MANAGEMENT OF CARRIERS OF HEMOPHILIA

Alison Street, VP Medical WFH
Head, Haemostasis/Thrombosis Unit
TheAlfred, MELBOURNE AUSTRALIA 3004
• It has been estimated that for each male with Factor VIII or IX deficiency that there may be five (5) female carriers of the responsible genetic mutation which has impact on

• her male offspring (50% chance of being affected)

• her female offspring (50% chance of being a carrier

AND
She may have symptoms of mild hemophilia if she has low factor levels (up to 80% of carriers)
Who are these women and how should we advise them?
<table>
<thead>
<tr>
<th>Carrier Type</th>
<th>Description</th>
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<tbody>
<tr>
<td>Obligatory carrier</td>
<td>The daughter of a man with hemophilia</td>
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<tr>
<td>Proven carrier</td>
<td>A woman with both an antecedent and a descendent relative with hemophilia. The gene must have passed through her.</td>
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<td>Probably carrier or possible carrier</td>
<td>The mother of an isolated case of hemophilia</td>
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<tr>
<td>Potential carrier</td>
<td>A female whose position in a family suggests that she might have an inherited the mutant gene, e.g. the sister of a male with hemophilia</td>
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• The woman may have bleeding problems (particularly with menses) and needs clinical assessment and measurement of the coagulation factor that is reduced in her male relatives

• Definitive testing is by genetic analysis
• Anne’s presentation introduces haemophilia and its inheritance pattern

• It describes the mutations responsible for F VIII and IX deficiency and their analysis

• It provides an algorithm for testing and web-based and literature resources
GENETICS

OF HEMOPHILIA A AND B

An Introduction for Clinicians,

2009

by

Carol K. Kasper, M.D.

and

Carolyn H. Buzin, Ph.D.

FÉDÉRATION MONDIALE DE L'HÉMOPHILIE
FEDERACIÓN MUNDIAL DE HEMOFILIA
• Clinician-scientists from hemophilia Centres in Iran, together with Professor Flora Peyvandi in Milan, Italy have contributed greatly to this literature
What information is critical to potential carriers?

• Advice that phenotype (plasma factor level) information is essential for procedures etc for personal safety

• Emphasis, that although factor levels may be reduced in carriers (up to 80%), normal factor levels do NOT exclude carrier status

• Provide information about haemophilia including DNA analysis

AND LISTEN TO CONCERNS
What are the implications of providing a genetics service?

• Implementation and resourcing of Genetic Testing Programs will take into account

• Diagnostic capacity

• Cultural considerations

• And require associated counselling and quality frameworks
Reasons for potential carriers to seek DNA analysis

- Knowledge of risk including phenotype assessment
- Informed reproductive options
- Preparedness for delivery
  - Preparedness for raising a child with haemophilia
Reasons for potential hemophilia carriers to NOT seek DNA analysis

- Result may not be necessary for personal decision making
- Fear of altering relationships/family concerns
Consultation with a specialised genetic counsellor is very valuable and may be a legal requirement. Clinicians should

- Ensure that counsellors understand the inheritance and clinical consequences of haemophilia to inform patients before testing and

- Provide complementary advice and support to “at risk” carriers
Care and treatment of Carriers

- With improved care and longevity of men with haemophilia, more carriers are being born

- We can define carriers by
  - Obligate/possible/phenotype status
  - DNA analysis
Genetic testing is performed as part of a supportive clinical encounter with

- Informed clinicians
- Genetic counsellors
- Excellent laboratory scientists
When should women know of their options?

• Aim to have discussions about the possibility and consequences of being a carrier before pregnancy

• so that women are tested and aware of their genetic status and reproductive options beforehand
Management of pregnancy

- Important to co-ordinate services of obstetrician, anesthetist and haematologist and to keep patient and her family informed.

- Factor level measurement at 34 weeks (Factor VIII levels may rise) informs safety of invasive procedures in mother.

- Knowledge of the gender of the foetus prepares obstetrician (and parents who wish to know) for delivery options.
So that we have our carrier patient well informed, anticipating the delivery of a son (possibly with haemophilia) in a safe environment by a skilled obstetrician.
Use of DDAVP in pregnancy in symptomatic carriers of FVIII deficiency

- Prescribers’ Information advises precaution in pregnancy and contra-indication in lactation

- Intermittent use to cover procedures in first and second trimesters of pregnancy has not been associated with harm to pregnancy or foetus

- Has been used safely to support epidural blockade
• Post partum use in von Willebrand disorder is recommended to reduce post-delivery fall in vWF/FVIII levels
Inspiring Mount Damavand