Congenital Heart Disease and GERD

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Congenital Heart Defects

- Defects of the heart at birth that are structural or functional
Congenital Heart Disease

- 4-8 cases per 1000 live births
- 40% of CHDs diagnosed in 1st year of life
- Primary reason undiagnosed is inability to detect small lesions by the practitioners
- 35 types of defects known
- Top 4: VSD, ASD, PDA, and Coarctation of the aorta
Cause of CHD

- Unknown in most cases
- May be genetic and/or environmental
- Some associated with certain chromosomal abnormalities (Down syndrome, DiGeorge syndrome)
- Maternal infection with rubella virus
- Medications: valproic acid, phenytoin, carbamazepine, warfarin, isotretinoin, lithium
- Diabetes and alcohol consumption can increase risk of CHD
Fetal Circulation

- Ductus Venosus
- Foramen Ovale
- Ductus Arteriosus
Transitional Circulation

- Cessation of right to left shunting.
- Lungs begin to function.
- The above changes occur due to:
  1. Ductus venosus closing due to placenta removal.
  2. Pulmonary vascular resistance decreases and flow to the ductus arteriosus becomes left-to-right.
  3. Left atrial pressure exceed right so that the foramen ovale closes.
Transitional Circulation
CHD: Acyanotic lesions

- Atrial Septal Defect (ASD)
- Ventricular Septal Defect (VSD)
- Patent Ductus Arteriosus (PDA)
- Coarctation of the Aorta
- Generally result in increased pulmonary blood flow, increased right and left ventricular pressure and volume overload, depending on the defect.
- Can result in right-to-left shunting from pulmonary hypertension
Atrial Septal Defect

- Opening separating the right atrium from the left atrium.
- Causes left-to-right shunting due to the right atrium pressure having a lower pressure than the left.
- This eventually leads to higher amount of blood that is highly oxygenated entering the lungs.
ASD (cont)

- Several forms of ASD-ostium secundum the most common and it spontaneously closes.
- Other forms require closure normally between 2-4 years of age.
- Most patients are asymptomatic.
- If not treated, eventually may lead to right ventricular hypertrophy and heart failure as well as right atrial enlargement (arrhythmias).
Ventricular Septal Defect

- Opening between the two ventricles.
- As ASD causes lungs to have increased amount of saturated blood delivered.
- For large defects, diagnosed at 4-6 weeks of life with signs of CHF, tachypnea, tachycardia, and failure to thrive.
- Moderate to large defects with heart failure are treated with digoxin, diuretics, and increased calorie dense formula.
- Surgery if growth failure, pulmonary hypertension, or cardiomegaly.
- If large defect and developing pulmonary hypertension, surgery by age 1.
Patent Ductus Arteriosus

- PDA is present in utero to shunt blood past the lungs into the aorta.
- It shunts right to left due to high pulmonary vascular resistance (PVR) and low SVR.
- It remains patent due to low oxygen tension and high levels of circulating prostaglandins.
PDA
Epidemiology

- Term: 1 in 2000 births
- Preterm: 20-60%
- <1200 grams at birth: PDA present in 80%
- <2000 grams at birth: 40%
- More common in female than male infants (2:1)
PDA Risks

- Bacterial endocarditis
- Calcification of the ductus
- Development of CHF and pulmonary hypertension
- Mortality rate if uncorrected: 33% by age 40 and 66% by age 60
Treatment of PDA

- Non-steroidal anti-inflammatory agents - 70-80% success rate
- Surgical Ligation – associated with higher incidence of chronic lung disease, neurosensory deficits, and possibly retinopathy of prematurity.
Contraindications for both indomethacin and ibuprofen

- Thrombocytopenia
- Coagulation defects
- Known or suspected necrotizing enterocolitis
- Significant renal problems
- Proven or suspected infection that is untreated
- If PDA is needed due to congenital heart disease where systemic blood flow or pulmonary flow is needed
- Bleeding—such as active intracranial hemorrhage or GI bleed
Indomethacin Dosing

- 1\text{st} dose is normally 0.2mg/kg/dose
- 2\text{nd} and 3\text{rd} dose depends on when first dose given.
- 0.1mg/kg/dose if less than 2 days postnatal age
- 0.2mg/kg/dose if 2-7 days postnatal age
- 0.25mg/kg/dose if >7 days postnatal age
Indomethacin Adverse Effects

- Decreased urine output and increased serum creatinine - hold for urine output <0.6ml/kg/hr
- Increased risk of NEC
- Decreased cerebral blood flow
- Decreased platelet aggregation
Ibuprofen

- **Dose:** 10mg/kg, followed by 5mg/kg q24 x 2 doses.
- If anuria or <0.6 ml/kg/hr urine output hold 2nd or 3rd dose until increases.
- Infuse over 15 minutes; use within 30 minutes of preparation.
- **Adverse Effects:** Sepsis, anemia, bleeding, apnea, decreased renal function, GI problems, respiratory failure.
Comparison of the two products

- May see less oliguria with ibuprofen than indomethacin
- Appear similarly effective
- No differences in survival or other outcomes noted in clinical trials
- Cost about the same.
Coarctation of the Aorta

- Narrowing or constriction of the aorta.
- Clinical presentation depends on age of patient, severity of the coarctation, and any other related defects.
- Treatment includes administration of PGE to maintain the ductus arteriosus, corrections of any metabolic acidosis, and maintaining perfusion.
Complications/Surgery

- For infants that are symptomatic, stabilize and surgically repair.
- Ideally surgery at 3-10 years of age for those diagnosed later.
- Long-term complications include hypertension, aortic aneurysm, endocarditis, aortic stenosis, coronary artery disease, recurrence of the coarct.
Treatment of CHD: Digoxin

- Controversial for use in acyanotic lesions.
- Normally reserved for decrease in left ventricular function.
- Side effects include GI problems, bradycardia and atrioventricular block.
- Maintenance doses: 5mcg/kg/day-preterm, 8-10mcg/kg/day for term newborns < 2months, 10-12mcg/kg/day for infants<2yo, and 8-10mcg/kg/day for >2yo.
Furosemide

- Loop diuretic to decrease preload.
- Decreases pulmonary edema due to left-to-right shunting or heart failure.
- Normal dose is 1-2mg/kg/dose q6-24 hours.
- Main adverse effects are decrease in electrolytes (K, Cl, Ca), metabolic alkalosis (hypochloremic), ototoxicity, and nephrocalcinosis.
Spironolactone

- Weak diuretic used to spare potassium depletion.
- May also help with the hyperaldosteronism associated with CHF.
- Normal doses of 1-3mg/kg/day given qd-bid.
- Adverse effects: hyperkalemia, N/V/D, metabolic acidosis
Thiazide Diuretics

- Used for chronic diuresis.
- Hydrochlorothiazide-2-4mg/kg/day q12-24 hrs. (>6 months give only 2mg/kg/day).
- Chlorothiazide-20-40mg/kg/day (or 2-8mg/kg/day of IV). (>6 months give only 20mg/kg/day or up to 4mg/kg/day IV)
- Adverse effects: hypokalemia, hyperglycemia, metabolic alkalosis, pancreatitis, GI problems, or hyperlipidemia.
Angiotensin-converting Enzyme Inhibitors

- Use to decrease SVR and/or decrease left-to-right shunting.
- Captopril - 0.25-0.75mg/kg/day divided q6-8hrs, may increase by 0.5mg/kg/day up to maximum of 6mg/kg/day.
- Enalapril - 0.1mg/kg/day and increase to 0.5mg/kg/day.
- Monitor renal function, potassium, blood pressure, white blood cell count.
Propranolol

- May decrease high catecholamine output.
- Start with a low dose and work up.
- May give initial 1mg oral dose. If tolerated give 1mg/kg/day divided 3 times a day. May titrate by 1mg every 3 days to 2mg/kg/day. (in infants)
- Adverse effects: hypotension and bradycardia; a increase in SVR and decrease in cardiac output causes intolerance in 20% of adults. Children also can have this problem.
Other Beta Blockers

- Metoprolol - better tolerated than propranolol
- Carvedilol - is the beta blocker that is now being used. Being studied more due to its added alpha 1 blockade (plus beta); reduced afterload (alpha) may offset the negative inotropic effects to make it better tolerated in adults. Can have profound vasodilation which can be offset by decreasing ACEI dose or diuretics. Studies underway.
Alprostadil (PGE1)

- Used to maintain patency of the ductus arteriosus in lesions that rely on its patency to maintain adequate flow to the systemic circulation or the pulmonary circulation.
- Normal dose is 0.025-0.1 mcg/kg/min. Titrate to the lowest dose (0.02-0.03 mcg/kg/min).
- Adverse effects include fever, apnea/tachypnea, hypotension, bradycardia, NEC, jitteriness, etc.; long-term may result in bone changes.
CHD: Cyanotic lesions

- Transposition of the Great Arteries (TGA)
- Tetralogy of Fallot (TOF)
TGA

- Aorta is connected to the right ventricle instead of the left. Pulmonary artery is connected to the left ventricle instead of the right.
- A PDA or ASD may help maintain some oxygenation.
- Surgical correction either arterial or atrial switch. Arterial is generally preferred if able.
TGA
Tetralogy of Fallot

- 4 anomalies: VSD, overriding aorta, right ventricular hypertrophy, and right ventricular outflow tract obstruction
- The severity of pulmonary obstruction determines onset of symptoms.
- If severe RVOT obstruction, need alprostadil.
- Survival for corrected TOF: 32 years 86%, 36 years 85%; Uncorrected: 66% 1 year, 40% at 3 years and 3% at 40 years.
RVOT obstruction

Tetralogy of
right atrium;
ventricle; PA,
artery; LA, left
left ventricle;
O₂ sat, oxygen
VSD, ventricular
effect; RVH,
hypertrophy;
right ventricular
tract. Arrows
direction of blood
through the VSD.

TOF
Treatment of “tet” spells

- Tet spells are caused by increased oxygen demand (i.e. physical exertion or stresses) that exceeds oxygen supply or infundibular spasm (causes dec. pulmonary blood flow).
- Knee-chest position to increase SVR.
- Supplemental oxygen
- IVF to increase SVR
- IV morphine
- IV propranolol or oral for chronic prophylaxis
CHD Summary

- Many agents available dependent on the patient’s needs.
- Surgical intervention is normally the definitive treatment.
- Need to monitor patients for adverse effects.
Gastro-esophageal Reflux

- Effortless retrograde movement of gastric contents into the esophagus
- Common condition: Peak incidence at 4 months of age (67%) for infants; typically outgrow.
- By 12 months of age, <5% have regular reflux.
- In older children, GER is similar to adults.
Gastro-esophageal Reflux Disease (GERD)

- GER should be considered a benign process that occurs prior to GERD.
- GERD is considered a pathologic process (reflux with complications).
- Not all reflux develops into GERD.
Incidence of Symptoms

- 2.3% of children 3-9 years of age* for GER
- 1.4% 10-17 years of age* for GER
- Incidence of GERD in infants, children, and adolescents in unknown.
- Need to differentiate between GER and GERD.
- Many disorders have similar symptoms so more difficult to diagnose.

*Based on pediatric-based survey of parents.
Risk Factors

- Infants lying down after feeding may cause reflux. Those with GERD have higher amounts of acid GER symptoms.
- Genetics may play a role. Autosomal dominant hereditary pattern seen in families.
- Obesity
- Smoking
- Cow’s milk allergy-2-5%
- GERD may contribute to asthma symptoms.
Common Symptoms of GER in Infants

- The happy spitter
- Regurgitation
- Vomiting but thriving
Common Symptoms of GERD in Infants

- Regurgitation
- Persistent vomiting (Failure to thrive)
- Esophageal Signs and Symptoms (Feeding refusal, arching, irritability, persistent crying, heartburn, hematemesis, anemia, sandifer’s syndrome (abnormal neck posturing, repetitive stretching, arching), stridor, wheezing, chronic cough, recurrent pneumonia
Common Symptoms of GERD in Children/Adolescents

- Intermittent vomiting in toddlers/young children
- Chronic heartburn or regurgitation with swallowing for older children/adolescents.
- Abdominal pain (60%), reflux or vomiting (>60%), and cough (60%)
- Food impaction
- Atypical GERD: may be pulmonary, nose, throat or ear symptoms such as cough, hoarseness, wheezing. These are all extraesophageal symptoms.
Complications

- Distal esophagitis
- Failure to thrive/delayed growth
- Esophageal strictures/perforation
- Pulmonary disease-wheezing, aspiration-related pneumonia, and apnea
- GI bleeding/hematemesis
- Heartburn or chest pain
- ALTE(Acute life threatening events)
Diagnosis of GER

- History and Physical
- Make sure meeting growth milestones
- Look at symptoms; diary kept by family of symptoms
- Empiric drug therapy
- If symptoms raise concern of GERD, further evaluation is done.
Diagnosis of GERD

- Esophageal pH monitoring (24 hours pH probe) - look for duration and frequency of reflux occurrences. (Most common initial)
- Endoscopy and biopsy - Looking for esophagitis, strictures, etc (If long-term therapy planned eventually do this test)
- Upper gastrointestinal series (UGI) - to look for anatomic anomalies.
- All of the above or a portion may be used by the gastroenterologist.
Treatment

- Non-pharmacological management-lifestyle changes
- Decrease gastric acid or enhance esophageal or gastric motility
- Surgery
Treatment of Infant GERD

- Conservative measures
- Reassurance of parents
- Postural management – Upright positioning during and after feeding. Prone position is thought to be best.
- Dietary changes: Try hypoallergenic formula for 1-2 (2-4) weeks if allergy to cow’s milk protein suspected; Thickening of infant formula and addition of cereal (may not help reduces vomiting episodes but not symptom scores) or feed less more frequently
- Medical management if necessary
Older Children and Adolescents

- Elevate the head of the bed and left side positioning may help
- Smaller more frequent meals
- Weight loss
- Avoid known LES relaxants (caffeine, alcohol, tobacco, spicy foods and chocolate)
- No clear benefit or added effect by doing the above when on pharmacologic therapy
Goals of Pharmacologic Therapy

- Eliminate symptoms
- Decrease frequency and duration of GER
- Heal esophagitis
- Prevent esophageal damage from chronic acid exposure
Therapy Endpoints

- Control of symptoms until spontaneous recovery
- Or failure to control symptoms proving need for surgery
- Treatment failure is lack of symptomatic improvement at maximum doses for at least 6 weeks (Some say try for 2-4 weeks)
Medical Management

- Step-up or step-down approach
- Suggest primary physician may place on therapy.
- If patient improves after 2-4 weeks stop therapy.
- If patients relapses quickly or after 2-4 weeks no response consult pediatric gastroenterologist.
Treatment of GERD

- Therapy is usually continued 6-8 weeks if clinical improvement is seen or longer dependent on child.
- GERD may in fact be a lifelong disease with apparent “wellness” when clinical reportable symptoms are absent or minimal and other times when the disease is apparent.
- H2 Receptor antagonists—ranitidine, famotidine, nizatidine, cimetidine
- PPIs—omeprazole or lansoprazole
- Prokinetic agents—metoclopramide
- Laparoscopic surgery
H2 Receptor Antagonists

- For mild to moderate GERD
- Cimetidine-30-40mg/kg/day TID-QID. Not used frequently anymore.
- Ranitidine-used most common- 4-5mg/kg/day up to 8-10mg/kg/day have been used. Divided twice daily to three times daily.
- Famotidine-1mg/kg/day divided twice daily
- Nizatidine-10mg/kg/day divided bid
- Tolerance effect to these compounds may occur over time requiring an increasing dose to achieve continued symptom relief and/or change in 24 hr pH probe.
Adverse Effects of H2 Blockers

- Minimal: headache, irritability, diarrhea, constipation, thrombocytopenia, may not like liquid preparation (for ranitidine)
- Cimetidine: gynecomastia, diarrhea, dizziness, agitation, drug interactions are more, hepatic enzyme inhibition.
Proton Pump Inhibitors

- Inhibit the H⁺/K⁺-ATPase proton pumps irreversibly.
- Best if given 30 minutes prior to breakfast (and dinner if twice daily). Have best effect if parietal cell is stimulated by a meal following a fast.
- Children metabolize the drugs more quickly- a 1 year old may need 3mg/kg/day for relief.
- Omeprazole-0.7-3.3mg/kg/day qd-bid. Most recently 1mg/kg qd or 0.5mg/kg bid has been recommended for GERD treatment. Some references suggest: <20kg 10mg qd, >20 kg 20mg qd.
- Lansoprazole-Similar to omeprazole but ≤30 kg 15mg qd, >30 kg 30mg qd
- Esomeprazole approved for 12 year olds and above
Omeprazole and Lansoprazone

- Granules may be mixed with acidic liquid such as apple, cranberry, grape, orange, pineapple, prune, tomato and given orally through the gastrostomy tube. Avoid grapefruit juice.
- May sprinkle on applesauce.
- Oral suspension can be made to go down a GT or jejunostomy for omeprazole.
- Lansoprazone suspension is not made to go down tubes (may clog). Need to open capsule and place granules in acidic liquid. ODT tablet can go through GT/NG if dissolved. Make bicarbonate suspension for JT.
Adverse Effects: PPI

- Elevated serum gastrin and hepatic transaminases
- Headache
- Diarrhea
- Nausea
- Dizziness
Sucralfate

- Mucosal protectant
- May be useful for mild to moderate esophagitis.
- May decrease pain with esophagitis.
- May improve oral intake of infants who have esophageal pain causing feeding aversion.
- Have not seen used.
Prokinetic Agents

- Use is much less than previously
- Improve contractility of the esophagus, increase lower esophageal sphincter pressure, and increase the rate of gastric emptying.
- Lack of evidence supporting use
- Concern that may cause CNS complications (irreversible) with metoclopramide
- Withdrawal of cisapride
- Metoclopramide-0.1-0.2mg/kg/dose tid to qid; Max: 10mg
Metoclopramide

- Dopamine antagonist that increases GI motility through smooth muscle stimulation by stimulating acetylcholine release from postganglionic nerve terminals.
- Also increases resting LES pressure and increases the rate of gastric and duodenal emptying.
- Few studies showing decreases number of GER episodes.
- Is associated with increased weight gain in infants with GERD.
Adverse Effects: Metoclopramide

- Drowsiness
- Restlessness
- Dry mouth
- Irritability
- Diarrhea
- Hyperactivity
- Lower seizure threshold
- Extrapyramidal effects
- Acute dystonic reaction
- Tardive dyskinesia
Surgery Indications

- Erosive esophagitis despite high-dose antisecretory therapy (PPIs), high-risk groups such as cystic fibrosis patients and neurologically impaired children, and pulmonary manifestations or sequelae of GERD such as aspiration pneumonia and apnea.

- Nissen fundoplication-360° wrap of the gastric fundus around the lower 2-3 cm of the esophagus. May still require pharmacologic management.
Adverse Effects of Fundoplications

- High incidence of adverse effects.
- Higher risk of bowel obstruction (5-10%)
- Gas-bloat syndrome—many place gastrostomy tube after surgery for gastric decompression in anticipation of this occurring.
- Infection
- Atelectasis or pneumonia
- Perforation; Persistent esophageal stricture
- Not always effective or permanent. 95% effective in otherwise normal children. 33% asymptomatic if neurologically impaired (many had recurrent pneumonia, vomiting, choking, gagging, etc).
Summary

- Definition
- Signs and symptoms
- Treatment