Medical Genetics

Genetic counseling

Lecture Objectives

By the end of this lecture, students should be able to:

1. understand the principle steps of **genetic counseling.**
2. understand unique features of genetic counseling in **Arabic/Islamic communities**.
3. be familiar with the general application of Hardy-Weinberg principle

Definition of Genetic Counseling

A process of communication and education which addresses concerns related to the development and/or transmission of a hereditary disorder

A communication between doctors and parents to know the recurrent risks for next children.

Essential Components of Genetic Counselling

Diagnosis

It's the primary goal

Risk Assessment

Know if the disease is dominant, recessive, or X/Y linked

Communication

Using easy terms (not medical) so people would understand + make a blueprint

Discussion of options

e.g: PGD (Preimplantation genetic diagnosis)

Long term contact & support

Follow up with the doctor

Where do GCs work?

GC: genetic counseling

- **Majority of genetic counselors work at:**
  - University medical centers
  - Private or public hospitals
- **Some genetic counselors:**
  - Work in laboratories
  - Coordinate research studies
  - Are employed by the state
  - Work in private industry

Steps in Genetic Counseling

1. Diagnosis: based on accurate family history, medical history, examination and investigation
2. Risk assessment
3. Communication
4. Discussion of options
5. Long-term contact and support

General Rules

1- seeks genetic counseling

Consultant ⇄ **Counselor**

strong communication & support

2- Information to understand

1. The diagnosis, prognosis, & possible treatment
2. The mode of inheritance & the risk of developing/transmitting
3. The choices/options available

3- Reach their own fully informed decisions without pressure or stress

Establishing the Diagnosis

1. History:
   - detailed information about the patient's family history (3-generations family tree)
2. Examination
3. Investigation:
   - chromosome and molecular studies
   - referral to specialists in other fields (e.g. neurology and ophthalmology)

Expanding the pedigree (family history) is helpful to get more accurate diagnosis (a good pedigree is the key to genetic study)

Difference between examination and investigation:
Examination→ physically examining the patient
Investigation→ e.g look at the pathology report, blood test…

Calculating and presenting the risk

Calculating by Punnet's square then give percentages of risks

Calculation of the recurrence risk:

Can be ***straightforward*** (Mendelian inheritance)

Or..Can be ***much more complex***, due to many factors, for example:

delayed age of onset

3- Communication

"Be Consistent & clear to avoid confusion"

- Example: There is a risk of 1 in 4 to have affected child; that means:
  - 25% chance to get an affected child

    25% chance in each pregnancy

  - Genes are made up of DNA molecules, which are the simplest building blocks of heredity.
  - They're grouped together in specific patterns within a person's chromosomes, forming the unique "blueprint" for every physical and biological characteristic of that person

Emphasize that a risk applies to *each* pregnancy

"Chance does not have a memory"

A couple has just had a child with an autosomal recessive disorder (recurrence risk equals 1 in 4)

That means that:

✗*A*- their next three children will be unaffected

√*B*- Each of their future children will have a recurrence risk of 1 in 4

Emphasize the good side of the coin

"Genetic counselors should not be seen exclusively as prophets of doom"

If a couple is faced with a probability of 1 in 25 that their next baby will have a neural tube defect, the counselor should tell them that:

✗ *A*- there 1 chance out of 25 that their next baby will be affected

√ *B*- there are 24 chances out of 25 that their next baby will **not be affected**

Discussing the Options

For example, ***if relevant***:

1- the availability of prenatal diagnosis
   - details of the techniques
   - limitations
   - associated risks
2- other reproductive options

should be brought up with great care and sensitivity

technically feasible & legally permissible

Communication and Support

Communication is a two-way process

As a genetic counselor, be ready to:

- Listen
- Present information in a clear, sympathetic **and appropriate manner**
- **take into account the complex psychological and emotional factors**
- **Offer an opportunity for further discussion and long-term support**
- **Create a network of genetic nurse counselors keeping genetic registers**
- **Offer contact with "Patient support groups"**

Unique features of genetic counseling in Arabic/Islamic communities.

- Consanguineous marriage is customary in the Middle East and parts of South Asia including Indo-Pak.

Population of children studied*	% of parents related	Prevalence of recessive disorders
Northern European	0.4	0.28%
British Pakistani	69	3.0 -3.3%

* Oxford Handbook of Genetics, Guy Bradly-Smith, Sally Hope, Helen Firch, Jane Hurst, Oxford Univ, 2010

Proportion of nuclear genes shared as a function of degree of relationship

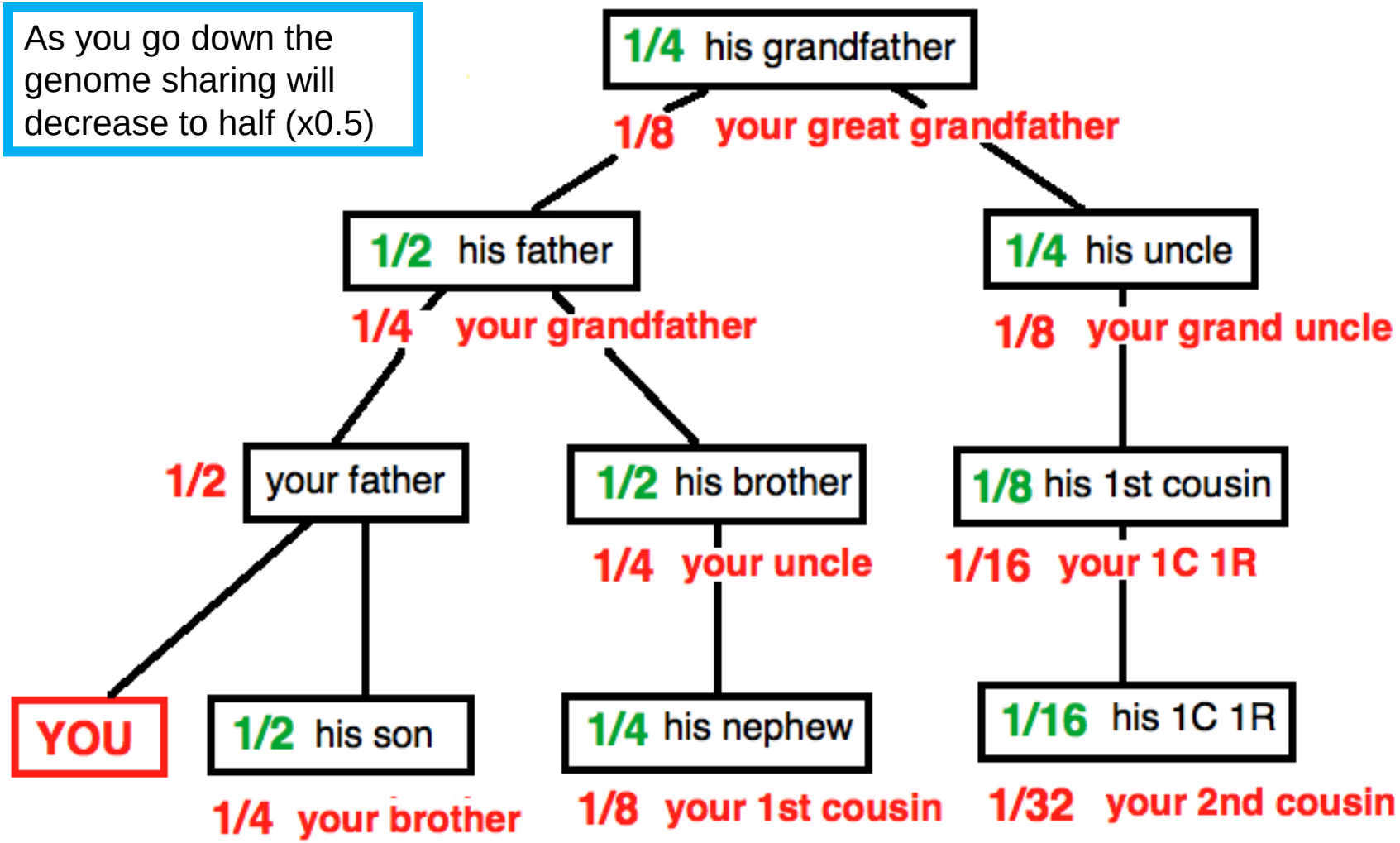
Relationship	Proportion of nuclear genes shared
Monozygotic twins	1 (100%)
1st –degree relatives (siblings, parent:child, dizygotic twins)	1/2 (50%)
2nd –degree relatives (half-sibs, double 1st cousins, uncle/aunt:nephew/niece)	1/4 (25%)
3rd –degree relatives (1st cousins, half-uncle/aunt:nephew/niece)	1/8 (12.5%)

Definitions:

Monozygotic: a single fertilized egg will separate to two

Dizygotic: 2 eggs are fertilized

As you go down the genome sharing will decrease to half (x0.5)



While Discussing the Options

The availability of prenatal diagnosis & other reproductive option should be:

- Brought up with great care and sensitivity
- Religiously & legally permissible
- Technically feasible

The frequency of alleles

Hardy-Weinberg principle

A mathematical process to calculate the allele frequency in a population

- Predicts how gene frequencies will be inherited from generation to generation given a specific set of assumptions.
- The Hardy-Weinberg principle states that in a large randomly breeding population, allelic frequencies will remain the same from generation to generation assuming that there is no mutation, gene migration, selection or genetic drift.

The Hardy-Weinberg Principle

- Mathematical relationship between allele frequencies and genotype frequencies
- The ***frequency of genotypes*** between individual mating can be predicted using the ***Punnett square***
- The frequency of particular ***alleles*** based on frequency of a phenotype within a population can be calculated by the ***Hardy-Weinberg principle***

Hardy-Weinberg principle
$p^2 + 2pq + q^2 = 1$

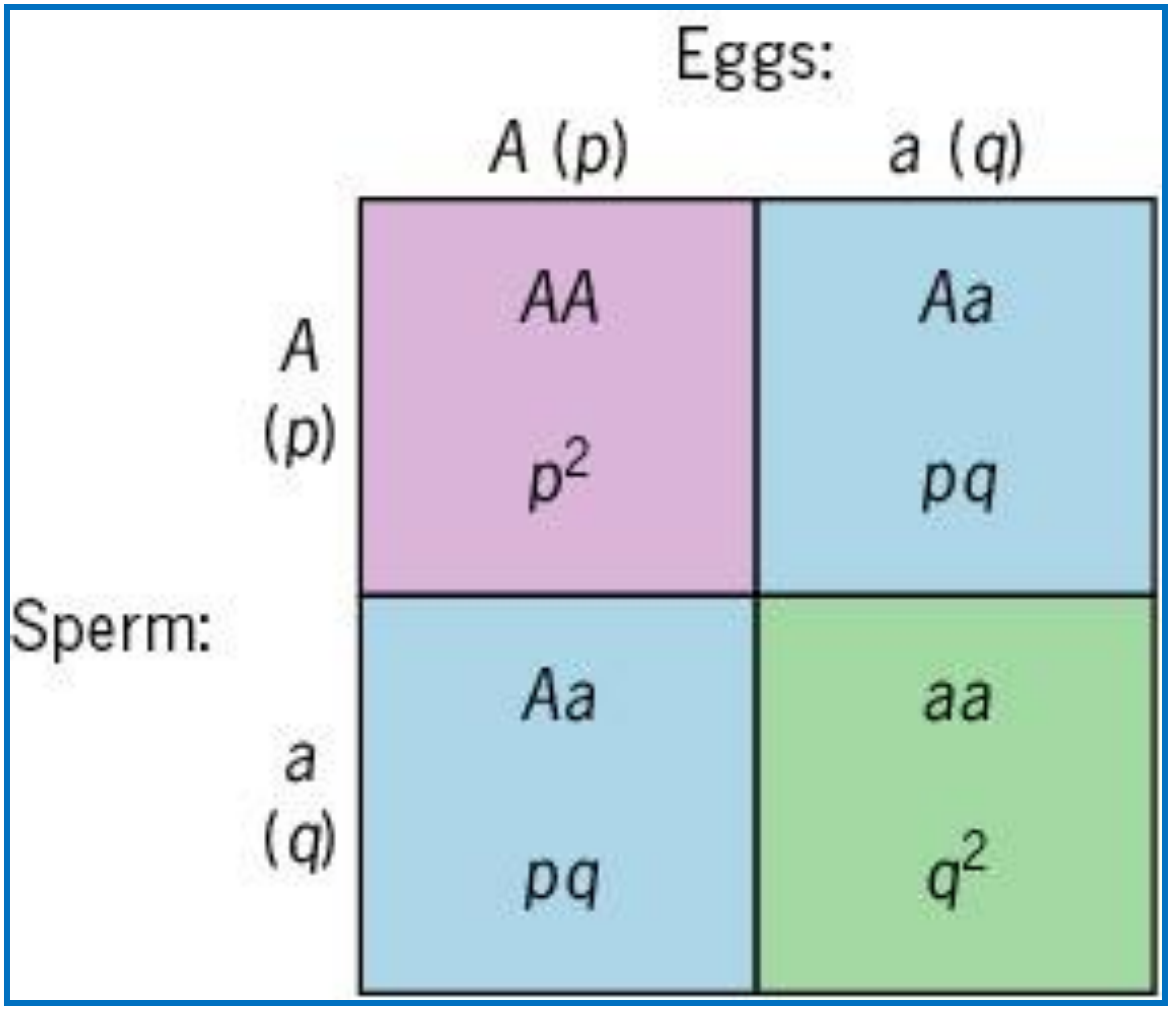
- For normal allele (A) : the frequency in the population is p
- For the mutant allele (a): the frequency in the population is q
- Because there are assumed to be only 2 alleles, p + q = 1

50% p , 50% q

- The frequency of:
  - the homozygote AA = p^2
  - the heterozygote Aa = 2pq
  - the mutant homozygote aa = q^2

	p	q
p	pxp	pxq
q	pxq	qxq

General Result



$p^2 + 2pq + q^2$

For a population to be in Hardy-Weinberg equilibrium, the following conditions must be met:

1. Random mating
2. Constant mutation rates
3. Large population sizes
4. Absence of migration

Take home message

- Genetic counseling is a communication process that deals with the risk of developing or transmitting a genetic disorder
- The most important steps in genetic counseling are diagnosis, estimation of a recurrence risk, communication of relevant information and the provision of long-term support.
- Genetic counseling should be non-directive and the genetic counselor should be non-judgmental
- The goal of genetic counseling is to provide accurate information that enables counselees to make their own fully informed decisions .

Take home message

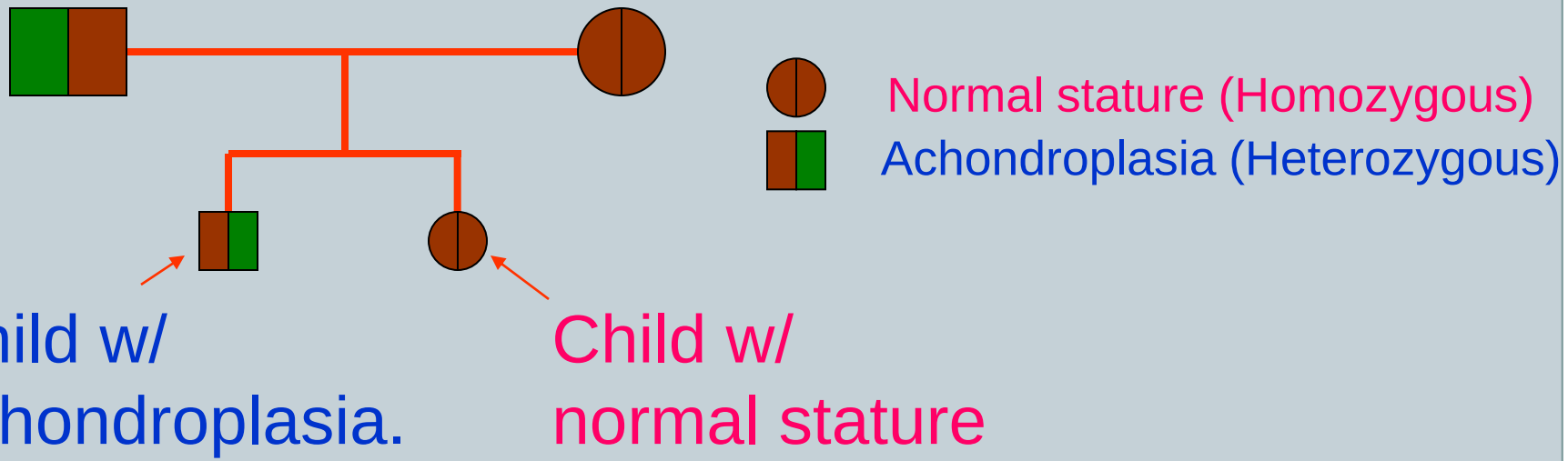
- Marriage between blood relatives conveys an increased risk for an autosomal recessive disorder in future offspring
- The frequency of particular alleles can be calculated by the Hardy-Weinberg principle

Genetic Counseling in Achondroplasia

- It is inherited in an AD manner.
- Homozygous achondroplasia is a lethal condition.
- > 80% of achondroplasia cases have parents with normal stature i.e.: **new gene mutation**.
- Such parents have a low risk of having another child with achondroplasia.
- Prenatal molecular genetic testing is available.

Genetic Counseling - Case

An individual with achondroplasia who has a reproductive partner with normal stature has a 50% risk in each pregnancy of having a child with achondroplasia.



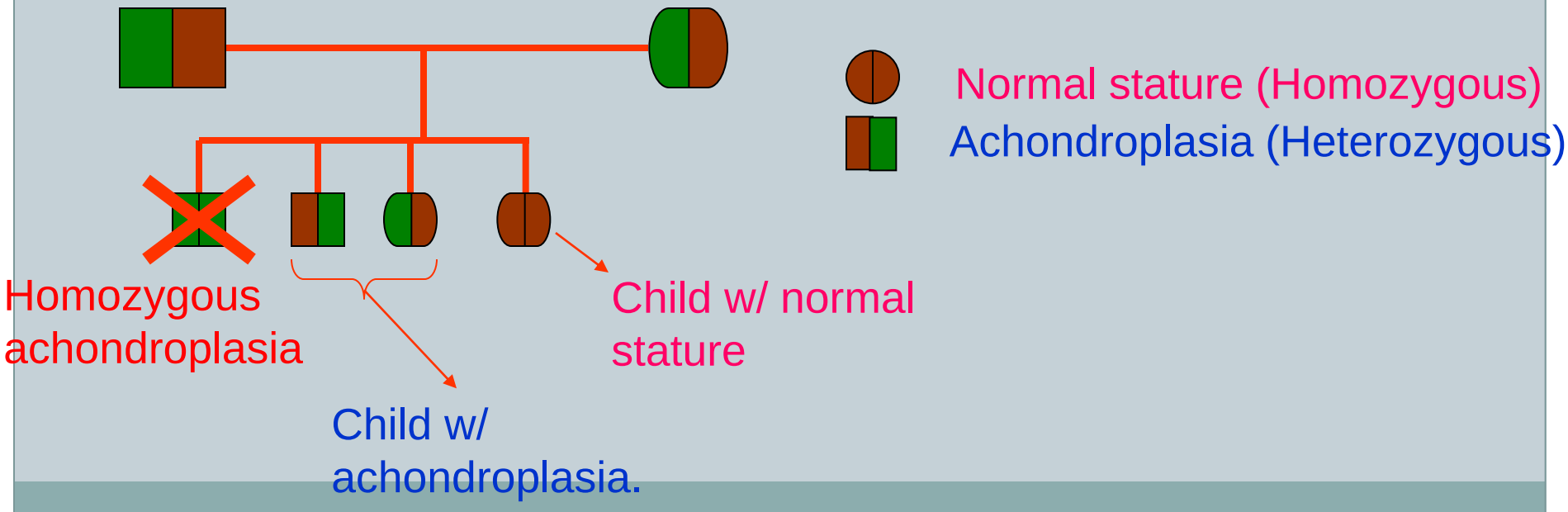
Genetic Counseling - Case

When both parents have achondroplasia, the risk to their offspring of having:

- normal stature: 25%

- achondroplasia: 50%

- homozygous achondroplasia (lethal): 25%



Thank you