Production of Increased Right-to-Left Shunting by Rapid Heart Rates in Patients with Tetralogy of Fallot

By Spencer B. King, M.D., and Robert H. Franch, M.D.

SUMMARY
A patient with tetralogy of Fallot who developed cyanosis and tachypnea during spontaneous attacks of paroxysmal atrial tachycardia had an increase in right-to-left shunting with a fall in arterial oxygen saturation from 96 to 43%. Duplication of the fast heart rate by atropine and atrial pacing reproduced these hemodynamic changes, while slowing the rate with propranolol reversed this effect. Subsequently, six patients with mild tetralogy of Fallot underwent rapid atrial pacing during cardiac catheterization. This primary increase in heart rate resulted in a fall in systemic oxygen saturation, an increase in percent right-to-left shunt, and an increase in the right ventricular outflow pressure gradient. These data suggest that further narrowing of the right ventricular infundibulum may occur during tachycardia. This experience indicates that paroxysmal atrial tachycardia should be added to the conditions that can cause increased cyanosis in some patients with tetralogy of Fallot. Other tachycardias may also augment right-to-left shunting.

Additional Indexing Words: Paroxysmal atrial tachycardia Atrial pacing Propranolol Atropine

The relationship of primary increases in heart rate to increasing cyanosis in tetralogy of Fallot has not been emphasized. This communication reports a patient with tetralogy of Fallot who had cyanosis and tachypnea precipitated by paroxysmal atrial tachycardia (PAT) occurring during cardiac catheterization. Subsequently, six patients with acyanotic or mild tetralogy of Fallot underwent atrial pacing in order that we might determine if right-to-left shunting increased as a result of a primary increase in the heart rate and, if it did, that we might elucidate the factors responsible for the increased cyanosis.

From Emory University Hospital Cardiac Catheterization Laboratory, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia.
Address for reprints: Dr. Franch, 401 Woodruff Building, Emory University Campus, Atlanta, Georgia 30322.
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Methods
Six children, age 7 months to 5 years, were referred for evaluation. Symptoms included easy tiring (patients 2, 4, and 5), squatting (patient 3), and cyanotic spells (patients 1 and 6). These patients were referred from a clinic population with generally poor dietary and maternal iron stores. Patient 6 was under treatment for marked iron-deficiency anemia. Patient 3 was significantly polycythemic, with a resting arterial saturation of 81%; the others were normocytic, had resting arterial oxygen saturations of 92% or greater (table 1), and were on oral iron therapy. Cardiac catheterization was done, with a mixture of Demerol-Phenergan-Thorazine (meperidine-promethazine-chlorpromazine) as sedation. The catheters were inserted via a cutdown into the median cubital or saphenous veins. Atrial pacing was done with a standard bipolar catheter with the tip in the area of the superior vena cava-right atrial junction or along the lateral right atrial wall with a DC variable-rate pacemaker. Pressures were measured with a Statham P23Db strain gauge and recorded on an Electronics for Medicine recorder. Pressure gradients were measured by pulling a no. 5 or 6 French thin-walled catheter with end and side holes from the main
### Table 1

Summary of Data on Six Cases with Tetralogy of Fallot

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Hematocrit %</th>
<th>Rhythm</th>
<th>Rate (beats/min)</th>
<th>O₂ saturation (%)</th>
<th>Systolic pressure (mm Hg)</th>
<th>Outflow gradient RV-PA (mm Hg)</th>
<th>Right-to-left shunting of systemic flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7 months</td>
<td>41</td>
<td>NSR</td>
<td>108</td>
<td>96</td>
<td>51</td>
<td>98</td>
<td>0</td>
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<tr>
<td></td>
<td></td>
<td>13.2</td>
<td>PAT</td>
<td>170</td>
<td>42</td>
<td>23</td>
<td>25</td>
<td>100</td>
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<tr>
<td>17 months</td>
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<td>NSR</td>
<td>110</td>
<td>92</td>
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<td>65</td>
<td>81</td>
<td>15</td>
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<tr>
<td></td>
<td></td>
<td>15.6</td>
<td>Paced</td>
<td>170</td>
<td>46</td>
<td>37</td>
<td>13</td>
<td>108</td>
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<tr>
<td>2</td>
<td>4 yr</td>
<td>40</td>
<td>NSR</td>
<td>100</td>
<td>95</td>
<td>83</td>
<td>73</td>
<td>110</td>
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<tr>
<td></td>
<td></td>
<td>12.3</td>
<td>Paced</td>
<td>150</td>
<td>84</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>3</td>
<td>11 yr</td>
<td>61</td>
<td>NSR</td>
<td>108</td>
<td>81</td>
<td>66</td>
<td>62</td>
<td>87</td>
</tr>
<tr>
<td></td>
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<td>66</td>
<td>48</td>
<td>48</td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>5 yr</td>
<td>40</td>
<td>NSR</td>
<td>90</td>
<td>97</td>
<td>82</td>
<td>75</td>
<td>97</td>
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<tr>
<td></td>
<td></td>
<td>12.9</td>
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<td>150</td>
<td>84</td>
<td>69</td>
<td>63</td>
<td>92</td>
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<tr>
<td>5</td>
<td>5 yr</td>
<td>39</td>
<td>NSR</td>
<td>118</td>
<td>98</td>
<td>83</td>
<td>77</td>
<td>95</td>
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<td></td>
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<td>NSR</td>
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<td>58</td>
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<td>160</td>
<td>59</td>
<td>43</td>
<td>43</td>
<td>82</td>
</tr>
</tbody>
</table>

Abbreviations: Hbg = hemoglobin; PA = pulmonary artery; RV = right ventricle; NSR = normal sinus rhythm; PAT = paroxysmal atrial tachycardia.
INCREASED RIGHT-TO-LEFT SHUNTING

pulmonary artery to the right ventricle. Oxygen saturations were measured on a Beckman DU spectrophotometer. The percent right-to-left shunt was calculated by substitution of the mixed venous (MV) and systemic artery (SA) blood oxygen saturations into the formula:

$$\frac{PVO_2 - SAO_2}{PVO_2 - MVO_2} \times 100 = \text{Right-to-left shunt (as percent of systemic flow)}$$

The pulmonary venous (PV) saturation is an assumed constant of 97%. Pulmonary venous blood samples obtained at catheterization via a foramen ovale in sedated patients with tetralogy of Fallot in our laboratory have shown an oxygen saturation in the normal range. When the heart rate changed from sinus rhythm to PAT or to atrial pacing, blood samples were obtained after a 3-5-min interval. Selective right ventricular cineangiography confirmed the presence of infundibular stenosis and a ventricular septal defect in all cases.

Paroxysmal Atrial Tachycardia and Cyanosis

The patient was a 7-month-old, 18 pound, female infant who was not cyanotic at rest. The pregnancy had been uncomplicated, and no abnormalities were noted at the time of delivery. At 4 months cyanotic tachypneic episodes of several minutes' to several hours' duration developed with feedings and at other times without apparent precipitating causes. On physical examination there was a grade 3/6 ejection systolic murmur along the left sternal border and a single second heart sound. The liver edge was palpated 2 cm below the right costal margin. The hemoglobin was 13.2 g/100 ml. Electrocardiography showed normal sinus rhythm and slight right ventricular hypertrophy, and the chest X-rays revealed no cardiomegaly and normal pulmonary vascularity. At the time of catheterization several episodes of PAT lasting up to 15 min occurred. During these arrhythmias the child was deeply cyanotic and tachypneic. Cyanosis would clear promptly when normal sinus rhythm was reestablished usually by an induced premature ventricular contraction. Systemic oxygen saturation, which was 96% during normal sinus rhythm, dropped to 42% when PAT began (table 1, patient 1). Systemic arterial blood pressure remained

Figure 1

16 mm cineangiographic frames in the anteroposterior position were obtained in patient 1, following the injection by hand of 6 ml (0.3 ml/lb) of a 1:1 sodium and meglumine diatrizoate mixture via a catheter in the right atrium. No side effects were noted. (A) During normal sinus rhythm with a rate of 108 beats/min. (B) During paroxysmal atrial tachycardia with a rate of 170 beats/min. Note the marked reduction in pulmonary artery opacification and the increase in right-to-left shunting during PAT.
unchanged. Pulmonary artery opacification, as shown by selective right atrial cineangiography (fig. 1), was dramatically reduced during PAT, while aortic opacification and percent right-to-left shunting were greatly increased.

For several days after the catheterization procedure, periods of deep cyanosis and tachypnea were observed. Each time PAT occurred the patient became cyanotic, and when normal sinus rhythm was reestablished, the cyanosis would clear.

PAT was diagnosed on the basis of sudden onset of a very regular rhythm at 170 beats/min during catheter manipulation in the atrium, failure of the P-R interval to shorten with tachycardia, and sudden breaks to normal sinus rhythm after premature ventricular contractions. Digoxin, 0.18 mg, was given intravenously, followed by 0.05 mg digoxin by mouth every 12 hr for the next 14 days. The arrhythmia was not controlled, and propranolol, 1 mg every 6 hr, was added. This was increased to a dose of 3 mg every 6 hr with control of the arrhythmia and the cyanosis and tachypnea. After being free of cyanosis for 6 months, the patient redeveloped cyanotic tachypneic episodes even in the absence of PAT.

Ten months after the first study she was again catheterized, and the data found are in table 1 (patient 1). No PAT developed during the procedure, but either rapid atrial pacing at 170 beats/min or acceleration to an identical rate with atropine produced a similar fall in arterial oxygen saturation and an increase in right-to-left shunting, as found previously with PAT. After administration of atropine, the heart rate continued to increase to 184 beats/min, and the aortic oxygen saturation dropped to 43%. Administration of 0.4 mg propranolol resulted in a decrease in heart rate to 133 beats/min and an increase in aortic oxygen saturation to 80%. The next day a Brock procedure was performed. After the right ventricular infundibulum was surgically

\[ \text{Aortic O}_2 \text{ Saturation (\%)} \]

<table>
<thead>
<tr>
<th>NSR</th>
<th>PACED</th>
</tr>
</thead>
<tbody>
<tr>
<td>90</td>
<td>50</td>
</tr>
<tr>
<td>80</td>
<td>70</td>
</tr>
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<td>70</td>
<td>60</td>
</tr>
<tr>
<td>60</td>
<td>50</td>
</tr>
</tbody>
</table>

**Figure 2**

Rapid atrial pacing resulted in a fall in aortic oxygen saturation in all patients.

**Figure 3**

Rapid atrial pacing increased the right-to-left shunt, expressed as percent of systemic flow.
enlarged, a sinus tachycardia of 180 beats/min produced no clinical cyanosis, and the child has remained free of cyanosis with no medication.

Atrial Pacing Studies

In order that we might establish whether increased heart rates produce an increase in right-to-left shunting, this child (patient 1) and five other children (patients 2 to 6) with acyanotic or mild tetralogy of Fallot underwent atrial pacing at a rate of 150 to 170 beats/min, thus simulating PAT (table 1). In all the patients, aortic oxygen saturation fell during rapid atrial pacing (mean, 19%) (fig. 2). The percent right-to-left shunt also increased in each case (fig. 3). Systolic and mean arterial pressures did not change appreciably (table 1). In the five patients in whom it could be measured, the right ventricular outflow-PA pressure gradient during pacing remained unchanged (one patient) or increased (four patients; mean, 14 mm Hg) (fig. 4). This occurred in spite of the marked increase in right-to-left shunting with a postulated fall in main pulmonary flow and a fall in the stroke volume from the right ventricle into the main pulmonary artery.

Discussion

The increase in the percent right-to-left shunt and the fall in arterial oxygen saturation during PAT and pacing were accompanied by a marked decrease in pulmonary artery opacification following selective right atrial angiography. Several explanations may be proposed to account for the shunting of blood away from the lungs. An unlikely factor is a primary decrease in systemic resistance. Although the systemic resistance was not accurately measured, the aortic systolic and mean pressures did not change on continuous pressure recording during onset of pacing, and right ventricular pressure remained the same or increased. It has also been shown that normal adult subjects exhibit no change in cardiac output or systemic resistance with PAT or rapid atrial pacingcompared to normal sinus rhythm. One normal child whom we paced showed no fall in mean arterial blood pressure or calculated systemic resistance. Atrial pacing then presumably produced a change in heart rate independent of any major change in systemic resistance in our patients.

Perhaps a more plausible explanation for the increase in percent right-to-left shunt during tachycardia is an increasing infundibular stenosis. If a decrease in main pulmonary artery blood flow and a decrease in right ventricular stroke volume across the stenotic region are postulated, then the increase in the gradient between the right ventricle and the pulmonary artery shown is most likely to be related to a decrease in the orifice across which the gradient is measured. The infundibular stenosis should increase in order to
maintain or increase the gradient at a time when the percent right-to-left shunt is increasing and the main pulmonary artery
blood flow is decreasing. In five of our
patients in whom the pulmonary artery pressure could be obtained during pacing, the
gradient between the right ventricle and the
pulmonary artery increased in four and was
unchanged in one at a time when the percent
right-to-left shunt was increasing and selective
right atrial cineangiography showed a de-
crease in pulmonary artery opacification. Glick
et al.5 and Sonnenblick et al.6 have shown in
normal subjects that the right ventricle gets
smaller during rapid atrial pacing due to a
shortened diastolic filling period. It is, there-
fore, not surprising that the narrowed outflow
tract of the right ventricle in tetralogy of
Fallot becomes even more stenotic during
rapid atrial pacing. Mason et al.7 increased the
left ventricular outflow pressure gradient in
patients with hypertrophic subaortic stenosis by
giving atropine. They postulated that the
increased heart rate was associated with a
decrease in left ventricular volume, thus
reducing the effective outflow orifice.7 Im-
proved contractile state of the myocardium
and splanchnic venous pooling may also
contribute to intensification of the outflow
obstruction.7

The interesting pressure flow-dynamics in
tetralogy of Fallot studied by Levin et al.8
have not been applied during arrhythmias or
pacing. What effect, if any, the prolonged P-R
interval and resulting fusion of the a and v
waves during atrial pacing has on differential
ventricular filling also has not been studied.
Other mechanisms that increase cyanosis, such
as a primary drop in systemic resistance,9 fall
in systemic venous return without change in
pulmonary-to-systemic flow ratios,10,11 and
increase in systemic venous flow during
exercise with a relatively fixed pulmonary
flow,12 do not seem to account for the
increased right-to-left shunting demonstrated
during these tachycardias. Rather it is postu-
lated that in some patients with tetralogy of
Fallot a rapid heart rate induced by sponta-
neous PAT, rapid atrial pacing, atropine, or
other causes may increase the right ventricular
outflow obstruction so that right-to-left shunt-
ing will be enhanced.

The recent descriptions of the prevention of
cyanotic tachypneic episodes13-16 with pro-
pranolol may be related to one or more of
these mechanisms: (a) beta-adrenergic re-
ceptor blocking effect which prevents in-
creased myocardial contractility and resulting
infundibular narrowing, (b) anti-arrhythmic
effect which prevents supraventricular ar-
rythmias, or (c) simply the prevention of
the development of sinus tachycardia with the
resulting decrease in right ventricular size and
infundibular narrowing. The effect of increas-
ing systemic resistance and the sedative effect
of propranolol may also play a role. Proprano-
lol was quite helpful in patient 1, whose
cineangiogram demonstrated variable right-to-
left shunting dependent on heart rate (fig. 1).
Atrial pacing or other methods of increasing
the heart rate may help identify patients who
would be benefitted by propranolol. Previous
studies have suggested that these patients will
most likely have histories of mild cyanosis and
clear-cut hypercyanotic episodes.13,14

This experience indicates that PAT should
be added to the list of conditions that can
increase right-to-left shunting and cyanosis in
some patients with tetralogy of Fallot. The
increased right-to-left shunting associated
with tachycardia appears to be caused by an
increasing infundibular stenosis. An increase
in heart rate from any cause may augment
right-to-left shunting.

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SPENCER B. KING and ROBERT H. FRANCH

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