Joanna McCosker is the Nurse Practitioner at the Queensland Haemophilia Centre, Queensland Children's Hospital, Brisbane.

WHAT DO WE KNOW ABOUT CARRIERS?

Joanna McCosker

In haemophilia care over the last two decades there has been a greater recognition and awareness of the significant bleeding complications that women experience, in particular carriers of haemophilia.[29] In haemophilia genetics, a 'carrier' is a female with an altered factor VIII (8) or IX (9) gene that can cause haemophilia if it is passed on to her children. Sometimes she may also have a bleeding tendency herself.

It is important to identify carriers by finding out who the females are in families with affected males. Drawing family trees or 'genograms' is an important tool to capture the females who are daughter of men with haemophilia (obligate carriers) and other girls and women who may be carriers so they can be involved in discussions and education regarding factor level testing and genetic testing. It is especially important as girls reach adolescence (menarche) and reproductive age (pregnancy), as it has been estimated that for every male with haemophilia there are four to five female carriers.[22]

Little is known about how women and girls in families with haemophilia are informed or discover they are carriers. In 2016 a literature review was undertaken to better understand from the published literature how communication of inheritance or knowledge of genetic information was passed onto females in families with haemophilia.

FINDING OUT YOU ARE A CARRIER

There is a gap in knowledge and understanding of carrier status and the risk of passing on haemophilia in many affected women of reproductive age. The literature suggests that over half of all carriers are unaware of their carrier status by the time they reach reproductive age.[2,23,25] Published studies consistently show that women have poor knowledge of inheritance and are unaware they are carriers at the time of pregnancy.[2,4,5,10,11] In general, studies on communication of genetic risk in families have identified gaps in the communication of genetic information, in particular the inheritance patterns and the risk of passing on the condition. Studies found parents and other family members do share genetic information, however that information is often misunderstood.[7,15,19,27,28]

WHAT IS THE IMPACT OF THIS?

The optimal management of immediate female relatives (mothers, sisters and daughters) of a person with haemophilia is to check their clotting factor levels, especially if bleeding symptoms are present, or before childbirth, invasive medical or dental procedures (where the skin or mucous membranes/inside of mouth, vagina, anus etc are scraped or cut), or tattoos and body piercings as these may result in bleeding complications.[1] However, if female relatives are unaware of their risk of being a carrier then how will they know to seek advice from health professionals? How can optimal health management be achieved if these girls and women are not aware of their health situation or have not been diagnosed?

Many mothers of children with haemophilia, despite having a known family history, were not aware of their carrier status until they had an affected son. Additionally, many of the daughters of males with haemophilia frequently question whether they are carriers, as do their relatives, although genetically they are obligate carriers and will automatically inherit the gene from their father. It is significant to note that over half of all carriers were unaware of their carrier state until their first pregnancy or birth of an affected son.[2,4,10] Carrier status appears to often only become relevant to women when they became pregnant or after the birth of a son.[2,16,17]

An interesting fact is the average age of carrier testing was found to be 30 years of age, but the average age of carriers at first pregnancy was 26 years of age.

>>

Managing bleeding in at-risk females is a common reason for testing of clotting factor levels, as it has been estimated that 30

WHAT IMPACTS ON COMMUNICATION OF CARRIER STATUS?

The family context

Haemophilia is a familial disease and the literature recognises the influence of the family context and its social system on how and to whom information is communicated about carrier status.[9,21,26] Communication can be complex with many factors that can influence the sharing and understanding of carrier information within families.[19,28]

Assumptions of prior knowledge

This may be due to a family history, and a presumed understanding of inheritance and genetic risk information may complicate communication within families.[20,21]

Gender lines

In one study inheritance and the risk of being a carrier were found to be infrequently discussed or not at all, even in families with a father or brother with haemophilia. In general, communication was found to follow gender lines with mostly mothers and sisters discussing genetic information.[26]

Obligate carriers

Communication patterns were found to be significant in how the experience of obligate carriers differed in comparison to possible carriers. The daughters of affected fathers (obligate carriers) appeared to have less understanding of haemophilia and of their carrier status than those who grew up with an affected brother.[9]

Other studies on the psychosocial needs of carriers have also found that knowledge of haemophilia inheritance and the possibility of being a carrier is poor, even in females who have first-degree relatives.[5,24]

WHEN TO TEST: REASONS FOR AND AGAINST

The ideal age of testing for carriers is largely debated in the literature and even in Australia the age may vary between the states and territories. International guidelines recommend that carrier testing should be delayed until minors are deemed competent to understand and participate in their own health decisions OR at the age of 18 years.[3,14]

The ongoing debate about the ideal age to perform carrier testing relates to concerns about whether finding out you are a carrier will cause psychological harm or will be a health benefit to the girl or woman and is a contributing factor to delays in carrier testing.

Reasons for carrier testing in minors:

- For the health benefit of the child – to help predict and manage symptoms.[3,6,12]
- Parents' peace of mind.[27]

Reasons against carrier testing in minors:

- The child is not prepared for that information and it is difficult to explain carrier risk to minors
- Psychological harm
- The burden of disclosure, as it can be difficult for parents to decide whether telling their child is more of a burden or a benefit.[8,7,18]
- Parental distress and anxiety around informing children of their carrier status
- Concern for the impact on the child's self-esteem and social identity. [8,13,18]

On the other hand, testing for clotting factor levels is recommended earlier than 16 years of age. Managing bleeding in at-risk females is a common reason for testing of clotting factor levels,[1] as it has been estimated that 30% of carriers have reduced factor levels. However, this may lead to an incidental finding of carrier status due to a low factor level.[14] Informing children of an incidental finding of carrier status is problematic and the arguments for and against are similar to the debate around the age of carrier testing and focus on psychological harm.[5]

% of carriers have reduced factor levels

WHERE DO WE GO FROM HERE?

More research is required in this area. We need further in-depth study of the experience of carriers, in particular, exploring how genetic information is communicated in families with haemophilia. The review highlighted a lack of communication within families, resulting in a lack of knowledge and awareness of carrier status throughout all life stages, in particular prior to pregnancy. Families and health professionals may find it helpful to discuss what activities or strategies could be developed to better assist families with talking about carrier status. Young girls and women need ongoing education and support to gain a much better understanding of their carrier status.[19]

REFERENCES

1. Australian Haemophilia Centre Directors' Organisation (AHCDO). Guidelines for the management of haemophilia in Australia. Canberra: National Blood Authority, 2016. https://www.blood.gov.au/haemophilia-guidelines

2.Balak DMW, Gouw SC, Plug I, Mauser-Bunschoten EP, Vriends HJT, van Diemen-Homan JEM et al. Prenatal diagnosis for haemophilia: a nationwide survey among female carriers in the Netherlands. Haemophilia 2012;18:584-592. DOI: 10.1111/j.1365-2516.2011.02742.x

3. Borry P, Fryns JP, Schotsmans P, Dierickx K. Carrier testing in minors: a systematic review of guidelines and position papers. European Journal of Human Genetics 2006 Feb;14(2):133-8. https://doi.org/10.1038/sj.ejhg.5201509

4. Cassis FR, Buzzi A, Forsyth A, Gregory M, Nugent D, Garrido C, et al. Haemophilia Experiences, Results and Opportunities (HERO) Study: influence of haemophilia on interpersonal relationships as reported by adults with haemophilia and parents of children with haemophilia. Haemophilia. 2014 Jul;20(4):e287-95. https://doi.org/10.1111/hae.12454

5. Dunn NF1, Miller R, Griffioen A, Lee CA. Carrier testing in haemophilia A and B: adult carriers' and their partners' experiences and their views on the testing of young females. Haemophilia 2008 May;14(3):584-92. https://doi.org/10.1111/j.1365-2516.2007.01649.x

6. Fenwick A. Are guidelines for genetic testing of children necessary? Familial Cancer. 2010 Mar;9(1):23-5. https://doi.org/10.1007/s10689-009-9278-0.

7. Forrest LE, Delatycki MB, Skene L, Aitken M. Communicating genetic information in families--a review of guidelines and position papers. European Journal of Human Genetics 2007 Jun;15(6):612-8. https://www.nature.com/articles/5201822.

8. Fryer A. Inappropriate genetic testing of children. Archives of Disease in Childhood 2000 Oct;83(4):283-5. https://adc.bmj.com/content/83/4/283.

9. Gregory M, Boddington P, Dimond R, Atkinson P, Clarke A, Collins P. Communicating about haemophilia within the family: the importance of context and of experience. Haemophilia 2007 Mar;13(2):189-98. https://doi.org/10.1111/j.1365-2516.2006.01417.x.

10. Knol HM, Voskuilen MA, Holterman F, Kluin-Nelemans JC, Meijer K. Reproductive choices and obstetrical experience in Dutch carriers of haemophilia A and B. Haemophilia 2011 Mar;17(2):233-6.

11. Lee CA, Chi C, Pavord SR, Bolton-Maggs PH, Pollard D, Hinchcliffe-Wood A et al. The obstetric and gynaecological management of women with inherited bleeding disorders--review with guidelines produced by a taskforce of UK Haemophilia Centre Doctors' Organization. Haemophilia 2006 Jul;12(4):301-36. https://doi.org/10.1111/j.1365-2516.2006.01314.x

12. Lewis C, Skirton H, Jones R. Can we make assumptions about the psychosocial impact of living as a carrier, based on studies assessing the effects of carrier testing? Journal of Genetic Counseling 2011 Feb;20(1):80-97. https://doi.org/10.1007/s10897-010-9327-8

13. McConkie-Rosell A, DeVellis BM. Threat to Parental Role: A Possible Mechanism of Altered Self-Concept Related to Carrier Knowledge. Journal of Genetic Counseling 2000 Aug;9(4):285-302. https://doi.org/10.1023/A:1009428328837.

14. McConkie-Rosell A, Spiridigliozzi GA. 'Family matters': a conceptual framework for genetic testing in children. Journal of Genetic Counseling 2004 Feb;13(1):9-29. https://doi.org/10.1023/B:JOGC.0000013379.90587.ef

15. Metcalfe A, Coad J, Plumridge GM, Gill P, Farndon P. Family communication between children and their parents about inherited genetic conditions: a meta-synthesis of the research. European Journal of Human Genetics 2008 Oct;16(10):1193-200. https://www.nature.com/articles/ejhg200884

16. Myrin-Westesson L, Baghaei F, Friberg F. The experience of being a female carrier of haemophilia and the mother of a haemophilic child. Haemophilia 2013 Mar;19(2):219-24. https://doi.org/10.1111/hae.12026.

17. Naicker T, Aldous C, Thejpal R. Haemophilia: A disease of women as well. South African Journal of Child Health 2016;10(1):29-32. http://www.sajch.org.za/index.php/SAJCH/article/view/961.

18. Plumridge G, Metcalfe A, Coad J, Gill P. Family communication about genetic risk information: particular issues for Duchenne muscular dystrophy. American Journal of Medical Genetics Part A. 2010 May;152A(5):1225-32. https://doi.org/10.1002/ajmg.a.33364.

19. Plumridge G, Metcalfe A, Coad J, Gill P. Parents' communication with siblings of children affected by an inherited genetic condition. Journal of Genetic Counseling 2011 Aug;20(4):374-83. https://doi.org/10.1007/s10897-011-9361-1 .

20. Ranta S, Lehesjoki AE, Peippo M, Kääriäinen H. Hemophilia A: experiences and attitudes of mothers, sisters, and daughters. Pediatric Hematology and Oncology 1994 Jul-Aug;11(4):387-97. https://www.ncbi.nlm.nih.gov/pubmed/7947011

21. Sorenson JR, Jennings-Grant T, Newman J. Communication about carrier testing within hemophilia A families. American Journal of Medical Genetics: Part C, Seminars in Medical Genetics 2003 May 15;119C(1):3-10. https://doi.org/10.1002/ajmg.c.10001.

22.Street AM, Ljung R, Lavery S. Management of carriers and babies with haemophilia. Haemophilia 2008;14(Suppl. 3):181-187. DOI: 10.1111/j.1365-2516.2008.01721.x

23.Tedgard U. Carrier testing and prenatal diagnosis of haemophilia – utilisation and psychological consequences. Haemophilia 1998;4:365-369. https://doi.org/10.1046/j.1365-2516.1998.440365.x

24. Tedgård U, Ljung R, McNeil TF. Long-term psychological effects of carrier testing and prenatal diagnosis of haemophilia: comparison with a control group. Prenatal Diagnosis 1999 May;19(5):411-7. https://www.ncbi.nlm.nih.gov/pubmed/10360508

25. Varekamp I, Suurmeijer TP, Bröcker-Vriends AH, van Dijck H, Smit C, Rosendaal FR et al. Carrier testing and prenatal diagnosis for hemophilia: experiences and attitudes of 549 potential and obligate carriers. American Journal of Medical Genetics 1990 Sep;37(1):147-54. https://doi.org/10.1002/ajmg.1320370134.

26. Varekamp I, Suurmeijer TP, Rosendaal FR, Bröcker-Vriends AH. The use of preventive health care services: carrier testing for the genetic disorder haemophilia. Social Science & Medicine 1993 Sep;37(5):639-48. https://www.ncbi.nlm.nih.gov/pubmed/8211278.

27. Vears DF, Delany C, Massie J, Gillam L. Why do parents want to know their child's carrier status? a qualitative study. Journal of Genetic Counseling 2016 Dec;25(6):1257-1266. https://doi.org/10.1007/s10897-016-9964-7.

28. Wilson BJ, Forrest K, van Teijlingen ER, McKee L, Haites N, Matthews E et al. Family communication about genetic risk: the little that is known. Community Genetics 2004;7(1):15-24. https://doi.org/10.1159/000080300.

29.Winikoff R, Amesse C, James A, Lee C, Pollard D. The role of haemophilia treatment centres in providing services to women with bleeding disorders. Haemophilia 2004;10(Suppl. 4):196-204. DOI: 10.1111/j.1365-2516.2004.01001.x