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What is Hemochromatosis?

Hemochromatosis is a disorder where too much iron accumulates in tissues and organs, resulting in iron overloading. If left undiagnosed and untreated, iron overloading can cause serious health problems, and can even be fatal.

In the United States, the majority of hemochromatosis cases are caused by variants in the *HFE* gene, namely *C282Y* and *H63D*. A recently-published review of HFE genotype frequencies reported that about 9% of the population carries one copy of the *C282Y* mutation and about 0.5% is *C282Y* **homozygous** (carries two copies of the *C282Y* mutation). The homozygous genotype is responsible for most cases of hemochromatosis,[1] but the proportion of people with this genotype who will develop the disorder (i.e., the **penetrance** of the genotype) is unknown.

Homozygous
Possessing two identical copies of a particular gene, one inherited from each parent.

Penetrance
Probability that manifestations of a gene change will be seen in an individual.

Hemochromatosis can be detected with simple blood tests and the treatment of choice, phlebotomy (bloodletting), is relatively easy and inexpensive. Early diagnosis and treatment of hemochromatosis provides a tremendous opportunity to reverse the course of the illness and to prevent the most serious health problems of advanced stage hemochromatosis, which are:

- cirrhosis of the liver,
- liver cancer,
- cardiomyopathy (heart muscle disorders), and
- heart failure.

More information about hereditary hemochromatosis can be found on the CDC Web site at: http://www.cdc.gov/genomics/info/perspectives/hemo.htm.

Why Is Hemochromatosis a Public Health Problem?

Research conducted by the CDC and others indicates that primary care physicians may lack the knowledge they need to be able to identify patients at risk for hemochromatosis.[2] These studies have also identified widespread misunderstanding among health care professionals about the appropriate diagnostic tests and treatments for hemochromatosis. Until the last decade,

diagnosis of hemochromatosis most commonly relied on diagnosing the triad of cirrhosis, diabetes mellitus, and skin bronzing, and was only confirmed through a liver biopsy that uncovered evidence of iron overload. These methods could only confirm later-stage hemochromatosis, even though early detection and treatment are essential to reducing serious illness and death from this disease.

When CDC surveyed 2,841 diagnosed hemochromatosis patients, over two-thirds (67%) had initially received various multiple diagnoses, including arthritis, liver disease, hormonal deficiencies, and diabetes.[2] These patients actually did have those conditions, but the underlying cause, iron overload, had been missed. Patients reported that they saw an average of 5 physicians before receiving a diagnosis of hemochromatosis, on average 9.5 years after the onset of symptoms. Reducing this time lag by increasing physicians' awareness of the early symptoms of hemochromatosis is clearly an important disease prevention opportunity.

Is Population Screening Recommended for Hemochromatosis?

Screening patients to detect and treat chronic diseases early has become an important part of medicine and public health.[3] The 1996 discovery of the HFE variants *C282Y* and *H63D* responsible for most cases of iron overloading held promise for prevention and earlier treatment of the serious health consequences of advanced stage hemochromatosis.[4] Hereditary hemochromatosis quickly moved into the public health spotlight as medical experts and patient support groups called for population screening.

When policy-makers evaluated population-based screening for hereditary hemochromatosis in the late 1990s, however, important knowledge gaps were identified.[5-7] For example, little is known about the clinical course of hemochromatosis, the likelihood of complications, or the prevalence of asymptomatic iron overload. In addition, reliable information about the prevalence and penetrance of the HFE variants is not available. To help fill in these knowledge gaps, the National Heart Lung and Blood Institute launched a 5-year study in 2001 of 100,000 adults in primary care settings.[8] The results of this study will help policy-makers to understand the benefits and risks of using primary care-based diagnostic screening for iron overload and hemochromatosis.

Genetic testing also raises issues related to ethical, legal, and social concerns. For more information, please see *Chapter 8, Genomics and Public Health: Ethical, Legal, and Social Issues*. Even when these issues are adequately addressed, decisions to institute population screening must also be supported with enough scientific evidence of public health effectiveness as well as with enough available resources to treat those patients identified through screening. For a population-based screening program to be effective, it must identify people who are at risk of developing the disease. For the program to be cost-effective as well, it should

identify only those people who are very likely to develop the disease and are thus most likely to benefit from intervention.[9] Benefits are proportional to the number of cases prevented; therefore, a screening program that fails to identify people who will develop the disease—or that identifies many people who would not have become ill, even in the absence of intervention—will have a less favorable cost-benefit ratio.

Although initial estimates of the percentage of at-risk individuals who would actually develop hemochromatosis were high, ranging from 40-70%,[10] more recent studies have reported clinical estimates ranging from <1-50%.[11-14] Inconsistencies regarding these estimates persist in the scientific literature. Further studies are warranted, including studies designed to find out more about the role of genetic and environmental factors.

At this time, therefore, public health policy-makers have concluded that additional information is needed before population-based screening for hereditary hemochromatosis can be recommended as a prevention strategy. Currently, enhanced case detection among individuals with hemochromatosis symptoms and family-based detection are the most practical strategies for early diagnosis and treatment of hemochromatosis.

CDC's Online Training on Hemochromatosis for Health Care Providers

Physicians and other health-care providers continually face the challenge of incorporating the rapidly expanding pool of genetics information and the accompanying new technologies into their everyday practices. Continuing medical education is required to stay abreast of this exponential growth in knowledge. The CDC's new online course entitled *Hemochromatosis: What Every Clinician and Other Health Care Professional Needs to Know* (http://www.cdc.gov/hemochromatosis/training/index.htm) provides training on:

- the genetics of hemochromatosis, and
- patient care for physicians and other healthcare providers.

The course was developed by the CDC, in collaboration with hemochromatosis experts throughout the United States. The goals of this educational campaign are to:

- promote health by increasing awareness and early detection of hemochromatosis, and to

- provide a strategy for health care providers for early intervention in the course of the disease.

The core curriculum for *Hemochromatosis: What Every Clinician and Other Health Care Professional Needs to Know* consists of six modules and a series of case studies. The Web-based self-instructional format was designed to appeal to busy practitioners with limited time for training. Course resources integrate research findings with clinical practice in an attractive, easy-to-use format. Module and course summaries, self quizzes, and a series of interactive case studies allow the learner to tailor the course to his/her own learning needs, style and interests.

Course content focuses on hemochromatosis as one of several diagnostic considerations in many clinical settings. Although clinical features, diagnostic testing, and patient treatment and management are addressed at length, the course avoids prescribing a specific course of physician action. Instead, the course integrates concepts related to hemochromatosis, iron overload and genetic diseases into everyday practice, and focuses on:

- learning to recognize the early, non-specific symptoms of hemochromatosis (e.g. fatigue, joint pain, weakness, weight loss, abdominal pain),
- learning about the recommended methods for diagnosing hemochromatosis,
- phlebotomy (bloodletting) treatment to reduce iron overload, and
- counseling hemochromatosis patients about the importance of family-based detection.

The course includes colorful, downloadable patient educational materials, as well as physician letter templates that can be customized to provide information for patients to pass on to family members. Links to additional resources are available, including links to referenced articles from the professional literature. Information on genetic testing, genetic counseling, and family-based detection are also included in the course, together with an easy-to-follow chart suggesting when genetic testing may be appropriate for hemochromatosis diagnosis.

Hemochromatosis: What Every Clinician and Other Health Care Professional Needs to Know
http://www.cdc.gov/hemochromatosis/training/index.htm

Core Curriculum
- Epidemiology,
- Pathophysiology,
- Clinical Features,
- Diagnostic Testing,
- Treatment and Management,
- Family-based Detection, and
- Case Studies.

Who Can Take This Course?
Physicians, health education specialists, nurses and others will benefit from this course.

Course Format
The Web-based format allows convenient, self-paced instruction over the Internet using a personal computer. Learners can focus on course components to suit their personal information needs. In addition, learners can "book mark" their place in the course and return to the Web site to complete the course in segments if desired.

Continuing Education Credits
The course provides free continuing education credits (CME, CNE, CHES and CEU) through CDC's online Public Health Training Network. Learners may immediately print a Continuing Education Credit Certificate upon completing the course.

Conclusion

CDC's Web-based training course *Hemochromatosis: What Every Clinician and Other Health Care Professional Needs to Know* provides a response to the need for easily accessible, reliable information on this genetic disease. The Web-based format of the course also meets the need for rapid, individualized learning and immediate access to additional resources; this makes it possible to update the course easily as new knowledge becomes available.

In addition, the course also serves as a model of Web-based instruction specifically designed for physicians. As new genetic variants are identified, physicians face the ongoing challenge of learning, interpreting, and applying new knowledge in their practice settings. CDC's course on hemochromatosis represents a positive step towards helping health care providers become prepared to meet these challenges.

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