NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

The Breathless Heart

by

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Part I – 2D Echocardiography and Color Doppler Report

Singh was an undergraduate at Smith College. In his junior year he had applied and landed an internship at Boston Children's Hospital. He currently was working in a cardiovascular research laboratory. He had specifically been drawn to this area of biology because it had impacted the lives of his family. His baby brother Pavit had died at 26 days old in 2003. Wishing to understand what happened to his brother, Singh asked his mother, Mena, about Pavit.

Mena related the events of that terrible time to Singh. "We were so happy when Pavit was born. You were so excited. From the start I had difficulty feeding Pavit. He was so fussy, refusing to nurse, panting, and sweating; he looked so pale to me. The doctor dismissed this when he was born and again at the first three-day checkup saying it was normal, India is hot. I could not sleep; I took him back five days later to a different doctor, Dr. May. Pavit was taken immediately from me. I remember sitting there for hours on those hard chairs. The new doctor performed an echocardiograph and color doppler to image the heart and blood vessels to see how they were working. I asked if all was good with my baby. I can recall the room becoming quiet, the welcoming smiles disappearing, heads shaking. I knew it was going to be bad. They told me that Pavit had congenital heart defect (CHD). I remember not hearing the rest of the diagnosis. I looked at the charts again when you asked me about them. All these big terms, patent ductus arteriosus (PDA), atrial septal defect (ASD), ventricular septal defect (VSD), and double outlet right ventricle (DORV)... I looked them up. The heart was malformed, and this somehow affected how Pavit's blood flowed. I know you will explain this better now to me."

Mena gave Singh the charts. He reviewed the first chart that showed the data from the echocardiograph and color doppler results (see below).

Chart 1. **Physical examination**

Congenital Heart Defect (CHD)

- Right atrium (RA) and right ventricle (RV) are dominant
- Patent ductus arteriosus (PDA) with right to left shunt
- Atrial septal defect (ASD) with a left to right shunt
- Ventricular septal defect (VSD) extending into muscular septum
- Double outlet right ventricle (DORV)
    - Aorta arises from the right ventricle and is to the right and side-by-side (anterior) with the pulmonary artery.
    - No evidence of aorta or pulmonary artery outflow obstruction.
        - No aorta or pulmonary valve stenosis
        - Severe pulmonary hypertension

Normal:

- Aortic arch is normal.
- Normal draining systemic and pulmonary veins
- Normal biventricular contractility
- Mitral and triscupid valves normal
- Aortic and pulmonary valves are normal

Paul, the postdoc, noticed Singh reviewing the chart. He looked it over and jotted a few questions down to assist Singh in unraveling what happened to Pavit.

Questions

1. a. How many chambers does the heart have?

   b. Which are superior and which are inferior?

2. What structures separate the chambers?

3. List the major vessels that:

   a. bring blood to the heart.

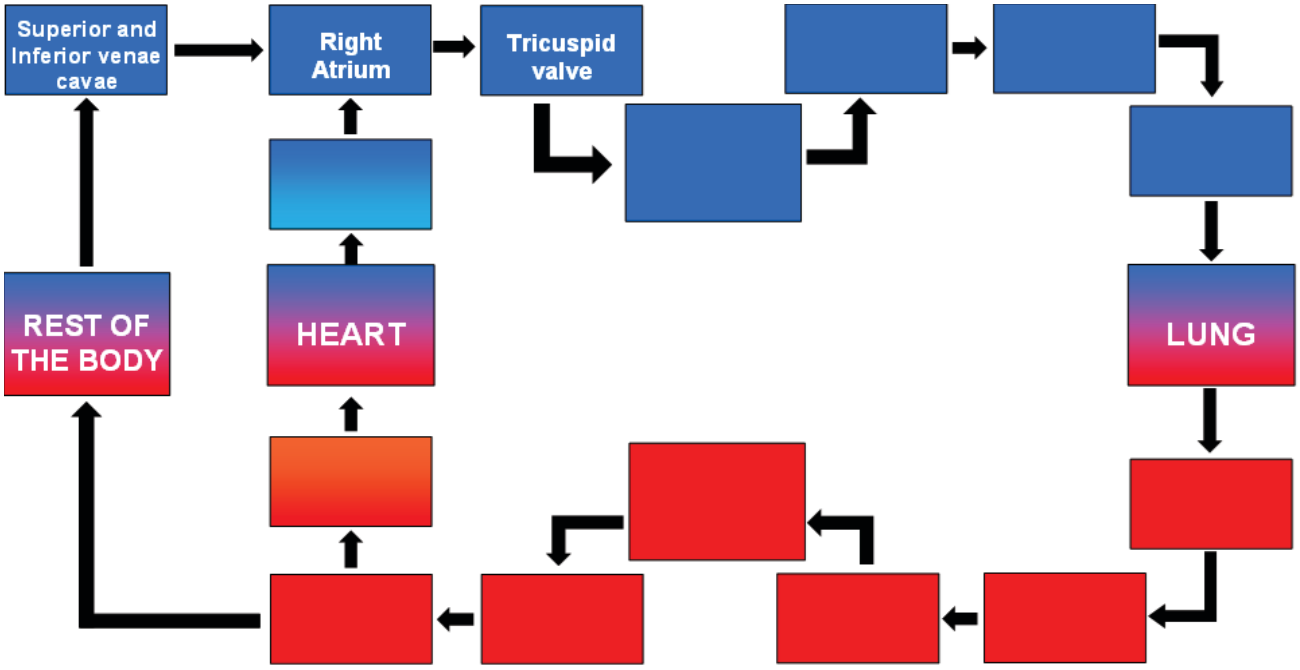
   b. take blood away from the heart.

4. Which chambers are these blood vessels associated with or connected to?

5. Singh then created a flow chart of the blood returning to the right atrium by the vena cava to being ejected into the aorta. Using the diagram on the next page, fill in the missing information as Singh would have using the word bank below:

Word Bank

Aorta	Coronary arteries	Coronary veins and sinus
Pulmonary veins	Pulmonary arteries	Pulmonary trunk
Right ventricle	Left ventricle	Left atrium
Pulmonary semilunar valves	Bicuspid valve	Aortic semilunar valves



6. a. What were the signs/symptoms that caused Dr. May to investigate further?

   b. Using a credible source, list the major signs/symptoms associated with CHD.

   c. Are they like Pavit's?

7. a. Why was a 2D echocardiography with color doppler performed on Pavit?

   b. What information do they each provide?

8. Were Pavit's valves normal?

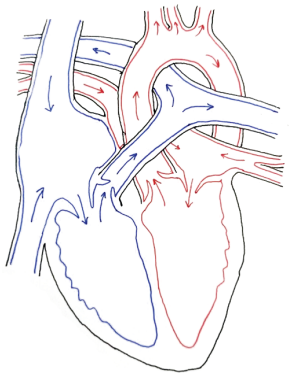
9. Paul told Singh that Pavit's heart and blood vessels were affected. Use reputable sources to answer the following questions for each of the malformations that were found:

   a. *Patent Ductus Arteriosus (PDA)*

      i. What is PDA with right to left shunt?

ii. Which of the following options is the new route for blood?
   (a) coronary arteries → aorta
   (b) aorta → body
   (c) right atrium → aorta
   (d) aorta → pulmonary trunk

iii. Would enough oxygenated blood enter the systemic circuit? Explain.



iv. Use an arrow to indicate on the flowchart used in Question 5 above where PDA would occur.

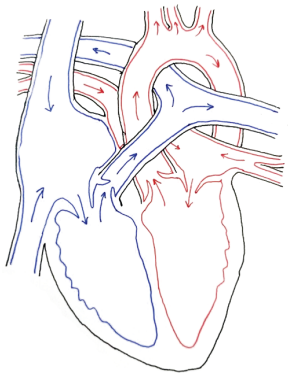
v. Indicate on the heart diagram to the right where PDA would be present:

b. *Atrial Septal Defect (ASD)*

i. What is ASD with a left to right shunt?

ii. Which of the following options is the new route for blood?
   (a) left atrium → coronary arteries
   (b) left ventricle → left atrium
   (c) left atrium → right atrium
   (d) aorta → left atrium

iii. Would enough oxygenated blood enter the systemic circuit? Explain.



iv. Use an arrow to indicate on the flowchart used in Question 5 above where ASD would occur.

v. Indicate on the heart diagram to the right where ASD would be present:

c. *Ventricular Septal Defect (VSD)*

i. What is VSD?

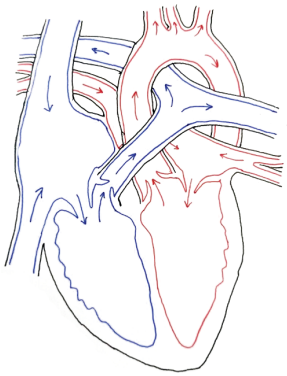
ii. Which of the following options is the new route for blood?
   (a) left ventricle → right ventricle
   (b) left ventricle → right atrium
   (c) left ventricle → left atrium
   (d) left ventricle → heart tissue

Normal ventricular pressure values:
Right ventricle: 25mmHg systolic; 4mmHg diastolic
Left ventricle: 120mmHg systolic, 10 mmHg diastolic

iii. Would enough oxygenated blood enter the systemic circuit? Explain.

iv. Use an arrow to indicate on the flowchart used in Question 5 above where VSD would occur.

v. Pavit presents with severe pulmonary hypertension; explain how VSD can lead to this.



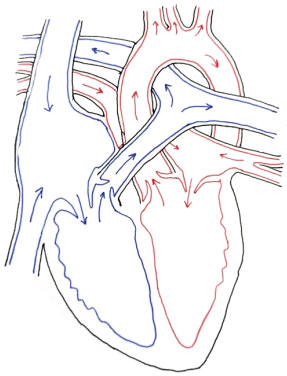
vi. Indicate on the heart diagram to the right where VSD would be present:

d. *Double Outlet Right Ventricle (DORV)*

i. What is DORV?

ii. Which of the following options is the new route for blood?

(a) right ventricle → pulmonary trunk and left ventricle
(b) right ventricle → aorta and coronary artery
(c) right ventricle → aorta and pulmonary trunk
(d) right ventricle → right and left atrium



iii. Would enough oxygenated blood enter the systemic circuit? Explain.

iv. Use an arrow to indicate on the flowchart used in Question 5 above where DORV would occur.

v. Indicate on the heart diagram to the right where DORV would be present:

10. Pavit's right side of the heart (right atrium and right ventricle) was dominant. Why?

Based on further discussions with Paul and conducting some literature research, Singh understood that sufficient cardiac output is vital in maintaining normal body function due to sufficient tissue perfusion and oxygenation. Therefore, the respiratory system is intimately linked to the cardiovascular system. He noted that two factors that affect the respiratory exchange of gases are the changes to blood flow and the surface area of alveoli. In addition, he learned that to meet the high metabolic oxygen needs of a newborn, the myocardium contractility is at its maximum. In addition, the myocardium is less compliant due to the disorderly organization of the higher amount of non-contractile proteins compared to

contractile proteins within the cardiac myocytes. As a result, stroke volume in neonates remains almost the same, decreasing the likelihood of increasing cardiac output with an increase in preload. Below are some definitions Singh noted.

Definitions

Cardiac Output (CO): volume of blood pumped by each ventricle in one minute.

CO = stroke volume × heart rate

- *Heart Rate (HR):* number of beats per minute.
- *Stroke Volume (SV):* volume (ml) of blood pumped out of the left ventricle with each beat.
- *Preload:* the force that stretches the cardiac muscle prior to contraction; associated with the volume of blood that fills the heart from venous return.
- *Afterload:* the amount of pressure that the heart needs to eject the blood during ventricular contraction.

Minute Ventilation (Total Ventilation): the amount of air that enters the lungs per minute.

Minute ventilation = respiratory rate × tidal volume

- *Tidal volume:* the normal volume (ml) of air inspired and expired with each breath.
- *Respiratory Rate:* the number of breaths per minute.

Alveolar Ventilation (AV): represents actual ventilation as it considers dead space. It represents the volume of air within the respiratory zone available for gas exchange per minute.

AV = respiratory rate × (tidal volume – dead space)

- *Dead Space:* the air in the conducting zones.

Pulmonary Capillary Perfusion (Q): the flow of blood to pulmonary capillaries.

Questions

11. How can neonates increase cardiac output if stroke volume remains the same?

12. a. Using one of the heart malformations, explain what would happen to heart rate.

    b. Pavit had normal biventricular contractility. Assuming stroke volume remained static, would cardiac output be affected? Explain using one of the malformations.

13. Pavit was panting, indicating his respiratory rate had increased. How would this affect:
    a. tidal volume?

    b. alveolar ventilation?

14. Would pulmonary capillary perfusion be affected by increased blood being received by the right ventricule? Explain.

15. a. Would alveolar ventilation and pulmonary capillary perfusion affect gas exchange?

    b. Based on your responses to Questions 13 and 14, would gas exchange be increased or decreased in Pavit?

Part II – Physical Examination

Setting the first chart aside, Singh proceeded to review the next set of notes. The document showed that Pavit was eight days old, and the doctor had performed a physical examination focused on the baby's appearance, respiratory rate, and heart rate.

A copy of the physical examination record is presented below.

Chart 2. **Physical examination**

Clinical data: 8-day old male neonate

Complaints of:

- Increased precordial activity: Day 2
- Breathlessness: Day 2
- Not accepting feeds: Day 2
- History of: cyanosis / sweating over forehead / fever

On examination:

- Heart rate (HR): 215 beats/minute (tachycardia)
- Respiratory rate (RR): 72 breaths/minute (tachypnea)

Questions

1. Why was the baby having increased precordial activity (visible pulsations on the anterior chest wall) and breathlessness?

2. How are these related to tachycardia and tachypnea documented? (Normal heart rate, 127–145 beats/min; normal respiratory rate is 40–44 breaths/min.)

3. What additional evidence shows a lack of tissue perfusion?

4. Would this be consistent with someone presenting with CHD?

Part III – Bloodwork

Singh felt his mother was wise to have sought a second opinion. It was clear that Dr. May had taken the case seriously; he had not only conducted tests on the heart and vessels, but the bloodwork notes also appeared detailed. To understand if the blood cells may have contributed to Pavit's condition, Singh spent the afternoon defining all terms on the bloodwork chart and tabulated the data for ease of analysis. He reached out to the librarian to obtain a reference book to look up normal pediatric blood values. The librarian provided him with the *Manual of Pediatric Hematology and Oncology*.

Definitions

Hematocrit (Hct): a measurement of the percentage of the total blood volume taken up by the red blood cells (RBCs).

Hemoglobin (Hbg): a measurement of the concentration of hemoglobin (gram/ deciliter) in the blood.

Mean corpuscular volume (MCV): a measure of the average volume, or size, of a single RBC.

MCV (fl) = hematocrit % × 1000 / erythrocyte count (10^{12} / L)

Mean corpuscular hemoglobin (MCH): is a measure of the average amount of hemoglobin in circulating erythrocytes.

MCH (pg) = hemoglobin (g/dl) / erythrocyte count (10^{12} / L)

Mean corpuscular hemoglobin concentration (MCHC): a measure of the concentration of hemoglobin in an average circulating erythrocyte.

MCHC (g/dl) = hemoglobin (g/dl) / hematocrit %

Red cell distribution width (RDW): a measure of the range of variation of RBC volume in a standard complete blood count.

Mean platelet volume (MPV): a measure of the average size of platelets found in blood.

Below is the bloodwork data.

Chart 3. **Bloodwork**

Bloodwork: 8-day old male neonate

Investigation done:

- C-reactive proteins (CRP): negative
- Complete blood count (CBC): data tabulated below with normal values for comparison
- Peripheral smear
  - Erythrocytes (RBC): anisocytosis and polychromasia
  - Leucocytes (WBC): neutrophilia
  - Platelets: increased

Table 1. Normal blood values versus Pavit's.

Source: One-week values from *Manual of Pediatric Hematology and Oncology* were used for the normal ranges (Philip, 2011): Table A1-4 Red Cell Values at Various Ages, Table A1-15 Normal Leukocyte Counts, Table A1-18 Normal Platelets Counts, and Table 1.1: Etiologic Classification and Major Diagnostic Feature of Anemia in Children.

	Normal (Mean + 2 SD)	*Pavit*
Erythrocytes count (RBC) (million cells / mm^3)	5.1	4.35
Hct (%)	54	38.2
Hbg (gram/ deciliter)	17.5	15.4
MCV (femtoliter/ cell)	*107*	*87.8*
MCH (picogram/ cell)	*34*	*35.4*
MCHC (grams/ deciliter)	*32.4*	*40.3*
RDW (%)	11.5–14.5	12.4
	Normal (Mean + 2 SD)	*Pavit*
White blood cells (WBC) (thousand cells / mm^3)	12.6	14.86
Differential Count	*thousand / mm^3*	*thousand / mm^3*
Neutrophils	5.5	7.82
Eosinophils	0.5	0.48
Basophils	0.5	0.45
Lymphocytes	5.0	5.21
Monocytes	1.1	0.90
	Normal (Mean + 1 SD)	*Pavit*
Platelet count (thousand / mm^3)	310.0 ± 68,000	482.0
MPV (fl)	8.9 ± 1.5	10.9

Questions

1. Describe the major functions of the formed elements in blood.
   - Erythrocytes (RBC):
   - White Blood Cells (WBC):
     - Neutrophils:
     - Eosinophils:
     - Basophils:
     - Lymphocytes:
     - Monocytes:
   - Platelets:

2. Why was a complete blood count performed?

3. What information would a differential blood count provide?

4. Why was a peripheral smear done? What was found?

5. a. What does anisocytosis of RBCs indicate?

   b. List a likely reason for this.

   c. How would this impact the RBC function?

6. The RBCs were also polychromatophilic.
   a. Why was this occurring?

   b. What hormone was likely responsible?

7. a. What could be the likely cause for the decrease in RBC, hematocrit, hemoglobin, or mean corpuscular volume?

   b. What specifically was the baby not receiving that could affect the hemoglobin structure?

   c. Would the absence of this molecule to the hemoglobin structure increase or decrease oxygen affinity?

8. Can a fever affect the hemoglobin affinity for oxygen?

9. a. Would Pavit's RBCs be capable of carrying sufficient oxygen?

   b. Does the peripheral smear support your answer?

10. What was the purpose of measuring MCV, MCH, MCHC, and RDW?

11. How would you test that the lack of a certain nutrient was affecting the RBC anatomy and physiology? Design experiments that can result with a more efficient RBC.

    Tests for anatomy: What would you measure?

    Hypothesis:

    Control:

    Experiment:

    Results: (Graph the data):

    Tests for physiology: What would you measure?

    Hypothesis:

    Control:

    Experiment:

    Results: (Graph the data):

12. C-reactive protein (CRP) was also measured.
    a. What is CRP?

    b. Why was the CRP tested?

    c. Why were Pavit's levels negative?

13. The baby had a fever indicative of an inflammatory response. An infection may be a likely contributor.
    a. What was examined to confirm this?

    b. What was the result?

14. What else could lead to an elevation of body temperature causing the baby to sweat?

15. Pavit's platelets and mean platelet volume were increased, indicative of thrombocytosis.
    a. What could have led to this?

    b. List one additional test besides the complete blood count you would conduct to confirm this.

Part IV – Treatment

Singh reached the conclusion that a malformed heart and defective RBC had contributed to Pavit's passing. Surgery was not an option for Singh's family who resided in India in 2003. During this time Mena was working for a recently launched computer company and while maternity leave was granted as part of the employment package, this leave was unpaid. Dad was a graduate student and supplemented the household income by doing odd jobs. The family simply lacked the resources needed to see a more prominent specialist. The best that could be afforded was treatment for severe pulmonary hypertension, edema, and oxygen deprivation.

Below is the treatment plan for Pavit.

Chart 4. Treatment recommendation

Prescription: 8-day old male neonate

- Tablet: lasilactone (pulvarised) taken every 8 hours
- Syrup: digoxin (elixir) taken every 8 hours
- O_2 inhalation through O_2 mask
- Expressed breast milk 20 ml given every 2 hours

Questions

1. Lasilactone was used to treat Pavit.
   a. Which of the conditions mentioned above did it help alleviate?

   b. What organ or organ system did it affect and what will it do?

   c. Lasilactone is a combination drug of furosemide and spironolactone. Describe the mechanism of action of these two compounds.

2. Digoxin was also prescribed for Pavit.
   a. Which of the conditions mentioned above did it help alleviate?

   b. What organ or organ system did it affect and what will it do?

   c. Describe the mechanism of digoxin.

3. Oxygen was also given to Pavit. Would it be effective? Explain.