PATHOPHYSIOLOGY OF CYANOTIC SPELL (TET SPELL)

Prepared by **Dr. Sidhartha Mullapudi**, DrNB (Cardiology), MD (General Medicine)
Last reviewed: October 2026

I CORE HEMODYNAMIC MECHANISM (THE SVR-TO-RVOT RESISTANCE RATIO)

- **Anatomical Prerequisite ("Tetralogy Physiology"):** In Tetralogy of Fallot (TOF), the Ventricular Septal Defect (VSD) is large and **non-restrictive** (equalizing systolic pressures between the Right Ventricle [RV] and Left Ventricle [LV]). Consequently, the direction and magnitude of ventricular ejection are governed entirely by the **dynamic balance between Right Ventricular Outflow Tract (RVOT) resistance and Systemic Vascular Resistance (SVR)**.
- **The Two Primary Hemodynamic Triggers:** A hypercyanotic spell ("Tet Spell") is an acute, paroxysmal, life-threatening reduction in pulmonary blood flow (Qp) with a simultaneous massive surge in **Right-to-Left (R-to-L) shunting** across the VSD into the overriding aorta, initiated by:
- **Dynamic Infundibular Spasm (Increased RVOT Resistance):** Acute catecholamine-mediated hypercontractility of the hypertrophied subpulmonary infundibular (conal) muscle bundles narrows or completely occludes the RVOT.
- **Acute Drop in Systemic Vascular Resistance (Decreased SVR):** Peripheral arterial vasodilation lowers aortic impedance, making it mechanically easier for deoxygenated RV blood to eject across the VSD into the low-resistance aorta rather than across the stenotic RVOT.

II PRECIPITATING PHYSIOLOGICAL TRIGGERS

- **Characteristic Diurnal and Behavioral Timing:** Peak incidence is between **2 and 6 months of age**, classically occurring **in the morning shortly after awakening** (when SVR is naturally low and sympathetic tone surges), or precipitated by **crying, feeding, defecation, fever, hot baths, dehydration, or painful venipuncture**.
- **Endogenous Catecholamine Surge:** Agitation, pain, or crying releases epinephrine and norepinephrine, stimulating beta-1 adrenergic receptors in the hypertrophied infundibular myocardium to increase **contractility (dP/dt)** and trigger dynamic muscular outflow tract closure.
- **Peripheral Vasodilation and Volume Depletion (Decreased SVR & Preload):** Fever, ambient heat, postprandial splanchnic vasodilation, or dehydration simultaneously lowers **SVR** and reduces **RV end-diastolic volume (preload)**—and a smaller, underfilled RV cavity brings the hypertrophied infundibular walls closer together, worsening dynamic obstruction.
- **Sinus Tachycardia:** Shortens diastolic ventricular filling time, further reducing RV preload and cavity size.
- **Mechanoreceptor Reflex / Bezold-Jarisch-Like Pathway:** Vigorous contraction of a Catecholamine-stimulated, underfilled RV may also activate ventricular mechanoreceptors (C-fibers), triggering reflex peripheral vasodilation that further drops SVR.

III THE SELF-AMPLIFYING VICIOUS CYCLE (GUNTHEROTH CASCADE)

- **Step 1 — Initial Trigger:** Sympathetic surge (crying/feeding/defecation) or peripheral vasodilation causes **increased dynamic RVOT obstruction** and/or **decreased SVR**.
- **Step 2 — Shunt Reversal Surge:** Deoxygenated RV blood is diverted away from the obstructed pulmonary artery and shunts massively **Right-to-Left across the VSD** into the aorta.
- **Step 3 — Arterial Hypoxemia and Tissue Hypoxia:** Systemic arterial oxygen tension (**PaO2**) and saturation (**SpO2**) plummet precipitously while arterial **PaCO2** rises.
- **Step 4 — Lactic Metabolic Acidosis:** Severe systemic tissue hypoxia triggers anaerobic glycolysis, generating **lactic acidemia (drop in arterial pH)**.
- **Step 5 — Medullary Respiratory Center Stimulation (Paroxysmal Hyperpnea):** Combined **arterial hypoxemia, hypercapnia, and acidemia** powerfully stimulate the carotid body chemoreceptors and central medullary respiratory center, producing **paroxysmal hyperpnea** (rapid, deep respirations).
- **Step 6 — The Thoracic Pump Amplification Loop:** Deep, rapid inspiratory efforts generate **markedly negative intrathoracic pressure**, which acts as a suction pump that **massively increases systemic venous return to the Right Atrium and Right Ventricle**. Because the RVOT remains clamped shut and acidemia/hypoxia further lower SVR (while increasing pulmonary vascular resistance), **virtually all of this augmented desaturated venous return is pumped directly across the VSD into the systemic aorta**—deepening hypoxemia and acidosis and locking the infant in a lethal positive-feedback loop until broken.

Stage of the Vicious Cycle	Pathophysiological Event	Targeted Therapeutic Interruption
Dynamic Infundibular Spasm & Tachycardia	Beta-1 adrenergic hypercontractility + small underfilled RV cavity	**IV Propranolol / Esmolol** (relieves spasm, slows HR) + **Isotonic Saline Bolus (10–20 mL/kg)** (expands RV cavity)
Fall in Systemic Vascular Resistance (SVR)	Peripheral vasodilation favors R-to-L shunting into aorta	**Knee-Chest Position / Squatting** (kinks femoral arteries) + **IV Phenylephrine** (pure alpha-1 agonist raises SVR)
Hypoxemia & Lactic Metabolic Acidosis	Anaerobic tissue metabolism lowers pH and PaO2	**100% Humidified Oxygen** + **IV Sodium Bicarbonate (1–2 mEq/kg)** (corrects acidemia)
Medullary Hyperpnea & Venous Return Surge	Acidemia drives deep breathing -> negative intrathoracic pressure -> venous return floods into aorta	**Morphine Sulfate (0.1–0.2 mg/kg)** or **Ketamine** (blunts central hyperpneic drive & sympathetic surge)

IV CLINICAL AND AUSCULTATORY CORRELATES

- **Paroxysmal Hyperpnea ("Air Hunger" Without Rales):** Rapid, deep, sighing Kussmaul-like respirations **without** pulmonary crackles, wheezing, or orthopnea—reflecting **pulmonary oligemia (starved lung perfusion)** and central acidotic drive rather than pulmonary congestion.
- **Characteristic Disappearance of the RVOT Systolic Murmur:** At baseline, the loud harsh crescendo-decrescendo systolic murmur of TOF at the left upper/mid sternal border is generated by turbulent forward flow across the stenotic RVOT (not across the large unrestrictive VSD, which is silent). **During a severe Tet spell, as the infundibulum spasms shut and RV blood shunts entirely into the aorta, antegrade flow across the RVOT falls to near-zero—causing the systolic murmur to soften markedly or disappear completely** (leaving a single loud S2 composed solely of A2). Reappearance of the systolic murmur is the bedside sign that the spell is breaking.
- **Hemodynamic and Neurological Sequelae:** Unabated cerebral hypoxia progresses from agitation to lethargy/limpness, syncope, **hypoxic seizures**, **cerebrovascular accidents (arterial stroke or cerebral venous sinus thrombosis)**, bradycardia, and cardiac arrest.
- **Physiology of "Squatting" in Older Children:** Toddlers and older unoperated children instinctively **squat** during exertion: squatting (1) **kinks the femoral and popliteal arteries**, acutely raising **SVR** and aortic pressure to force RV blood into the lungs, and (2) **traps highly desaturated venous blood in the lower extremities**, temporarily reducing the return of acidotic, low-PO2 venous blood from the exercising leg muscles to the right heart.

V PRACTICAL CONSIDERATIONS IN THE INDIAN CLINICAL CONTEXT

- **Iron-Deficiency Anemia as a Potent Spell Catalyst:** Nutritional iron deficiency is widespread in Indian infants. In a cyanotic infant with TOF, a hemoglobin of 10 to 12 g/dL represents **severe relative anemia** with microcytic, hypochromic red blood cells. Iron deficiency simultaneously (1) reduces systemic arterial oxygen content (accelerating tissue lactic acidosis), (2) lowers systemic vascular resistance via hypoxic vasodilation, and (3) replaces flexible normocytes with **rigid, non-deformable microcytes** that sludge in the cerebral microcirculation—dramatically increasing both the **frequency of Tet spells** and the risk of **pediatric ischemic stroke**. Routine screening of **MCV, serum iron, and ferritin** with oral iron repletion is mandatory.
- **Summer Dehydration and Gastroenteritis:** In tropical Indian summers or during acute infantile diarrhea, volume depletion simultaneously drops RV preload and SVR, acting as a frequent precipitant of life-threatening spells requiring prompt oral/intravenous rehydration.

KEY REFERENCES

- **Guntheroth WG, Morgan BC, Mullins GL:** Physiologic studies of paroxysmal hyperpnea in cyanotic congenital heart disease, *Circulation*, 1965.
- **Libby P, Bonow RO, Mann DL, Tomaselli GF, Bhatt DL, Solomon SD:** *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*, 12th Ed., Elsevier, 2022.
- **Apitz C, Webb GD, Redington AN:** Tetralogy of Fallot, *The Lancet*, 2009.