defibrillation: range and relationship to body weight. (abstr)
Circulation 57 (suppl II): II-204, 1978
15. Standards for Cardiopulmonary Resuscitation and Emergency
Cardiac Care. JAMA 227: 837, 1974
16. Connell PN, Ewy GA, Dahl CF, Ewy MD: Transthoracic imped-
ance to defibrillator discharge. Effect of electrode size and electrode-
18. Ewy GA: Effectiveness of direct current defibrillation: role of
paddle electrode size: II. (letter) Am Heart J 93: 674, 1977
19. Hoyt R, Grayzel J, Kerber R: Intracardiac current in defibril-
ation. Effect of paddle size. (abstr) Circulation 59 (suppl II):
II-192, 1979
20. Thomas ED, Ewy GA, Dahl CF, Ewy MD: Effectiveness of
direct current defibrillation: role of paddle electrode size. Am
Heart J 93: 463, 1977
21. Parker MR: Defibrillation and synchronized cardioversion. In
Advanced Cardiac Life Support. Dallas, American Heart
Association, 1975
22. Geddes LA, Tacker WA, Cabler DP, Chapman K, Rivera BS,
Ilder H: Decrease in transthoracic resistance during successive
ventricular defibrillation trials. Med Instrum 9: 179, 1975
23. Dahl CF, Ewy GA, Ewy MD, Thomas ED: Transthoracic im-
pedance to direct current discharge: effect of repeated countershocks. Med Instrum 10: 151, 1976
24. Chambers W, Miles R, Stratbucker R: Human chest resis-
tance during successive countershocks. (abstr) Circulation 56
(suppl III): III-183, 1977
25. Kerber RE, Sarnat W: Factors influencing the success of ven-
tricular defibrillation. Circulation 60: 226, 1979
26. Tacker WA, Geddes LA, Cabler PS, Moore AG: Electrical
threshold for defibrillation of canine ventricles following myoc-
ardial infarction. Am Heart J 88: 476, 1974

Oral Prostaglandin E2 in Ductus-dependent
Pulmonary Circulation

ERIC D. SILOVE, M.D., J. YASHU COE, M.B., M. F. SHIU, M.D., JANE D. BRUNT, B.S.C.,
ANTONY J. F. PAGE, M.B., SHYAM P. SINGH, M.B., and MURRAY D. MITCHELL, M.A., D. PHIL.

SUMMARY Prostaglandin E2 (PGE2) was administered orally, in doses of 12–65 µg/kg at intervals of 1–4
hours, to 12 neonates in whom the pulmonary circulation depended on patency of the ductus arteriosus. After
an oral dose, both oxygen saturation (SaO2) and plasma PGE2 concentration increased consistently within
15–30 minutes, reaching values comparable to those during i.v. infusions. Treatment continued for 5 days to 4
months. In eight infants, PGE2 withdrawal resulted in a decrease of SaO2, from a mean of 75 ± 7% to
57 ± 10% (± SD).

The ductus remained responsive for long periods — in four infants, for over 3 months. Consequently, surgery
could be delayed until the infants and their pulmonary arteries had grown. Side effects during oral therapy
were similar to those during i.v. infusion but were less severe in this series. The effectiveness and simplicity of
oral PGE2 administration have advantages over i.v. administration, especially for long-term treatment.

INFUSIONS of the E-type prostaglandins are widely
used to maintain patency of the ductus arteriosus in
neonates with severely reduced pulmonary blood
flow.1–4 Therapy usually continues for hours or days;
the longest reported course of i.v. therapy has been 29
days in one infant.5 We have briefly described the effi-
cacy of long-term oral prostaglandin E2 (PGE2)6–10 and
now report our experience of oral therapy in 12 pa-
tients. In particular, we tested (1) whether oral PGE2
consistently maintained ductus patency; (2) whether
oral PGE2 could easily be substituted for i.v. therapy;
(3) the requirements of dosage and frequency of ad-
ministration; and (4) whether the ductus remained
PGE2-dependent after a period of months.

Patients and Methods

This study was approved by the Research Ethical
Committees of both the Children's Hospital and the
Central Birmingham Health District. Informed paren-
tal consent was obtained in each case.

Twelve infants with severely diminished pulmonary
blood flow were treated with oral PGE2. Their mean
weight was 2.90 kg. The clinical features are given in
table 1. In patients 2, 3, 4, 6, 11 and 12, the surgeons
considered the pulmonary arteries, as shown by
angiography, to be too small to attempt a shunt oper-

From the Department of Pediatric Cardiology, Children's
Hospital, Ladywood Middleway, Birmingham, and Nuffield
Department of Obstetrics and Gynaecology, University of Oxford,
John Radcliffe Hospital, Oxford, England.

Presented in part at the 52nd Scientific Sessions of the American
Heart Association, Anaheim, California, November 1979.

Dr. Mitchell is a Medical Research Council Senior Research
Fellow.

Address for correspondence: Dr. E. D. Silove, Children's
Hospital, Lady Middleway, Birmingham B16 8ET, England.

Received October 9, 1979; revision accepted July 11, 1980.
Circulation 63, No. 3, 1981.
The route and duration of PGE₂ administration are shown in table 1. For oral therapy, tablets dissolved in water were first given through a nasogastric tube for 12–24 hours and were later given orally; in case 1, the i.v. preparation was given orally. Initially, oral PGE₂ was given hourly, and each dose was 12–65 µg/kg. The dose and frequency of administration were adjusted depending on the clinical response. Cardiac catheterization was repeated in five infants at varying intervals after therapy had commenced.

In eight infants, the effects of PGE₂ withdrawal and reintroduction were studied at various ages (table 2). A radial arterial cannula (Abbocath 22G) was introduced for repeated blood oxygen analysis. Arterial oxygen tension (Pao₂) was measured with an Instrumentation Laboratories pH/Blood Gas Analyzer (Model 413) and oxygen saturation (Sao₂) with an American Optical Oximeter. For the purpose of analysis, Pao₂ measurements were converted to Sao₂ values using the appropriate oxygen dissociation curves. The significance of changes in Sao₂ was obtained using the t test for paired data. During the study, the skin temperature, radial arterial pressure and ECG were monitored continuously. Skin temperature was measured with a surface temperature probe (Yellow Springs Instruments, Series 409) taped just proximal to the great toe. Arterial pressure was measured with a Hewlett-Packard strain-gauge transducer (Model 1280) and pressure module (Model 78205).

At the time of study, seven of the eight patients had been stabilized on oral PGE₂ therapy and one on an i.v. infusion. Repeat studies were performed in two infants. Most of the infants on oral therapy had been receiving hourly doses (table 2) up to the time of the withdrawal study. Normal feeding continued during the study. Sao₂ was measured immediately before the last oral dose or before discontinuation of i.v. infusion, then at 15-minute intervals for the first hour and then every 30 minutes until the reintroduction of PGE₂ therapy was clinically indicated. Additional blood samples were then taken to determine the rate of response to oral doses of PGE₂.

In five patients, measurements of plasma PGE₂ concentration were made to coincide with some of the arterial oxygen measurements. Plasma concentrations were measured by specific radioimmunoassay after extraction and chromatographic procedures described and validated previously. Briefly, plasma was acidified to pH 3 with citric acid and extracted twice with a mixture of cyclohexane and ethyl acetate. Samples were then applied to microcolumns containing silicic acid, and, after a wash procedure, PGE₂ was eluted with a methanolic mixture of cyclohexane and ethyl acetate. Recovery of PGE₂ was monitored in each sample by the addition of 1200 cpm tritiated material before extraction began. The final radioimmunoassay has a sensitivity of 1 pg and 50% inhibition of initial binding at 5–6 pg. Buffer blanks run through the entire assay procedure were consistently undetectable. The intra-assay coefficient of variation was 8%. The significance of changes in plasma PGE₂ concentration produced by PGE₂ therapy was obtained using the t test for paired data.

At the initial and subsequent cardiac catheterization studies, the diameter of the main right pulmonary artery was measured on anteroposterior projections of the cineangiograms. The measurement was made just proximal to the division of the main right pulmonary artery, and correction was made for magnification.

**Results**

**Dosage and Duration of PGE₂ Therapy (table 1)**

The total course of treatment lasted 6–145 days and the oral course lasted 5–130 days. The oral dose ranged from 12–65 µg/kg, administered at intervals of 1–4 hours. The initial oral dose was 30–45 µg/kg/hour, except in patient 1, who received 12 µg/kg/hour. After 1–3 weeks, the frequency was reduced in most cases to 2-hour intervals and in some, after 4 weeks, to 4-hour intervals. When PGE₂ was infused i.v., the smallest effective dose was used. This was usually as low as 0.002–0.006 µg/kg/min.

**Arterial Blood Oxygen Saturation**

In each patient, oral PGE₂ therapy produced an increase in oxygen saturation, usually within 15–20 minutes and invariably within 2 hours of commencing treatment. The mean Sao₂ during oral therapy was not significantly different from the mean value during i.v. therapy (fig. 1). In eight infants who had been stabilized on i.v. or oral therapy for periods of 1–10 weeks, Sao₂ decreased during the period of 2–5 hours after the last dose of PGE₂, from a mean of 75 ± 7% to 57 ± 10% (± sp) (table 2, figs. 2–5). Within 15 minutes of reintroduction of oral PGE₂, Sao₂ increased and by 30–45 minutes had almost reached prewithdrawal values (figs. 3–5). However, in one patient (case 2) in whom Sao₂ had been allowed to remain in the region of 40–50% for 2 hours, reintroduction of therapy was effective only after several hourly doses.

After the last dose of PGE₂, Sao₂ remained above 60% for at least 2 hours in seven studies and for at least 3 hours in four studies (table 2, figs. 2, 4, 5). The response of Sao₂ to withdrawal and reintroduction of PGE₂ therapy was not related to the age of infants at the time of the study.

**Plasma PGE₂ Measurements (table 3)**

Plasma PGE₂ concentrations were measured in patients 2, 3, 4, 6 and 7. After discontinuation of therapy, plasma PGE₂ concentrations were 20–142 pg/ml in individual patients. A constant i.v. infusion of 0.002–0.006 µg/kg/min produced a mean plasma PGE₂ concentration of 95 pg/ml. Within 15 minutes after an oral dose, the plasma concentration reached a mean of 77 pg/ml, and at 45–60 minutes reached a maximal mean value of 130 pg/ml. The change in plasma PGE₂ concentration was accompanied in each case by the appropriate change in Sao₂ or Pao₂ (figs. 3 and 5). The dose response to oral PGE₂ was tested...
only in one patient in whom the maximal plasma concentration almost doubled when the dose was doubled (fig. 5).

**Clinical Observations and Adverse Effects**

The skin temperature followed the changes in $P_{aO_2}$ or $S_{aO_2}$ fairly closely. There were no significant changes in heart rate or blood pressure. Brief apneic spells occurred in three patients during i.v. therapy, but occurred in only one patient during oral therapy. Transient bradycardia accompanied the apnea. During i.v. therapy, two infants developed severe diarrhea that progressed to necrotizing enterocolitis in one. Both recovered after i.v. nutrition and continued i.v.

### Table 1. Clinical Summary

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (days)</th>
<th>Weight (kg)</th>
<th>Diagnosis</th>
<th>RPA diameter (mm)</th>
<th>Age (days)</th>
<th>Weight (kg)</th>
<th>RPA diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
<td>2.55</td>
<td>TGA, VSD, PA</td>
<td>2.5</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>1.2</td>
<td>2.34</td>
<td>PA, intact IVS</td>
<td>2.0</td>
<td>29</td>
<td>2.88</td>
<td>2.5</td>
</tr>
<tr>
<td>3</td>
<td>2.0</td>
<td>2.50</td>
<td>PA, VSD</td>
<td>3.0</td>
<td>75</td>
<td>4.12</td>
<td>6.0</td>
</tr>
<tr>
<td>4</td>
<td>1.5</td>
<td>2.96</td>
<td>PA, VSD</td>
<td>2.5</td>
<td>64</td>
<td>3.36</td>
<td>3.5</td>
</tr>
<tr>
<td>5</td>
<td>3.0</td>
<td>3.15</td>
<td>TA</td>
<td>3.5</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>6</td>
<td>3.0</td>
<td>3.05</td>
<td>PA, single V</td>
<td>3.0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>7</td>
<td>1.7</td>
<td>3.78</td>
<td>TA</td>
<td>3.0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>8</td>
<td>1.3</td>
<td>3.54</td>
<td>PA, single V</td>
<td>3.0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>9</td>
<td>5</td>
<td>2.92</td>
<td>PA, intact IVS</td>
<td>2.5</td>
<td>68</td>
<td>4.60</td>
<td>4.0</td>
</tr>
<tr>
<td>10</td>
<td>1.0</td>
<td>3.20</td>
<td>PA, VSD</td>
<td>4.0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>11</td>
<td>60</td>
<td>1.82</td>
<td>PA, intact IVS</td>
<td>3.0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>12</td>
<td>2.0</td>
<td>3.0</td>
<td>PA, TA</td>
<td>2.5</td>
<td>69</td>
<td>4.35</td>
<td>3.0</td>
</tr>
</tbody>
</table>

*Duration of therapy is given in parentheses.

Abbreviations: MPA = main pulmonary artery; RPA = right pulmonary artery; LPA = left pulmonary artery; IV = intravenous; TGA = transposition of the great arteries; VSD = ventricular septal defect; PA = pulmonary atresia; IVS = interventricular septum; TA = tricuspid atresia; V = ventricle; PDA = patent ductus arteriosus.

### Table 2. PGE2 Withdrawal Studies

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age at study (days)</th>
<th>PGE2 dose at study</th>
<th>Oxygen saturation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>µg/kg Frequency</td>
<td>Before dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>16</td>
<td>50</td>
<td>hourly</td>
</tr>
<tr>
<td>3</td>
<td>35</td>
<td>22</td>
<td>3-hourly</td>
</tr>
<tr>
<td>4</td>
<td>29</td>
<td>15</td>
<td>3-hourly</td>
</tr>
<tr>
<td>5</td>
<td>50</td>
<td>35</td>
<td>hourly</td>
</tr>
<tr>
<td>6</td>
<td>20 i.v.*</td>
<td>—</td>
<td>i.v.</td>
</tr>
<tr>
<td>7</td>
<td>6</td>
<td>33</td>
<td>hourly</td>
</tr>
<tr>
<td>8</td>
<td>30</td>
<td>35</td>
<td>hourly</td>
</tr>
<tr>
<td>11</td>
<td>81</td>
<td>50</td>
<td>2-hourly</td>
</tr>
<tr>
<td>12</td>
<td>71</td>
<td>29</td>
<td>2-hourly</td>
</tr>
</tbody>
</table>

*On i.v. infusion, 0.005 µg/kg/min.

Oxygen saturation values shown were those measured immediately before the last oral dose of PGE2 and at intervals after the dose or after discontinuation of i.v. infusion.
TABLE 1. (Continued)

<table>
<thead>
<tr>
<th>Age (days) at commencement of PGE2 therapy*</th>
<th>Complications of oral and i.v. therapy</th>
<th>Clinical course</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>Oral</td>
<td></td>
</tr>
<tr>
<td>6 (4)</td>
<td>12 (11)</td>
<td>i.v. — apnea, bradycardia</td>
</tr>
<tr>
<td>-</td>
<td>1 (30)</td>
<td>—</td>
</tr>
<tr>
<td>1 (18)</td>
<td>18 (69)</td>
<td>i.v. — apnea, necrotizing enterocolitis; Oral — apnea</td>
</tr>
<tr>
<td>1 (15)</td>
<td>16 (133)</td>
<td>i.v. — apnea, diarrhea</td>
</tr>
<tr>
<td>1 (1)</td>
<td>2 (5)</td>
<td>—</td>
</tr>
<tr>
<td>3 (16)</td>
<td>2 (1)</td>
<td>Oral — diarrhea</td>
</tr>
<tr>
<td>2 (1)</td>
<td>3 (21)</td>
<td>Oral — transient diarrhea</td>
</tr>
<tr>
<td>-</td>
<td>2 (48)</td>
<td>—</td>
</tr>
<tr>
<td>5 (1)</td>
<td>6 (76)</td>
<td>—</td>
</tr>
<tr>
<td>-</td>
<td>1 (8)</td>
<td>Oral — transient diarrhea</td>
</tr>
<tr>
<td>-</td>
<td>60 (59)</td>
<td>Oral — transient diarrhea</td>
</tr>
<tr>
<td>-</td>
<td>2 (116)</td>
<td>—</td>
</tr>
</tbody>
</table>

PGE2 at a lower dose. Four infants developed diarrhea while on oral PGE2. In three it was transient and improved when the dose was reduced, but in one infant it was severe, necessitating a period of i.v. therapy.

Outcome

The outcome of each case is shown in table 1. In five patients who were recatheterized, growth of the pulmonary arteries had occurred.

Discussion

PGE1 and PGE2 infusions have significantly improved the management of neonates whose pulmonary blood flow is dependent on patency of the ductus arteriosus. It has been suggested that the preferred route of administration is via an umbilical artery catheter, positioned immediately proximal to the aortic end of the ductus arteriosus, but there is little evidence that i.v. infusion is any less effective. Both routes of administration have practical limitations and a significant incidence of side effects. Consequently, infusions of PGE have almost always been used for short periods only. However, we found that PGE2 was easier to administer orally and continued to be effective for months. When side effects occurred, they could usually be eliminated or their severity could be reduced by decreasing the dosage. Operations could

TABLE 3. Plasma PGE2 Concentration During Therapy

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (days)</th>
<th>Dose (µg/kg/min)</th>
<th>Plasma PGE2 concentration (pg/ml)</th>
<th>Age (days)</th>
<th>Dose (µg/kg)</th>
<th>Plasma PGE2 concentration (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2'</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>16</td>
<td>50</td>
<td>93</td>
</tr>
<tr>
<td>3</td>
<td>18</td>
<td>0.002</td>
<td>82</td>
<td>35</td>
<td>23</td>
<td>18</td>
</tr>
<tr>
<td>4</td>
<td>16</td>
<td>0.003</td>
<td>45</td>
<td>35</td>
<td>45</td>
<td>25</td>
</tr>
<tr>
<td>6</td>
<td>19</td>
<td>0.006</td>
<td>33</td>
<td>30</td>
<td>35</td>
<td>70</td>
</tr>
<tr>
<td>7</td>
<td>20</td>
<td>0.005</td>
<td>220</td>
<td>19</td>
<td>40</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td></td>
<td>95</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

± SD = 86  ± 33 = 78  ± 89
be postponed while the infants and their pulmonary arteries grew, with consequent decrease in operative risk. The pulmonary arteries were initially considered to be too small for successful anastomotic operations in six of our 12 patients. All 12 patients gained weight during treatment with oral PGE₂ for 1-5 months and those who were recatheterized had objective evidence of increased pulmonary arterial size.

The effectiveness of orally administered PGE₂ in relaxing the ductus was demonstrated both by clinical improvement and by an increase in arterial oxygen content. The appreciable increase in plasma concentration of PGE₂ within 15-30 minutes after an oral dose implies rapid absorption. An hourly oral dose of 30-45 µg/kg resulted in a plasma PGE₂ concentration comparable to that achieved by a continuous i.v. infusion. Although doses at 1-2-hour intervals may seem problematic, the ease of administration to the awake or sleeping baby surprised even the most skeptical.

Some of our planned studies were designed to determine the minimal requirements of PGE₂ in terms of dosage frequency. Arterial oxygen tensions and saturations usually decreased to unacceptable levels if oral PGE₂ was administered less frequently than every 2 hours during the first few weeks of therapy, but there were exceptions (fig. 5). Perhaps this difficulty may be overcome by developing less rapidly metabolized derivatives of PGE₂ or by a slow-release preparation.

None of our patients required an increased dose of PGE₂ as time progressed. In fact, we could usually reduce the dose, but in no case could we stop the drug before surgery. Even after many months of responding to therapy, the ductus seemed to retain its preference to constrict when PGE₂ was withdrawn for a matter of hours. In the one patient in whom the SaO₂ had been allowed to remain at 40-50% for 2 hours, subsequent reintroduction of PGE₂ resulted in slower improvement. This observation suggests that the degree of constriction of the ductus may determine its responsiveness to PGE₂ therapy. Indeed, Olley et al.¹⁴

---

**Figure 1.** Pre-dose and maximal arterial oxygen saturation (SaO₂) values in 11 infants given an oral dose of PGE₂ and in four during an i.v. infusion. After oral PGE₂, mean SaO₂ increased by 18%, from 57 ± 3% to 75 ± 2% (SEM) (p < 0.01). Maximal SaO₂ values after an oral dose were not significantly different from values during i.v. infusion.

**Figure 2.** PGE₂ withdrawal studies in eight infants (10 studies) showing changes in arterial oxygen saturation (SaO₂). Measurements at time 0 were made immediately before the last dose of PGE₂. Subsequent measurements were made at intervals after the last dose or (in case 6) after discontinuation of i.v. infusions. In each case, SaO₂ increased soon after an oral dose, then decreased over a period of hours. A logarithmic scale is used to indicate time.

**Figure 3.** Arterial oxygen saturation (SaO₂) and plasma PGE₂ concentration in an infant given i.v. and oral PGE₂. Three hours after discontinuation of i.v. infusion, oral PGE₂ was given hourly (doses as shown). Both SaO₂ and plasma PGE₂ increased within 15 minutes of the first oral dose.
suggested that when the ductus arteriosus is fully closed, it no longer responds to PGE.

Complications of oral therapy were only seen early in the course of treatment. Four of 12 patients developed diarrhea during oral therapy, but it was usually transient and was simply and effectively managed by dose reduction in three patients, although one patient required prolonged i.v. infusion. When diarrhea occurred during i.v. therapy in two infants, it was more severe and progressed to necrotizing enterocolitis in one of them. Dose-related apnea occurred transiently in one infant during oral therapy but occurred in three patients during i.v. infusions. None of our patients suffered from hypotension, bradycardia, pyrexia or muscle twitching, which are commonly associated with i.v. therapy. Increase in skin temperature to normal values was probably a result of improved cardiac output rather than of the systemic vasodilator effect of PGE because the increase in skin temperature was not associated with systemic hypotension. Thus, the incidence of adverse effects during i.v. and oral PGE therapy was similar, but the side effects associated with oral therapy were less problematic and could usually be managed by dose reduction.

In the early part of our study we usually commenced treatment with an i.v. infusion of PGE and found that a dose as low as 0.002–0.006 μg/kg/min was usually effective. This is less than 10% of the generally recommended dosage. Because we showed that a similar clinical response was obtained by oral therapy, we now reserve i.v. therapy for infants who develop diarrhea that does not respond to a decreased oral dose.

We recommend an initial oral regimen of 30–45 μg/kg/hour. If there has been no significant response within 2 hours, the dose should be increased to a maximum of 65 μg/kg/hour. After a few hours, it may again be possible to reduce the hourly dose. For the first 2 weeks of oral PGE therapy, hourly doses of 30–45 μg/kg are usually necessary. For practical reasons, we have tried to reduce the frequency rather than the size of the doses, but with little success in patients younger than age 3 weeks. It is always a matter of trial, preferably with the aid of repeated arterial oxygen measurements.

Oral administration of PGE proved effective for both short- and long-term therapy. The chief indication for long-term therapy is probably to ensure that the baby becomes a better surgical candidate, and this was indeed achieved. Our study has also provided new information concerning the response of the ductus to PGE over a period of many months. Our success in these cases has prompted us to extend the use of long-term oral PGE therapy to include infants with other complex congenital heart anomalies in which ductus patency is beneficial.
Acknowledgment
The authors thank Professor A. C. Turnbull, Nuffield Department of Obstetrics and Gynaecology, University of Oxford, for departmental facilities for PGE₂ estimations.

References
Oral prostaglandin E2 in ductus-dependent pulmonary circulation.

Circulation. 1981;63:682-688
doi: 10.1161/01.CIR.63.3.682

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1981 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on
the World Wide Web at:
http://circ.ahajournals.org/content/63/3/682