experimental Investigation

The present investigation was undertaken in two parts. From May, 1949, until July, 1950, we had the instrument available in the home of one of us and made arrangements to be called to St. Mary's Hospital, the Postgraduate Medical School, and Queen Charlotte's Hospital when cases of foetal distress or neonatal asphyxia arose. In this phase of the investigation we had only two successful cases; in the 30 other calls we received the baby had either recovered or died by the time we arrived. The useful control period caused by the delay in arriving at the hospital was clearly too long for all but the exceptional cases. For a period of nine weeks, from July to September, 1950, one of us (K.W.C.), financed by a grant from the Medical Research Council, was enabled to work in the Rotunda and the Coombe Hospitals in Dublin. During this period there were 1,083 deliveries of viable foetuses in the labour wards of the two hospitals, and on most occasions it was possible to be present within 10 minutes of a call.

As the cases reported here have been delivered at five different hospitals, and this treatment was applied only at the invitation of the responsible clinicians, there was a widely varying background of other methods of resuscitation which was not under our control. Before attempting to stimulate the phrenic nerve we insisted only that the air passages of the baby should be emptied as thoroughly as possible, by mucus catheter or by direct intubation, depending on the practice of the hospital. While stimulation was proceeding oxygen was applied, again by one of several methods, but the best and simplest seemed to be a baby-sized anaesthetic mask and balloon reservoir which was in use at the Rotunda Hospital. Even with the excellent co-operation which we received in Dublin it was neither possible to be present with the stimulator at every delivery nor possible to be called to every second asphyxiated case. We can report, therefore, only the results we obtained, and it will not be possible to deduce from this investigation whether neonatal morbidity or mortality would be affected in a statistically significant fashion by this method of treatment.

Before a baby was treated an assessment was made of its clinical condition. We have used the simple classification of "slightly," "moderately," and "severely" ill infants, but we would stress that this diagnosis had to be made rapidly and the gradations are not clearly defined. "Slightly ill" babies were those who at birth had moderate but diminished muscular tone and were somewhat cyanosed. They would generally have taken some spontaneous respirations but had not established adequate oxygenation as judged by the colour of the mucous membranes. "Moderately ill" babies were those who appeared to have no muscular tone and were very deeply cyanosed.

"Severely ill" babies had no muscular tone, generally had taken no respirations at all, had relaxation of the anal sphincter, and included those who had white asphyxia. All babies treated in Dublin were followed to their own homes after discharge, and an attempt was made to get the mothers to bring them back to their hospitals. Dr. W. D. Brophy has kindly seen those at the Rotunda.

The results of our investigation are divided into four sections. Each section is completed by the inclusion of the appropriate case histories. The total number of cases treated was 29, of which 25 recovered. Measurements were made on 19 of the cases.

(a) Relation between Current and Degree of Illness

The diagram shows the current required, as defined above, in those babies in whom measurements were made. In some cases it was possible to make more

Diagram showing currents required for those babies in whom measurements were made.

than one measurement, and the clinical conditions of the infant might have altered in the interval. The points joined by a line indicate repeated observations on one infant and the arrow indicates the passage of time.

It will be observed that there seems to be some relationship between the current required and the sickness of the baby, as defined above. We feel that this relationship is a function of the neuromuscular system under consideration and not other factors, for the following reasons: (1) When, after a period of stimulation, the neck at the site of the electrode and the skin of the back underlying the indifferent electrode were thoroughly cleaned with ether the resistance diminished slightly but the current required was not lowered. (2) If more than one reading was possible on a baby the current required diminished (in all but one case) if the baby was improving and increased the longer the baby

was dead, and there were not necessarily parallel skin-resistance changes.

If it is correct to say that the current required for stimulation is a function of the sickness of the baby, this is most probably related to the degree of oxygenation of the tissues, which can be correlated with *in vitro* observations on muscle-nerve preparations. These show that in anoxia a stronger stimulus is required to evoke a maximal response of nerve (Lorente de N6, 1947).

(b) Expansion of the Lungs by Phrenic-nerve Stimulation Alone

In most of the cases in which death subsequently occurred the baby had taken some spontaneous respirations before death, but we have pathological material from three cases in which the time of death was accurately known and the baby had taken no respirations and no other method of artificial respiration had been used. This material gives us information whether stimulation of the phrenic nerve alone, with adequate movement of the diaphragm, is capable of expanding the lungs. This is important, for more effort is necessary to separate the adherent alveolar surfaces than to take subsequent breaths (Wilson and Farber, 1933).

Case Histories

Case 1. St. Mary's Hospital.—The patient was born on April 5, 1950, and was a second female twin born 75 minutes after the first. At delivery the child was blue and flaccid and made no attempt to breathe. The heart was slow and stopped 13 minutes later. Stimulation was started on the right phrenic nerve two minutes after the heart had stopped. Dr. J. P. M. Tizard auscultated the chest while this proceeded; he heard an air-entry over the right lower chest anteriorly and noted that the heart restarted at 16 beats a minute. Stimulation rapidly became less effective and the heart stopped. After five minutes the stimulation was quite ineffective and was not continued. Post-mortem examination showed that there was almost complete aeration of the right middle lobe and some aeration of the right lower lobe. The heart showed a bicuspid aortic valve and the brain bilateral superficial tentorial tears.

Case 2. Coombe Hospital.—This patient was born on July 30, 1950, by breech delivery. The foetal heart was irregular and rapid. The after-coming head very suddenly passed through the pelvis and delivery occurred five minutes later. The heart beat could not be heard or felt and there were no signs of life. Phrenic-nerve stimulation was applied first on the right side and then on the left, with more effect on the right. Post-mortem examination 24 hours later showed that the whole thoracic pluck sank in water, but the right lung by itself floated, while the left sank. There were bilateral tentorial tears. Section showed moderate aeration of the right lung.

Case 3. Rotunda Hospital.—This was a case of difficult forceps delivery on August 8, 1950. The heart rate at delivery was 60 a minute, but this stopped in five minutes. There were no respiratory movements. Stimulation started directly after the heart had stopped, with reasonably effective movement of the diaphragm; the left side was stimulated more than the right. Post-mortem examination 12 hours later showed bilateral tentorial tears, right greater than left.

The entire thoracic pluck floated. Sections showed moderate aeration but many intra-alveolar squaïtes.

From these cases we conclude that this method of artificial respiration is capable of expanding the lungs, in which respect it does not differ from other techniques, but here the normal muscles are being called into play and there cannot be the danger of pulmonary emphysema or distension of the stomach, which are present with the positive-pressure methods.

(c) Evidence for the Efficacy of the Method in Saving Life

From the Table it is seen that four babies died out of the 29 treated. Of the 25 who lived all of those slightly ill and moderately ill survived (except the one

Results of Cases Treated

Condition	No.	Recovered	Died	Average Current (Initial Reading) (mA)	No. of Observations of Initial Reading
Slightly ill ..	14	14*	0*	20	9
Moderately ill	6	6	0	36	3
Severely ill ..	9	5	4	61	7

* One died at 13 weeks and 1 day (see text).

case discussed below). As the chance of survival without aid is greatest for those least ill it is obvious that the efficacy of the method would be best illustrated by those cases which were severely ill. However, bearing in mind our definition of degrees of illness, we believe that the figures for those less than severely ill show promise for the method. The four cases in which the patients were thought to be severely ill and subsequently died are here described.

Four Fatal Cases

Case 4. Rotunda Hospital.—The mother was a primipara and was admitted, one week post-mature with a floating head, for induction of labour. Castor oil, a hot bath, and an enema were given, and also quinine and "pitocin." The membranes ruptured spontaneously on July 13, 1950, labour began on the 15th, and meconium was noticed in the early hours of the 16th. At midday a vaginal examination revealed that the os was still only three-quarters dilated and the occiput was posterior in the high mid-strait. There was a large caput and the head appeared to be jammed in the pelvis. The anaesthetic was continued and the patient taken to the theatre for caesarean section. The head was difficult to disengage from the pelvis, and there was a great deal of meconium in the amniotic fluid.

A male infant of 8 lb. (3.6 kg.) was delivered at 12.35 p.m. He was completely flaccid and the heart was beating slowly. Phrenic-nerve stimulation was attempted after pharyngeal aspiration, but, although the abdomen moved, the effect was poor and an air entry could not be heard. Oxygen was given by mask. The baby gradually became pink and cried a little. He was put in an oxygen tent and large quantities of fluid and meconium continued to come from the mouth and nose. When he became more blue direct intubation was attempted and oxygen was run in by catheter. He died at 4.30 p.m.

Post-mortem examination showed that there was a large left-sided pneumothorax, with a collapsed left lung and one emphysematous bulla on the lingula. The right lung was also collapsed. There were some clots over the posterior hemispheres of the brain. It seems almost certain that the pneumothorax was the result of the positive-pressure oxygen therapy which was given without an adequate safety valve.

Case 5. Coombe Hospital.—This baby was the second of twins and was born on August 18, 1950, with the cord round the neck; delivery was by breech extraction after some placental separation. The heart had been slow before

delivery and stopped after delivery. It had started again with an intracardiac injection of nikethamide, and mouth-to-mouth respiration was used. Phrenic-nerve stimulation was started 25 minutes after delivery and good breath sounds were heard with each stimulation. Treatment was stopped after 20 minutes, and the baby remained pink in an oxygen tent. The infant died 24 hours after birth, shortly after being given a feed from a teaspoon while lying in the tent. Post-mortem examination showed that the lungs were moderately well aerated. There was evidence of inhalation of amniotic debris and signs of early bronchopneumonia. Small bilateral tentorial tears were present, with very little haemorrhage.

Case 6. Rotunda Hospital.—The baby was born on August 21, 1950, and weighed 5 lb. 10 oz. (2.6 kg.). It was delivered by an emergency lower-segment caesarean section for severe ante-partum haemorrhage with air hunger. At birth the baby had white asphyxia without response to skin stimulation. A good colour was rapidly obtained with phrenic-nerve stimulation. Two days after birth the baby's condition was not satisfactory. X-ray examination did not reveal any massive collapse of the lungs. Death occurred three days after birth. At post-mortem examination there were some subarachnoid haemorrhages over the posterior part of the frontal lobes and some extravasation of blood in the right tentorium. The right lung floated in water, but the left sank.

Case 7.—Rotunda Hospital.—This was a case of difficult forceps delivery on August 3, 1950; the baby was blue and flaccid. It was treated with moderate success 20 minutes after delivery, and breathed spontaneously and irregularly after half an hour's treatment. It was kept in an oxygen tent, but respiration improved only slightly, and it brought up large quantities of blood-stained mucus. Death occurred 12 hours after delivery. Post-mortem examination showed bilateral blood-stained pleural effusions and apparent haemorrhages in the lungs. The upper lobes floated in water, the lower lobes sank. There was some extravasation of blood around the right suprarenal gland. The brain was normal. Sections showed emboli in the pulmonary arteries, a finding with which we were previously unfamiliar.

Severely Ill Patients Who Survived

The following five reports are of patients who were thought to be severely ill and who have lived.

Case 8. St. Mary's Hospital.—This case has been previously described (Cross, 1950). The patient was under Dr. Reginald Lightwood and Mr. Leslie Williams. Briefly, after a difficult instrumental delivery per vaginam, there was a period of three and a quarter hours' severe cyanosis with irregular gasping respiration. The baby was twice thought to be dead by the resident obstetric officer, and immediately before treatment was started single gasps were being made at less than one a minute. Three-quarters of an hour's treatment with the stimulator rendered the baby pink and capable of adequate spontaneous respiration. This baby has been followed up by Dr. Lightwood for 20 months; he reports that the baby milestones have been passed at normal times and that this infant appears to be in all respects normal.

Case 9. Rotunda Hospital.—Lower-segment caesarean section was performed on August 5, 1950, for prolapse of the arm and cord of 1 hour and 40 minutes' duration with marginal placenta praevia. An 8-lb. (3.6-kg.) baby was delivered with marked asphyxia pallida; it made no attempt at spontaneous respiration. There was an immediate and excellent response to phrenic-nerve stimulation, which was discontinued within three minutes, as the baby was then pink and breathing satisfactorily. It has made excellent progress, weighing 13 lb. 12 oz. (6.2 kg.) at 12 weeks.

Case 10. Rotunda Hospital.—This baby—6 lb. 11 oz. (3 kg.)—was born on August 16, 1950, after a very difficult forceps delivery, when the mother had been 64 hours in labour. After bathing in hot and cold water and being given oxygen for 10 minutes from the Rotunda mask,

phrenic-nerve stimulation was continued for 15 minutes with only moderately good air entry, and the baby was then left in an oxygen tent breathing spontaneously. Since discharge the baby has made very good progress and is developing normally. Weight 12 lb. 2 oz. (5.5 kg.) at 12 weeks.

Case 11. Rotunda Hospital.—The mother suffered from toxæmia of pregnancy, and forceps delivery was undertaken for transverse arrest of the head. At birth—weight 8 lb. 2 oz. (3.7 kg.)—the face of the baby was blue, but the body was strikingly white and flaccid. After bathing in hot water and skin stimulation had failed, satisfactory stimulation of the phrenic nerve was carried out for 10 minutes, at the end of which time spontaneous respirations were occurring often enough to keep the baby pink in an oxygen tent. Progress since discharge has been good, the weight at 12 weeks being 13 lb. 12 oz. (6.2 kg.).

Case 12. Rotunda Hospital.—A multipara was delivered on July 24, 1950, of an 8-lb. (3.6-kg.) female child by breech extraction. The right arm had been extended and the left was in the nuchal position. Twenty minutes after delivery the baby was flaccid and blue, and had taken no spontaneous respiration. Positive-pressure artificial respiration had been given from the Rotunda oxygen mask with little or no improvement. Good response to phrenic-nerve stimulation was obtained, and after 10 minutes' treatment the baby was breathing spontaneously. She had gained 8 oz. (227 g.) by the seventh day, when mother and child were discharged from the hospital. The home is rather poor, but the baby was progressing satisfactorily at 8 weeks, when she weighed 10 lb. 11 oz. (4.8 kg.). The mother has not responded to repeated appeals to bring the baby for examination.

An examination of these results cannot give certain evidence of the efficacy of the method, but in the opinion of the clinicians responsible and the labour ward sisters all those labelled severely ill were thought to be dying, yet five of the nine have lived. In the four cases in which death occurred it appears that causes other than neonatal asphyxia could be put forward.

(d) After-effects of Electrical Stimulation

As the current we were using was considerably larger than that required for the adult, we thought it was necessary to examine those babies who recovered to see if there was any sign of permanent injury from the high dosage which had been employed. All but two of the babies who have survived the neonatal period have been followed up for three months and no damage has been noted, although we must confess that the examination was a rather general one, for there was no specific type of injury which we could visualize as being likely to arise.

One patient, the first of twins, who had been regarded as slightly ill at birth, died at the age of 13 weeks. Forceps were applied for persistent occipito-posterior position, and on delivery the baby was breathing poorly and was somewhat cyanosed. Good respiratory movements were obtained with a peak current of only 11 mA. After discharge both twins had made slow progress, which was not surprising, as it was with some difficulty that the mother was persuaded to increase the diet above 3 oz. (85 ml.) of half milk and water with four teaspoonfuls of sugar only three times a day. At 12 weeks of age the baby weighed 8 lb. 11 oz. (3.9 kg.), which represented a gain of 9 oz. (255 g.) less than her sister in the same period, and was well below the average rate of gain for the group. The child was unexpectedly found dead, and post-mortem examination showed severe congestion of both lungs, with many alveoli filled with exudate; these changes were consistent with pneumonia.

It is still too early to say whether the resuscitation of babies who had suffered from severe cyanosis has

resulted in children with any mental derangement. Case 8, however, has so far showed no signs of abnormality.

We have failed to find any ill effects attributable to phrenic-nerve stimulation or any other abnormalities which may result from the survival of a severely cyanosed child.

Discussion

Whenever measurements are made it is necessary to give some idea of the errors involved. In Section (a) above, errors in the potential and resistance readings, together with other undetermined instrumental errors, probably amount to 10%, but there are two large errors which we have not estimated: (1) The current necessary to obtain "adequate movement of the diaphragm" will depend very greatly on the positioning of the electrodes, and this will vary from case to case and also during any one case; (2) the process of estimating when "adequate movement of the diaphragm" is obtained is itself subject to a large error, for diaphragmatic movement is estimated from the protrusion of the abdomen. Both these errors are unsatisfactory, but under the urgent conditions of treating these babies, many of whom seemed moribund, we did not consider it necessary at this stage to improve our methods.

The exact choice of $\frac{1}{4}$ millisecond pulse duration is not entirely arbitrary. It is long enough to induce a propagated response in the nerve, but is probably too short to excite muscles directly in the adult with the current used for operation. This factor is useful in experimental work with the adult. It appeared, however, that we generally caused direct stimulation of the sternomastoid in the infant, quite apart from other muscles supplied by the upper part of the brachial plexus; we have not sought to avoid this, because the movement produced would tend only to expand the thorax, and this effect can be increased by fixing the arm in an abducted position. This was well shown in one baby, not mentioned in this series because he had multiple congenital abnormalities, including a grossly deficient diaphragm. By stimulating the accessory muscles we improved the colour of the infant and air entry was heard, although there was never any visible movement of the epigastrium.

The effects of phrenic-nerve stimulation in the newborn seem to differ markedly from those in the adult, in that inhibition of spontaneous respiration, which is reported by Sarnoff and which we confirmed in the adult, does not occur. This has the advantage that the dangers of overventilation are not so great as we had at first feared. Stimulation is stopped when the baby is no longer cyanosed, and is restarted if cyanosis returns.

The repetition frequency of stimulation of 100 c./sec. is high enough to ensure a smooth contraction of the diaphragm and has the advantage that it can be locked to the mains supply frequency.

We would suggest that those who intend to use the apparatus can best familiarize themselves with the anatomy of the part by experimenting on their own phrenic nerves. For self-experimentation, and when one is working on an infant, it is convenient to have the machine fitted with a loudspeaker so that a buzz is made when impulses are passing and one can correlate the noise with any movement the infant may make.

It is clearly not possible to compare our results with those obtained with other methods, for the series is too small and too many factors enter into the consideration

of each case. Such a comparison is urgently required and should be undertaken in centres where there is an established routine for treating neonatal asphyxia, and where enough cases of this variable condition occur, so that treated cases and controls can be studied.

Summary

An instrument is described which is capable of performing artificial resuscitation when electrodes are applied to the neck over the site of the phrenic nerve. Experiments on the treatment of asphyxia neonatorum are described together with appropriate case histories taken from 29 subjects. Results are given which show the method to be promising and the line for further experiments is suggested.

This work has been possible only because of the kind co-operation of many people, as our appointments carry no clinical responsibilities. Post-mortem examinations of most of the cases at the Rotunda Hospital were made by Dr. J. H. D. Widdes and the pathological material was examined by Professor W. D. Newcomb and Dr. D. M. Pryce, to all of whom we are very grateful. We would also like to thank the Medical Committees of the English hospitals, the Masters and staff of the Rotunda and Coombe Hospitals, and the many clinicians who have co-operated with us. Our thanks are particularly due to the Medical Research Council for a grant to one of us (K. W. C.) which made possible the clinical work at Dublin, and to Mr. K. F. Tindall for help in constructing the instruments.

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The pioneer health centre of the Union of South Africa was set up at Polela, Natal, in 1940, and up to date 39 have been opened. They aim primarily to prevent disease and to promote health, but curative medical treatment is also given. On the whole patients are encouraged to go to private practitioners in case of illness, so no encroachment is made on private practice; on the contrary, routine medical examinations and home visits result in more patients attending the doctors' surgeries. All persons in the area covered by a centre, whether they are ill or not, are encouraged to attend the centre for routine medical examination, and the assessment of health and ill-health is based on environmental and social as well as individual pathology. Preventive services such as immunization against infectious diseases, antenatal examinations, and so on are provided by the centres. Each centre is left as much freedom as possible to carry out experiments and adapt itself to local needs; in short, each is a research centre. They are still embryonic; the training scheme being developed in Durban plans to give each medical officer a minimum of six months' training, and to appoint at least two to every centre, preferably one man and one woman. The health-centre movement has had to cope with both official prejudices and the opposition of herbalists and witch-doctors. One of their biggest advantages is the scope they give for the employment of the African on health work among his own people. They cater mainly for Africans, but also for non-Europeans and in certain cases Europeans; one result of their work is the increasing confidence the people are showing in hospital treatment (see *S. Afr. med. J.*, 1946, **20**, 326). The centres are also educating in sanitation, diet, and hygiene.

BRUCELLA ABORTUS ENDOCARDITIS

BY

F. DUDLEY HART, M.D., F.R.C.P.

Assistant Physician, Westminster Hospital

ALAN MORGAN, M.B.

Department of Morbid Anatomy, Westminster Medical School

AND

BRIAN LACEY, M.B., B.Sc.

Department of Bacteriology, Westminster Medical School

Infections due to *Brucella abortus* are not uncommon in this country. They remain long undiagnosed and for many months blood-stream infection persists. Until recently, no therapy was effective. It is therefore surprising that no fully proved case of endocarditis due to this organism has so far been recorded in British journals, although in 1936 Rennie and Young described a case which was not proved bacteriologically at necropsy. To date, only three reported cases can be said to satisfy all the required criteria in life and at necropsy (Rothman, 1935; Spink and Nelson, 1939; Spink, Titrud, and Kabler, 1942).

Chemotherapy and antibiotics have yet to be proved effectual in *Brucella* endocarditis. Spink *et al.* (1948) reported a case in which streptomycin and sulphadiazine appear to have inhibited the growing powers of the organism but did not save the patient.

Now that aureomycin and chloramphenicol have both been given with satisfactory results in uncomplicated *Br. abortus* infections, the following case is worth reporting, as courses of "aureomycin," chloramphenicol, penicillin, and streptomycin did nothing to alter the progress of the disease. Admittedly chloramphenicol was given too late to have any effect, but with none of the drugs mentioned was the fever lowered; in fact a Jarisch-Herxheimer reaction appeared to be caused by aureomycin. Dihydrostreptomycin together with aureomycin as used by Heilman (1949) and Herrell and Barber (1949) was contemplated, but was withheld until too late.

Case History

The patient, a male labourer aged 48, was first noticed to have a "bad heart" at the age of 7. In 1917 he was rejected for military service on this account. As he had suffered from dyspepsia for the past five years he had been drawing extra unpasteurized milk from the estate on which he worked in order to supplement his gastric diet.

He was first seen in the out-patient department on July 26, 1949, complaining of palpitations of six months' duration, malaise and fatigue for one year, and shivering attacks with night sweats for three weeks. The heart was found clinically to be enlarged to the left. Loud harsh systolic and faint soft diastolic murmurs were heard at the aortic area, and a systolic thrill was palpable at the same site. The E.C.G. was normal; haemoglobin 92% (Haldane); screening and radiographs of the heart showed some prominence of the ascending aorta, rounding of the cardiac apex with slight enlargement of the left ventricle, and calcification of the aortic valves. Clinically and radiologically the picture was that of aortic stenosis, compatible with the diagnosis of a long-standing rheumatic condition.

He returned on August 17, 1949, with fever, and was admitted as a case of subacute bacterial endocarditis superimposed on a long-standing rheumatic aortic stenosis. His temperature was ranging between 100 and 104° F. (37.8 and 40° C.). His B.P. was 120/85. Slight clubbing of the