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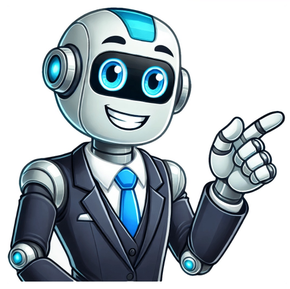

Hemochromatosis is a disorder characterized by excessive iron accumulation in body tissues that leads to the dysfunction of various organs. Normally, iron absorption is tightly regulated, but in hemochromatosis, the body absorbs too much iron, which it cannot excrete. Hereditary hemochromatosis, the most common form, is an autosomal recessive disorder predominantly found in individuals of European descent. The disorder is caused by mutations in HFE, resulting in increased iron absorption. Excess iron is deposited in organs, including the liver, pancreas, heart, and skin, often leading to conditions such as liver disease, diabetes, heart failure, and skin discoloration, known as "bronze diabetes." The types of hereditary hemochromatosis vary based on genetic mutations. Type 1 is the most common, while types 2, 3, and 4 are rarer variants. Secondary hemochromatosis can occur due to frequent blood transfusions or certain hematological disorders. The symptoms of hemochromatosis typically appear in adulthood and may include fatigue, joint pain, and skin darkening, among others. Diagnosis is made through blood tests measuring iron levels and genetic testing. Treatment of hemochromatosis primarily involves regular phlebotomy to remove excess iron from the body, and early detection can prevent severe organ damage. Objectives: Identify the clinical features of hemochromatosis.Determine the appropriate evaluation for a patient with suspected hemochromatosis.Compare the management options available for hemochromatosis.Apply interprofessional team strategies to improve care coordination and outcomes in patients affected by hemochromatosis. Access free multiple choice questions on this topic. Primary hemochromatosis is an autosomal recessive disorder, particularly among those of northern European descent, that disrupts the body's ability to regulate iron absorption, leading to systemic iron overload. Despite the high prevalence of the gene mutation, the condition often shows variable clinical expression with low penetrance. Excess iron accumulates in critical organs, including the liver, pancreas, heart, joints, skin, and pituitary gland, leading to cellular dysfunction. The condition is typically diagnosed in middle age; women are often diagnosed later in life due to the iron loss associated with menstruation. Symptoms are generally nonspecific, and many cases are discovered through elevated transaminase, ferritin, and transferrin saturation levels.While primary hemochromatosis is hereditary, secondary hemochromatosis can develop from disorders in erythropoiesis or as a result of treatments involving blood transfusions, such as in thalassemia, sickle cell anemia, and hereditary spherocytosis. These secondary conditions lead to iron accumulation from damaged red blood cells, further complicating iron regulation. Phlebotomy is the primary treatment, reducing iron levels and improving organ function. In severe cases, particularly when liver damage is extensive, liver transplantation may be necessary. Relatives of individuals with hereditary hemochromatosis are advised to undergo genetic testing to assess their risk.Retained iron is primarily deposited in the parenchymal cells in hereditary hemochromatosis, whereas transfusional hemochromatosis predominately results in iron deposition in the reticuloendothelial cells. The excess iron is deposited in the cells as hemosiderin, eventually leading to cell death and replacement of these cells by a fibrous deposition that causes destruction or impairment of organ function. Hereditary hemochromatosis is traditionally classified into 4 classes or types with some additional subtypes.Type 1 hereditary hemochromatosis occurs in patients who are typically homozygous for loss-of-function mutations in HFE. These mutations cause increased iron absorption despite an average dietary iron intake. While more than 100 HFE mutations can cause Type 1 hereditary hemochromatosis, the most common mutation is the p.Cys282Tyr or C282Y variant; the second most common mutation is the p.His63Asp or H63D mutation.[1] HFE is present on the short arm of chromosome 6 (6p21.3). The resultant anomaly is a decreased hepcidin production or a state of hepcidin resistance.[2] This is considered the classic form of hereditary hemochromatosis, is inherited in an autosomal recessive fashion, and disproportionately affects males.[3][4]Type 2 hereditary hemochromatosis is also inherited in an autosomal recessive fashion without a predilection for either sex. Historically, this disease was referred to as "juvenile" hemochromatosis, and the typical age of onset is in adolescence or early adulthood (15 to 20 years). Type 2 hereditary hemochromatosis has 2 subtypes, 2a and 2b. Type 2a is due to a mutation in the gene initially referred to as hemojuvelin but now known as HFE2. Type 2b is due to mutations in the hepcidin antimicrobial peptide (HAMP) gene on chromosome 19.Type 3 hereditary hemochromatosis, also inherited in an autosomal recessive fashion, has a typical age of onset of 30 to 40 years. This type is due to mutations in the transferrin-receptor gene (TFR2) on chromosome 7.[5]Type 4 hereditary hemochromatosis is the only known type to be inherited in an autosomal dominant fashion. Historically, this subtype was known as ferroportin disease, as the relevant mutations occur in the ferroportin transport protein known as ferroportin/solute carrier family 40 member 1, encoded by SCL40A1 on chromosome 2. The age of onset of type 4 hemochromatosis is highly variable and may be as early as 10 years or as late as 80 years.[2]Hereditary hemochromatosis is the most common autosomal recessive disorder in White populations, with a prevalence of 1 in 300 to 500 individuals.[6] Hereditary hemochromatosis types 2, 3, and 4 are seen worldwide, but type 1 is primarily seen in people of northern European descent.[7] The prevalence of hemochromatosis is the same in Europe, Australia, and other Western countries, with excess in people of Celtic or Scandinavian origin. Hemochromatosis is less prevalent in patients of African descent. White individuals have a 6 times higher risk of developing the disease than Black individuals.In hemochromatosis, men are affected 2 to 3 times more often than women. The estimated ratio between men and women is 1.8:1 to 3:1. Women with hemochromatosis become symptomatic later in life than men due to the blood loss and consequent iron excretion associated with menstruation. The disease usually becomes apparent in men in the fifth decade; in women, it often presents in the sixth decade. In contrast, juvenile hemochromatosis may appear in persons aged 10 to 30. Analyses of a p.C282Y homozygous genotypic subset have revealed the greatest morbidity is in those patients older than 60.[8] The main risk factors for hemochromatosis include:[9]C28Y homozygosity (most significant risk factor)Positive family historyNorthern European heritageHemochromatosis affects the liver, pancreas, heart, thyroid, joints, skin, gonads, and pituitary. Excessive alcohol consumption and viral hepatitis worsen liver and pancreatic toxicity. Micronodular cirrhosis occurs in 70% of patients with unmanaged hemochromatosis, significantly increasing the risk of hepatocellular carcinoma, a leading cause of death. Pancreatic iron deposition primarily manifests as diabetes, affecting about 50% of homozygous individuals; the risk of developing diabetes is elevated in heterozygotes.Arthropathy causes joint pain without destruction, resembling degenerative joint disease but with calcium pyrophosphate crystals in the synovial fluid. Cardiac symptoms stem from iron accumulation, leading to heart failure and arrhythmias. Iron overload also causes hypogonadism and skin hyperpigmentation.Iron overload in macrophages impairs phagocytosis, leading to decreased immunity and an increased risk of infections from organisms like Aeromonas, Listeria, Yersinia enterocolitica, and Vibrio vulnificus.[10][11][12][13] Patients with hemochromatosis should avoid handling or consuming raw shellfish due to a heightened risk of sepsis from V vulnificus. Excess iron deposits in the thyroid gland can cause hypothyroidism, with men experiencing an 80-fold greater risk than normal. While iron deposition in the adrenal and parathyroid glands rarely results in clinical symptoms, iron overload in hemochromatosis can occur due to massive oral intake, increased absorption with normal intake, or excessive red blood cell production or transfusion. Hereditary Hemochromatosis HFE mutations cause increased iron absorption despite normal dietary iron intake. HFE regulates the production of hepcidin, the protein product of HAMP, which is a circulating peptide hormone.[14] Hepcidin, made predominately in the liver, inhibits dietary iron absorption in the duodenum and its release by splenic macrophages. HFE-related mutations are responsible for 90% of the cases of hereditary hemochromatosis in people of Northern European descent. Heterozygotes may have abnormalities in clinical markers of iron metabolism but do acquire iron overload. Heterozygotes do have an increased risk of diabetes over the general population due to unknown mechanisms.[15][16] Secondary Hemochromatosis Causes of secondary hemochromatosis include erythropoietic hemochromatosis, a condition that results from excess iron absorption because the patient is producing excessive amounts of red blood cells. This often occurs due to an underlying disease of the red blood cells that causes them to be more fragile and, therefore, to have a shortened lifespan. When the cells are destroyed, their iron is deposited in the body tissues. The same mechanism is in effect in patients who receive multiple, usually chronic, transfusions of red blood cells. Other less common conditions, such as porphyria cutanea tarda, can cause iron overload. Erythropoietic hemochromatosis follows the prevalence of the underlying disease and is found in a broader range of ethnicities than the hereditary form of the disorder. Furthermore, excessive iron consumption can also cause hemochromatosis. Historically, this has resulted from drinking beer prepared in steel drums. Accidental and intentional overdoses of iron can result from the consumption of some over-the-counter dietary supplements.[17]Clinical signs of hemochromatosis are dictated by the organ system most severely affected. Patients are usually asymptomatic until adulthood, and often, a diagnosis will not be made until multiple systems are affected. Almost all patients complain of severe fatigue. Other early manifestations include arthralgias and lethargy. Patients are typically symptomatic for up to 10 years before diagnosis. A high index of suspicion, combined with a thorough family history, is required to diagnose hemochromatosis. Women with hemochromatosis become symptomatic later in life than men due to the blood loss and consequent iron excretion associated with menstruation.[18]The following late manifestations occur when iron is deposited progressively in various tissues:Koilonychia: Koilonychia affects the thumb and index finger, and it has been observed in 50% of patients. However, in 25% of patients, all nails are affected.Secondary diabetes: Looking at the lateral aspects of the nails during the examination may reveal finger prick marks indicating diabetes, and an abdominal examination may be suggestive of lipodystrophy as a clue towards insulin administration.Diffuse hyperpigmentation: Skin discoloration is seen in more than 90% of patients with hemochromatosis and is one of the earliest manifestations of the disease. Although it may be mild, hyperpigmentation is more evident in sun-exposed areas of the skin. Other cutaneous manifestations may involve ichthyosiform changes and skin atrophy on the anterior aspects of the legs.Arthropathy: This occurs due to calcium pyrophosphate crystal deposition in the joints. Arthropathy can present with arthritis, chondrocalcinosis, and joint swelling, commonly involving metacarpophalangeal and proximal interphalangeal joints. Other commonly affected areas include knees, wrists, hip, back, neck, and feet.Liver involvement: Jaundice may or may not be present; liver dysfunction is encountered in 75% of patients. Jaundice is usually absent earlier in the course of the illness. Liver disease can present with abdominal pain, hepatomegaly, cirrhosis, portal hypertension, ascites, and splenomegaly. While cirrhosis only occurs in 10% to 15% of patients, the risk of hepatocellular carcinoma increases in patients with coexisting hemochromatosis and cirrhosis. The risk of hepatocellular carcinoma may amount to 30% of patients. A hepatic bruit may indicate hepatocellular carcinoma, and hepatic hum may suggest portal hypertension in such patients.Cardiac involvement: This can lead to restrictive or dilated cardiomyopathy, arrhythmias, and cardiac failure. Clinicians should listen for the third and fourth heart sounds in suspected cases.Endocrine dysfunction: This can lead to diabetes, pituitary hypogonadism, manifested by decreased libido and impotence in men and amenorrhea in women, hypopituitarism, thyroid dysfunction, adrenal dysfunction, parathyroid defects, and osteoporosis.[19] Gynecomastia and decreased body hair can be secondary to both chronic liver disease and hypogonadism. Partial loss of body hair is seen in 60% of patients, and complete hair loss is seen in 12% of patients. The pubic region is the most commonly involved area.Cancers: When compared with the general population, the risk of hepatocellular carcinoma is increased by 20-fold in patients with hemochromatosis.Infections: Patients with iron overload are at increased risk of infection from Yersinia enterocolitica, Listeria monocytogenes, and V vulnificus.Cranial nervous system: Hereditary hemochromatosis has been thought to lead to Parkinson disease, chorea, and tremors through its iron deposition in the basal ganglia, dentate, red nuclei, and the substantia nigra.[13] Laboratory Studies Evaluation of hemochromatosis begins with serum transferrin saturation or serum ferritin concentration testing.[20] The mainstay of diagnosis requires a transferrin saturation greater than 45% or a serum ferritin greater than 200 µg/L in females or 300 µg/L in males.[2] Transferrin saturation testing in erythropoietic hemochromatosis may not be as effective in testing for iron overload in these patients. Ferritin specificity can be affected by inflammatory conditions. Ferritin is a "phase reactive protein," and in conditions of inflammation, indicated by an increase in either the erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), ferritin may appear elevated, giving a false level of concentration. Ferritin levels above 200 mcg/L in women or 300 mcg/L in men or a transferrin saturation of >40% in women or 50% in men should lead to further testing.Transaminases are usually elevated but are generally not higher than twice normal.[21] Additionally, fasting blood glucose levels need to be checked for diabetes. Glycosylated hemoglobin levels might not be reliable in patients with high red cell turnover.[22] In the United States, where the HFE mutation is prevalent, further genetic testing for the mutations C282Y and H63D should be obtained.[23] Genetic testing for these mutations will confirm the diagnosis in over 90% of cases. For a more comprehensive discussion of the evaluation of hemochromatosis, please see StatPearls' companion reference, "Laboratory Evaluation of Hereditary Hemochromatosis." Imaging Studies Echocardiography can be used to identify and evaluate the severity of cardiomyopathy in patients with hemochromatosis. A chest radiograph may indicate cardiomegaly and increased pulmonary vascular markings, but is not diagnostic of cardiac disease. Magnetic resonance imaging (MRI) of the liver is a noninvasive way to measure liver iron content.[24] The contrast of hepatic iron excess with the relative paucity of splenic iron is highly suggestive of hepcidin deficiency.[25] Additional Testing Liver biopsy is the most sensitive and specific test for measuring liver iron content and can also assess liver damage. On histopathological analysis with Perls Prussian blue staining, there is a classic pattern in which iron deposits are primarily in hepatocytes and biliary epithelial cells, with slight involvement of Kupffer cells. A liver biopsy is indicated in the following situations:Elevated liver enzymes in a diagnosed case of hemochromatosisSerum ferritin levels greater than 1000 mcg/LAdditional tests that need to be conducted in patients with high ferritin levels are echocardiogram for cardiomyopathy, hormone levels to evaluate hypogonadism, and bone densitometry to evaluate for osteoporosis.[26][27] All relatives of patients with hemochromatosis should be offered genetic testing.The conventional therapy for primary hemochromatosis is phlebotomy. By removing circulating erythrocytes, the major mobilizer of iron in the body, iron toxicity can be minimized.[28] Patients may require 50 to 100 phlebotomies of 500 mL each to reduce iron levels to normal. Phlebotomy is usually performed once or twice a week. Once iron levels have normalized, lifelong but less frequent phlebotomy is required, typically 3 to 4 times a year. The objective is to obtain a ferritin level of less than 50 µg/L.[29][30] Iron removal through phlebotomy improves insulin sensitivity, skin pigmentation, and fatigue; cirrhosis, hypogonadism, and arthropathy remain unchanged. Erythrocytapheresis has been suggested as an alternative to phlebotomy as it operates more rapidly.[9] Erythrocytapheresis has been shown to improve cognition, fatigue, and the ferritin level quickly.[31]Alcohol should be strictly prohibited in this condition due to its potential to accelerate liver and pancreatic toxicity. Phlebotomy rarely reverses preexisting end-organ damage. Treatment for associated dysfunction, such as insulin for pancreatic dysfunction, remains essential. Early detection of hemochromatosis allows for treatment that can prevent end-organ dysfunction, resulting in minimal mortality or morbidity. However, severe end-organ damage often leads to a life expectancy of less than two years following diagnosis.Although chelation is not as effective in hereditary hemochromatosis, it is of more benefit in erythropoietic hemochromatosis, where phlebotomy is not typically an option.[32] Deferoxamine is an intravenous iron-chelating agent. Deferiprone and deferasirox are oral iron chelators. Deferoxamine, deferiprone, and deferasirox are all equivalent in efficacy in the mobilization and excretion of iron.[33] In combination with phlebotomy, erythropoietin is sometimes administered to maintain the hemoglobin concentration while forcing iron mobilization. Patients who have end-stage liver disease may be candidates for liver transplantation. Initial studies have shown that compared to patients with non-hemochromatosis causes, patients with iron overload disorders who undergo liver transplantation have lower survival rates.[34][35] However, the reduced survival rates were noted to be due to cardiac complications and infections. Data accumulated over recent years showed an increase in posthepatic transplant survival with hepatocellular carcinoma.[9] A 1-year posttransplant survival of approximately 89% and a 5-year survival of about 78% were noted. Since hepatocellular carcinoma accounts for around 30% of mortality in patients with hemochromatosis, all patients should undergo surveillance with ultrasounds and alpha-fetoprotein levels every 6 months.Due to the involvement of multiple organ systems, several differential diagnoses must also be considered when evaluating patients with clinical features of hemochromatosis, including:Iron overload from chronic transfusion Hepatitis B and CMetabolic dysfunction associated steatotic liver disease (MASLD; formerly nonalcoholic fatty liver disease or NAFLD)Excessive iron supplementationDysmetabolic hyperferritinemiaHereditary aceruloplasminemiaAlcoholic liver diseasePorphyria cutanea tardaMarrow hyperplasiaHemolytic anemiaBiliary cirrhosisIf left untreated, hemochromatosis can lead to progressive liver damage and cirrhosis, hepatocellular carcinoma, and other complications associated with iron overload in the tissues and organs.[36] The prognosis has improved in the last few decades with advances in diagnosis and management of this condition. Hepatic fibrosis or cirrhosis is the main prognostic indicator at the time of diagnosis. Early diagnosis and regular treatment with phlebotomy can decrease most of the complications associated with hemochromatosis.Patients are more likely to develop cirrhosis in the presence of additional factors like alcohol use disorder or hepatitis. Other complications of hemochromatosis include:Hepatocellular carcinomaDiabetes mellitusHeart failureHypogonadismOsteoporosisOwing to multiple organ system pathologies, the involvement of various specialties may be required in the management of patients with hemochromatosis, including:Gastroenterology and hepatologyEndocrinologyCardiologyRheumatologyDermatologyPatients should be educated that regular treatment with phlebotomy and chelating agents can prevent most hemochromatosis complications. Alcohol should be avoided. Patients should also avoid supplements that contain iron or vitamin C, which promotes iron absorption. There are no special diet recommendations for patients with hemochromatosis.Patients should avoid eating raw or undercooked shellfish. This is because of the risk of bacterial infections, especially those caused by Vibrio vulnificus, which thrives in iron-rich environments.Management of hemochromatosis requires an interprofessional effort from healthcare clinicians, including the patient's primary care clinicians, gastroenterologists, and hepatologists. If complications arise from progressive iron overload, patients should be referred to consultants for managing complications, such as endocrinologists, orthopedics, and cardiologists. Nurses should educate patients that alcohol should be strictly prohibited in this condition because it can accelerate liver and pancreatic toxicity. Genetic counseling for family members is advocated for those patients with the hereditary form. 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Hemochromatosis: Ferroptosis, ROS, Gut Microbiome, and Clinical Challenges with Alcohol as Confounding Variable. Int J Mol Sci. 2024 Feb 25;25(5) [PMC free article: PMC10931627] [PubMed: 38473913]36.Rawla P, Sunkara T, Muralidharan P, Raj JP. Update in global trends and aetiology of hepatocellular carcinoma. Contemp Oncol (Pozn). 2018;22(3):141-150. [PMC free article: PMC6238087] [PubMed: 30455585] Disclosure: Joann Porter declares no relevant financial relationships with ineligible companies. Disclosure: Prashanth Rawla declares no relevant financial relationships with ineligible companies. Haemochromatosis is an inherited condition where iron levels in the body slowly build up over many years.This build-up of iron, known as iron overload, can cause unpleasant symptoms. If it is not treated, this can damage parts of the body such as the liver, joints, pancreas and heart.Haemochromatosis most often affects people of white northern European background and is particularly common in countries where lots of people have a Celtic background, such as Ireland, Scotland and Wales. Symptoms of haemochromatosis usually start between the ages of 30 and 60.Common symptoms include:Read more about symptoms of haemochromatosis See a GP if you have:persistent or worrying symptoms that could be caused by haemochromatosis – particularly if you have a northern European family backgrounda parent or sibling with haemochromatosis, even if you do not have symptoms yourself – tests can be done to check if you're at risk of developing problemsTalk to the GP about whether you should have blood tests to check for haemochromatosis.Read more about tests for haemochromatosis There's currently no cure for haemochromatosis, but there are treatments that can reduce the amount of iron in the body and reduce the risk of damage.There are 2 main treatments.venesection (phlebotomy) – a procedure to remove some of your blood; this may need to be done every week at first and can continue to be needed 2 to 4 times a year for the rest of your lifechelation therapy – where you take medicine to reduce the amount of iron in your body; this is only used if it's not easy to regularly remove some of your bloodYou do not need to make any big changes to your diet to control your iron levels if you're having treatment, but you'll usually be advised to avoid:breakfast cereals containing added ironiron or vitamin C supplementsdrinking too much alcoholRead more about how haemochromatosis is treated Haemochromatosis is caused by a faulty gene that affects how the body absorbs iron from your diet.You're at risk of developing the condition if both of your parents have this faulty gene and you inherit 1 copy from each of them.You will not get haemochromatosis if you only inherit 1 copy of the faulty gene but there's a chance you could pass the faulty gene on to any children you have.If you do inherit 2 copies, you will not necessarily get haemochromatosis. Only a small number of people with 2 copies of this faulty gene will ever develop the condition. It's not known exactly why this is.Read more about the causes of haemochromatosis If the condition is diagnosed and treated early on, haemochromatosis does not affect life expectancy and is unlikely to result in serious problems.But if it's not found until it's more advanced, the high iron levels can damage parts of the body.This can lead to potentially serious complications, such as:liver problems – including scarring of the liver (cirrhosis) or liver cancerdiabetes – where the level of sugar in the blood becomes too higharthritis – pain and swelling in the jointsheart failure – where the heart is unable to pump blood around the body properlyRead more about complications of haemochromatosis Haemochromatosis UK is a patient-run UK charity that provides information and support to people living with haemochromatosis. Page last reviewed: 29 March 2023 Next review due: 29 March 2026 Haemochromatosis is a genetic iron storage disease in which the body absorbs excessive amounts of iron from the diet. Excess iron is usually metabolised and excreted from the body, but in haemochromatosis, excess iron is deposited in the liver, pancreas, heart, endocrine glands and joints. Who gets haemochromatosis? Haemochromatosis is ten times more common in males than in females and usually presents at between 40 and 60 years of age. What is the cause of haemochromatosis? Haemochromatosis is caused by mutations in the HFE gene with autosomal recessive inheritance. Two mutations identified in the HFE gene are C282Y and H63D. Haemochromatosis is the most common single-gene inherited disorder in whites, with one in ten persons carrying one abnormal gene. For an individual to have haemochromatosis they must have inherited a defective gene from each parent. A person who has one defective gene and one normal gene is a carrier and will lead a perfectly healthy life. However, the carrier is able to pass on the defective gene to a son or daughter. Up to half of all patients with porphyria cutanea tarda carry at least one HFE gene mutation and this may contribute to the increased stores of liver iron seen in these patients. What are the signs and symptoms of haemochromatosis? The four main features characterise haemochromatosis are: Cirrhosis of the liver Diabetes mellitus Increased skin pigmentation Heart failure. How does haemochromatosis affect the skin? Increased pigmentation affects more than 90% of patients. Skin pigmentation is often one of the first signs of the disease and may precede the other features by many years. Hyperpigmentation is most evident on sun-exposed skin, particularly on the face. The colour of skin can be slate grey or brownish bronze. Ichthyosis-like changes (scaling) Skin thinning Partial loss of body hair; the pubic region is most affected. Koilonychia (thinned spoon-shaped nail), usually of the thumb and index and middle fingers Haemochromatosis can be associated with the disease porphyria cutanea tarda (PCT). PCT may cause fragility and blistering of the skin, especially on the backs of the hands. How does haemochromatosis affect other body organs? Enlarged liver occurs in more than 95% of patients and is often accompanied by chronic liver disease (cirrhosis) and liver failure. Diabetes mellitus, often requiring insulin therapy, is seen in 30-60% of patients. Cardiomyopathy (disease of the heart muscle) Loss of sex drive, impotence in men, absent or irregular menstrual periods and early menopause in women Arthritis, commonly in the knuckle and first joint of the first two fingers General symptoms including chronic fatigue, weakness, lethargy and apathy Patients with haemochromatosis may develop one or more of the above symptoms over a period of time as iron slowly accumulates and deposits in organs. Often the disease is not diagnosed until routine blood tests show elevated blood iron levels. Patients often seek help because of tiredness, abdominal discomfort, joint pains, and general malaise experienced over a prolonged period of time. How is the diagnosis of haemochromatosis made? Several tests can be done to confirm the diagnosis of haemochromatosis. Laboratory studies show elevated levels of iron in the blood and body stores. serum iron concentrations greater than 150 mcg/dL and serum ferritin levels > 500 ng/mL. 92% of patients with haemochromatosis have transferrin saturation greater than 62%. X-rays may show an enlarged heart, and blood tests may show liver disease or diabetes, increased blood vessels in the lungs and restrictive cardiomyopathy on echocardiograms. Genetic tests for the C282Y and H63D mutations are widely available. These tests can be performed to confirm the diagnosis or as a screening mechanism for early detection of at-risk individuals. What is the treatment for haemochromatosis? Treatment of haemochromatosis consists of regular removal of blood and is similar to making a blood donation (venesection therapy or phlebotomy). Every mL removed contains a 0.5 g of iron. Depending on the amount of iron overload the procedure may initially be performed once weekly or once monthly. This regularity of treatment continues until serum ferritin levels fall back to normal; this may take up to 2 years or more. After this, lifelong maintenance therapy needs to be set in place as excess iron continues to be absorbed. On average venesection is required every 3–4 months to prevent build-up and maintain healthy levels. Regular monitoring of serum ferritin, transferrin saturation, haematocrit and haemoglobin is necessary throughout the treatment process. It is essential to detect haemochromatosis as early as possible so that venesection can be instituted to prevent the build-up of iron and potential complications. Once complications such as diabetes and cirrhosis have developed, they cannot be reversed. Tiredness and abdominal pain should diminish, and increased pigmentation of the skin should fade over time once treatment has started. Arthritis, however, may fail to improve with venesection. Haemochromatosis cannot be treated with a low iron diet. However, some foods affect the way the body absorbs iron. The following dietary tips may play a small part in reducing the symptoms of the disease. Minimise alcohol intake, particularly with meals – alcohol may lead to increased iron absorption and increase the risk of liver disease. Avoid eating offal (liver, kidney etc.) and red meat – iron absorption from red meat is 20–30% compared with 1–20% for vegetables and grains. Avoid vitamin supplements or tonics containing iron or vitamin C - vitamin C enhances the absorption of iron from the diet. If treatment begins early, people can expect to lead a normal life with normal life-expectancy. However, if treatment is delayed until after diabetes, cirrhosis, hypogonadism, or hypopituitarism develop, these processes cannot be reversed.Therapeutic phlebotomy (bloodletting)One of the mainstay treatments of hemochromatosis is therapeutic phlebotomy (bloodletting), which is when blood is removed from the body. This serves to decrease overall iron stores and is a generally safe and effective practice. Therapeutic phlebotomy is generally performed once the iron level is high enough. Typically, one unit of blood is taken per week initially until the blood iron level is slightly below normal. Thereafter, therapeutic phlebotomy is performed as needed depending on the blood iron level. This method of treatment requires routine blood laboratory testing to ensure that an appropriate amount of blood is being removed from the body. On average, men require therapeutic phlebotomy twice as often as women do. It may take more than a year to normalize body iron levels.MedicationFor people who cannot receive therapeutic phlebotomy, a drug called an iron chelator can be given. Deferoxamine, an iron chelator, acts to bind iron, soaking it up from the blood and allowing it to be removed from the urine and feces.Dietary changesPeople with hemochromatosis should never take iron supplement pills. You should also restrict your intake of vitamin C. In addition, you should limit your consumption of red meat since it has a high iron content. You should also avoid alcohol since it increases the chance of liver damage in people with hemochromatosis. Some advise the avoidance of raw shellfish since it can cause an infection in people with hemochromatosis.PreventionThe genetic causes of HH cannot be prevented because they are inherited. However, there are certain measures that can be taken to lessen the severity of the disease. For example, people with HH should never take iron supplements and should follow the dietary modifications listed in the previous section. Regular care from a physician who treats HH should be obtained in order to prevent permanent complications from HH.On the other hand, the environmental causes of hemochromatosis are more preventable. For each type of environmental cause, the prevention strategy is given below:Excessive dietary iron intake: Avoid excessive iron supplements.Excessive blood transfusions: Physicians should monitor and limit the amount of blood you receive or consider giving you iron chelators.Chronic liver disease: The underlying cause of liver disease should be managed.Porphyria cutanea tarda: This will likely be treated with bloodletting and medication.Sideroblastic anemia: This will likely be treated with pyridoxine and iron chelation will be used if needed.If you receive a diagnosis of HH, then it may be prudent for your relatives to undergo genetic testing to check for the disease before symptoms begin. Haemochromatosis is a common inherited disorder, which causes the body to absorb more iron than usual from food.Haemochromatosis tends to be under-diagnosed, partly because its symptoms are similar to those caused by a range of other illnesses.Treatment includes regularly removing blood until iron levels normalise. Haemochromatosis (iron overload disorder) is one of the most common hereditary diseases. Around one in 200 Caucasian Australian people have a genetic predisposition to this disease – meaning that they may get it. Haemochromatosis is characterised by the excessive absorption of iron. Normally, excess iron is safely stored in various joints and organs in the body, particularly the liver. In a person with haemochromatosis, iron stores keep rising and, over time, the liver enlarges and becomes damaged, leading to serious diseases such as cirrhosis. Other problems that can be caused by excessive iron include heart disease, diabetes and arthritis. Both sexes are at risk, but women tend to develop the condition later in life, since regular menstrual periods deplete the body of iron. Haemochromatosis tends to be under-diagnosed, partly because its symptoms are similar to those caused by a range of other illnesses. Iron is a vital trace mineral Red blood cells contain a protein called haemoglobin, which carries oxygen. Iron is needed for production of this particular protein, and the iron in food is absorbed via the small intestine. The human body has no method of excreting excess iron, so any excess is normally stored in the liver, with no ill effects. The body typically stores around one gram or less of iron at any given time. However, a person with haemochromatosis absorbs a great deal more iron from their food than is necessary. Iron stores of five grams or more build up inside the body. Organs such as the liver, heart and pancreas are affected and ultimately damaged. Without treatment, haemochromatosis can cause premature death. Symptoms of haemochromatosis Early haemochromatosis has no symptoms. However, in its later stages, haemochromatosis presents a variety of symptoms, and not all people will experience the same signs. Many symptoms are similar to those caused by other illnesses, which partly explains why haemochromatosis may be overlooked as a possible diagnosis. Some of the symptoms include: weakness and lethargy weight loss joint pain, usually in the joints of the second and middle fingers abdominal pains liver dysfunction sexual dysfunctions, such as impotence and low sex drive disorders of the menstrual period, such as early menopause loss of body hair skin darkening Causes of haemochromatosis Haemochromatosis is a recessive gene disorder caused by mutations of the haemochromatosis (HFE) gene. To develop a recessive gene disorder a person needs to inherit the gene mutation from both parents. If a person inherits only one mutated HFE gene, they are known as carriers. Around one in seven people carry the mutated HFE gene. A carrier won't develop the condition themselves, but may pass the mutation on to their children. If two carriers conceive, their child has a 50 per cent chance of inheriting one mutated HFE gene and becoming a carrier, and a one in four chance of inheriting both mutated HFE genes and developing the disease. A simple blood test can establish whether a person is carrying the mutated HFE genes. Treatment for haemochromatosis A person with haemochromatosis is treated with venesection. This is a procedure similar to blood donation, where around 500 mls of blood is removed until iron in the blood is reduced to normal levels. Depending on the severity of the condition, this may take around one and a half years of twice-weekly visits. Once iron levels are normal, venesection needs to be performed three or four times every year for life. If haemochromatosis is treated in its earliest stages before severe organ damage has occurred, there is no reduction in life expectancy – other things being equal. Lifestyle changes with haemochromatosis A person with haemochromatosis can better manage their condition by making a few simple lifestyle changes, including: not taking iron supplements not taking vitamin C supplements, as vitamin C increases iron absorption. reducing alcohol intake, as metabolising alcohol can stress an already compromised liver. reducing or limiting iron-rich foods such as offal. You should have a healthy, nutritious diet. This will include foods with the small amount of iron that you continue to need. Haemochromatosis cannot be treated by diet. Preventing organ damage from haemochromatosis If a person is diagnosed before significant symptoms arise, they can prevent organ damage and disease symptoms by maintaining iron in the normal range. However, a person diagnosed with the condition should notify all blood relatives so they can be tested for the HFE genes and treated if necessary. Anyone with disorders including liver disease, cardiomyopathy, arthritis or impotence should be tested for haemochromatosis. This underlying condition (haemochromatosis) could be causing their secondary illnesses. Prompt treatment can reverse some organ damage and symptoms, and prevent further damage. Where to get help Hereditary hemochromatosis, The Merck Manual of diagnosis and therapy, eds R. Berkow, M. Beers, A. Fletcher & R. Bogin. Merck & Co. Inc., Whitehouse Station, NJ, USA. Haemochromatosis , Haemochromatosis Australia. This page has been produced in consultation with and approved by: This page has been produced in consultation with and approved by: This page has been produced in consultation with and approved by: