LACK OF AWARENESS OF HEMOCHROMATOSIS
IN THE HEALTHCARE COMMUNITY
AND THE DETRIMENTAL EFFECTS OF LATE DIAGNOSIS

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As thesis advisor for ANNE MEYER,

I have read this paper and find it satisfactory.

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Date
Précis

Hereditary Hemochromatosis (HH) is a genetic condition characterized by excessive iron absorption in the body. HH is termed autosomal recessive, which means that a person must have two genes in order to develop symptoms of the disease. A mutation on the HFE gene causes high levels of iron to be absorbed from the diet. As iron builds up in the bloodstream, it is deposited in various organs. The most likely organ for iron deposition is the liver, but it can also occur in the heart, pancreas, lungs, and brain. Common symptoms of HH include fatigue, joint pain, depression, impotence, bronzing of the skin, abdominal pain, memory problems, early menopause, and loss of body hair. Diagnosis of HH tends to occur between ages 40 to 60, after iron levels reach toxic levels. As iron levels rise in the body, conditions such as diabetes mellitus, cirrhosis, liver failure, liver cancer, infertility, weakening of the heart, and heart failure may occur. If undiagnosed or untreated, HH can cause early death.

HH is the most common genetic disorder in the United States. Approximately 1 in 200 people have HH and 1 in 10 people are carriers for the disease. HH affects both men and women equally. Women naturally lose blood and iron during menstruation and pregnancy; therefore, men tend to show symptoms earlier in life and often have more complications. The disease is most commonly seen in people of European descent.

Treatment of HH is relatively simple and can prevent many complications of the disease. The most common treatment to manage iron overload is regular blood-letting, referred to as phlebotomy. Patients with HH also need to reduce the amount of iron in their diets, limit vitamin C intake, and avoid alcohol. Certain drugs may be used to treat HH, but these are generally used as a last resort. Treatment of HH requires minimal lifestyle changes,
yet has the ability to prevent many severe complications. Despite HH’s high occurrence in the population, many people, including medical professionals, have never heard of or know little about the condition. A lack of awareness of HH in the healthcare community may lead to late or no diagnosis, as well as unnecessary, devastating long-term effects.

To address this issue, a survey was conducted to assess the level of awareness of HH among people who work in the healthcare community. The goal of the survey was to question participants about factual information regarding knowledge of HH, rather than asking for opinions, judgments, or values. Participants of the survey included physicians, nurse practitioners, registered nurses, licensed practical nurses, and healthcare students. Out of 54 medical professionals and students surveyed, eight participants (14.8%) correctly identified HH as a condition of iron overload in the body. Primary care providers also answered questions regarding the frequency of diagnosis or screening for HH in their practice. Accurate identification of HH among physicians was 100%, but 70% of primary care providers stated that they had never diagnosed HH, and 20% reported that they “rarely” diagnosed the disease. Thus, it seems that even if primary care providers are aware of the condition, they are not applying their knowledge of HH to their own practice and identifying the disease in patients.

Although further research is needed in order to confirm the results of this study, the survey demonstrates that there is an inadequate level of awareness of HH among people who work in healthcare. Given the results, it is clear that education about HH must be increased and medical professionals need to apply knowledge of HH to their practice. This will allow patients with the condition to be properly diagnosed and treated to reduce, or even prevent, the devastating complications associated with HH.
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**Introduction**

Hereditary hemochromatosis (HH) is an autosomal recessive blood disorder that is characterized by an increase in iron absorption, which can lead to excessive iron deposits in organs and eventual organ failure (Phatak, Bonkovsky, & Kowdley, 2008). Despite the common belief that it is a rare disease, HH is actually the most common genetic disorder in the United States. However, there is little public awareness of the disease. Patients with HH often have symptoms long before they receive the correct diagnosis and get proper treatment. One study found that diagnosis of HH takes an average of nine and a half years after the onset of symptoms (Centers for Disease Control and Prevention, 2007). Late diagnosis of HH can cause detrimental effects such as diabetes mellitus, cirrhosis, liver failure, heart failure, and premature death. Because of the delay between onset of symptoms and diagnosis, it appears that the level of awareness of HH in the medical community is inadequate. In order to determine the awareness of HH among medical personnel, a survey was performed targeting people who currently work in the healthcare community. The goal of the survey was to question participants about their factual knowledge regarding HH, rather than asking for opinions, judgments, or values.

**History**

HH was first described in 1865, by the French doctor, Armand Trosseau. For the next 25 years it was called “bronze diabetes” and thought to be extremely rare (Moalem, 2007). In 1889, German pathologist Friedrich von Recklinghausen identified iron as the cause of pigment changes seen in the disease and renamed the condition hemochromatosis. Successive medical researchers considered HH a disease that caused cirrhosis in alcoholics. Even as late as the 1960s, it was still believed to be a nutritional disorder related to alcohol intake,
although a study of over 300 published cases of HH, organized by J. H. Sheldon in 1934, revealed that HH was a familial disorder in which tissues have an abnormal affinity for iron. Sheldon also determined that HH was not a complication of alcoholism, diabetes, cirrhosis, or copper excess (Machado, Ravasco, Martins, Almeida, Camilo, & Cortez-Pinto, 2009).

Effective treatment for HH was not available until 1952, when W. D. Davis and W. R. Arrowsmith proposed repeated phlebotomy. Meanwhile, autopsy studies had begun to show a much higher prevalence of the disease in the general population than previously expected. By the end of the 1980s, researchers concluded that HH should be diagnosed through screening, and saturation of total iron-binding capacity (TIBC) was recognized as the best test for HH (Felitti, 1999). Unfortunately, numerous supporting studies did not lead to a change in clinical practice.

In 1996, more than 130 years after the initial description of HH, the gene responsible for HH, the HFE gene, was finally discovered (Moalem, 2007). As a result, the myth that all patients with HH were alcoholics was dispelled. Researchers have since estimated that the C282Y mutation occurring on the HFE gene originated 60 to 70 generations ago. Assuming approximately 15 to 20 years per generation, this means that the appearance of HH can be dated to between 600 to 1100 C.E. (Moalem, Percy, Kruck, & Gelbart, 2002).

Since the discovery of the HFE gene, two main theories have been advanced to explain both the origin and the prevalence of HH. Medical historians believe that HH can be traced to Vikings who lived in early medieval Scandinavia, where it evolved as a method to minimize iron deficiency in a poorly nourished population with harsh living conditions. Women with HH were able to avoid common iron deficiency and have more children, therefore spreading the HH mutation. Complications of HH in women were offset through
menstruation and pregnancy. Men with HH were also able to survive the negative effects, perhaps because of frequent blood loss from battle. After the Vikings became carriers of HH, they spread it to other parts of Europe during nearly 250 years of raiding and conquering (Moalem, 2007). Researchers often point to the very high frequency of the C282Y mutation on the British Isles to support their claims that HH is Scandinavian in origin (Moalem et al, 2002).

The current prevalence of HH can be traced to 1347, when the bubonic plague, or Black Death, devastated Europe. The explanation rests on the role of macrophages, the part of the white blood cell involved in the immune response. Some infectious diseases use iron in macrophages as a source of food and energy. When a disease encounters a macrophage, it feeds and multiplies, due partially to the availability of iron. People with HH, however, have less iron in their macrophages than people without the disease. By the time the plague struck Europe, the number of people with HH had increased considerably. When these people were exposed to the bubonic plague, their macrophages essentially starved the pathogen of iron and stopped it from spreading throughout the body. People with HH were more likely to survive the plague and pass the mutation on to their children (Moalem, 2007). This substantially increased the percentage of Europeans who had HH. Today, regions in Europe with the highest mortality rates during the initial phases of the plague (Northern Europe, Belgium, England, and France) now have the highest prevalence of HFE mutations (Moalem et al., 2002).

Prevalence

Although once thought to be a rare disorder, recent research shows that HH is more common than originally believed. HH is the most common genetic mutation in people of
European descent (Moalem, 2007). Approximately 1 in 10 people of the Caucasian population in the United States are heterozygous, thus, carriers of the disease. About 1 in 200 people in the Caucasian population is homozygous, therefore will show clinical manifestations of HH (Schrier & Bacon, January 2008). Roughly one million people in the United States have the disease (National Heart Lungs and Blood Institute, 2009). Research shows that HH affects both men and women equally; however, males tend to have a higher incidence of cirrhosis than females (Regan, 2009).

Despite the high prevalence of HH, the disorder often goes undiagnosed and untreated until the late stages of the disease. In one study, patients reported that before receiving the diagnosis of HH, they saw an average of three different doctors and the correct diagnosis took more than nine years. Common misdiagnoses of HH include arthritis, gallbladder and liver disease, stomach disorders, diabetes, mental health disorders, and hormonal deficiencies. In many cases these diagnoses were indeed correct, but did not identify the underlying cause of the problem: iron overload (Weinberg, 2004; Centers for Disease Control and Prevention, 2007). “A lot of diseases mask hemochromatosis; it’s a bigger problem than we realize,” said one HH patient (J.R., personal communication, January 30, 2010).

**Pathophysiology**

Iron is an essential part of a person’s diet and performs many vital functions within the human body. Iron is responsible for oxygen transport through the bloodstream, red blood cell production, DNA synthesis, and numerous enzymatic processes in metabolism (Weinberg, 2004). Without enough iron in the diet, the immune system functions poorly, skin
becomes pale, and people feel dizzy, confused, cold, and very fatigued (Moalem, 2007). Too much iron, however, can also cause many adverse effects.

The gene responsible for regulating iron absorption from the diet is called the HFE gene (Mayo Clinic, 2008). HH is typically caused by mutations on the HFE gene. Since the disease is autosomal recessive, a person must inherit two mutated genes for the disorder to be expressed, which is termed homozygous. The two main mutations that can occur on the HFE gene are the C282Y mutation, which accounts for 90 to 95% of cases, and the H63D mutation. A C282Y mutation is associated with a more severe form of iron absorption than a H63D mutation. People who are heterozygous for HH are generally asymptomatic, but in rare cases, they may also exhibit signs and symptoms of the disease (Plaut & McLellan, 2009).

Iron stores in the body are regulated by intestinal absorption in the duodenum (Regan, 2009). Most people absorb roughly one to two milligrams of iron per day from their diets (about 10% of ingested iron), which is then equally excreted through sweat, sloughing skin cells, urine, and the gastrointestinal tract (Schrier & Bacon, January 2008). When iron stores are adequate, the HFE gene signals the intestines to absorb less iron to avoid excess iron accumulation (Mayo Clinic, 2008). Due to a mutation in the HFE gene, people with HH can absorb anywhere from two to four milligrams per day, which is about 30% of ingested iron, but the excretion rate remains the same (Schrier & Bacon, January 2008). Once iron is absorbed, the only physiologic pathway for iron excretion is blood loss (Centers for Disease Control and Prevention, 2007). Premenopausal women tend to have lower iron levels and fewer complications from HH than men since they regularly lose blood and iron during menstruation and pregnancy (Bring, Partovi, Ford, & Yoshida, 2008).
**Signs and Symptoms**

Over time, people with HH deposit excess iron accumulation in organs such as the liver, heart, brain, pancreas, and lungs (Plaut & McLellan, 2009). The liver is the most common organ for iron deposition (Mayo Clinic, 2008). A person without HH has about three to four grams of total iron in his or her body at any given time (Moalem, 2007). A person with HH starts to show symptoms once approximately 15 to 20 grams of iron accumulate in the body. Men typically become symptomatic in their 40s and women with HH show symptoms approximately 15 years after menstruation ceases (Centers for Disease Control and Prevention, 2007). Estimates suggest that nearly half of all people with HH are asymptomatic (National Heart Lungs and Blood Institute, 2009).

Early symptoms of HH include arthralgia, fatigue, depression, impotence, skin hyperpigmentation, abdominal pain, increased susceptibility to bacterial infections, premature menopause, memory problems, and loss of body hair (Weinberg, 2004; Plaut & McLellan, 2009). The most common complaints of HH are fatigue and joint pain (Iron Disorders Institute, 2009). Over 70% of patients have liver function abnormalities, weakness and lethargy, and skin hyperpigmentation at the time of diagnosis (Regan, 2009). Other signs of HH found through lab tests include high blood sugar levels, hypothyroidism, and abnormal liver function tests. Increasingly high iron levels lead to cirrhosis, liver failure, liver cancer, diabetes mellitus, infertility, psychiatric disorders, cardiomyopathy, and heart failure (Mayo Clinic, 2008; Moalem, 2007). If untreated, these diseases caused by HH can, and do, lead to death.
Diagnosis

Current clinical guidelines recommend that testing for HH should be performed if a person has any unexplained signs or symptoms that may be associated with HH. People should especially be examined for HH if they know of a family member with the condition, since it is an inherited disorder (Centers for Disease Control and Prevention, 2007). In 1999, changes in the Medicare Reimbursement Policy caused serum iron to be taken off routine blood panel screenings. A primary care provider must now look specifically for signs and symptoms of iron overload and order particular tests to detect HH (Weinberg, 2004). Thus, HH is not likely to be routinely diagnosed, unless primary care providers are familiar with the prevalence of HH and can identify early symptoms. One patient with homozygous HH said, “I think all CBC’s [complete blood count] should include an iron panel. It should be a mandatory part of a CBC” (C.R., personal communication, January 30, 2010).

Diagnosis of HH typically does not occur until the ages 40 to 60, when iron levels have already reached toxic levels (Plaut & McLellan, 2009). Diagnosis is made through a variety of laboratory tests. In 1997, the Centers for Disease Control and Prevention (CDC) recommended that transferrin saturation, a major iron-binding and transport protein in serum, be used as the initial diagnostic test for HH. In order to determine the transferrin saturation level, a fasting blood draw is done to measure serum iron and total iron-binding capacity (TIBC). Serum iron measures the amount of circulating iron bound to transferrin and shows the level of iron in the body. However, serum iron can be affected by inflammation, menstruation, time of day, diet, and presence of hepatitis. Therefore, serum iron alone cannot be used solely as a diagnostic tool (Centers for Disease Control, 2007). Transferrin saturation is calculated by dividing serum iron by TIBC and multiplying by 100% (serum iron/TIBC)
A normal range for transferrin saturation is 16 to 45%. Transferrin saturation within the normal range eliminates the possibility of HH (Regan, 2009). If a person has a transferrin saturation percentage greater than 45%, the primary care provider should proceed with a serum ferritin test, which measures the amount of iron stored in the body (Centers for Disease Control, 2007).

A normal serum ferritin for men and postmenopausal women is below 300 ng/mL and below 200 ng/mL for premenopausal women (Iron Disorders Institute, 2006). A serum ferritin level greater than normal in the absence of other causes of iron overload, warrants the diagnosis of HH and treatment can begin (Centers for Disease Control and Prevention, 2007). Severe symptoms of HH are likely if ferritin levels are greater than 1,000 ng/mL, since there is a close correlation between serum ferritin levels and the level of excess iron in the body (Regan, 2009).

Confirmation of HH after an elevated iron panel can occur in one of three ways. Phlebotomy is the most common method of choice used to confirm HH. Each phlebotomy treatment removes approximately 500 mL of blood. A weekly or biweekly phlebotomy treatment, for approximately fifteen treatments, confirms a HH diagnosis by measuring the total amount of iron removed from the body. The goal is to lower the serum ferritin level to about 20 ng/mL (Centers for Disease Control and Prevention, 2007). The removal of more than two grams of iron using phlebotomy, without producing iron deficiency, confirms diagnosis of HH (Iron Disorders Institute, 2006).

The second method for confirming diagnosis of HH after a patient presents with an elevated serum ferritin level is HFE genetic testing for C282Y mutation homozygosity or other mutations on the HFE gene (Phatak et al., 2008). Approximately 85% of the cases of
HH in the United States are due to a mutation of the HFE gene. Other causes are still unknown (Plaut & McLellan, 2009). Therefore, if a patient tests negative for HFE mutation, but has symptoms and lab results indicating iron overload, treatment should be considered. HFE genetic testing by itself is insufficient for diagnosis of HH due to the incomplete knowledge regarding the causes of the disease. Positive genetic testing for HH must be combined with elevated transferrin saturation or serum ferritin to obtain a diagnosis (Centers for Disease Control and Prevention, 2007).

Another method of confirming HH after getting elevated iron levels is liver biopsy. Since liver biopsy directly evaluates the amount of iron per gram of liver tissue, it is more commonly used for prognostic reasons to determine the level of damage from HH (Centers for Disease Control and Prevention, 2007; Weinberg, 2004). Once used as the definitive confirmation test for HH, liver biopsy is now recommended for patients with high risk of liver involvement or liver damage from HH. Most health care providers use liver biopsy in patients with elevated liver enzymes and serum ferritin levels greater than 1,000 ng/mL (Schrier & Bacon, 2009).

Other noninvasive imaging studies, such as computed tomography (CT) and magnetic resonance imaging (MRI) are used to determine iron content in organs in patients with a reduced risk of liver involvement. However, these procedures do not necessarily confirm diagnosis of HH (Schrier & Bacon, 2009).

**Screening**

Since the disease is common and complications can be easily prevented with early diagnosis and treatment, the question of community screening has been raised and much debate has ensued. Concerns—at both national and international levels—include: incomplete
knowledge about disease penetrance, the potential for discrimination with insurance and employment, potential for increased anxiety in people who may never develop manifestations of the disease, cost effectiveness of screening, compliance with clinical management, and whether screening should be by iron studies or genetic testing (Allen, Nisselle, Collins, Williamson, & Delatycki, 2008). One major concern regarding screening is that people who test positive may never return for confirmation testing or may not take action to treat their disease. A study performed in Italy found that 67% of people who had elevated iron levels upon screening did not return for definitive testing (Allen et al., 2008).

In 2006, the U.S. Preventive Services Task Force (USPSTF) recommended against routine screening for HH in the asymptomatic general population based on “poor predictability of future risk for disease” (Regan, 2009, p.26). The CDC and the American College of Physicians also do not currently recommend population screening for HFE mutations due to the uncertainty of proportion of people affected by the disease and inefficiency of screening. All three organizations do encourage screening for patients with clinical symptoms and/or a family history of HH, since these patients are considered high risk for the condition. Primary care providers may also offer screening to asymptomatic individuals if the patient is aware of the risks and benefits of screening (Centers for Disease Control and Prevention, 2007; Phatak et al, 2008). Early detection of HH may reduce morbidity of patients and, ultimately, long-term healthcare costs for individuals who are found to have HH (Laudicina, 2006).

**Treatment and Management**

Initial treatment and long-term management of HH often depends on the level of iron in the body and associated symptoms at the time of diagnosis. In addition to treatment of HH,
diseases caused by HH also need separate management, such as liver disease and diabetes mellitus (National Heart Lungs and Blood Institute, 2009). Phlebotomy is the most common treatment and management method for HH. Phlebotomy works by stimulating the bone marrow to make new red blood cells as old ones are extracted. Iron is moved out of iron stores in the body to make more hemoglobin. Therefore, phlebotomy reduces the patient’s iron level and can restore it to a healthy level. If phlebotomy is started early enough in the course of iron accumulation, most overload complications can be prevented (Centers for Disease Control and Prevention, 2007). Phlebotomy is considered the easiest, cheapest, and most effective option for removing accumulated iron stores; it is regarded as the gold standard for treatment of HH. Phlebotomy is recommended for patients with ferritin levels greater than 300 ng/mL for men and greater than 200 ng/mL for women and hemoglobin values of 12.5 g/dL or greater (Bring et al., 2008; Weinberg, 2004).

The unit of blood removed typically contains 200 to 250 mg of iron and reduces serum ferritin by about 30 ng/mL per phlebotomy (Weinberg, 2004; Centers for Disease Control and Prevention, 2007). Frequent serum ferritin tests are the most reliable and easiest way to monitor progress of phlebotomy. The most common side effects of phlebotomy include fatigue, dehydration, and nutrient deficiency (Weinberg, 2004). Regular phlebotomy treatment often resolves or improves symptoms of HH. A homozygous HH patient said, “I believe that hemochromatosis causes all kinds of diseases that can be prevented, and prevented in a way that doesn’t even require drugs. It just requires phlebotomies” (C.R., personal communication, January 30, 2010). However, cirrhosis is not reversible through phlebotomy, and improvement with diabetes mellitus is rarely seen (Bring et al., 2008; Weinberg, 2004).
During the initial “de-ironing” phase, blood is drawn once or twice a week until the level of iron returns to a normal range (Plaut & McLellan, 2009). The de-ironing phase can take three months to one year, depending on the patient and initial iron levels (Centers for Disease Control and Prevention, 2007). One patient with homozygous HH who underwent an extensive de-ironing phase said,

I went through about three years of very high-levels of phlebotomy. At first it was every week for the first year… I had a lot of trouble with dehydration. Then we settled in that about all I could handle was every two weeks and still function well. I did that really for the remainder of the three years. I actually wound up a little iron deficient. (M.L., personal communication, February 21, 2010).

It is important not to remove too much iron during the de-ironing phase, as forced anemia may result (Centers for Disease Control and Prevention, 2007). Once iron levels return to normal again, phlebotomy is recommended four to six times per year to prevent recurrent iron overload. The amount of blood drawn depends on the patient’s age and weight, overall health, and the severity of iron overload (Mayo Clinic, 2008).

Most blood removed through phlebotomy of an HH patient is not used for blood donation or transfusions. In 1999, the Food and Drug Administration (FDA) announced that blood from patients with HH and iron overload is safe for transfusion as long as the facility meets certain criteria. A person cannot contract HH from a blood transfusion since the disorder results from a genetic mutation (Centers for Disease Control and Prevention, 2007).

Another option for management of HH is monitoring dietary iron intake. This is often performed in conjunction with phlebotomy treatment. Iron is found in numerous food sources and many over-the-counter vitamins (Plaut & McLellan, 2009). There are two types of
dietary iron: heme iron and non-heme iron. Heme iron originates from foods such as red meat and is more easily absorbed by the body. Non-heme iron comes from foods such as grains, nuts, fruits, vegetables, iron fortified foods, or contaminated iron sources, such as water, soil, and cooking utensils, and is not as easily absorbed by the body (Weinberg, 2004). Calcium is the only known substance that inhibits the absorption of both types of iron. Tannins, fiber, eggs, and salts impair the absorption of non-heme iron. Substances that increase iron absorption include vitamin C supplements, sugar, fat, and alcohol (Iron Disorders Institute, 2006). Alcohol is one of the most potent non-genetic modifiers of iron absorption. However, the absolute risk of alcohol, at any level of consumption, is unknown (McCune, 2008).

People with HH should also avoid raw shellfish if iron levels are elevated because shellfish may contain bacteria, *Vibro vulnificus*, which may be fatal to people with high iron levels (Iron Disorders Institute, 2006).

A third option for treatment of HH is iron chelation. Chelation involves the use of medications that selectively bind excess iron and increase iron excretion, typically through urine and stool (Barton, 2007). This treatment is generally used for patients who cannot tolerate phlebotomy. Reasons that people may not be able to endure phlebotomy include poor venous access, forced anemia from too much phlebotomy, and interference with quality of life (Regan, 2009). Chelation is used only when absolutely necessary, as it lacks the same efficacy of phlebotomy treatment (Centers for Disease Control and Prevention, 2007).

Three iron chelating agents are currently available for clinical use: deferoxamine, deferiprone, and deferasirox (Barton, 2007). Deferoxamine is the most widely used chelating agent and is administered by subcutaneous infusion pump over an 8- to 12-hour period (Regan, 2009). Infusion typically takes place for five to seven days per week. Patients may
also take vitamin C supplements below 250 mg per day concurrently with deferoxamine in order to increase iron excretion (Bring et al., 2008). Potential side effects of deferoxamine include redness and pain around the infusion site, high-frequency hearing loss, and visual impairment. These adverse effects may be reversed upon discontinuation of the medication (Regan, 2009). Patients may also notice reddish colored urine, but this is normal (Bring et al., 2008). The course of therapy varies with each patient, but it is often required for at least two years (Regan, 2009). Patient compliance is a concern with deferoxamine due to the stringent infusion routine, high cost, and potential adverse reactions (Barton, 2007).

Deferiprone and deferasirox are oral medications used for iron chelation, and are generally less expensive than deferoxamine. However, the FDA has not approved deferiprone for use in the United States. Potential side effects include abdominal pain, nausea, vomiting, diarrhea, skin rashes, and elevated serum creatinine (Regan, 2009). Chelating agents may also impair growth and skeletal changes in young children (Bring et al., 2009). Patient compliance with oral iron chelation medications tends to be much higher than compliance with deferoxamine (Barton, 2007).

**Prognosis**

Early diagnosis and treatment of HH are essential in order to prevent severe complications of the disease. Treatment may help prevent, delay, or even reverse some of the complications of HH. The outlook for patients with HH depends on how much organ damage is present at the time of diagnosis. If diagnosis and treatment take place early, a normal lifespan is possible. On the other hand, late diagnosis and lack of treatment have devastating effects, since not all symptoms of HH can be reversed (National Heart Lungs and Blood Institute, 2009). Failure to correctly identify HH is particularly problematic. One study
showed that people who received early diagnosis and treatment had an improved life expectancy of seven years compared to those who received late diagnosis (Phatak et al., 2008).

The major determinant of prognosis for HH is the occurrence of cirrhosis in a patient. One study reports that survival of HH was shortened in patients with cirrhosis and diabetes, but survival was normal in patients without cirrhosis. An analysis of the causes of death in patients with HH found that patients were 119 times more likely to have hepatocellular carcinoma, 10 times more likely to have cirrhosis, 306 times more likely to have cardiomyopathy, and 14 times more likely to have diabetes mellitus (Schrier & Bacon, May 2008).

**Research Question**

Does the lack of awareness among medical personnel about the existence and prevalence of hereditary hemochromatosis result in late diagnosis of the disease, resulting in improper treatment, increased medical expenses, and life-threatening complications for patients with this disease?

**Methodology**

A survey was conducted in order to assess the actual level awareness of hemochromatosis among people who work in the healthcare community. The target population for the survey was members of the healthcare population, which included physicians, nurse practitioners, physician assistants, pharmacists, registered nurses (RNs), licensed practical nurses (LPNs), healthcare educators, nursing students and physician assistant students. A primary sampling unit was chosen as opposed to random sampling since the research question targets a specific population. The survey received Human Studies
Approval from the Washington State University Office of Grants and Research Development (OGRD) prior to implementation and participants signed a consent form before completing the survey (see Appendices I and II).

Participants were contacted through an intercept questionnaire and participation in the study was voluntary and anonymous. An open-ended survey style was selected, in order to prevent the results from being skewed by successful guesswork among participants. Surveys were completed through a self-administered questionnaire in order to improve time efficiency. Healthcare professionals and students were surveyed at the Washington State University Riverpoint Campus in Spokane, Washington, and at various regional hospitals, clinics, and healthcare facilities.

Responses to the completed surveys were manually entered into an Excel spreadsheet. Assumptions were not made about missing data and no information was entered into empty fields. If a questionnaire contained terminology regarding an elevated iron level in the body, the participant was judged to have correctly identified the disorder and data was interpreted as actual awareness of the disease. Answers by primary care providers regarding the frequency of diagnosis or screening in practice for HH were also recorded.

**Results**

Fifty-six healthcare professionals were contacted to complete the survey regarding awareness of HH. A total of 54 (n=54) healthcare professionals participated in the study. The rate of participation was 96.4%. Of the 54 participants, 11 were male (20.4%) and 43 were female (79.6%). The average age of participants was 42 years, with a median of 42 years. The average reported experience working in healthcare was 18.1 years, with a median of 12 years. Four of the participants were physicians (7.4%), six participants were nurse
practitioners (11.1%), 22 participants were RNs/LPNs, (40.7%), one participant was a physician assistant student (1.9%), and 21 participants were nursing students (38.9%). Eight RNs and two nurse practitioners also reported being healthcare educators.

Of the 54 participants, 19 people answered “yes” when asked if they had ever heard of HH (35.2%). This included four physicians, six nurse practitioners, five RNs/LPNs, one physician assistant student, and three nursing students. A total of eight participants correctly identified HH as a disorder of iron overload (14.8%) (See Table 1).

Table 1. Survey Results

<table>
<thead>
<tr>
<th>Role in Healthcare</th>
<th>Number of Participants</th>
<th>Answered “yes” if they had heard of HH</th>
<th>Correctly identified HH</th>
<th>Percent correctly identified according to role in healthcare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physicians</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>100%</td>
</tr>
<tr>
<td>Nurse Practitioners</td>
<td>6</td>
<td>6</td>
<td>1</td>
<td>16.7%</td>
</tr>
<tr>
<td>RNs/LPNs</td>
<td>22</td>
<td>5</td>
<td>1</td>
<td>4.5%</td>
</tr>
<tr>
<td>Nursing Students</td>
<td>21</td>
<td>3</td>
<td>1</td>
<td>4.8%</td>
</tr>
<tr>
<td>PA Students</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>Total</td>
<td>54</td>
<td>19 (35.2%)</td>
<td>8 (14.8%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Correct symptoms of HH listed on the survey

<table>
<thead>
<tr>
<th>Symptom of HH listed</th>
<th>Number of participants who listed each symptom</th>
<th>Percent of total participants (n=54)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>1</td>
<td>1.9%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3</td>
<td>5.6%</td>
</tr>
<tr>
<td>Bronze skin</td>
<td>4</td>
<td>7.4%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3</td>
<td>5.6%</td>
</tr>
<tr>
<td>Liver disease</td>
<td>4</td>
<td>7.4%</td>
</tr>
<tr>
<td>Cardiovascular problems</td>
<td>1</td>
<td>1.9%</td>
</tr>
<tr>
<td>Neurological problems</td>
<td>2</td>
<td>3.7%</td>
</tr>
</tbody>
</table>
Correct symptoms of HH listed on the survey were evaluated (see table 2). Of the four physicians surveyed, three listed only advanced symptoms of HH, which included diabetes, liver disease, and bronze skin. Only one of the physicians listed early-stage symptoms in addition to advanced symptoms of HH, such as asymptomatic and fatigue. Treatments listed were phlebotomy (eight participants, 14.8% of total participants) and dietary iron restriction (two participants, 3.7% of total participants).

The primary care providers (four physicians and six nurse practitioners) who participated in the survey also answered questions regarding diagnosis and screening for HH in their practice. The average length of reported experience working in healthcare among primary care providers was 25.3 years with a median of 31 years. Of the 10 primary care providers (physicians and nurse practitioners), seven participants (70%), answered that they had never diagnosed HH, two participants (20%) answered that they diagnosed it “rarely,” and one participant (10%) answered that he/she did not work as a primary care provider. In regard to screening, eight participants (80%) answered that they do not screen for HH and two participants (20%), both physicians, answered that they do screen for HH. One of the two physicians who screens for HH answered, “I screen for this about once every three months in my adult inpatient practice.” The other answered, “yes- ferritin, TIBC, iron.” The physician assistant student, who is not a primary care provider yet, answered, “still just a student, but have worked with primary care provider’s who do screen for it. They screen mostly in individuals of Northern European descent.”

Discussion

Results of this study indicate that there is little awareness of HH among healthcare professionals and students. According to the results, roughly 15% of people in the healthcare
community can correctly identify HH. Given the prevalence of the disease, the knowledge of HH in the healthcare community is inadequate to properly diagnose, educate, and treat the disease.

It is worth noting that 70% of primary care providers said that they had never diagnosed HH, and 20% of primary care providers stated that they “rarely” diagnose HH. According to one statistic, the average doctor sees 11 patients per day (Moore & Wasson, 2007). This calculates out to be approximately 220 patients per month. Since 1 in 200 people have homozygous HH in the United States, each primary care provider should see about one homozygous HH patient per month in his or her practice. The average length of work experience among primary care providers in this study group was 25.3 years, yet 70% self-reported they had never diagnosed HH.

According to the American Academy of Nurse Practitioners (2009), there are 125,000 nurse practitioners actively practicing in the United States and 62% of them see three to four patients per hour. Nurse practitioners may be responsible for the initial diagnosis of HH, but will often refer care for the primary treatment of the disease to a specialist. Only one of six (16.7%) nurse practitioners identified the disease correctly. All six nurse practitioners stated that they have never diagnosed HH. Given these statistics, there needs to be an increase of awareness of HH among nurse practitioners working as primary care providers for proper diagnosis of HH to occur.

This study shows that primary care providers do not know to identify and diagnose HH as often as patients present with it. One study found that it took an average of nine and a half years from the onset of symptoms to the diagnosis of HH (Centers for Disease Control and Prevention, 2007). The reason for the delay of diagnosis is simple—not enough people in
the healthcare community are aware of the disorder. One patient with homozygous HH, whose brother had been previously diagnosed, said,

I went to a primary care doctor and the first thing she did was get a little laptop computer out. I know she was looking up hemochromatosis—she asked me how to spell it…She ran some tests and said, you don’t have hemochromatosis, your labs are absolutely normal. I found out later she didn’t do an actual iron panel…I insisted on seeing a specialist and I was found to be homozygous for hemochromatosis (C. R., personal communication, January 30, 2010).

Physicians in particular seemed to be aware of the disease in this study. However, the reported rate of diagnosis compared to the prevalence of the disease does not reflect the high identification rate of HH found in the survey.

Another interesting result of the study was the identification of symptoms associated with HH listed by physicians. Although all symptoms listed were correct, three of four physicians only listed severe, end-stage symptoms. Only one physician acknowledged that HH could be asymptomatic and also listed less severe symptoms of HH, such as fatigue. This raises the question of whether or not most physicians only look for advanced symptoms of HH. Since significant organ damage may have already occurred with late diagnosis of a patient with HH, it is essential to promote early diagnosis. Primary care providers need to be observing for both early and late signs of the disease.

In addition to primary care providers, RNs/LPNs and healthcare students had low rates of identification of HH. Only one RN, one physician assistant student, and one nursing student correctly identified the condition of HH out of 44 total RNs/LPNs, nursing students, and physician assistant students. Although RNs and LPNs may not be responsible for
diagnosing HH, they are accountable for educating patients and the public about the disease. Their knowledge about HH is particularly important when counseling patients about the treatment and management of their disorder. RNs and LPNs also spend more time with patients than primary care providers do. This extra time allows RNs and LPNs to observe and identify early symptoms of HH. In rare cases, RNs and LPNs can contribute to the correct diagnosis of HH. One homozygous HH patient reported that “the doctor said he couldn’t take credit for the diagnosis of hemochromatosis since the extra iron test was the nurse’s idea” (M.L., personal communication, February 21, 2010).

**Limitations**

A limitation of the study was the small sample size. More generalizable data may have been collected if a larger group of participants was used. Another limitation of the study was the availability of primary care providers to participate in the survey. Many physicians and nurse practitioners were unavailable or difficult to locate due to the busy nature of their jobs. If the survey were repeated, it would also be beneficial to ask participants to estimate the prevalence of HH. Many participants made comments about how rare the disorder must be since they had never heard of it. It would be interesting to compare the perceived prevalence among medical personnel and the actual prevalence of HH.

Given that relatively no research currently exists regarding the level of awareness of HH among the healthcare community, further research is needed to expand upon the findings of this original study. It would also be beneficial to conduct a survey specifically targeting primary care providers to investigate the level of knowledge and awareness of HH among medical professionals who are responsible for identifying and diagnosing the disease.
Conclusion

HH is one of the most common genetic disorders in the United States, but diagnosis of the disease takes an average of 9.5 years after the onset of symptoms. Treatment and management of the disorder remains fairly simple and can significantly improve outcomes of patients with HH. Delayed diagnosis of HH leads to increased health complications, elevated healthcare costs, and higher morbidity rates among patients.

The results from this study show a relatively low level of awareness of HH among people who work in the healthcare community. This reduced level of awareness of HH among medical personnel may be partially responsible for delayed diagnosis of people with HH. Although physicians in this study were able to correctly identify the disease, the majority of primary care providers had never diagnosed the disease in their practice. This shows a significant breakdown between the knowledge of the disease and application to practice. Despite limitations of the study, similar findings would likely result if the survey were repeated using a larger sample size.

Further research may provide additional insight into the external validity of the level of awareness of HH among healthcare professionals. This study provides a useful foundation for understanding the current knowledge deficit regarding HH in the United States. It also demonstrates the need for increased education, awareness, and application to practice among healthcare professionals regarding the symptoms, diagnosis, and treatment of HH.
References


Appendix I. Consent form for surveys

Awareness of Hemochromatosis in the Healthcare Community Survey

As part of my research for the Honors College Thesis at Washington State University, I am looking at the level of awareness and knowledge about Hereditary Hemochromatosis in the healthcare community. Dr. Mary Sobralske, assistant professor at the College of Nursing, is overseeing this project.

- The survey should take approximately 1-3 minutes.
- Your identity will be kept private at all times. (Please do not write your name on the survey.)
- The information you submit in the survey will be kept confidential and will be stored in a secured, locked file at Washington State University, College of Nursing in Spokane.
- Only the researcher and mentor will look at your answers.
- Information gained from these surveys may be used for written articles.
- You will receive a copy of this signed consent form today.

Researcher’s Signature_____________________________________

CONSENT STATEMENT:

I have read this entire consent form and agree to participate in this survey. I understand that participation in this research study is voluntary and I have the right to drop out or ask questions at any time. If I have questions about the study, I can contact the researcher, Anne Meyer at 509-432-9476 or acmeyer11@gmail.com. If I have any questions about my rights as a participant, I can contact the Washington State University IRB at 509-335-3668 or irb@wsu.edu.

Participant’s signature ____________________________ Date ___________

Print Name_________________________________________
Appendix II. Survey

AWARENESS OF HEMOCHROMATOSIS IN THE HEALTHCARE COMMUNITY SURVEY

What is your role in the healthcare industry?

___Physician
___Nurse Practitioner
___Pharmacist
___Nurse (RN or LPN)
___Healthcare Educator Please state healthcare field:________________
___Healthcare Student Please state healthcare field:________________
___Other: ___________________________________________________

Gender: Male______ Female______
Age:___________
Years of experience working in healthcare:___________
Have you ever heard of Hereditary Hemochromatosis? _____Yes _____No

If so, describe the condition:
_____________________________________________________________________
_____________________________________________________________________
_____________________________________________________________________

What are some common signs and symptoms of the condition?
_____________________________________________________________________
_____________________________________________________________________
_____________________________________________________________________

Name one kind of treatment for the condition:
_____________________________________________________________________
_____________________________________________________________________
_____________________________________________________________________

If you are primary care provider, how often do you diagnose Hereditary Hemochromatosis?
_____________________________________________________________________
_____________________________________________________________________
_____________________________________________________________________

If you are a primary care provider, do you ever screen for Hereditary Hemochromatosis?
_____________________________________________________________________
_____________________________________________________________________
_____________________________________________________________________

Appendix III. Consent form for interviews

AWARENESS OF HEMOCHROMATOSIS IN THE HEALTHCARE COMMUNITY INTERVIEW

As part of my research for the Honors College Thesis at Washington State University, I am looking at the level of awareness and knowledge about Hereditary Hemochromatosis in the healthcare community. Dr. Mary Sobralske, assistant professor at the College of Nursing, is overseeing this project.

With your permission, by participating in this interview, you are agreeing to be recorded in order to keep an accurate record of your answers. Your answers to the questions may be published, but your name and personal information will not be released. You can refuse to be tape recorded and still be interviewed and participate in the research study. You do not have to answer any questions you feel uncomfortable with and you can stop the interview at anytime.

- The interview should take approximately 30 minutes.
- Your identity will be kept private at all times.
- The cassette tape and any information you release in the interview will be kept confidential and will be stored in a secured, locked file at Washington State University, College of Nursing in Spokane.
- Only the researcher and mentor will look at your file and listen to your recorded interview.
- Information gained from these interviews may be used for written articles.
- You will receive a copy of this signed consent form today.

Researcher’s Signature_____________________________________

CONSENT STATEMENT:

I have read this entire consent form and agree to participate in this interview. I understand that participation in this research study is voluntary and I have the right to drop out or ask questions at any time. If I have questions about the study, I can contact the researcher, Anne Meyer at 509-432-9476 or acmeyer11@gmail.com. If I have any questions about my rights as a participant, I can contact the Washington State University IRB at 509-335-3668 or irb@wsu.edu.

Participant’s signature ______________________________________ Date ___________

Print Name_______________________________________________
Appendix IV. Interview questions

LACK OF AWARENESS OF HEMOCHROMATOSIS IN THE HEALTHCARE COMMUNITY AND THE DETRIMENTAL EFFECTS OF LATE DIAGNOSIS

Interview Questions

Today’s Date _________________________

Location of Interview_________________________________________

Year of Birth _________________________ Age Today_____________

1. What year did you receive a diagnosis of Hereditary Hemochromatosis? (How long ago were you diagnosed?)
2. What symptoms (if any) did you have at the time of your diagnosis?
3. How long did you seek medical help before you received a diagnosis?
4. How many doctors/primary care providers did you see before receiving your diagnosis?
5. Do you remember your initial lab values upon diagnosis? If so, what were they?
6. How do you currently manage your disease?
7. What is your opinion about community screening for HH?
8. If you had had the option to get tested before your diagnosis, would you have done it?
9. If you have children, do you plan on getting them tested for HH or have you already had them tested?
   a. If not, why?
   b. If so, why?
10. Is there anything else you would like to share about your experience with HH?