Congenital Diaphragmatic Hernias: Part 1

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KEY POINTS

- Congenital diaphragmatic hernia is a rare defect in the diaphragm leading to the herniation of abdominal contents into the thorax. This results in difficulties with oxygenation and ventilation.
- The main issues initially are pulmonary hypoplasia and pulmonary hypertension.
- Management involves resuscitation and stabilization in the form of invasive monitoring, early intubation and optimisation of ventilation and pulmonary hypertension.
- Congenital diaphragmatic hernias are not a surgical emergency.

INTRODUCTION

Congenital diaphragmatic hernia (CDH) is a developmental defect in the diaphragm that involves the protrusion of abdominal organs into the thorax (Figure 1). It is a rare defect with a worldwide prevalence of between 1:3500 and 5000 of live births. The key clinical features of CDH are underdevelopment of the lungs (ie, pulmonary hypoplasia; PH) and abnormal development of the pulmonary vasculature leading to persistent pulmonary hypertension of the newborn (PPHN). PH and PPHN occur as a direct consequence of the herniation of the abdominal contents into the thoracic cavity and the resulting compression of the growing lungs. The size of the defect and hence the degree of PH and PPHN determine the severity of the condition, which may be life threatening.[1]

AETIOLOGY AND ASSOCIATED CONDITIONS

The aetiology of CDH remains uncertain. Less than 2% of cases are familial; chromosomal disorders, however, are seen in 10% to 15% of cases. The most common of these include trisomies 13, 18 and 21; Cornelia de Lange syndrome; Beckwith-Wiedemann; Fryns syndrome; and CHARGE syndrome. A further 30% of CDH cases are associated with structural anomalies involving the cardiovascular, genitourinary and central nervous systems as well as the limbs.[2]

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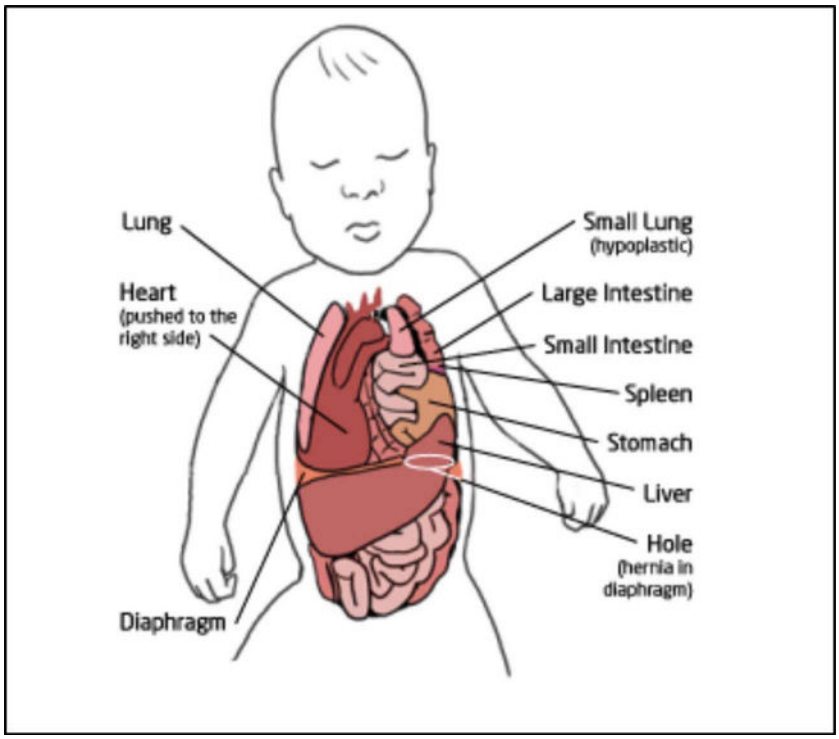

Figure 1. Illustration of a baby with a left-sided congenital diaphragmatic hernia. Abdominal contents can be seen in the thoracic cavity.

TYPES OF DEFECTS

Hernias may be located on the left or right side of the diaphragm or may be bilateral. Hernias may be referred to as right or left sided or bilateral. In a small number of cases, the diaphragm is weak but remains intact. This is known as an eventration. Defects may be classified as either Bochdalek or Morgagni.

Bochdalek

The vast majority (about 95%) of defects occur via the Foramen of Bochdalek. These defects are posterolateral and are mostly left sided with a small proportion being right sided. They are bilateral in 2% of cases. Intestinal herniation occurs in both right- and left-sided hernias, with the stomach usually involved in left-sided defects. Right-sided defects frequently involve liver herniation. Liver involvement can also occur with left-sided defects.[3]

Morgagni

Approximately 5% of hernias occur via the foramen of Morgagni. These involve much smaller defects in the anterior part of the diaphragm, just posterior to the sternum within the central tendon. Approximately 90% of these are right sided and have been linked with better outcomes.[3,4]

PATHOPHYSIOLOGY

CDH involves inhibition of the normal development of the lungs and pulmonary vasculature (Table 1). As a result of lung compression, there is underdevelopment of the airways and abnormal lung parenchyma. Abnormalities involve decreased terminal

Pathophysiology of congenital diaphragmatic hernia
1. Pulmonary hypoplasia
2. Vascular remodelling and pulmonary hypertension
3. ±Left ventricular hypoplasia

Table 1. Key Concepts of the Pathophysiology of Congenital Diaphragmatic Hernia

branching of the bronchioles, which leads to hypoplasia and dysregulated differentiation of type 2 pneumocytes.[1,5,6] Vascular remodelling leads to changes in the vascular bed. Intrapulmonary arteries become hypertrophied and muscular, leading to severe PPHN. The pulmonary vessels have an exaggerated response to vasoactive substances such as endothelin 1, which adds further to the development of PPHN.[6,7]

There may be an element of left ventricular (LV) hypoplasia, particularly in large left-sided defects. This occurs as a result of mechanically induced cardiac rotation, which leads to reduced blood flow across the foramen ovale. As a result, there is reduced LV filling, leading to LV hypoplasia. A hypoplastic LV occurring in combination with high pulmonary artery pressures and associated right ventricular (RV) dysfunction often leads to PPHN that is difficult to treat.[8]

PRENATAL DIAGNOSIS AND PREDICTORS OF SEVERITY AND PROGNOSIS

Between 50% and 60% of cases are diagnosed antenatally on routine ultrasound imaging. Diagnosis of right-sided hernias is more difficult because the sonographic appearance of the liver and foetal lung are extremely similar. Diagnosis is confirmed with foetal MRI followed by high-resolution ultrasound.

High-resolution ultrasound determines foetal measurements including lung area to head circumference ratio (LHR). Based on the LHR and position of the liver, CDH can be divided into extreme (<15%), severe (15%-25%), moderate (26%-35%) and mild (36%-45%) categories.[9,10] Predictors of poor prognosis are outlined in Table 2.

MANAGEMENT OF CDH IMMEDIATELY AFTER BIRTH

Conflicting evidence has resulted in controversy as to the preferred means of delivery and timing of delivery. Delivery should be planned whether it is via induced vaginal delivery or caesarean section.[11] The mode of delivery should be guided by maternal status.[11] It is important to remember that CDH is not a surgical emergency. Immediate management after birth involves resuscitation and stabilization in the form of monitoring, endotracheal intubation and transfer to a specialist centre (Table 3).

Essential monitoring includes heart rate, pre- and postductal saturations and invasive blood pressure. Early intubation is key. This is because the stomach, intestines and potentially other organs are in the thorax. Intubation prevents air from entering the stomach and bowel, which would cause further mechanical compression of the already restricted lungs. Insertion of a nasogastric tube (NGT) is also indicated to decompress the stomach and relieve thoracic pressure, improving ventilation.[11] Feeding via the NGT should not be commenced until surgical repair is complete.

An inspired oxygen fraction (FiO_2) to achieve preductal oxygen saturations (SpO_2) >92% is standard. Postductal saturations should be between 80% and 95%. The purpose of pre- and postductal oxygen saturation monitoring is to detect right to left shunting of blood through the ductus arteriosus that may occur as a result of high pulmonary vascular pressures (Figure 2).[11] A difference between the preductal saturations (right hand) and postductal saturations (left land or either foot) of ≥10% suggests marked pulmonary hypertension. Echocardiography should be carried out early to determine the extent of PPHN and to determine the presence of structural or functional cardiac defects.[12]

Additional standard investigations include cranial and renal ultrasound in light of the occurrence of associated central nervous system and genitourinary anomalies. Formal neonatal, genetic and surgical referrals should be requested in advance.

Predictors of Poor Prognosis
1. Low birth weight
2. Cardiac anomalies
3. Chromosomal anomalies
4. Left ventricular hypoplasia
5. Severe pulmonary hypertension
6. Observed to expected lung-to-head ratio <25%
7. Predicted lung volume <15%
8. Total lung volume <20 mL
9. Small contralateral lung
10. Right-sided CDH
11. Bilateral CDH
12. Large defect

Table 2. Predictors of Poor Prognosis. CDH indicates congenital diaphragmatic hernia

Immediate Management
1. Immediate intubation 2. Monitoring: Pre- and postductal saturations aiming for postductal SaO_2 between 80% and 95% 3. NGT insertion with frequent or continuous suction 4. IV access; umbilical line may also be used 5. Transfer to ICU 6. Invasive blood pressure monitoring

Table 3. Immediate Management of a Congenital Diaphragmatic Hernia. ICU indicates intensive care unit; IV, intravenous; NG, nasogastric tube

MANAGEMENT OF CDH IN THE CRITICAL CARE UNIT

Following delivery and initial stabilization, neonates will require transfer to a critical care unit for ongoing management. Close attention will need to be paid to oxygenation, ventilation and haemodynamics, and quick action must be taken in the event of deterioration (Figure 3).

Oxygenation and Ventilation

Ventilating patients with CDH can be complex, with protective ventilation strategies allowing permissive hypercapnia being shown to have higher survival rates.[13] The core aims are to ensure adequate tissue oxygenation whilst minimising barotrauma of the hypoplastic lung. To achieve this, intubation, protective mechanical ventilation and decompression of the abdomen via an NGT should occur early.[11] Pressure-controlled ventilation is preferred to reduce barotrauma. Peak inspiratory pressures (PIP) should not exceed 25 cm H_2O with peak end expiratory pressures maintained between 3 and 5 cm H_2O. This may lead to mild hypercapnia (6.9-9.3 kPa), which should be tolerated.[11]

In cases of high FiO_2 requirements, pre- to postductal SaO_2 difference >10%, or in cases of hypercapnia with high PIP, there may be a role for high-frequency oscillatory ventilation (HFOV).[11] Hypoxia and excessive hypercapnia can lead to significant acidosis and cause worsening PPHN. HFOV is therefore used as a rescue therapy. It works by applying a constant distending pressure (mean airway pressure) with pressure variations oscillating at very high rate around that distending pressure. This leads to very small tidal volumes and but avoids large changes in pressures and volumes that are seen in conventional ventilation and can result in improved gas exchange with better oxygenation and reduction in $PaCO_2$.

Pulmonary Hypertension

PPHN is common in CDH, and an echocardiogram within 24 hours after birth is essential.[11,14] This reveals the presence and severity of the PPHN as well as information about congenital defects and overall function. High pulmonary vascular resistance

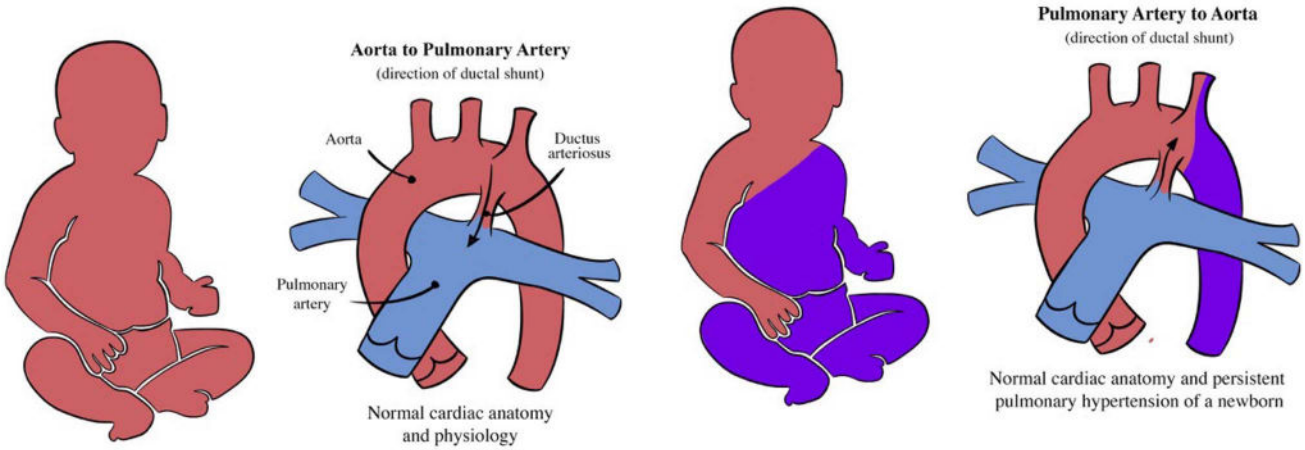

Figure 2. Illustration of blood flow across the patent ductus arteriosus (PDA) after birth. The image on the left illustrates normal physiology, in which oxygenated blood flows from the aorta into the pulmonary artery via the PDA. The image on the right illustrates the physiology in the event of persistent pulmonary hypertension of the newborn. In this instance, pressures are higher in the pulmonary artery compared with the aorta, so deoxygenated blood flows from the pulmonary artery into the aorta via the PDA. This results in blood that is relatively more hypoxemic distal to the PDA.

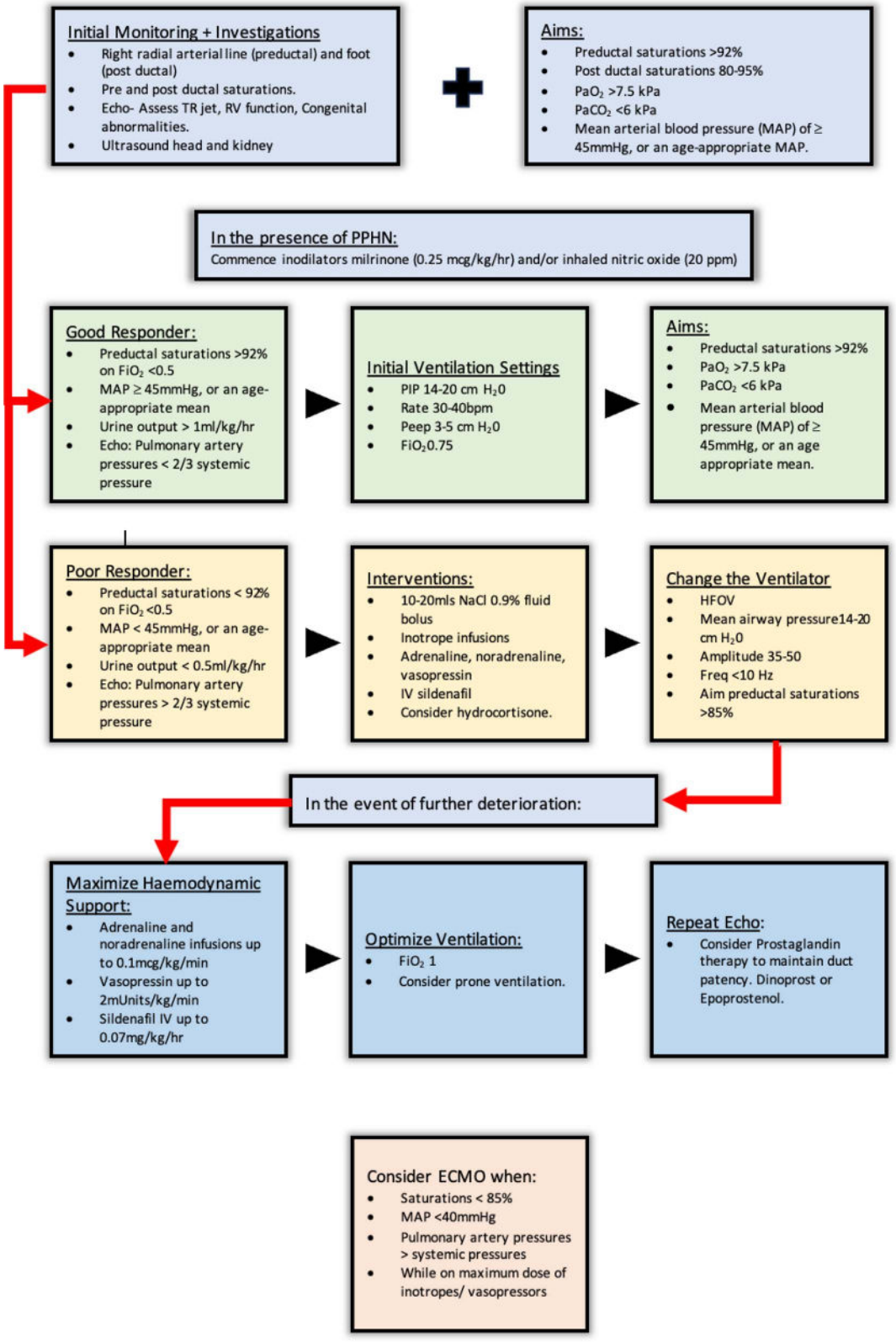

Figure 3. Algorithm for the management of congenital diaphragmatic hernia in the critical care unit. Echo indicates echocardiogram; ECMO, extracorporeal membrane oxygenation; FiO_2, fraction of inspired oxygen; freq, frequency; HFOV, high-frequency oscillatory ventilation; IV, intravenous; $PaCO_2$, partial pressure of arterial carbon dioxide; PaO_2, partial pressure of arterial oxygen; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure; PPHN, persistent pulmonary hypertension of the newborn; MAP, mean arterial pressure; mL, millilitre; NaCl, sodium chloride; RV, right ventricle; TR, tricuspid regurgitation.

means that that blood will back up into the right heart, leading to high pressures within the RV. RV pressures are measured using the tricuspid regurgitation jet and right ventricular end diastolic pressures. Flattening of the intraventricular septum suggests moderate PPHN. Bowing of the septum into the LV suggests severe PPHN.[14]

High pulmonary vascular pressures will result in a bidirectional or right to left shunt across the patent ductus arteriousus (PDA). Right to left shunting occurs because pulmonary vascular pressure is higher than that of the systemic circulation. Right to left shunting may also occur if the patient has a patent foramen ovale or atrial septal defect.[14]

Pulmonary artery pressures that are the same or higher than systemic pressures indicate a requirement for intervention to reduce shunting via the PDA. This is achieved by reducing pressures in the right heart and maintaining adequate systemic pressures.[14]

Treating PPHN requires reducing pulmonary vascular tone. This involves the use of pulmonary vasodilators and mitigating factors that increase pulmonary vascular tone, such as hypoxia, severe hypercarbia, pain or agitation, mechanical compression from air in the stomach and acidosis. Intubation and adequate ventilation is therefore essential, as are stomach decompression (via NGT) and adequate analgesia and anaesthesia.

Pulmonary vasodilators are widely used in the treatment of PPHN. Inhaled nitric oxide is a potent selective pulmonary vasodilator that is often used as a first-line agent.[15] An intravenous infusion of sildenafil may be added as a second-line agent followed, if necessary, by a prostaglandin (Dinoprost or epoprostenol), which is used to maintain the patency of the PDA.[11,16] A PDA allows for blood to be offloaded from the right heart and thus relieves right ventricular pressure. This, however, will have the undesired effect of reducing postductal saturations as deoxygenated blood from the right heart is pumped to the systemic circulation.

It is important to remember that PPHN causes RV impairment.[14] The workload of the right heart is significantly higher when pumping against high pulmonary pressures. Milrinone, which is a potent inodilator, is often used as it both decreases PVR and improves RV contractility,[17] resulting in improved oxygenation.[18]

Maintenance of SVR is necessary to reduce shunting across the PDA. Noradrenaline and adrenaline infusions are commonly used in the setting of reduced LV function or hypotension. Hydrocortisone may have a role failing maximum inotropic and vasopressor therapy.[11]

Serial echocardiograms should guide response to treatment and the necessity for second- and third-line agents as well as determine changes in haemodynamics.

Sedation

Adequate sedation is necessary to achieve effective ventilation and reduce pulmonary hypertension. Intravenous (IV) infusions and boluses are the preferred route given that the patient will be nil by mouth. Suitable agents include morphine, fentanyl, clonidine, dexmedetomidine and midazolam. Muscle relaxation is not routinely required although may be needed to facilitate high-frequency oscillatory ventilation.

Antimicrobials

There is little evidence surrounding the use of prophylactic antimicrobial in CDH. Indications for antimicrobial treatment may include the presence of maternal risk factors such as a group B strep or clinical signs and biochemical markers of infection.

Extracorporeal Membrane Oxygenation

Extracorporeal membrane oxygenation (ECMO) is used in circumstances in which conventional ventilatory therapy, as in cases of trialled HFOV, has failed pre- or postsurgery. Criteria for ECMO include[11]

- Inability to maintain preductal saturations >85% or postductal saturations >70%
- Increased $PaCO_2$ and acidosis with pH <7.15 despite optimization of conventional ventilator management
- Peak inspiratory pressure >28 cm H_2O or mean airway pressure >17 cm H_2O is required to achieve saturation >85%
- Inadequate oxygen delivery with metabolic acidosis as measured by elevated lactate ≥5 mmol/L and pH <7.15
- Systemic hypotension, resistant to fluid and inotropic therapy, resulting in urine output <0.5 mL/kg/h for at least 12 to 24 hours
- Oxygenation index ≥40 present for at least 3 hours

When considering ECMO, it is important to bear in mind the inherent risk involved, especially since the benefits of ECMO remain unclear.[12]

FUTURE DIRECTIONS

The aim of prenatal intervention is to reduce the extent of lung hypoplasia and promote normal lung development. Fetoscopic endoluminal tracheal occlusion (FETO) is a minimally invasive transuterine intervention. It works by deploying a balloon in the foetal trachea. This acts to prevent the efflux of pulmonary fluid from the trachea by way of occlusion. It also stretches the foetal lung accelerating lung growth, increasing the number of alveoli and capillary vessels and preventing the remodelling of pulmonary arterioles. The balloon is removed at 32 to 34 weeks of gestation.[19] FETO, however, is still considered experimental due to the increased risk of premature birth.[19] FETO is currently being studied in ongoing randomised control trials such as the TOTAL trial. The consensus statement from the CDH Euro Consortium recommends that FETO should not be performed outside of these trials pending their results.[19]

SUMMARY

CDHs are rare developmental defects. The pathophysiological processes are complex and dynamic. PH and premature lungs require thoughtful ventilation, while the pathophysiological effects of PPHN on haemodynamic stability should not be underestimated. Despite goal-directed therapy in the form of ventilation strategies, haemodynamic support and multidisciplinary input, management in the intensive care unit is often challenging, with prognosis varying considerably on a case-by-case basis.

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