# Haemochromatosis

## *A future focus for continuing education in general practice*

Megan Young, MBBS, MPH, is Registrar in Public Health, Brisbane Southside Public Health Unit, Queensland.

Marie-Louise Dick, MBBS, FRACGP, MPH, is Senior Lecturer in General Practice, School of Medicine, University of Queensland, and a general practitioner in private practice, Brisbane, Queensland.

Peter O'Rourke, BSc, BA, PhD, GCEd, is Associate Professor in Biostatistics, School of Population Health, University of Queensland.

**INTRODUCTION**
This study aimed to assess the educational needs of general practitioners with regards to the diagnosis and management of hereditary haemochromatosis.
**METHODS**
A questionnaire was mailed to all 216 GPs in a suburban division of general practice, with a response rate of 91 (42.1%). The survey covered GPs' knowledge of the symptoms, signs, diagnosis, management and prognosis of haemochromatosis; attitudes toward management; beliefs regarding the prevalence of haemochromatosis and its relationship to other conditions; and management practices.
**RESULTS**
The relative prevalence, symptoms, signs, diagnostic requirements and prognostic factors associated with haemochromatosis were generally well recognised. The specifics of management is an area of educational need; in particular, venesection goals, dietary recommendations and the role of liver biopsy in diagnosis. Respondents were generally not comfortable managing haemochromatosis without specialist support, most commonly from a gastroenterologist. Of 80% of GPs who reported having patients with haemochromatosis, 41% primarily managed the condition.
**DISCUSSION**
The management of haemochromatosis in general practice could be improved by an educational campaign targeting GPs and the referral of uncomplicated patients back to their GPs from specialist services.

Hereditary haemochromatosis is the most common inherited metabolic disorder[1] and the most common genetic disease in people of northern European descent.[2] It has an estimated frequency in Australia of 1:300,[3] and can result in significant morbidity[2] and premature mortality.[4] Early diagnosis of haemochromatosis and treatment by venesection can restore normal life expectancy, reduce symptoms, and help to prevent end-organ damage.[4]

Much of the literature, however, suggests that hereditary haemochromatosis is underdiagnosed and therefore undertreated.[5–7] In a large international survey of people with haemochromatosis, an average of 3.5 physicians had been consulted about symptoms related to the disease before a diagnosis was made.[2] A survey of physicians in the USA concluded that many had inadequate knowledge about the diagnosis and treatment of haemochromatosis.[8]

Education of physicians has often been cited as necessary for improving early case detection.[5,9,10] A recent study in the USA found that the haemochromatosis case detection rate increased – and cases were detected at an earlier stage of iron overload – after an extensive physician educational program that was conducted in conjunction with a screening study.[11] It was unclear, however, whether the educational program alone was responsible for these changes. A study by Barton et al[12] also lends support to the benefits of physician education on case detection.

Learning needs surveys help to target educational messages.[13] No such surveys have been undertaken in Australia in regards to haemochromatosis. This study aimed to assess the educational needs of general practitioners in Brisbane, Queensland, with regard to haemochromatosis in order to improve the diagnosis and management of this disease.

## Methods

A cross sectional postal survey was conducted of all 216 GPs in the catchment area of a capital city division of general practice between June and August 2002. This sample was considered to be representative of metropolitan GPs and of sufficient size to estimate the proportion of GPs practising according to the Australian Gastroenterology Institute guidelines for the diagnosis of haemochromatosis.[14] An error of 10%, a confidence level of 95%, and an anticipated response rate of 50% required 160 GPs to be approached. The study was approved by the University of Queensland's School of Population Health Ethics Committee.

A questionnaire was developed following a thorough literature review, focus group discussions with individuals diagnosed with haemochromatosis, and interviews with selected Brisbane GPs. After piloting, the final questionnaire covered knowledge of the relative prevalence, symptoms, signs, diagno-

sis, management and prognosis of haemochromatosis; attitudes toward management; and practices with respect to screening, diagnosis, and management.

The division viewed the questionnaire which was then mailed to all GPs with a letter detailing the study, confidentiality procedures, and the voluntary nature of participation. A single reminder was sent to nonresponders 3 weeks later.

Responses were entered directly into the Statistical Package for Social Sciences (SPSS) version 11.0 (SPSS Inc., Chicago, Illinois). In addition to frequency distributions for each question, analysis allocated scores to correct responses to knowledge questions according to the recommendations of the Australian Gastroenterology Institute,[14,15] and summed these to give a knowledge score. Questions answered conditionally were excluded from this calculation. Categorical variables were assessed for confounding by a number of demographic variables by chi-squared tests, while one way analysis of variance was used for continuous variables. EpiInfo version 6 was utilised to compare respondent demographic proportions with those of the Australian GP population by chi-squared goodness of fit tests, while student t-tests were used to compare means.

**Table 1. Demographic characteristics of respondents compared with the medical labour force 1998 estimates***

| Demographic characteristic | | Responding sample (n=91) | Australian GPs | p value |
|---|---|---|---|---|
| Sex | Men | 50.5% | 66.8% | <0.001 |
| | Women | 49.5% | 33.2% | |
| Age | <35 | 12.1% | 14.6% | 0.360 |
| | 35–44 | 36.3% | 33.1% | |
| | 45–54 | 34.1% | 28.3% | |
| | 55> | 17.6% | 24.0% | |
| Practice numbers: | Solo | 10.0% | 19.4% | 0.003 |
| | 2–4 | 34.4% | 42.9% | |
| | 5> | 53.3% | 37.7% | |
| Mean hours worked: | Total | 35.9 | 45.3 | <0.001 |
| | Men | 43.5 | 51.6 | <0.001 |
| | Women | 27.9 | 34.2 | <0.001 |

*Percentages may not sum to 100% due to missing values

**Table 2. Percentage of GPs indicating the need to test for haemochromatosis***

| Situation | Test always | Test sometimes | Test never | Unsure |
|---|---|---|---|---|
| Family history | **95** | 5 | 0 | 0 |
| Elevated LFTs | 71 | **29** | 0 | 0 |
| Elevated serum iron | **78** | 21 | 0 | 0 |
| Transferrin saturation >45% | **88** | 8 | 0 | 3 |
| Chronic fatigue | **34** | 59 | 2 | 4 |
| Diabetes mellitus | **29** | 63 | 4 | 4 |
| Cardiomyopathy | 44 | **45** | 6 | 4 |
| Arthritis | 17 | **52** | 15 | 12 |
| Peripheral neuropathy | 8 | 45 | **20** | 22 |
| Asthma | 1 | 6 | **71** | 17 |
| Porphyria cutanea tarda | **19** | 13 | 11 | 54 |

*Percentages may not sum to 100% due to missing values
Percentages in bold indicate testing recommendations[14]

## Results

Ninety-one of the 216 posted questionnaires were completed and returned, giving a response rate of 42.1%. The demographic characteristics of responding GPs are shown in *Table 1* where they are compared with national figures estimated from the Australian medical workforce data.[16]

### Knowledge

When asked to rank the prevalence of haemochromatosis against a number of other conditions likely to be encountered in general practice, GPs generally correctly believed it to be less common than peptic ulcer disease, and more common than cystic fibrosis and multiple sclerosis. General practitioners were also familiar with the well documented signs and symptoms of haemochromatosis.

Respondents were asked how often they would test for haemochromatosis in given situations (*Table 2*). Overall, a high index of suspicion was indicated. Participants' knowledge of the management of haemochromatosis was limited in some areas (*Table 3*). Many were unaware of the role of haemoglobin monitoring in venesection regimens and the need to avoid vitamin C supplements. A substantial proportion incorrectly believed that liver biopsy should be used to confirm the diagnosis (45%), and that patients should be encouraged to adopt low iron diets (50%).

Participants who indicated that venesection should be guided by the haemoglobin and/or the serum ferritin were asked to indicate the goal level/s of maintenance therapy. Of those who felt that haemoglobin should guide venesection, 64% gave a goal level. One GP correctly indicated a level of 110 g/L for males and five GPs correctly indicated this level for females. Responses ranged

from 110–185 g/L. Of participants who believed that serum ferritin should guide venesection, 75% and 69% gave goal levels for males and females respectively. Responses ranged from 10–700 µg/L. Fifteen GPs (17%) correctly indicated levels of less than 100 µg/L for males, and 15 GPs (17%) correctly indicated levels of less than 100 µg/L for females.

More than 80% of GPs recognised the significance of cirrhosis of the liver and diabetes at the time of diagnosis on the prognosis of patients with haemochromatosis.

The highest possible knowledge score was 54. The score distribution was approximately normal with a slight left skew (data not shown). The mean was 33.5 (or 62%), with scores ranging from 23–45 (43–83%). This knowledge score was compared using one way analysis of variance across age groups, sex, and categories of hours worked per week. No statistically significant differences were found.

### Practices

Participants indicated they had screened between zero and 300 asymptomatic patients in the past 12 months, with a median of eight. They had considered a diagnosis of haemochromatosis because of aspects of the history and/or examination in between zero and 200 patients over the past 12 months, with a median of three.

General practitioners reported a high degree of uncertainty when managing patients with haemochromatosis. Sixty-seven percent indicated they required a specialist's opinion in all cases of haemochromatosis. A further 13% felt they needed a specialist's opinion in complicated cases, and 17% did not feel comfortable managing the disorder at all.

Despite this, 73 of the 91 respondents (80%) indicated that they currently had patients with haemochromatosis. The majority of these (60%), had four or fewer patients with the disorder in their care. *Table 4* indicates how these GPs managed their patients with haemochromatosis at the time of the survey. Referring for management primarily by a specialist was the most common practice (69% of GPs, n=50).

For 48% of GPs (n=35), all their patients with haemochromatosis were being primarily managed by a specialist. Thirty GPs (41%) primarily managed at least one of their patients with haemochromatosis. The other eight GPs did not indicate their management practice.

General practitioners who primarily managed at least one of their patients with haemochromatosis were noted to have slightly higher mean knowledge scores compared to those who did not primarily manage any of their patients with haemochromatosis (35.4 vs. 33.3, $p$=0.045). While not statistically significant, more male GPs than female GPs appeared to primarily manage patients with haemochromatosis (54.3 vs. 36.7%, $p$=0.155). No such trend was noted across age groups or hours worked per week.

Of the 73 GPs who had patients with haemochromatosis under their care, 73% referred patients to a gastroenterologist, with 51% of GPs referring all of their patients with haemochromatosis to these specialists. Other specialists and health professionals did not feature as highly in the referral practices of these GPs.

## Discussion

Respondents' knowledge of haemochromatosis overall was good. The disease was acknowledged to be comparatively common, its common presenting signs and symptoms were well recognised, and general prognostic indicators were known. The specifics of the management of haemochromatosis, particularly the goals for venesection, dietary recommendations and the role of liver biopsy, represented an area of educational need for the GPs in this study. General practitioners' overall knowledge about the condition was associated with their level of practical experience with it, although because of the cross sec-

**Table 3. GPs' beliefs about selected management practices for haemochromatosis***

| Practice | Yes (%) | No (%) | Unsure (%) |
|---|---|---|---|
| Confirm diagnosis with genetic test | **84** | 13 | 2 |
| Confirm diagnosis with liver biopsy | 45 | **39** | 16 |
| Venesection guided by haemoglobin | **50** | 39 | 11 |
| Venesection guided by ferritin | **85** | 3 | 12 |
| Patients should avoid uncooked shellfish | **12** | 31 | 55 |
| Patients should avoid iron supplements | **96** | 2 | 1 |
| Patients should avoid vitamin C supplements | **44** | 20 | 35 |
| Patients should adopt a low iron diet | 50 | **30** | 19 |

* Percentages may not sum to 100% due to missing values

Percentages in bold indicate recommended practices[14]

**Table 4. Management of patients with haemochromatosis***

| Practice | Number of GPs |
|---|---|
| Venesection at GP's practice – GP manages regimen | 15 |
| Venesection elsewhere – GP manages regimen | 23 |
| Specialist manages venesection regimen | 50 |
| Chelation therapy | 2 |
| Erythrocytapheresis | 1 |

*Cells are not mutually exclusive

tional nature of the study, it is not clear whether knowledge preceded or followed this experience.

Despite the apparently high index of suspicion, a median of only eight asymptomatic patients and three otherwise 'symptomatic' patients were tested for the condition in the past 12 months. Respondents were generally not comfortable managing haemochromatosis without specialist (predominantly gastroenterologist) support. Only 41% of those GPs who reported having patients with haemochromatosis primarily managed the condition.

There were several limitations inherent to the study. First and foremost, although GPs are often poor survey responders,[17] the response rate of 42.1% may well represent significant response bias. The survey instrument underwent rigorous piloting, and question wording was carefully selected to be as nonconfrontational as possible, but GPs who felt a lack of knowledge on the topic may not have participated. The results may therefore over represent the true knowledge level of Brisbane GPs. Similarly, both the confidence expressed about managing the disease and the proportion of GPs primarily managing the disease may be inflated.

The questionnaire asked GPs to recall their practice over a 12 month period. The accuracy of these results would therefore be subject to recall error. The direction of the effect of this error is unknown.

The responding population was similar in age distribution to that of Australian GPs, but comprised more women, fewer doctors from solo practices, and more doctors from large practices (□5 GPs). Both men and women in the sample also worked fewer hours than the general GP population. As no statistically significant differences were found with respect to age, gender or practising hours across most of the range of outcomes, it is quite possible that the demographic differences between the GPs surveyed and the larger general practice population would not substantially affect the results. The survey was limited to GPs in one metropolitan centre and, while it is not unreasonable to generalise the results to other metropolitan GPs, this may not be appropriate for rural GPs. In particular, limited access to specialist services would be likely to result in reduced referral practices by rural GPs.

Despite its limitations, the study points to the benefits of a pilot educational campaign targeting Australian GPs about haemochromatosis in order to standardise diagnostic and management practices. The benefits of educational programs on case detection in the USA has been suggested by Hover et al[11] and Barton et al.[12]

Specific educational messages to the GPs in the study area should include the role of genetic testing versus liver biopsy in confirming the diagnosis, the goals for venesection, and appropriate dietary recommendations. Interactive sessions have been shown to result in moderately large changes to practice behaviours, and would be favoured over didactic sessions[18] when planning such a program. These messages could be reinforced by encouraging specialists to refer uncomplicated patients back to their GPs, thus increasing GPs' practical experience with haemochromatosis. Should a positive evaluation result from such a pilot campaign in regard to changes in GPs' knowledge and practices, a wider rollout would be recommended.

Conflict of interest: none.

## Acknowledgment

The authors would like to thank the Brisbane Inner South Division of General Practice and Haemochromatosis Society Australia Inc.

For practical information on haemochromatosis, The Gastroenterological Society of Australia's information booklet for health professionals 'Haemochromatosis: a guide for clinical practice in the era of genetic testing' is available electronically at: www.gesa.org.au/members_booklets/haemochromatosis/haemochromatosis_2nded.pdf

## References

1. Bacon BR, Sadiq SA. Hereditary hemochromatosis: presentation and diagnosis in the 1990s. Am J Gastroenterol 1997;92:784–789.
2. McDonnell SM, Preston BL, Jewell SA, et al. A survey of 2851 patients with hemochromatosis: symptoms and response to treatment. Am J Med 1999;106:619–624.
3. Leggett BA, Halliday JW, Brown NN, et al. Prevalence of haemochromatosis amongst asymptomatic Australians. Br J Haematol 1990;74:525–530.
4. Niederau C, Fischer R, Purschel A, et al. Long term survival in patients with hereditary hemochromatosis. Gastroenterology 1996;110:1107–1119.
5. Adams P, Brissot P, Powell LW. EASL International Consensus Conference on Haemochromatosis. J Hepatol 2000;33:485–504.
6. Prows CA. Hereditary hemochromatosis. Nurs Clin North Am 2000;35:707–717.
7. Motulsky AG, Beutler E. Population screening in hereditary hemochromatosis. Annu Rev Public Health 2000;2165–2179.
8. Acton RT, Barton JC, Casebeer L, et al. Survey of physician knowledge about hemochromatosis. Genet Med 2002;4:136–141.
9. Powell LW, George DK, McDonnell SM, et al. Diagnosis of hemochromatosis. Ann Intern Med 1998;129:925–931.
10. Brittenham GM, Franks AL, Rickles FR. Research priorities in hereditary hemochromatosis. Ann Intern Med 1998;129:993–996.
11. Hover A, McDonnell SM, Burke W. Changing the clinical management of hereditary hemochromatosis: translating screening and early case detection strategies into clinical practice. Arch Intern Med 2004;164:957–961.
12. Barton JC, Barton NH, Alford TJ. Diagnosis of hemochromatosis probands in a community hospital. Am J Med 1997;103:498–503.
13. Wetterhall SF, Cogswell ME, Kowdley KV. Public health surveillance for hereditary hemochromatosis. Ann Intern Med 1998;129:980–986.
14. Australian Gastroenterology Institute. Haemochromatosis. Sydney: Australian Gastroenterology Institute, 1999.
15. Australian Gastroenterology Institute. Haemochromatosis: a guide for health care providers. Mod Med 1999;42:51–54.
16. Australian Institute of Health and Welfare. Medical labour force 1998. Canberra: Australian Institute of Health and Welfare, 2000.
17. McAvoy BR, Kaner EF. General practice postal surveys: a questionnaire too far? BMJ 1996;313:732–734.
18. Thomson O'Brien M, Freemantle N, Oxman A, et al. Continuing education meetings and workshops: effects on professional practice and health care outcomes (Cochrane Review). In: The Cochrane Library Issue 1. Update Software: Oxford, 2002.

AFP

**Correspondence**
Email: megan_young@health.qld.gov.au