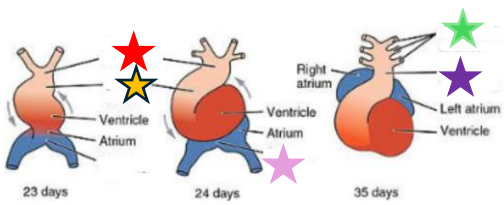
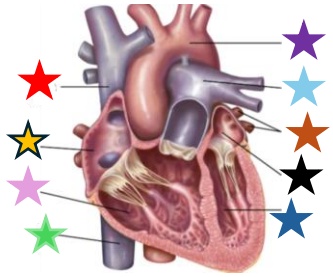
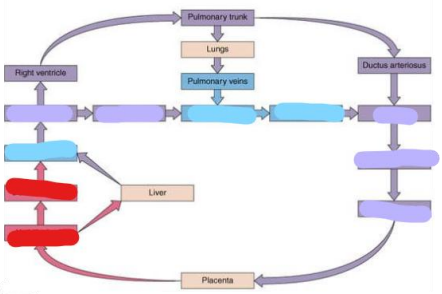
Integrated physiology Week 5 **CV changes across the lifecycle**	
What germ layer is the heart derived from?	Mesoderm **formed at week 7
5 steps in heart looping	1. Heart starts out as **2 endocardial tubes** 2. 2 tubes fuse into **single primitive heart tube** 3. Primitive heart tube elongates & differentiates into **5 regions** 4. **Looping process** → C and S shaped loops 5. 4 heart chambers formed
4 regions of elongated primitive heart tube and what they become	• **Bulbus cordis + primitive ventricle** → ventricles • **Primitive atrium** → atria • **Sinus venosus** → Atria and SA node • **Truncus arteriosus** → Aorta and pulmonary artery
	Endocardial Tubes Primitive heart tube Truncus arteriosus Bulbus Cordis Primitive ventricle Primitive atrium
	Truncus arteriosus Bulbus Cordis Sinus Venosus Aortic arch arteries Truncus arteriosus
When does fetal heart begin pumping?	• DAY 35 • 4 chambered heart



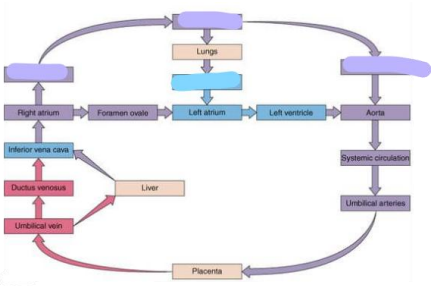
- Superior vena cava
- Right Atrium
- Right Ventricle
- Inferior Vena Cava
- Aorta
- Pulmonary artery
- Pulmonary Veins
- Left atrium
- Left Ventricle

When do atrioventricular valves form?

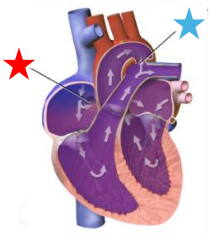
- week 5-9



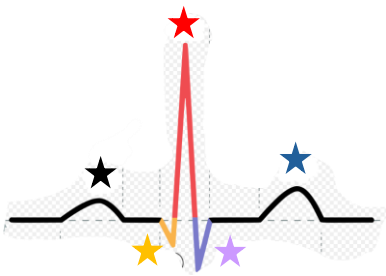
1. Umbilical vein
2. Ductus venosus
3. Inferior vena cava
4. Right atrium
5. Foramen ovale
6. Left atrium
7. Left ventricle
8. Aorta
9. Systemic circulation
10. Umbilical arteries



1. Right Ventrical
2. Pulmonary Trunk
3. Ductus arteriosus
4. Pulmonary veins



- Foramen ovale (RA → LA)
- Ductus arteriosus (PT →Aorta)



- **P wave:** Atrial contraction
- **Q:** Interventricular septum depolarizes
- **R:** Ventricles contract
- **S:** Upper ventricles contract
- **T wave:** Ventricles repolarize

Difference between systemic and pulmonary circulation

Systemic: oxygenated blood goes from heart to body

Pulmonary: deoxygenated blood from body goes to heart, then to lungs

3 bipasses in fetal heart and their location	**Foramen ovale** right to left atria **Ductus venosus** liver bypass **Ductus arteriosus** pulmonary artery to aorta
Blood pathway for ductus venosus	• Bypass liver • Shunts from umbilical vein to inferior vena cava
Fetal oxygenated blood pathway (8)	Placenta → umbilical vein → RA → foramen ovale → LA → LV → Aorta → systemic circulation
Fetal deoxygenated blood pathway (8)	Superior/inferior Vena Cava → RA → RV → pulmonary artery → ductus arteriosus → aorta → umbilical arteries → placenta
Eustacian valve function	• Directs oxygenated fetal blood from inferior vena cava toward foramen ovale • Directs less oxygenated fetal blood from superior vena cava toward right ventrical
Foramen ovale function and what blood is prioritised?	Lung bypass: shunts blood from RA to LA • This blood is more oxygenated and prioritized for upper body and brain (organ development)
Ductus arteriosus function and location	LOC – connects pulmonary artery to descending aorta • Lung bypass

Ductus Venosus function and location	Located in fetal liver, connects umbilical vein to inferior vena cava • Liver bypass
Difference between adult and fetal blood vessels	Fetus: **arteries take deoxy** and **veins take oxy** **This is because placenta takes over lung function
Why is there less demand for oxygenated blood in fetus LOWER body?	All major organs are in upper body Aorta preferentially sends less oxygenated blood to lower body
Eustacian valve location	Opening of inferior vena cava into Right atrium
What forces fetal blood to bypass lungs	Fetal lungs are fluid filled not air filled – causing high resistance Blood takes easier pathway through ductus arteriosus
Where do umbilical arteries arise from	• Internal iliac arteries (pelvis) Carry deoxy blood from fetus to placenta
Is any blood sent to liver or lungs?	• Yes small amountenough for tissue to develop

What causes foramen ovale to close	Baby's first breath causes lung expansion Blood goes to lungs then LA Increase pressure in LA forces FO closure
What causes ductus venosus closure	Clamping umbilical cord = loss of placental circulation Ductus venosus collapses and closes Umbilical vein/artery close
What causes ductus arteriosus closure	Loss of placental prostaglandins cause vasoconstriction → ductus arteriosus closes
What is 'the hole in the heart' birth defect	Foramen ovale stays open
Define stroke volume and cardiac output	SV – amount of blood pumped by LV (mL) CO – total volume pumped per minute (L/min)
What allows adaption when metabolic demands change	Homeostatic mechanisms
Difference in SV, HR, CO between children and adults	Child HR: 130-150 Adult HR: 60-100 Child SV: 2-4 mL/contraction Adult SV: 70-120 mL/contraction Child CO: lower Adult CO: higher

Why do children have higher HR but lower CO compared to adults?	Lower SV is compensated by a higher HR Children have higher metabolic needs
Difference between skeletal and cardiac muscle	Cardiac – decreased capacity for regeneration ** lack of satellite cells to help repair unlike muscle cells
What is myocardial infarction and why is it so bad?	**Blood flow to heart is blocked** – causing cell death **Cardiac tissue cannot regenerate** – cells replaced with nonfunctional fibrous tissue
New treatment for heart cell damage	Pluripotent stem cell-derived cardiomyocytes
What precedes CV disease	Vascular dysfunction
3 modifyable risk factors fir CVD	• Smoking • Cholesterol • Weight/adiposity
3 independent CV risk factors	• Ethnicity • Age • Sex

CV risk for 45 y/o males and females	Males with 2+ risk factors ~ %50 of CVD before 80 Females with 2+ risk factors ~ %31 chance of CVD before 80
3 hallmarks of aging that affect the heart	• Impaired Ca^{2+} homeostasis • Neurohormonal signaling • Mitochondrial dysfunction and ROS
2 age associated cardiac pathologies	• Heart failure • Fibrillation (atrial and ventricular)
Difference between atrial and ventricular fibrillation	Ventricular is more life threatening than atrial
3 layers of heart wall	• **Epicardium**: outer layer • **Myocardium**: middle, cardiac muscle • **Endocardium**: inner layer, minimize surface friction **Pericardium surrounds heart
Functional change to aging heart	• Diastolic dysfunction
Structural change to aging heart	• Left ventricular hypertrophy (because of increased work load) **Can lead to diastolic dysfunction and ventricular fibrillation

Molecular change to aging heart	• Mitochondrial dysfunction • Ca^{2+} signaling change • Neurohormonal
Which layer is most relevent in heart failure	• Myocardium
What is an intercollated disk	• Separates individual cardiac muscle cells
6 steps in excitation contraction coupling in heart muscle	1. **Action potential**: electrical signal travels down sarcolemma 2. D**epolarization**: sarcolemma depolarize, spreads down T tubules 3. **Ca^{2+}** released from sarcoplasmic reticulum 4. **Ca^{2+} causes more Ca^{2+}** to be released 5. **Cross bridge cycling** actin and myosin, Ca^{2+} and ATP required 6. **Relaxation** Ca^{2+} pumped back into SR, thick and thin filaments detach
What is heart failure	Heart cannot pump blood efficiently, body does not get sufficient nutrients ** Progressive condition → stages of severity
3 common causes of heart failure	• Coronary artery disease • Myocardial infarction • Aging
What part of the heart is mostly affected by heart failure	Left ventricle → decreased blood volume and oxygen to all of body

2 causes of death from heart failure	• Insufficient cardiac output • Ventricular fibrillation
What is arrhythmia	• Irregular heart beat
What is ventricular fibrillation	Ventricles beat very **irregularly** and **fail to pump blood** properly Type of arrhythmia **Can lead to cardiac arrest
Heart failure treatment	Slow progression
Heart contraction breakdown (5)	**P wave** atrial contraction **Q** interventricular septum depolarizes **R** ventricles depolarize and contract **S** upper ventricles depolarize **T wave** ventricles repolarize (relax)
What is needed for ventricular fibrilations	Defibrillator to reset heartbeat
What is Diastole and Systole	**Diastole** – filling (relax) **Systole** – Pumping (contract)

4 functional changes in left ventricular dysfunction and other name	**Diastolic dysfunction** • Slow cardiomyocyte relaxation • Ventricular thickening + fibrosis • Ventricles refill very late in diastole
Consequence of ventricular fibrosis	Stiffer heart
Difference between dysfunction and healthy heart diastole	**Dysfunctional** refills very late in diastole
Why does aging heart hypertrophy	Myocytes die – heart has to work harder Remodeling – fibrosis and hypertrophy
Why is myocardium hypertrophy a bad thingin ventricular dysfunction	Ventricular chamber narrows • Contributes to diastolic dysfunction
How does increased ROS affect the heart?	Too much ROS damages Ca^{2+}regulatory proteins • Causes Ca^{2+} build up in cells • Contributes to ventricular fibrillation
Difference between healthy and unhealthy myocardium hypertrophy	Healthy – there is a proportional increase in capillary number Unhealthy – not accompanied by capillary increase

3 consequences of narrow LV	• Cardiac output not maintained • Harder for blood to leave heart • Heart failure
Function of Ca^{2+} in heart	Intracellular Ca^{2+} signaling controls contraction and relaxation
How does abnormal Ca^{2+} release affect heart?	Contributes to arrhythmias and ventricular fibrillation **Ca^{2+} leaks out and disrupts normal signaling
What produces ROS	Mitochondria - Produces ROS under cellular stress
What is oxidative stress	Too much ROS overwhelms the cell
To an extent, how does exercise combat ROS	Exercise induces ROS, but also produces antioxidants
Function of β-adrenergic receptors (3)	• Interface between SNS and CVS • Binds adrenaline and noradrenaline to trigger physiological changes • Vasodilator

What are catecholamines, function?	Homeones and neurotransmitters like **adrenaline and noradrenaline** Regulate stress response – increase HR, BP, and metabolism
Catacholamines in 65+ years (4)	• Elevated levels of catecholamines • This overstimulates β-adrenergic receptors • Induces fight/flight pathway • Leads to arrhythmias
How do functional changes in disfunctional LV cause heart failure?	1. Loss of cardiac cells/age related damage changes LV filling rate 2. Refill occurs later in diastole (inefficient or incomplete) 3. Ventricle can't relax, affects next contraction 4. CO can't be maintained 5. Heart failure
How does chronic β-adrenergic stimulation affect heart	• Disrupts Ca^{2+} regulatory proteins • Change in contractility and CO decreases • Build up of Ca^{2+} in cells • Contributes to ventricular fibrillation
What makes estrogen cardioprotective? (4)	• Mitigates ROS • ↑HDL and ↓LDL • Dampen Ca^{2+} changes in release • Modulate β-adrenergic response **research in mice and young people
CVD mitigation (4)	• Diet • Exercise • Alcohol • Smoking
Heart condition medications (5)	• Vasodilators • B blockers • Implanted defibrillator • ROS scavenging agents • Hear transplant