Chapter 7

Tetralogy of Fallot

Matthew P. Monteleone

Case Scenario

A 6-week-old, former 32-week preterm infant weighing 3.2 kg presents with a history of vomiting and lethargy for urgent ventriculoperitoneal shunt revision. He is followed by cardiology for unrepaired tetralogy of Fallot. Noncardiac history is remarkable for a 4-week stay in the neonatal intensive care unit for respiratory and nutritional support and placement of a ventriculoperitoneal shunt to treat obstructive hydrocephalus related to a perinatal intraventricular hemorrhage. He was discharged two weeks ago on full oral feeds and no respiratory support. His only current medication is cholecalciferol.

Parents report that no hypercyanotic spells or "tet spells" have been noted at home. Elective cardiac surgical repair is planned in the next several months. The infant has not had anything by mouth in over 12 hours and is receiving maintenance fluids with dextrose through a 24-gauge peripheral intravenous line.

On physical examination vital signs are SpO_2 93% on room air, heart rate 155 beats/minute, blood pressure 71/40 mm Hg, respiratory rate 38 breaths/minute, and temperature 36.8°C. The infant is sleepy but arousable and cries appropriately.

The most recent echo shows the following:

- *Severe right ventricular outflow tract obstruction, peak gradient 80 mm Hg by continuous wave Doppler; turbulence begins below the pulmonic valve with the main gradient at the valvular level*
- *Large anterior malalignment ventricular septal defect present with bidirectional shunting*
- *Patent foramen ovale with predominantly left-to-right flow*
- *Normal biventricular systolic function*

Key Objectives

- Describe the classic anatomy of tetralogy of Fallot.
- Identify typical physical examination and diagnostic test findings associated with tetralogy of Fallot.
- Understand the pathophysiology and treatment options for a hypercyanotic or "tet" spell.
- Understand considerations for the anesthetic perioperative care for the patient with uncorrected tetralogy of Fallot.

Pathophysiology

Who was Fallot and what is the history of the discovery and treatment of this lesion?

Tetralogy of Fallot (TOF) was first described in 1671 by Niels Stensen. The syndrome was eventually named for Etienne Fallot, who published the classic description in 1888 based on autopsy-confirmed diagnoses. Tetralogy of Fallot is the most common form of cyanotic heart disease and represents up to 10% of all congenital heart defects. It was first palliated surgically with a systemic-to-pulmonary artery shunt in 1944 by Blalock, Taussig, and Thomas. The first complete repair was reported by Lillehei in 1954; in the current era most cases are repaired within the first 6 months of life.

Clinical Pearl

Tetralogy of Fallot is the most common form of cyanotic heart disease and represents about 10% of all congenital heart defects.

What are the four defects present in classic TOF?

Tetralogy of Fallot with pulmonary stenosis (TOF/PS) is generally thought of as classic TOF. Although TOF is one of the most successfully repaired cardiac lesions, if left unrepaired, mortality in the first several years of life can approach 50%.

Although variants exist, classic TOF consists of a large, nonrestrictive ventricular septal defect (VSD), right ventricular outflow tract obstruction (RVOTO), an overriding

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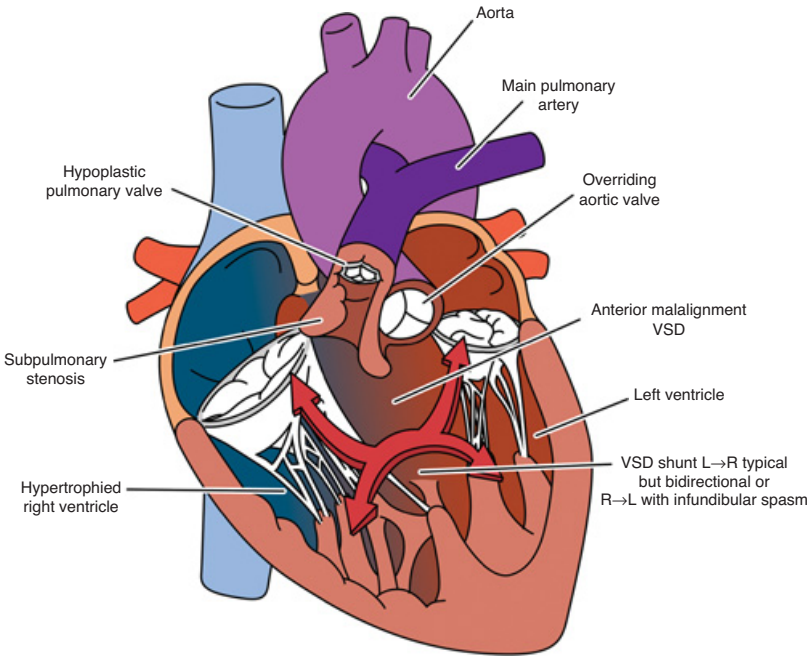

Figure 7.1 Tetralogy of Fallot. Drawing by Ryan Moore, MD, and Matt Nelson.

aorta, and right ventricular hypertrophy (RVH). Although named for Etienne Fallot, it was Maude Abbott in 1924 who first labeled the four classic findings as *tetralogy of Fallot*. (See Figure 7.1.)

What is meant by an "overriding aorta"?

Aortic override is created by the malalignment of the infundibular and ventricular septum. Essentially, part of the aortic valve exists on the right side of the septal plane. The aortic valve, therefore, "overrides" the interventricular septum and VSD.

What are the characteristics of the VSD in TOF?

Understanding the characteristics of the VSD in TOF is essential in order to appreciate the pathophysiology of this lesion. The VSD is large and perimembranous, often similar in diameter to the aortic annulus. This means that it is typically nonrestrictive or unrestrictive, with equal right and left ventricular pressures. The amount and direction of shunting are therefore dependent on the balance between the resistance to pulmonary blood flow, which is dependent on the degree of RVOT obstruction, and systemic vascular resistance (SVR). In contrast, a restrictive VSD is generally small and has a pressure gradient across the defect; flow is determined by the size of the VSD.

What is meant by RVOTO and what variations exist?

Right ventricular outflow tract obstruction is a key feature of TOF; the extent of obstruction can be variable, with obstruction at the valvular, subvalvular, or pulmonary artery level. The pulmonary valve is often thickened and dysplastic with some degree of hypoplasia. There is compensatory RVH as a consequence of the RVOTO. Obstruction can also exist at multiple levels and may be ***fixed and/or dynamic*** in nature. Fixed components occur at the valvular and supravalvular levels while dynamic components can exist due to the hypertrophied RV infundibulum and muscle bundles. Echocardiography can estimate the pressure gradient across the right ventricular outflow tract (RVOT), describe the anatomic level of obstruction and may delineate whether a dynamic obstructive component is present. Patients with a larger dynamic component of RVOTO are more likely to experience frequent tet spells during crying or agitation and may be treated with ß-blockers to decrease heart rate and contractility.

Clinical Pearl

The extent of RVOTO can be variable in TOF, with obstruction at the valvular, subvalvular, and/or pulmonary artery level that can be fixed and/or dynamic. The variable degrees of outflow tract obstruction account for the varying levels of symptomatology experienced by different patients.

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Are other important cardiac lesions or abnormalities associated with TOF?

Approximately 25% of patients with TOF will also have a right-sided aortic arch (RAA) with mirror-image branching of the head and neck vessels. The origin of the subclavian artery may also be aberrant, with either the right subclavian artery arising from the descending aorta or the left subclavian artery arising from the pulmonary artery. Subclavian artery anatomy is important to consider when determining the optimal placement of an arterial line. Coronary abnormalities are also present in 5%–12% of TOF patients, with the most common anomaly being origination of the left anterior descending artery from the right coronary artery, crossing the RVOT/infundibular surface.

Patients with TOF may also have an atrial septal defect (ASD) or patent foramen ovale (PFO); when this finding is present the syndrome may be referred to as ***pentalogy of Fallot***. Other associated lesions can include anomalous pulmonary venous drainage, left-sided superior vena cava, interrupted inferior vena cava, patent ductus arteriosus (PDA), a bicuspid pulmonary valve (PV), and pulmonary artery stenosis. All imaging and cardiac catheterization studies should be reviewed completely in the preanesthetic period for the presence of other associated anomalies.

Approximately 25% of patients with TOF will also have chromosomal abnormalities, most commonly trisomy 21 and chromosome 22q11.2 microdeletions. In these patient subsets the anesthesiologist must be alert for craniofacial abnormalities, immune deficiencies, hypocalcemia, and other conditions associated with genetic syndromes.

Clinical Pearl

The presence and significance of an aberrant subclavian artery should be noted, particularly when considering placement of an arterial line.

Are there other anatomic variations of TOF?

There are several important variants of TOF involving variations in pulmonary valve and pulmonary artery anatomy.

Tetralogy of Fallot/PS Stenosis of the RVOT, PV, and main pulmonary artery exists; the PV is often bicuspid and may be dysplastic.

Tetralogy of Fallot/Pulmonary Atresia (PA) Pulmonary atresia is present, along with variable hypoplasia of the main pulmonary artery. Depending on the nomenclature used, the term tetralogy of Fallot may be completely dropped and the patient's disease referred to as PA/VSD. Pulmonary artery anatomy may be complex and varies widely from patient to patient. The central pulmonary arteries may or may not be confluent, and pulmonary blood flow (PBF) may be dependent on flow supplied by a PDA. Alternatively, the patient may carry the description of TOF/PA/major aortopulmonary collateral arteries (MAPCAs); in this disease the spectrum may include a lack of central confluent pulmonary arteries and PBF may be augmented or supplied by large collaterals from the aorta. There is a wide spectrum of anatomic variants with this type of disease. (See Chapter 10.)

Tetralogy of Fallot/Absent Pulmonary Valve (APV) These patients typically have enlarged main and branch pulmonary arteries; there is often compression of the airway and resultant development of tracheobronchomalacia. The child may require mechanical ventilation, high levels of positive end expiratory pressure and even prone positioning to keep the airways open. In less severe cases, airways may remain open on moderate ventilator settings, but obstruction can occur when a transesophageal echocardiography probe or other esophageal device is placed. (See Chapter 9.)

What occurs during a "tet spell"?

A "tet" or hypercyanotic spell is a sudden and significant increase in the degree of RVOTO, with the resultant decrease in PBF resulting in a significant drop in the child's hemoglobin–oxygen saturation. The degree of RVOTO is the primary driver in determining the severity of spells. Deoxygenated systemic venous return from the body to the right side of the heart will be shunted across the VSD (R-to-L) if RVOTO significantly increases or SVR abruptly falls so that right-sided ventricular pressures are greater than left-sided pressures. While these spells may occur spontaneously, hypovolemia, acidosis, hypoxia, and/or RV infundibulum spasm with resultant increased RVOTO are among the usual contributing causes. Infundibular spasm results from increased sympathetic activity, tachycardia, and increased cardiac contractility. Agitation and pain are usual triggers. The cycle of hypoxia and acidosis can make the spell perpetuate and worsen; immediate treatment is indicated.

Clinical Pearl

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What is meant by a "pink tet"?

As with many congenital cardiac lesions, there is a spectrum of disease severity in TOF. A "pink tet" is a child with minimal RVOTO who generally has normal systemic oxygen saturations. The active physiology is similar to an unrestrictive VSD; they may have pulmonary overcirculation from excessive flow across the VSD and signs of congestive heart failure.

Clinical Pearl

The term "pink tet" describes a child with minimal RVOTO who generally has normal systemic oxygen saturations.

How and when is TOF with PS usually repaired?

All patients with TOF will require intervention at some time, but the optimal timing for surgery remains a matter of debate. Most centers advocate total repair in infancy unless specific anatomic features preclude this. Patients with significant RVOTO may require the placement of a systemic-to-pulmonary artery shunt prior to definitive repair. The goals of surgical repair are to close existing septal defects, to provide a patent and competent RVOT, and if necessary, to correct branch pulmonary artery stenosis. (See Figure 7.2.)

Anesthetic Implications

What diagnostic tests should be reviewed prior to anesthetizing a patient with TOF?

The ***echocardiogram*** is the highest-yield study. It should describe intracardiac anatomy, aortic arch pattern, presence or absence of a PDA, and relevant coronary artery anatomy. The VSD and infundibular septum can be visualized, and blood flow across the RVOT can be imaged (with Doppler) to assess the degree of RVOTO. Finally, pulmonary artery anatomy can be examined should the child have a TOF variant.

A ***cardiac catheterization*** report, if available, should be reviewed. However, cardiac catheterization is generally not routinely performed for TOF patients unless there is a desire for angiographic imaging or invasive assessments (e.g., the child with MAPCAs). Likewise, computed tomography and magnetic resonance imaging studies, if available, are certainly helpful in defining anatomy.

An ***electrocardiogram*** (***ECG***) will be consistent with the amount of RVH, showing right axis deviation and upright and peaked T waves in the right precordial leads.

Chest radiography may show the classic "boot-shaped" heart. Right ventricular hypertrophy results in an upturned cardiac apex and the shadow of the main pulmonary artery appears smaller, leading to the classic boot shape.

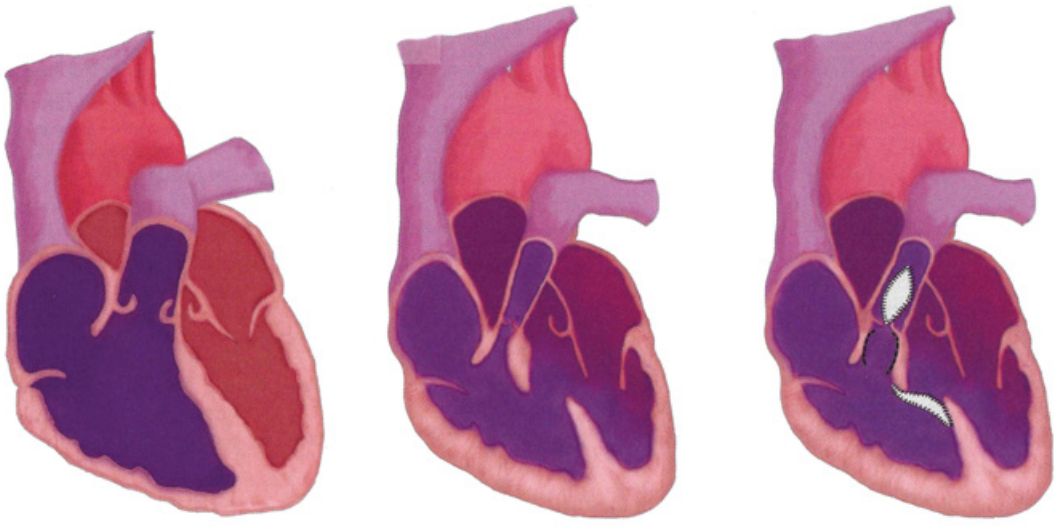

Figure 7.2 Schematic illustration of tetralogy of Fallot. (A) Normal heart. (B) Tetralogy of Fallot illustrating infundibular stenosis, ventricular septal defect (VSD), overriding aorta, and right ventricular hypertrophy. (C) Surgically repaired heart showing resection of obstructing muscle in the right ventricular outflow tract, patch closure of the VSD, and patch arterioplasty used to widen the main pulmonary artery at and/or above the pulmonary valve. From M. L. Schmitz M. L., Ullah S., Dasgupta R., et al. Anesthesia for right-sided obstructive lesions. In Andropoulos D. B., Stayer S., Mossad E. B., et al., eds. *Anesthesia for Congenital Heart Surgery*, 3rd ed. John Wiley & Sons; 2015: 516–41. With permission.

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Review of a recent complete blood count with ***hemoglobin and hematocrit*** is useful. A higher than normal hematocrit is indicative of more frequent cyanotic spells.

Clinical Pearl

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What questions are important during the preoperative assessment?

Inquiries should be made regarding cardiac symptomatology, specifically tet spells: have they been observed by the parents, and if so, how frequently? The parents should also be asked about any ongoing issues related to prematurity, including respiratory issues, apneic events, and recent exposure to illnesses. As the infant in this case scenario has been vomiting, it would be prudent to ask about recent wet diapers and the presence of tears in order to assess the state of hydration.

What remarkable physical examination findings may be observed in a TOF patient?

A child with TOF and a stenotic RVOT will have a harsh systolic ejection murmur heard best over the left upper sternal border. In fact, if there is no murmur, there should be concern for decreased flow across the RVOT. This could occur during a tet spell or in the child with pulmonary atresia. The child with a PDA or MAPCAs may also have a continuous murmur.

Clinical Pearl

A child with TOF and a stenotic RVOT generally has a harsh systolic ejection murmur; if no murmur is auscultated there should be concern for decreased flow across the RVOT.

Should a peripheral intravenous line be placed before induction? What options are available for induction?

When planning anesthetic induction in the patient with TOF without preexisting peripheral intravenous (PIV) access one should consider the risk of decreasing SVR with inhalational agents versus the challenge and sympathetic stimulation of awake PIV placement. This risk/benefit calculation is best made in patient specific context, considering the degree of RVOTO, degree of hydration, difficulty of IV placement, and other patient or anesthetic considerations. As the spectrum of disease severity can vary widely in patients with TOF, not all unrepaired TOF patients necessarily require placement of a PIV prior to induction of anesthesia. In fact, many children with TOF will have an increase in oxygen saturation during a mask induction with sevoflurane. Even though sevoflurane reduces SVR and may cause tachycardia, anesthesia causes a significant decrease in oxygen consumption, which leads to an improvement in the mixed venous oxygen saturation.

If mask induction is chosen, plans for rapid post-induction placement of an PIV, with phenylephrine readily available if needed to increase SVR, would be prudent. It is worth noting that many infants with TOF appear robust for their age, as their parents feed them frequently to avoid agitation, which may precipitate hypercyanotic spells. Consequently, it may not always be easy to obtain PIV access and the use of ultrasound may be helpful. If the patient is actively experiencing hypercyanotic spells or is volume depleted, a PIV placement with fluid resuscitation prior to induction is prudent.

Ketamine is another induction agent that can be useful in the uncorrected TOF patient. It can be given intramuscularly if necessary. While it will increase heart rate and contractility, it will also increase SVR and may prevent a hypercyanotic spell due to the decrease in SVR which can be associated with mask induction.

In this patient, given his vomiting, a rapid sequence PIV induction with the use of neuromuscular blockade prior to intubation would be appropriate.

Clinical Pearl

It is helpful to have ketamine readily available when inducing a patient with TOF as it can be given IM in patients without IV access.

Immediately after intubation and confirmation of endotracheal tube position oxygen saturations suddenly fall to 60%. How should this be treated?

Mainstays of therapy for hypercyanotic spells fall into the following major categories:

- Increasing SVR
- Decreasing sympathetic stimulation
- Volume expansion

Inspired oxygen concentration (FiO_2) should be increased to 100%. Oxygen is a potent pulmonary vasodilator, will decrease PVR, and may serve to reduce hypoxic pulmonary vasoconstriction. Administration of phenylephrine is the initial intervention to increase SVR. Phenylephrine doses

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as high as 5–10 mcg/kg may be needed, though an effect may be seen initially with doses of 2–3 mcg/kg. A phenylephrine infusion may be considered if the patient requires multiple boluses.

If the patient's legs and torso are accessible, bringing the child's knees to his chest can increase SVR. Hepatic compression may also increase preload. To further increase preload, IV fluid boluses should be given to fill the right heart, dilate the RVOT, and ultimately increase cardiac output and blood pressure.

To decrease sympathetic effects, the ß-blocker esmolol can be utilized to decrease heart rate and contractility, relieving RV infundibular spasm. The appropriate dose is typically 50–250 mcg/kg/minute. Sevoflurane can also treat infundibular spasm via its action as a negative inotrope and by decreasing sympathetic stimulation via increasing anesthetic depth.

Clinical Pearl

Treatments for a tet spell include administration of 100% oxygen, phenylephrine, IV fluid bolus(es), knee-to-chest position if possible, esmolol and increasing depth of anesthesia while maintaining SVR.

What considerations exist during the maintenance of anesthesia?

Generally, anesthesia management principles for a child with TOF are similar to those for a healthy child with the added focus on avoidance of R-to-L shunting and hypercyanotic spell triggers. Hypotension and significant decreases in SVR should be avoided as they may increase the R-to-L shunting of blood across the VSD and cause systemic hypoxia. Hypovolemia will likely be poorly tolerated, so careful attention to fluid status is essential. Light anesthesia, pain, or agitation may increase catecholamines and RVOTO, causing R-to-L shunting and hypoxia. Muscle relaxation, along with a judicious amount of opioid (fentanyl) and volatile agent (sevoflurane), will provide an appropriate balanced anesthetic for this patient. Additionally, the anesthesiologist must be prepared to manage hypercyanotic spells and possible associated hemodynamic instability.

What considerations exist for postoperative care?

If the case is uneventful, extubation in the operating room and recovery in the post-anesthesia care unit is appropriate. If, on the other hand, the perioperative course is complicated by hypercyanotic spells and hemodynamic instability or continued fluid shifts are expected, the patient should be admitted to an intensive care unit postoperatively. Given this child's history of prematurity, monitoring for postoperative apnea is appropriate. A child who was previously thought to have an unobstructed RVOT who now shows signs of hypercyanotic episodes may need to be put forward for urgent surgical repair. In all perioperative patients with unrepaired congenital heart disease, cardiology consultation is suggested.

Suggested Reading

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