Carriers

What do parents, young girls and adolescents need to know?

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Disclosures

- Sanofi-Genzyme: ISTH Congress May 2019
- Roche Ad Board: Hemlibra masterclass Feb 2019
- SHIRE (Takeda) Personalising Haemophilia Summit 2019
- Trans Tasman NovoNordisk Meeting for Nurses: November 2018
- CSL: WFH Congress 2018
- Pfizer Summit: 2015
- NovoNordisk: member of Global haemophilia network Support Committee (3 years - 2014 – 2016)
- NovoNordisk Changing Possibilities Grant 2014
- Novo Nordisk sponsorship of QCH outreach dinner education meetings yearly
- SHIRE (Takeda) honoraria March 2019 speaker – money donated to QHC research cost centre

Carrier confusion??

A carrier is typically defined as a person who has a genetic mutation for a disease that can be passed onto a child, but who doesn't have symptoms.

In haemophilia:

Women who have the genetic mutation can also be **symptomatic.**

Affected males pass their genetic mutation to their daughters

Obligate carriers

All daughters of a male with haemophilia

Mothers of one son with haemophilia, **and**

who have at least one other family member with haemophilia or

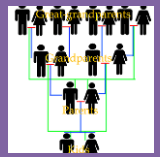
who have a family member who is a known carrier

Mothers of two or more sons with haemophilia

Possible carriers

All daughters of carriers

Mothers of one son with haemophilia but who do not have any other affected family members



Sisters, mothers, maternal grandmothers, aunts, nieces, & female cousins of carriers

So… what is the problem?

For every 1 male with haemophilia there are up to 5 female carriers!!

Women face many haemostatic challenges over their lifetime

Menstruation and child birth are unique to women

Females with the haemophilia gene bleed too!

The research says….

…Over half of all carriers are unaware of their carrier status…

- by the time they reach reproductive age,
- at the time of pregnancy…
- or until the birth of an affected son

(Balak et al, 2012)

Should we be concerned?

… Median age of carrier testing (diagnosis) was 28 -30 years old….

HOWEVER

the average age of carriers at first pregnancy was 26 years old!!??

(Balak et al., 2012).

- Delayed diagnosis is a barrier to appropriate management and timely treatment

(Byams et al., 2011)

Risk factors & complications

Increased risk of bleeding symptoms: epistaxis, bleeding after invasive procedures (surgery, dental, piercings), heavy menstrual bleeding & possible muscle / joint bleeds after trauma (Byams et al., 2011).

Impaired daily activities & Quality of Life

Bleeding risk to the pregnant woman & the baby: increased morbidity during pregnancy, labour and delivery

Self-Administered Bleeding Assessment Tool (Self-BAT)

- The online Self-Administered Bleeding Assessment Tool (Self-BAT) is freely accessible on the Let's Talk Period website and assesses past and present bleeding symptoms and generates a quantitative Bleeding Score (BS).

- https://letstalkperiod.ca/

Dr. Paula James

Consequences of bleeding in women

- Prolonged & painful periods
- Iron deficiency & anaemia
- Increased mortality & morbidity
- Limitations in daily activities /work /sport
- Adverse psychological / emotional effects
- Reduced Quality of Life
- Unnecessary procedures

Carrier status: What do we know?

Gaps in knowledge

Gaps in understanding

- carrier status
- factor levels versus genetic testing
- Risk of passing on haemophilia & inheritance patterns

Why carrier specific clinics

Specific health care needs

Assess bleeding risk

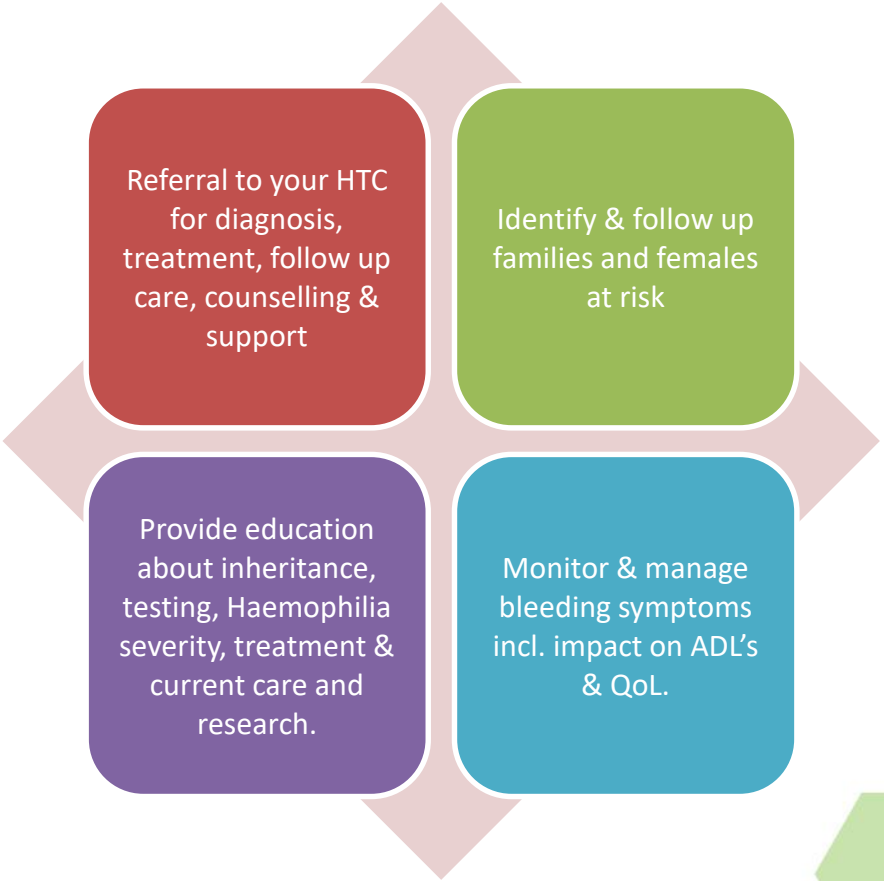
Identify optimal patient treatment strategies

Deliver appropriate care & avoid unnecessary “interventions”

Assess effect of treatment modalities

AIM to educate and reinforce importance of early diagnosis and recognition of bleeding symptoms

…Your family history is an important roadmap to understand and manage your risk proactively …



Newborn to toddler

- Obtain family history
- Inheritance - draw a family tree (pedigree)
- Risk assessment
    - Identify obligate carriers
    - Identify potential carriers
- Measure factor levels ? (only if clinical need & urgency)

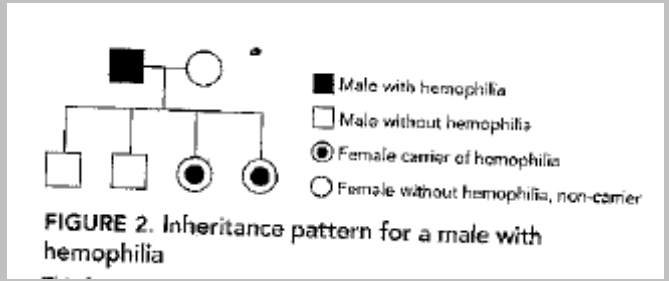


FIGURE 2. Inheritance pattern for a male with hemophilia

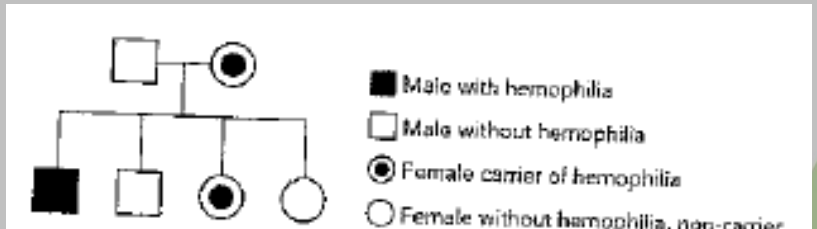
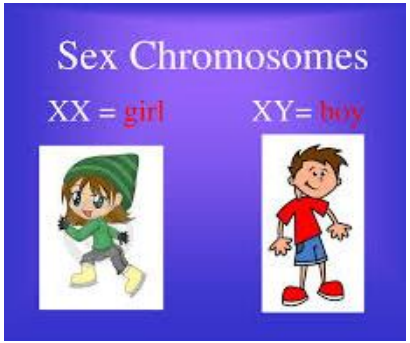


FIGURE 3. Inheritance pattern for a female carrier of hemophilia

WFH 2015. Genetic Counselling for haemophilia, (25).

Pre schoolers

- Update family tree (new siblings?)
- Focus on parent education
- Inheritance / Haemophilia education
- Terminology – age appropriate games, drawings to reinforce concepts
- Investigate factor levels, bleeding symptoms…
    - 30% of carriers have reduced factor levels
    - factor levels not always indicative of bleeding problems
    - factor levels not related to severity of Haemophilia in the family
- Factor levels versus genetic testing



School age to early adolescence

- Change from parent focused to the child/ young girl
- Pre menarche (plan for start of periods)
- Post menarche - monitor — QoL / HMB / Anaemia /iron deficiency
- Education: inheritance, terminology, current treatments & care, research
- Reinforce knowledge – promote informed decision making
- What is genetic testing and counselling?
- Referrals to gynaecologist, genetic counsellor, psychologist…

Adolescence to early adulthood

- Genetic counselling & genetic testing
- Ongoing monitoring if HMB /iron deficiency
- Ongoing education - inheritance, current treatment, reproductive choices
- Support informed decision making around genetic testing, pregnancy and delivery
- Referrals to gynaecologist, genetic counsellor, psychologist

Genetic testing

Ideal age of testing?

- Ethical concerns – age of informed consent
- Cultural, social & religious reasons may impact on decision to find out carrier status.
- In Australia …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]
- Done well before pregnancy !!

Other issues

- Helpful to have genetic mutation identified first in “index” (affected) person
- Counselling & support provided prior to help understand the chance (risk) of being a carrier and follow up
- May take months for results to come back
- Consent needed to share your genetic information amongst related family members

Reasons for carrier testing in minors

For the health benefit of the child – to help predict and manage symptoms if factor levels are low.[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]

"Being a carrier is a genetic designation, not a diagnosis. It says nothing about how you are clinically."

Marion A. Koerper, MD medical adviser of the National hemophilia Foundation (NHF)

Thank you !

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