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## **Pathophysiology**

Hyperlipidemia is a term used when there are elevated lipids in the plasma. It is also referred to as Dyslipidemia. It is a metabolic disorder involving a level of lipoproteins that increase the risk for atherosclerosis. Lipoproteins are molecules that carry cholesterol in the bloodstream. They are divided into different classes according to their size and density. The classes are: very low density lipoprotein (VLDL), intermediate density lipoprotein (IDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL).

The lower density lipoproteins are the particles that migrate to inflamed areas of blood vessel walls. There, they are oxidized and form fatty streaks and atherosclerotic plaques. Other cardiovascular risk factors, determine the acceptable level of LDL a person should have. Triglycerides (TG) are formed from dietary fats, they are large lipid molecules that also contribute to the formation of atherosclerotic plaques. Total cholesterol in the blood comes from dietary fats as well as liver synthesis.

HDL is a protective lipoprotein, its function is to remove excess cholesterol from the blood vessels and transport it back to the liver to be excreted as bile. It also prevents oxidization of LDL, which, in turn, prevents atherogenesis. Thus a higher HDL is considered cardioprotective, whereas a low HDL is considered a cardiovascular risk factor.

Dyslipidemia is thought to arise as a result of behavioral factors such as dietary consumption of fats and physical inactivity. It has also been linked to genetics and family history. Secondary causes include obesity, diabetes, hypothyroidism, renal disease, hepatic disorders, alcoholism and other endocrine disorders. Certain medications also can contribute to dyslipidemia such as thiazide diuretics, steroids and beta-blockers (Dunphy, Winland-Brown, Porter, & Thomas, 2007).

## **Past Medical History**

### ***Medical Conditions-***

- Hyperlipidemia since 1996
- Pheochromocytoma in 1996
- Seasonal allergies
- Multiple seborrheic lesions on her back
- Hemorrhoids
- History of UTIs
- Hypothyroidism since 2007
- Low back pain with right side radiculopathy diagnosed with an L4/L5 disc herniation
- Degenerative disc disease and spinal stenosis in 2008
- Lipomas on her abdomen, right thigh and right arm.

### ***Surgeries/Hospitalizations-***

- Removal of left adrenal gland and pheochromocytoma tumor April 1996.
- Right breast biopsy 1996 and 2009.
- Left breast biopsy 1991 and 2008.
- Tonsillectomy as a child.
- Microdiscectomy 2008.

***Previous Health Care-*** She gets routine care on a regular basis at Sioux Rapids Family Care Clinic under the care of Sue Terrell ARNP. She has annual wellness and screening exams as recommended. She has

been followed in the past at Rochester Mayo for her pheochromocytoma. She has not been seen there since 2007.

**Preventive Screenings-** Last PAP test with CBE was 9/09, Last Mammogram 5/10, She had a screening colonoscopy in 2008. She has not had a Dexascan.

**Immunizations-** Last Tdap 10/29/07, she has not had an influenza, pneumonia or shingles vaccine.

**Allergies-** Normodyne caused bronchospasms

**Medications-**

Claritin PRN

Calcium with vitamin D 600mg daily

Synthroid 0.075mg daily

Simvastatin 80mg daily

ASA 81mg daily

Fish Oil 1000mg twice a day

Preparation H to hemorrhoids PRN.

**Social/Personal History:**

Married white female who lives on a farm with her husband. Her life has been spent on the farm as a housewife and partner on the farm. They raise livestock on their farm where she is an active participant in the feeding and handling of the animals. She smokes about ½ a pack of cigarettes per day, uses no alcohol and drinks 4 cups of decaffeinated coffee each day. She is active in the Lutheran Church. She has no regular exercise program with her physical activities coming from her daily farm chores.

**Family History:**

Her father was deceased at age 71 with emphysema, her mother deceased at age 83 from “old age” . She was in good health prior to her death. She has 3 brothers alive and well with 1 brother deceased at age 47 from an MI. She has 2 sisters alive and well. Her paternal grandmother had breast CA at age 40 and she had a paternal cousin who also had breast CA. She has 2 daughters and 1 son each alive and well.

**Chief Complaint and HPI:**

This patient is seen at this visit for review of lab results and follow up of her hyperlipidemia and cholesterol lowering medication. Over the past 6 months, she had been having her cholesterol lowering medication adjusted. In February 2010, her lipids were elevated [*I did not see these values*]. Her Simvastatin was increased from 20mg daily to 40mg daily at that time. She returned in May 2010, at which time the lipid profile was still elevated and not at goal. Her Simvastatin was again increased to 80mg daily.

Today she arrives at her visit and complains of muscle weakness and leg cramps. The leg cramps started in March 2010 and at that time were rare but since the beginning of summer, she has noticed them regularly along with feeling general muscle weakness. She stated that she does not feel as strong as she once was, noticing the weakness most when she is carrying heavy buckets of feed and water to the livestock on the farm. Activity worsens the leg cramps while rest relieves the leg pains.

**Review of systems:**

**General:** Denies fever, chills, weight changes, fatigue, night sweats, or sleep disturbances.

**HEENT:** Denies visual changes, hearing loss, headaches, nasal congestion, ear pain, enlarged or tender lymph nodes in her neck. She states that she did have a cold about 2 weeks ago that included a sore throat that lasted for 2 days. Her last eye exam was in January 2010. Her last dental exam was in the summer of 2009.

**Cardiovascular:** Denies chest pain or palpitations, lightheadedness or edema.

**Respiratory:** Denies shortness of breath or wheezing. She does admit that the cold that began 2 weeks ago included a productive cough that has lingered and continues today. She states she coughs more at night than during the day and expectorates yellow phlegm. She has been taking Vitamin C and Zinc lozenges to improve her symptoms.

**GI:** Denies constipation or diarrhea, has had no change in bowel habits and no blood in her stool. She has had no difficulties with her hemorrhoids. Denies indigestion, heartburn, nausea or vomiting.

**Endocrine:** Denies excessive thirst or hunger, heat or cold intolerances, diaphoresis, or enlarged thyroid. Denies brittle nails or hair. She states that she was diagnosed at age 50 with a Pheochromocytoma resulting in her right adrenal gland with the tumor being removed. She recalls the symptoms she experienced that lead to her diagnosis included: palpitations, anxiety, nervousness, sudden high blood pressure and a rapid pulse. She states that she has not experienced any similar symptoms since her surgery.

**GU:** Denies urinary urgency or frequency, painful urination, vaginal discharge, itching or redness. She denies any breast lumps or nipple discharge.

**MS:** See HPI. Complains of general muscle weakness. She has been experiencing leg cramps that have been increasing in frequency over the last 6 months. She denies any joint stiffness or swelling, denies limited ROM.

**Skin:** Denies dry skin, rashes, changing or concerning moles. Denies abnormal hair or nail growth. She does state that she has several lipomas located on her abdomen and on each arm.

**Neuro:** Denies change in consciousness, syncope, seizures, weakness, paralysis, or loss of memory.

**Psych:** Denies depression, mood changes, difficulty concentrating, anxiety or irritability.

## Physical Exam

**GENERAL:** 63 year old pleasant Caucasian female, alert, cooperative, well-groomed, answering questions appropriately. No acute distress noted. T-98.4 P-72 R-16 BP-#1 -142/90 , #2 – 140/90, Wt- 176lbs. Ht- 64” BMI-30.21

**HEENT:** Head is normocephalic, eyes clear, conjunctiva pink, corneal light reflexes symmetrical, PERRLA, red reflexes present bilat. No hemorrhages or exudates noted on fundoscopic examination. External auditory canals are clear. TMs pearly gray with good light reflexes, no redness, drainage, bulging or retraction. Nasal and oral mucosa pink and moist, nasal mucosa somewhat boggy with clear drainage noted. Posterior pharynx without erythema, exudates, or lesions. Teeth in fair condition.

**NECK:** Supple without adenopathy or thyromegaly.

**LUNGS:** Respirations regular, lungs clear and somewhat diminished to auscultation upper and lower lobes bilat. No wheezes, rales, or rhonci noted.

**HEART:** Regular rate and rhythm. No ectopic beats or murmurs appreciated. Extremities without clubbing, edema, or cyanosis. Peripheral pulses 2+ bilat upper and lower extremities.

**ABDOMEN:** Bowel sounds normoactive X 4 quads. Abdomen soft, round and nontender. No hernias or organomegaly palpated. Large 5-6 cm oval soft tissue mass noted right upper quad consistent with her 2007 documented history of a lipoma in that area of her abdomen. No discoloration, redness, warmth or tenderness of the mass. It is soft yet fixed and non-movable. No inguinal adenopathy noted.

**BREASTS:** Exam deferred. Last CBE was 9/2009 and she has recently had a mammogram in May 2010.

**GU:** Exam deferred, patient will be making another clinic visit for her annual pap exam within the next month to coincide with the conditions of her insurance for routine screening.

**SKIN:** Skin warm, pink and dry. No rash or lesions of concern. She does have multiple seborrheic lesions on her back. She also has a 3-4cm soft tissue mass on her right arm and a 3-4cm soft tissue mass on her right thigh. These masses are consistent with her documented lipomas in these areas and have not changed in size since they were first documented in 2007. No discoloration, redness, warmth or tenderness of the masses. The masses are soft yet fixed and non-movable. No epitrochlear adenopathy noted.

MS: All joints with full range of motion. No tenderness, nodules, deformities, erythema, edema, or swelling. Gait steady. Muscle strength 5/5 equally upper and lower extremities bilat.

NEURO: Cranial nerves II-XII grossly intact. All deep tendon reflexes brisk to upper and lower extremities bilat.

PSYCH: Normal mentation. Alert and oriented X3.

### Laboratory Data

<u>Lipid Profile 8/2010</u>	<u>5/2010</u>
Cholesterol – 171	196
Triglyceride – 255 H	251
HDL – 37 L	44
LDL – 83	102

AST – 18

ALT – 14

- *Lipid Profile. In this case the rationale was to evaluate Simvastatin dose adjustment. Her total cholesterol is decreasing and her LDL is decreasing, although her TG continues to be elevated without improvement. Her HDL is also low and has actually decreased.*
- *AST/ALT. Completed to evaluate liver function in relation to the increasing Simvastatin dose adjustments. Her AST/ALT remains WNL.*

*Other lab that could have been completed would include:*

- *CBC r/o anemia which could produce general weakness and muscle aches.*
- *Chem Profile to monitor thyroid effects looking at renal functions and evaluate for a decreased GFR which can occur with hypothyroidism. Also leg cramps can be caused by hypokalemia, hyponatremia, hypoglycemia and other electrolyte imbalances induced by dehydration.*
- *TSH considering her hx of hypothyroidism should be re-evaluated as this can be a cause of dyslipidemia as well as muscle weakness. Her TSH and free T4 were WNL 6 months previously checked.*
- *FBS to evaluate blood glucose levels. She is at an increased risk for Metabolic Syndrome due to her high cholesterol with low HDL, her increased BMI, and her borderline HTN state. Taking thyroid medications can also increase blood glucose levels.*
- *Complete UA with specific attention to protein indicating possible renal impairment with the hypothyroidism.*
- *CK to evaluate myopathy complaints. Evaluate for muscle breakdown and potential for rhabdomyolysis complications.*
- *EKG may be beneficial to evaluate for any target organ damage due to the hyperlipidemia and HTN.*
- *Calcium Score CT scan through Planet Heart could screen for atherosclerosis considering her increased risk for CAD due to hypercholesterolemia, hx of smoking, borderline HTN.*

(Dunphy, Winland-Brown, Porter, & Thomas, 2007)

#### FRAMINGHAM SCORE:

Age 60-64 Female	10
TC 160-199	1
Smoker	2
HDL <40	2
Systolic BP 140-159 untreated	3
Total	18pts

10 year cardiac risk of 6% (National Institute of Health, 2001)

#### Assessment

1. Dyslipidemia
2. Hypertension
  - Differential Diagnosis – Metabolic Syndrome
3. Hypothyroidism
4. Myopathy probably secondary to Cholesterol lowering medication

#### Plan

##### **Problem #1: Dyslipidemia**

**Immediate Treatment:** Discontinue Simvastatin 80mg daily. Initiate Simcor 40/500 PO every day at bedtime. Increase ASA to 325mg PO daily take 30 minutes prior to Simcor dose.

**Long Term Rx or Tx:** Goal for this patient is to lower her LDL  $\geq$  160. She has multiple risk factors but her Framingham score was <10%. This patient should continue practicing therapeutic lifestyle changes (TLC) (National Institute of Health, 2001). Simvastatin is a 1<sup>st</sup> line drug of choice. These statins reduce LDL by about 30-40%. Simvastatin has had an LDL lowering effect on her cholesterol level and her LDL is currently below goal at 83. Her TGs remain high and unchanged and her HDL remains low. According to ATP III, treatment would now consist of addressing TGs. This may be achieved by adding nicotinic acid or fibrate. Changing the type of statin therapy or reducing the dose may also reduce the myopathy the patient is experiencing (Dunphy, Winland-Brown, Porter, & Thomas, 2007). *(The FNP I am precepting with wanted to address TG by ordering Simcor. Simcor contains Simvastatin and Niacin, her hope is that the Niacin will have a TG reducing effect. The dose of Simcor is 40/500, this is 40mg less than the Simvastatin 80mg dose she has been on. The FNP is hoping the decreased dose will relieve the myopathy the patient is experiencing considering her LDL is well below goal, reducing the Simvastatin is acceptable).*

**Further Testing:** Consider CBC, Chem Panel and Uric Acid to further evaluate blood sugar and lytes, Simcor can elevate blood glucose levels. Niacin can reduce platelet count and phosphorus levels and increase uric acid levels (Abbott Laboratories, 2009). Also re-evaluate TSH with Free T3 and T4.

**Patient Education:** Teach patient to take Lipid lowering agents at bedtime to coincide with circadian rhythm of the liver producing cholesterol at night. This medication should be taken with a low-fat snack to reduce GI symptoms. Educate patient on the side effects and use of Simcor including: muscle weakness and the significant flushing and pruritis that goes along with taking Niacin. Educate on taking her ASA for pretreatment 30 min before Simcor dose to counter the flushing side effects. Encourage to notify if myopathy worsens before follow-up appointment. Educate about lab values and the difference and ratio of TC, LDL, HDL, and TG. Encourage TLC including low fat and high fiber diet, weight management and increased physical activity. Discuss the Framingham Heart Score with patient to help motivate the patient to adhere to diet, exercise, and drug treatment. Encourage smoking cessation to reduce risk factors.

**Follow-up:** 6-8 weeks to re-evaluate lipid profile and Simcor.

**Referral made:** Could be referred to dietician for nutrition consultation.

**Cost issues:** Simcor is not on \$4 list and cost approx \$75 for 30 day supply. Simvastatin is about \$25 for 30 day supply. This patient is covered by insurance and it appears Simcor to reduce the TG will be the most cost effective choice. Cost will increase if atherosclerosis resulting in heart damage or stroke occurs.

**Research implications:** Research in the use of cholesterol lowering medications and recommended guidelines for treatment continues. The National Heart Lung and Blood Institute are working on ATP IV and these new research based guidelines are expected to be released Fall 2011.

**Ethical and legal implications:** Primary care providers have a responsibility to evaluate and treat patients with dyslipidemia through patient teaching, medication therapy, and follow-up. There is a documented correlation between dyslipidemia and coronary events. Elevated lipid levels present the greatest risk factors for the development of coronary artery disease (CAD) which claims the lives of approximately 700,000 people in the U.S. each year (Dunphy, Winland-Brown, Porter, & Thomas, 2007).

## **Problem #2: Hypertension**

**Immediate Treatment:** Lifestyle modification counseling. (*Other treatment may have included adding a low dose HCTZ 12.5mg PO daily to her medication regimen*) (Dunphy, Winland-Brown, Porter, & Thomas, 2007).

**Long Term Rx or Tx:** This patient is just at the borderline between prehypertension and stage I hypertension. 1<sup>st</sup> line therapy for a BP of 140/90 should include lifestyle modification as well as a low dose HCTZ for continued BP at this level and above (Dunphy, Winland-Brown, Porter, & Thomas, 2007). (*The FNP that I am with did not want to address HTN at this time. She stated that the patient will follow-up again for lipids in 6-8 weeks and will see where the BP is at that time*).

**Further Testing:** An EKG to assess for other target organ damage and labs to include FBS and lipids to r/o metabolic syndrome.

**Patient Education:** Life style modification regimen including weight reduction for BMI <25. Teaching patient to use BMI for goal rather than pounds. Teach patient principals of the DASH diet including low fat diet and increasing fruits and vegetables may decrease SBP 8-14mmHg. Restricting sodium to 2.4g or 6gm of sodium chloride per day may have a SBP reduction of 2-8mmHG. Increasing physical activity by engaging in aerobic activity for 30 min on most days can reduce the SBP 4-9mmHg. She does not consume alcohol but limiting alcohol intake can also have SBP reduction benefits. Encourage smoking cessation to reduce risk factors as well as lower BP (Dunphy, Winland-Brown, Porter, & Thomas, 2007).

**Follow-up:** She is returning to clinic in 6-8 weeks for lipid profile and medication review. Will follow up with BP at that time and see how lifestyle modification is going for her.

**Referral made:** Could be referred to cardiologist if evidence of target organ damage is present.

**Cost issues:** Following lifestyle modification has virtually little cost impact other than purchasing healthier foods which do increase the grocery bill. If she needs to be put on HCTZ the cost is minimal as a 30 day supply is on the \$4 list or \$10 for a 90 day supply. The cost issue increase as HTN is ignored and target organ damage occurs. Newer and multiple medications required to control severe hypertension increases the cost. The hospitalizations can be costly when heart failure or kidney failure occur that started due to poorly control HTN.

**Research implications:** Research is continually being conducted to identify biological and other mechanisms responsible for abnormal blood pressure control, risk factors, and susceptibility to target organ damage. Understanding the causes and finding the approaches that best control high blood pressure are studied by the National Institutes of Health and the American Heart Association (National Institutes of Health, 2010). The guidelines and standards for treatment are recommendations of the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (Dunphy, Winland-Brown, Porter, & Thomas, 2007).

**Ethical and legal implications:** Primary care providers have a responsibility to screen, evaluate, educate, and treat patients as well as the community with information on high blood pressure. Hypertension affects more than 50 million people in the U.S. and is the most common chronic health care problem seen in primary care. Numerous studies have shown the relationship of hypertension and the development of

target organ damage resulting in CAD, kidney damage, heart failure, and stroke (Dunphy, Winland-Brown, Porter, & Thomas, 2007).

### **Problem #3: Hypothyroidism**

**Immediate Treatment:** Continue Synthroid 0.075mg PO daily.

**Long Term Rx or Tx:** Patient should remain on Synthroid and have TSH monitored every 6 months due to her age and naturally decreasing albumin levels may affect thyroid dosing.

**Further Testing:** as described above.

**Patient Education:** Teach patient to take this medication on an empty stomach in the morning as it can cause insomnia and other medications and foods can reduce absorption. Emphasis is on lifelong replacement therapy and follow-up. Educate on the signs and symptoms of hypothyroidism as well as hyperthyroidism. Encourage patient to layer clothing if they have cold intolerance and avoid getting burns when trying to get warm with heating pads etc. Instruct to stay with same brand of thyroid preparation due to the bioavailability differences between types of thyroid replacement.

**Follow-up:** TSH and free T4 biannually for this patient since over age 60

**Referral made:** Could be referred to endocrinologist considering her history of pheochromocytoma as well as her hypothyroidism.

**Cost issues:** Levothyroxine is on the \$4 list at Walmart. As long as the thyroid replacement is adequate, little health damage typically occurs. The emphasis on life long replacement is important as hypothyroidism can also cause multiple medical problems and symptoms.

**Research implications:** Hypothyroidism affects four times more frequently in women than men. There are no clinical recommendations for the routine screening of hypothyroidism but most clinicians try to screen women over 40 years of age. There are American Association of Clinical Endocrinologists is the organization who sets the standards for all endocrine related diseases.

**Ethical and legal implications:** Many comorbid conditions are related to hypothyroidism. It is the primary care provider responsibility to recognize symptoms of hyper and hypothyroidism, screen, and follow-up with thyroid lab values to ensure proper medication doses are being ordered.