Top Ten Things Rheumatologists Should (And Might Not) Know About Detection and Treatment of Hemochromatosis

By Justin Cottrell; and Paul Adams, MD, FRCPC

This brief report summarizes some common issues related to hereditary hemochromatosis (HH) and its impact on patients with comorbid rheumatic diseases.

1. **HH screening.** Individuals with HH and iron overload without related complications benefit from early diagnosis and treatment. Population screening is not recommended.[1] A serum transferrin saturation and ferritin concentration is appropriate for initial diagnosis and for screening first-degree relatives of patients with HH.

2. **HH and iron overload diagnosis.** Homozygosity for the C282Y mutation in the *HFE* gene is typical. Iron overload is suspected by a ferritin > 300 µg/L in men or > 200 µg/L in women. Transferrin saturation is often elevated but has significant biological variability.[2]

3. **Genetic testing.** In most provinces, genetic testing for the C282Y and H63D mutations of the *HFE* gene is done in provincial laboratories without charge. Genetic testing for rare iron genes (*e.g.*, ferroportin, hemojuvelin, hepcidin, transferrin receptor 2) is available but not recommended; you can find out more at *www.invitae.com*. Due to stigmatization, genetic testing of children is not recommended.

4. **False positive elevations in iron tests.** Serum ferritin commonly rises with inflammation; other causes of an elevated ferritin include daily alcohol use, obesity, and fatty liver.[3] Extreme elevations of serum ferritin can be seen in histiocytosis and Still's Disease. None of these conditions have iron overload.

5. **HH treatment.** Phlebotomy (500 mL) once a week until iron levels return to normal is the primary treatment for HH and serum ferritin levels should be checked monthly or bi-monthly.[4] Maintenance phlebotomy is not always required, particularly in women. Avoidance of iron supplements, vitamin C supplements, and uncooked shellfish is also recommended.

6. **HH arthropathy distribution.** Chronic, indolent pain and joint stiffness of the joints, including the wrists, knees, hips, feet, shoulders, and ankles may be observed. Arthropathy is generally symmetrical and polyarticular. Acute bilateral destruction of the metacarpophalangeal joints (Figure 1) may resemble rheumatoid arthritis (RA); however bony swelling may occur which is indistinguishable from pyrophosphate-associated arthropathy. Disease-specific changes include subchondral radiolucency of the femoral head with atypical stripping of the cartilage from subchondral bone, and hook-like osteophytes on the second and third metacarpal heads.

7. **HH arthropathy findings.** Histological changes include abnormal iron deposits, minimal synovial inflammation,

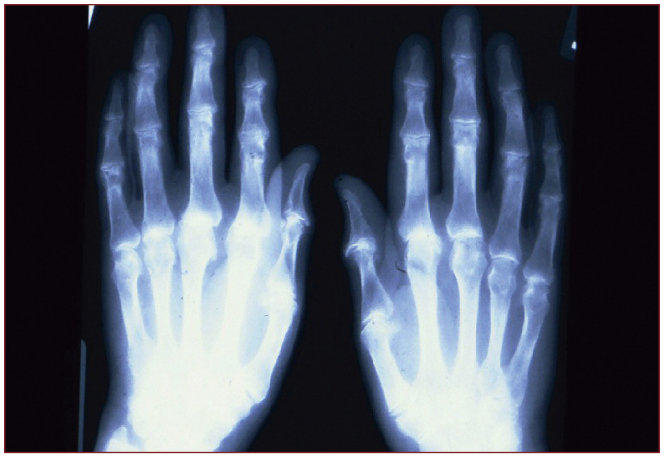

Figure 1. X-rays of the hands of a surgeon with hemochromatosis, who could not operate because of pain in the knuckles.

and calcium pyrophosphate dihydrate (CPPD) deposition, particularly in the knees and triangular cartilage. Synovial histology in HH arthropathy resembles osteoarthritis (OA) but increased neutrophils are present.

8. **HH arthropathy treatment.** Control of symptoms using analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), and acetaminophen is beneficial. In severe cases, joint replacement is warranted and is more frequent in hemochromatosis patients.[5]

9. **Other HH symptoms.** End organ damage can lead to liver enlargement, fibrosis, cirrhosis, liver failure or death and increased risk for developing liver cancer. Weakness, lethargy, darkness of the skin, diabetes mellitus, heart disease, thyroid disease, and reproductive problems due to pituitary abnormalities leading to impotence, loss of libido, amenorrhea and generalized osteoporosis may be present.

10. **Other iron overload syndromes.** Other iron overload syndromes include transfusional iron overload, juvenile hemochromatosis, aceruloplasminemia, African iron overload, neonatal, or perinatal iron overload.

References

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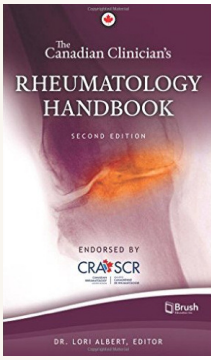
Book Review



The Canadian Clinician's Rheumatology Handbook, 2nd Edition

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This book is the second edition of a handbook written to support a national rheumatology curriculum for internal medicine trainees in Canada. Dr. Lori Albert is the lead author and editor of this volume which comprises chapters written by academic rheumatologists from across Canada. The comprehensive and well written chapters reflect the expertise of each author.

Each chapter provides a logical and comprehensive approach to major clinical presentations of rheumatic conditions. The chapters are introduced with a list of "key concepts," followed by important questions to ask during history taking as well as the clinical features to assess during the physical examination. A discussion of the recommended lab investigations, differential diagnosis, and treatment possibilities makes each chapter a complete overview of the topic.

In addition to very thorough coverage of the major clinical problems in rheumatology, a separate chapter addresses the clinical assessment and management of certain "rheumatologic emergencies".

Not only are the basics of the musculoskeletal (MSK) examination described, there is also a detailed joint examination complete with illustrations. Techniques for joint aspiration and injections are likewise detailed. Separate chapters discuss an approach to selection and interpretation of laboratory tests used in rheumatology, plus interpretation of imaging used to assess the MSK system.

The *Canadian Clinician's Rheumatology Handbook* is an excellent, comprehensive resource geared to residents in rheumatology, internal medicine, and family practice, and would be a useful asset for practicing physicians or allied health professionals working in rheumatology.

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