THE MANAGEMENT OF SERIOUS HEART DISEASE IN THE NEONATE AND INFANT

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Incidence

Congenital cardiovascular defects are a major cause of death among infants. Where living standards are highest, deaths from congenital malformations account for 15 - 20% of the total infant mortality.[1] Roughly half of all deaths from congenital malformations are caused by congenital malformations of the circulatory system.[2] MacMahon and his colleagues[3] determined that 60% of infants with congenital heart defects are dead by the end of the first year of life and of these 35% are dead by the first month of life. The incidence of congenital heart defects among infants born alive has been recorded as 3·2/1,000 by MacMahon,[3] 6·8/1,000 by Harris and Steinberg,[4] 6·0/1,000 by McIntosh and his co-workers,[5] 7·0/1,000 by Richards and her colleagues[6] and 6·4/1,000 by Carlgren.[7] Keith and his co-authors[8] state that it may safely be assumed that approximately 6 babies in 1,000 live births are born with congenital heart defects and it is not unreasonable to accept this figure. With an estimated 453,000 births in the South African population in one year (1963)[9] there are an estimated 2,718 infants born each year in the Republic who have congenital cardiovascular defects (Table I).

TABLE I. THE ESTIMATED NUMBER OF BABIES WITH CONGENITAL HEART DISEASE BORN ANNUALLY IN THE REPUBLIC

Race	*Number of births* per annum	*Number of infants born annually estimated to have congenital heart disease*
White	77,900*	468
Coloured	76,347*	456
Asiatic	23,790*	144
Bantu	196,716*	1,650
	78,686†	
Total	452,739	2,718

*Registered births (1963).
†Estimated number of non-registered births on the safe assumption that at least 60% of Bantu register their newborn.

The chief sources of error in determining the incidence of congenital heart disease are unevenness and variation in statistical coverage, lack of certified and qualified personnel, uncertainty of diagnosis in the newborn and young infant, inadequate studies during life, lack of adequate follow-up examinations, failure to recognize or note defects at autopsy and differences in death certification. Furthermore, the frequency of other causes of death in infancy, particularly infections which may be associated with or unrelated to heart disease, probably accounts for much of this error. Precision and standardization of terminology, diagnostic and recording procedures are the only means whereby comparisons can be made on a national and international level. The incidence of congenital abnormalities in general increases as diagnostic facilities and observation periods following birth are extended. Inadequate diagnosis of congenital heart anomalies in the newborn is illustrated by comparison with those extending to 1 year of age.

Race

There is no factual data to support a racial difference in the frequency of congenital heart disease and until such data are made available, and in view of the numerous reports from other countries, it seems reasonable to assume that there is in fact, no such difference. Schrire[10] points out that the Bantu population at risk is not known, but there is no reason to believe that the Bantu population at risk is any different from any other racial group. Bradlow[11] is of the opinion that the incidence of congenital heart disease is probably the same in all races in South Africa. Stamler[12] has shown in an extensive and comprehensive review that little difference exists in the incidence of congenital heart defects between the Negro and the White.

Survival

From figures in Table II it is estimated that 1,630 infants in the Republic will succumb annually with congenital heart disease in the first year of life. The survivors of all infants born each year with congenital heart disease are estimated to number 1,188, of which a further 271 will die within the next 10 years with congenital heart disease. At the age of 10 years, the estimated number of survivors will be 917 patients, i.e. of the total number of infants born alive each year with congenital cardiovascular defects, 60% will die in the first year of life, a further 10% will die within the next 10 years and 30% will survive 10 years of age and will account for the number of cases of congenital heart disease in the general South African population group, viz. 2/1,000 survive from an initial 6/1,000. This figure is in accordance with the findings of Miller and others[13] who determined the prevalence rate of congenital heart disease in elementary school children to be 2·1/1 000 and supports the findings of Morton *et al.*[14] as well as Gardiner and Keith.[15]

TABLE II. THE ESTIMATED NUMBER OF DEATHS IN THE REPUBLIC IN INFANTS WITH CONGENITAL HEART DISEASE IN THE FIRST YEAR OF LIFE

Race	*Number of infants born each year estimated to have congenital heart defects*	*Estimated number of infants who succumb annually to congenital heart disease in the first year of life*
White	468	280
Coloured	456	274
Asiatic	144	86
Bantu	1,650	990
Total	2,718	1,630

The number of survivors accounts for the estimated 30,000 individuals with congenital heart defects over the age of 10 years in the Republic. Studies of congenital heart disease in the period of life after infancy give only an approximate incidence of the disease since the greatest mortality during the earlier years of life leaves a minority at later ages.

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The importance of the problem of congenital heart disease is such that proper recognition of its role as a cause of neonatal and infantile morbidity and mortality is necessary. Furthermore, in addition to the magnitude of the problem, it is imperative that a correct approach be formulated in the diagnosis, management and treatment of such abnormalities in the young and that the very high prevalence rate of congenital heart disease in infants and children, as compared to that of older school children and adults, be made more generally known.

The advent of cardiac surgery and the introduction of catheterization and cardiac cine-angiographic techniques into clinical medicine has led to the specialized qualification of individuals possessing special skills in the handling of the infant and who are trained at special centres where the standards of training have been developed.[16] The recent establishment of the American Board of Pediatric Cardiology as well as the creation of an increasing number of Chairs in Pediatric Cardiology in the United States and also in Europe point to the growing importance of this field. The forthcoming International Symposium on the Heart and Circulation in the Newborn and Infant to be held in Chicago firmly establishes this new aspect of medicine on firm ground.

Since the greatest incidence of, and mortality from, congenital heart disease occurs in the first year of life and because cyanosis owing to heart disease constitutes one of the major presenting features, this report attempts to formulate an approach to the infant with cyanosis from heart disease.

Cyanosis

Cyanosis is a sign of emergency, and congenital heart disease is an important cause of this sign in the infant. It is true that every infant who has cyanosis does not necessarily have heart disease. The causes of cyanosis in the newborn are listed in Table III. Extensive or microscopic neuronal damage may cause episodic transient or permanent cyanosis. With cerebral damage, neurologic signs are seldom present in the first 48 hours of life except as manifested by periods of apnoea and Cheyne-Stokes episodes. A history of traumatic delivery, foetal distress and a poor Apgar rating may help in differentiation. The infant with cerebral cyanosis is furthermore likely to have depressed gasping respirations, whereas the infant with respiratory or cardiac cyanosis is likely to breathe normally or, more usually, faster than normal. The presence of congenital heart disease may be suspected when those signs and symptoms listed in Table IV A and B develop, or when there are other anomalies or syndromes whose association with cardiac malformations is well recognized.[17] Typical examples (but by no means all) are mongolism, Turner's syndrome, Ellis-Van Creveld syndrome, the rubella syndrome and in infants with cleft palate, hypertelorism, and poly- or syndactyly.

TABLE III. THE CAUSES OF CYANOSIS IN THE NEWBORN

1. *Disorders of the central nervous system*
   - a. Developmental — i.e. prematurity
   - b. Congenital — i.e. various malformations
   - c. Inflammatory — i.e. due to bacteria, viruses, fungi and protozoa
   - d. Traumatic — i.e. intercranial and intracerebral haemorrhage and oedema
   - e. Metabolic — i.e. hypoxia, drug-induced depression, inborn metabolic errors and tetany
2. *Disorders of the respiratory system*
   - a. Intrinsic or extrinsic airways obstruction at the following levels:
     (1) Oro-pharynx, (2) Larynx, (3) Trachea, (4) Bronchi.
     Examples. Choanal atresia, macroglossia, mandibular hypoplasia, thyroglossal cysts or goitre, laryngeal oedema, stenosis, spasm, webs, cysts or paralysis, tracheal stenosis or absence of tracheal rings, vascular rings, papillomata, haemangiomata, hygromata, fibromata and other tumours, etc.
   - b. Primary non-expansion of the lungs
     Examples. Atelectasis, hypoplasia or agenesis of the lungs, pneumonia, haemorrhage or hyaline membrane disease
   - c. Secondary non-expansion of the lungs
     Examples. Air, fluid or blood in the pleural cavity or mediastinum; diaphragmatic herniae, paralysis or eventration; lobar emphysema; lung or thoracic cage cysts; tracheo-oesophageal fistulae, tumours, etc.
3. *Disorders of the cardiovascular system*
   - a. Peripheral circulatory insufficiency, physiologic or pathologic, the latter being associated with shock-producing syndromes.
   - b. Congenital malformations of the heart.
   - c. Inflammatory conditions of the heart, e.g. myocarditis/endocardial fibroelastosis.
   - d. Functional cardiac derangements resulting from arrhythmias, heart block or secondary to anaemias or arteriovenous fistulae.
   - e. Metabolic disorders such as glycogen storage disease.
4. *Biochemical and metabolic disorders*
   - a. Drug-induced (secondary or acquired) methaemoglobinaemia due to nitrites and aniline dyes
   - b. Congenital methaemoglobinaemia or sulfhaemoglobinaemia
   - c. Congenital haemoglobinopathy M.
   - d. Polycythaemia neonatorum

TABLE IVA. SYMPTOMS AND SIGNS SUGGESTING A CARDIAC DISORDER IN THE NEWBORN

1. Cyanosis
2. Increasing respiratory rate
3. Retractions of the thoracic cage or xiphoid
4. Easy fatiguability when feeding
5. Stridor or choking spells
6. Vomiting
7. Increase or irregularity in the heart rate
8. Profuse sweating
9. A heart murmur
10. Failure to gain weight
11. Increasing polycythaemia
12. A large cardiac shadow on X-ray

Numbers 1 - 11 all demand a chest X-ray

TABLE IVB. SIGNS AND SYMPTOMS OF HEART FAILURE

(In addition to some of the above)

1. Rapid respirations	Early
2. Enlargement of the heart	Early
3. Engorgement of the liver	Early
4. Râles in the lungs	Late
5. Pitting oedema	Late
6. Sudden weight increase	Late

A baby with cyanosis from congenital heart disease has a markedly abnormal cardiac anatomy and this is the reason that he manifests cyanosis at such an early age.

Generally speaking, the earlier the cyanosis, the worse the anomaly or the more incompatible the anatomy with normal (extra-uterine) life. Some of the cardiac malformations producing cyanosis may produce a murmur directing attention to the heart, but it must be emphasized that there are some of these same cardiac malformations producing cyanosis in which no heart murmur or an insignificant heart murmur may be heard, e.g. in transposition of the great vessels and in pulmonic atresia complex. One should therefore not be misled by the absence of a murmur in the cyanotic infant who might well have serious heart disease. Furthermore, every cyanotic infant with a heart murmur does not necessarily have heart disease and other causes of cyanosis must be considered.

It should be remembered that in addition to developmental cardiac anomalies, there are other important cardiac causes for cyanosis in the infant. Congestive heart failure is such a cause and the basis may or may not be a congenital heart defect. Other causes may be infection, i.e. myocarditis, to which the neonate is particularly susceptible, and arrhythmias, i.e. paroxysmal tachycardia. Of the non-cardiac causes of congestive heart failure, anaemia from various causes and arteriovenous communications elsewhere may contribute to the cause of cyanosis. If congestive heart failure is present, this should never be accepted as a final diagnosis. A cause must be sought and found if possible while (or after) active measures are undertaken to treat the heart failure. Often the condition of the infant will improve and, if so, the physician's hand in undertaking active investigatory measures can be delayed for a brief period of time. Generally speaking, the earlier the onset of cardiac failure, the worse the prognosis for the same reasons as when cyanosis is observed early. A single episode of heart failure is probably sufficient indication for the immediate establishment of a definitive diagnosis.

Diagnosis

The diagnosis of heart failure in the infant is not an extremely difficult one. Progressive enlargement of the liver in a baby is more important than palpating a liver 2 cm. below the costal margin. In such patients, auscultation of the heart yields little information regarding the diagnosis of heart failure *per se* but auscultation of the chest may yield valuable information regarding the presence or absence of pulmonary oedema. The management of the infant with heart failure has recently been described in detail[18,19] and will not be discussed in this paper. For a baby with a congenital heart defect to have gone into heart failure at an early age, digitalis alone will rarely ensure prolonged survival. The physician should not delay steps to make a diagnosis nor delay the time when further investigations should be undertaken, following successful digitalization and other measures to treat the heart failure. An important feature requiring emphasis is the frequent liability of cyanotic infants to become acidotic. Rapid deep respirations may be the presenting feature of a lowered pH or low CO_2 and the possibility of acidosis should be considered and confirmed before instituting therapy. Cyanosis from heart disease is a grave sign and the mortality is high, particularly in infancy. The physician should not be deceived by the apparent well-being of the infant at any one time, for many of these may die during or after investigative, diagnostic and surgical procedures but may be just the ones to be saved by correct diagnosis and treatment.

One factor in determining the survival of the infant with cyanosis due to congenital heart disease is the time of diagnosis of the heart lesion ; early and accurate diagnosis having been proven to improve the salvage rate. It is wrong to think that the steps necessary to make a diagnosis will jeopardize the infant's life, for it should be realized that his life is already jeopardized. The safety and efficacy that has been developed in the past few years has resulted in a mortality rate associated with cardiac catheterization of 0·2% in children and adult patients in good clinical condition. Even in the ill cyanotic newborn, the mortality rate of cardiac catheterization and angiocardiography is as low as 5%—this figure being related to the clinical condition of infants requiring such procedures.[20] Cardiac catheterization in the cyanotic infant with congenital heart disease is nevertheless justified and imperative in view of the generally poor prognosis. Persistence of cardiac failure is not a contraindication to further study and if the baby's course seems to be one of deterioration in spite of adequate medical measures, urgent study is required to establish a diagnosis and surgery is necessary as soon as a definitive diagnosis has been established. Numerous centres in the United States have developed units where cardiac catheterization is undertaken at any time of the day or night, which reflects the urgency of the problem, particularly in the young infant.

It has been held that a specific and accurate diagnosis cannot be made in the first 4 weeks of life. Today, it is possible to obtain a great deal of information by clinical examination and it is possible to make a reliable and reasonably accurate diagnosis (without special investigative procedures) at a few hours of age. Evaluation of data may at times be extremely difficult and there will be an occasional case in which a definite and exact clinical diagnosis will be in question. The management and handling of an ill cyanotic infant requires the exacting skill of a team trained in the management of such patients and who are continually being confronted by problems in this age group. Such management differs markedly from the management of patients with heart disease at any other age and such infants require expert knowledge in the approach to heart disease and the specialized techniques and care which are necessary to establish a diagnosis at so young an age.

A cyanotic 'spell' with sudden increasing cyanosis and laboured breathing or loss of consciousness in a cyanotic baby demands immediate treatment in the form of morphine and oxygen. Although the mechanisms for such attacks are still controversial[21,22] their development indicates a severe form of obstruction to the pulmonary blood flow. The first such spell constitutes a clear warning which, if unheeded, may lead to early and sudden death. Such infants should receive priority for immediate study and surgical treatment. It is important to recognize such attacks as well as milder forms of a similar nature which may resemble the various epilepsies.

Anaemia. An important concept in infants with heart disease is that the lower the haemoglobin in a cyanotic

baby, the lower the reduced haemoglobin and therefore, the less evident the cyanosis. Since anaemia as a physiological (as well as a pathological) entity is frequent in infancy and is aggravated by a cyanotic infant who feeds poorly and has a low intake of iron-containing solids, correction of the anaemia and elevation of the haemoglobin will result in an increase in the quantity of reduced haemoglobin. The necessary correction of the anaemia is frequently effective in alleviating symptoms resulting from anoxaemia and although beneficial to the infant's immediate condition, will rarely obviate the need for surgical intervention, but may delay it for a short while until the operative risk may be less.

Radiological evaluation of cardiac chamber hypertrophy and dilatation as well as pulmonary blood flow in the infant by conventional X-ray methods, though important, can be misleading. Some ill infants with heart abnormalities have chest radiographs within the normal range. Many malformations causing cyanosis in the infant do have characteristic patterns, and in some conditions the anatomic arrangement may be suggestive, whereas in other cases of the same malformation, such clues may be absent or minimal and can be missed or misinterpreted. Overpenetration results in normal lungs appearing avascular, whereas underpenetration suggests pulmonary vascular engorgement. All too often, technically poor films, inadequately centred films and films taken at the wrong phase of respiration produce a picture of an artificially enlarged heart in the infant. The frequency with which the thymic shadow obscures important features or adds to the contour of the cardiac silhouette, suggesting the presence of cardiomegaly, are important features that need emphasis.

ECG. Much has been written about the electrocardiogram in the normal neonate and infant and it has been established that there are changes at this stage of life that reflect metabolic changes, haemodynamic adaptations and maturation.[23,24] Such changes are not present in the electrocardiogram of the older child and adult and an awareness of such differences are of considerable importance in the assessment of this tool in the younger age group.

GENERAL CONSIDERATIONS

Optimal Time for Investigations

The time to study an infant with cyanosis due to heart disease is when serious heart disease is suspected, when it should be considered necessary to undertake surgical treatment immediately. Investigative measures should not be postponed until the infant is older, when, it is believed, it will be safer to undertake catheterization, angiocardiographic and surgical procedures. It must be conceded that an attempt to improve the infant's condition should be made with all possible measures but, failing this, further postponement will increase the mortality. The type of baby who is cyanosed early is a poor-risk baby and simple living is dangerous for him. Many of such babies are so ill they cannot feed, have to be fed with a naso-gastric tube, require constant and continuous oxygen and careful handling. The survival rate in such infants is tremendously increased by cardiac investigation followed by surgery and the dangers are not greatly increased when the operation is performed by a careful trained manipulator.

Major Cardiac Anomalies

An infant may have one of many entities and one has to consider the whole field of congenital heart disease.[25] The range of cardiac malformations in the neonate and infant is much wider than that of the older infant and child or adult because the range of the many anomalies causing cyanosis are incompatible with prolonged survival without surgery. The serious congenital heart defects which may present in the newborn period are listed in Table V. Reference to Table V shows that such anomalies are divided into 5 major groups. Careful judgement is required in the differential diagnosis of these conditions and in the selection of cases for surgery. It is the clinician's responsibility to furnish the surgeon with as much detailed information as is possible, for there is little doubt that more infants can be saved and salvaged by making a more accurate and definitive diagnosis. It is today not in the best interest of the patient nor sufficient to establish a diagnosis by grouping of a clinical entity. It has only recently been appreciated that subtle but important distinctions alone separate one condition from another. The specific size and situation of chambers and vessels and the presence or absence of associated anomalies are all important factors in determining the ultimate prognosis, and the surgical mortality rate is directly related to the proper selection of patients for operation.

TABLE V. SERIOUS HEART LESIONS IN EARLY INFANCY

1. *Left-sided lesions*
   a. Hypoplastic left heart syndrome
      (i) Mitral and/or aortic atresia
      (ii) Mitral and/or aortic stenosis
   b. Coarctation of the aorta
   c. Other
2. *Transposition of the great vessel complexes*
3. *Large left to right shunts*
   a. Ventricular septal defect
   b. Atrio-ventricular canal defects
   c. Patent ductus arteriosus
   d. Atrial septal defect
   e. Combinations of the above
   f. Anomalous pulmonary venous drainage
4. *Obstructive right-sided lesions*
   a. Pulmonic stenosis with or without intact septum
   b. Pulmonic atresia with or without intact septum
   c. Tricuspid atresia and/or stenosis
   d. Other
5. *Primary myocardial diseases*
   a. Myocarditis
   b. Endocardial fibroelastosis
   c. Other

It has been the belief that even if the diagnosis is made and the lesion is operable, the surgical mortality is prohibitive. Not too infrequently, with delays in establishing a diagnosis, the surgeon is called in when the condition of the infant has deteriorated, thus adding to the risk. In expert hands (i.e. experienced surgeons having had intensive training in the treatment of such cases) the mortality rate of cardiac surgery in the infant compares favourably with other types of surgery in this age group. Cooley and Hallman[26] report that of 450 infants with cardiovascular abnormalities in the first year of life, no less than 59% (233 cases) were operated at below 3 months of age; many

of these being operated on within a few days of birth. The survival rate of the 450 infants undergoing surgery was 72%. The present availability of corrective surgical techniques for the majority of the cardiovascular abnormalities causing early death (available only at very few South African centres at present) suggests that ample opportunity exists for lessening this toll of death. The feasibility of undertaking open-heart surgery in small infants has been developed by Sloan *et al.*[27] and Cooley and Hallmann[26] and has recently been commented on by Baffes and his colleagues.[28]

Risk of Mortality

It should not be assumed that the infant who dies generally has a bizarre kind of malformation, intractable and incurable by surgery. The infant who dies or is allowed to die very frequently does not have an incurable lesion although there is a very small group for whom nothing can be done at present. It must be emphasized that 50 - 70% of neonates with heart lesions causing cyanosis today have correctable (partially or completely) defects, and soon a greater percentage may have correctable defects. All causes for cyanosis are as important as each other, no matter how complex the anomaly may seem or may actually be. Once immediate steps have been taken to establish a diagnosis, and if it is impossible to control heart failure by medical measures, immediate operative treatment should be considered for a total or partial correction. Failure to carry out such a procedure is almost certain to lead to the infant's death, bearing constantly in mind that operation in infants with congenital heart defects has everything to offer the patient, with a marked reduction in mortality rate as compared to the very high mortality rate without operation.

Sixty per cent of babies with complete transposition of the great vessels who do not have surgical treatment are dead by the end of the third month. Survival beyond birth is not possible in those cases without some form of communication between the systemic and pulmonary circulation. Even those babies with some form of communication between the two circulations have a poor prognosis and by 6 months, 85% will have died. By one year of age, 92% of such patients will have died.[29] The need for surgical treatment is obvious and various types of procedures have been developed which have increased the chances for survival tremendously (Table VI). Today, with surgical treatment, the survival rate can be nearly as high as 70%.

Results with Surgical Treatment

In tricuspid atresia, the median age of death in 119 cases reviewed by Fontana and Edwards[30] was 6·5 months. Approximately 60% of patients born with this defect die within the first year of life. Three types of surgical procedure have been developed by Glenn, by Blalock and by Potts—all devised to shunt blood, thereby increasing pulmonary blood flow. With such procedures, the mortality rate can be reduced to 20% (Table VI).

In tetralogy of Fallot, the most dangerous years are the first 2 years of life. In analysis of cases seen at autopsy[8] 55% of patients with this anomaly were dead before their first birthday. With surgical treatment, it is possible to reduce this mortality rate considerably.

The infant with pulmonic stenosis, an intact ventricular septum and a right-to-left shunt at the atrial level, may die in a matter of hours after birth. Pulmonary valvotomy, a relatively simple procedure, can dramatically and instantaneously turn a moribund infant *in extremis* into a pink healthy infant. Although 50% of patients with this anomaly survive into adult life, the other 50% die during infancy and early childhood. Surgery offers such infants (particularly those with severe obstruction to the pulmonary blood flow) the only chance of survival.

TABLE VI. MORTALITY AND SURVIVAL RATES FROM CONGENITAL HEART DISEASE IN THE FIRST YEAR OF LIFE[8, 26]

Cardiac anomaly	*Mortality rate without surgery in the first year of life*	*Mortality rate with surgery in the first year of life*	*Survival rate with surgery in the first year of life*
Complete transposition of the great vessels	95%	33%	67%
Tricuspid atresia	60%	20%	80%
Tetralogy of Fallot	55%	16%	84%
Pulmonic stenosis		10%	90%
Pulmonic atresia	95%	60%	40%
Total anomalous pulmonary venous drainage	78%	52%	48%

In a review of pulmonary atresia, Fontana and Edwards[30] state that 95% of infants with this anomaly have died within 1 year of birth if they do not have surgical treatment. With operation, the mortality can be reduced to 60% with 40% surviving.

While increasing numbers of cases of total anomalous pulmonary venous drainage are being recognized in adults, it must be realized that in the majority of cases death occurs in infancy. Almost 78% of patients with this anomaly die within 1 year of birth.

The above few examples of the more common cardiac anomalies causing cyanosis in the infant have been briefly presented, with details of the high mortality rate associated with these conditions in infancy. Early diagnosis and surgery offer these babies the only chance of survival.

SUMMARY

The significantly greater incidence of congenital heart disease in the neonatal and infancy period is presented. The management of the baby with heart disease and cyanosis is emphasized.

The high mortality rate of congenital heart disease in infancy is mentioned, reflecting the height of the present challenge. Cardiac surgery can be successfully performed on infants in the first weeks of life.

Exact diagnosis in early infancy adequately facilitated by investigations and early surgery has been shown to reduce the mortality rate of congenital cardiovascular defects considerably.

Today, infants with serious congenital heart defects may grow up toward productive adulthood, who would have been hopelessly doomed before present diagnostic and corrective procedures were developed.

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