Prostaglandin E\textsubscript{1}, Therapy*  
Is It Associated with a Higher Incidence of Wound Infection in the Cyanotic Neonate?

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Prostaglandin (PGE\textsubscript{1}) may be used to maintain ductal patency in the infant with cyanotic congenital heart disease, but the risk of infection may be increased. Between October, 1976 and December, 1982, 38 neonates with complex cyanotic congenital heart disease required operations creating systemic-to-pulmonary artery shunts. Of 13 patients who did not receive PGE, therapy, none developed a wound infection. Of 25 patients who did receive PGE, therapy, four (16 percent) developed a significant wound infection. The two patient groups were similar when compared by age and weight at operation, by severity of heart disease and by the presence of other congenital anomalies. Pathogenic Staphylococcus epidermidis was recovered from all infected wounds, all of which responded favorably over a period of two to four weeks with a short course of antibiotics and wound debridement.

Prostaglandin (PGE\textsubscript{1}) is a drug of proved efficacy in improving oxygenation in infants with ductus-dependent pulmonary blood flow.\textsuperscript{1,4} It is often used in the infant with severe cyanotic congenital heart disease to maintain ductal flow in anticipation of palliative or reparative surgery, thus allowing maximal oxygenation at the time of the operation. The risk of infection for the infant who receives PGE, is not mentioned prominently in the literature as a complication.\textsuperscript{5} However, previous investigators have shown PGE\textsubscript{1} to adversely affect neutrophil function by inhibiting lysosomal enzyme release. The response was dose-related.\textsuperscript{6} The literature on transplantation cites the role of prostaglandin E\textsubscript{2} (PGE\textsubscript{2}) in adversely affecting the immune response by suppressing blast transformation, lymphocyte cytotoxicity, lymphokine production, antibody formation and macrophage activity.\textsuperscript{7} This article reports a higher than expected incidence of wound infection in neonates undergoing treatment with prostaglandin prior to surgery.

Patients Studied

All neonates requiring a systemic-to-pulmonary artery shunt in the first 28 days of life at the University of Nebraska Medical Center were studied. There were 38 neonates involved between the period October, 1976 and December 31, 1982; 27 were males and 11 were females. The age at operation ranged from one day to 28 days (median two days), and the weight at operation ranged from 2.0 to 4.78 kg (mean 3.3 kg). Types of shunts included formalin infiltration of patent ductus arteriosus (PDA) 29/38, and Waterston, 9/38. Severity of heart disease ranged from pulmonary atresia (PA) with intact septum—3/38, through severe tetralogy of Fallot (ToF)—11/38, to complex cyanotic heart disease with at least one other significant congenital anomaly—9/38, including 4/38 with asplenia syndrome. Of 38 patients studied, 25 received PGE, and 13 did not. The infections under study were wound infections of sufficient severity to require removal of sutures and opening the incision down to the rib over at least one-fourth the length of the incision (Table 1).

There were 13 neonates who did not receive prostaglandin. Eight of the 13 were operated on prior to mid-1977 when PGE became available. Age at operation ranged from hours to 28 days (median two days), and weight ranged from 2.0 to 3.04 kg (average 3.03 kg). All patients had severe cyanotic heart disease and four (30 percent) infants had a significant extracardiac anomaly, including two with asplenia syndrome. Waterston shunts were performed in eight and formalin infiltration of PDA in five. Eight of 13 (61 percent) survived to leave the hospital. None was noted to have a wound infection.

Twenty-five patients were treated with PGE. Age at operation ranged from one day to 26 days (median two days). Weight ranged from 2.2 to 4.78 kg (mean 3.39 kg). Extracardiac congenital anomalies were present in six (24 percent), with two having asplenia

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**Table 1—Patients Studied (N = 38)**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Lesion</th>
<th>Shunts</th>
<th>PA with Intact Septum</th>
<th>Tetralogy of Fallot (Severe)</th>
<th>Complex Cyanotic CHD</th>
<th>Age at Operation</th>
<th>Weight at Operation</th>
<th>PDA/Formalin</th>
<th>Waterston</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>11</td>
<td>1 to 28 days (Median 2 days)</td>
<td>2.0 to 4.78 kg (Average 3.3 kg)</td>
<td>29</td>
</tr>
</tbody>
</table>

PA = pulmonary atresia; CHD = congenital heart disease; PDA = patent ductus arteriosus
syndrome. Formalin infiltration of PDA was used in 24 patients, and a Waterston shunt in one patient. Of 25 patients, 15 (60 percent) survived to leave the hospital. Of 25 patients, four had a significant wound infection (Table 2).

The four patients with wound infections ranged in age at the time of operation from one to 26 days (median two days), and weight at operation ranged from 2.2 to 4.78 kg (mean 3.3 kg). The time on PGE1 infusion for this group ranged from 18 hours to 26 days (median two days) compared to a range of four hours to five days (median one day) for the noninfected group. Of the four infected patients, two had asplenia syndrome. Wound infections were noted from three days to six days postoperation. All patients were receiving an appropriate dose of synthetic penicillin and aminoglycoside at the time infection was noted. A pure culture of Staphylococcus epidermidis was grown from each of the wounds. All four patients survived to leave the hospital.

**DISCUSSION**

The results from the study of our patient data point to an increased incidence of infection in cyanotic neonates receiving PGE1 (p value = .13). All wound infections were found in the PGE1 group, which translates to an infection rate of 16 percent in the treated group versus 0 percent in the non-treated group. While the sample size is small, the increased incidence is disturbing, as our data are similar to the data of Kugler et al who report sepsis and wound infections (4/27) were of concern in a similar patient population treated with PGE1. The two groups were matched for weight, age at shunt, and percentage with extracardiac defects. The only significant difference was in the type of shunt used, with 60 percent of the non-PGE1, treated group receiving a Waterston shunt and 95 percent of the PGE1 group receiving formalin infiltration of the PDA; however, none of the group reported by Kugler et al was reported to have had formalin infiltration. The group of four infected infants included one who was maintained on PGE1 for 26 days because of poor oxygenation. A modified Blalock-Taussig shunt at two days of age had closed. This was the only patient who had a wound infection while

<table>
<thead>
<tr>
<th>Patient</th>
<th>Date of Operation</th>
<th>Age at Operation</th>
<th>Days on PGE1</th>
<th>Infection Noted</th>
<th>Organism</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9/20/79 (Home on 10/6/79)</td>
<td>2 days</td>
<td>1 day</td>
<td>3rd day postop (patient receiving ampicillin and kanamycin)</td>
<td>Staphylococcus (epidermidis)</td>
<td>Asplenia syndrome, Ventricular inversion, Small subaortic RV</td>
</tr>
<tr>
<td>2</td>
<td>7/17/81 (Home on 8/5/81)</td>
<td>26 days</td>
<td>26 days</td>
<td>9th day postop (patient receiving methicillin and gentamycin)</td>
<td>Staphylococcus (epidermidis)</td>
<td>Asplenia syndrome, Abdomino situs ambiguous</td>
</tr>
<tr>
<td>3</td>
<td>2/20/82 (Home on 3/5/82)</td>
<td>1 day</td>
<td>2 days</td>
<td>6th day postop (patient receiving ampicillin and gentamycin)</td>
<td>Staphylococcus (epidermidis)</td>
<td>Asplenia syndrome, BT shunt (4 mm)-failed 6/22/81</td>
</tr>
<tr>
<td>4</td>
<td>7/5/82 (Home on 8/4/82)</td>
<td>3 days</td>
<td>36 hours</td>
<td>4th day postop (patient receiving methicillin and gentamycin)</td>
<td>Staphylococcus (epidermidis)</td>
<td>Hypoplastic right heart, 2/4 (Severe)</td>
</tr>
</tbody>
</table>

RV: right ventricle; VSD: ventricular septal defect; PA: pulmonary atresia; FDA: patent ductus arteriosus; TAPVR: total anomalous pulmonary venous return; d-TGV: dextrotransposition of the great vessels; AV: atrioventricular; BT: Blalock-Taussig, TS: tricuspid atresia
receiving PGE₁.

The median time of administration of PGE₁ was two days for the infected group, compared to a median time of one day for the noninfected group. There did not appear to be a correlation between length of time on PGE₁ and increased susceptibility, and all except one patient had been off PGE₁, at least two days (Table 3). Weight did not seem to be a correlating factor, although Lewis et al suggested this might be the case. All infants were receiving the same prophylactic antibiotic regimen, so the use of antibiotics to avoid infection may not be totally effective. Both patients with asplenia syndrome who did receive PGE₁ had wound infections. Those with the asplenia syndrome not receiving PGE₁ did not develop wound infections. It is known that immunity in asplenia syndrome is not normal, but these patients are prone to develop disseminated infections rather than localized wound infections. Of the two asplenic patients in the non-PGE₁ group, one died a day after operation. The organism cultured from each wound infection was Staphylococcus epidermidis, frequently considered a benign organism. Acid-fast organisms were looked for in the wound culture of patient 4, but none was found. None of the patients developed signs of disseminated infection, which was in contrast with Kugler et al who found an increased rate of sepsis in their patients. There was a period of at least five months between cases of infection, suggesting that infection was not of a common environmental etiology.

In conclusion, caution must be observed in the use of PGE₁, as with any other new therapy. PGE₁ may not have been the cause of increased wound infections in the operated cyanotic neonates, but information must be collected in order to determine if PGE₁ is the likely cause. This institution continues to use PGE₁ for the therapeutic effect of increasing oxygenation and optimizing the clinical condition of these critically ill neonates.

REFERENCES