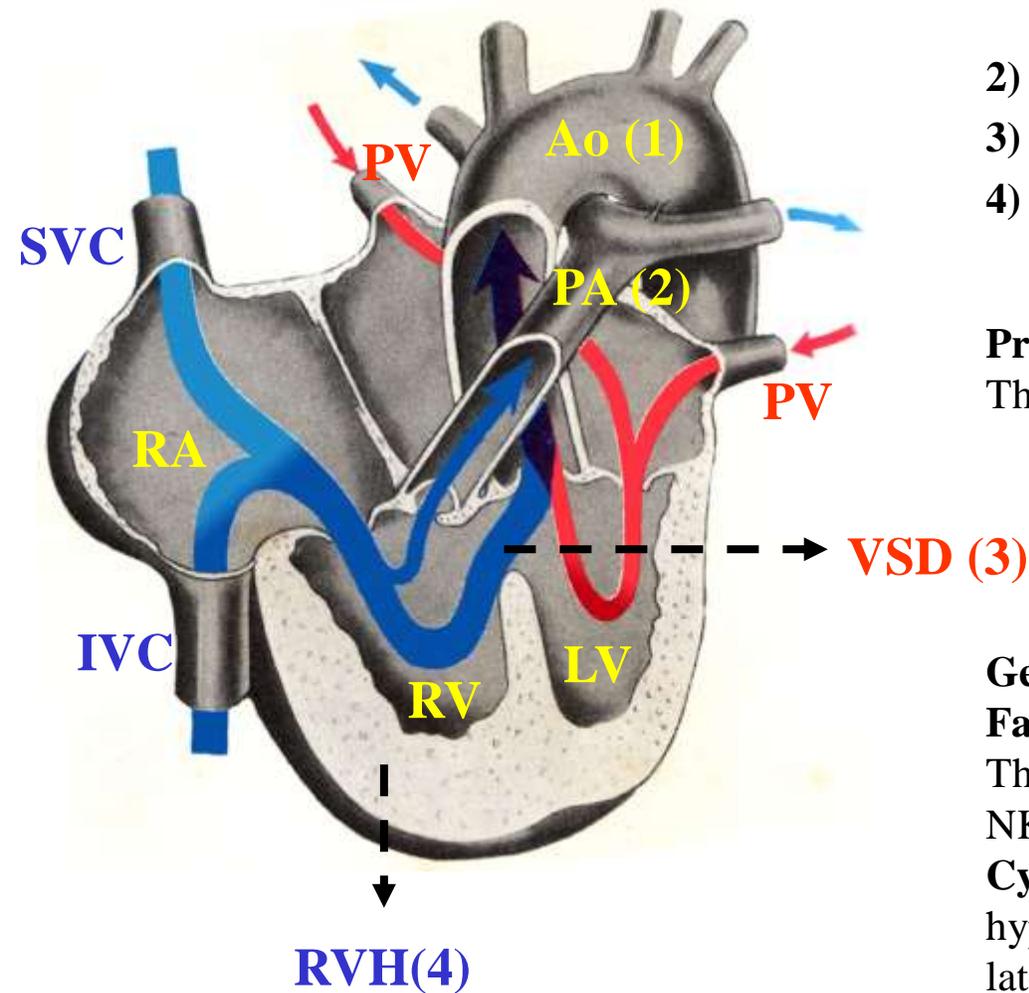


# Tetralogy of Fallot

It consists of a right ventricular outflow tract obstruction, a malalignment ventricular septal defect, an overriding aorta, and right ventricular enlargement/ hypertrophy (RVE/RVH).



- 1) **Ao:** dextropositioned, large and “overriding” the septum. Posterior wall of the Ao and mitral valve anterior fascicle with fibrous continuity.
- 2) **PA:** hypoplastic with valvular, infundibular or infundibulo-valvar PS.
- 3) **VSD:** mid-basal, infracristal and large ( $>1 \text{ cm}^2/\text{m}^2$ ).
- 4) **RVH:** secondary (right intraventricular pressure = systemic).

**Prevalence:** 400 cases each 100,000 babies born, 9 to 10% of congenital heart diseases. The most frequent one is cyanotic congenital heart disease after 1 year.

**Gender:** distribution in TOF is approximately equal.

**Familial background:** families have been reported in siblings, parents and offspring. The entity is observed in Alagille’s syndrome with mutation in the jagged 1 gene, NKX2.5 mutations and chromosome 22q11.2 deletion (**Momma 2001**).

**Cyanosis:** In Tetralogy of Fallot often cyanosis is not present at birth, but increasing hypertrophy of the right ventricular infundibulum and patient’s growth, cyanosis occur later in the first year of life (**Tubman 1991**).

## Brief history

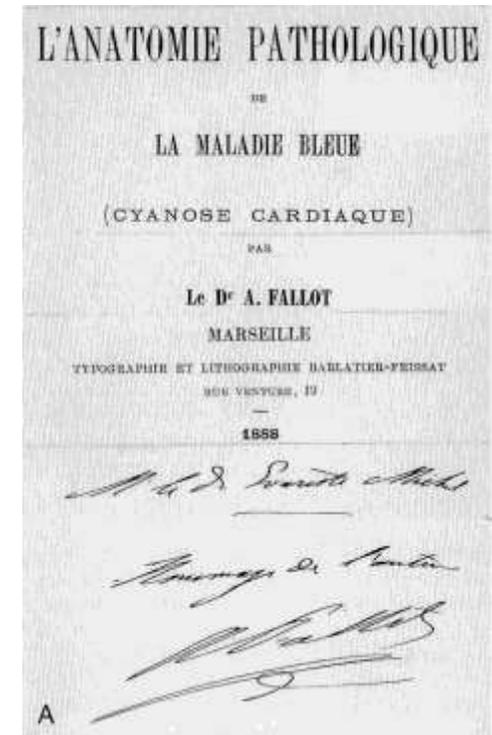
The chronicle of tetralogy of Fallot is part of a dramatic evolution in cardiology, cardiac surgery, and understanding of the developing heart. Many new tools and concepts have evolved since Steno of Denmark first described the defect in 1673, and since Fallot of Marseilles coined the term tetralogy in 1888. Four major eras of progress can be recognized. The 1st, the era of pathologic anatomy, culminated in the publication of Maude Abbott's Atlas of Congenital Cardiac Disease in 1936. The next, the era of clinicophysiology and surgery, was highlighted by the 1st Blalock-Taussig anastomosis in 1944, by open-heart surgery 10 years later, and by a new team approach to cardiology. The 3rd, or infant era, began in the mid 1970s with successful intracardiac repair in infants, the rise of echocardiography, and the introduction of prostaglandin therapy. The current era of cardiac development (beginning in the 1990s) gives hope for early understanding of the molecular basis of tetralogy. Tribute is due to the surgical and medical pioneers, and to the pioneer patients and their families, for revolutionary changes in diagnosis and treatment. The challenge of the next 100 years lies in increased understanding of the molecular biology of the defect and in preserving the blend of humanism, scholarship, and skill that have graced the advances of the past 3 centuries (Neill 1994).



**Niels Steensen; Latinized to Nicolaus Steno or Nicolaus Stenonius, who first described the defect in 1673 (1666–1677).**



**Étienne-Louis Arthur Fallot;  
Marsella, 1850 - 1911**



## Genetic aspects

### Phenotypes associated with TOF

1. CATCH 22 monosomy 22q11.2: DiGeorge syndrome (DGS) comprises thymic hypoplasia, hypocalcaemia, outflow tract defects of the heart, and dysmorphic facies. It results in almost all cases from a deletion within chromosome 22q11;
2. Down trisomy 21 ([Tubman 1991](#));
3. Velocardiofacial syndrome (Shprintzen-Goldberg): Shprintzen-Goldberg syndrome is a rare and lethal association of craniosynostosis with features of Marfan syndrome.<sup>1</sup> It has been traced to a defect of chromosome 15.<sup>2</sup> Cardiac features include progressive aortic root dilatation. To our knowledge, there is no known association of this syndrome with congenital heart defects ([Pauliks 2005](#));
4. Goldenhar's syndrome (oculoauriculovertebral dysplasia): The oculo-auriculo-vertebral spectrum (OAVS) or goldenhar syndrome is a non-random association of microtia, hemifacial microsomia with mandibular hypoplasia, ocular epibulbar dermoid, and cervical vertebra malformations. CHDs have been reported in 5-58% of these patients. They report a 20 year old male patient diagnosed with TOF and oculo auriculo vertebral syndrome ([Prem 2015](#));
5. Absent thumb and first metacarpal;
6. Absent of pectoralis major muscle (congenital pectoral dysplasia or Poland's syndrome);
7. Syndactyly;
8. Brachydactyly with hypoplasia of the ipsilateral hand;
9. Under development of the left arm secondary to an isolated left subclavian artery, and hypoplasia of a hand;
10. Alagille's syndrome.

### Alagille's syndrome (ALGS)

**Other denominations:** Alagille-Watson Syndrome, arteriohepatic dysplasia (AHD), cardiovertebral syndrome, cholestasis with peripheral, pulmonary stenosis, hepatic ductular hypoplasia, hepatofacioneurocardiovertebral syndrome, paucity of interlobular bile ducts, Watson-Miller syndrome.

ALGS is a genetic disorder that can affect the liver, heart, and other parts of the body.

One of the major features of ALGS is liver damage caused by abnormalities in the bile ducts. These ducts carry bile (which helps to digest fats) from the liver to the gallbladder and small intestine. In ALGS, the bile ducts may be narrow, malformed, and reduced in number (bile duct

paucity). As a result, bile builds up in the liver and causes scarring that prevents the liver from working properly to eliminate wastes from the bloodstream. Signs and symptoms arising from liver damage in ALGS may include a yellowish tinge in the skin and the whites of the eyes (jaundice), itchy skin, and deposits of cholesterol in the skin (xanthomas).

ALGS is also associated with several heart problems, including impaired blood flow from the heart into the lungs (pulmonic stenosis). Pulmonic stenosis may occur along with a hole between the two lower chambers of the heart (ventricular septal defect) and other heart abnormalities. This combination of heart defects is called tetralogy of Fallot.

People with ALGS may have distinctive facial features including a broad, prominent forehead; deep-set eyes; and a small, pointed chin. The disorder may also affect the blood vessels within the brain and spinal cord (central nervous system) and the kidneys. Affected individuals may have an unusual butterfly shape of the bones of the spinal column (vertebrae) that can be seen in an x-ray.

Problems associated with ALGS generally become evident in infancy or early childhood. The severity of the disorder varies among affected individuals, even within the same family. Symptoms range from so mild as to go unnoticed to severe heart and/or liver disease requiring transplantation.

Some people with ALGS may have isolated signs of the disorder, such as a heart defect like tetralogy of Fallot, or a characteristic facial appearance. These individuals do not have liver disease or other features typical of the disorder.

**Causes:** In more than 90% of cases, mutations in the JAG1 gene cause ALGS. Another 7% of individuals with ALGS have small deletions of genetic material on chromosome 20 that include the JAG1 gene. A few people with ALGS have mutations in a different gene, called NOTCH2. The JAG1 and NOTCH2 genes provide instructions for making proteins that fit together to trigger interactions called Notch signaling between neighboring cells during embryonic development. This signaling influences how the cells are used to build body structures in the developing embryo. Changes in either the JAG1 gene or NOTCH2 gene probably disrupt the Notch signaling pathway. As a result, errors may occur during development, especially affecting the bile ducts, heart, spinal column, and certain facial features.

### **Inheritance pattern**

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered or deleted gene in each cell is sufficient to cause the disorder.

In approximately 30 to 50% of cases, an affected person inherits the mutation or deletion from one affected parent. Other cases result from new mutations in the gene or new deletions of genetic material on chromosome 20 that occur as random events during the formation of reproductive cells (eggs or sperm) or in early fetal development. These cases occur in people with no history of the disorder in their family.

## **Clinical manifestations**

The signs and symptoms of ALGS and their severity vary, even among people in the same family sharing the same gene mutation.

### **Liver**

In some people, problems in the liver may be the first signs and symptoms of the disorder. These signs and symptoms can occur in children and adults with ALGS, and in infants as early as the first 3 months of life. **Jaundice.** Jaundice—when the skin and whites of the eyes turn yellow—is a result of the liver not removing bilirubin from the blood. Bilirubin is a reddish-yellow substance formed when hemoglobin breaks down. Hemoglobin is an iron-rich protein that gives blood its red color. Bilirubin is absorbed by the liver, processed, and released into bile. Blockage of the bile ducts forces bilirubin and other elements of bile to build up in the blood. Jaundice may be difficult for parents and even health care providers to detect. Many healthy newborns have mild jaundice during the first 1 to 2 weeks of life due to an immature liver. This normal type of jaundice disappears by the second or third week of life, whereas the jaundice of ALGS deepens. Newborns with jaundice after 2 weeks of life should be seen by a health care provider to check for a possible liver problem. **Dark urine and gray or white stools.** High levels of bilirubin in the blood that pass into the urine can make the urine darker, while stool lightens from a lack of bilirubin reaching the intestines. Gray or white bowel movements after 2 weeks of age are a reliable sign of a liver problem and should prompt a visit to a health care provider. **Pruritus.** The buildup of bilirubin in the blood may cause itching, also called pruritus. Pruritus usually starts after 3 months of age and can be severe. **Xanthomas.** Xanthomas are fatty deposits that appear as yellow bumps on the skin. They are caused by abnormally high cholesterol levels in the blood, common in people with liver disease. Xanthomas may appear anywhere on the body. However, xanthomas are usually found on the elbows, joints, tendons, knees, hands, feet, or buttocks.

### **Other signs and symptoms of ALGS**

Certain signs of ALGS are unique to the disorder, including those that affect the vertebrae and facial features.

**Eyes.** Posterior embryotoxon is a condition in which an opaque ring is present in the cornea, the transparent covering of the eyeball. The abnormality is common in people with ALGS, though it usually does not affect vision. A large number of ocular manifestations may occur in ALGS. Posterior embryotoxon is the most important diagnostically. Posterior embryotoxon is a prominent, centrally positioned Schwalbe's line. It generally does not affect vision. It occurs in many (56-95% of different series) ALGS patients, but has also been reported to occur in 20% of normal eyes. Axenfeld anomaly (iris strands) is seen in 13% of ALGS patients.

**Face.** Many children with ALGS have deep-set eyes, a straight nose, a small and pointed chin, large ears, and a prominent, wide forehead. These features are not usually recognized until after infancy. By adulthood, the chin is more prominent.



**Facial abnormalities:** The typical facies in childhood consist of a prominent forehead, deep set eyes with moderate hypertelorism, a small pointed chin, and a saddle or straight nose. This has been termed triangular facies. The typical facies in adults with ALGS do not resemble the childhood features. The forehead becomes less prominent, and the chin is more protuberant.

**Skeleton.** The most common skeletal defect in a person with ALGS is when the shape of the vertebrae—bones of the spine—gives the appearance of flying butterflies. This defect, known as "butterfly" vertebrae, rarely causes medical problems or requires treatment.



**Skeletal abnormalities:** The characteristic manifestation of ALGS is the sagittal cleft or butterfly vertebrae, which is found in 33-87% of patients. Due to a failure of the fusion of the anterior arches of the vertebrae, the vertebral body is split sagittally into paired hemivertebrae. This anomaly may occur in other syndromes and also in healthy individuals. It is generally not of structural significance.

Butterfly vertebrae of T5 and T6, with vertebral anomalies at T4, T7, T8 and T9 in an infant with ALGS.

**Heart and blood vessels.** People with ALGS may have the following signs and symptoms having to do with the heart and blood vessels: heart murmur—an extra or unusual sound heard during a heartbeat. A heart murmur is the most common sign of ALGS other than the general symptoms of liver disease.<sup>1</sup> Most people with ALGS have a narrowing of the blood vessels that carry blood from the heart to the lungs.<sup>1</sup> This narrowing causes a murmur that can be heard with a stethoscope. Heart murmurs usually do not cause problems.

heart walls and valve problems. A small number of people with ALGS have serious problems with the walls or valves of the heart. These conditions may need treatment with medications or corrective surgery. Blood vessel problems. People with ALGS may have abnormalities of the blood vessels in the head and neck. This serious complication can lead to internal bleeding or stroke. ALGS can also cause narrowing or bulging of other blood vessels in the body.

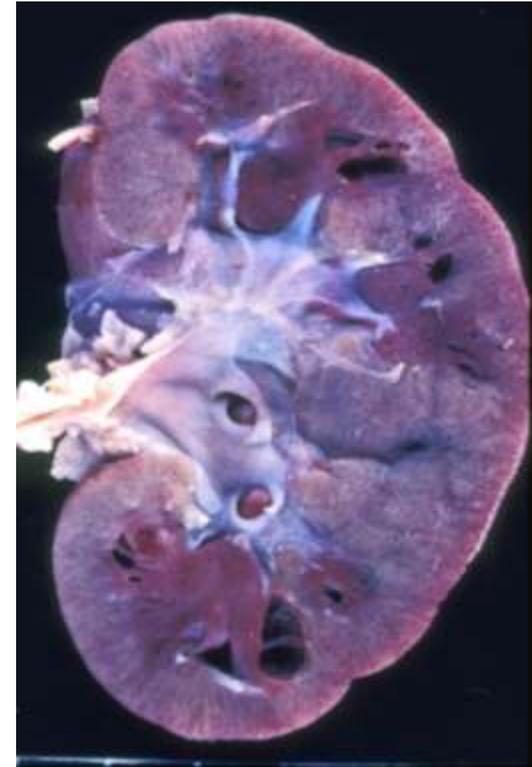
**Kidney disease.** A wide range of kidney diseases can occur in ALGS. The kidneys are two bean-shaped organs, each about the size of a fist, that filter wastes and extra fluid from the blood. Some people have small kidneys or have cysts—fluid-filled sacs—in the kidneys. Kidney function can also decrease.

**Central Nervous System abnormalities:** Stroke, intracranial bleeding and other CNS vascular anomalies occur in patients with ALGS, and have contributed significantly to morbidity and mortality. Intracranial bleeding has occurred in up to 15% of cases presenting with liver disease in some series, and is fatal in approximately one third of events. The majority of this bleeding has occurred in the absence of a significant coagulopathy. Head trauma, generally of a minor nature, has been associated with a minority of these bleeding events. Structural vascular lesions, including aneurysms and moyamoya, have been identified in some patients with ALGS



Aneurysm of the external carotid artery in an adolescent with ALGS.

**Renal abnormalities:** It is now recognized that renal abnormalities are an important feature of ALGS. Major structural disease can occur, including cystic and dysplastic kidneys, solitary kidney, and duplicated ureters. Renal artery stenosis is a cause of systemic hypertension. Tubular disease, including renal tubular acidosis, tubulointerstitial nephropathy, and glomerular lipidosis has been seen in ALGS. Renal transplantation has been described in ALGS. ALGS individuals undergoing liver transplantation are generally considered at increased risk of nephrotoxicity from immune suppressants and should be managed with renal-sparing protocols.



Diffuse renal cystic dysplasia in a patient with ALGS.

## Diagnosis

The diagnosis of ALGS was traditionally made with the combination of bile duct paucity in association with at least three of five major criteria: cholestasis, heart murmur, embryotoxon, butterfly vertebrae and facies. These diagnostic criteria substantially underestimated the number of patients ultimately shown to have JAGGED1 mutations, and overestimated the incidence of major criteria. Subsequent studies have shown that many patients have mild or subclinical manifestations, and that JAGGED1 mutations have highly variable expressivity. The identification of JAGGED1 mutations and the availability of molecular testing have greatly improved the understanding about and diagnosis of ALGS. It has confirmed the clinical impression that nearly all minimally affected relatives who manifest one or two minor features of ALGS will carry the gene mutation. Since the transmission risk for their progeny is high, it seems appropriate to designate these mutation positive individuals as ALGS. Therefore, revised criteria for clinical and molecular diagnosis has been proposed. Some mutation positive individuals will have only one or even no clinical features, yet may have severely affected progeny.

**Table 1:** Revised Diagnostic Criteria for the Diagnosis of ALGS

ALGS Family History <sup>a</sup>	Paucity	Jagged1 or Notch2 mutation	Number of criteria needed
Present or absent	Present	Identified <sup>b</sup>	Any or no features
None (proband)	Present	Not identified <sup>c</sup>	3 or more features
None (proband)	Absent or unknown	Not identified	4 or more features
None (proband)	Absent or unknown	Identified	1 or more features
Present	Present	Not identified	1 or more features
Present	Absent or unknown	Not identified	2 or more features
Present	Absent or unknown	Identified	Any or no features

Major clinical criteria include cholestasis, consistent cardiac, renal, ocular disease, butterfly vertebrae, or characteristic "Alagille" facies of childhood or adulthood.

a. Family History = ALGS present in a first degree relative

b. Identified = JAGGED1 mutation may have been identified in clinical or research laboratory

c. Not Identified = Not identified on mutation screening, or not screened for

## **Complications**

The complications of ALGS include liver failure, portal hypertension, and growth problems. People with ALGS usually have a combination of complications, and may not have every complication listed below.

**Liver failure.** Over time, the decreased number of bile ducts may lead to chronic liver failure, also called end-stage liver disease. This condition progresses over months, years, or even decades. The liver can no longer perform important functions or effectively replace damaged cells. A person may need a liver transplant. A liver transplant is surgery to remove a diseased or an injured liver and replace it with a healthy whole liver or a segment of a liver from another person, called a donor.

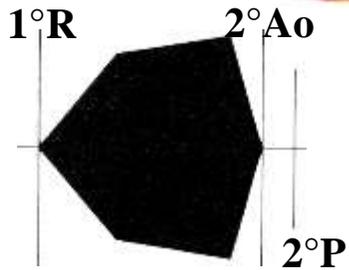
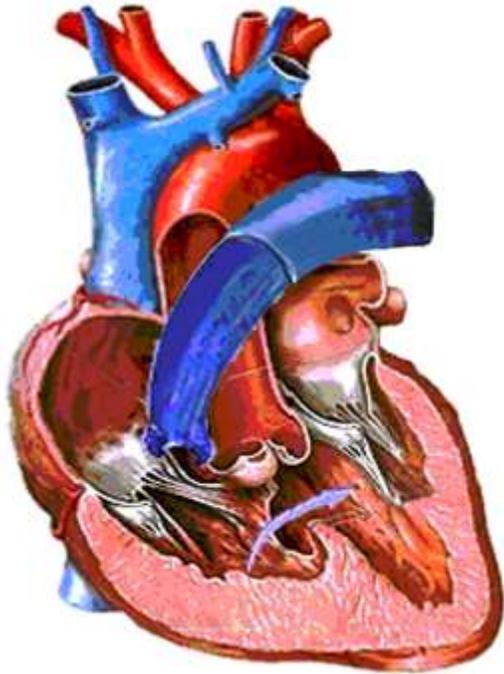
**Portal hypertension.** The spleen is the organ that cleans blood and makes white blood cells. White blood cells attack bacteria and other foreign cells. Blood flow from the spleen drains directly into the liver. When a person with ALGS has advanced liver disease, the blood flow backs up into the spleen and other blood vessels. This condition is called portal hypertension. The spleen may become larger in the later stages of liver disease. A person with an enlarged spleen should avoid contact sports to protect the organ from injury. Advanced portal hypertension can lead to serious bleeding problems.

**Growth problems.** ALGS can lead to poor growth in infants and children, as well as delayed puberty in older children. Liver disease can cause malabsorption, which can result in growth problems. Malabsorption is the inability of the small intestine to absorb nutrients from foods, which results in protein, calorie, and vitamin deficiencies. Serious heart problems, if present in ALGS, can also affect growth.

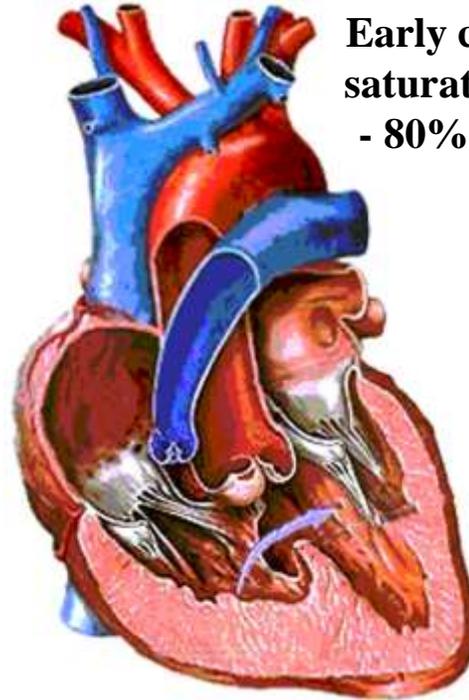
**Malabsorption.** People with ALGS may have diarrhea—loose, watery stools—due to malabsorption. The condition occurs because bile is necessary for the digestion of food. Malabsorption can lead to bone fractures, eye problems, blood-clotting problems, and learning delays.

# Types of TOF by degree of severity

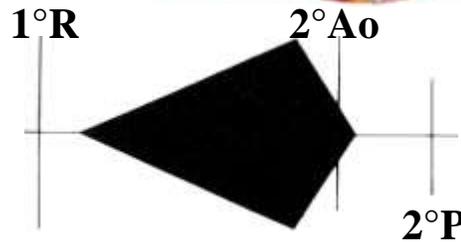
Pink-Fallot	Classical TOF (moderate)	TOF with pulmonary atresia, pseudo-truncus or extreme
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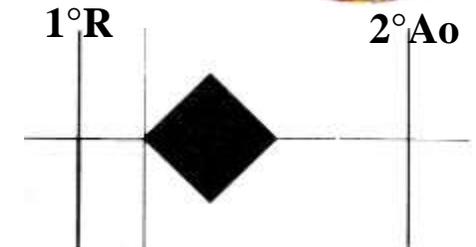
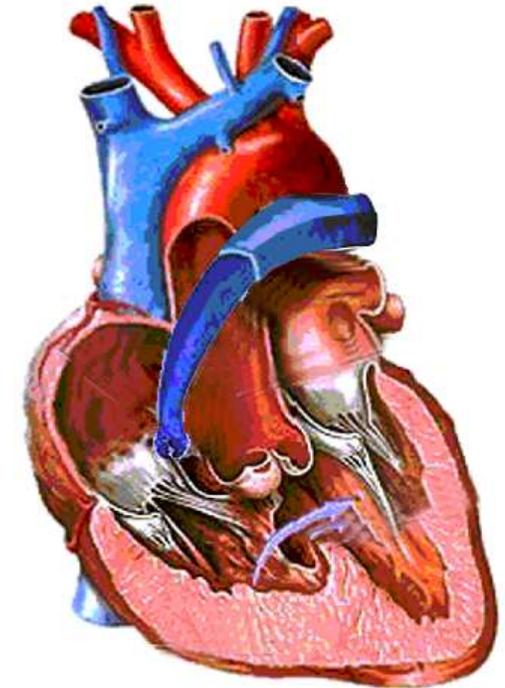
Intense murmur + mild cyanosis  
 Less evident RVH  
 Late or absent cyanosis  
 Saturation of O<sub>2</sub> 90% to 100%.



Early cyanosis:  
 saturation of O<sub>2</sub>  
 - 80% to 89%



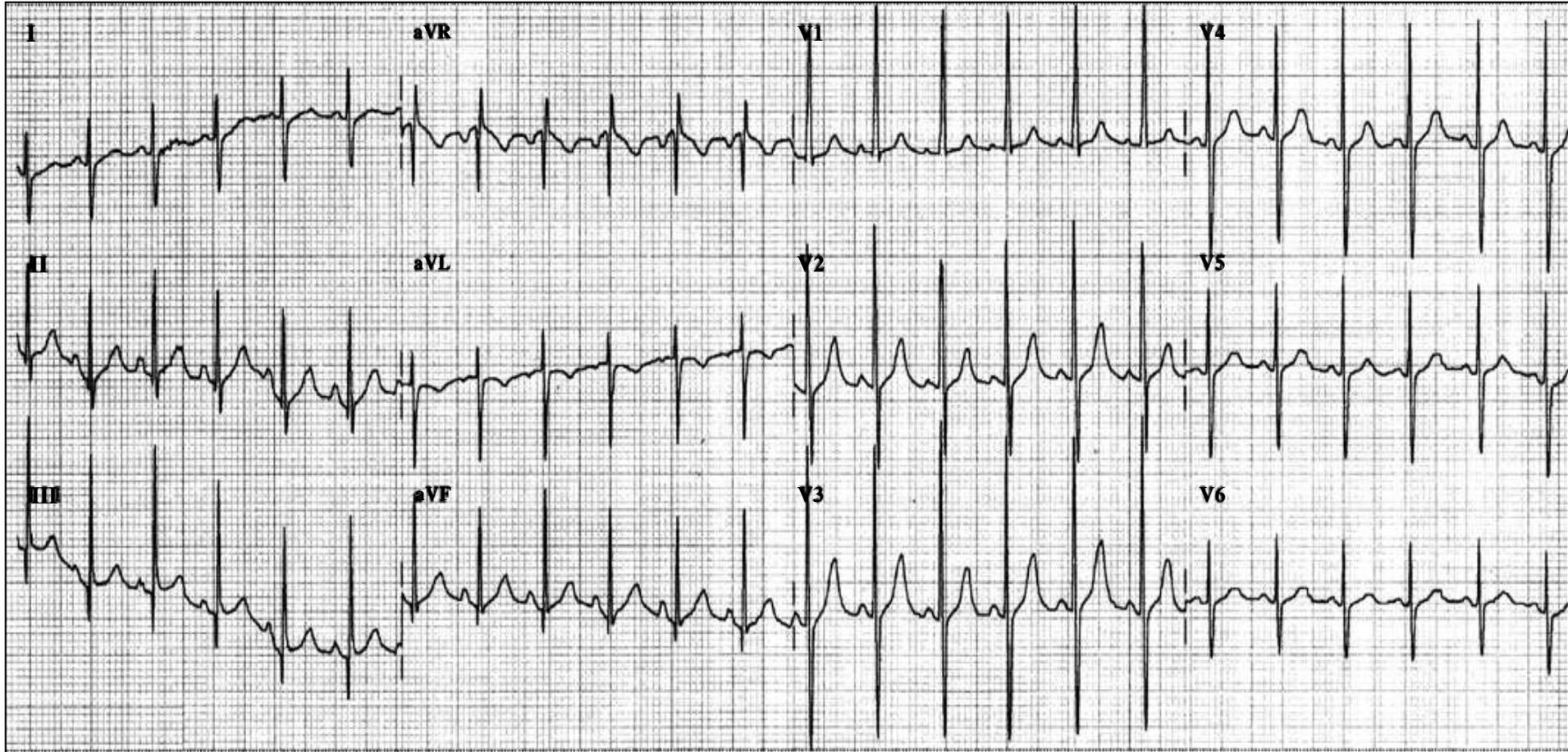
Systolic RVH of adaptation: R/S (R>S) in V3R and V1 with notch at the foot of the R wave and sudden transition from V1 to V2, i.e., predominantly positive QRS complexes in V1 for rS type complexes in V2. The sign is present in 50% of these cases.



**Mild murmur + intense cyanosis**

## Classical TOF (moderate)

**Name:** MBFR; **Age:** 9 months; **Sex:** M; **Ethnic group:** Caucasian; **Weight:** 7.8 Kg; **Height:** 78 cm;  
**Number:** 720; **Date:** 11/20/2001; **Medication in use:** propranolol

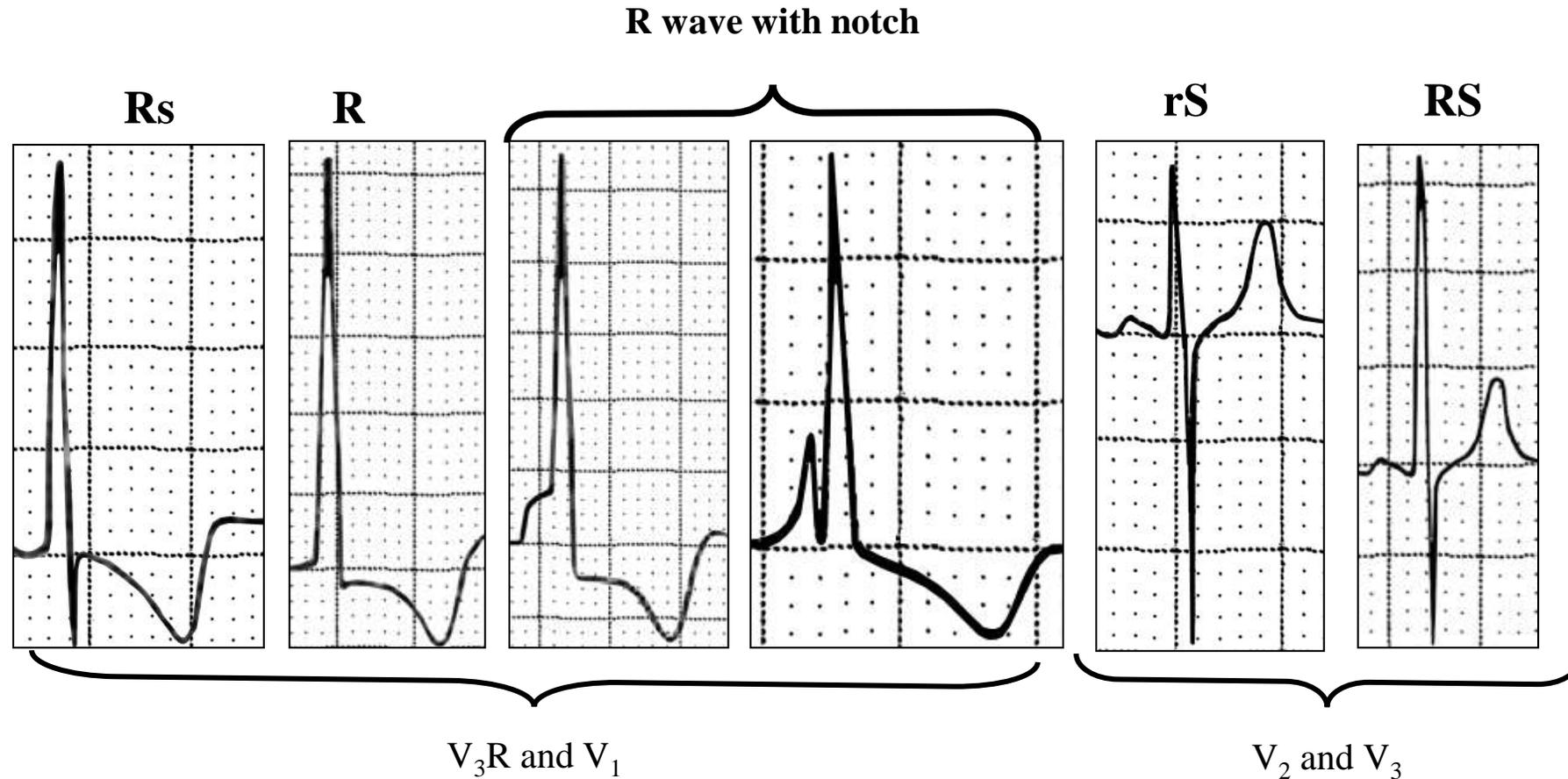


Sinus tachycardia (HR: 130 bpm: the normal heart rate in this age range is between 90 and 120 bpm) + RVH; AQRS  $104^\circ$ . In this age range, generally  $\hat{S}\hat{A}QRS$  is less than  $+90^\circ$ . Morphology: I and aVL. rS, III qR, II and aVF: qRs, aVR: QR with R wave of 6 mm in  $V_1$  and Rs and RS from  $V_2$  to  $V_6$ . The sudden transition from  $V_1$  to  $V_2$  stands out, i.e., predominantly positive QRS complexes in  $V_1$  toward RS type complexes in  $V_2$ . The sign is considered typical of TOF and it is present in 50% of the cases.

## RVH in TOF

Systolic RVH of adaptation. The RV adapts to a regime of systemic pressure: RV = LV pressure. E.g.: TOF, where right intraventricular pressure does not exceed the systemic one. There is RV latero-postero-basal selective hypertrophy.

QRS morphologies in V1 and V3R may be:



V<sub>2</sub> and V<sub>3</sub> display rS or RS pattern because they face the inferior region of the not so hypertrophied free and trabecular wall.

Characteristics of QRS complexes in TOF in V<sub>3</sub>R and V<sub>1</sub> and in V<sub>2</sub> and V<sub>3</sub>.

## Summary of VCG in TOF

In TOF the VCG reflects the balance of electrical forces of the right and left ventricles.

In severe forms flow is markedly decreased, there is marked right ventricular dominance. The RMSV is increased, the LMSV is decreased and the horizontal loop is clockwise. In the mild forms of TOF, in which there is less obstruction by a systemic to pulmonary shunt, the LMSV is usually normal and the horizontal loop demonstrates a figure-eight or CCW rotation. Following shunt operation, an increase in the LMSV and a change of the horizontal loop from the CW to a figure-eight or CCW configuration reflect the increase in pulmonary blood flow. A very high LMSV suggests excessive pulmonary blood flow from too large a shunt. A change from a CCW to a CW horizontal loop occurs in conjunction with progressive severity of TOF owing to increasing right ventricular outflow obstruction.

In infants under 2 years of age, similar relationships are seen. Following surgical repair, relief of right ventricular hypertension is reflected by a return of the RMSV towards normal, in spite of the development of right bundle branch block.

# ECG/VCG correlation of a classical TOF

**Name:** MBFR  
**Height:** 78 cm.

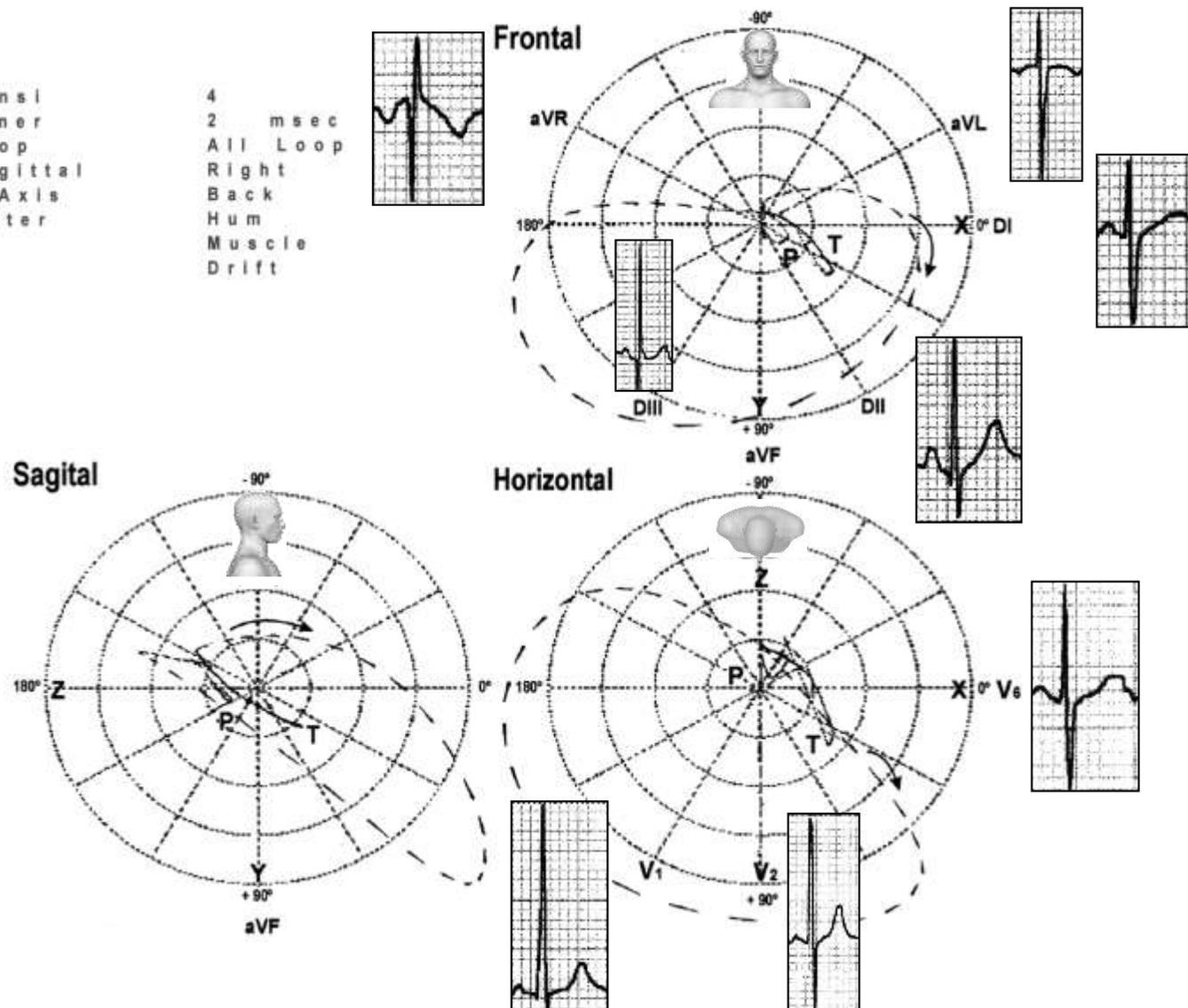
**Age:** 9 months  
**Number:** 720.

**Sex:** M.  
**Date:** 11/20/2001.

**Race:** W. **Weight:** 7.800 Kg.  
**Medication in use:** propranolol.

Sensl  
Timer  
Loop  
Sagittal  
Z Axis  
Filter

4  
2 msec  
All Loop  
Right  
Back  
Hum  
Muscle  
Drift

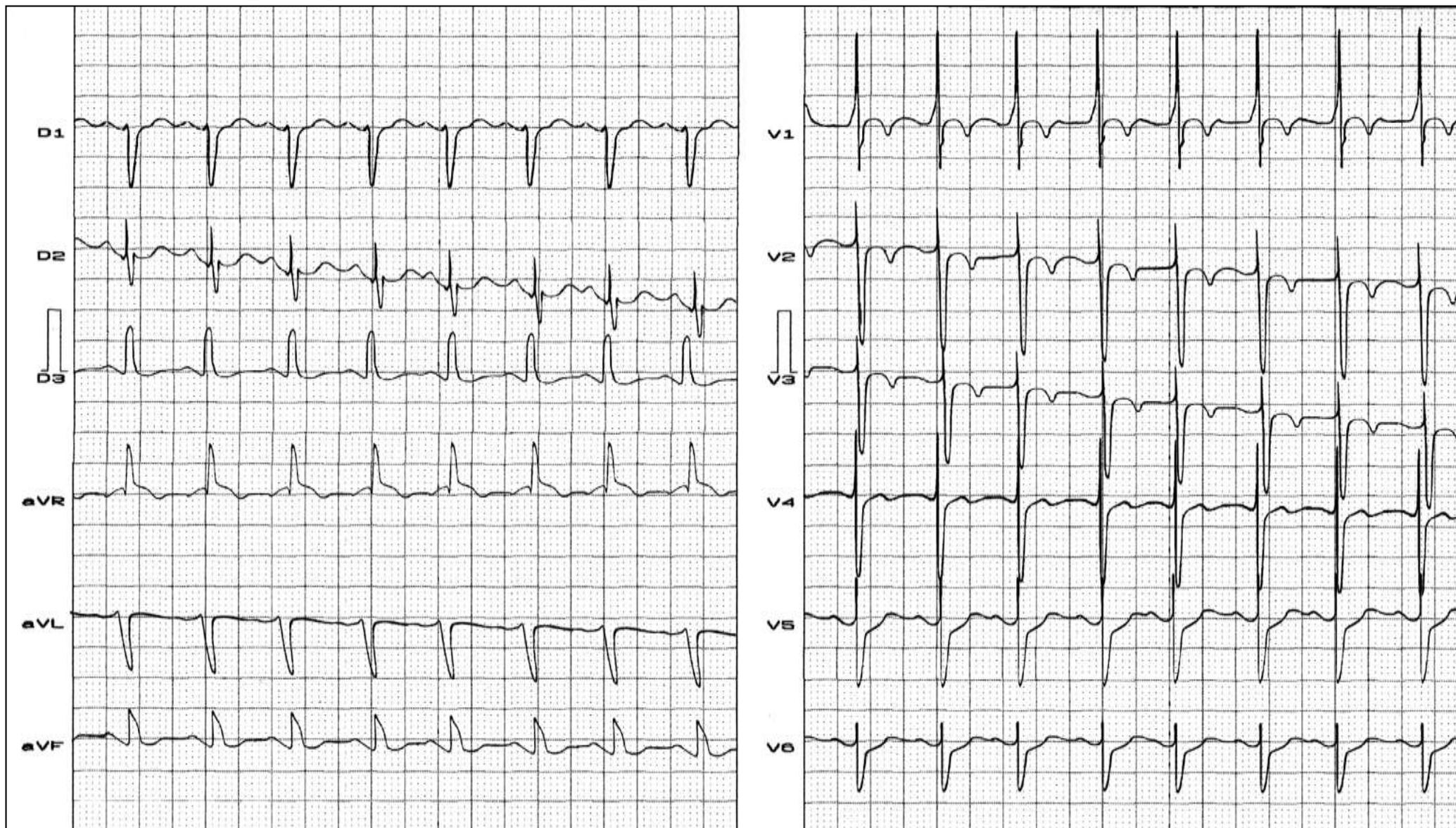


Clockwise rotation or figure in 8 in 80% of case in the frontal plane. 10% of patients have CCW and superior loop.

Near 90% of patients have marked RV dominance and clockwise rotation in the horizontal plane. In TOF with highest O<sub>2</sub> saturation 90% have counterclockwise rotation or figure in 8.

Predominantly CW rotation and did not appear to be influenced by changes in saturation.

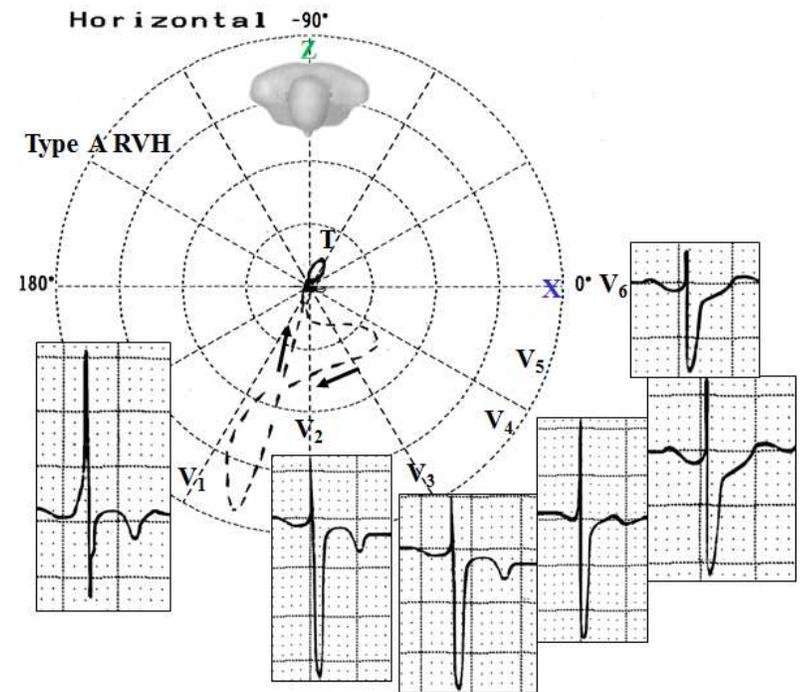
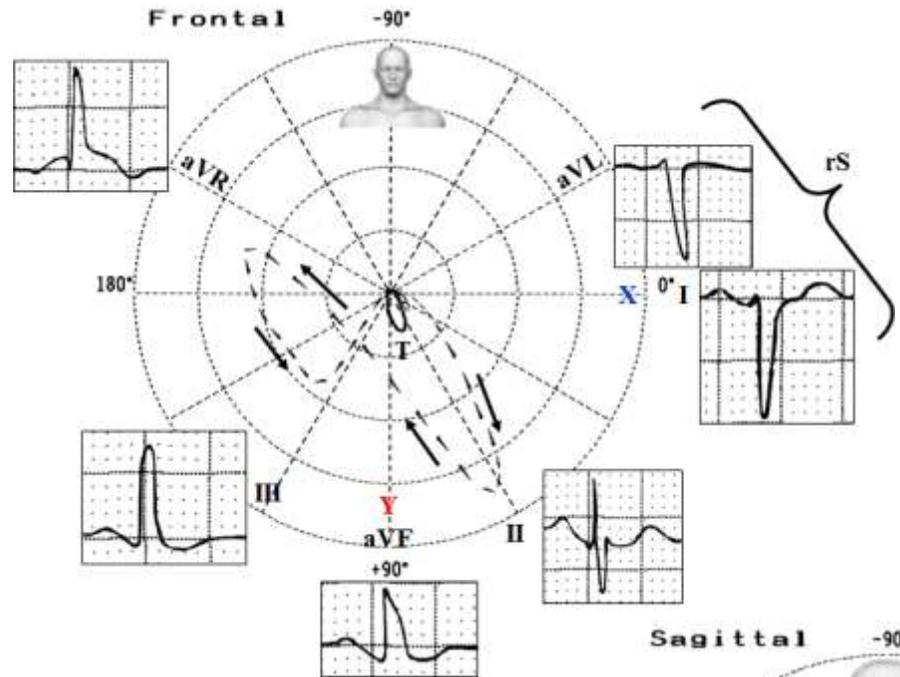
Name: MS; Age: 11 y/o; Sex: M; Ethnic group: Caucasian; Weight: 19 Kg; Height: 1.30 m; Date: 2/28/1996



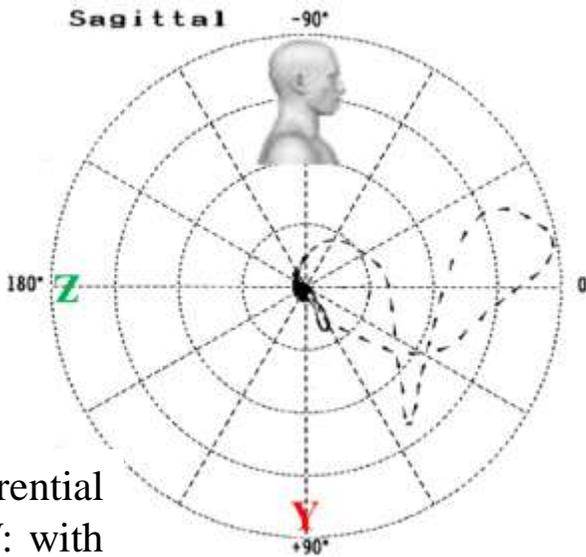
**Clinical diagnosis: Classical TOF.**

**ECG diagnosis: RVH:  $\hat{S}\hat{A}QRS: +150^\circ$ .** Precordial leads: R/S (R>S) in V<sub>1</sub> with notch in the foot of R and sudden transition from V<sub>1</sub> to V<sub>2</sub>, i.e., predominantly positive QRS complexes in V<sub>1</sub> toward rS type complexes in V<sub>2</sub>. The sign is present in 50% of these cases of TOF.

# ECG/VCG correlation of classical TOF



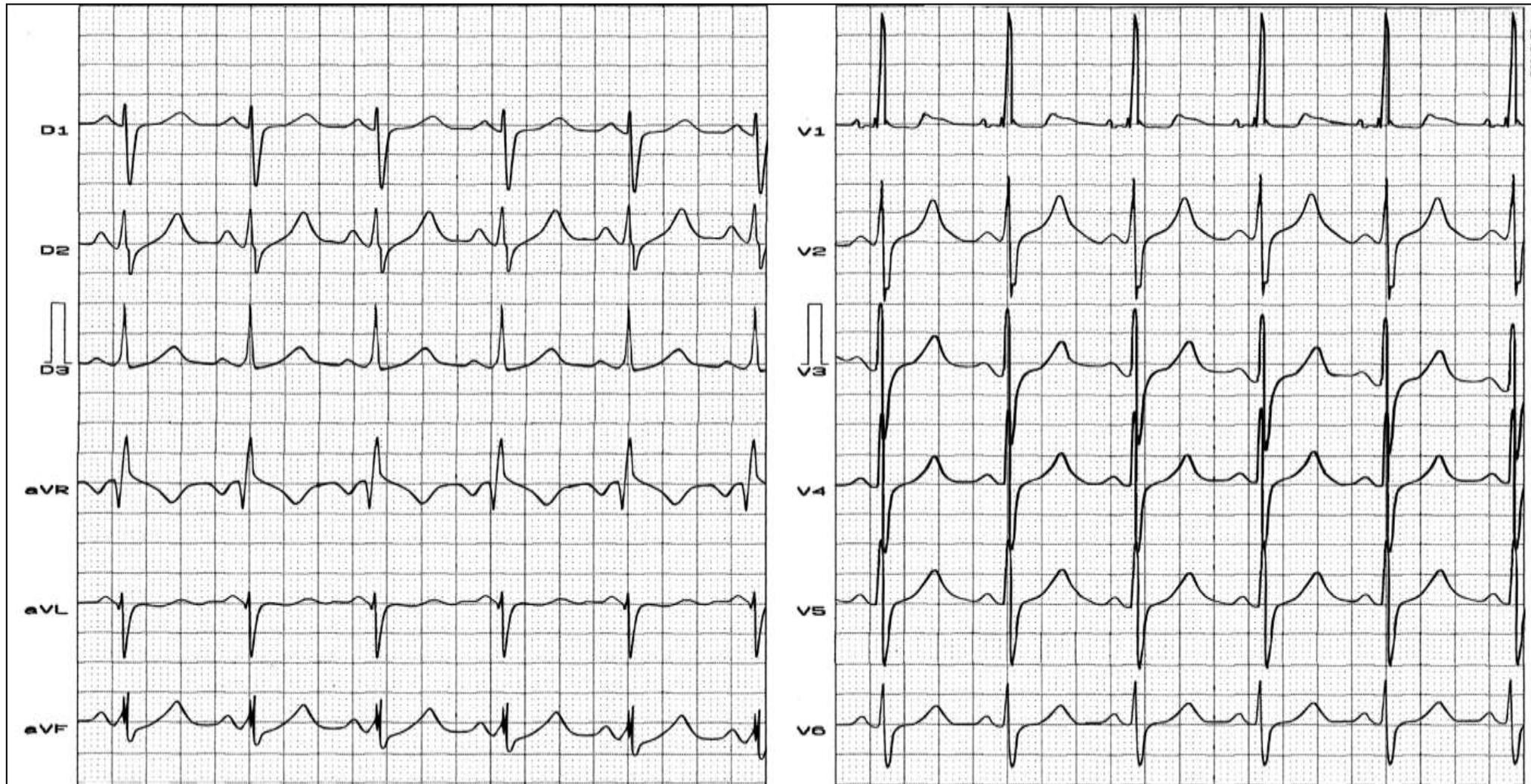
**Sensi.** 2  
**Timer** 2 mse  
**Loop** All Loop  
**Sagittal** Right  
**Z Axis** Back  
**Filter** Hum  
**Muscle**  
**Drift**



**HP** - Rs in  $V_1$ : present in 60% with characteristic notch in the ascending limb to R: systolic RVH of adaptation. QRS loop with eight-like rotation (20% of TOF cases). Sudden transition from  $V_1$  to  $V_2$  predominantly positive complexes in  $V_1$ , predominantly negative rS type from  $V_2$ . Present in 50% of TOF.

**FP** - Valuable for the differential diagnosis between TOF and DORV: with no initial q;  $\hat{S}\hat{A}QRS$ : Shift below and to the right:  $+150^\circ$  in the right inferior quadrant; Sat below and to the left.

Name: MA; Age: 20 days; Sex: M; Ethnic group: Asian; Weight: 2,900 g; Height: 47 cm; Date: 8/4/2000

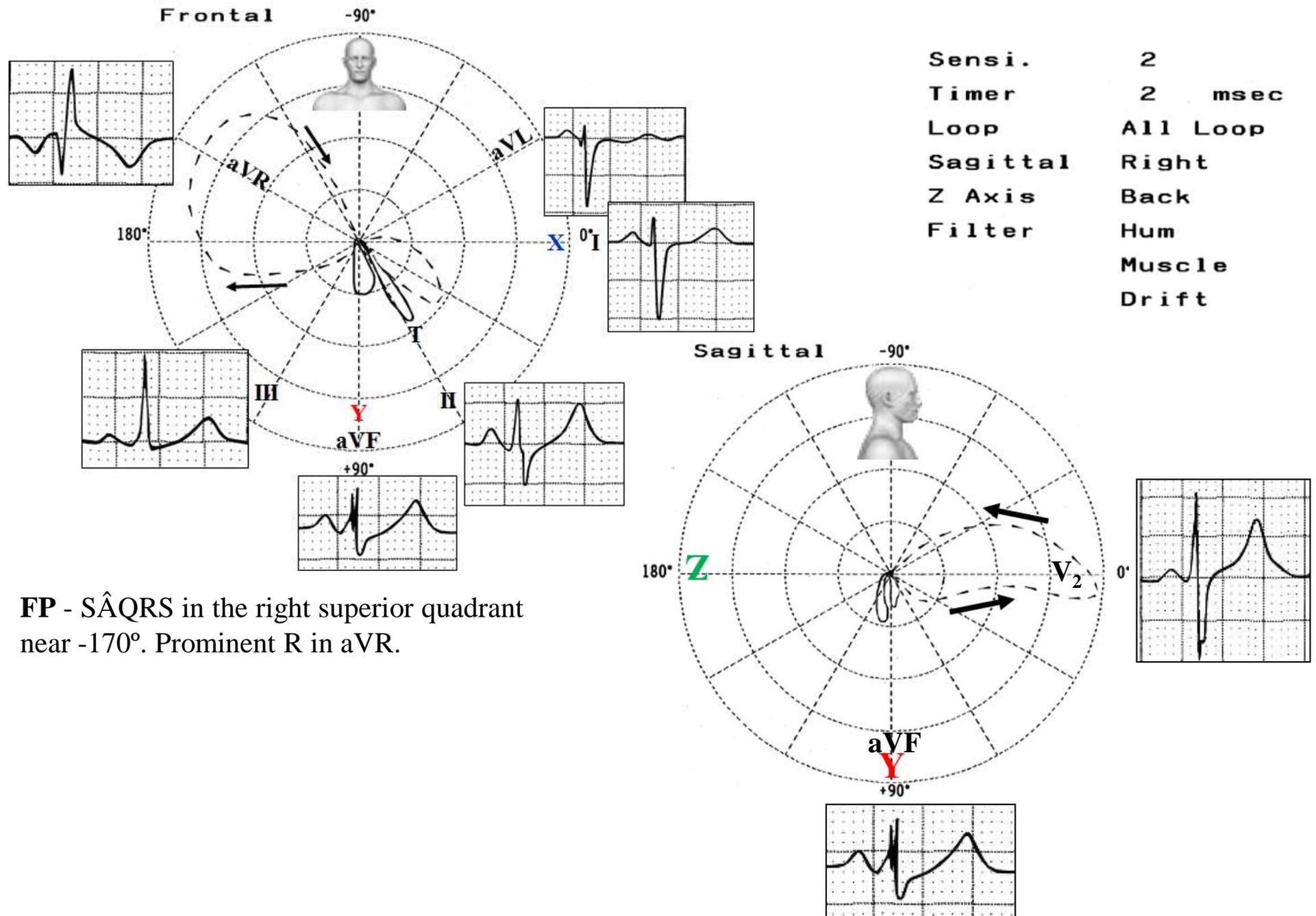


**Clinical diagnosis: Tetralogy of Fallot (TOF).**

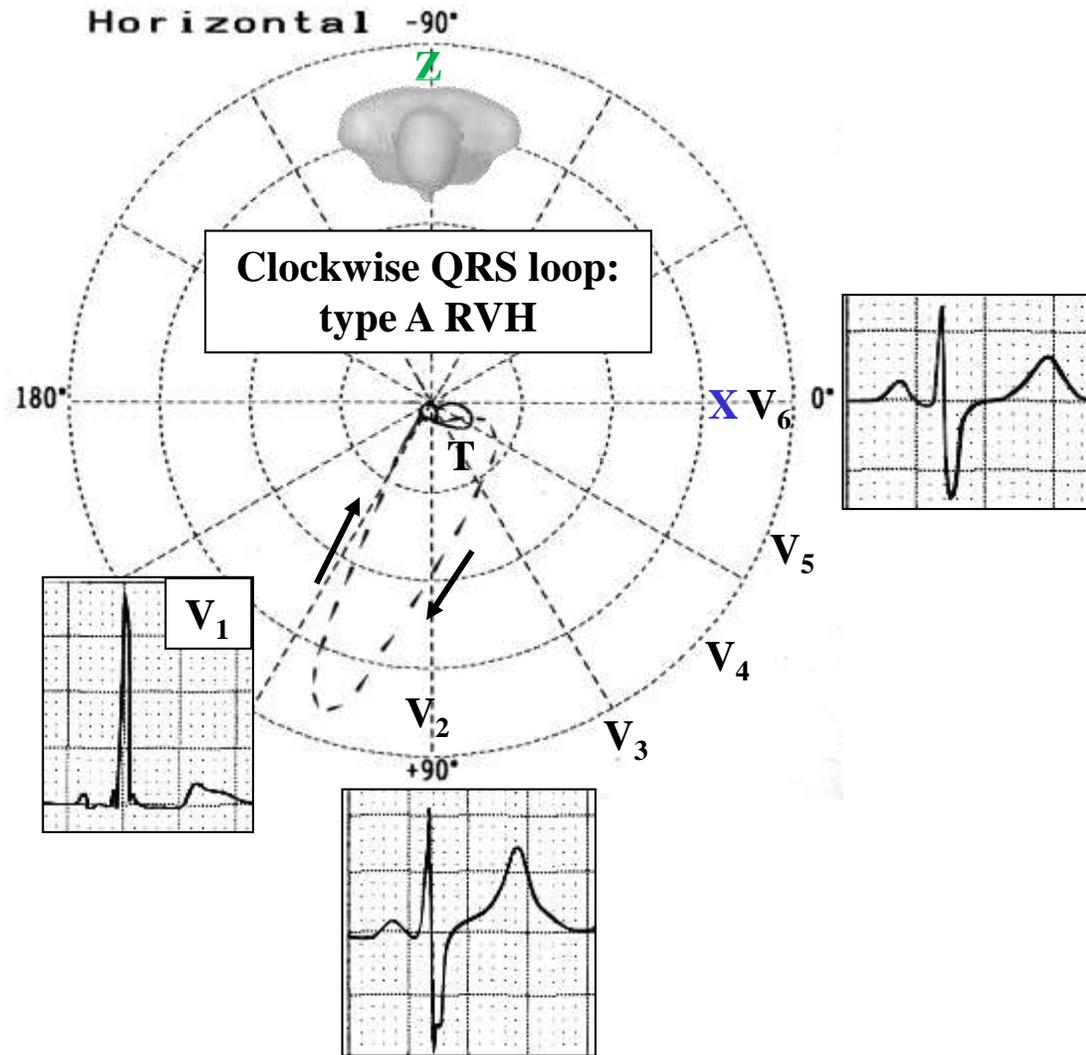
**ECG diagnosis:** SR; HR: 81 bpm; P wave: SAP  $+50^\circ$  forward; duration: 70 ms; PR: 100 ms. In newborn babies the normal PR interval is 80 ms to 120 ms (80 to 120 ms); QRS:  $\hat{S}\hat{A}\hat{Q}\hat{R}\hat{S}$  in the right superior quadrant near  $-170^\circ$ . In normal newborn babies, in average  $\hat{S}\hat{A}\hat{Q}\hat{R}\hat{S}$  is around  $+125^\circ$ , and it may reach  $180^\circ$ , i.e. in the right inferior quadrant:  $\hat{S}\hat{A}\hat{Q}\hat{R}\hat{S}$  to the right. Prominent R in aVR. HP: pure R wave with notch at the foot of the ascending limb and sudden transition from  $V_1$  to  $V_2$  RS type complexes from  $V_2$ - $V_6$ . The sign is present in 50% of these cases of TOF.

**Conclusion:** RVH.

# ECG/VCG correlation of classical TOF in the FP and RSP



# ECG/VCG correlation of classical TOF in the HP

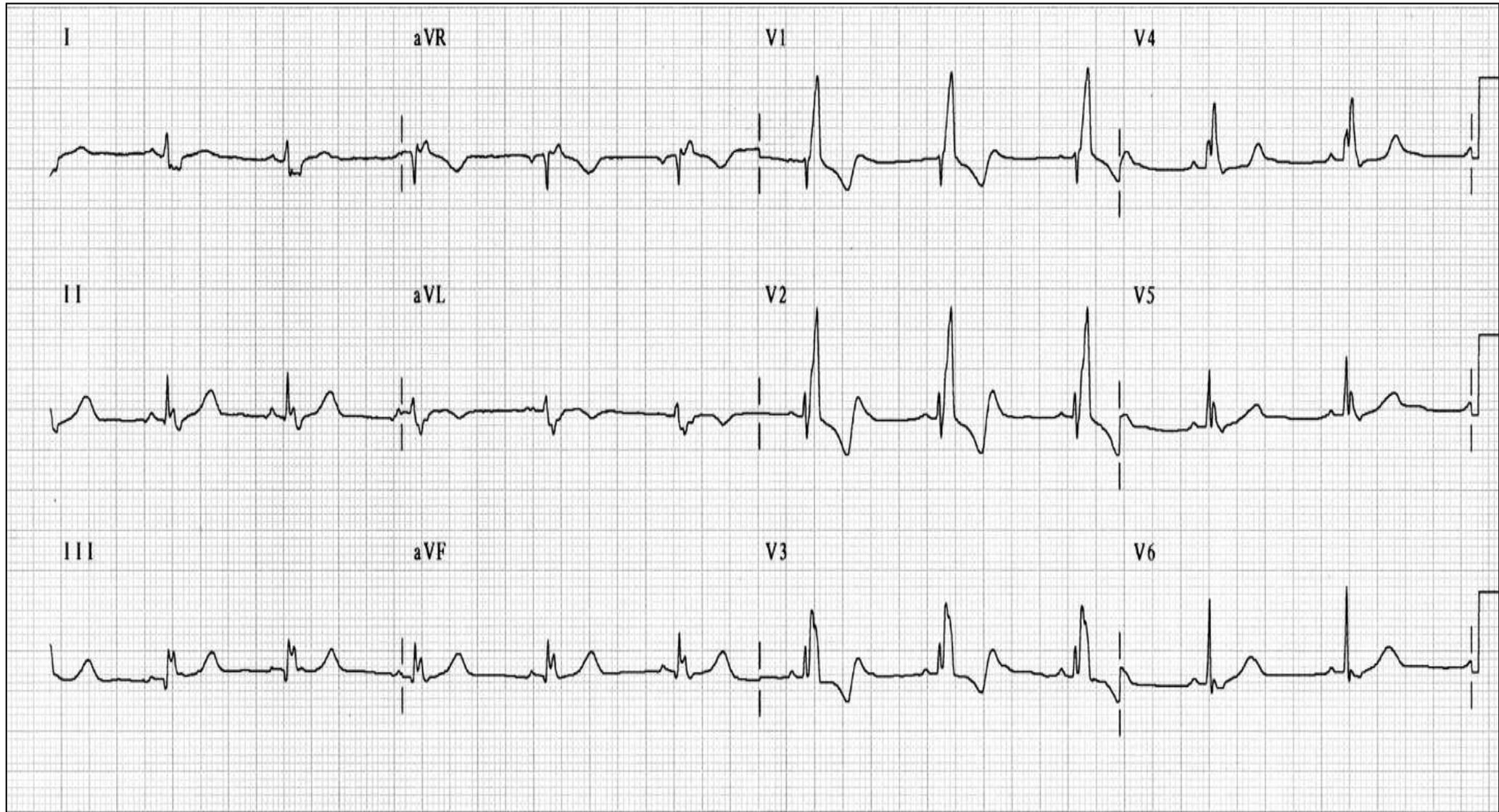


In newborn babies, if the voltage of R is equal or greater than 10 mm, it strongly suggests RVH; however, this diagnosis may not exist with up to 29 mm within the first 7 days of life and 26 mm within the remaining 21 days. In our case, pure R presents 19 mm with 20 days of life. T wave: it may be of positive polarity in V<sub>1</sub> in the first day of life, remaining negative since the third day. Positive T wave beyond such time, suggests RVH as in this case.

In the first two weeks of life, the location of the QRS loop is in the right anterior quadrant and with clockwise rotation.

Since the third or fourth weeks, the initial vector may head forward and to the left, and rotation may be like an eight (transitional phase of Cooskey).

**Name:** CYM; **Sex:** F; **Age:** 17 y/o; **Ethnic group:** Asian; **Weight:** 44 Kg; **Height:** 1.55 m; **Date:** 02/19/2004; **Medication in use:** nothing stated

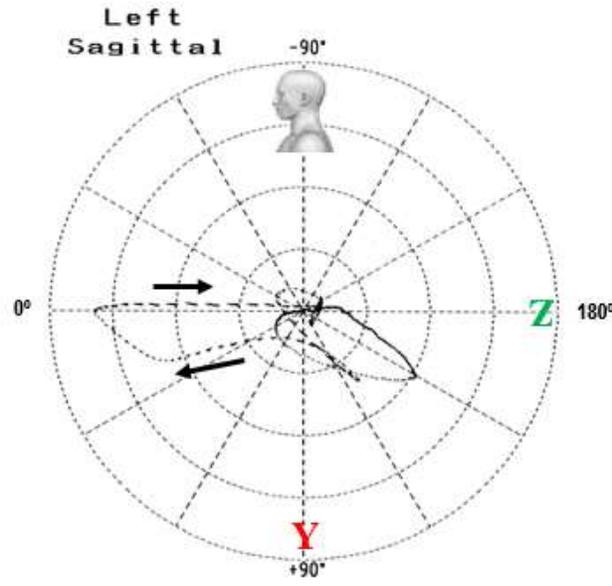
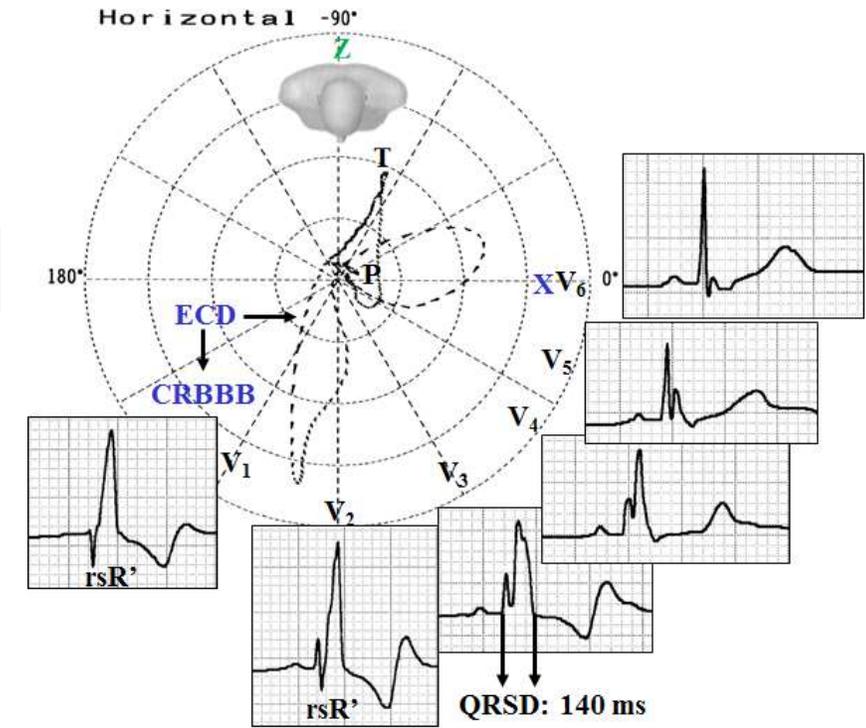
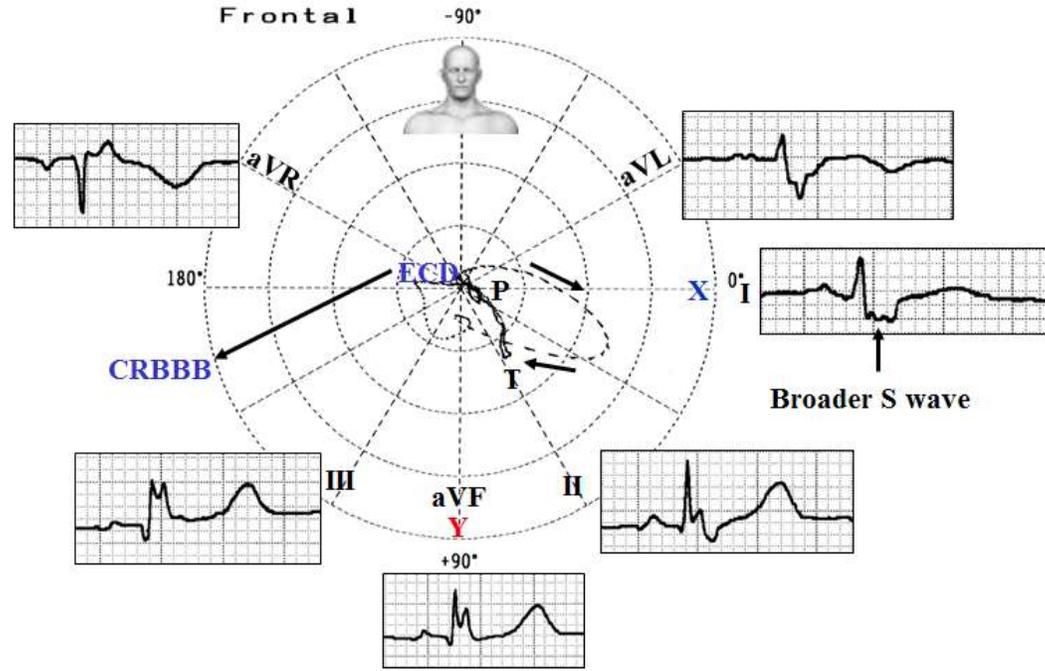


**Clinical diagnosis:** late post-operative (15 years) of total correction of Tetralogy of Fallot.

**ECG diagnosis:** SR; HR: 64 bpm; P wave:  $\hat{S}\hat{A}P$   $+40^\circ$  forward; PR interval: 129 ms; QTc: 479 ms; SAT:  $+60^\circ$ ; QRS:  $\hat{S}\hat{A}QRS$ :  $+118^\circ$ ;  $\hat{S}\hat{A}QRS$  duration: 141 ms; rsR' in V1 and V2; broader S wave in left leads.

**Conclusion:** CRBBB.

# ECG/VCG correlation of post-operative TOF

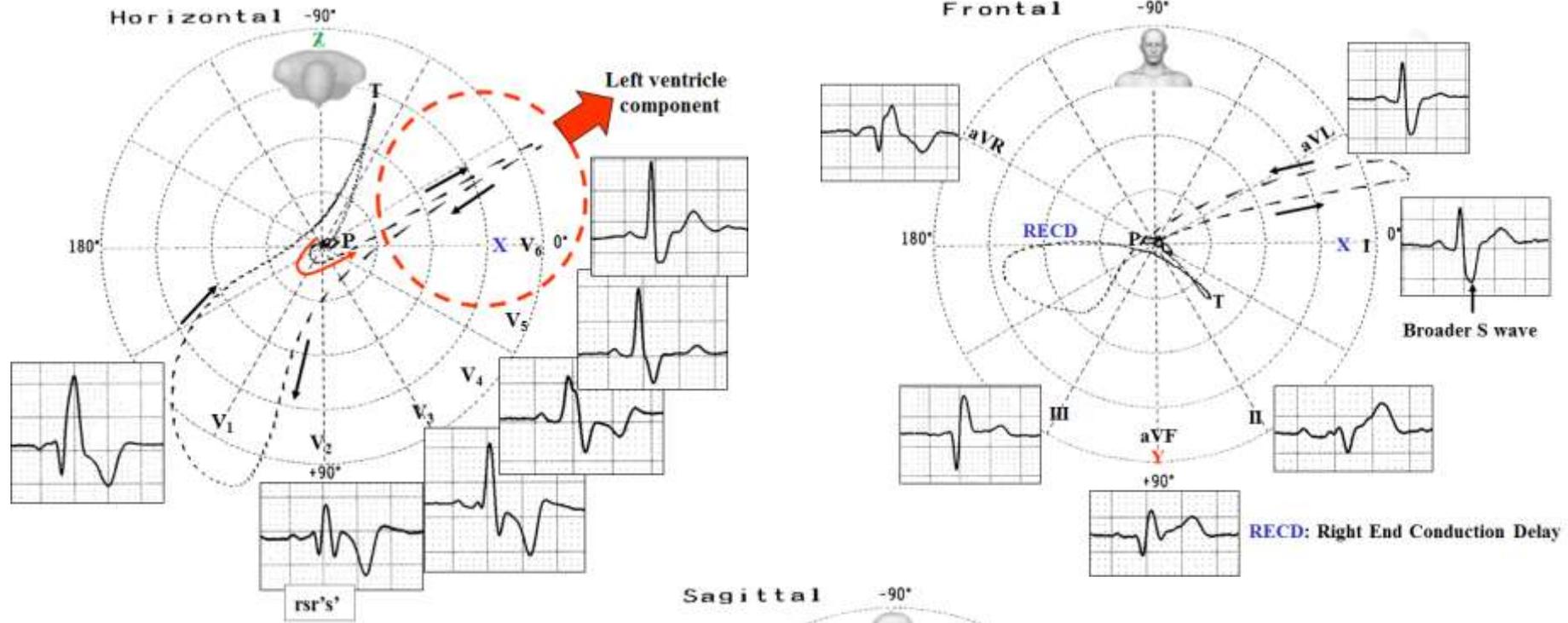


QRS loop with **ECD** in “glovesfinger”

Sensi.	4
Timer	2 msec
Loop	All Loop
Sagittal	Left
Z Axis	Back
Filter	Hum
	Muscle
	Drift



# ECG/VCG correlation



**HP** - Tetrphasic QRS complex in V<sub>2</sub> is indicative of RV lateropostero-basal selective hypertrophy: typical of Fallot's tetralogy. Glove finger morphology. RBBB pattern.

**FP** - SÂQRS near 180° (difficult determination). CCW rotation.

# Fallot´s pentalogy: another Brugada phenocopy

Brugada Syndrome (BrS) is a congenital cardiac channelopathy that affects repolarisation in patients with apparent structurally normal hearts predisposing them to malignant ventricular arrhythmias and sudden cardiac death. It is characterized by two distinct ECG patterns. Type-1 has a “coved” ST-segment elevation ( $\geq 0.2$  mV) with inverted T-wave in the right precordial leads and Type-2 has a “saddleback” appearance (Bayés de Luna 2012). Indistinguishable Brugada ECG patterns, referred to as Brugada Phenocopies (Baranchuk 2012; Anselm 2012), continue to emerge in the absence of true congenital BrS and their etiology is diverse including metabolic, structural, and ischemic causes. Pentalogy of Fallot (POF) is a congenital heart defect that includes the 4 classical characteristics of Tetralogy of Fallot (TOF) along with an atrial septal defect (Brickner 2000). We describe the first case in literature of an electrocardiographic Brugada Phenocopy emerging postoperatively in a patient who underwent surgical POF repair.

## Case report and ECG description

A 7 year-old girl with POF and otherwise unremarkable medical history underwent total surgical repair. Her preoperative 12-lead ECG (Figure 1) showed: sinus rhythm, heart rate 60 bpm, P-wave duration 85 ms, PR interval 167 ms, QRS duration 79 ms, QT interval 380 ms, QTc 424 ms, with extreme right axis deviation ( $-150^\circ$ ). In lead V1 she had a notched R-wave in the ascending peak.

The surgical technique consisted of right ventriculotomy and resection of the RVOT without valve replacement. A Gore-Tex patch was used to close both ventricular and atrial communications.

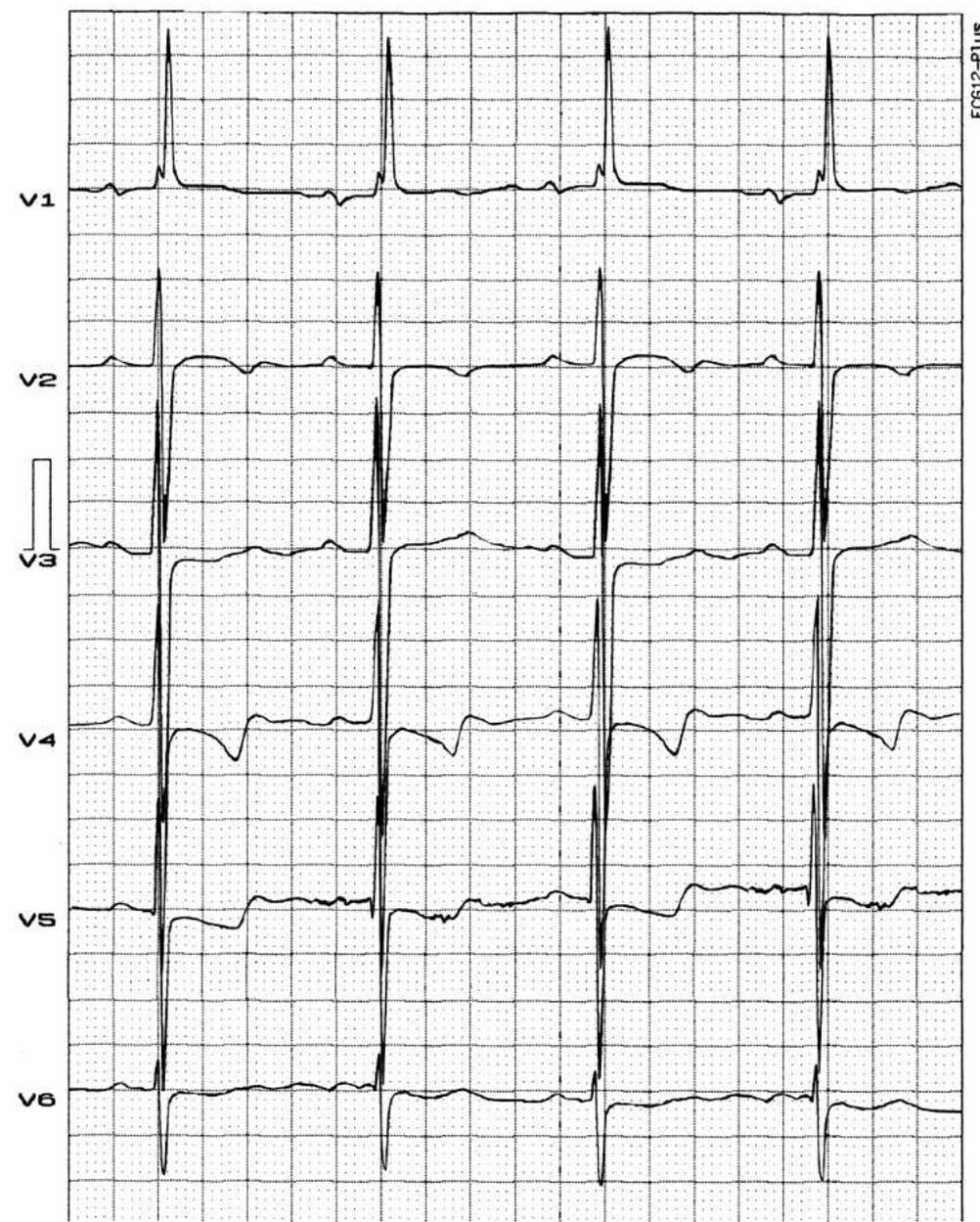
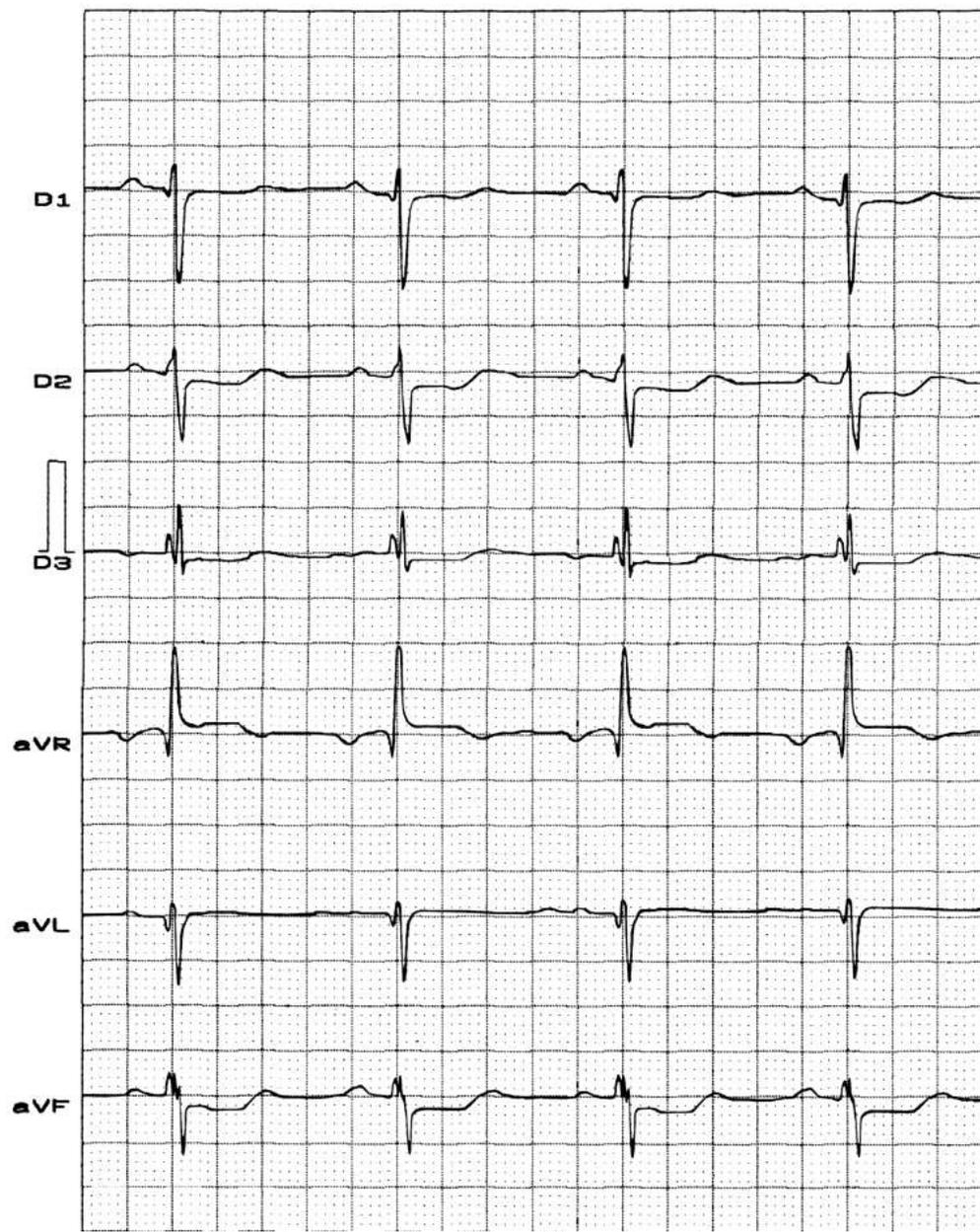


Figure 1: Preoperative electrocardiogram Sinus rhythm, heart rate 60 bpm, P-wave duration 85 ms, PR interval 167 ms, QRS duration 79 ms, QT interval 380 ms, QTc 424 ms, with extreme right axis deviation ( $-150^{\circ}$ ). In lead V1 she had a notched R-wave in the ascending peak.

During the immediate postoperative period her 12-lead ECG (Figure 2) showed: sinus rhythm, heart rate 107 bpm, P-wave duration 85 ms, PR interval 200 ms, QRS duration 120 ms, with extreme right axis deviation ( $-160^\circ$ ). The ECG pattern was consistent with a Brugada Type-1 ECG pattern (coved). There was also ST-depression in the lateral (V4-V6) and inferior leads (II, III, aVF).

Her postoperative hospital stay was unremarkable and she was discharged home after 7 days. During outpatient follow-up an ECG performed at 3 months postoperatively (Figure 3) showed: sinus rhythm, heart rate 65 bpm, P-wave duration 60 ms, PR interval 166 ms, QRS duration 120 ms, with extreme right axis deviation ( $-160^\circ$ ). The ECG showed resolution of the Brugada Type-1 ECG pattern observed earlier; however, continued to show complete RBBB with an rsR in V1 and V2, and RsR' in V3. There was also prominent R-wave with wide S-wave in I, aVL, V5 and V6. There were negative T-waves in V1-V4 and ST-depression in V4-V6. This pattern was also observed during long-term follow-up.

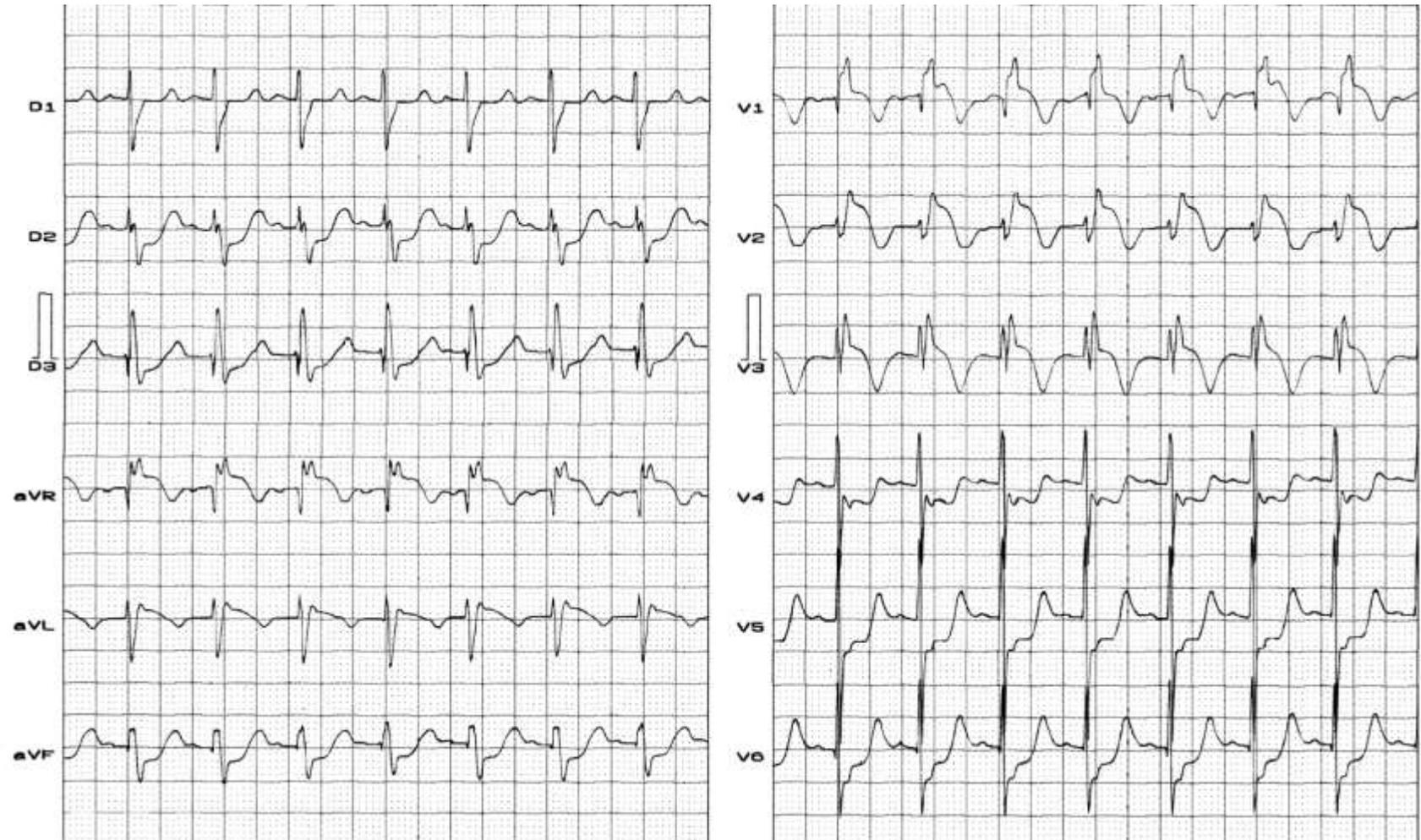


Figure 2: Immediate postoperative electrocardiogram

Sinus rhythm, heart rate 107 bpm, P-wave duration 85 ms, PR interval 200 ms, QRS duration 120 ms, with extreme right axis deviation ( $-160^\circ$ ). The ECG pattern was consistent with complete right bundle branch block (RBBB) with an rsR complex in V1, rsR' in V2 and RSR' in V3. There was a prominent R-wave in I, aVL, V5 and V6. There was ST-elevation and T-wave inversion in the right precordial leads consistent with a Brugada Type-1 ECG pattern. There was also ST-depression in the lateral (V4-V6) and inferior leads (II, III, aVF).

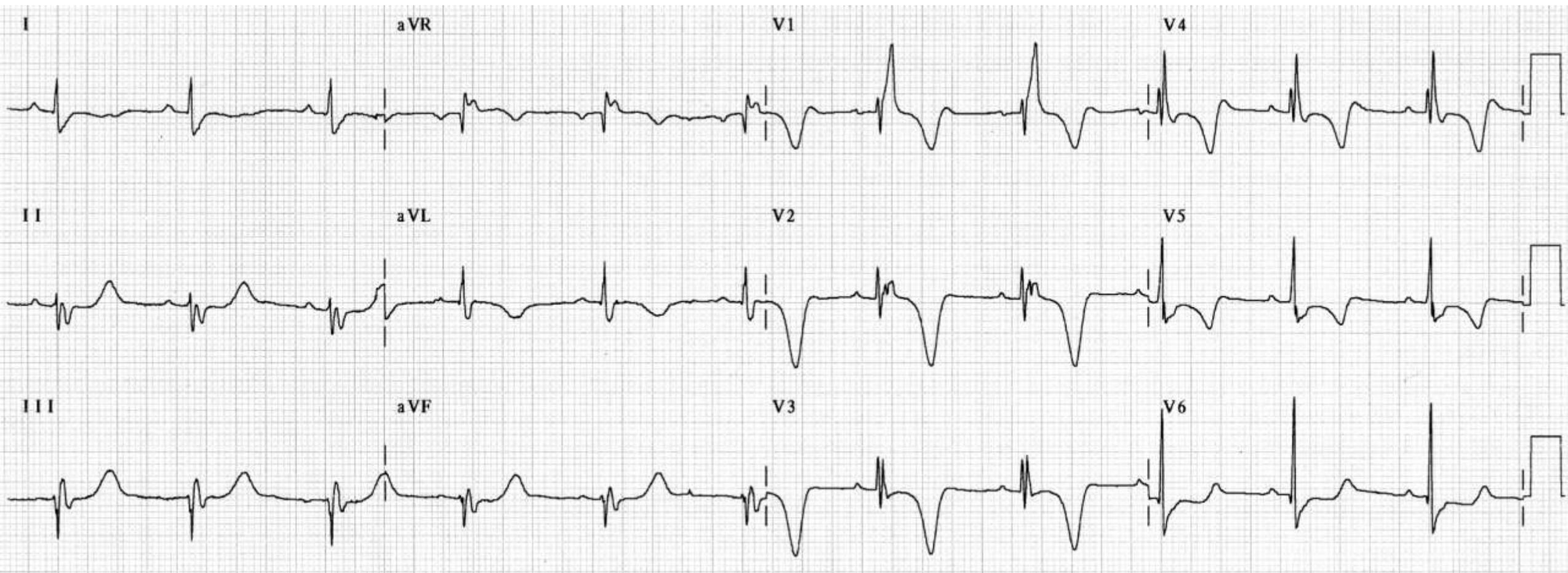


Figure 3: 3 month postoperative electrocardiogram

Sinus rhythm, heart rate 65 bpm, P-wave duration 60 ms, PR interval 166 ms, QRS duration 120 ms, with extreme right axis deviation ( $-160^{\circ}$ ). The ECG showed resolution of the Brugada Type-1 ECG pattern however continued to show complete RBBB with an rsR in V1 and V2, and RsR' in V3. There was also prominent R-wave with wide S-wave in I, aVL, V5 and V6. There were negative T-waves in V1-V4 and ST-depression in V4-V6.

## Points to Ponder

TOF is one of the most commonly encountered cyanotic congenital heart lesions with a prevalence of approximately 3.9 per 10,000 live births in the United States ([Centers for Disease Control and Prevention 2006](#)). The defect occurs approximately equally in both males and females and accounts for about 7 to 10 percent of all congenital heart lesions ([Report of the New England Regional Infant Cardiac Program 1980](#)). In about 10% of cases, an atrial septal defect is associated with TOF ([Rao 1971](#)) resulting in the so-called POF.

Brugada Phenocopies are continuing to emerge as distinct clinical entities. Recently, we updated the criteria for defining a Brugada Phenocopy ([Anselm 2012](#)) as follows: (i) the ECG pattern has a Brugada Type-1 or Type-2 morphology; (ii) the patient has an underlying condition that is identifiable; (iii) the ECG pattern resolves after resolution of the underlying condition; (iv) there is a low clinical pre-test probability for true BrS determined by lack of symptoms, past medical history and family history; (v) negative provocative testing with flecainide, procainamide, ajmaline, or other sodium channel blockers; (vi) negative genetic testing (non-mandatory criterion). The patient in this case report satisfied criteria (i) through (iv); however, this case introduces an additional caveat to point (v) in that provocative testing may not be required if there has been recent manipulation of the RVOT.

In this patient, we observed a transient Brugada Type-1 ECG pattern during the immediate postoperative period which resolved at 3 month follow-up leaving the patient with a persistent complete RBBB.

Interestingly, Gelband et al. ([Gelband 1971](#)) demonstrated that surgical right ventriculotomy was strongly associated with RBBB and they attributed the changes in right ventricular activation to the surgical ventriculotomy itself. Their postoperative ECG's, however, were taken ([Abramov 2005](#)) days after surgery and not in the immediate postoperative period as in our case. Hence, in their surgical cases the ST-segment elevation in the right precordial leads may have resolved by the time their postoperative ECG's were recorded.

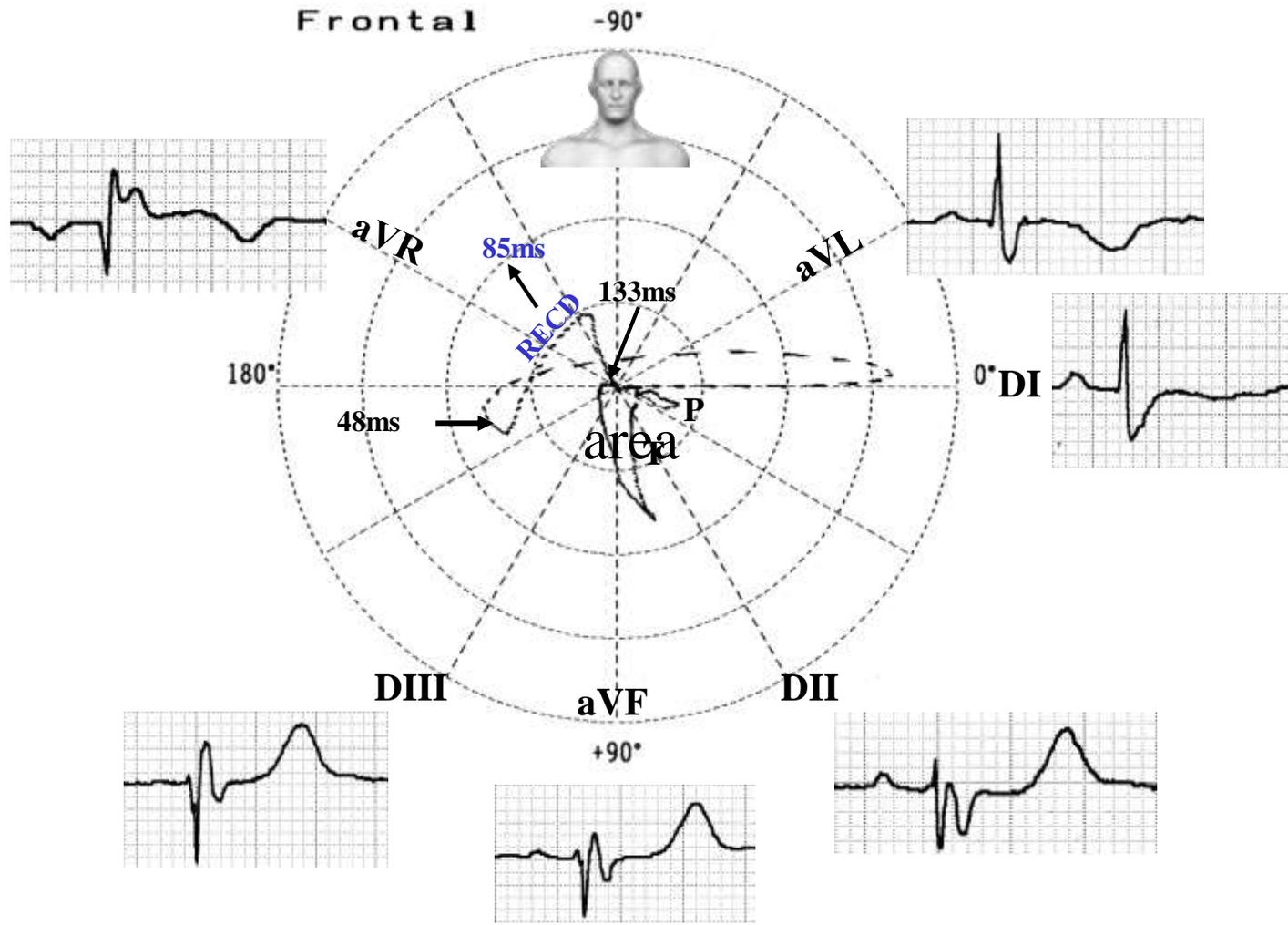
We hypothesize that in our case, manipulation of the RVOT during surgical POF repair may aggravate the anterior RVOT epicardium resulting in a transient Brugada Phenocopy during the immediate postoperative period. As such, we suggest that point (v) of the Brugada Phenocopy definition be revised as follows: negative provocative testing with flecainide, procainamide, ajmaline, or other sodium channel blockers (non-mandatory if RVOT manipulation has occurred within the last 96 hours). We chose the 96 hour cut-off because prior studies have shown that most surgical chest tubes should be removed within the first 24 hours postoperatively 9 and most epicardial pacing wires are removed by the 4th postoperative day because they begin to deteriorate Elmi 2002).

## **Conclusion**

Brugada Phenocopies exhibit Type-1 or Type-2 ECG patterns in the absence of true congenital BrS. This is the first case report of a patient with surgically corrected POF demonstrating a Brugada Type-1 ECG pattern during the immediate postoperative period that resolved in follow-up. The mechanism of this transient pattern may be associated with manipulation of the anterior RVOT epicardium.

# Late post-operative ecg/vcg correlation four months after surgery

Name: RCPL; Age: 7 years; Gender: female; Ethnic group: mixed; Weight: 26.000Kg; Height: 1.23m; Date: 12/12/03; Medication used: none stated.



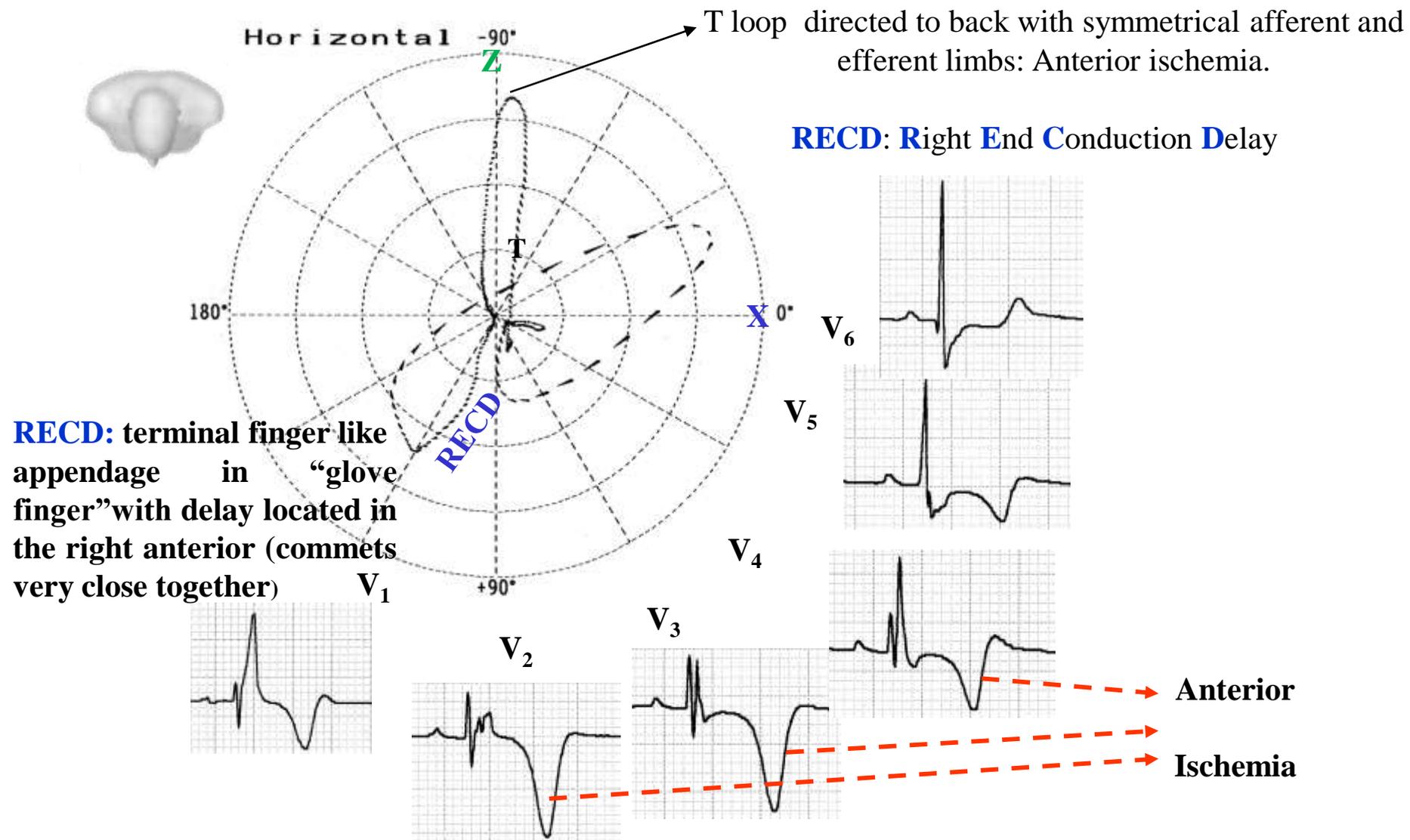
Diagnosis: CRBBB QRSD: 133 ms (>120ms). RECD (85ms) located on RVOT area.

# Late pos-operative ECG/VCG correlation four months after surgery

Name: RCPL; Age: 7 years; Gender: female; Ethnic group: mixed; Weight: 26.000Kg; Height: 1.23m  
used: none stated.

Date: 12/12/03

Medication



**Diagnosis:** CRBBB Grishman Type or Kennedy Type 1 (afferent limb behind X orthogonal leads). Anterior Ischemia: Deep negative symmetrical broad base T waves

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