MANAGEMENT OF CARRIERS OF HEMOPHILIA

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- **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

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HERSELF

She may have symptoms of mild hemophilia if she has low factor levels (up to 80% of carriers)

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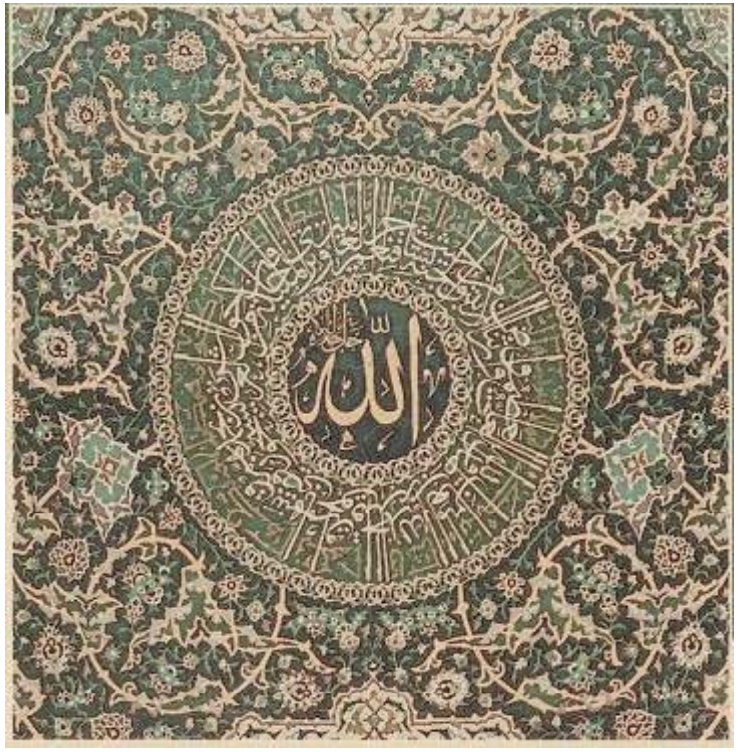

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Who are these women and how should we advise them?

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Obligatory carrier	**The daughter of a man with hemophilia**
Proven carrier	**A woman with both an antecedent and a descendent relative with hemophilia. The gene must have passed through her.**
Probably carrier or possible carrier	**The mother of an isolated case of hemophilia**
Potential carrier	**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**

- **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**

WFH Publication

Genetics of Haemophilia

Anne Goodeve

Sheffield Molecular Genetics Service

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On WFH website www.wfh.org

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- **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**

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GENETICS

OF HEMOPHILIA A AND B

An Introduction for Clinicians,

2009

by

Carol K. Kasper, M.D.

and

Carolyn H. Buzin, Ph.D.

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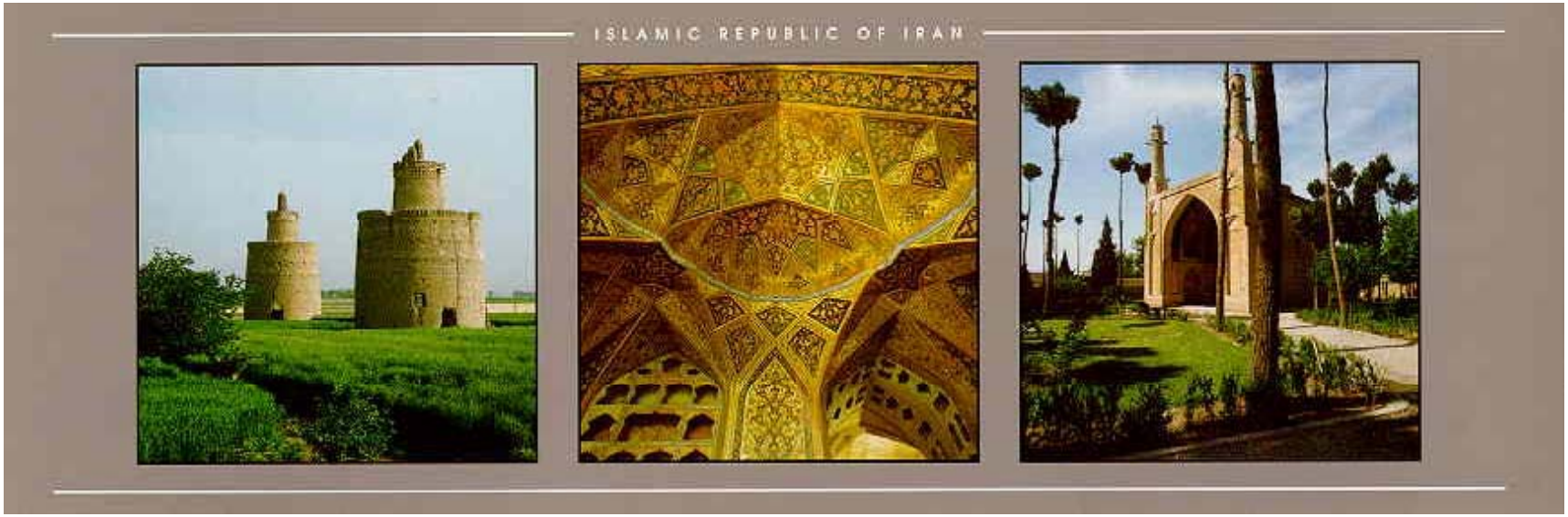
- **Clinician-scientists from hemophilia Centres in Iran, together with Professor Flora Peyvandi in Milan, Italy have contributed greatly to this literature**



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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

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What are the implications of providing a genetics service?

- **Implementation and resourcing of Genetic Testing Programs will take in to account**
- **Diagnostic capacity**
- **Cultural considerations**
- **And require associated counselling and quality frameworks**

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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**

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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**

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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

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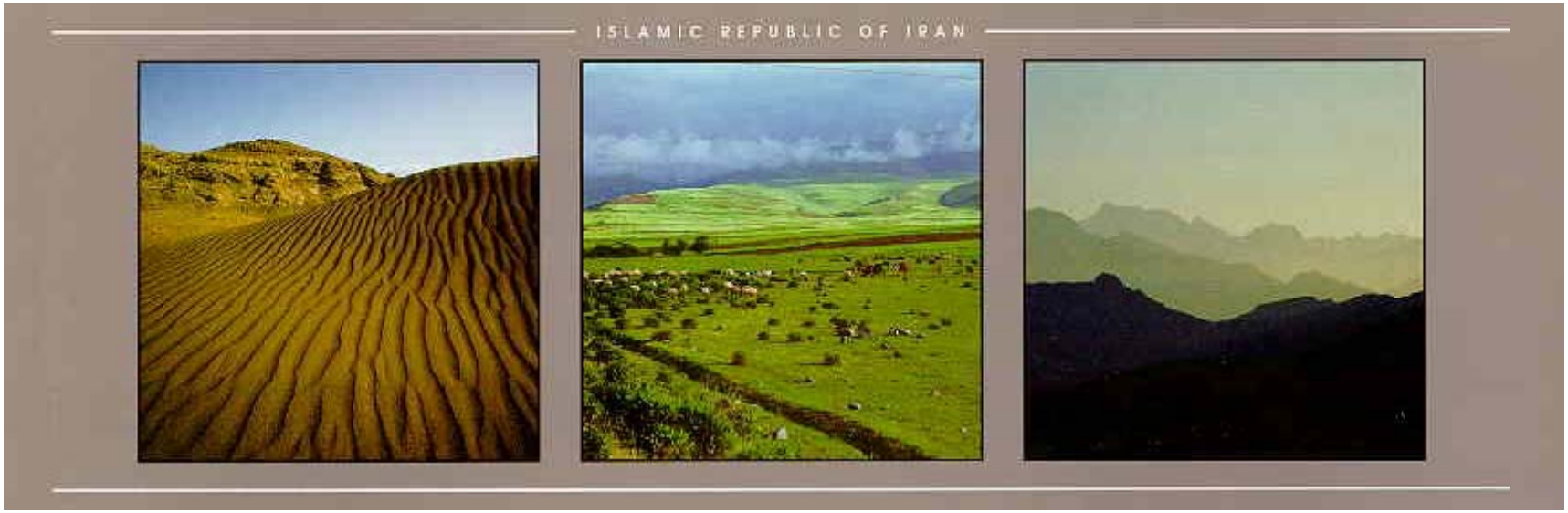

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Care and treatment of Carriers

- **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**

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Genetic testing is performed as part of a supportive clinical encounter with

- **Informed clinicians**
- **Genetic counsellors**
- **Excellent laboratory scientists**

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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**

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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

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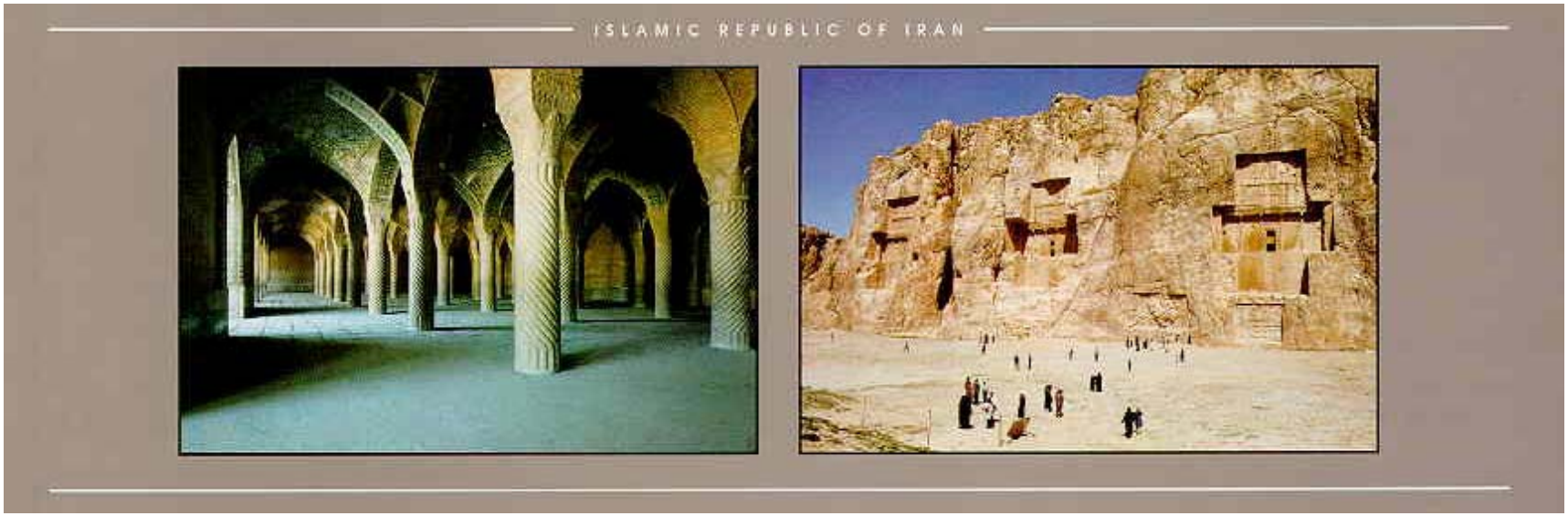

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Use of DDAVP in pregnancy in symptomatic carriers of FVIII deficiency

- **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**

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- **Post partum use in von Willebrand disorder is recommended to reduce post-delivery fall in vWF/FVIII levels**

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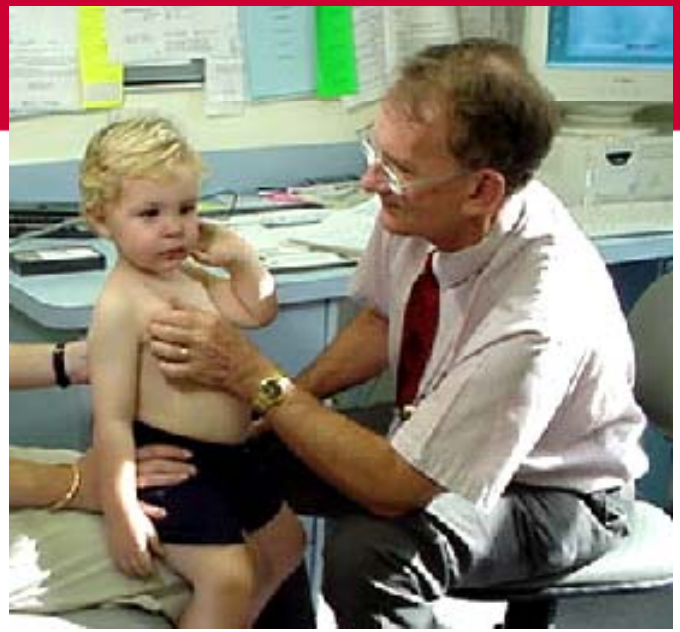

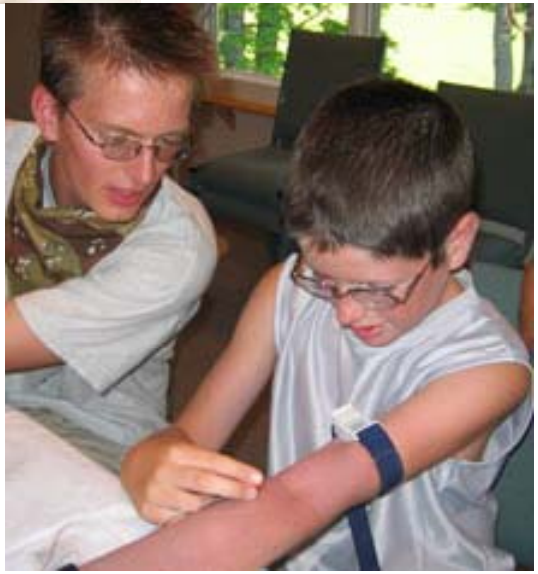

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Inspiring Mount Damavand

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