

Consanguinity in Saud population

Professor Arjumand Warsy,
B.Sc, M.Sc, Ph.D, FACB

BCH 590

[1424-1425]

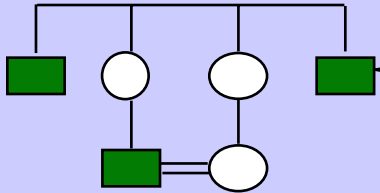
- *Consanguinity literally means “related by blood”*
- *Consanguineous marriages are “marriages between blood relatives”*
 - Genetists usually classify unions between second cousins or closer as consanguineous
 - Consanguinity is a Greek word meaning
con=shared
sanguis=blood so consanguinity means related by blood

Globally, the most common form of consanguineous union contracted is between first cousins, in which the spouses share 1/8 of their genes inherited from a common ancestor, and so their progeny are homozygous (or more correctly autozygous) at 1/16 of all loci. Conventionally this is expressed as the coefficient of inbreeding (F) and for first cousin offspring,

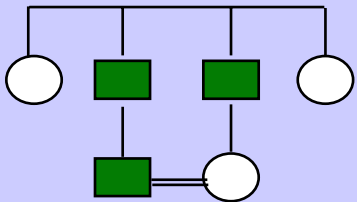
cousanguinity

- Although marriages between close biological kin are preferential in many parts of the world, there still is a great lack of knowledge of this central feature of human kinship structure. As an introduction to the subject, brief summaries are presented on topics such as the religious and legal backgrounds to consanguineous marriage in different societies, sociodemographic aspects of marriages between close biological kin, fertility in consanguineous unions, and the effects of consanguinity on rates and patterns of morbidity and mortality. Unfortunately, in many of the more populous countries representative information on consanguineous marriage and its outcomes is sparse or even unavailable. In others, legislation introduced within the present generation may be exerting a marked effect on traditional patterns of marriage preference, an example being the 1981 Marriage Law of the People's Republic of China which prohibits marriage between couples related as first cousins or closer. It is envisaged that this lecture can serve both as a spur to continuing data collection on consanguinity, and as a baseline against which future changes in marriage practices and their outcomes can be assessed.

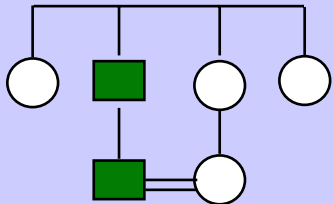
Types of Consanguinity



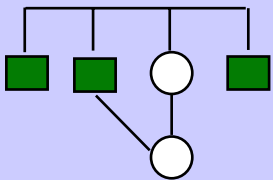
- Matrilateral parallel cousins
- Allowed in Islam and in Indians (Hindus)



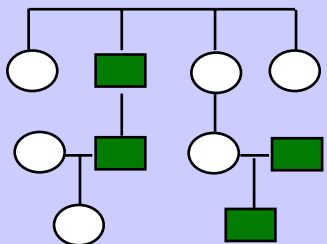
- Patrilateral parallel cousins
- Allowed in Islam and in Indians (Hindus)
- Prohibited in China



- Cross-cousins
- Allowed in Islam and in Indians (Hindus)



- Uncle- Neice
- Commonest form in India
- Prohibited in Islam



- Second Cousin
- Allowed in Islam and in Indians (Hindus)

Parents

Brothers and sisters

Collateral consanguinity

First Cousins

Second Cousins

Third Cousins

Third Cousins once removed

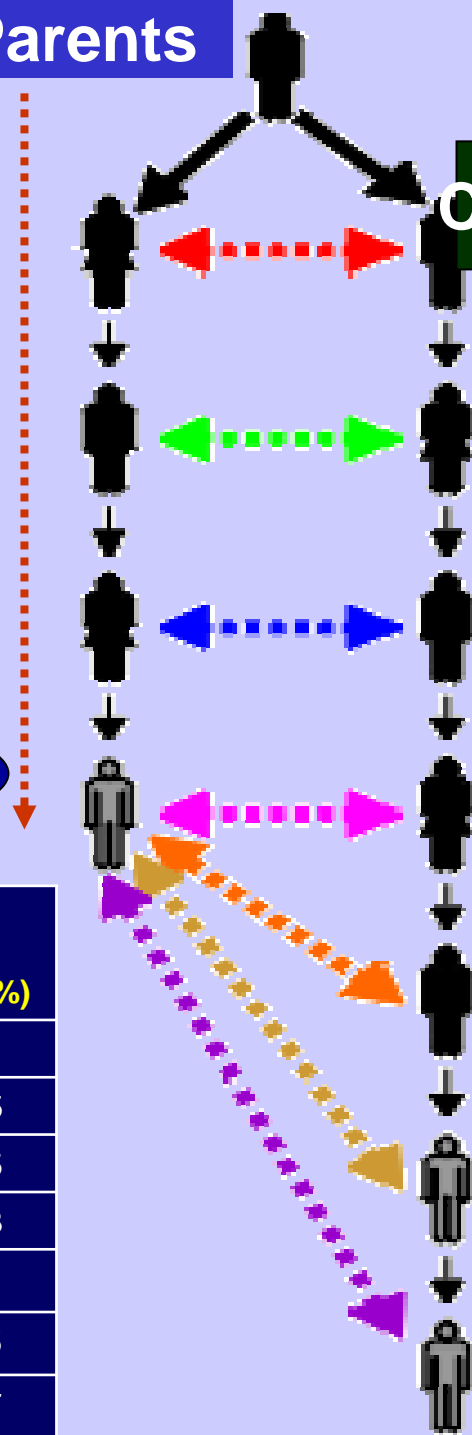
Third Cousins twice removed

Third Cousins 3 times removed

Lineal consanguinity

In the line of decent

Relation	Proportion of Shared genes	Chance of Homo by descent (%)
1 st degree	1/2	1/4 25
2 nd degree	1/4	1/8 12.5
3 rd degree	1/8	1/16 6.25
4 th degree	1/16	1/32 3.13
5 th degree	1/32	1/64 1.5
6 th degree	1/64	1/128 0.75
7 th degree	1/128	1/256 0.37



Historical Aspects

Queen Victoria (1819-1901 A.D)

was married to her first cousin Prince Albert of Germany



Gregor Mendel (1822-1884 A.D)

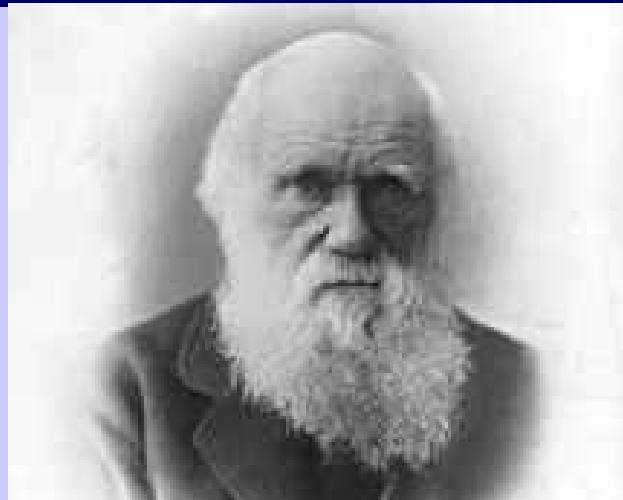
the father of modern genetics, was married to his cousin



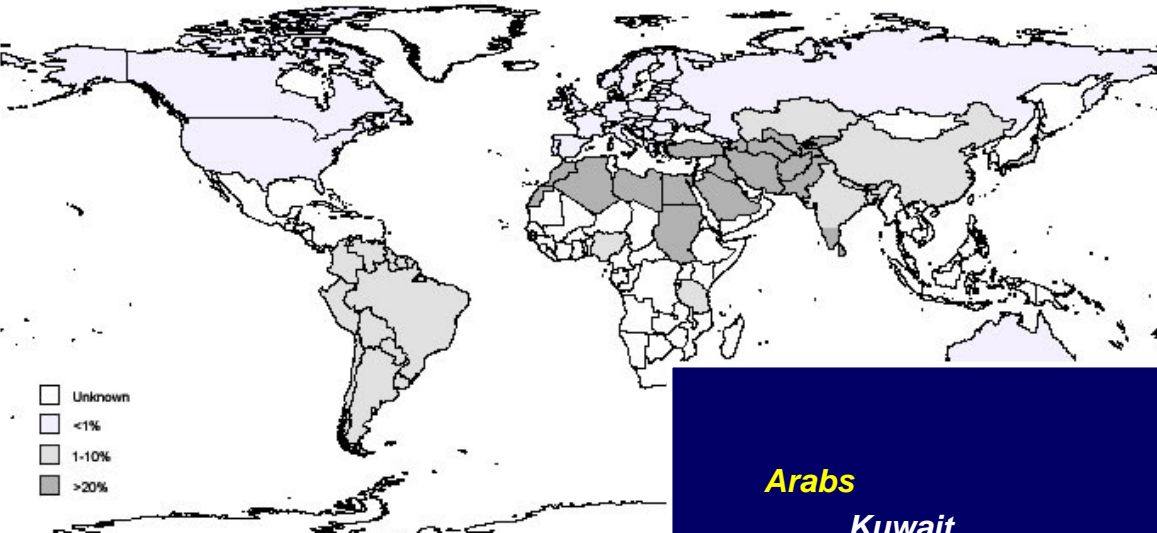
During the 19th and 20th centuries First cousin marriages are quite common in Europe and in many countries Asia.

Charles Darwin (1809-1882 A.D)

was married to his first cousin, Emma Wedgewood



The 20th and 21st Century A.D Global Prevalence of Consanguinity*



Highest prevalence of consanguinity in:
N.Africa, S. and W. Asia
and Arabian Peninsula

Arabs

<i>Kuwait</i>	<i>54</i>
<i>Syria</i>	<i>33</i>
<i>Egypt</i>	<i>28</i>
<i>Lebanon</i>	<i>25</i>
<i>Algeria</i>	<i>23</i>
<i>Jordan</i>	<i>50</i>
<i>Saudi Arabia</i>	<i>52-67.7</i>

Asians

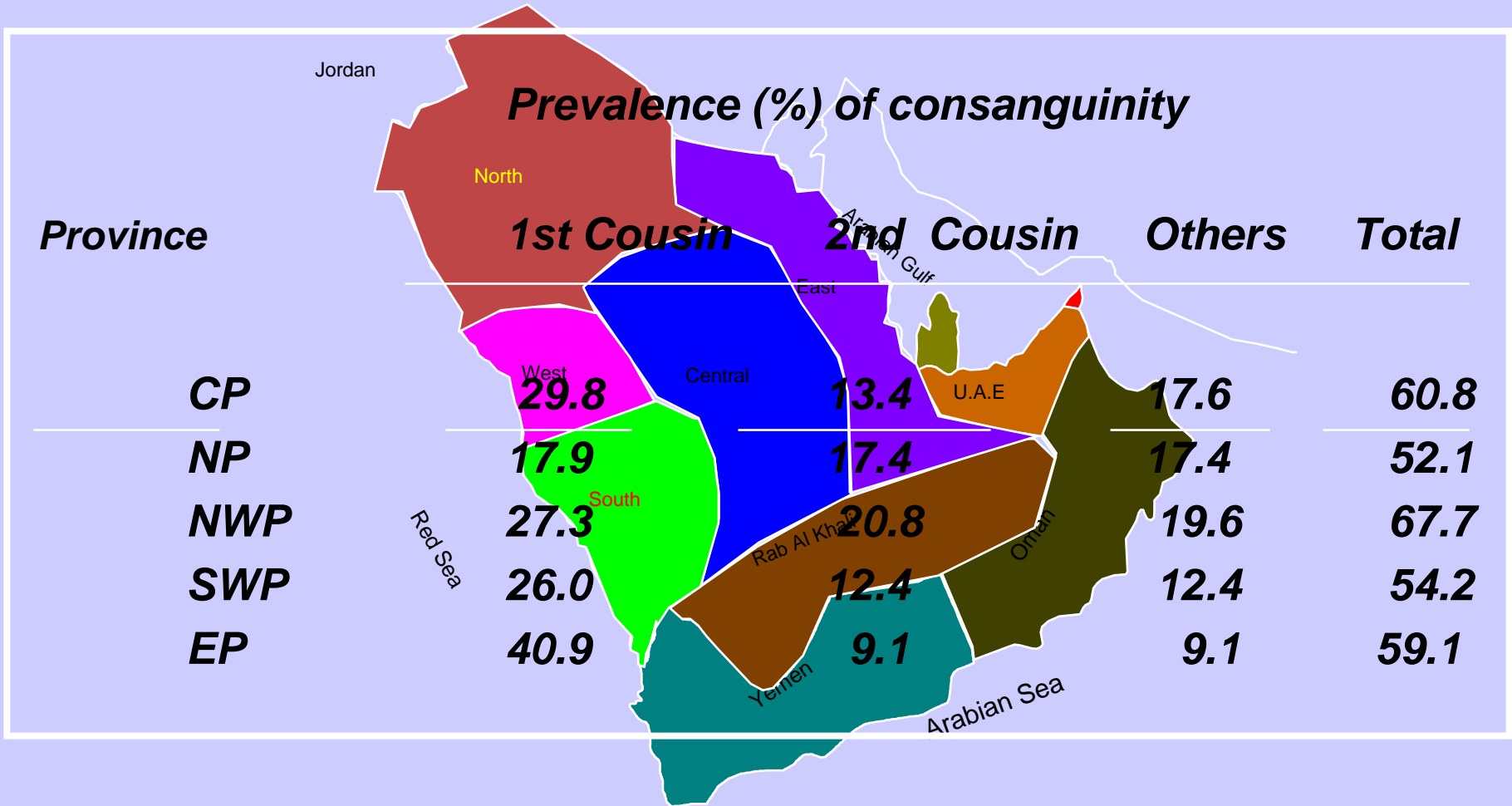
<i>Pakistan</i>	<i>38 - 49</i>
<i>India</i>	<i>5 - 61</i>
<i>Japan</i>	<i>1.6 - 3.9</i>

Americas

<i>Brazil</i>	<i>0.62 - 9.0</i>
<i>Some States of USA</i>	<i>Illegal</i>

Prevalence (%) of consanguinity

PREVALENCE OF CONSANGUINITY IN SAUDI ARABIA



Consanguinity

Practiced for centuries worldwide

Has several advantages and **some disadvantages**

Contributing factors

Indicates that any advantage of this type of union outweighs the disadvantage

- Economic
- Psychological
- Social

Maintenance of family structure and property

Stronger family ties

Greater marriage stability and durability

Closer relationship with in-laws

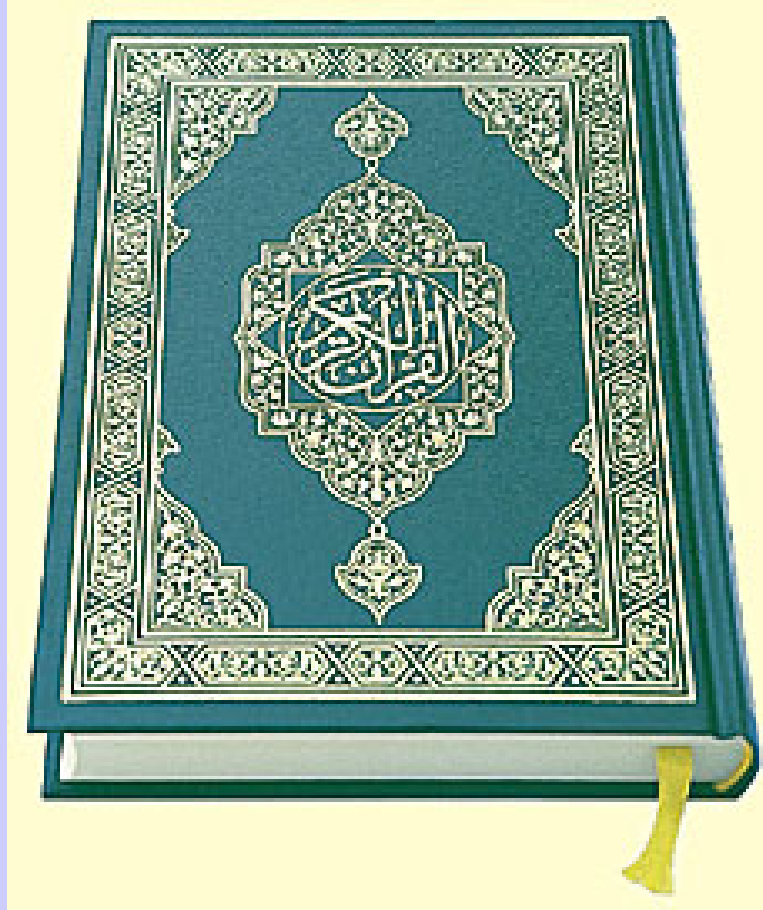
Rare disorders seen in highly endogamous communities

Financial advantages relating to dowry or bride wealth

To secure political alliance

Increased frequency of homozygotes

In Islam



Consanguinity in Islam (610 A.D)



Prohibited to you (for marriage) are:
your mothers daughters sisters
father's sisters mother's sisters;
brother's daughters sister's
daughters foster-mothers (who
gave you suck) foster-sisters; your
wives' mothers; your step-
daughters under your guardianship
born of your wives to whom ye have
gone in no prohibition if ye have not
gone in; (those who have been)
wives of your sons proceeding from
your loins; and two sisters in
wedlock at one and the same time
except for what is past; for Allah is
Off-Forgiving Most Merciful.

وَسَاءَ سَبِيلًا ﴿٢٢﴾ حُرِّمَتْ عَلَيْكُمْ أُمَّهَاتُكُمْ
وَبَنَاتُكُمْ وَأَخَوَاتُكُمْ وَعُمَّتُكُمْ وَخَالَاتُكُمْ وَبَنَاتُ
الْأَخِ وَبَنَاتُ الْأُخْتِ وَأُمَّهَاتُكُمُ اللَّاتِي أَرْضَعْنَكُمْ
وَأَخَوَاتُكُم مِّنَ الرَّضْعَةِ وَأُمَّهُت نِسَائِكُمْ
وَرَبِّبَاتِكُمُ اللَّاتِي فِي حُجُورِكُم مِّن نِّسَائِكُم
الَّتِي دَخَلْتُم بِهِنَّ فَإِن لَّمْ تَكُونُوا دَخَلْتُم بِهِنَّ
فَلَا جُنَاحَ عَلَيْكُمْ وَحَلَائِلُ أَبْنَائِكُمُ الَّذِينَ
مِّنْ أَصْلَابِكُمْ وَأَنْ تَجْمَعُوا بَيْنَ الْأُخْتَيْنِ
إِلَّا مَا قَدْ سَلَفَ إِنَّ اللَّهَ كَانَ غَفُورًا رَّحِيمًا ﴿٢٣﴾

Prophet Mohammad(PBUH) saying on close kin marriages (570-632 A.D)

- Prophet Mohammad(PBUH) recommended his followers to **marry outside their families** and outside their clans.
- The Prophet (PBUH) once told one of his companions to **choose a wife from a tribe** different to his, and then to choose for his **son a wife from a third tribe**, and to seek for his other **son a girl from yet another tribe**

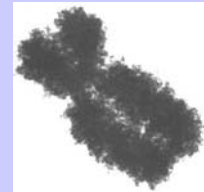
Genetic disorders



Types of genetic defects

Multifactorial

Chromosomal



Mitochondrial

Single gene

Autosomal

Sex -linked

X

Y

Dominant

Recessive

Inherited Haemolytic Anaemias



Abnormal Hb structure

HbS, HbC, HbD,
HbE,

AR

Unstable Hb

Hb Hammersmith
Hb Zurich, Hb Koln

AD

Abnormal Hb synthesis

α - thalassaemia
 β - thalassaemia

AR

Abnormal RBC membrane

- Hereditary Spherocytosis
- Hereditary elliptocytosis
- Hereditary Stomatocytosis

AD

Enzymopathies

- G-6-PD def

XR

- HNSHA- \downarrow PK, HK, GPI, PFK,
GR, GS, PGK, AK def. \uparrow ADA

AR

Consanguinity and Autosomal Recessive Disorders

- *There are around 400 different very rare disorders in human population (carrier frequency $< 1\%$).*
- *Even if consanguineous marriages are very common in a population, these disorders remain rare (birth rate < 0.3 per 1000), but is several times more than in random matching.*
- *In customary consanguineous, rare disorders (e.g. deafness, mental retardation, congenital malformation) is to be anticipated.*
- Expressed in **homozygotes**
- Parents of affected individuals are generally normal
- Consanguineous marriages favor the manifestation of **rare recessively** inherited disorder.

CONSANGUINITY AND RECESSIVE DISORDERS

- *Consanguineous marriages favour the manifestation of rare recessively inherited disorder (carrier, frequency <1%).*
 - Most inborn errors of metabolism
 - Some congenital malformation
 - Genetic forms of deafness
 - Mild to moderate mental retardation
- *For common recessive genes, a carrier has a relatively higher chance of marrying another carrier. The rate of homozygous births is approx. doubled in first cousin marriages:*
 - Hb S
 - α -Thalassaemia
 - β -Thalassaemia

Autosomal Recessive (AR) disorders

	A	a
A	AA	Aa
a	Aa	aa

Each offspring has **25%** chance of being affected by SCA and 50% chance of being a carrier

What is the probability that two heterozygotes will get married to each other?

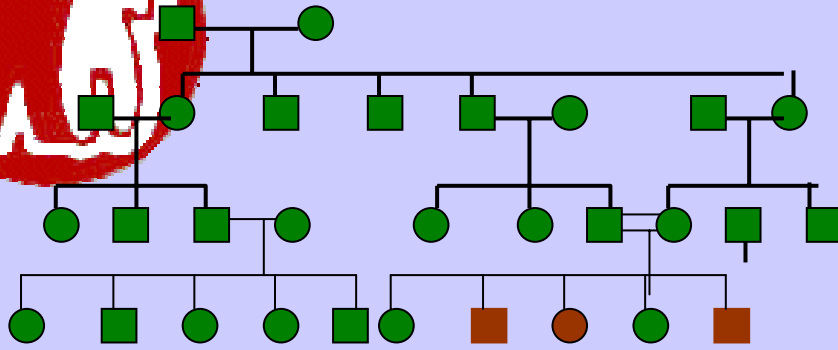
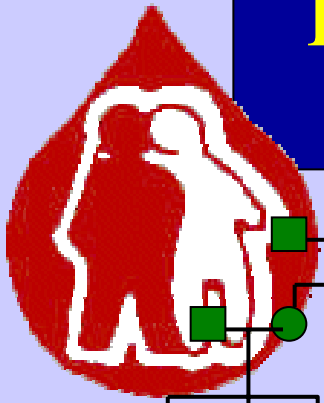
Frequency of the heterozygotes in the population

Consanguinity

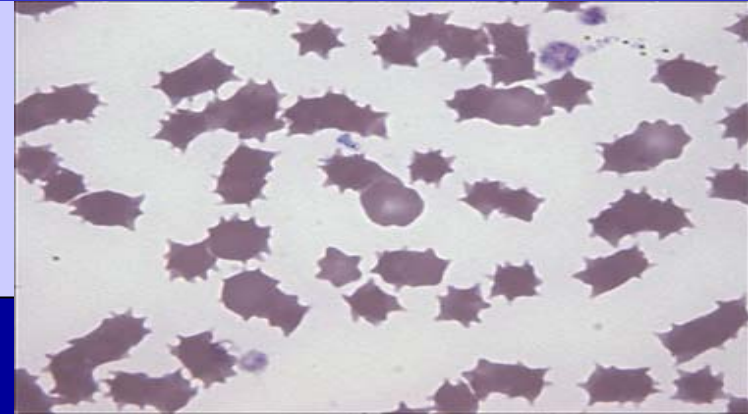
Consanguinity \uparrow the chance of marriage between carriers

Frequency of the mutant allele

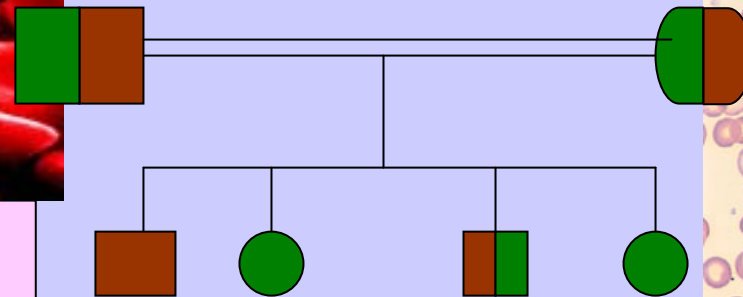
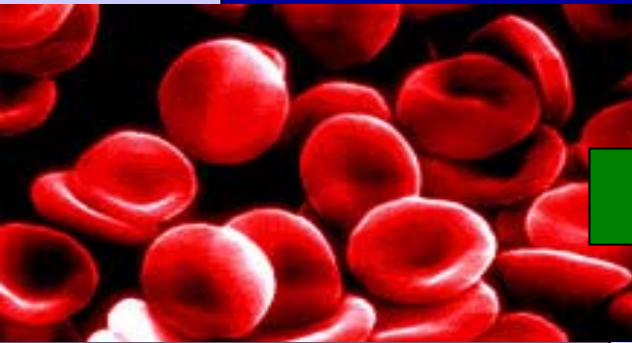
Family tree of an autosomal recessive disorder



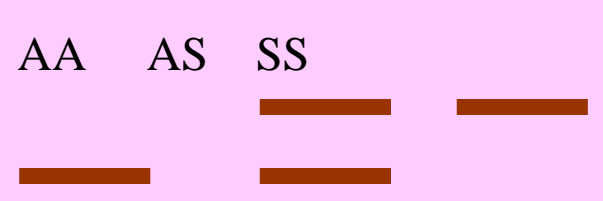
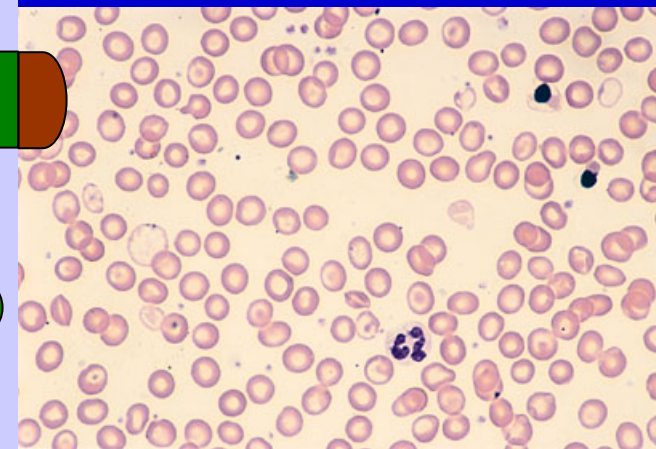
Acanthocytosis

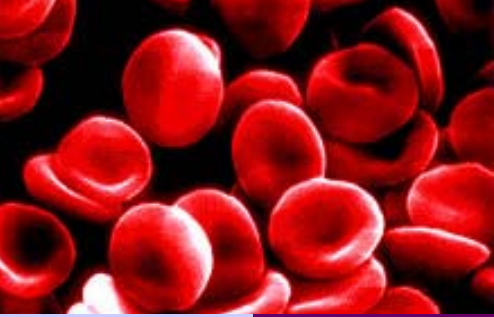


A family with sickle cell disease

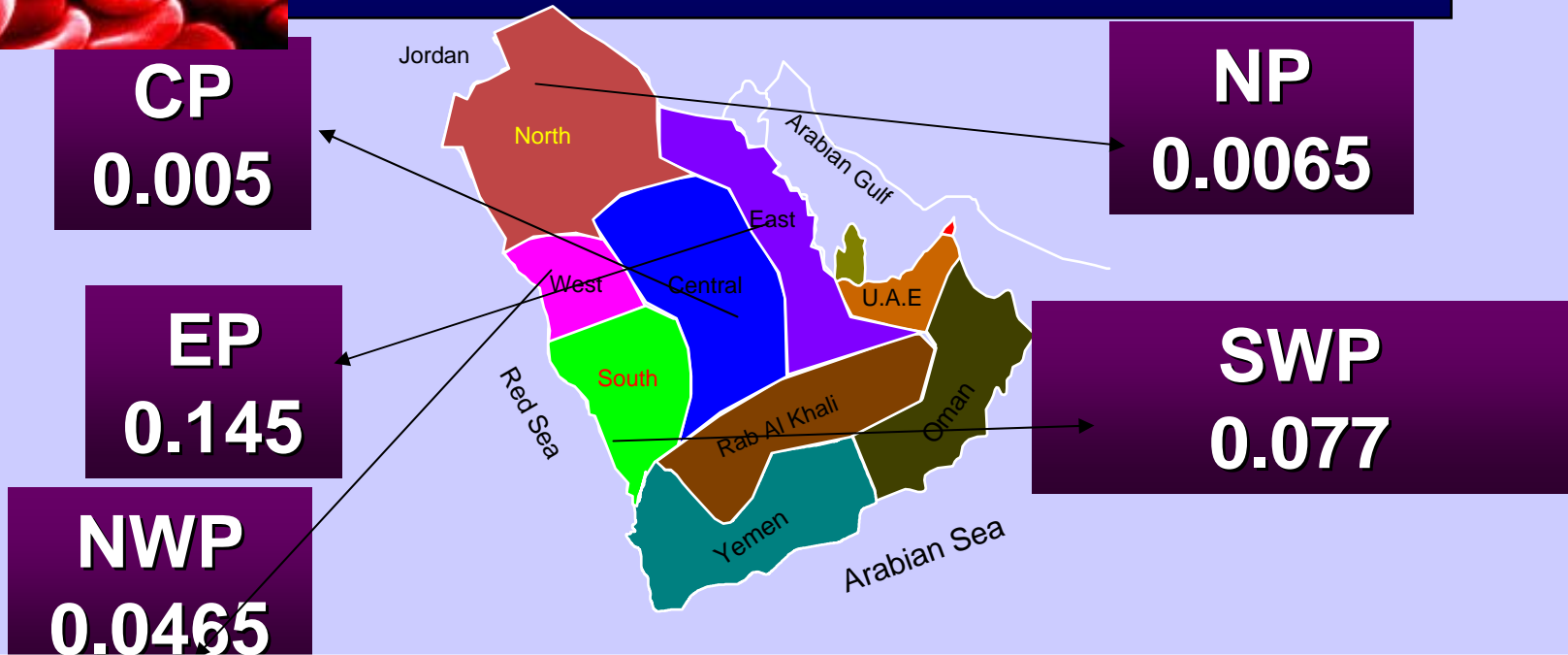


β -thal



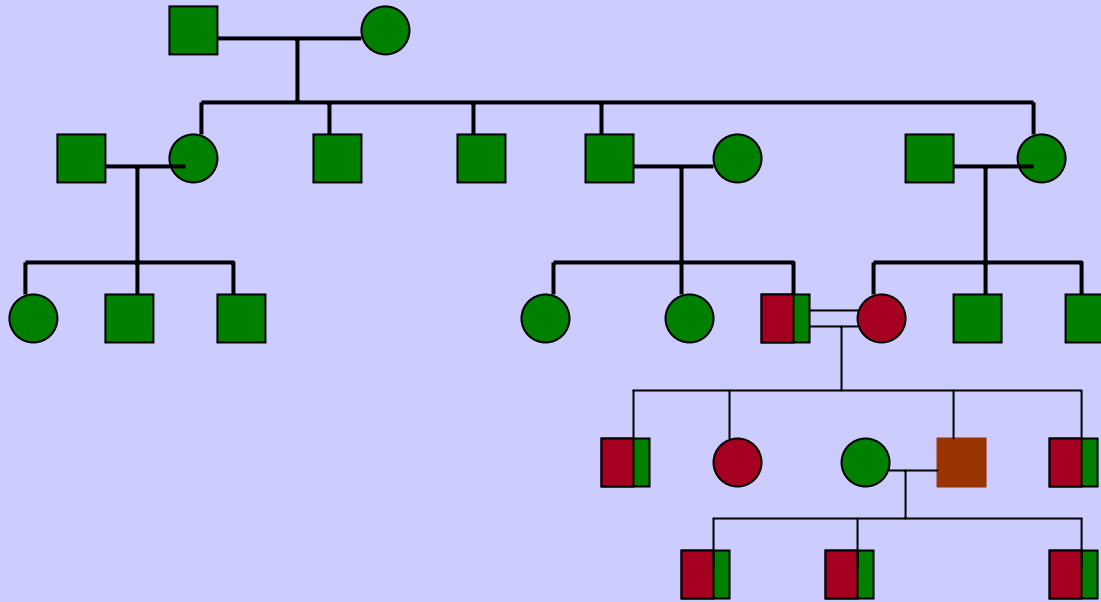


Hb S gene frequency in Saudi Arabia



Province	Hb S Carrier Frequency	Homozygous births/1000		Multiplication factor 30% IC/ random	P-Value
		Random	30% First cousin		
EP	21.3	12.0	14.3	1.2	NS*
CP	0.83	0.009	0.08	8.9	S
SWP	12.0	3.25	5.5	1.7	NS*
NWP	7.54	0.8	1.6	2.0	NS*
NP	1.3	0.030	0.21	7.0	S

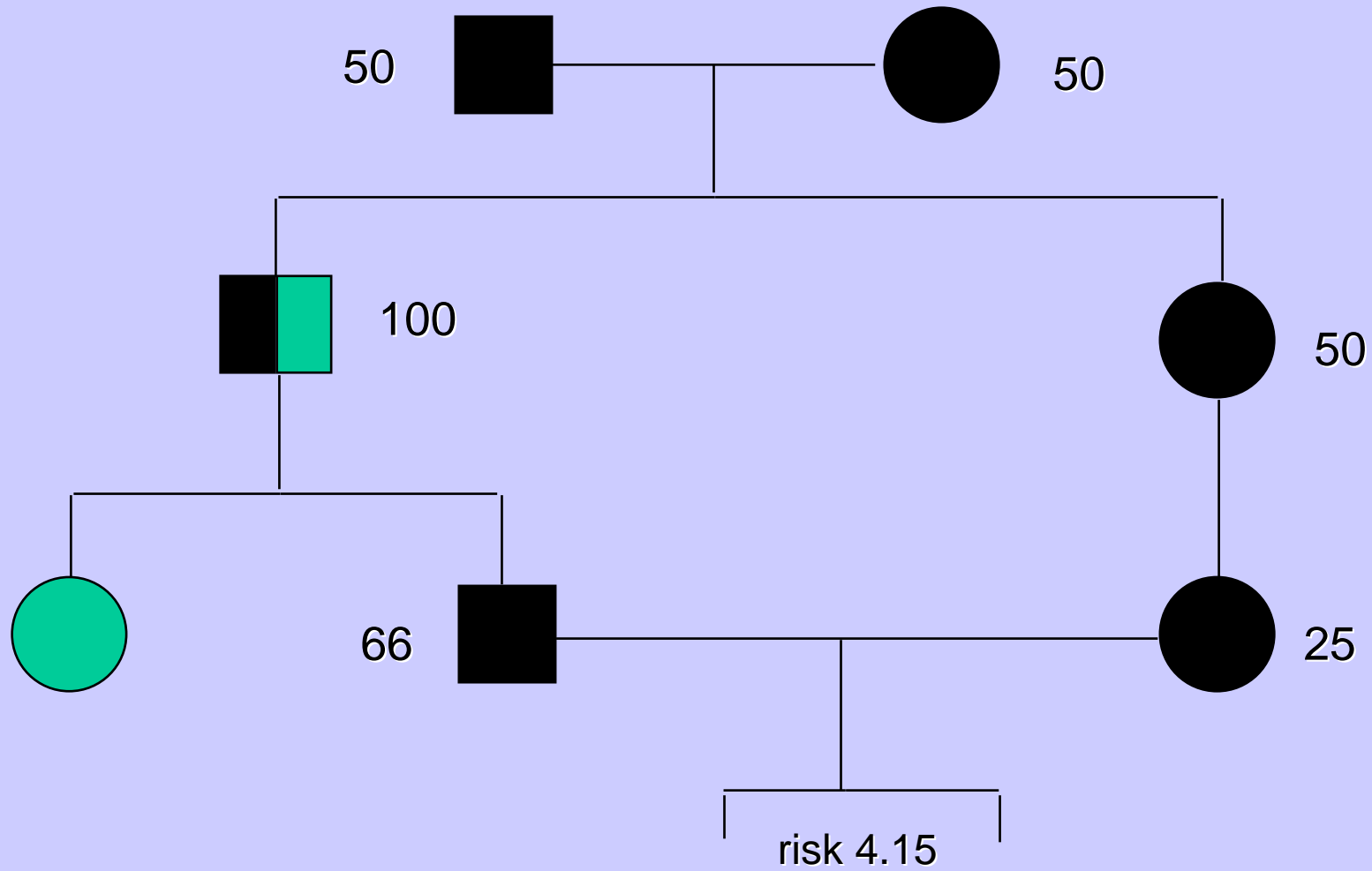
Consanguinity ↑ Quasi (pseudo)-dominance in AR



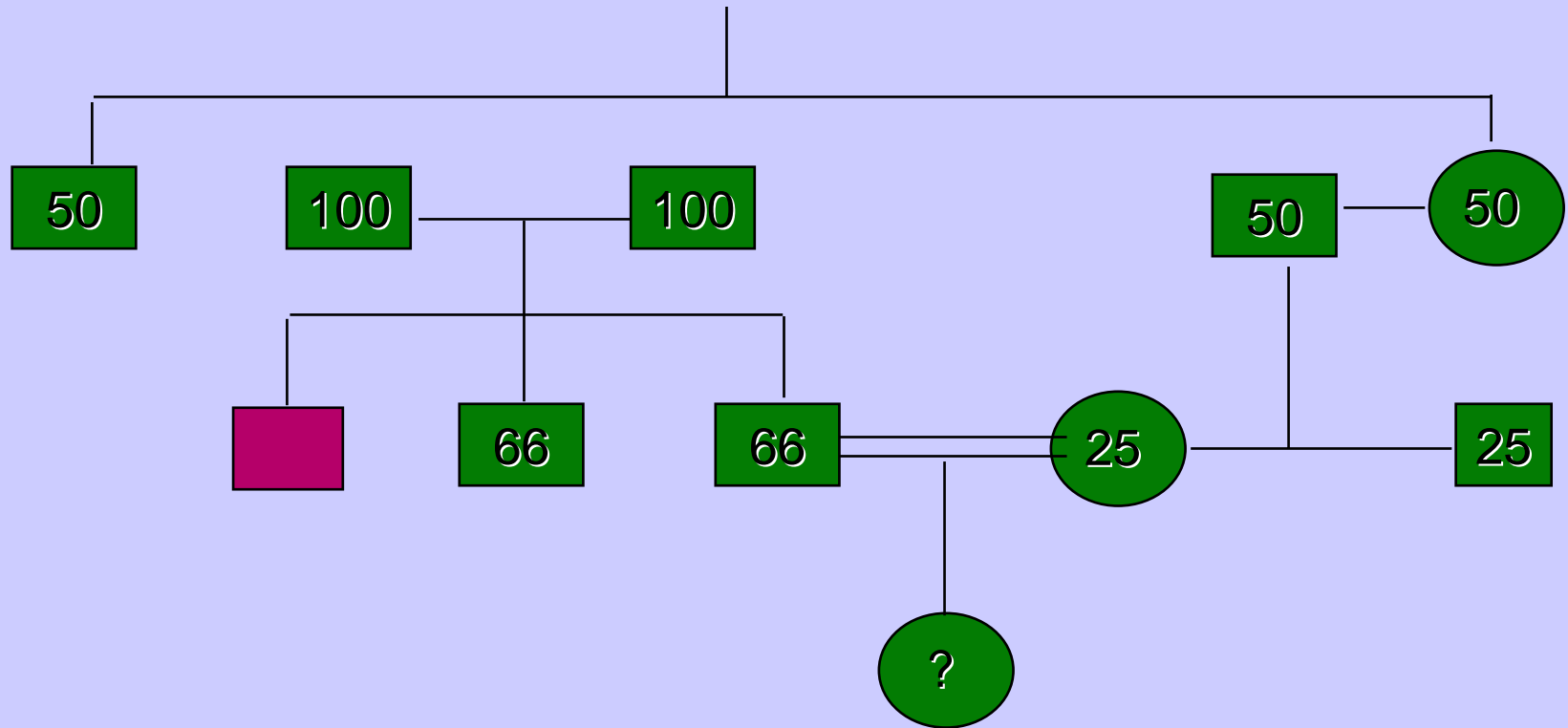
	S	S
A	AS	SS
S	AS	SS

Chance in offsprings
 Carriers---50%
 Homozygous---50%

Genetic Risk in Consanguineous Marriage

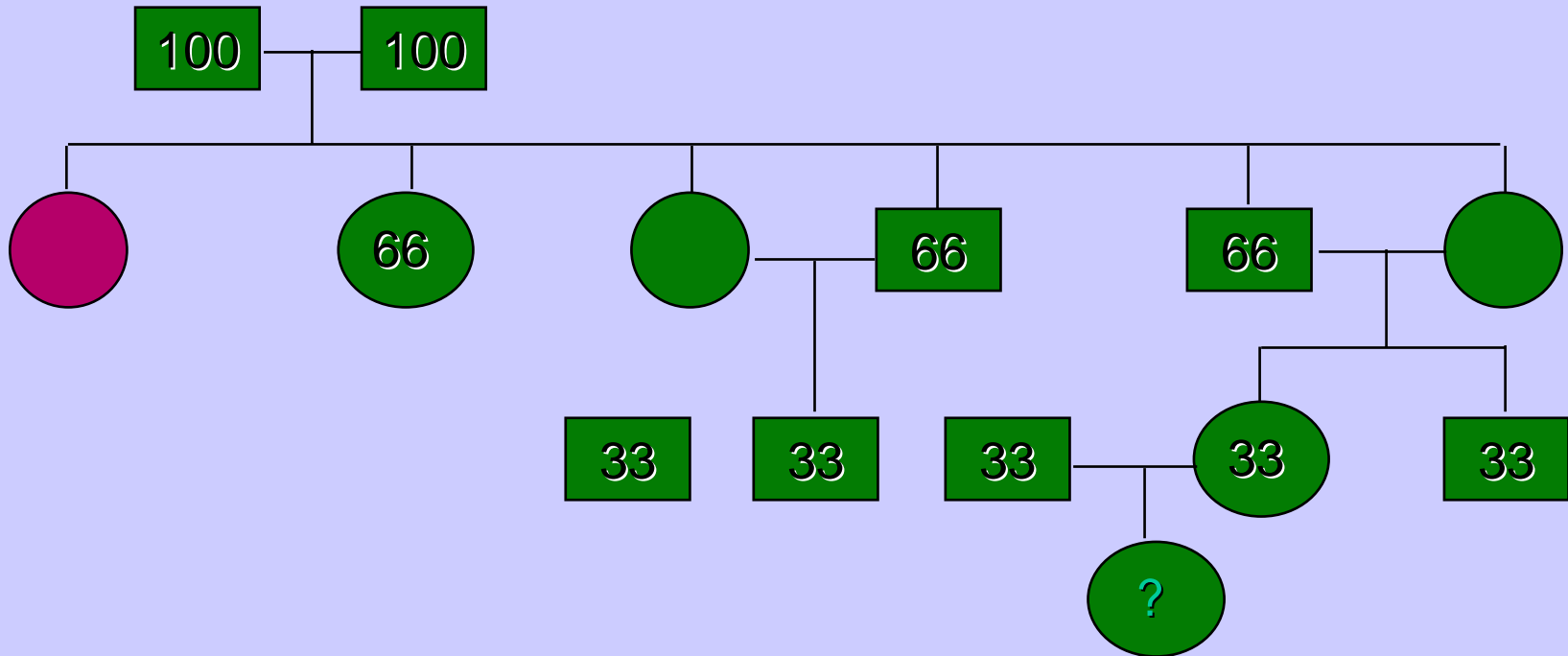


Genetic risk for consanguineous couples - Sibling affected



- Chance of affected persons, healthy siblings is carrier = 66%
- Chance that affected persons 1st cousin is carrier = 25%
- Chance that both cousins are carrier = 25% of 66% = 16.5%
- Chance of an affected child/pregnancy = $16.5/4 = 4.15\%$

Genetic risk for consanguineous couples - Aunt affected



- Aunt or uncle has a AR disorder
- Chance of healthy aunts being carrier = 66%
(Risk on the basis of relationship + Population risk)
- Chance that each of their offspring is carrier = 33%
- Chance that both first cousins are carriers = 33% of 33% = 10.9%
- Chance that each pregnancy is affected by same disorder = $10.9/4 = 2.7\%$

Contribution of
genes as
predisposing factors
in common diseases
of adulthood

Higher prevalence of major adult disorders
(e.g. common causes, CHD)*

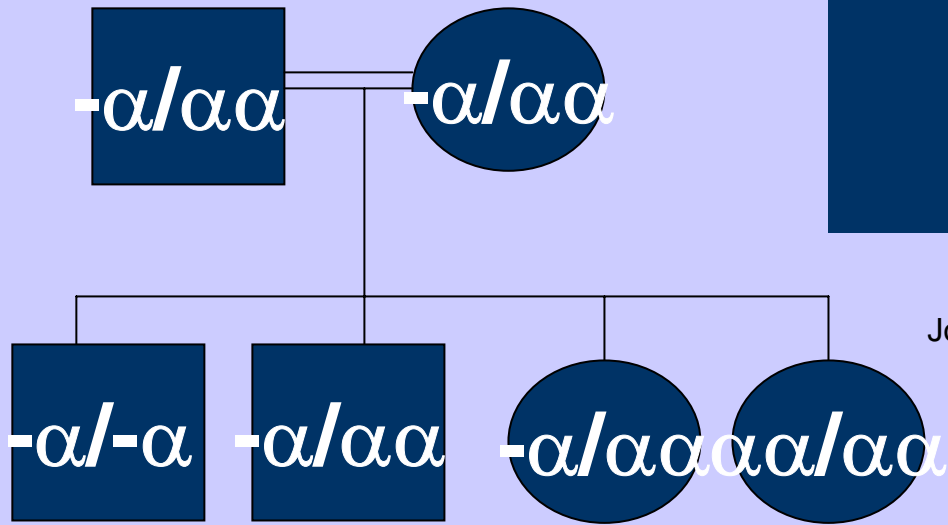
If a genetic disorder exists in the family?

- Consanguineous marriages have serious implications as genetic risk is increased.
- Social benefits/genetic risks

It is important for the counsellor to provide clear information on the precise genetic risk

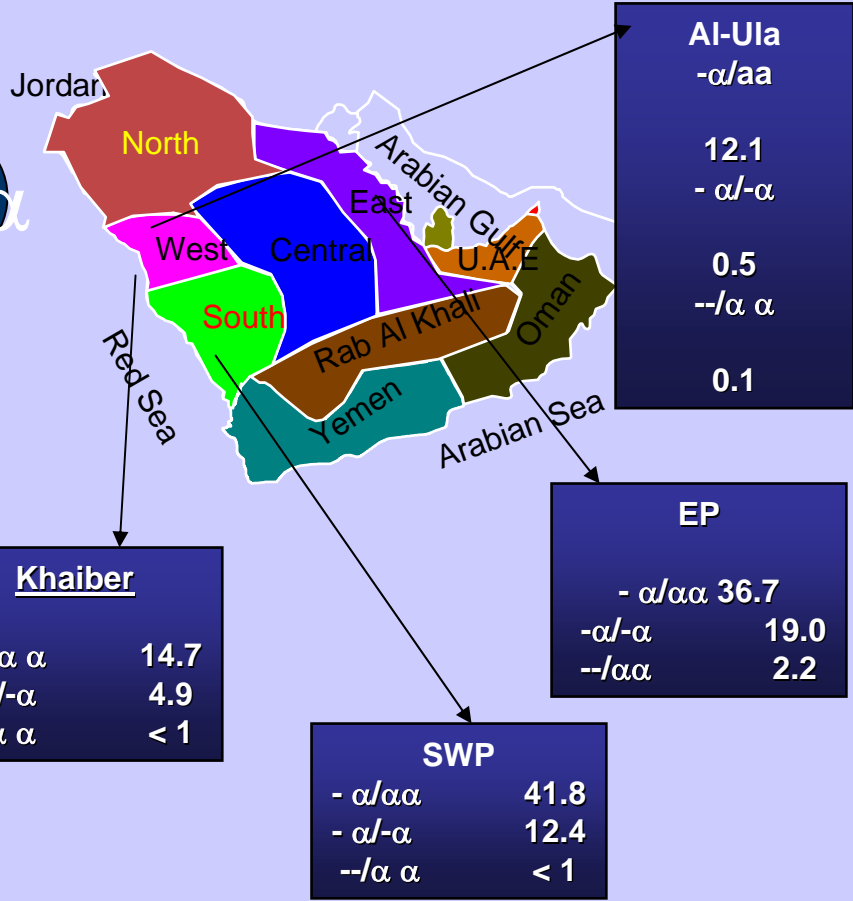
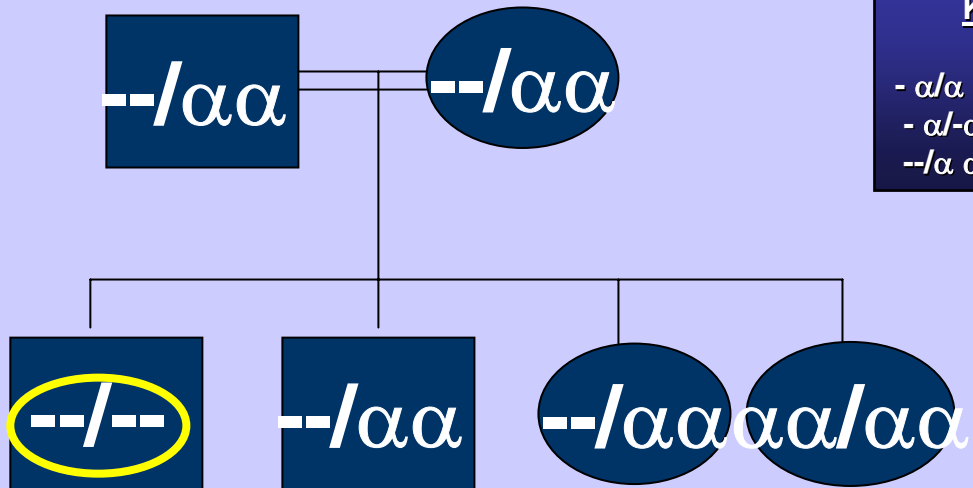
Risk increases with closeness of relationship

α Thalassaemia-2



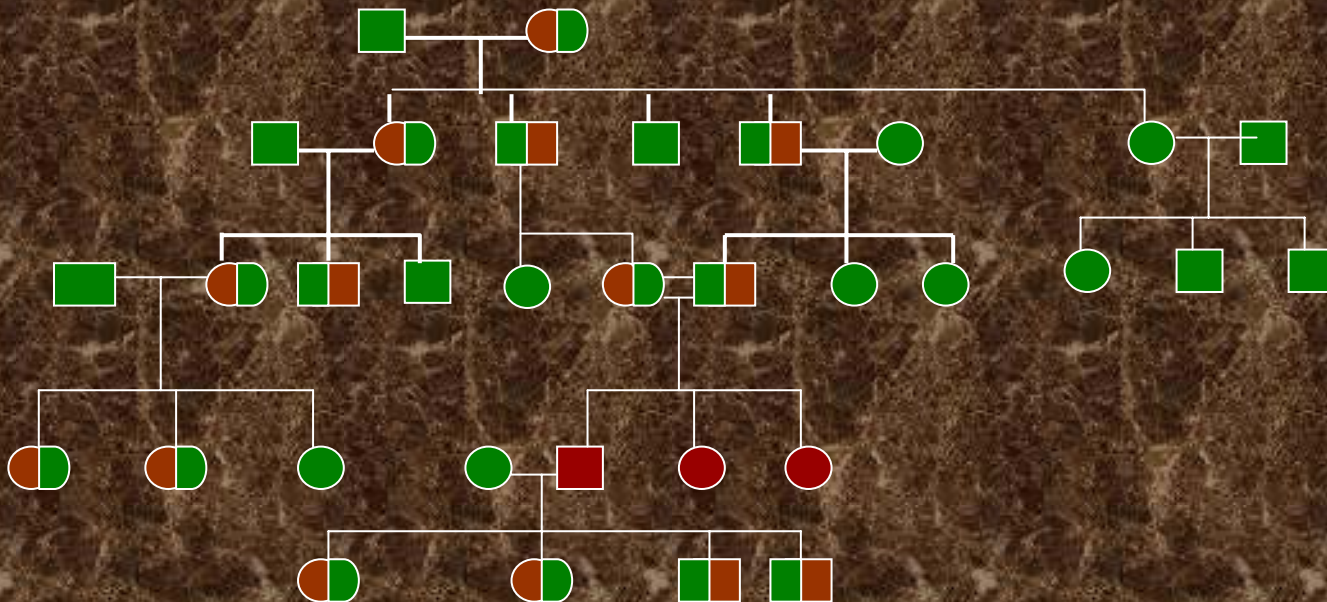
Inheritance of α Thalassaemia

α Thalassaemia-1



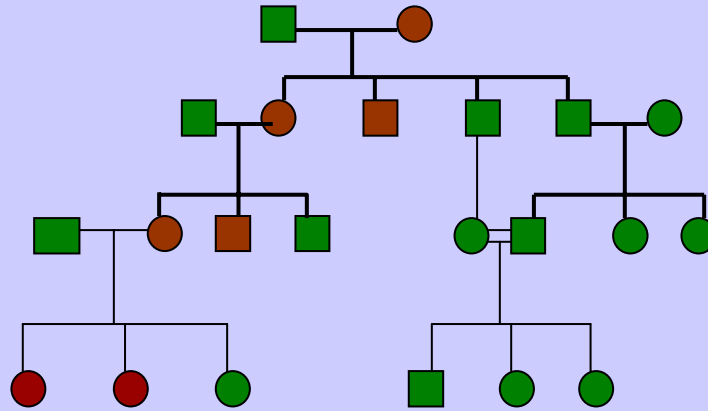
Consanguinity and AD disorders

- AD disorders are expressed in **heterozygotes**.
- Affected individuals transmit it to **50%** of their children.
- **Un-affected** individuals do not transmit it to their children
- **Consanguinity** may increase the number of **homozygous births**.
- If a homozygous will marry a normal person **100%** children will be affected

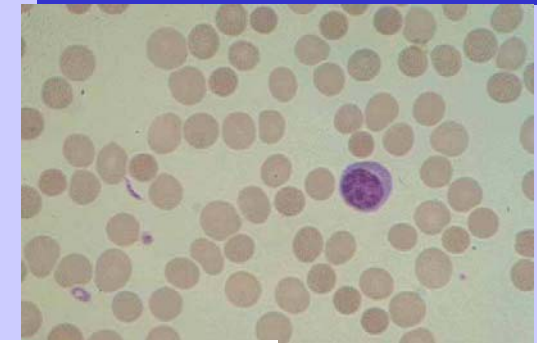


Autosomal Dominant Inheritance

	D	d
d	Dd	dd
d	Dd	dd



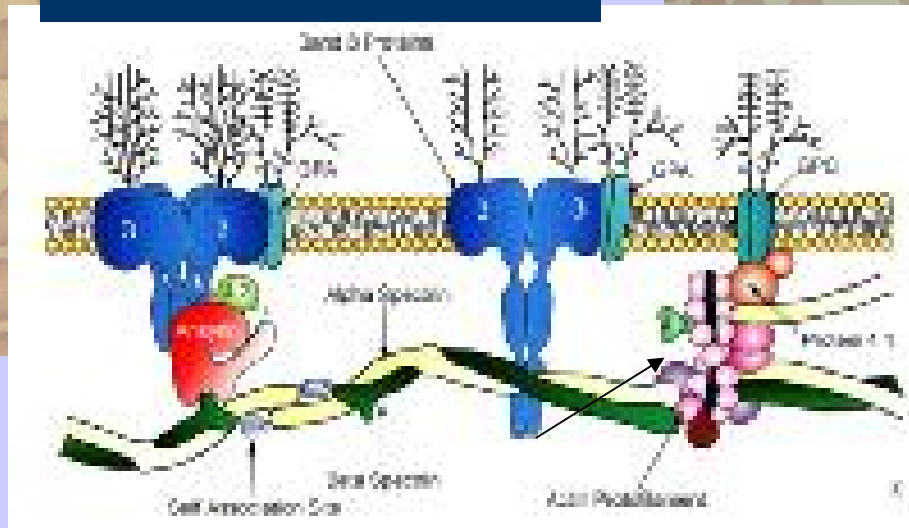
Hereditary spherocytosis



Membrane disorders

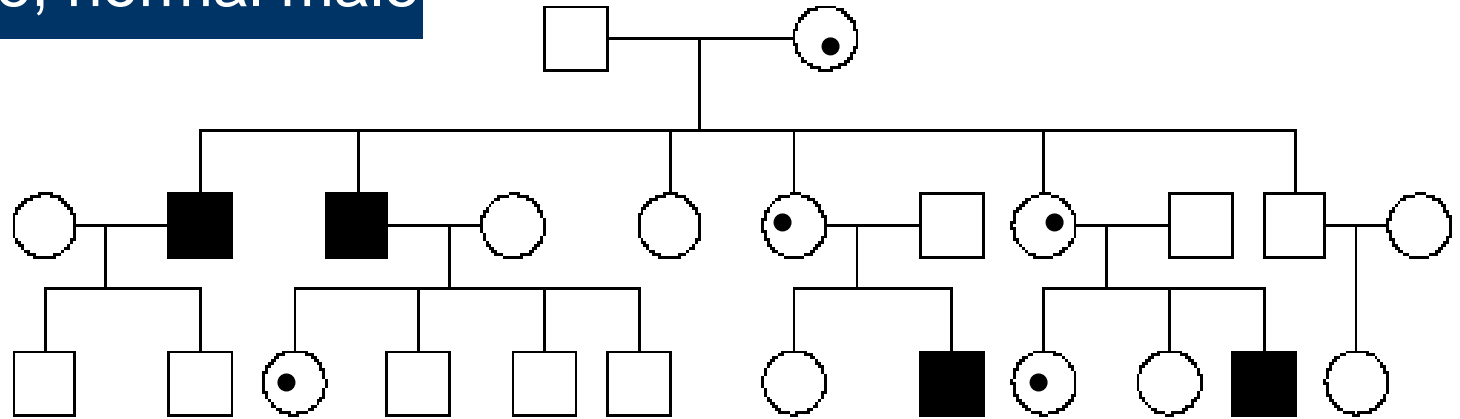


Elliptocytosis

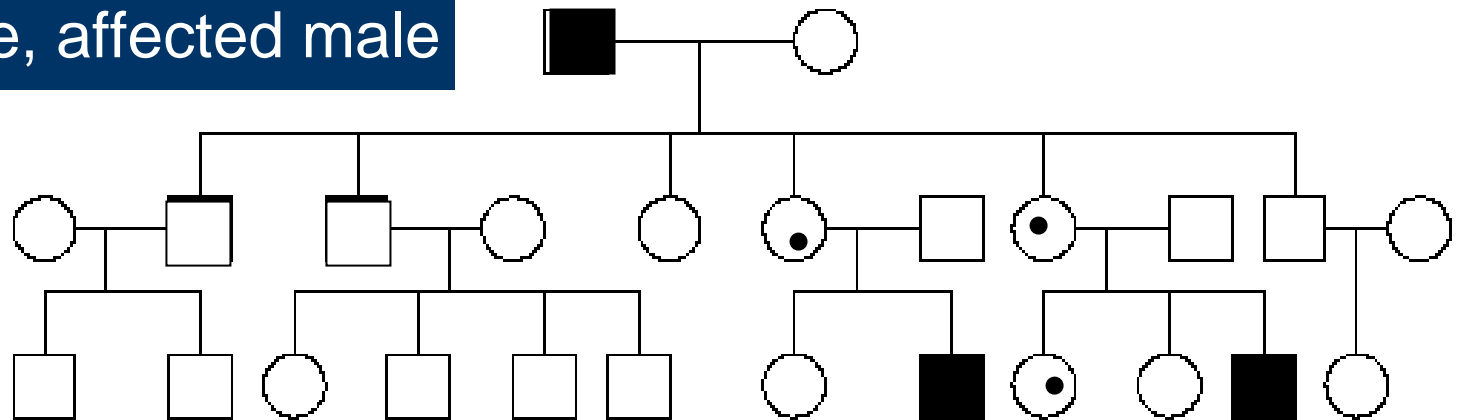


X-linked Recessive Disorders

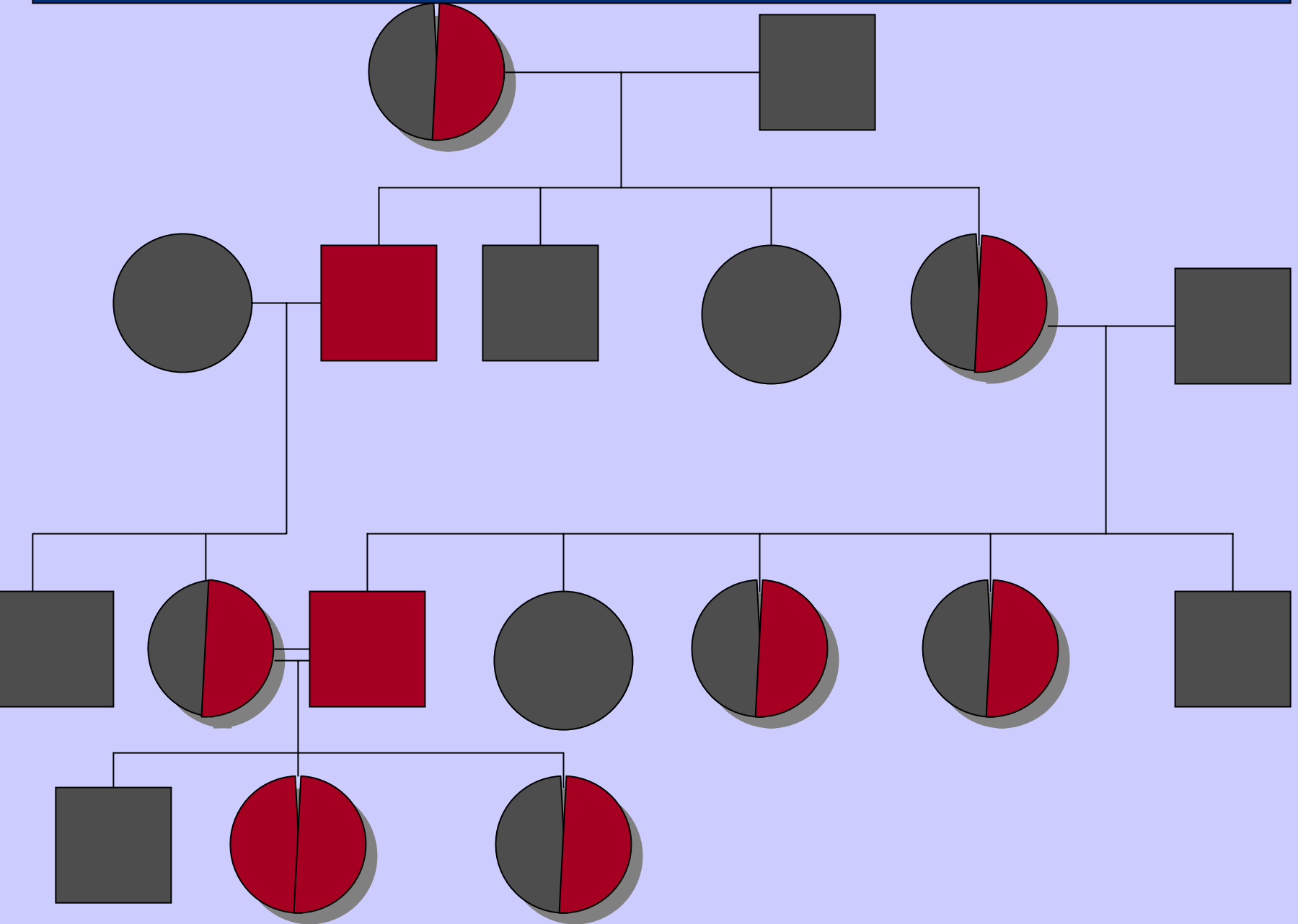
Carrier female, normal male



Normal female, affected male



A typical Family Tree in a family with XR disorder





Genetic anaemias in Saudi Arabia

Polymorphic

- Haemoglobinopathies:
 - Structural
 - Hb S [AR]
 - Biosynthetic
 - Thalassaemias (α and β) [AR]
 - Enzymopathies
 - G-6-PD deficiency [XR]

Non-polymorphic (Rare)

- Hb E [AR]
- Hb C [AR]
- Hb Riyadh [AR]
- Hb O-Arab [AR]
- Hb D-Punjab [AR]
- Hb Riyadh [AR]
- Hb F Dammam [AR]
- Hereditary spherocytosis [AD]
- Hereditary elliptocytosis [AD]
- Hereditary pyropoikilocytosis [AD]
- PK, HK deficiency [AR]

Conclusions

- Consanguinity occurs at a **high frequency** in many parts of the world and has been practiced for generations
- Despite its advantages e.g marriage stability, the **disadvantages** have serious consequences i.e. expression of **rare genetic disorders**
- **Rare disorders are more frequently seen in endogamous cultures**
- Islam does not prohibit consanguinity, however **Prophet Mohammed's (PBUH) recommendation needs to be followed** to avoid development of homozygous states of genetic disorders
- **Pre-marital screening** may help for some diseases.