# Case report

A 54-year-old Asian male patient, non-smoker, presented with recurrent cold with productive cough, copious expectoration, anosmia, rhinorrhea, headache and progressively increasing exertional shortness of breath for last 7 years. He had been previously treated with antibiotics, antihistamines and bronchodilators, but the response was only partial and temporary. His past history was significant as he had frequent visits to the pediatrician for recurrent respiratory infections. His family history revealed no parental consanguinity. He had been married for the last 28 years, but had no children.

**Physical examination:** blood pressure of 120/80 mmHg, pulse rate 60bpm regular. **Lungs**: Diffuse ronchi and bilateral coarse crackles (more on the left side) were heard. **Heart:** apical impulse(ictus cordis) is covered with one digitalis pulp and palped on the right side in fifth intercostal space at the point of intersection with the *right midclavicular line*. Heart sounds were heard best on the right side of the chest. There was bilateral hippocratic fingers with focal bulbous enlargement of the terminal segments (grade 2 digital clubbing).

We request: ECG, VCG, Chest X-ray, Ultrasound of the abdomen and genetic screening.

**Questions**: 1) What are the diagnostic keys? ; 2) Which is the ECG diagnosis?; 3) Which is the VCG diagnosis and why?

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Paciente asiático, masculino, 54 anos não-fumante, apresentado com resfriado recorrente, tosse produtiva, expectoração abundante, anosmia, rinorréia, dor de cabeça e progressiva falta de ar aos esforços nos últimos 7 anos. Ele havia sido reiteradamente tratado com antibióticos, anti-histamínicos e broncodilatadores, com resposta apenas parcial e temporária. Na sua história passada refere frequentes visitas ao pediatra para infecções respiratórias recorrentes.

A história familiar não revela consanguinidade. Casado há 28 anos, sem filhos.

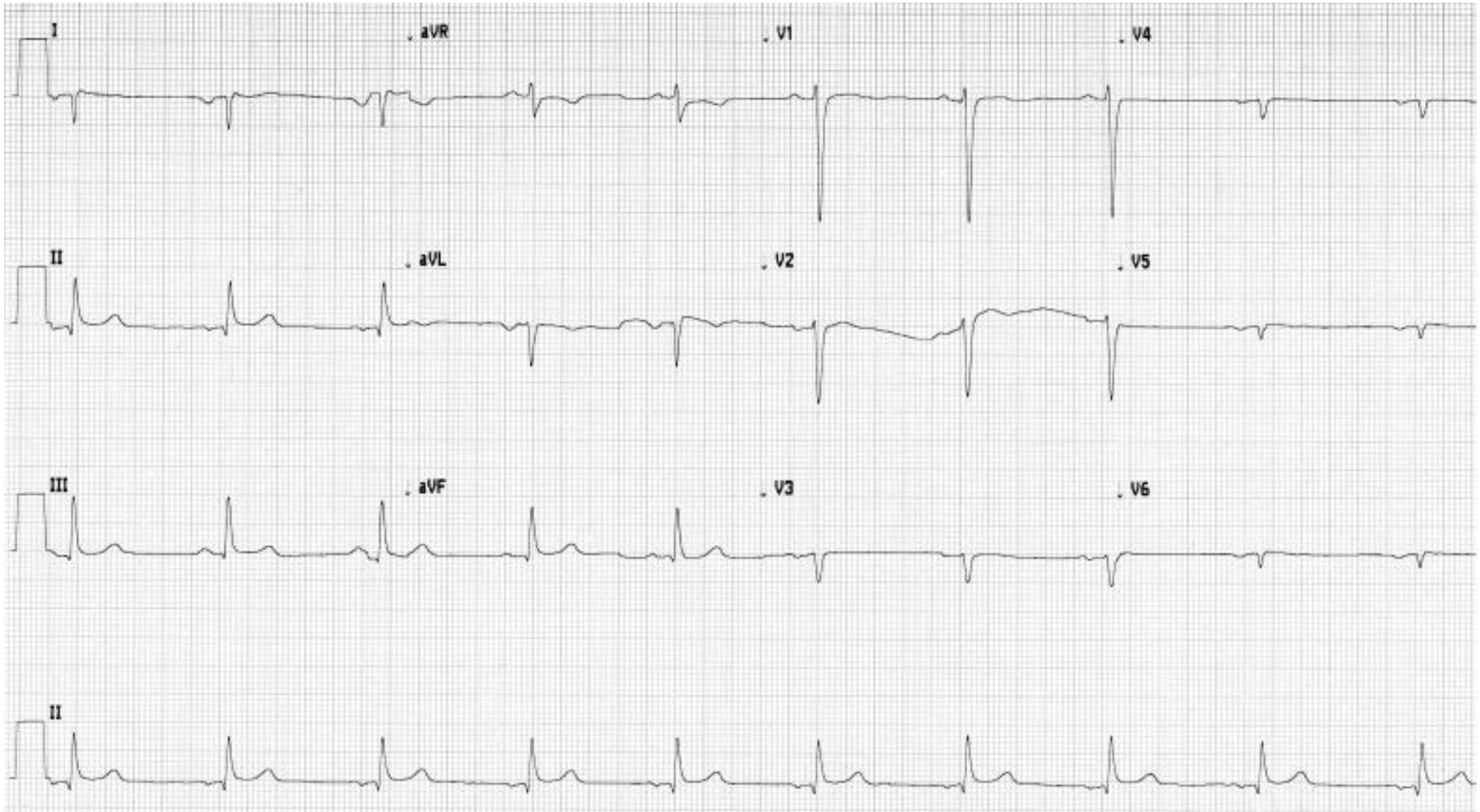
**Exame físico:** PA:120/80 mmHg, FC: 60bpm regular. **Pulmões:** roncos difusos e crepitações grosseiras bilaterais (mais à esquerda).

**Coração:** ictus cordis palpável no lado direito no quinto espaço intercostal na intersecção com a linha hemiclavicular direita se cobre com uma polpa digital. Os sons cardíacos ouvidos no lado direito do peito.

Dedos hipocráticos bilaterais com alargamento bulboso focal dos segmentos terminais (grau 2 clubbing).

Solicitamos ECG, VCG, radiografia de tórax, ultrassom do abdômen e rastreamento genético.

**Perguntas** Qual é o diagnóstico clínico?; 2) Qual é o diagnóstico eletrocardiográfico? 3) Qual é o diagnóstico VCG e por quê?


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II

# Colleagues opinions

Estimado Potro:1. Presenta dextrocardia en el electrocardiograma (habria que confirmar sino presenta un situs inversus)
2. Tríada de sinusitis, bronquiectasias y *situs inversus* descripta en en 1933 por (1)
Diagnostico: Síndrome de Kartagener
Un abrazo
Martín Ibarrola

Dear Andrés,

1. The patient has dextrocardia on ECG. I do not know if he has also situs inversus.
2. Manes Kartagener (1) first recognized this clinical triad situs inversus, chronic sinusitis, and bronchiectasis as a distinct congenital syndrome in 1933.

*1.Kartagener M. Zur pathogenese der bronchiectasien. I Mitteilung:bronchiectasien bei situs viscerum inversus. Betr Klin Tuberk. 1933. 83:498-501.*

Hola Tincho

Si pones Kartagener and Baranchuk en Google, te sale un lindo paper que escribmos hace unos anios. Se tradujo al frances, chino, ingles, espaniol y portugues. Por ahi andan todas las versions, creo. Hermoso caso

AB

Fibrilación auricular permanente en un paciente con síndrome de Kartagener y miocardiopatía isquémica 1 Mohammad Haqqi MD, 1 Genevieve Digby, 1 Adrian Baranchuk MD FACC. 1 División de Cardiología, Hospital General de Kingston, Universidad de Queen Caso de Reporte Palabras clave: Síndrome de Kartagener, disquinesia ciliar primaria, fibrilación auricular permanente, dextrocardia, coronariopatía.

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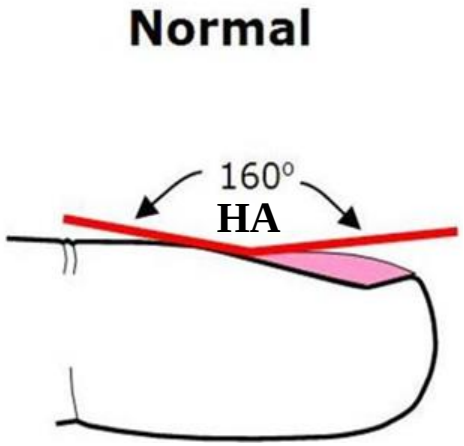
A Kingston cardiologist has been the first to prove what we always assumed: shovelling snow can kill you.
But it took a newcomer from Argentina to figure this out.
Dr. Adrian Baranchuk had heard that shovelling causes heart attacks — or at least be a trigger for some people — and when eight such patients turned up on his ward one day he tried to look up the scientific evidence to get the details. Only there wasn’t any.
Meanwhile, the continent’s two big associations of cardiologists both had guidelines warning heart patients not to shovel.
He couldn’t understand how all those cardiologists could give people advice without any studies to base it on.
That set Dr. Baranchuk in motion. He searched through Kingston General’s records for two winters, starting after the first snowfall each year and adding up the heart attacks — exactly 500, as it turned out.

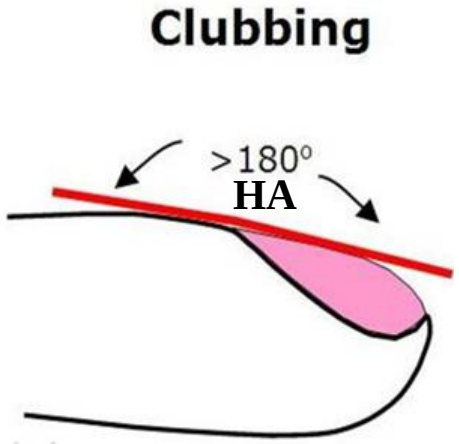
# Final comments by Andrés Ricardo Pérez-Riera

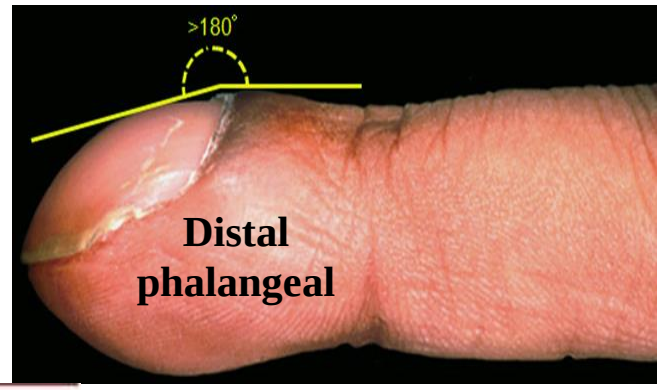
# Final conclusions - Primary Ciliary Dyskinesia (PCD) associated with dextrocardia: Kartagener syndrome

**Clinical diagnosis clues in the present case:**

1. His past history was significant: he had frequent recurrent respiratory infections.
2. Even married for 24 years, he had no children, which may suggest infertility for male sterility, which is a common finding in Kartagener syndrome.
3. Grade 2 of digital clubbing: Hippocratic fingers with focal bulbous enlargement of the terminal segments are frequent in Kartagener syndrome. The hyponychial angle (HA) and the distal phalangeal depth/interphalangeal depth (DPD/IPD) ratio are determined on profile shadow projections of the index fingers.

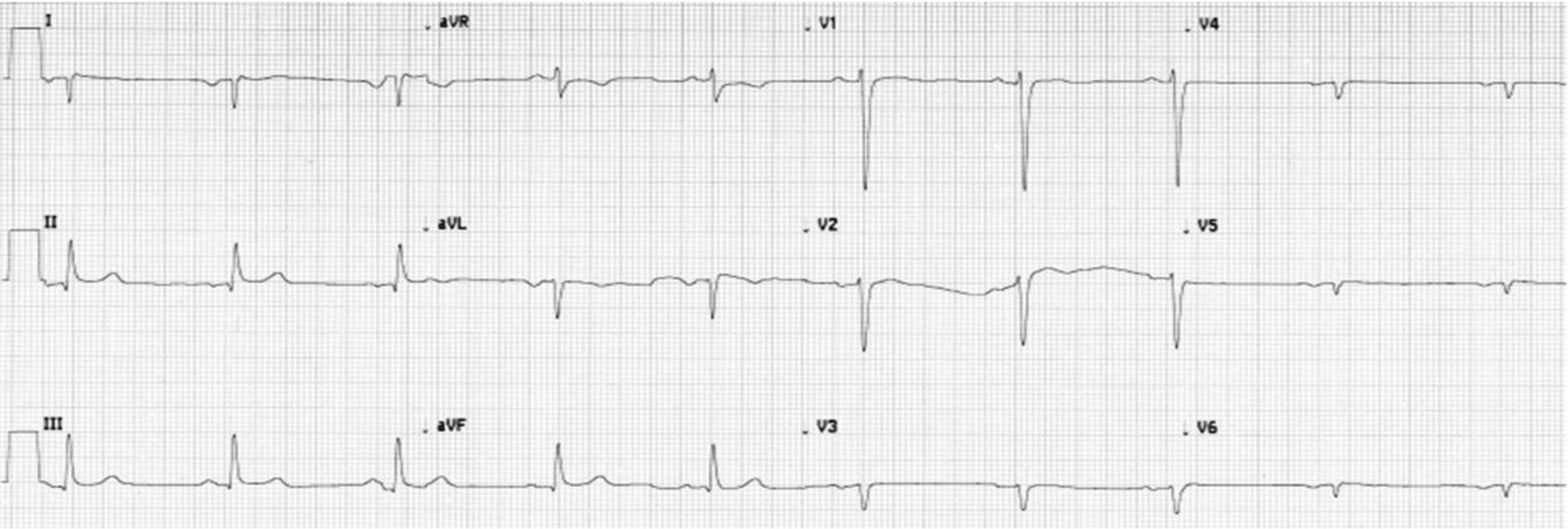


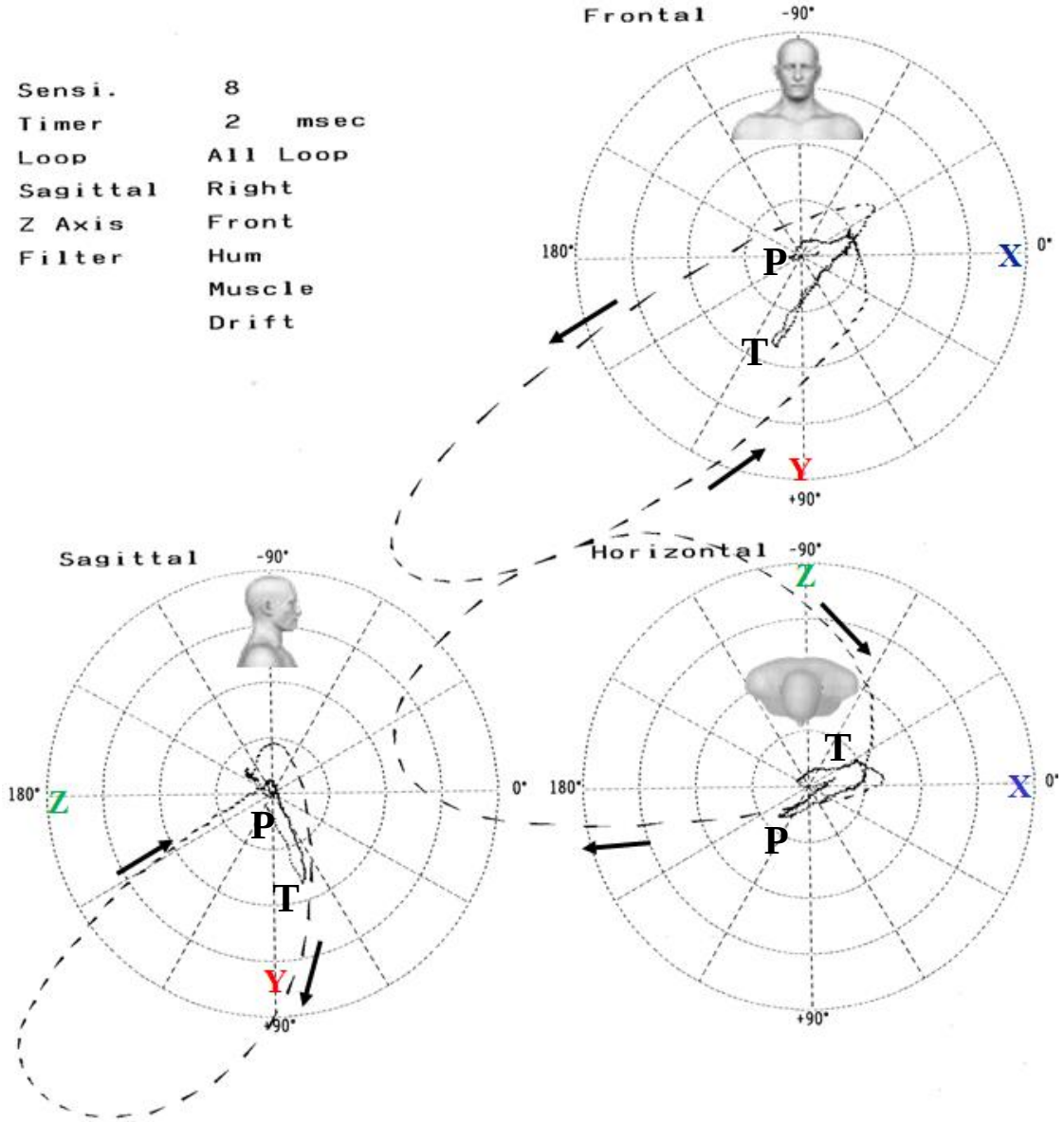

| | |
|---|---|
| Grade 1 | Fluctuation and softening of the nail bed |
| Grade 2 | Increase in the normal 160° angle between the nail bed and the proximal nail fold. |
| Grade 3 | Accentuated convexity of the nail |
| Grade 4 | Clubbed appearance of the fingertip |
| Grade 5 | Development of a shiny or glossy change in nail and adjacent skin with longitudinal striations |

4. Apical impulse(ictus cordis) is palped on the right side in fifth intercostal space at the point of intersection with the *right midclavicular line*.
5. Heart sounds were heard best on the right side of the chest.
6. ECG/VCG features.



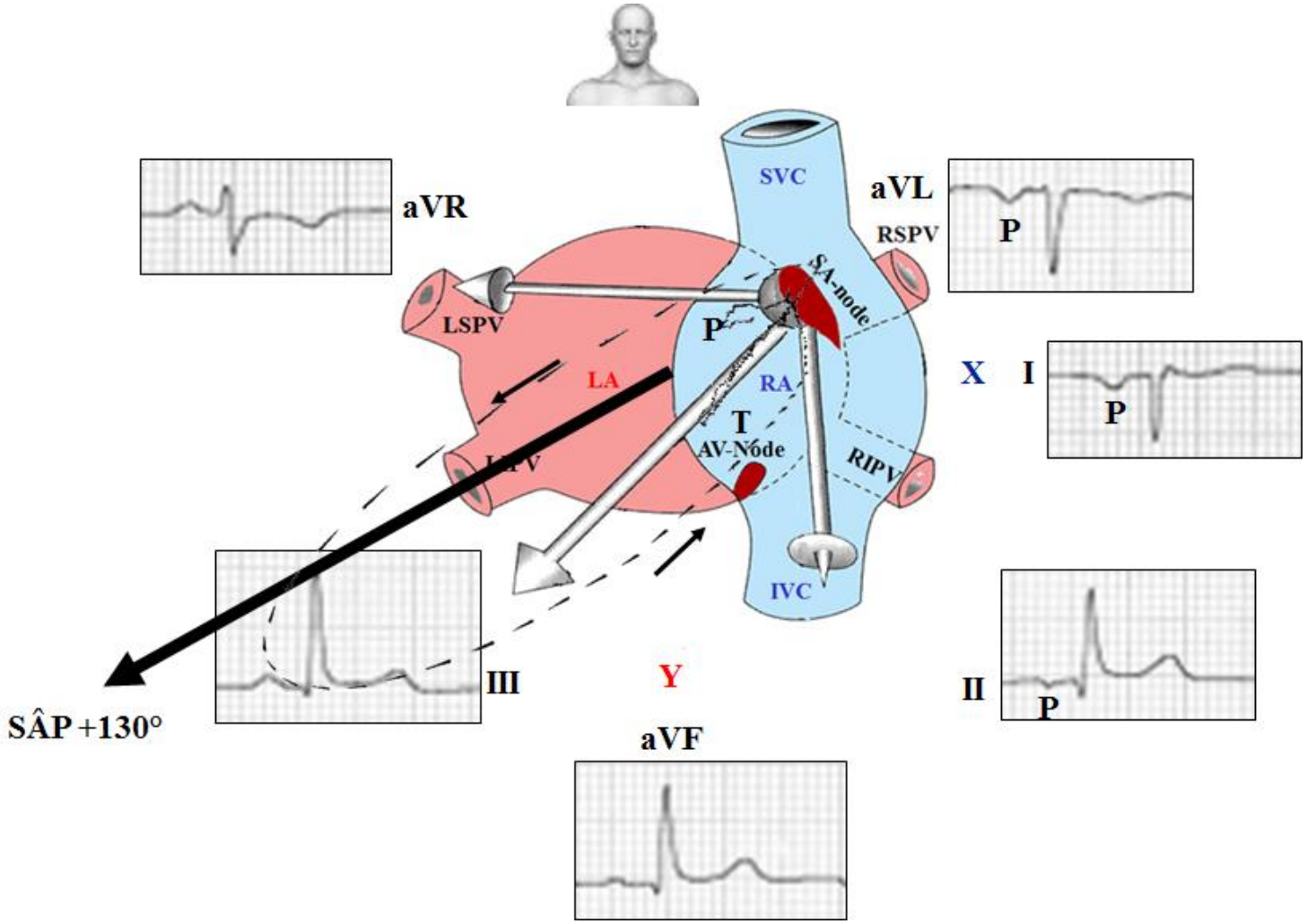

**ECG diagnosis: Lead I:** P, QRS and T waves inverted or upside down. **Lead II:** represented the usual lead III and vice versa. aVR and aVL are reversed and prominent negative deflections are seen in aVL rather than in aVR. aVF is unaffected.
P axis (SÂP) to the right and below, pointing at around +130º. Negative P wave in aVL and I, positive in III and aVR.
**Precordial leads: From V1 to V6** QRS complexes show progressive decreasing R/r wave amplitude: Reverse progression of r wave in precordial leads from V1 to V6 (decreasing). V1 is the equivalent of the usual V2 and vice versa.
**Conclusion:** Truly dextrocardia.

# The vectorcardiogram in the three spatial planes: Frontal (FP), Horizontal (HP) and Right Sagittal (RSP)




The P, QRS and T loops are the mirror or reciprocal image of situs solitus. P loops axis is directed from left to right, pointing at around +130° in the FP, to front and righward in the HP. QRS loop is located predominantly on right inferior quadrant in the FP, in the right posterior quadrant in the HP and inferior posterior quadrant in the RSP.

# ECG/VCG correlation in the frontal plane




SÂP vector is directed from left to right, top to bottom, pointing at around +130°. This fact will yield negative P wave in aVL and I, positive in III and aVF and aVR.

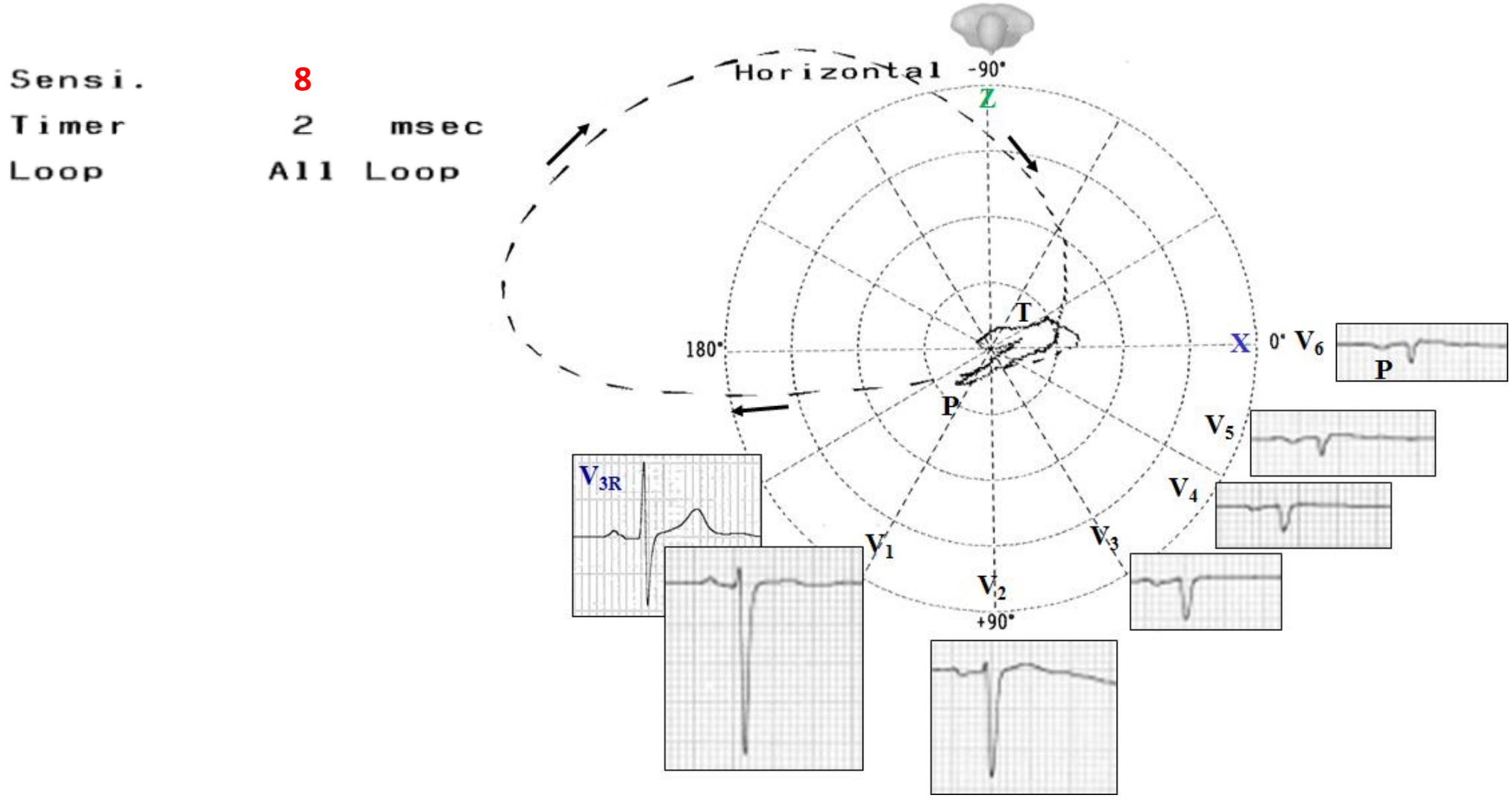
**Lead I:** P, QRS and T waves inverted or upside down.

**Lead II:** represented the usual lead III and vice versa.

aVR and aVL are reversed and prominent negative deflections are seen in aVL rather than in aVR.

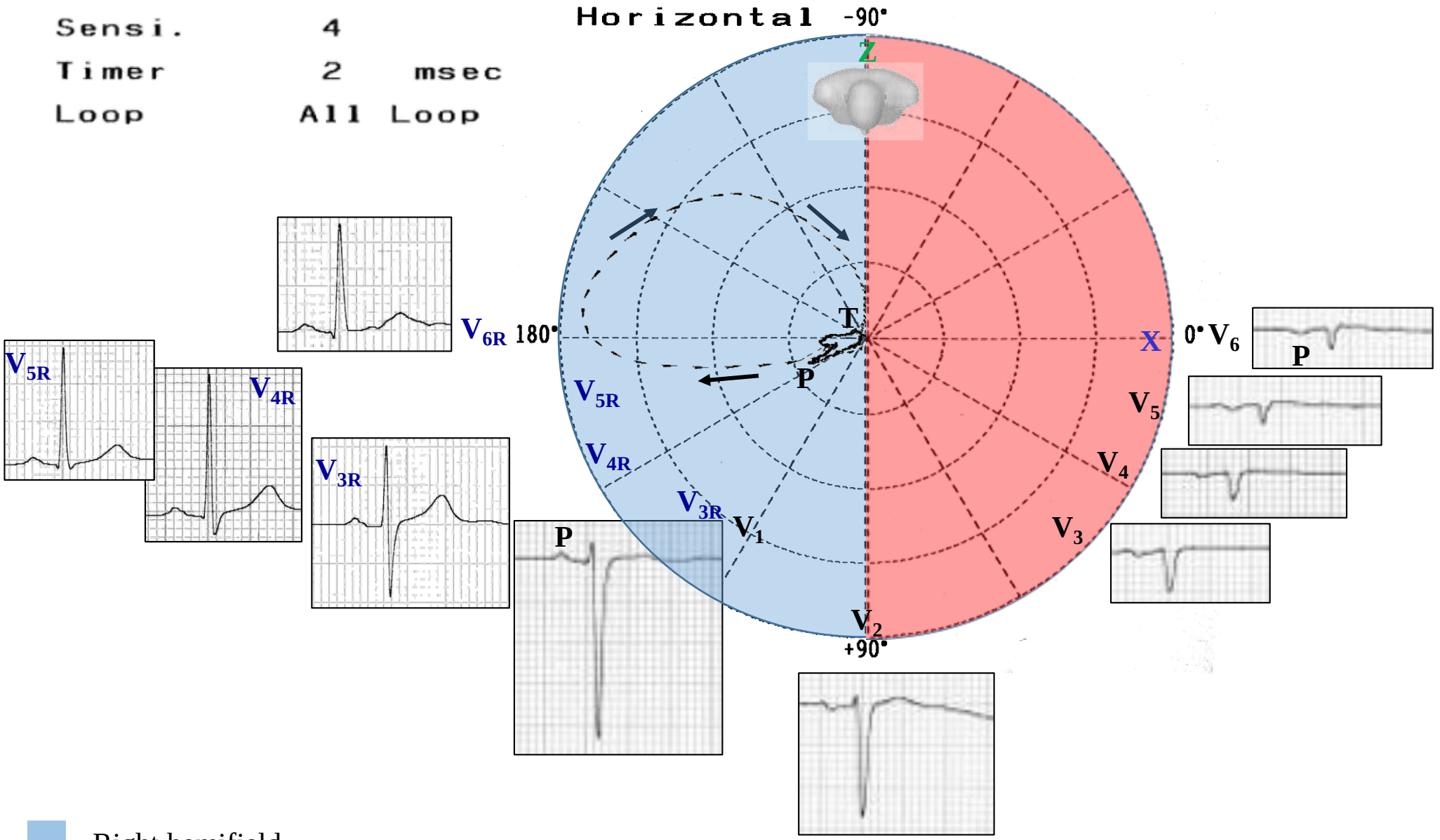
aVF is unaffected.

# ECG/VCG correlation in the Horizontal Plane and accessory lead $V_{3R}$




P loop pointed to front and rightward (P wave positive in V1 and negative in V6), initial 10 ms vector forward and to the right, QRS loop área is located predominantly on right posterior quadrant (it is in the left posterior quadrant in situs solitus), counterclockwise rotation, reverse progression of r wave in precordial leads $V_1$ to $V_6$ (decreasing). This last one is very importante for the differential diagnosis with accidental misplacement of the limb lead electrodes.

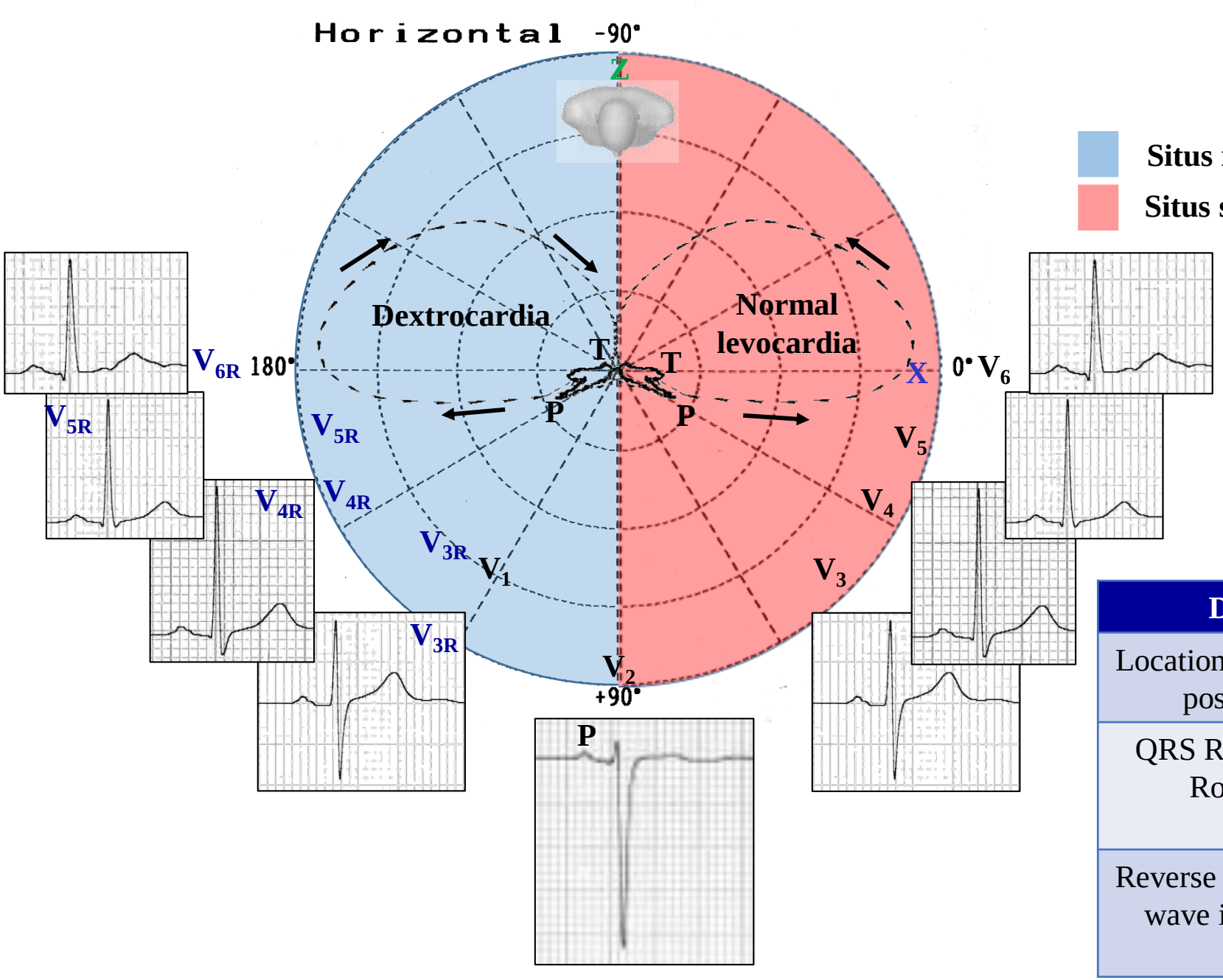
# ECG/VCG correlation in the horizontal plane with left and right precordial leads

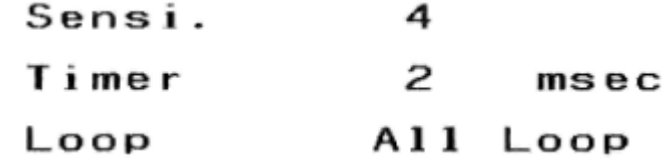



Right hemifield

Left hemifield

# P, QRS and T loops with mirror image in the HP: concomitant loops with situs inversus and situs solitus




**Situs inversus: truly dextrocardia (the present case)**

**Situs solitus: normal levocardia**

**Right hemifield**

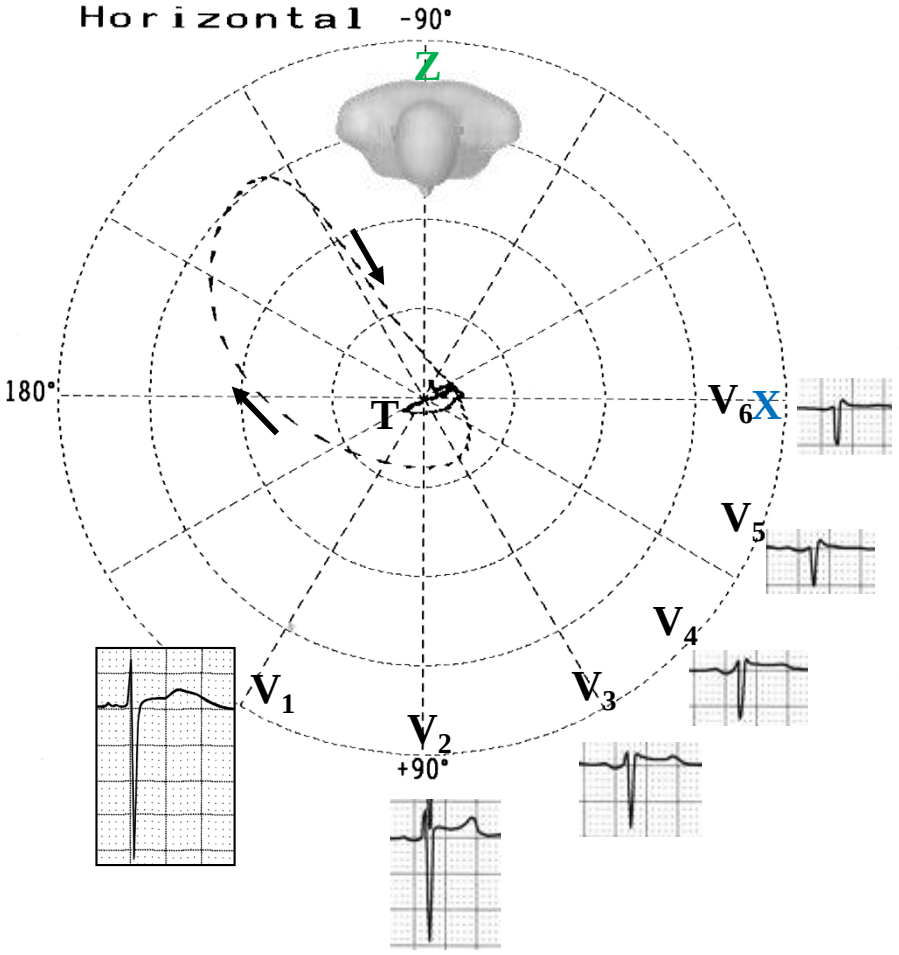
**Left hemifield**

| Dextrocardia | Normal heart |
|---|---|
| Location of QRS loop: Right posterior quadrant | Location of QRS loop: Left posterior quadrant |
| QRS Rotation: Clockwise Rotation (CW-R) | QRS Rotation: Counterclockwise Rotation (CCW-R) |
| Reverse progression of the R wave in precordial leads | Normal progression: increased R wave from V1-V4 |

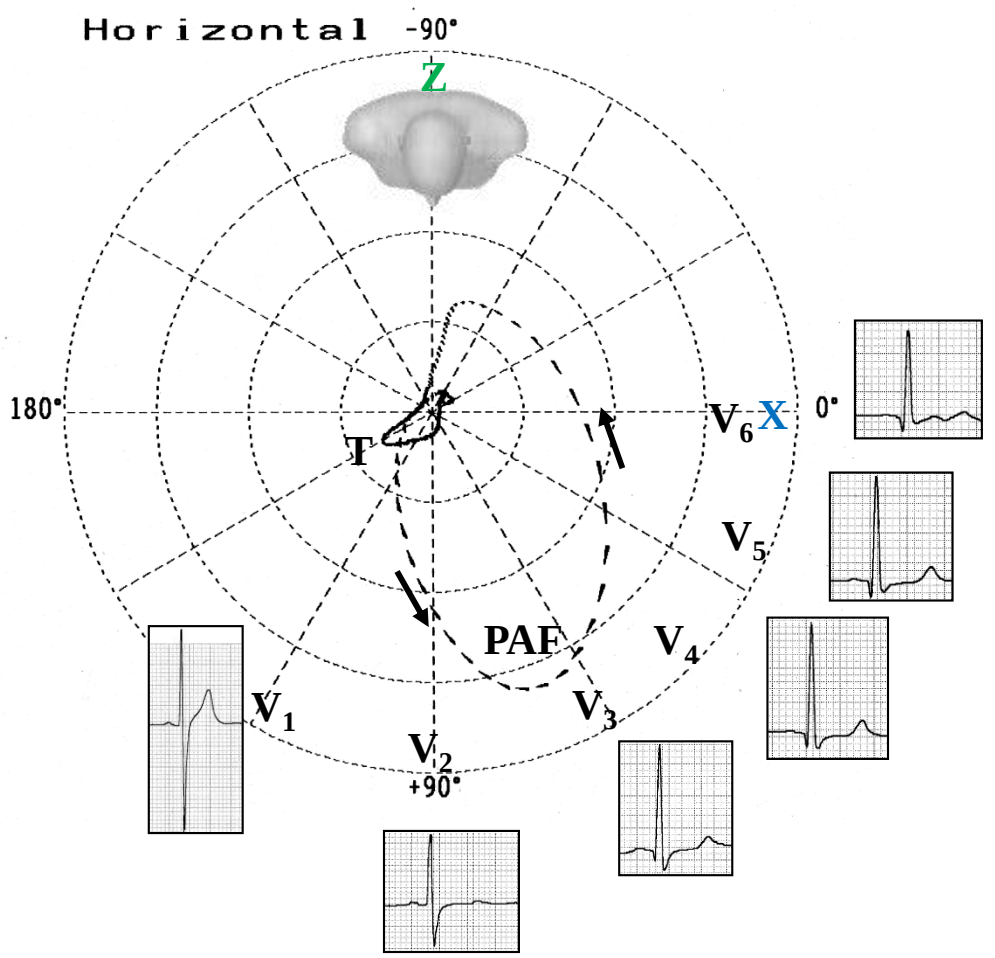
# Criteria for the differential diagnosis between normal and simple true dextrocardia

| | Normal | Simple true dextrocardia |
|---|---|---|
| Initial 10 to 20 ms vector | Forward and to the right | Forward and to the left |
| QRS loop rotation | Counterclockwise | Clockwise |
| Location and voltage of maximal vector | Left posterior quadrant. Voltage does not exceed 2 mV. | Right posterior quadrant. The maximal vector represents the systemic or arterial ventricle. Voltage does not exceed 2 mV. |
| I Lead | Positive P; qRs type QRS and positive T. | Negative P, QRS and T. |
| aVL-aVR | The first positive and the second negative: P, QRS and T. | The first negative and the second positive: P, QRS and T. |
| II-III | Variable | Usual image of II in III and vice-versa. |
| $V_1$ - $V_2$ | rS | There may be initial q: qRs. |
| $V_5$ -$V_6$ | qRs or Rs with positive T wave. | rS or rSr' with negative T. |
| Progression of r wave in precordial leads | Progressive increase of R wave voltage from $V_1$ to $V_5$ . | Reverse progression: R wave of decreasing voltage from $V_2$ to $V_5$ . |
| T loop | To the left and in adults, slightly forward: always positive in $V_2$ -$V_6$. | To the right and in adults, slightly forward: negative T in $V_5$ -$V_6$. |

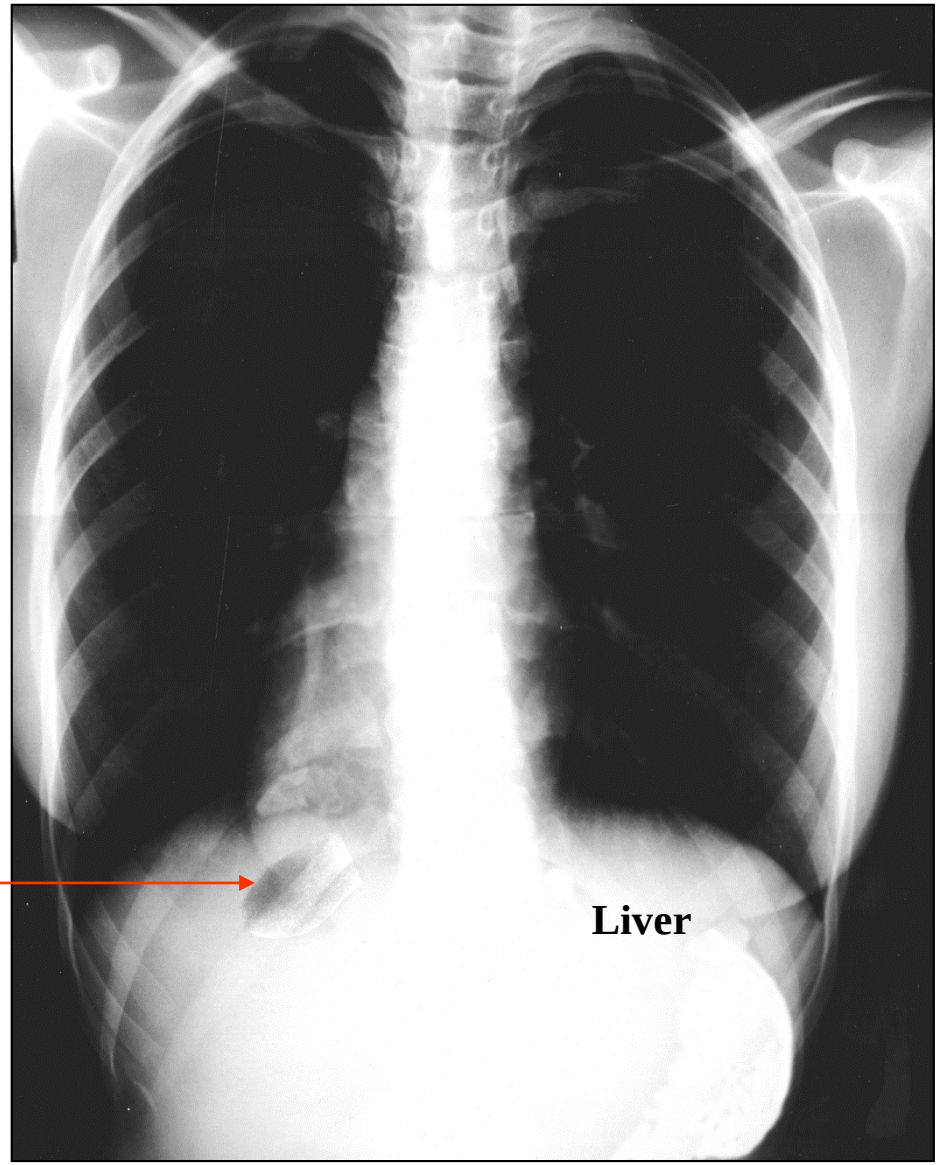
**True dextrocardia**




**Dextroposition or pseudo-dextrocardia**




| | |
|---|---|
| Predominant location of QRS loop: right posterior quadrant | Predominant location of QRS loop: left anterior quadrant |
| QRS rotation: clockwise | QRS rotation: Counterclockwise |
| Reverse progression of the R wave in precordial leads | Prominent Anterior QRS Forces (PAF) |




Typical radiography of a true dextrocardia with "situs inversus," gastric chamber to the right and liver to the left. Heart at the right (dextrocardia), inverted atrial position, liver at the left, gastric chamber and spleen at the right. Situs inversus: mirror image or insolitus.

# Genetic background: Mutations in the Genes that Cause Human Primary Ciliary Dyskinesia

| Human Gene | Human Chromosomal Location | Chlamydomonas Ortholog | Ciliary Ultrastructure in Subjects with Biallelic Mutations | Presence of Laterality Defects | Percentage of Individual with Biallelic Mutations | MIM No. |
|---|---|---|---|---|---|---|
| DNAH5 | 5p15.2 | DHC ? | ODA defect | Yes | 15–21% of all PCD, 27–38% of PCD with ODA defects | 608644 |
| DNAI1 | 9p21-p13 | IC78 | ODA defect | Yes | 2–9% of all PCD, 4–13% of PCD with ODA defects | 244400 |
| DNAI2 | 17q25 | IC69 | ODA defect | Yes | 2% of all PCD, 4% of PCD with ODA defects | 612444 |
| DNAL1 | 14q24.3 | LC1 | ODA defect | Yes | na | 614017 |
| CCDC114 | 19q13.32 | DC2 | ODA defect | Yes | 6% of PCD with ODA defects | 615038 |
| TXNDC3 (NME8) | 7p14-p13 | LC5 | Partial ODA defect (66% cilia defective) | Yes | na | 610852 |
| DNAAF1 (LRRC50) | 16q24.1 | ODA7 | ODA + IDA defect | Yes | 17% of PCD with ODA + IDA defects | 613193 |
| DNAAF2 (KTU) | 14q21.3 | PF13 | ODA + IDA defect | Yes | 12% of PCD with ODA + IDA defects | 612517, 612518 |

| Human Gene | Human Chromosomal Location | Chlamydomonas Ortholog | Ciliary Ultrastructure in Subjects with Biallelic Mutations | Presence of Laterality Defects | Percentage of Individual with Biallelic Mutations | MIM No. |
|---|---|---|---|---|---|---|
| DNAAF3 (C19ORF51) | 19q13.42 | PF22 | ODA + IDA defect | Yes | na | 606763 |
| CCDC103 | 17q21.31 | PR46b | ODA + IDA defect | Yes | na | 614679 |
| HEATR2 | 7p22.3 | Chlre4 gene model 525994 Phytozyme v8.0 gene ID Cre09.g39500.t1 | ODA + IDA defect | Yes | na | 614864 |
| LRRC6 | 8q24 | MOT47 | ODA + IDA defect | Yes | 11% of PCD with ODA + IDA defects | 614930 |
| CCDC39 | 3q26.33 | FAP59 | IDA defect + axonemal disorganization | Yes | 36–65% of PCD with IDA defects + Axonemal disorganization | 613798 |
| CCDC40 | 17q25.3 | FAP172 | IDA defect + axonemal disorganization | Yes | 24–54% of PCD with IDA defects + Axonemal disorganization | 613808 |
| RSPH4A | 6q22.1 | RSP4, RSP6 | Mostly normal, CA defects in small proportion of cilia | No | na | 612649 |
| RSPH9 | 6p21.1 | RSP9 | Mostly normal, CA defects in small proportion of cilia | No | na | 612648 |

| Human Gene | Human Chromosomal Location | Chlamydomonas Ortholog | Ciliary Ultrastructure in Subjects with Biallelic Mutations | Presence of Laterality Defects | Percentage of Individual with Biallelic Mutations | MIM No. |
|---|---|---|---|---|---|---|
| HYDIN | 16q22.2 | hydin | Normal, very occasionally CA defects | No | na | 610812 |
| DNAH11 | 7p21 | DHC ß | Normal | Yes | 6% of all PCD, 22% of PCD with normal ultrastructure | 603339 |
| RPGR | Xp21.1 | na | Mixed | No | PCD cosegregates with X-linked Retinitis pigmentosa | 300170 |
| OFD1 | Xq22 | OFD1 | nd | No | PCD cosegregates with X-linked mental retardation | 312610 |
| CCDC164 (C2ORF39) | 2p23.3 | DRC1 | Nexin (N-DRC) link missing; axonemal disorganization in small proportion of cilia | No | na | 312610 |

CA = central apparatus; IDA = inner dynein arm; MIM = Mendelian Inheritance in Man; na = not available; N-DRC = nexin–dynein regulatory complex; ODA = outer dynein arm; PCD = primary ciliary dyskinesia.

*Knowles MR, Daniels LA, Davis SD, Zariwala MA, Leigh MW. Primary ciliary dyskinesia. Recent advances in diagnostics, genetics, and characterization of clinical disease. Am J Respir Crit Care Med. 2013 Oct 15. 188(8):913-22.*

# Differential diagnoses of Human Primary Ciliary Dyskinesia

- Adenoid hyperplasia
- Allergic bronchopulmonary aspergillosis
- Alpha1-Antitrypsin Deficiency
- Bronchial obstruction
- Chronic Obstructive Pulmonary Disease
- Chronic aspiration
- Congenital cartilage deficiency
- Cystic fibrosis
- Foreign body aspiration
- Idiopathic interstitial pneumonias
- Idiopathic nasal polyposis
- Immunosuppression
- Inhalation of toxic substances
- Interstitial lung diseases, including idiopathic pulmonary fibrosis
- Malignancy
- Postinfectious bronchiectasis
- Pulmonary sequestration
- Samter triad
- Severe atopy
- Tracheobronchomegaly
- Tumor
- Yellow nail syndrome