

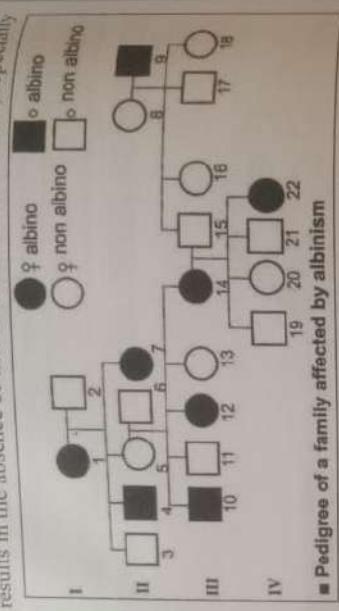
Patin & Gauthier

Albinism

Question 1-

Albinism is a hereditary abnormality that results in the absence of the melanin in the skin cells, especially in the cells of hair root.

The adjacent document presents the pedigree of a family in which some of its members shown in black are affected. 1- Is the allele of the abnormality dominant or recessive? Justify your answer.



2- Discuss logically the chromosomal localization of the gene responsible for albinism.

We study individual (individuals, P<sub>n</sub> bases), P follows:

Most Q requires takes place

At birth, In an example taken from the table

3- Woman 22 marries an albino man, her family predicts that all her children will be albino. Is this prediction compatible with the answer of question a? Justify.

4- Based deduce th

In order -22 acco

Woman 22 gave birth to a non-albino girl Ghada. To eliminate any doubt that the albino man is not the real father of Ghada, we determine the blood groups: Abo. & Rhesus of Ghada & her parents, the father is of blood group [o, Rh+], the mother is of blood group [B, Rh-] & their daughter is of group [o, Rh-].

N.B The allele of Rh<sup>+</sup> dominates the allele of Rh<sup>-</sup>.

4- After a logical reasoning of the obtained results concerning the blood groups & taking into consideration the non-albino phenotype of Ghada, can we confirm that Ghada is the daughter of this couple? Justify the answer.

5- Formulate a hypothesis to explain the non-albino phenotype of Ghada.

Question N°

Lesch-Nyhan Lesch-Nyhan This disease Doc-1 pre has some affected b 1- Is the dominant

discuss 2- Discuss

localizatio 3- Are tw

twins? Ju

We study individual (individuals, P<sub>n</sub> bases), P follows:

Most Q requires takes place

At birth, In an example taken from the table

4- Based deduce th

In order -22 acco

DNA or test C<sub>4a</sub> ④

Naurogy

bio

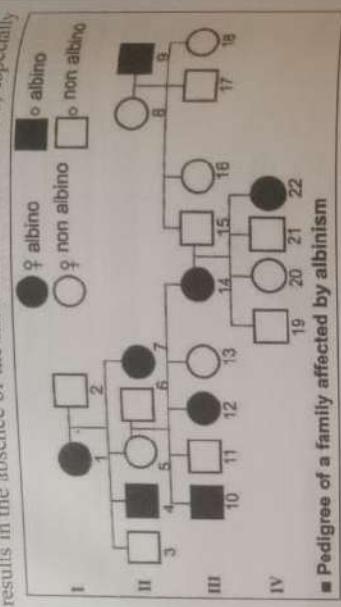
Patin de Génétique

Albinism

Question 1-

Albinism is a hereditary abnormality that results in the absence of the melanin in the skin cells, especially in the cells of hair root.

The adjacent document presents the pedigree of a family in which some of its members shown in black are affected. 1- Is the allele of the abnormality dominant or recessive? Justify your answer.



2- Discuss logically the chromosomal localization of the gene responsible for albinism.

We study individual (individuals, P<sub>n</sub> bases). P follows:

Most Q requires takes place

At birth, In an example taken from the table

3- Woman 22 marries an albino man, her family predicts that all her children will be albino. Is this prediction compatible with the answer of question a? Justify.

4- Based deduce th

In order -22 acco

Woman 22 gave birth to a non-albino girl Ghada. To eliminate any doubt that the albino man is not the real father of Ghada, we determine the blood groups: Abo. & Rhesus of Ghada & her parents, the father is of blood group [o, Rh+], the mother is of blood group [B, Rh-] & their daughter is of group [o, Rh-].

N.B The allele of Rh<sup>+</sup> dominates the allele of Rh<sup>-</sup>.

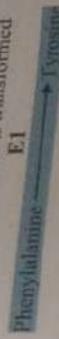
4- After a logical reasoning of the obtained results concerning the blood groups & taking into consideration the non-albino phenotype of Ghada, can we confirm that Ghada is the daughter of this couple? Justify the answer.

DNA  
or a  
test  
Car  
④

5- Formulate a hypothesis to explain the non-albino phenotype of Ghada.

**Question 14****Phynylketonuria**

Phenylketonuria is a hereditary metabolic disease characterized by mental retardation of an amino acid: phenylalanine. In the normal individual, the amino acid phenylalanine is transformed into tyrosine under the effect of an enzyme E1 as indicated below:



1. Formulate a hypothesis concerning the origin of this disease.

The following document shows a portion of mRNA which is responsible for the synthesis of the E1 in the normal person & abnormal one.

**Portion of mRNA responsible for the synthesis of E1 in the normal person:**

... UAU ACC CCC GAA CCU GAC AUC CUU GCC UCU

**Portion of mRNA responsible for the synthesis of E1 in the abnormal person:**

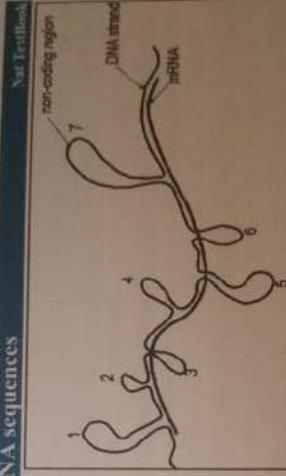
... UAU ACC CCC AAA CCU GAC AUC CUU GCC UCU

2. By the help of the genetic code table, write down the sequence of amino acid for each portion.
3. Compare the sequence of mRNA and amino acids between the normal & abnormal person.
4. Verify if the hypothesis is validated.

**Question 15-****Coding & noncoding DNA sequences**

The next document is obtained by using a synthesis radioactive mRNA and the corresponding DNA strand, in the case of certain proteins.

1. Using your acquired knowledge, explain the back loops of DNA observed.
2. Certain gene mutations have no effect on the phenotypic expression; formulate a hypothesis to explain such a result.

**Question 16:**

In a book entitled "artisans of heredity", one author wrote: "Protein synthesis is not made directly from the manual instruction but remotely from a copy of the concerned instruction".

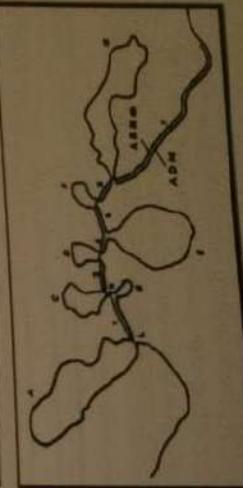
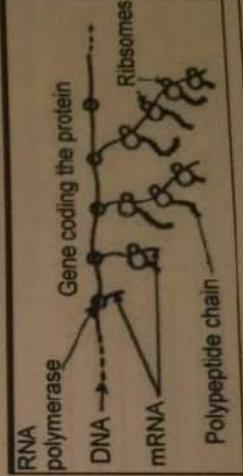
1. Justify the following statements "instruction manual" and "copy this instruction".

**Document 1 shows the activity of a bacterial gene:**

2. Name the protein synthesis stage observed.

Document 1 shows an experiment of molecular hybridization between eukaryotic gene coding for the ovalbumin protein and mRNA of ovalbumin.

3. Give the significance revealed from the organization of this gene.
4. Referring to document 2 and your acquired knowledge, represent schematically the steps of expression of the gene coding for ovalbumin.

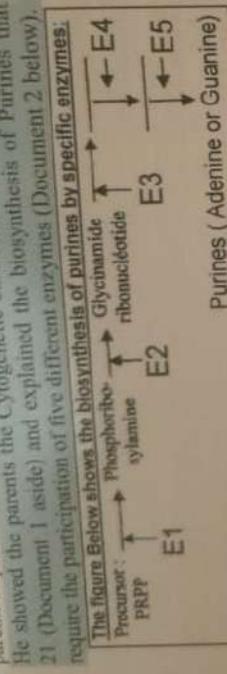


**Serious Metabolic Disease and Prenatal Diagnosis.****Question 1-11-**

**Part-A:** Corentin, son of Alan and Beatrix, presents a serious mental retardation since birth. The couple is expecting a second child and wants to know if there is a risk for the fetus to be affected also.

The doctor, based on clinical symptoms of Corentin, suspected a certain anomaly. He had to do certain tests to verify his suspicion and upon the parents request, he explained the biochemical origin of this anomaly. He showed the parents the Cytogenetic card of a normal chromosome 21 (Document 1 aside) and explained the biosynthesis of purines that require the participation of five different enzymes (Document 2 below).

The figure Below shows the biosynthesis of purines by specific enzymes.

**Document 3**

| Mental activity | Number of fragments 21q22.1 | Activity of E2 enzyme (a.u) | Blood rate of purines (mmole/l) |
|-----------------|-----------------------------|-----------------------------|---------------------------------|
| Normal          | 2                           | 100                         | 79                              |
| Retardation     | 3                           | 150                         | 118.5                           |

He also showed them blood dosages performed on individuals differing by their mental activity according to the number of copies of the fragment 21q22.1 in the pair of chromosomes no 21. (Document 3)

1- Compare the results of the normal individual and the individual suffering from mental retardation (document-3), and then draw out the cause of mental retardation observed in affected individuals.

2. Formulate a hypothesis concerning the locus of the gene responsible for the synthesis of enzyme-E2.

DNA extraction is performed from cells taken from Alan, Beatrix, their son Corentin and from the Ira cells. Each sample is submitted to the action of restriction enzymes; the obtained DNA fragments are separated by electrophoresis. The radioactive DNA probe used is able to hybridize specifically a genetic marker found under several different allelic forms and whose locus is closely linked to that of "Gart" gene which is located on fragment (21q 22.1) of chromosome 21. Document 4 represents the results obtained after autoradiography.

- 3- Indicate the method that must be used to extract fetal cells knowing that the mother is in the tenth week of gestation.
- 4- Deduce the cause of the mental retardation of Corentin.

- 5- Specify whether the fetus will suffer from mental retardation.

- 6- Name a test that could be used to further confirm the cause of Corentin's disease.

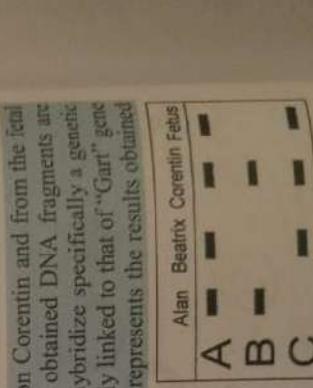
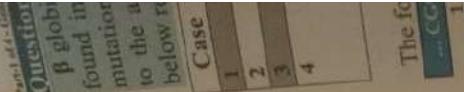
**Part-B- Document 5: Cellular cultures.**

**Culture-1:** The neurons degenerate when they are cultured in a medium enriched in purines.

**Culture-2:** The cells of mice CHO have lost the capacity to synthesize purines, due to the fact that a gene homologous to the human gene coding for enzyme E2 is inactive. In a medium deprived of purines, cells of mice CHO degenerate.

**Culture-3:** Hybridomes, resulting from the hybridization of human cells and CHO mice cells, are cultured in a medium deprived of purines. Some of them lose spontaneously the human chromosome 21 and can survive in the medium deprived of purines.

7- Interpret each of the results of the cellular cultures and then conclude the causes of the disease.



Part I - Case Studies  
**Question-2**  
 We are interested in events that accompany reproduction at the molecular level. Female rabbits mate with males in order to produce sperm cells that will fertilize eggs in the genital tract of the female rabbit. One event that was observed under our microscope was the removal of the testes from a male rabbit.

Document 1 shows two main aspects of spermatogenesis where the testes were removed.

1. Explain the aspect V

2. Determine

Document 2 shows that of the three populations of germ cells, the first population is the largest in Mr. Z.

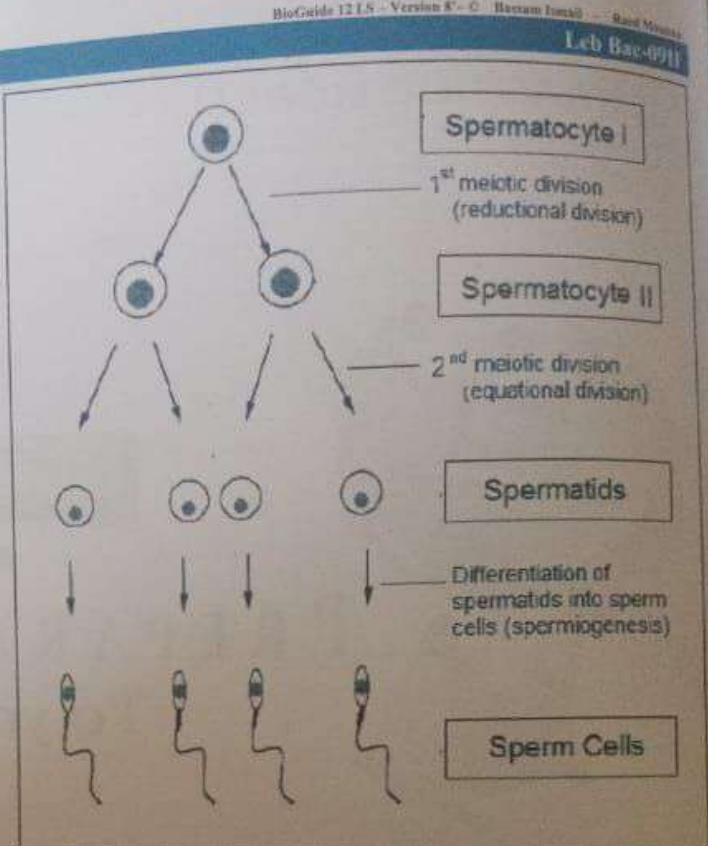
Document 3 shows a drawing of a sperm cell.

#### Part I - Case Studies

**Question-1- A Case of Sterility**  
 Mr. X and Mr. Y are two adult sterile men. We perform different tests to specify the origin of this defect.

Document 1 shows certain stages of spermatogenesis. The germ cells, whose names are framed in boxes, are found in the wall of the seminiferous tubules.

- 1- Describe the different stages of spermatogenesis represented in document 1.



We perform a quantitative study for the amount of DNA of the germ cells extracted directly, by biopsy, from a fragment of the testicles of these two sterile men and that of a fertile man Mr. Z.

3 different populations of germ cells are obtained. The number of each cell population, as well as the amount of DNA in each of them is shown in doc 2.

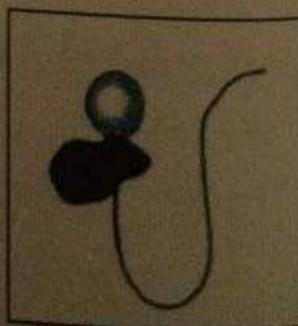
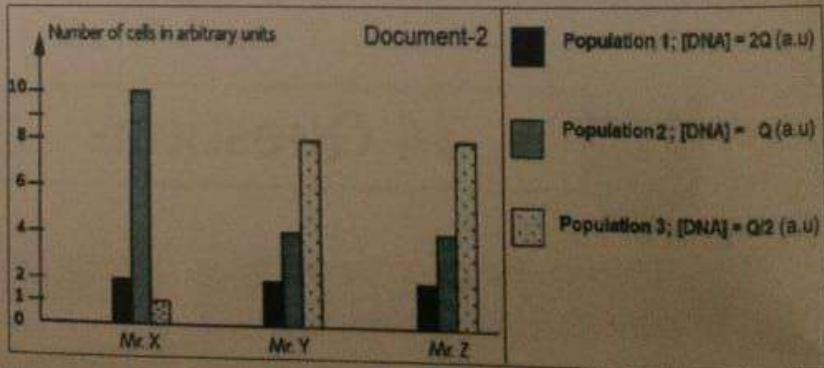
- 2- Indicate the germ cells corresponding to each of the three populations shown in document-2. Justify.

- 3- Explain the variation of the number of germ cells of the three populations in the fertile man Mr. Z.

- 4- Determine, by referring to document 2, the cause of sterility of Mr. X.

Microscopic observations of the semen of Mr. Y showed sperm cells, where the majority of these cells showed an aspect identical to that schematized in doc 3.

- 5- Explain the origin of the sterility of Mr. Y.



**Document 3**

### Reproduction and Male Fertility

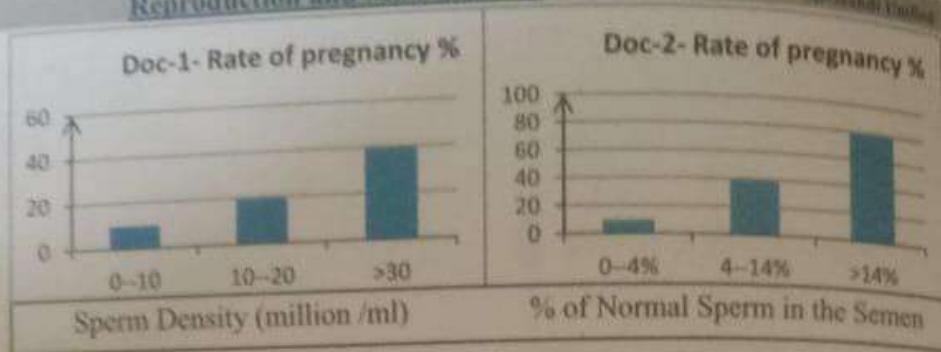
Biofinals 12 U.S - Version E. ©. Review French - Biofrench

Al-Maktabat

#### Question-28-

Document 1 represents the results of 2 studies which are performed to determine the factors affecting the male infertility.

(The pregnancy rate reflects the rate of male fertility).



1- 1-1. Analyze the obtained results.

1-2. Draw out the factors which affect the male infertility.

In men there are several known risk factors for infertility: medications, long term alcohol use, smoking, environmental exposure to chemicals and heat such as saunas....note that if the sperm density in men is between 5 and 10 million/ml, the men are more likely to have male infertility that can be healed by staying away of its causes.

**Doc 2**

- Mrs. Z. which was trying hard to have a baby but with no result. All the tests indicated that she is normal. The sperm test of Mr. Z which is a chemist shows that its sperm density is around 12 million/ml.

2-1- Identify, using documents 1 & 2, the cause of absence of pregnancy for Mrs.Z.

2-2- Propose a solution for the problem of family Z.

For another couple Y: Mrs. Y is exposed to spontaneous abortion after each pregnancy. To identify the problem, the doctor performed a karyotype of the aborted embryo; document 3 represents the obtained karyotype.

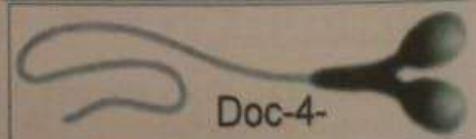
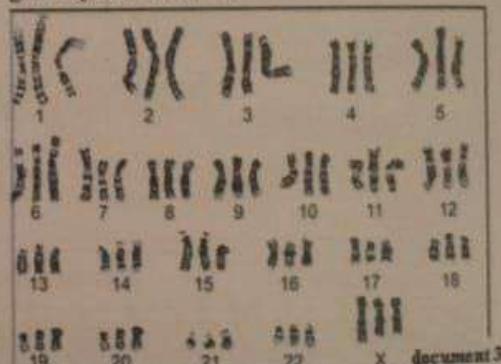
3- Indicate the chromosomal formula for this karyotype.

4- Indicate the abnormality that is revealed by this karyotype.

5- Formulate 2 hypotheses that explain the origin of such abnormality.

- In order to find the real cause of the abnormality shown by the embryonic cell, we observe under microscope the sperm cells of the father Y: we notice that they almost have the aspect represented in document 4:

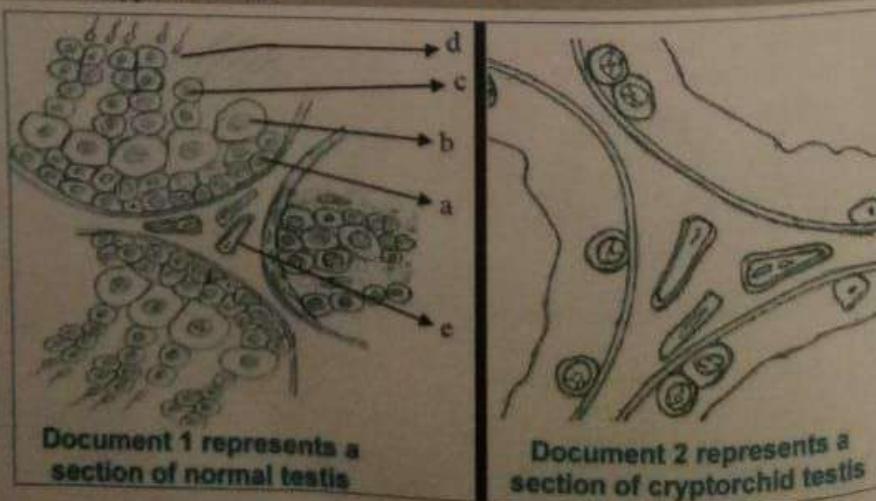
6- Draw out from document 4, the real cause of the abnormality that has led to the abortion of the embryo.



#### Question-29-

Cryptorchidism is an anomaly that affects males of mammals (especially humans) reaching adulthood if their testes were developed in the abdominal cavity instead migrate into the scrotum (or scrota). It locates outside abdomen. Some secondary sexual characteristics are manifested in a cryptorchid but it is sterile.

### Cryptorchidism

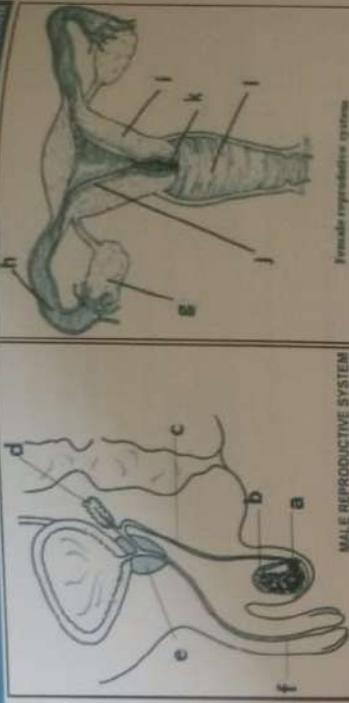


### Sterility

#### Question -25-

Reproduction is the process that ensures the survival of species. Sexual reproduction involves two individuals of opposite sexes and belonging to the same species. It necessitates the presence of a specialized and organized reproductive system.

Documents (1 & 2) represent the male & female human reproductive systems.



- 1-1. Label documents 1 and 2 (from a to l).

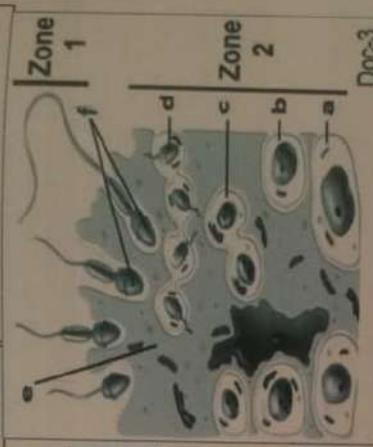
- 1-2. State the function of organs a-c-d-h.

- 2- A section of a seminiferous tubule present inside organ (a) was viewed under the microscope. Document 3 shows a detailed view of this section.

- 2-1. Name the process revealed in this figure.

- 2-2. Draw a table that shows the name of the cells a-b-c-d-e-f, the number of chr / cell & whether the chromosome is made up of 1 or 2 chromatids.

Two cells were taken from cells of document 3 & karyotyped. The results are shown in documents 4 & 5.



Doc3

|    | Document 5 |   |   |   |   |   |   |
|----|------------|---|---|---|---|---|---|
| 6  | X          | X | X | X | X | X | X |
| 7  | -          | - | - | - | - | - | - |
| 8  | -          | - | - | - | - | - | - |
| 9  | -          | - | - | - | - | - | - |
| 10 | -          | - | - | - | - | - | - |
| 11 | -          | - | - | - | - | - | - |
| 12 | -          | - | - | - | - | - | - |

Document 4



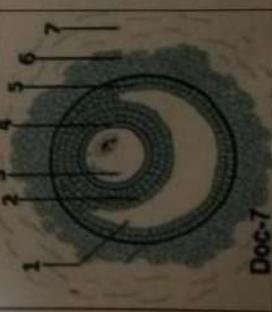
Document 6

Doc-7 represents detailed schematic drawing of structure (e) in doc-6

4-3. Label document 5 (1 to 7).

4-4. Schematize oogenesis. Given  $2n=6$ . (Chr 2, 12 & sex chr).

4-5. Draw a table that shows the different cells involved in oogenesis & the number of chr in the nucleus of each cell and the number of chromatids per chr.



Doc-7

Document 6 represents structures observed in a cross section of organ g in document 2.

- 4-1. Name structures (a-b- c- d- e).

- 4-2. Name event X.

- part 1 of 1 : Questions
- Name the phenomenon that occurs in doc 1; at what age begins & when it stops.
  - Label the structures a to c.
  - Compare documents 1 & 2.
  - Using docs 1, 2 & your knowledge, explain why a cryptorchid is sterile, but it may develop secondary sexual characteristics.

#### Semen analysis

**Question-30-** In a fertility clinic 4 males performed semen analysis the results are shown in the documents below:

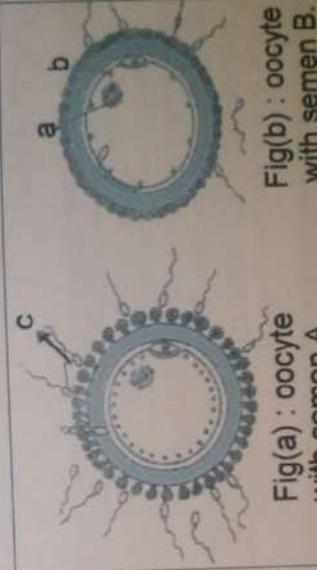
|  |           | Document-1 | Forward progression towards oocyte | % Motility | Morphology of sperm cells | Number of sperm cells       |
|--|-----------|------------|------------------------------------|------------|---------------------------|-----------------------------|
|  | Fertility | > 60%      | Present                            | > 50%      | > 30% Normal              | > 40 million/ml             |
|  |           | < 30%      | Not present                        | < 30%      | Between 20 to 65% Normal  | Between 10 to 12 million/ml |

**Male (B) is infertile, document (2) shows the semen analysis as recorded in the clinic:**

|  |           | Document-2 | Forward Progression towards oocyte | % Motility | Morphology of sperm cells | Number of sperm cells |
|--|-----------|------------|------------------------------------|------------|---------------------------|-----------------------|
|  | Fertility |            |                                    |            |                           |                       |

1- Compare the semen of males A & B.

A medical team in this clinic had done in vitro experiments to study the medical case of male (B). They brought healthy oocytes blocked at metaphase 2 of meiosis and place them with the semen of (A) and with the semen of B as in Fig(a) and Fig(b) respectively.



The results of observation of the two experiments are recorded in the following document 3 as seen below:

**Doc-3- Figure (a)**

|                                                       |                                                   |
|-------------------------------------------------------|---------------------------------------------------|
| Efficiency of movement and fertilization is 70%       | Efficiency of movement and fertilization is null. |
| Forward progression towards the oocyte is 70%         | Forward progression towards the oocyte is null.   |
| Hyperactive sperms                                    | Hypoactive sperms                                 |
| Presence of protein called cathepsin in the flagellum | Absence of this protein in the flagellum.         |

**2- After analyzing Figures a & b, conclude the cause of infertility of male (B) & the role of protein cathepsin.**

**3- Referring to your knowledge, indicate the changes that follow Fig(a) at the level of oocyte & spermatozoon.**

**4- Label a, b, and c (of Fig. a and b).**

**Male (C) is infertile the following document represents the results of semen analysis.**

|  |           | Doc-4- Forward Progression towards oocyte | % Motility     | Morphology of sperm cells | Number of sperm cells                                             |
|--|-----------|-------------------------------------------|----------------|---------------------------|-------------------------------------------------------------------|
|  | Fertility | < 30%                                     | Slightly found | < 30% moves normally      | < 30% normal sperms<br>Presence of sperms with two heads normally |

**5- What hypothesis you can formulate concerning the cause of infertility of male(C).**

**6- Explain, by referring to spermatogenesis, how would the abnormal sperm cells (with 2 heads) of male (C) be formed.**

**Male (D) is exposed to vasectomy, the vas deferens on each side is sectioned and the cut ends are tied thus preventing the release of spermatozoon from testes. The results of the semen test are recorded in document 5.**

|  |           | Doc-5- Forward Progression towards oocyte | % Motility | Morphology of sperm cells | Number of sperm cells |
|--|-----------|-------------------------------------------|------------|---------------------------|-----------------------|
|  | Fertility | 0                                         | 0          | 0                         | 0                     |

**7- Explain why there is no sperm in the semen (document 5) knowing that the semen is ejected.**

## Transmission of hereditary characteristics in Drosophila

### First Cross

|                                              |          |                                             |
|----------------------------------------------|----------|---------------------------------------------|
| <p>Females F1<br/>Gray body<br/>Red eyes</p> | <b>X</b> | <p>Males<br/>Black body<br/>Purple eyes</p> |
|----------------------------------------------|----------|---------------------------------------------|

We obtain in F1 100% drosophilae having gray body, red eyes and well-formed wings.

- 1- Indicate the dominant allele and recessive allele for each of the studied genes.

### Second Cross

We perform, in drosophilae, two other experimental crosses 1 and 2, represented in the adjacent figures.

- 2- Name the type of the performed crosses.

- 3- Explain the results obtained in the first cross.

|                                                       |          |                                                |
|-------------------------------------------------------|----------|------------------------------------------------|
| <p>Females F1<br/>Gray body<br/>Well-formed wings</p> | <b>X</b> | <p>Males<br/>Black body<br/>Deformed wings</p> |
|-------------------------------------------------------|----------|------------------------------------------------|

|                                      |
|--------------------------------------|
| 4368 gray body and well-formed wings |
| 796 gray body and deformed wings     |
| 820 black body and well-formed wings |
| 4324 black body and deformed wings   |

The results of the two crosses put in evidence the existence of a certain type of genetic recombination during meiosis in female drosophila F1.

- 4- Name this type of genetic recombination and illustrate by explanatory schematic drawings the behavior of the corresponding chromosomes of the second cross.
- 5- Determine, by referring to the first and second crosses, whether the genes responsible for eye color and form of wings are linked or independent.
- 6- Calculate the percentage of recombination between the studied genes in each of the two crosses.

- 7- Knowing that the percentage of recombination between the genes of eye color and form of wings is 8%, establish a factorial map which reveals the location of the three studied genes on a chromosome.

**Question-1**

We propose to study certain particularities of sexual reproduction in mice. We measured the quantity of DNA present in different cells; the results are indicated in document-1.

| Cells of the mouse | Liver | Pancreas | Spermatogonium | Sperm |
|--------------------|-------|----------|----------------|-------|
| DNA quantity (pg)  | 6.2   | 6.2      | 6.2            | 3.1   |

- 1- Compare the obtained results. Name the biological phenomenon that is at the origin of the observed differences.

Geneticists crossed a mouse having curly hair & malformed eyes with a mouse having smooth hair & normal eyes, all the individuals of F1 have curly hair & normal eyes.

- 2- What can you conclude?

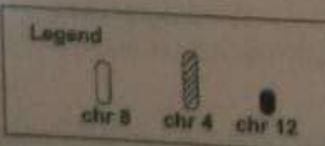
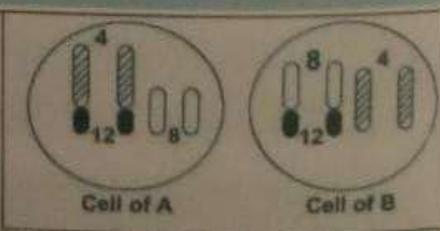
The results of the F2 issued from the self-cross F1 x F1 among themselves are the following:

42 mice with smooth hair & normal eyes.  
127 mice with curly hair & normal eyes.  
41 mice having curly hair & malformed eyes.  
14 mice with smooth hair & malformed eyes.

- 3- Calculate the phenotypic proportions of the F2 generation.

- 4- Make a chromosomal representation of the genotype of an individual of F1.
- 5- Specify the type of genetic recombination (assortment) responsible for the phenotypic proportions of F2.
- 6- Illustrate the genetic assortment which is responsible for producing the gametes by F1.
- 7- Make the necessary chromosomal factorial analysis to verify the phenotypic proportions obtained in F2.

Upon crossing mouse A with B, we obtain a hybrid individual AB of a normal phenotype yet their descendants may include individuals with trisomy.

**Document 2**

**N.B. Only the chromosomes 4, 8 and 12 are represented.**

- 8- By restricting only to chr 4, 8, & 12, schematize the chr of the gametes produced in each of the cells A & B of doc-2 as well as the chr of one cell of the hybrid mouse AB.

- 9- Schematize the chromosomes of the gametes produced by mouse AB & specify the abnormal gamete which is at the origin of producing an embryo with trisomy 12 after its fertilization with a normal gamete of mouse with non-attached chromosomes.

**Question-1**

We propose to study certain particularities of sexual reproduction in mice. We measured the quantity of DNA present in different cells; the results are indicated in document-1.

| Cells of the mouse | Liver | Pancreas | Spermatogonium | Sperm |
|--------------------|-------|----------|----------------|-------|
| DNA quantity (pg)  | 6.2   | 6.2      | 6.2            | 3.1   |

- 1- Compare the obtained results. Name the biological phenomenon that is at the origin of the observed differences.

Geneticists crossed a mouse having curly hair & malformed eyes with a mouse having smooth hair & normal eyes, all the individuals of F1 have curly hair & normal eyes.

- 2- What can you conclude?

The results of the F2 issued from the self-cross F1 x F1 among themselves are the following:

- 3- Calculate the phenotypic proportions of the F2 generation.

42 mice with smooth hair & normal eyes.  
127 mice with curly hair & normal eyes.

41 mice having curly hair & malformed eyes.  
14 mice with smooth hair & malformed eyes.

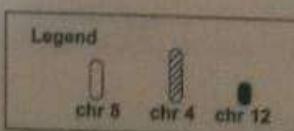
- 4- Make a chromosomal representation of the genotype of an individual of F1.

- 5- Specify the type of genetic recombination (assortment) responsible for the phenotypic proportions of F2.

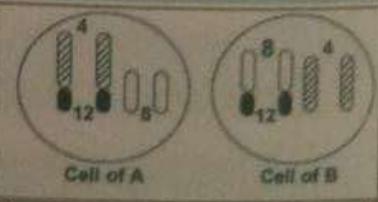
- 6- Illustrate the genetic assortment which is responsible for producing the gametes by F1.

- 7- Make the necessary chromosomal factorial analysis to verify the phenotypic proportions obtained in F2.

Upon crossing mouse A with B, we obtain a hybrid individual AB of a normal phenotype yet their descendants may include individuals with trisomy.



■ Document 2



N.B. Only the chromosomes 4, 8 and 12 are represented.

- 8- By restricting only to chr 4, 8, & 12, schematize the chr of the gametes produced in each of the cells A & B of doc-2 as well as the chr of one cell of the hybrid mouse AB.

- 9- Schematize the chromosomes of the gametes produced by mouse AB & specify the abnormal gamete which is at the origin of producing an embryo with trisomy 12 after its fertilization with a normal gamete of mouse with non-attached chromosomes.

**Question-31-**

Documents 1 and 2 represent the results of spermograms, of two owners of semen: one fertile (semen of Mr. X) and the other sterile (semen of Mr. Y).

**Doc-1- Spermogram of Mr.X**

| Mobility                                                                                                                                 | After 1hr | After 4hr | Properties                       |
|------------------------------------------------------------------------------------------------------------------------------------------|-----------|-----------|----------------------------------|
| % of normal mobility                                                                                                                     | 55        | 45        | Ejaculation volume : 4.2 ml      |
| % of decreased mobility                                                                                                                  | 5         | 5         | Viscosity : Normal / PH: 7.8     |
| % of immobile forms                                                                                                                      | 40        | 50        | Numeration: $53.10^6$ sperm / ml |
| Vitality: 88% of living forms (1 <sup>st</sup> hr) on 100 spermatozooids observed. It was noted : Typical Forms: 61% Atypical forms: 39% |           |           |                                  |

**Doc-2- Spermogram of Mr.Y**

| Mobility                                                                                                                                | After 1hr | After 4hr | Properties                      |
|-----------------------------------------------------------------------------------------------------------------------------------------|-----------|-----------|---------------------------------|
| % of normal mobility                                                                                                                    | 1         | 0         | Ejaculation volume : 0.8 ml     |
| % of decreased mobility                                                                                                                 | 6         | 0         | Viscosity : Normal / PH: 7.6    |
| % of immobile forms                                                                                                                     | 93        | 100       | Numeration: $2.10^6$ sperm / ml |
| Vitality: 8% of living forms (1 <sup>st</sup> hr) on 100 spermatozooids observed. It was noted : Typical Forms: 60% Atypical forms: 40% |           |           |                                 |

Vitality: 8% of living forms (1<sup>st</sup>hr) on 100 spermatozooids observed. It was noted : Typical Forms: 60% Atypical forms: 40%

- 1- Compare the two spermograms. Conclude the possible causes of the sterility of Mr. Y.
- 2- Mr. X cannot have children with Madam X. Formulate two hypotheses about the possible causes of the sterility of this couple.

In order to verify the hypothesis, the following studies were done:

- We extract some proteins from zona pellucida of oocytes of fertile mice then we mark them by a radioactive isotope, and then we put them in the presence of spermatozoa of fertile mouse. It is found that the radioactivity appears at the level of the external side of the cell membrane of sperm-head.
- We place these marked sperms in the presence of mature oocytes. There is no fertilization.
- Spermatozoa which have not been put in contact with these previous proteins are still able to fertilize.

3- What do these observations reveal?

**Question-32-**

Doc-1 shows the diagrams of three transverse & partial microscopic sections of an individual before puberty and two pubescent individuals one of which is normal & the other sterile.

1- Annotate the figure of section B.

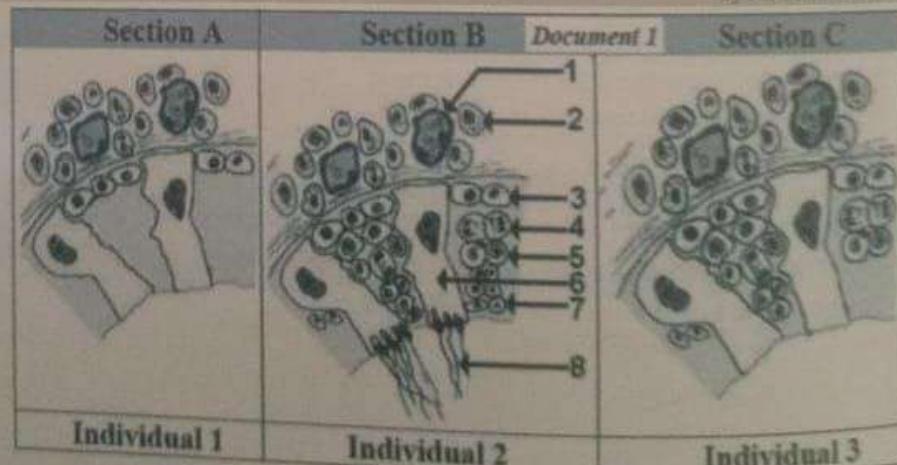
2- Compare the 3 sections.

3- Based on doc 1, specify which section belongs to the immature, sterile and the normal individuals.

4- Formulate a hypothesis explaining the possible cause of sterility of this individual.

To clarify the cause of infertility, the sterile individual was injected with daily doses of the hormones involved in the regulation of testicular function: H<sub>1</sub>, H<sub>2</sub>, H<sub>3</sub>, and H<sub>4</sub>. The results of injections are shown in the following table:

5- Using doc 2, determine the exact cause of sterility for this individual.



| Doc-2-Hormone                 | Results         |
|-------------------------------|-----------------|
| H <sub>1</sub> : Testosterone | Sperms produced |
| H <sub>2</sub> : LH           | No effect       |
| H <sub>3</sub> : FSH          | No effect       |
| H <sub>4</sub> : GnRH         | No effect       |

**Question -4-****Transmission of traits in drosophila**

In order to study the transmission of two traits in drosophilae, the body color and the bristle size, we perform the following crosses:

**First cross:** crossing drosophila having ebony body and short bristles (drosophila A) with drosophila having gray body and normal bristles (drosophila B).

**Second cross:** crossing drosophila having also ebony body and short bristles (drosophila A) with drosophila having also gray body and normal bristles (drosophila C). The results of the two crosses are shown in the document 1:

| Result of the 1 <sup>st</sup> cross between A and B | Result of the 2 <sup>nd</sup> cross between A and C |
|-----------------------------------------------------|-----------------------------------------------------|
| 50% drosophilae having gray body & normal bristles  | 50% drosophilae having gray body & normal bristles  |
| 50% drosophilae having gray body & short bristles   | 50% drosophilae having ebony body & normal bristles |

1. By referring to the results obtained in document 1:

- 1-1. Determine the dominant and the recessive allele for each trait.  
1-2. Specify the possible genotypes of drosophilae A, B & C.

Document 1

Third cross: crossing drosophila A with drosophila D. The result is shown in document 2:

| Result of the 3 <sup>rd</sup> cross between A and D                                                                                                                                                                                                                                                | Document 2 |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| <ul style="list-style-type: none"> <li>• 226 drosophilae with gray body and short bristles.</li> <li>• 224 drosophilae with ebony body and normal bristles.</li> <li>• 24 drosophilae with gray body and normal bristles.</li> <li>• 26 drosophilae with ebony body and short bristles.</li> </ul> |            |

- 2-1. Name the third cross.  
2-2. Explain the results shown in document 2. Justify your answer by using a punnet square.  
3- Illustrate this chromosomal recombination that permits to show the behavior of chromosomes in the third cross.

**Question -5-****Transmission of hereditary traits**

By Mr. Mahmoud El-Said

In Drosophila flies, the character "reduced wings" is recessive with respect to the character "normal wings", the character "red eyes" is recessive with respect to the character "normal eyes" and the character "dark body" is recessive with respect to the character "normal body".

We crossed female having normal eyes and normal wings with a male having red eyes and reduced wings. We obtained the following results in the descendants:

|                                               |
|-----------------------------------------------|
| 144 flies having normal wings and normal eyes |
| 5 flies having normal wings and red eyes      |
| 6 flies having reduced wings and normal eyes  |
| 145 flies having reduced wings and red eyes   |

- 1- Deduce the genotypes of both parents.  
2- Calculate the % of different phenotypes obtained.

Another cross is done between a female fruit fly (drosophila), heterozygous for the characters "normal body" and "normal wings", and a male having dark body and reduced wings.

The following results are obtained in the offsprings:

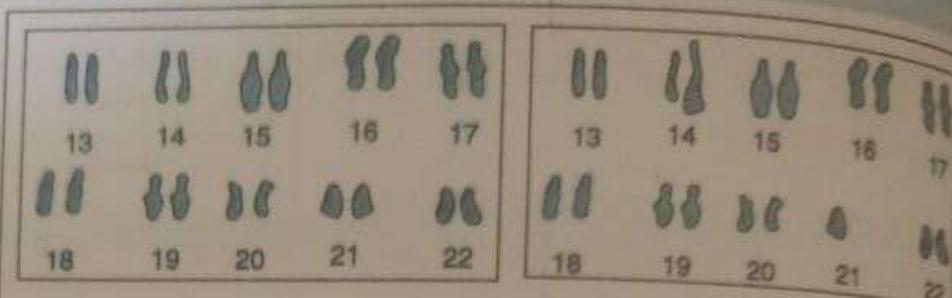
- 234 flies having normal body and normal wings
- 17 flies having normal body and reduced wings
- 13 flies having dark body and normal wings
- 236 flies having dark body and reduced wings

- 3- Explain the obtained results.  
4- Make the necessary chromosomal factorial analysis to verify the obtained phenotypic %.

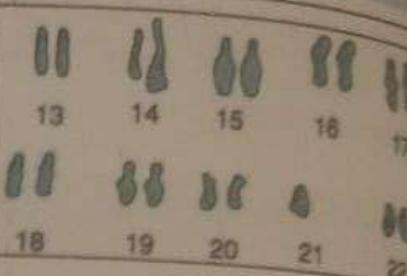
**Question 3****Analysis of Partial Karyotypes**

In the framework of studying human chromosomal abnormalities, we prepare the karyotypes of parents of normal phenotype (document 1) and those of their children (document 2); one of these children has trisomy 21. Only certain pairs of chromosomes, from number 13 to 22, are represented.

- 1- Compare the partial karyotypes of the father and the mother. What can you draw out?



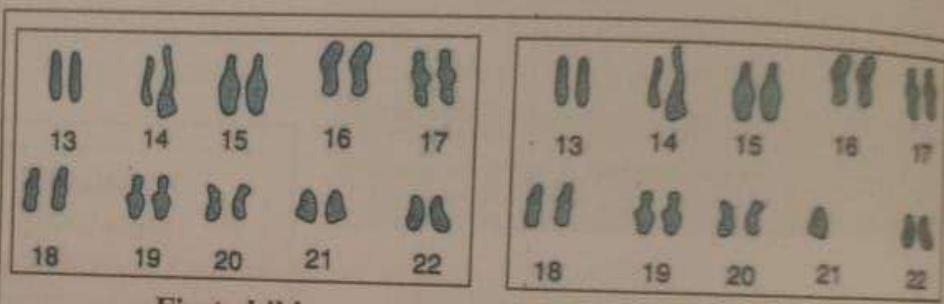
Father



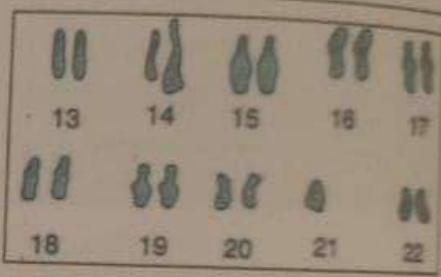
Mother

Document 1

- 2- Explain why the first child is affected with trisomy 21 and the second presents normal phenotype.



First child



Second child

Document 2

- 3- Schematize, for the mother, the phase of meiosis that is at the origin of trisomy 21 in the first child. (Limit your answer to chrs 14 & 21).

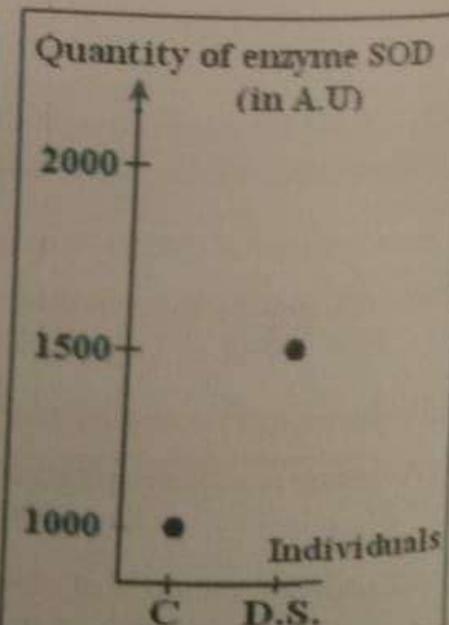
- 4- Make a chromosomal analysis considering only chromosomes 14 and 21 in order to determine the proportions of normal and abnormal children of this couple.

One of the manifestations of Down syndrome (trisomy 21) is mental retardation. Biochemical analyses relate this manifestation to an abnormally high level of a protein "P" in the brain of individuals with this syndrome. This protein is coded by a gene located on chromosome 21.

- 5- Propose an explanation concerning the presence of protein "P" in quantities greater than normal in the brain of individuals with Down syndrome.

On the other hand, we measured the level of an enzyme, superoxide dismutase (SOD), in the red blood cells of unaffected control individuals (C) and in those of others with Down syndrome (D.S.). This enzyme is coded by a single gene and is involved in the synthesis of protein "P". Document 3 shows the results of SOD measurement.

- 6- Determine, with reference to document 3, the probable chromosomal location of the gene coding for the enzyme SOD.



Document 3

**Dihybrid crosses and recombination****Point of a question****Qu**

In the field of studying the transmission of the four traits : body color, wing length, eye color & the size of the abdomen in a fruit fly drosophila, the following experiment was done :

(Wing &amp; body genes traits)

- A long wing striped body male crossed with a vestigial wings black body female which gives 100% long wing striped body F1.

- 1-1. Derive out the suitable conclusion(s).
- 1-2. Identify the genotypes of each parent & F1 generation.

When members of F1 are crossed, F2 generation was obtained:

307 long striped, 104 long black, 99 vestigial striped & 34 vestigial black.  
2-1. Give the phenotypic proportion of each type in F2.

2-2. Derive a conclusion concerning the relation between these two genes.

2-3. Make the necessary factorial analysis to verify the proportion of the obtained phenotypes.

- 2-4. Name & illustrate the type of recombination that took place.

(Abdomen &amp; Eyes traits)

**2<sup>nd</sup> cross:** Knowing that narrow allele dominates wide one for the abdomen trait, similarly red allele dominates the purple one for the eye trait.

A cross was done between females having narrow abdomen & red eyes with males' drosophilae having wide abdomen & purple eyes that hatch to the following:

208 drosophila having wide abdomen &amp; purple eyes

213 drosophila having narrow abdomen &amp; red eyes.

3- Using logical reasoning, specify the genotypes of each parent.

4.

Explain the obtained results.

5. Schematize the chromosomes of each of the obtained phenotypes.

**3<sup>rd</sup> cross:**

**1<sup>st</sup> cross:** we crossed two pure lines of drosophilae, one having stripped body and wide abdomen, the other having black body and narrow abdomen. All the drosophilae obtained in F<sub>1</sub> generation have stripped body and narrow abdomen.

**423 drosophila having stripped bodies and wide abdomen**  
**77 drosophila having black bodies and wide abdomen,**  
**73 drosophila having stripped bodies & narrow abdomen,**  
**427 drosophila having black bodies & narrow abdomen.**

Document-2

**According the 2<sup>nd</sup> cross:**

6-1. Calculate the % of the phenotypes obtained.

6-2. Name this cross.

6-3. Interpret the obtained results.

6-4. Name &amp; represent the type of assortment that took place.

6-5. Make the necessary factorial chromosomal analysis to verify the phenotypic % obtained.

6-6. Calculate the distance between these two genes.

7- Is the body &amp; the eyes genes are linked or not? Justify.

8. Give a representation for a diploid cell hybrid for the all 4 studied traits.

9- Draw the most logical factorial map for all the linked genes knowing that the distance between abdomen & eyes genes are just 0.5CM & the distance between eyes & body is 16.5 CM.

## DNA Alteration

## Question -2-

The Xeroderma pigmentosum is a disease that results in skin lesions which can develop into cancerous tumors and eye lesions. We are interested in the causes of this disease and the relative influence of genes and environment on its appearance.

The body cells have, in their nucleus, enzymes that can repair DNA whenever this latter shows alterations. One of these enzymes is the ERCC3 which is coded by the gene G-ERCC3.

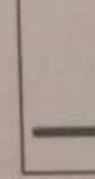
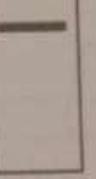
We present in document 2 the nucleotides sequence of a fragment of the non-transcribed strand of the gene G ERCC3 of a healthy individual (allele G1) and the sequence of the equivalent fragment of an individual affected by xeroderma pigmentosum (allele G2).

| Allele | nucleotides sequence of the fragment |
|--------|--------------------------------------|
| G1     | 1 12<br>...AAG AAG AGC AAC...        |
| G2     | 1 12<br>...AAG AAG AGA AAC...        |

Document 2

|            |            | NUCLEOTIDE  |                          | POSITION 2               |                          |                  |                          |  |
|------------|------------|-------------|--------------------------|--------------------------|--------------------------|------------------|--------------------------|--|
|            |            | U           | C                        | A                        | T                        | G                |                          |  |
| NUCLEOTIDE | POSITION 1 | U           | UCU<br>UCC<br>UCA<br>UCG | serine                   | UAU<br>UAC<br>UAA<br>UAG | tyrosine<br>stop | UCG<br>UCC<br>UCA<br>UCC |  |
|            |            | C           | CUU<br>CUC<br>CUA<br>CUG | leucine                  | CCU<br>CCC<br>CCA<br>CCG | proline          | CAU<br>CAC<br>CAA<br>CAG |  |
| NUCLEOTIDE | POSITION 1 | A           | AUU<br>AUC<br>AUU<br>AUG | isoleucine<br>methionine | ACU<br>ACC<br>ACA<br>ACG | threonine        | AAU<br>AAC<br>AAA<br>AAG |  |
|            |            | G           | GUU<br>GUC<br>GUA<br>GUO | valine                   | GCU<br>GCC<br>GCA<br>GCG | alanine          | GAU<br>GAC<br>GAA<br>GAG |  |
|            |            | A: Adenine  |                          | U: Uracile               |                          | G: Guanine       |                          |  |
|            |            | C: Cytosine |                          |                          |                          |                  |                          |  |

Document 1

|                            | Reference electrophoresis                                                           | Individual A                                                                         | Individual B                                                                          | Individual C                                                                          |
|----------------------------|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|
| ERCC3 (coded by allele G1) |  |  |  |  |
| ERCC3 (coded by allele G2) |                                                                                     |   |   |  |

Document 3

- 1- Determine using the genetic code table (doc.1), the amino acid sequence of the portion of each of the enzymes ERCC3 coded by the allele G1 and by the allele G2.

We can separate, by electrophoresis, the enzyme ERCC3 coded by the allele G1 and enzyme ERCC3 coded by allele G2. Electrophoresis is performed for three different individuals: A, B and C. Individual A is affected with Xeroderma pigmentosum & individuals B & C are not. The results are presented in doc.3.

- 2- Write the genotypes of individuals A, B and C. Justify the answer.

- 3- Specify the dominant allele and the recessive one.

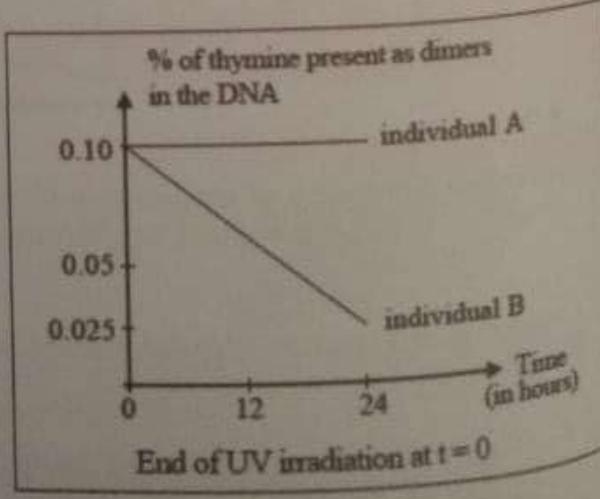
Upon exposure to ultra violet sunlight rays, the DNA of skin cells undergoes alterations, particularly the formation of dimers between 2 successive thymines (T-T). We measure the evolution of the percentage of dimers in the two individuals A and B after being subjected to irradiation with ultraviolet rays. The measured results are presented in document 4.

- 4- Analyze the obtained results in document 4.

- 5- Based only on the previous given:

- 5-1. Explain the results of document 4.

- 5-2. Specify the factors that determine the development of the studied disease.



Document 4

**Question 3-****Origins of Phenylketonuria**

In hepatic cells, the enzyme phenylalanine hydroxylase, PAH, is responsible for the transformation of phenylalanine into tyrosine. Its absence or its inactivity results in the accumulation (high amount) of phenylalanine in the blood which becomes toxic at a dose exceeding 20mg/dl which leads to the destruction of the nerve cells in individuals affected with phenylketonuria. This disease has different origins and is manifested by irreversible mental retardation.

- 1- Pick out the consequence of the high amount of phenylalanine in the blood.

|                       |   | NUCLEOTIDE POSITION 2    |                          |                          |                  |                          |                                |                          |
|-----------------------|---|--------------------------|--------------------------|--------------------------|------------------|--------------------------|--------------------------------|--------------------------|
|                       |   | U                        | C                        | A                        | G                |                          |                                |                          |
| NUCLEOTIDE POSITION 1 | U | UUU<br>UUC<br>UUA<br>UUG | phenylalanine<br>leucine | UCU<br>UCC<br>UCA<br>UCG | tyrosine<br>stop | GUU<br>GUC<br>GUA<br>GUG | cysteine<br>stop               | UCAG                     |
|                       | C | CUU<br>CUC<br>CUA<br>CUG | leucine                  | CCU<br>CCC<br>CCA<br>CCG | proline          | CAU<br>CAC<br>CAA<br>CAG | histidine<br>glutamine         | GUU<br>GUC<br>GCA<br>GCG |
|                       | A | AUU<br>AUC<br>AUA<br>AUG | isoleucine<br>methionine | ACU<br>ACC<br>ACA<br>ACG | threonine        | AAU<br>AAC<br>AAA<br>AAG | asparagine<br>lysine           | GUU<br>GUC<br>GAA<br>AGG |
|                       | G | GUU<br>GUC<br>GUA<br>GUG | valine                   | GCU<br>GCC<br>GCA<br>GCG | alanine          | GAD<br>GAC<br>GAA<br>GAG | aspartic acid<br>glutamic acid | GUU<br>GUC<br>GGA<br>GGG |

A: Adenine    U: Uracile    G: Guanine    C: Cytosine

**Document 1**

Document 2 represents a part of the gene coding for the enzyme PAH of a healthy individual and that of the equivalent fragment of an individual suffering from phenylketonuria.

- 2- Determine, using the genetic code table the sequence of amino acids of the part of the enzyme PAH coded by each of these two alleles.

- 3- Explain how the modification in the nucleotide sequence of the allele leads to the appearance of phenylketonuria.

Two normal couples had two newborns with high plasma concentration of phenylalanine that exceeds 20 mg/dl.

- 4- Indicate if the allele of the disease is dominant or recessive. Justify the answer.

In order to determine the origin of the disease in these two newborns, N1 and N2, these couples consulted a doctor who recommended DNA analysis for all the family members. The obtained results are presented in doc-3.

Moreover, the doctor proposed another test, where he injected the newborns with phenylalanine followed by injection of BH4, an organic substance normally present in the organism and that is indispensable for the normal activity of PAH. The obtained results are presented in document 4.

- 5- Indicate the possible origin of the disease in the case of the newborn (N1). Justify the answer by referring to documents 3 and 4.

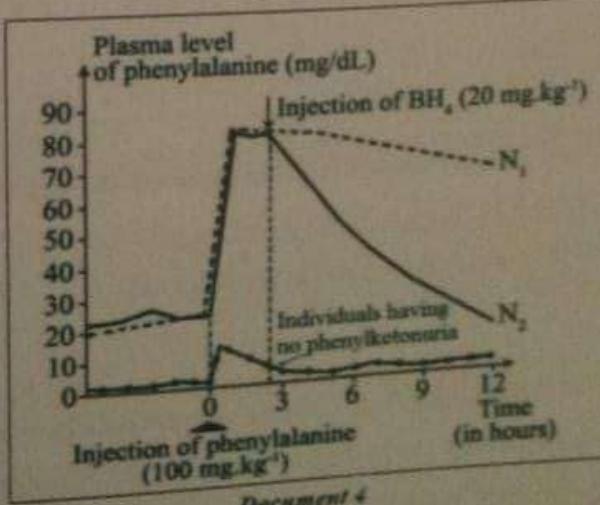
- 6- Determine, by referring to documents 3 and 4, the possible origin of the disease in the case of the newborn (N2).

| Alleles  | Nucleotide sequence of the non-transcribed strand of DNA from codon 277 to codon 283 |
|----------|--------------------------------------------------------------------------------------|
| Normal   | TAT ACC CCC GAA CCT GAC ATC                                                          |
| Diseased | TAT ACC CCC AAA CCT GAC ATC                                                          |

**Document 2**

| Alleles  | F <sub>1</sub> | M <sub>1</sub> | N <sub>1</sub> | F <sub>2</sub> | M <sub>2</sub> | N <sub>2</sub> |
|----------|----------------|----------------|----------------|----------------|----------------|----------------|
| Normal   | —              | —              | —              | —              | —              | —              |
| Diseased | —              | —              | —              | —              | —              | —              |

F: Father    M: Mother    N: Newborn

**Document 3**

**Question-5-****Genetics & Cancer**

Billions of cells of the organism, having limited lifespan, are continuously renewed due to cellular divisions controlled by a system of regulation. The dysfunction of this system of regulation can produce a clone of cells, thus forming a tumor. This latter, is benign as long as it is controlled but it can evolve into a malignant tumor: cancer.

This cancerous cells lose their contact with their neighboring cells; they tend to migrate and colonize other tissues: this is metastasis.

1-Pick out from the text:

1-1-the cause of the appearance of tumor,

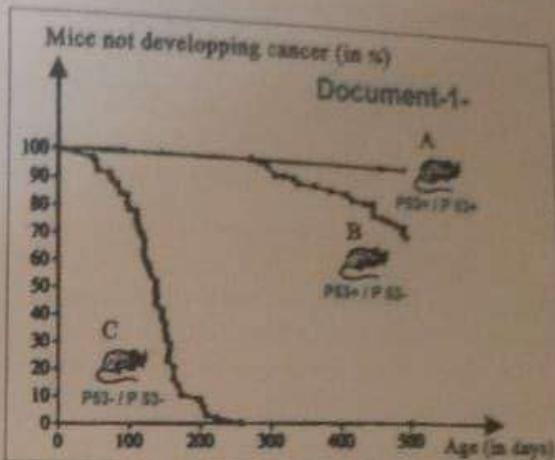
1-2-the definition of metastasis.

In order to better understand the origin of this type of cancer, several studies have been carried out on the gene p53 coding for protein p53. This protein intervenes in the regulation of the cell divisions.

**Study 1:**

The development of this type of cancer is studied in three lots of mice as function of their genotypes concerning the gene p53. Two alleles of this gene, p53+ (normal) and p53- (muted) are only considered. The results of this study are shown in document 1.

2-Interpret the obtained results shown in doc 1.



Doc 2 shows the nucleotides sequence of the non-transcribed strand of each of the two alleles involved of this study.

3-Specify the type of mutation at the origin of this cancer.

| Document-2  |             | Sequence of the nucleotides of the non-transcribed DNA strand |
|-------------|-------------|---------------------------------------------------------------|
| Gene p53    | 1244        | 1250                                                          |
| Nº of codon | Allele p53+ | GGC GGC ATG AAC CGG AGG CCC                                   |
| Allele p53- |             | GGC GGC ATG AAC CGG AGT CCC                                   |

4-Explain how the modification in the nucleotide sequence leads to appearance of this type of cancer.

**Study 2:**

Researchers have studied the mutations detected in three groups of individuals: individuals of group 1 are non-smokers and non-alcoholic consumers, those of group 2 are smokers but non-alcoholic consumers and those in group 3 are smokers and alcohol consumer. The results are shown in doc 3.

5-Show that the consumption of tobacco is a risk factor for cancer.

| Group                                             |        |              |                                    |
|---------------------------------------------------|--------|--------------|------------------------------------|
| Document-3                                        | 1      | 2            | 3                                  |
|                                                   | Number | 3            | 5                                  |
| Mutations detected at the level of gene P53       | Type   | Substitution | Substitution                       |
| Result : Number of individuals affected by cancer | Low    | Moderate     | High                               |
|                                                   |        |              | Substitution, deletion & insertion |

6-Justify the high number of individuals affected by cancer in the case of simultaneous consumption of alcohol & tobacco.

A-Two Template DNA strands that represent two alleles of a given gene are given to study:

1      6      9      13      20      27      30      35

Normal: AAACCCGGA --- TCGGTAGAATTCTCCGGATTAAG

Mutant: AAACCCGGA --- TGGTAGATTCTCCGGATTAAG

In the aim to study them, many restriction enzymes are used; the restriction sites of these enzymes are given in the table below.

- Pick out from the given table the enzymes that can be used to cut these two DNA strands (alleles).
- Complete the missing codon of this gene if the enzyme Bam HI has a restriction site within it.
- Indicate the type of the mutations that lead to the formation of two alleles from this gene. Justify while précising the modified nucleotides and their consequences on the corresponding protein.
- Make for the two alleles of the gene, the restriction map (electrophoresis result) in the case of use of the enzyme Hae III. Is this enzyme able to help in the detection of the genetic polymorphism of these two alleles? Justify.
- Draw for the other enzymes the restriction maps (electrophoresis results) for the two alleles.
- Are all the mutations between these two alleles revealed by using these enzymes? Justify.

| Enzyme  | Recognition site | Cleavage site |
|---------|------------------|---------------|
| Hae III | CCGG             | CC   GG       |
| Eco RI  | GAATTC           | G   AATTC     |
| Bam HI  | GGATCC           | G   GATCC     |
| Not I   | GCGGCCGC         | G   CGGCCGC   |

B- We use a radioactive DNA probe with the sequence GGAC to reveal the different fragments obtained by the enzyme Hae III, the DNA fragments are incubated after electrophoresis in the presence of the probe in order to make hybridization.

- Define hybridization.
- Indicate the necessary treatment that should precede the hybridization.
- Draw the result of the autoradiography done after the hybridization with the above probe of the DNA fragments separated by electrophoresis.
- Is this method able to detect the genetic polymorphism of this gene? Justify.

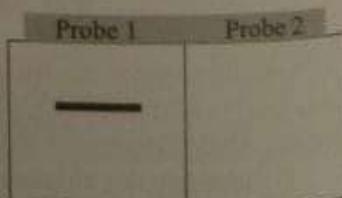
Two other probes are used to test whether an individual is affected or normal; the sequences of these two probes are given as follow.

Probe 1: ACCAATCTAAA  
Probe 2: AGCCATCTTAA

The restriction fragments of this individual are incubated with each of these two probes alone; an autoradiography reveals after hybridization the results shown in the document beside.

- To which allele does each probe act?

- What can these results reveal? Derive a conclusion concerning his phenotype.



Result of autoradiography

**Question 10:**

**Protein and Gene Mutation**  
**FSH** hormone is produced by the pituitary gland during the female sexual cycle. Its role is to stimulate the follicles (structures containing ova) inside the ovary leading to their maturation, in which ovulation occurs and the oocyte becomes ready for fertilization. Any absence or modification in this hormone, the female becomes **sterile**.

The amino acid sequence of human and monkey are given in document 1 →.

- 1- Compare these sequences & derive a conclusion.

Doc2 shows the molecular mass of the 20 amino acids & doc 3 shows partial genetic code table.

| Molecular mass in gr/mol: H <sub>2</sub> O: 18gr/mol |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|------------------------------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala                                                  | Arg | Asn | Asp | Cys | Gln | Gly | His | Ile | Leu | Lys | Met | Phe | Pro | Ser | Thr | Trp | Tyr | Val | Glu |
| 89                                                   | 166 | 110 | 112 | 121 | 86  | 75  | 155 | 120 | 145 | 146 | 100 | 96  | 115 | 105 | 92  | 170 | 181 | 117 | 99  |

**Doc-3- Genetic Code:**

|     |     |     |     |     |     |     |     |     |     |     |      |     |     |      |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|------|
| CUU | CAU | GUU | AGA | GAA | AAU | UCU | AAA | CAA | GAU | UUU | UGA  | GCG | AUG | UAA  |
| Leu | His | Val | Arg | Glu | Asn | Ser | Lys | Gln | Asp | Phe | Stop | Ala | Met | Stop |

- 2- Determine the transcribed strand of DNA of each mammal, and conclude the origin of their difference.

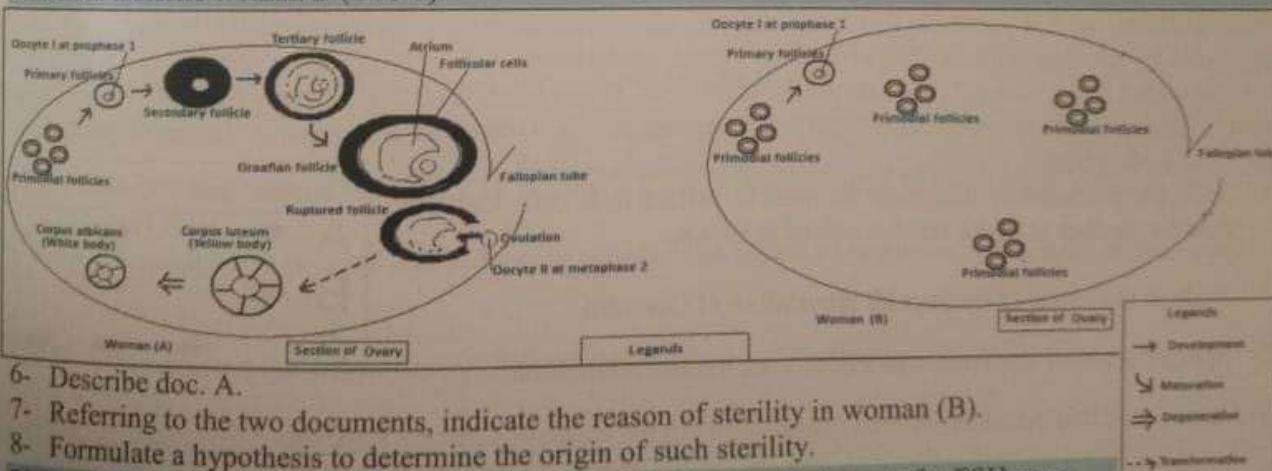
- 3- Calculate the molecular mass of Human chain.

The adjacent document 4 shows the chromatography of cats FSH from amino acid at site 2 till site 7.

- 4- Establish the constituent of this chain by referring to doc 2.

- 5- Formulate a hypothesis to explain the difference in FSH behavior between the monkeys and human.

Document 6 below reveals transverse sections of two ovaries one for a fertile woman A (Doc-a) and the other for a sterile woman B (Doc-b):



- 6- Describe doc. A.

- 7- Referring to the two documents, indicate the reason of sterility in woman (B).

- 8- Formulate a hypothesis to determine the origin of such sterility.

The sterile woman shows the following sequence of DNA (transcribed strand) for FSH gene.

Codons: 1    2    3    4    5    6    7

.... ACT GTA CAA TTT CTT CTT .....

- 9- Determine the m-RNA and the amino acid sequence for this DNA. Derive a conclusion.

The injection of FSH hormone for this woman during 6 months leads to the following results.

- 10- Referring to the results of part (9) & the result of the table, show if your hypothesis is validated.

| No. of follicles | Follicle | Primordial | Primary | Secondary | Tertiary | Graafian |
|------------------|----------|------------|---------|-----------|----------|----------|
| Before Treatment | 300000   | 20         | 5       | 0         | 0        |          |
| After Treatment  | 150000   | 100000     | 25000   | 200       | 24       |          |

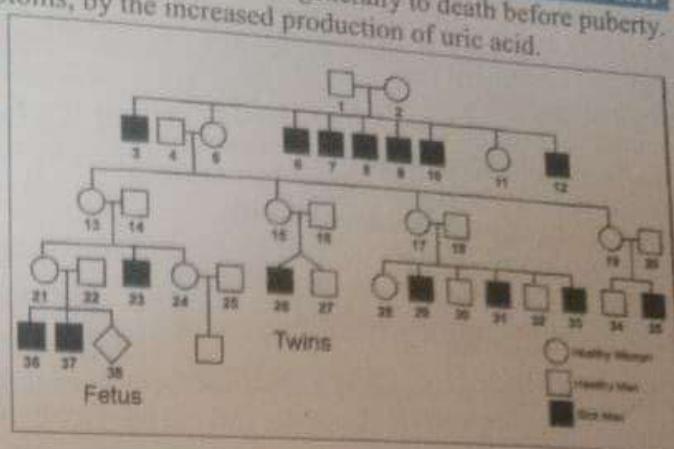
**Lesch-Nyhan syndrome**  
This disease is characterized, beside other symptoms, by the increased production of uric acid.

Doc-1 presents the pedigree of a family that has some members, figured in black, who are affected by Lesch-Nyhan syndrome.

1. Is the allele responsible for the disease dominant or recessive? Justify.

2. Discuss logically, the chromosomal localization of the sickness gene.

3. Are twins 26 & 27 identical or fraternal twins? Justify & write their genotypes.



We study the mode of action of the mutant allele responsible for Lesch-Nyhan syndrome. In a healthy individual the nucleotides are continuously hydrolyzed liberating purines and pyrimidines (nitrogenous bases). Part of these bases (purines), are degraded progressively into hypoxanthine, then into uric acid as follows: Nucleotides → purine bases → hypoxanthine → uric acid.

Most of the hypoxanthine is continuously recovered to synthesize new nucleotides. This synthesis requires certain enzymes such as HGPRT (hypoxanthine - guanine - phosphoribosyl transferase), and takes place according to the following reaction: Hypoxanthine → HGPRT → purine bases → nucleotides

At birth, we notice that the sick individual has a high concentration of uric acid in the blood.

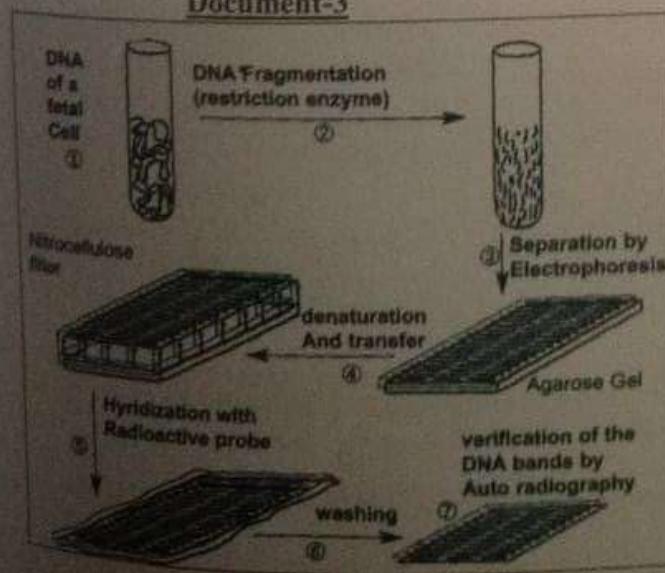
In an experiment, we culture, in the same medium containing hypoxanthine, two types of cells, one is taken from a healthy individual, and the other type is taken from a sick one. The results are presented in the table of document- 2.

| Doc-2: Culture of cells taken from: | Healthy individual      | Sick individual             |
|-------------------------------------|-------------------------|-----------------------------|
| Observation                         | Multiplication of cells | No Multiplication of cells. |

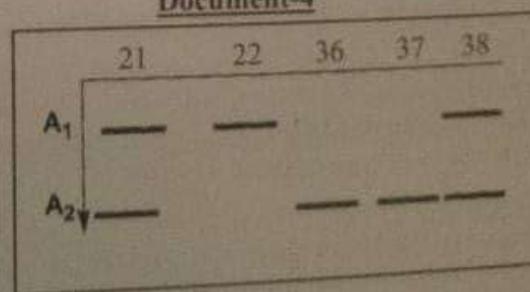
4. Based on the given information, and knowing that nucleotides are used in the replication of DNA, deduce the cause of the sickness.

In order to prepare a prenatal diagnosis of fetus- 38, we fragment the DNA of the family of the couple 21-22 according to the technique schematized in doc-3. The results are shown in doc-4.

**Document-3**



**Document-4**



5. Describe the technique used in document-3.

6. Referring to document-4, identify the mutant allele. Conclude the phenotype of the

and 4-1-Denotia

Daltonism

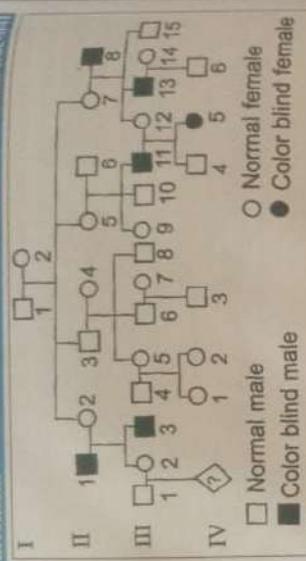
Question 4-

BioGuide 1218 - Version E-G. BioGuide

Document 1

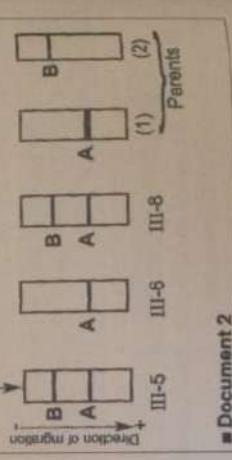
- A. Color blindness (daltonism) is a defect in vision of colors. This defect is due to a gene localized on the non-homologous segment of chromosome-X. Document-1 represents the pedigree of a family, whose certain members are affected.
- Is the allele responsible for color blindness dominant or recessive? Justify.
  - 2- Identify the genotypes of the individual III<sub>5</sub>, her parents, and her husband.
  - 3- Individual (III<sub>1</sub>) is expecting a child and is worried if her child will be color blinded. Make a table of the cross to find the probability of the child to be color blinded.

- B. In this family, medical analyses are performed to individual (III<sub>8</sub>), who presents physical and sexual troubles. Equally, medical analyses were done to his parents, his sister (III<sub>5</sub>) and his brother (III<sub>6</sub>).
- Document 1



- Among the medical analyses done, was testing for glucose-6-phosphate-dehydrogenase (G6PD) due to a gene located on non-homologous segment of X. G6PD is an enzyme whose synthesis of G6PD of form A and G6PD of form-B respectively (A & B are normal active). We can distinguish the two forms by electrophoresis.
- Doc-2 shows the electrophoresogram obtained for individuals III<sub>5</sub>, III<sub>6</sub>, and III<sub>8</sub>, and for their parents:

4. Compare the electrophoresograms of the two individuals III<sub>5</sub> and III<sub>6</sub>.
- 5- Indicate, to which of the two parents of the individual III<sub>8</sub>, the electrophoreograms 1 and 2 correspond. Justify the answer.
- 6- Determine the possible disorder that caused the troubles in individual III<sub>8</sub>. Identify the parent whose responsible for that. Then name the phase of meiosis during which the disorder took place & then schematize the behavior of the chromosome in this parent which leads to this abnormality.



■ Document 2

- A study was done on the male descendants originated from women, whose fathers are color blind and have a G6PD of form-B. These women are of normal color vision like individual III<sub>2</sub> but their electrophoreogram is like that of individual III<sub>5</sub>. The husbands of these women are of normal vision and have a G6PD of form-A, their genotype can be represented by XY
- 7- Specify the genotype of these women.
- The descendants produced are the following:

- 75 Males with normal color vision and G6PD of form-A.  
71 Males with color blindness and G6PD of form-B.  
4 Males with normal color vision and G6PD of form-B.  
4 Males with color blindness and G6PD of form-A.
- 8- How can you explain the obtained results? (a table of cross is not required) and then name & illustrate the type of assortment that took place.

Document 2  
of a which has  
2. What in  
8. Make a  
produces th

**Question 4-**

**A- Document 1** represents the pedigree of a family whose certain members, colored in black are affected by hemophilia B. This disease is observed only in male individuals. The presence of this gene in two copies in a genotype provokes the death of the embryo.

1- Is the allele responsible for this disease dominant or recessive? Justify the answer.

2- Is this gene sex-linked? Justify the answer.

3- Indicate the genotype of each of the individuals 8, 13 and 14. Justify, for each genotype, the answer.

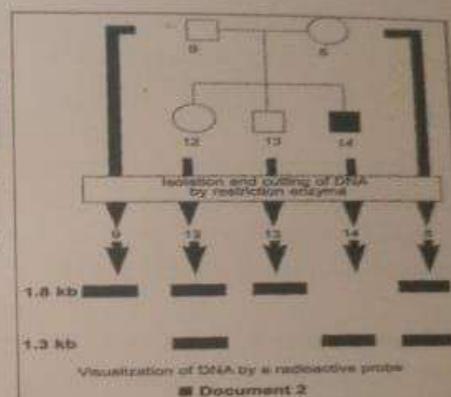
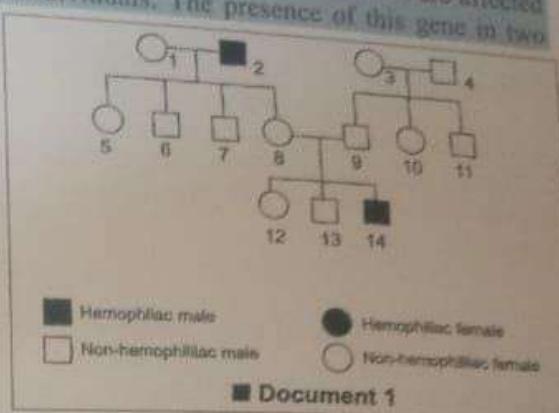
4- Make the necessary analyses to determine the possible proportions of the descendants of female-5 in each of the following cases:

- If her husband is not affected by hemophilia.
- If her husband is affected.

We performed a special technique for the analysis of DNA of the couple 8-9 & their children 12, 13, & 14.

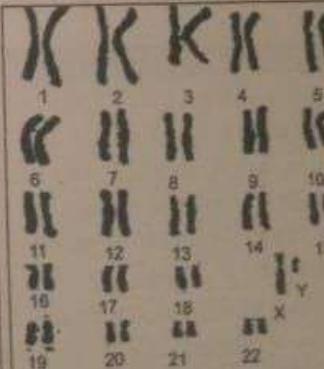
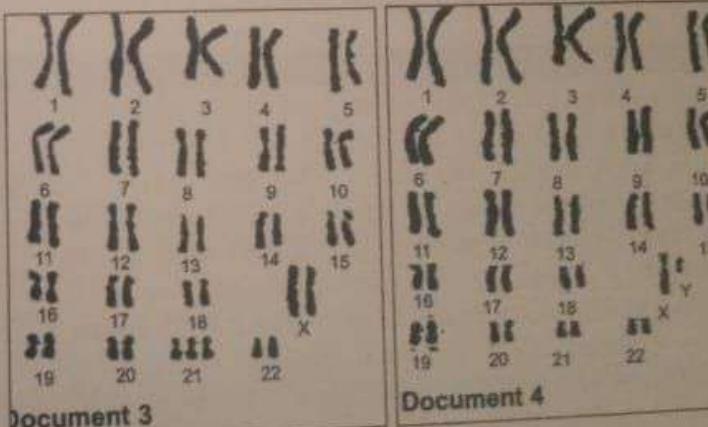
We obtained different DNA fragments of variable lengths measured in kilo bases (document-2).

5- By referring to document-2, identify the allele of the hemophilia-B.



**B- Document-3** presents the karyotypes of an individual with an abnormality while document-4 presents the karyotype of a normal individual.

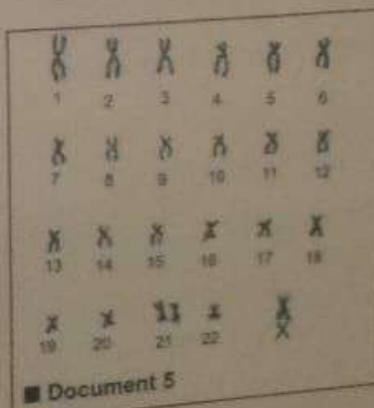
6- Compare these two karyotypes. What is the abnormality revealed?



Document-5 is a karyotype of a spermatocyte-II that is obtained from a man of a normal karyotype. This spermatocyte-II is identical to that which has allowed the birth of the individual affected by the abnormality (document-3).

7- What information does document-5 provide?

8- Make a labeled diagram of the anaphase stage of the division, which produces this type of spermatocyte-II. (Present, only, in the diagram the sex chromosomes X and Y and the pair of chromosomes concerned with the disease).



Part-1 of 4 - Genetics  
Question-7-

Blood groups of the ABO system are determined by a gene located on chr.9. This gene exists in 3 alleles A, B, & O. A & B are codominant to each other but dominates allele O.

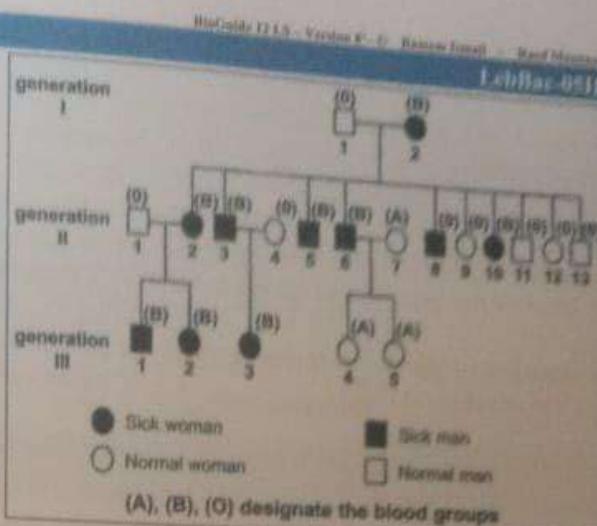
The given pedigree shows the transmission of 2 hereditary traits: blood group & a dominant autosomal genetic disease manifested by a reduced fingers & undeveloped patella.

Designate the normal by "n" & mutant allele for the disease by "N".

1- What information in the adjacent document reveals that the two studied genes are linked?

2- Schematize chromosomally the genotypes of parents I<sub>1</sub> & I<sub>2</sub>. Justify.

3- What is the genotype of the person II<sub>8</sub>? How can we explain the appearance of this genotype in the offspring of parents I<sub>1</sub> & I<sub>2</sub> without using the table of cross?



Question-8-

Cystic fibrosis

Lab Bac-661

Document-1 represents the pedigree of a family of whom some members, figured in black, are affected by a disease called cystic fibrosis, a hereditary disease manifested by respiratory and digestive troubles.

This disease is determined by a mutant allele of a gene called CF. This gene is located on chromosome-7, & very close to a non-coding region that has restriction sites recognized by the restriction enzyme Taq 1.

The non-coding region close to the functional dominant allele-N has four restriction sites for enzyme Taq 1, while the non-coding region close to the mutated recessive allele-m has three restriction sites.

The length of the restriction fragments is expressed in kilo base (kb), document-2.

1- Indicate the possible genotypes of individuals II<sub>4</sub> and II<sub>5</sub>. Justify the answer.

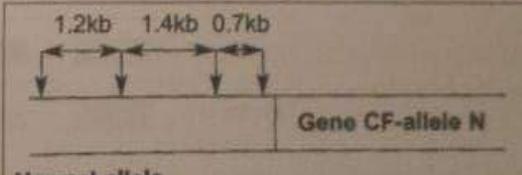
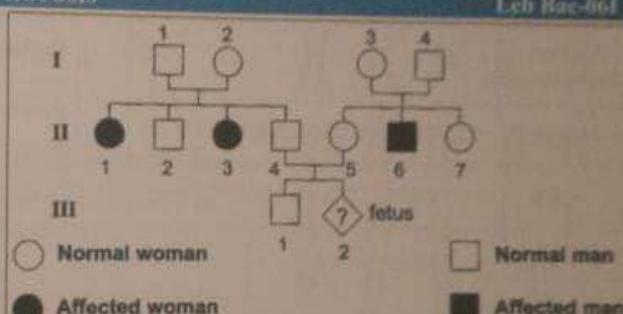
2- Determine the genetic risk of couple II<sub>4</sub> and II<sub>5</sub> to have a sick child.

3- Specify the site at which mutation took place.

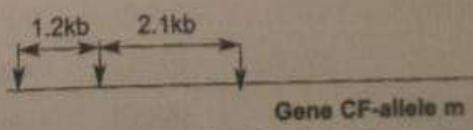
Document-3 shows the results of electrophoresis of the restriction fragments obtained by Southern blot technique for individuals II<sub>4</sub>, II<sub>5</sub> and their children.

4- After analyzing the obtained results, conclude the real genotype of each of individuals II<sub>4</sub>, II<sub>5</sub> and the fetus.

5- Based on the above analysis, is this couple in risk of having affected children? Justify the answer.



Normal allele



Mutant allele

Fragment size

|        | II-4 | II-5 | III-1 | III-2 |
|--------|------|------|-------|-------|
| 2.1 kb |      | —    | —     | —     |
| 1.4 kb | —    | —    | —     | —     |
| 1.2 kb | —    | —    | —     | —     |
| 0.7 kb | —    | —    | —     | —     |

## Part-I of 4 - Genetics

**Question-5:**

Document-1 represents the pedigree of a family with some of its members, shown in black, having a rare hereditary disease that occurs mainly in males and very rarely in females.

- Verify if the allele responsible for the disease is dominant or recessive.
- Discuss logically the chromosomal localization of the gene responsible for this disease (without considering female-20).

- Illustrate, chromosomally, the genotype of each of the individuals 13 and 16. Justify the answer.

Female-20 presents, besides her disease, an abnormality, which is manifested by the absence of menstruation, absence of the development of mammary glands...

To identify this abnormality we perform the karyotype of female-20, document-2.

- Write the chromosomal formula of this female. Give the name of the abnormality revealed by the karyotype.
- Based on the karyotype, how can you explain the appearance of the disease in female-20?

- Knowing that this chromosomal abnormality results from an error in meiosis during spermatogenesis, schematize the chromosomal behavior of the concerned chromosomes only (consider one case only).

**Question-6:**

Hemoglobin A is consisted of 4 chains of globin: 2 alfa & 2 beta. The synthesis of the beta is controlled by a gene located on chr.11. This gene exists in several forms of alleles such as allele HbA that leads to the formation of normal hemoglobin A & allele HbS that leads to the formation of abnormal hemoglobin S, only persons possessing 2 HbS alleles have a disease called sickle cell anemia.

Doc-1 presents the % of the 2 types of hemoglobin in 3 persons P, M & R.

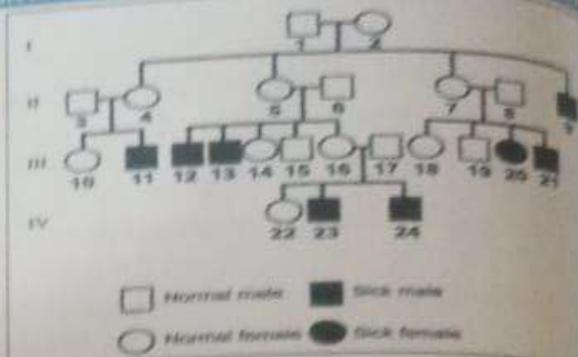
- Write the genotype of each of these persons. Justify in reference to doc-1.

- Identify the sick persons.

We study the % of the alpha & beta globin chains present in the blood of the fetus from the 6th month before birth till the 9th month after birth, the results are shown in document-2.

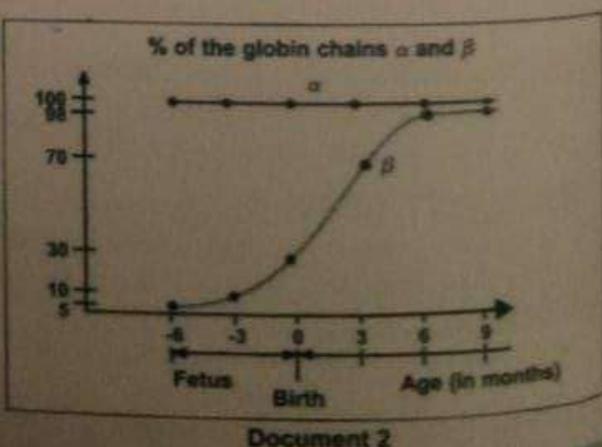
- Tabulate document-2.

- Justify, in reference to doc-2, that sickle cell anemia is not manifested until 6 months after birth.



|              | Person P | Person M | Person R |
|--------------|----------|----------|----------|
| Hemoglobin A | 100%     | 0%       | 50%      |
| Hemoglobin S | 0%       | 100%     | 50%      |

Document 1



**Sickle cell Anemia**

Mr. X & Mrs. X have a daughter suffering from sickle cell anemia (doc-1), the hereditary sickness whose mode of transmission is autosomal recessive, is characterized by the abnormality of the beta-globin molecule which leads to the deformation of RBC cells.

Mrs. X is pregnant & the couple demand prenatal diagnosis to know if their 2nd child will be affected by sickle cell anemia.

1- Identify the genotype of Mr. X & Mrs. X & their daughter.

2- Based on the logical reasoning, find the probability of this couple to have an affected child.

Doc-2 reveals the sequence of parts of the non-transcribed strand for beta-globin alleles: HbA is the normal allele while HbS is the mutant allele.

A direct diagnostic method by radioactive probe is done for the family, many copies of the part of beta-globin gene can be obtained from the DNA of each person by this technique, these copies are separated in two lots & each is placed in the presence of a different radioactive probe (Doc-3). Each probe is capable to bind to either HbA or HbS, the result of autoradiography are shown in Doc-4.

| Position of the nucleotide | 1                    | 10 | 20 |
|----------------------------|----------------------|----|----|
| HbA                        | CTCCTGAGGAGAAGTCTGCC |    |    |
| HbS                        | CTCCTGTGGAGAAGTCTGCC |    |    |

Document 2

|           |                          |
|-----------|--------------------------|
| Probe n°1 | GAGGACACCTCTTCAGACGG     |
| Probe n°2 | GAGGA<br>CTCCTCTTCAGACGG |

Document 3

|           | Mr. X      | Mrs. X     | Daughter   | Fetus      |
|-----------|------------|------------|------------|------------|
| Probe n°1 | [redacted] | [redacted] | [redacted] |            |
| Probe n°2 | [redacted] | [redacted] |            | [redacted] |

Document 4

3- Specify, based on doc-2, the location of the mutation & its type.

4- Determine, in reference to doc-2 & 3, which allele corresponds to each probe used.

5- Do the results of doc-4 confirm the genotypes you have indicated in part 1? Justify. Draw out the genotype & the phenotype of the fetus.

6- Justify why prenatal diagnosis is more accurate than then pedigree in detecting a genetic disease.



Document 1

Part of 4 - Genetics  
**Question-10**  
Hemophilia  
abnormality  
factor is the c  
segment of c  
responsible fo  
Document-1  
disease. Wom  
her fetus.

1- Indicate th

2- Show, by

3- Determin

To clarify t  
were done.

4- Does th

The secon  
sick perso  
electropho

Because v  
codes for  
mark a p  
This zone  
present i  
and the re

5- Specif

the fetus

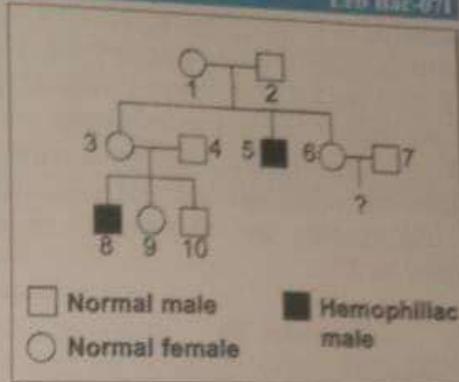
6- We e  
In this c

**Question-10-**

**Hemophilia**  
Hemophilia A is a genetic recessive disease due to an abnormality of a blood coagulation factor; factor VIII. This factor is the expression of a gene located on the non-homologous segment of chromosome-X. We designate, by h, the allele responsible for the disease and by N the normal allele.

Document-1 reveals the pedigree of a family that expresses this disease. Woman-6 is pregnant and asks for prenatal diagnosis for her fetus.

- 1- Indicate the genotypes of persons 6 and 7. Justify the choice.

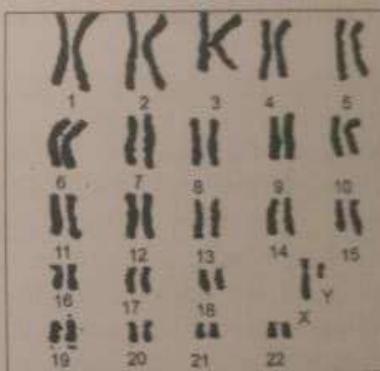


- 2- Show, by logical reasoning, that this pedigree does not permit a sure diagnosis concerning the fetus.

- 3- Determine the genetic risk of this child to be hemophiliac.

To clarify the diagnostic problem of hemophilia in the fetus, two tests were done. The first test is a karyotype of the fetus, doc- 2.

- 4- Does this karyotype solve this problem? Justify the answer.



The second test is the analysis of the DNA of chromosome-X. The DNA of the mother, the fetus, and the sick person- 8, are subjected to restriction enzymes. The obtained DNA fragments are separated by gel electrophoresis, and then hybridized by a probe.

Because we cannot use an intragenic probe to distinguish the hemophilia allele from the normal allele that codes for factor VIII, we use probe ST14 that can mark a polymorphic zone, very close to this gene. This zone has 10 alleles, but only alleles 3 and 5 are present in this family. An autoradiography is done and the results are shown in document-3.

|          | Mother       | Fetus       | Person 8    |
|----------|--------------|-------------|-------------|
| Allele 3 | [Faint band] | [Dark band] |             |
| Allele 5 | [Dark band]  |             | [Dark band] |

Document 3

- 5- Specify, starting from the analysis of the obtained autoradiogram, the real genotype of the mother and the fetus.

- 6- We estimate a 4% recombination between the polymorphic zone and the gene coding for factor-VIII. In this case, is the second test reliable for diagnosing hemophilia in the fetus? Justify the answer.

Partie 4 - Genetics  
Question-12-

Phenylketonuria is a disease caused by a deficit in a hepatic enzyme - PAH - responsible for the transformation of an amino acid, phenylalanine, into another one called tyrosine. In Europe, the risk of being heterozygous is 1/50.

Document 1 shows the pedigrees of two families A and B which some members are affected with this disease. Couples (3, 4) of family A and (1, 2) of family B ask for a prenatal diagnosis.

1- Through a rigorous analysis of the pedigree of family B, determine:

a- Whether the allele responsible for the disease is dominant or recessive.

b- The location of the gene responsible for the disease.

2- Determine the genetic risk for each fetus to be affected with this disease.

Three mutations were determined to be at the origin of phenylketonuria. Document 2 shows a part of the codon sequences that correspond to three regions X, Y, and Z of the normal allele, and of the three mutant alleles that are responsible for this disease.

Doc-2

| Codon         | 278.....<br>( Region X) | 282.....<br>( Region Y) | 310.....<br>( Region Y) | 314.....<br>( Region Z) | 406.....<br>( Region Z) | 410 |
|---------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-----|
| RNA           | ACC CCC GAA CCU GAC...  |                         |                         |                         |                         |     |
| Normal allele | ACC CCC GAA CCU GAC...  | UCU CUG GGU GCA CCU ... |                         | AUA CCU CGG CCC UUC     |                         |     |
| Mutant 1      | ACC CCC AAA CCU GAC...  | UCU CUG GGU GCA CCU...  |                         | AUA CCU CGG CCC UUC     |                         |     |
| Mutant 2      | ACC CCC GAA CCU GAC...  | UCU CCG GGU GCA CCU...  |                         | AUA CCU CGG CCC UUC     |                         |     |
| Mutant 3      | ACC CCC GAA CCU GAC...  | UCU CUG GGU GCA CCU ... |                         | AUA CCU UGG CCC UUC     |                         |     |

3- For each allele responsible for the disease, locate the mutation and indicate its type.

In order to diagnose the fetuses, the following DNA tests were carried out in both families.

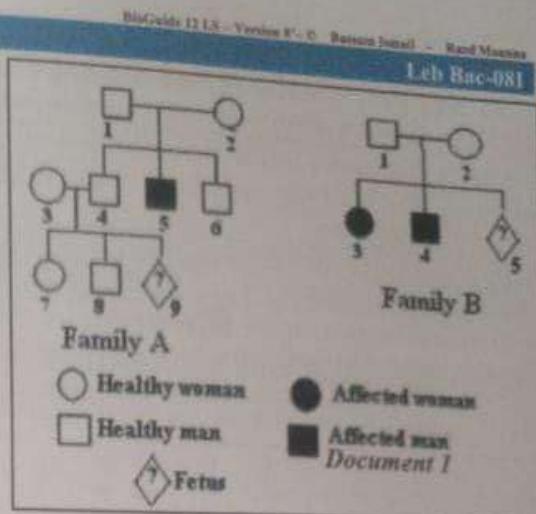
1<sup>st</sup> test: DNA is extracted from parental and fetal cells and is subjected to restriction enzymes. Hybridization technique is then carried out using two radioactive DNA probes that are complementary to a specific "region X". One of the probes is specific for the normal allele; the other is specific for a mutant allele. The results are shown in document 3.

4- Draw out the genotypes of the individuals of family A in document 3.

5- Justify that the test performed is not sufficient to establish the diagnosis of family B.

2<sup>nd</sup> test: Family B is subjected to a second DNA test yet using other restriction enzymes. This method reveals a restriction site (cleavage site) at the level of region Z, while regions X and Y remain intact. The results of this test are shown in document 4.

6- Show the importance of the second test in order to obtain an exact diagnosis concerning the fetus of family B.



| Document 3   | P      | M      | E     | P      | M      | E     |
|--------------|--------|--------|-------|--------|--------|-------|
|              | Father | Mother | Fetus | Father | Mother | Fetus |
| Normal probe | ●      | ●      |       | ●      | ●      | ●     |
| Mutant probe |        | ●      | ●     |        |        |       |

Family A      Family B

| Document 4    | Father        | Mother | Fetus |
|---------------|---------------|--------|-------|
|               | Normal allele | —      | —     |
| Normal allele | —             | —      | —     |
| Mutant allele | —             | —      | —     |

**Question-13:** Phenylketonuria is a recessive Autosomal disease that affects 1/10,000 of newborns world-wide. This disease is related to a deficiency in an enzyme called PAH.

In normal conditions, this enzyme metabolizes phenylalanine into tyrosine, in the presence of a co-factor DHBP. This deficiency leads to an increase in the amount of phenylalanine in the blood accompanied with serious troubles.

A study performed on 1,200 children selected from an isolated community, showed that 30 children were heterozygous for PAH.

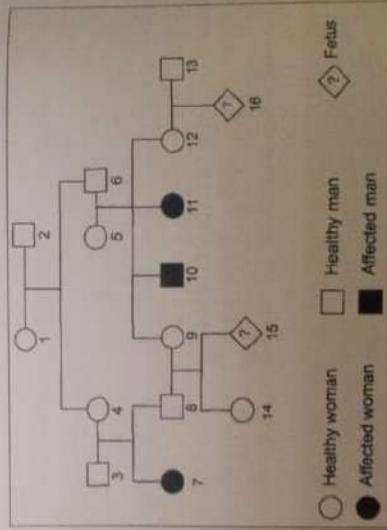
1- Calculate the proportion of heterozygous children in this community; and then determine the genetic risk for a child to be affected with phenylketonuria

2- Identify the g

2- Compare the genetic risk obtained to the worldwide risk. Formulate a hypothesis that explains the difference between these two risks.

In order to verify the formulated hypothesis, a study was carried out on a family of this community, which pedigree is shown in the following document.

3- By referring to the pedigree, justify that the disease is recessive and Autosomal.



4- Determine, for each of the fetuses 15 and 16, the risk to be affected.

5- Verify if obtained results confirm the formulated hypothesis. Justify the answer.

**Daughter-7 marries an affected man. Their first child was normal. All the tests performed confirm that the child is legal, and that the husband, unlike his wife, has a normal amount of PAH.**

6- Determine the probable cause of the disease of the husband of daughter-7.

7- Justify, genetically, the birth of a normal child by this couple.

Duchenne Myopathy is a Seg

**Question -14-**

Duchene Myopathy is a degenerative disease of muscle fibers which is due to a gene carried on the non-homologous segment of X. Boys affected with myopathy do not synthesize an inactive form of it.

Document 1 represents the pedigree of a family having one member of its family affected with the disease.

Doc-1

1- Determine, using doc-1, whether the allele responsible for the disease is dominant or recessive.

2- Identify the genotypes of the parents.

3- Determine the probability of the fetus to be affected.

Parents (1&2) who are expecting a baby want to know whether their fetus is at risk of developing the disease. They consult a doctor who proposes a prenatal diagnostic test by applying Southern Blot technique. The results are shown in document 2 →

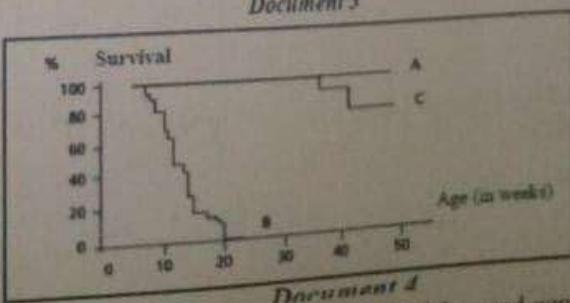
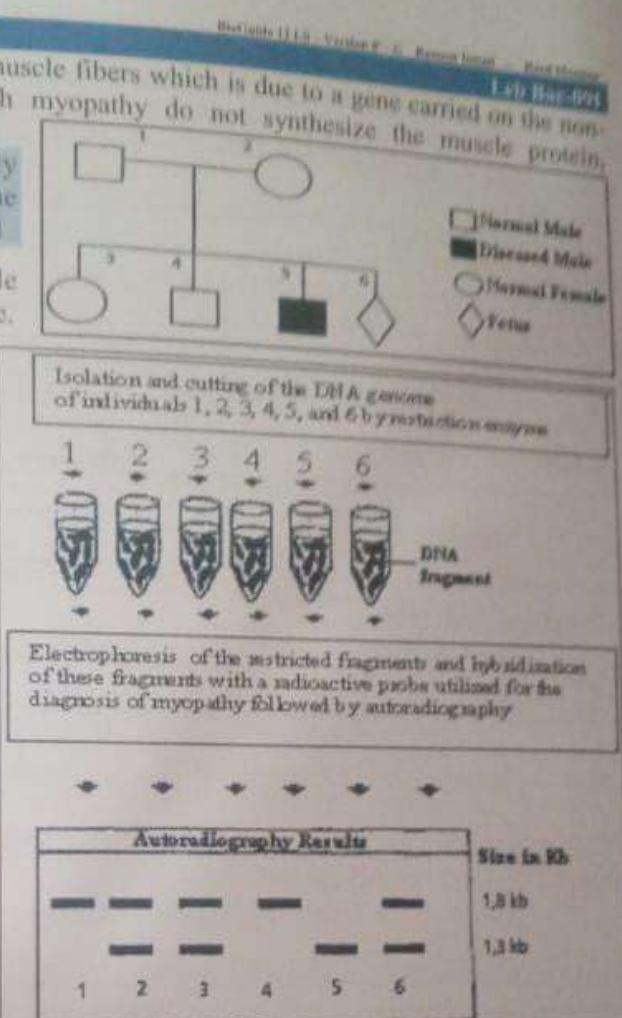
4- Identify, by referring to document 1 and the autoradiography of document 2, the allele causing the disease. Justify the answer.

5- Specify the sex and the phenotype of the fetus.

A gene therapy is applied for the first time on mice attaining myopathy similar to Duchene myopathy in humans. This technique consists of injecting the dystrophin gene into a diseased organism by means of a virus vector which is harmless to mice and human species. After this treatment, transversal sections are taken from the diaphragm muscle (respiratory muscle) of 3 groups of mice (A, B and C), then incubated with anti-dystrophin fluorescent antibodies and observed under a fluorescent microscope. The results obtained within 16-18 weeks are shown in doc-3.

Document 4 reveals the percentage of survival of the three groups of mice in function of time.

6- Interpret the results obtained in each of docs 3&4. Conclude concerning the efficiency of the used gene therapy.



**Retinitis Pigmentosa**

Retinitis pigmentosa, a hereditary disease, is the main cause of visual impairment (30% of visual deficiencies). The disease starts by affecting night vision and reducing the visual field. It is caused by progressive degeneration of rod cells, which are photoreceptor cells of the retina containing the protein rhodopsin.

To understand the origin of this disease, we study the structure of proteins encoded by different alleles of the rhodopsin gene.

The rhodopsin gene consisting of 1044 pairs of nucleotides encodes a protein of 348 amino acids.

Document 1 represents a portion of the nucleotide sequences of the alleles of the rhodopsin gene and the of the amino acids sequences of the corresponding proteins in individuals with normal phenotype and individuals with retinitis pigmentosa.

| Individual's phenotype             | Portion of the nucleotides sequence of the allele | portion of the amino acids sequence of the protein    |
|------------------------------------|---------------------------------------------------|-------------------------------------------------------|
| normal                             | 391<br>↓<br>...CTG GCC ATC GAG CGG TAC...         | 408<br>↓<br>131<br>↓<br>...Leu-Ala-Ile-Glu-Arg-Tyr... |
| Affected with retinitis pigmentosa | 391<br>↓<br>...CTG GCC ATC GAG CTT TAC...         | 408<br>↓<br>131<br>↓<br>...Leu-Ala-Ile-Glu-Leu-Tyr... |

Leu = leucine, Ala = alanine, Ile = isoleucine, Glu = glutamic acid, Arg = arginine, Tyr = tyrosine.

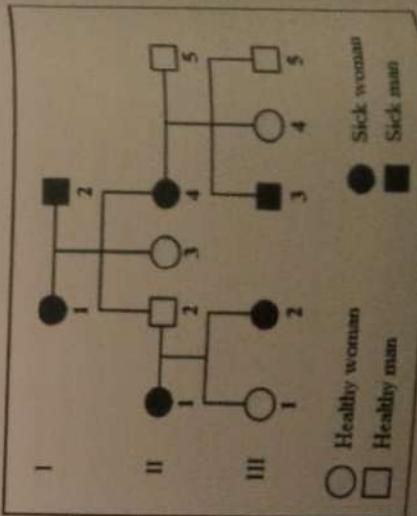
**Document 1**

- Pick out from the text the cause of retinitis pigmentosa.
- Compare the two nucleotides sequences and the two amino acids sequences presented in document 1.
- Draw out the origin of this disease.

- 3- Explain how the modifications in the nucleotides sequence of the allele (doc.1) lead to the appearance of the previously mentioned symptoms of retinitis pigmentosa.

Document 2 presents the pedigree of a family having some of its members affected with retinitis pigmentosa.

4. Specify if the allele responsible for the disease is dominant or recessive and indicate its chromosomal location.



5. Determine the genotypes of individuals II3 and II4.
6. Woman III2 married her cousin III3; determine the risk for this couple to have children with retinitis pigmentosa.

**Document 2**

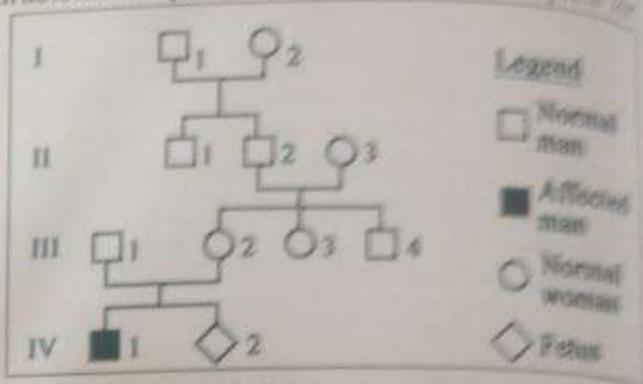
**Fragile X Syndrome****Question -17-**

Fragile X syndrome is the most common cause of hereditary mental retardation. The gene FMR1 which is responsible for this disease is located on the non-homologous segment of the X sex chromosome. The alleles at the origin of the abnormal phenotype are characterized by the repetition of CGG triplets for more than 200 times.

Couple III1- III2 (document 1), who already had an affected child, expects another one and would like to know if it will be affected or not.

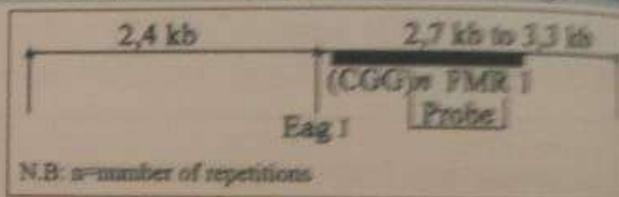
Father III1 has no abnormal allele depending on his DNA finger printing.

1- Justify that the gene is localized on X chromosome.



2- Propose an explanation for the appearance of the disease in individual IV1 (document 1).

The fragment of DNA which carries the FMR1 gene is isolated. A very close site to this gene is recognized by the restriction enzyme EagI. For a complicated reason, this site is no more recognized by the enzyme when the number of repetitions of CGG triplets exceeds 200. Document 2 shows the position of this cleavage site in normal alleles.



The DNA of certain individuals of this family is cut and a specific radioactive probe of the FMR1 gene is used. The obtained bands are presented in document 3.

3- Identify the band(s) corresponding to the alleles of the disease and those corresponding to the normal alleles.

| Individuals | III3 | III1 | III2 | IV1 | IV2 |
|-------------|------|------|------|-----|-----|
| 5,8 kb      |      |      |      | —   |     |
| 3,2 kb      |      |      | —    | —   |     |
| 2,8 kb      | —    | —    | —    |     | —   |

*Document 3*

4- Determine whether the fetus IV2 will be affected or not by the fragile X syndrome.

5- Pose the problem that arises from the study of document 3 concerning the origin of the disease in IV1.

Document 4 shows the position and the number of repetitions of CGG triplet for the allele of FMR1 gene. The alleles having a number of repetitions between 54 and 200 are expressed normally but might be subjected to instability during gametogenesis. This instability can be manifested by an increase in the number of triplets.

6- Explain, based on what precedes, the real origin of the disease in IV1.

|                |  |                                       |
|----------------|--|---------------------------------------|
| $(CGG)_n$      |  |                                       |
| $n = [6-33]$   |  | Alleles found in normal individuals   |
| $(CGG)_n$      |  |                                       |
| $n = [54-200]$ |  | Alleles found in affected individuals |
| $(CGG)_n$      |  |                                       |
| $n > 200$      |  |                                       |

**Question -21-**

Dysuria is a disease that consists of a difficulty in urinating. It's related to excessive formation of urinary calculi ("stones" in urinary tracts).

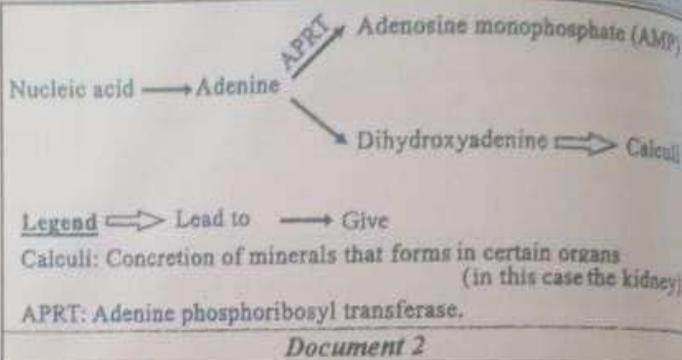
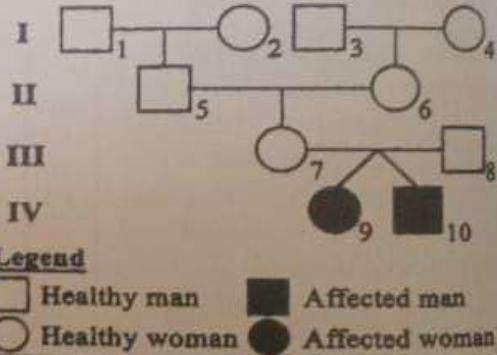
A family, which has twins suffering from dysuria, consults a doctor. He prescribed many tests whose results are presented in doc 1.

Doc 2 shows the reactions of metabolism of adenine related to the formation of calculi.

1- Justify by referring to doc 1 and 2, the dysuria detected in the twins.

**Dysuria**

| Document-1- Measurements                          | Control      | Twins         |
|---------------------------------------------------|--------------|---------------|
| Quantity of Adenine (mg) in urine excreted/ 24hrs | 1.5          | 40            |
| Dihydroxyadenine (constituent of calculi)         | Not detected | High Quantity |
| % of active APRT enzyme                           | 100          | 0             |

**Document 2****Document 3**

In order to clarify the problem observed in the twins, a more detailed analysis concerning members of their family was performed. The pedigree of their family was performed. The pedigree of their family is shown in doc 3.

2- Formulate, by referring to doc 3, two hypotheses explaining the appearance of the disease in the twins.

3- Knowing that the gene exists only in two allelic versions, specify if the allele responsible for the disease is dominant or recessive.

4- Show that the gene is not carried by a sex chromosome.

5- Indicate the possible genotype(s) of each of the individual I<sub>1</sub> & III<sub>8</sub>. Justify the answer.

Blood tests concerning the amount of active enzyme APRT were performed in members of this family. The results are represented in doc 4.

6- Show, by referring to doc 4, that at the molecular level, the two alleles are codominant.

| Member of the family | % of active APRT |
|----------------------|------------------|
| III <sub>7</sub>     | 50               |
| III <sub>8</sub>     | 50               |
| II <sub>5</sub>      | 50               |
| II <sub>6</sub>      | 100              |
| IV <sub>9</sub>      | 0                |
| IV <sub>10</sub>     | 0                |

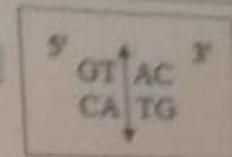
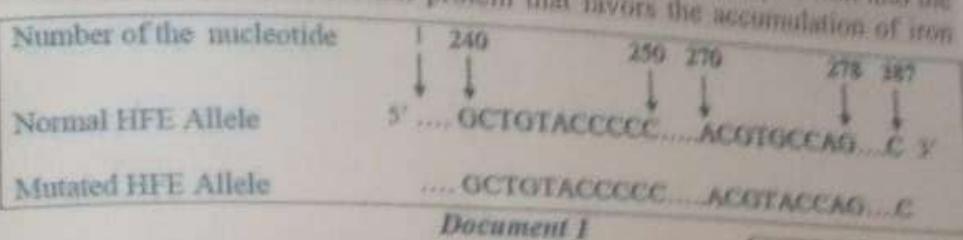
Genetics  
Question - 22-

Hemochromatosis appears after the age of 40 years and is characterized by the accumulation of iron in the body. It is a recessive disease linked to the HFE gene which is located on chromosome 6. This gene has two alleles: the normal allele which codes for a membrane protein that regulates the entry of iron into the cells, and the mutated allele which codes for an abnormal protein that favors the accumulation of iron inside the cells.

Document 1 presents the partial sequence of nucleotides of the two alleles, the normal and the mutated ones.

Document 2 presents the restriction site of a restriction enzyme RsaI.

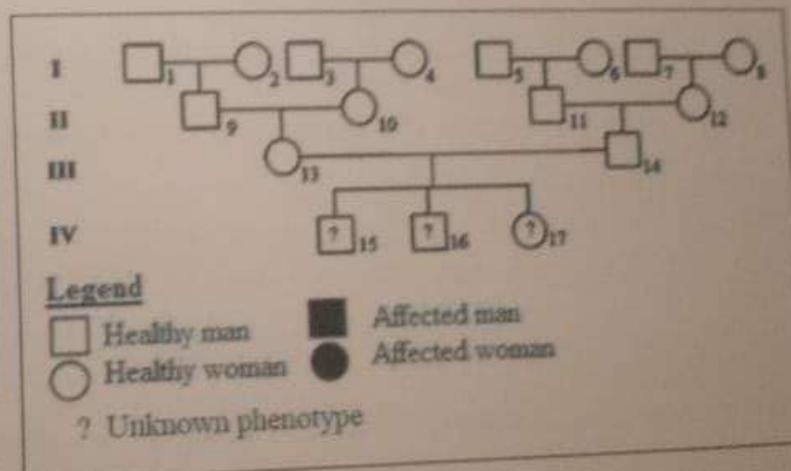
1- Specify, by referring to document 1, the origin of hemochromatosis.



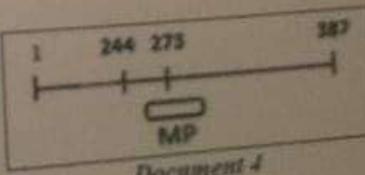
The frequency of heterozygotes in a certain population is 1/10.

A healthy couple, older than 40 years, belongs to this population. This couple would like to know if their three children, who appear healthy, have a risk to develop the disease. That's why they consult a doctor who, as a first step, establishes for this family a pedigree which is shown in document 3.

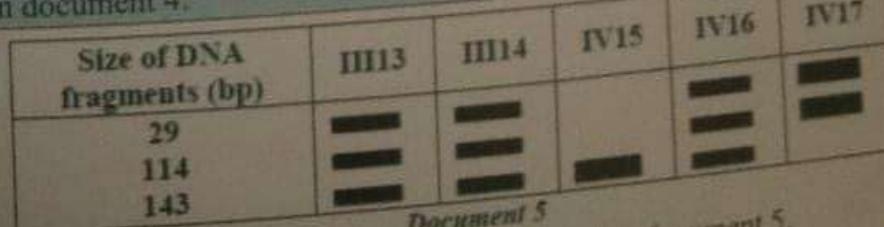
3- Calculate the risk for this couple, III13 and III14, to have an affected child.



As a second step, the doctor performs DNA analysis by applying the southern blot technique using the restriction enzyme RsaI and a radioactive molecular probe (MP) which is complementary to a specific sequence of HFE gene. This probe can fix to the whole or to a part of the recognized sequence as shown in document 4.



Document 5 shows the results obtained by this technique for certain members of this family.



4- Explain the absence of the 244 bp fragment in the electrophoreogram presented in document 5.

5- Establish the diagnosis for each of the children in document 5.

**Question -23-** Cystic Fibrosis  
Certain mutations which are at the origin of genetic diseases may protect against other diseases. In order to clarify this observation, the following studies are performed.

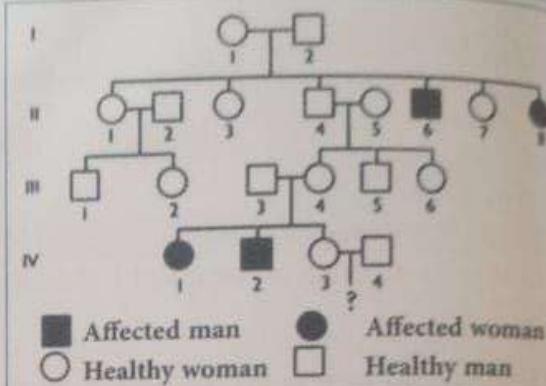
### Study 1:

**Study 1:** Cystic fibrosis is a severe disease manifested by respiratory and digestive troubles. The origin of the disease is a mutation of the gene coding for the protein CFTR leading to the modification of amino acid 508. The protein CFTR is present in the plasma membrane of the cells. It allows the exchange of Cl<sup>-</sup> ions and therefore, the exchange of water.

The alteration of this protein blocks the passage of the Cl- ions and water leading to an increase in the viscosity of the mucus, particularly at the level of the lungs and the digestive tract. In a well-defined population, 1 out of 20 persons are heterozygous.

Document 1 shows the pedigree of a family whose some members are affected by cystic fibrosis.

- 1- Pick out:**



- ### 1-2 The consequences of the mutation at the cellular level.

- 2- Indicate if the allele responsible for the disease is dominant or recessive. Justify the answer.

- 3- Determine the chromosomal localization of the gene responsible for cystic fibrosis.

- 4- Specify the genotype of each of the individuals II8, III3, IV2 and IV3.

- 5- Determine the risk for couple [V3 and V4] to have a child affected by cystic fibrosis.

Three lots of mice are genetically modified by integrating the human gene coding for CFTR protein in their genome. The mice of lot 1 are homozygous for the normal allele, the mice of lot 2 are homozygous for the mutated allele, and the mice of lot 3 are heterozygous. *Salmonella typhi* is used as a challenge agent.

Salmonella typhi bacteria have been ingested by the mice of the three lots. The number of intestinal cells infected by Salmonella typhi is estimated. The results are shown in document 2.

| Doc-2   | Lot 1                              | Lot 2                              | Lot 3                         |
|---------|------------------------------------|------------------------------------|-------------------------------|
| Mice    | Homozygous for the normal alleles  | Homozygous for the mutated alleles | Heterozygous for this gene    |
| Results | Numerous infected intestinal cells | No infected intestinal cells       | Few infected intestinal cells |

The infection by this bacterium leads to Typhoid fever which is manifested by a very serious inflammation of the digestive tract leading to death in the absence of any antibiotic.

- 6- Justify, referring to what precedes, that some mutations which are at the origin of genetic diseases may protect against other diseases.

## Diagnosis of Galactosemia

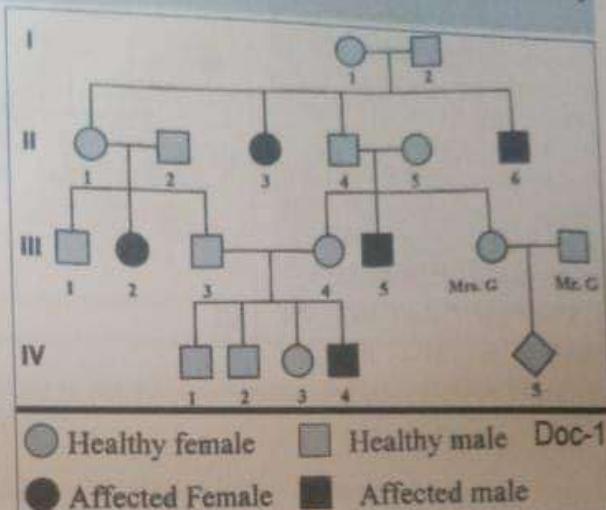
Galactosemia is a genetic disease which results from a deficiency in the enzyme transforming galactose to glucose. Several days following the consumption of milk or milk products, the following clinical signs appear like vomiting, diarrhea,.... On the long term, infants would show retarded growth and later they may have mental retardation.

Mr. and Mrs. G are expecting a child. Mrs. G is worried because several members in her family are affected this disease as shown in the pedigree presented document 1.

1. Indicate if the allele responsible for the disease dominant or recessive. Justify the answer.

2. Determine the chromosomal location of the gene responsible for this disease.

3. Specify the possible genotype(s) of Mrs. G and individual IV-4.



Worldwide, the probability of individuals to be heterozygous is 1/100.

4. Determine risk for the expected child, IV-5, to be diseased.

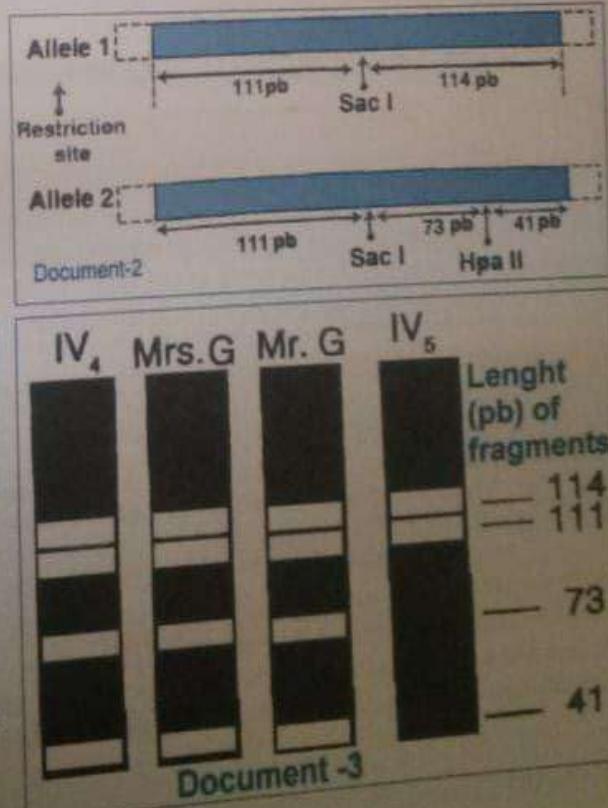
The GALT gene is responsible for galactosemia. Document 2 shows the cleavage sites of two restriction enzymes, Sac I and Hpa II, at the level of a part (from nucleotide 1367 nucleotide 1605) of two alleles this gene: Allele 1 & allele 2.

Document 3 represents the results of electrophoresis obtained after the combined action of enzymes, Sac I and Hpa II on allele 1 and allele 2 of GALT gene of certain family members.

5. Indicate, by referring document 2, the number size of restriction fragments obtained by the enzymatic digestion 1 and allele 2.

6. Determine the allele which corresponds to the mutant one.

7. Verify if the fetus IV-5 will be affected by galactosemia.





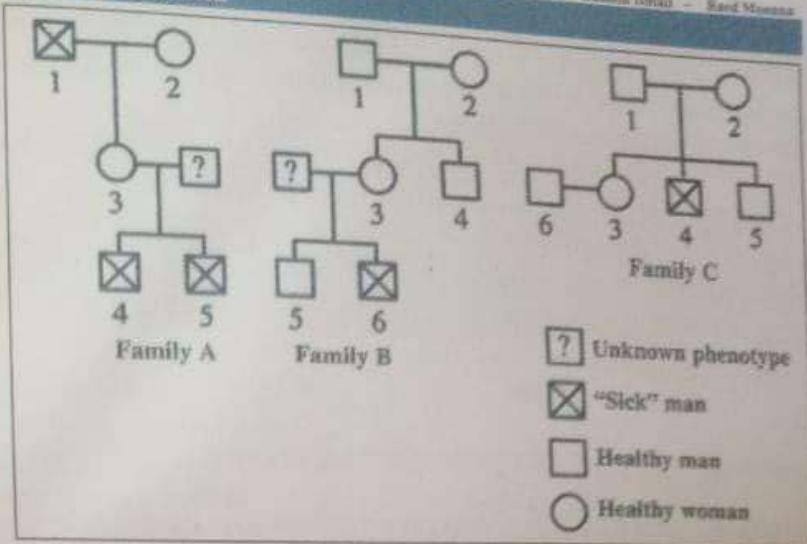
### Question 33

There is a type of anemia, characterized by a very fast destruction of the red blood cells.

This is a genetic anomaly which is caused by the absence of a molecule called glucose-6-phosphate dehydrogenase (G6PD), an enzyme which intervenes in the glucidic cycle metabolism in the red blood cells. A study applied on three different families allowed the tracing of their genealogical trees.

### Origin of Anemia

BioGuide 12 LS - Version F - © Barron's Test Prep - Barron's Test Prep



1- Among the three families, determine the one which allows recognizing if the responsible allele is a dominant or a recessive one.

2- Knowing that the individual number 1 of family C does not carry the responsible allele, show that the gene is located on the part of chromosome X which does not have an equivalent part on Y. we will designate the two alleles by N or n.

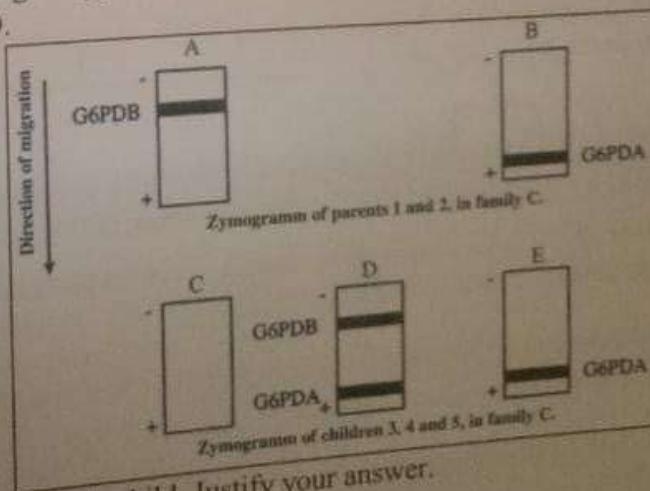
3- Write the possible genotype(s) for all family C members. Justify briefly your answer.

4- Determine the risk, for the woman number 3 in family C, to give birth to a child who suffers from a G6PD deficiency. What would be this risk if the expected child is to be a boy?

In family "C", one of its members has two possible genotypes. In order to make a final decision, a more detailed study is made on the gene coding for G6PD.

The locus of the gene may be occupied by one of the alleles A and B that govern the synthesis of two molecules having the same enzymatic activity, G6PD-A and G6PD-B. The locus may also be occupied by an inactive allele.

On a nitrocellulose paper, we put protein extracts of the red blood cells of different members of family "C" and by electrophoresis, the various enzymes are separated. (Zymograms A, B, C, D, and E).



5- Indicate the zymogram of each parent (1 and 2) and each child. Justify your answer.

6- Make a schema, for each individual 3 and 4 of family C, of the chromosome pair involved. Then place the alleles of the G6PD gene on these chromosomes.

**Question-35- Study of a genetic disease: Huntington chorea.**

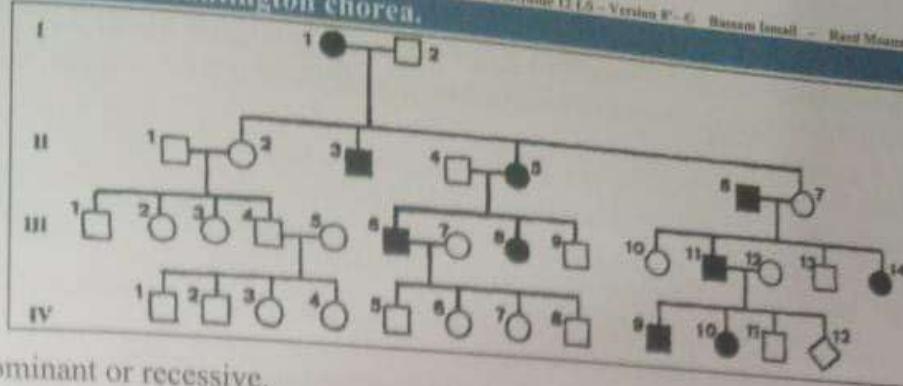
**A-** Huntington disease is a very serious neurological affection.

Document 1 shows the genealogical tree of a certain family-A where the disease is observed.

**Doc.1→**

1- Determine if the allele responsible for the disease is dominant or recessive.

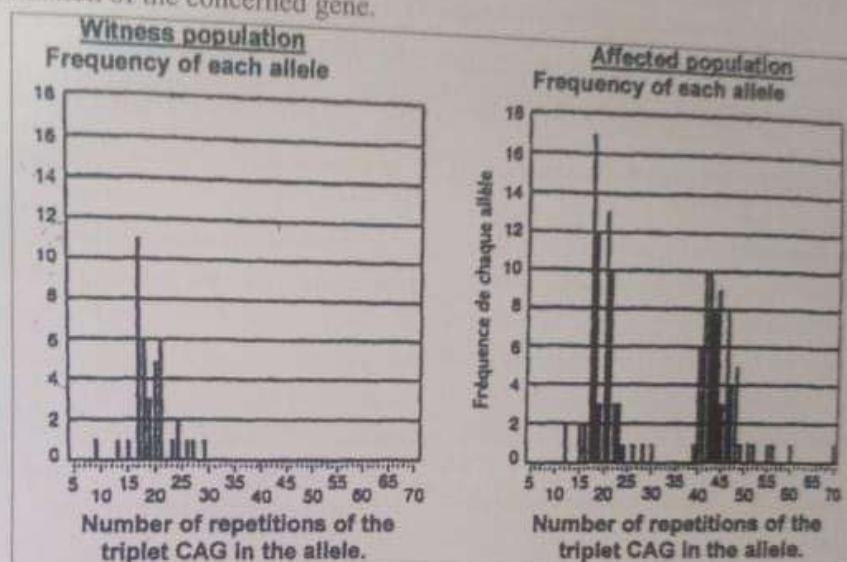
2- Determine the chromosomal localization of the concerned gene.



**B-** The abnormality responsible for this disease has been identified in 1993; it corresponds to a mutation due to the abnormal repetition of the nucleotide triplet-CAG in a gene called IT 15. Here are given the frequencies of the varied alleles of gene IT 15 in two populations: the witness population is composed of 20- healthy persons, while the affected population is composed of 71- sick persons.

**Doc.2**

3- Compare the obtained results. What can you conclude concerning the number of repetitions of the triplet CAG in the normal and the mutated alleles?

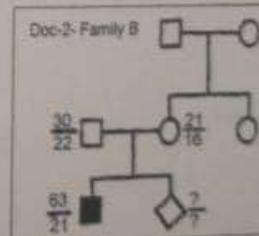


**C-** An investigation of the alleles of gene IT 15 has been carried out in members of family-B; the obtained results show the number of repetitions of the triplet CAG, detected for each allele (doc.3)

4- Using the results revealed by the number of repetitions of the CAG-triplet:

4.1- Give the genotypes of the individuals II<sub>1</sub>, II<sub>2</sub> and III<sub>1</sub>. (Choose suitable symbols for the normal and defective or abnormal alleles).

4.2- Explain the surprising genotype of the affected son III<sub>1</sub>.



**D-** The couple II (1, 2) was worried about the fetus III<sub>2</sub> (since they have an affected son III<sub>1</sub>). A physician demands DNA-analysis to ask the parents questioning. The result of DNA-analysis is shown in document-4. (30 and 22 refer to the number of repetitions of CAG-triplets)

**Doc-4**

5- 5.1- Referring to the DNA-analysis, specify the genotype and phenotype of the coming child concerning the studied disease.

The result of DNA-analysis of the fetus was interesting.

5-2. Formulate a hypothesis, issued from the fact that the disease is due to an abnormal increase in the number of repetitions of CAG-triplets, to explain the surprising result of the fetus.

Assume that the surprising state of the fetus is due to an error during meiosis in the course of parent(s) gametogenesis.

5-3. Illustrate chromosomally the behavior of chromosomes during meiosis and fertilization, in both parents, showing the origin of such surprising result concerning the coming child.

30 ————— ↓ Sense of migration

22 —————

• In USA, about 1 in every 500 people has familial hypercholesterolemia; you only have to receive the mutant gene from one of your parents to have the disease. If you have one mutant gene and one normal gene, you are considered to be "heterozygous" for the disease. People who receive a mutant gene from both parents are considered to be "homozygous" for the disease. People who are homozygous for the disease are at a greater age, but, fortunately, the homozygous status is relatively rare.

• People with familial hypercholesterolemia begin to have high LDL blood levels in early childhood. Although normal LDL levels are considered to be under 200 mg/dL, people with familial hypercholesterolemia often have values that top 250 mg/dL in childhood and greater than 300 mg/dL in adulthood. People with two copies of the mutant gene can have cholesterol levels that reach 1200 mg/dL.

• The next pedigree represents a family whose some members are affected by familiar hypercholesterolemia.

1. Show, by using the information of the text, that the allele responsible for the disease is dominant.

2. Calculate the probability of having a sick child in the following cases:

2.1. Marriage of the female III-1 with an affected male.

2.2. Marriage of the female III-11 with a heterozygous male.

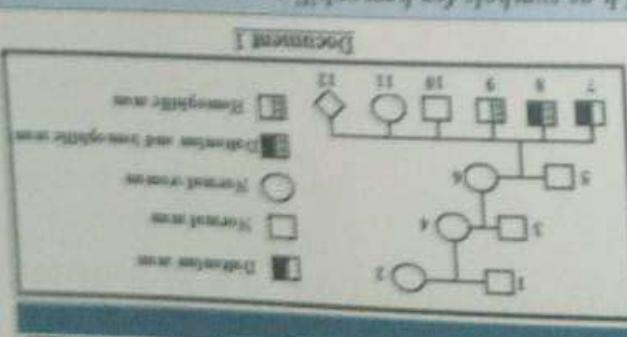
3. Write the genotype of each of individual III-1, II-5, and II-6. Justify the answer in each case.

4. Make the necessary factorial analysis to find the phenotypic percentages of each descendants of the marriage between the male III-6 and a normal female. Give the cholesterol level of each descendant.

#### **Familial Hypercholesterolemia**

| Document 2 |   |   |   |   |   |       |
|------------|---|---|---|---|---|-------|
|            | 1 | 3 | 4 | 6 | 6 | Fetus |
| A1         | — | — | — | — | — | —     |
| A2         | — | — | — | — | — | —     |
| A3         | — | — | — | — | — | —     |

and as symbols for datumism and it and its symbols for remington.

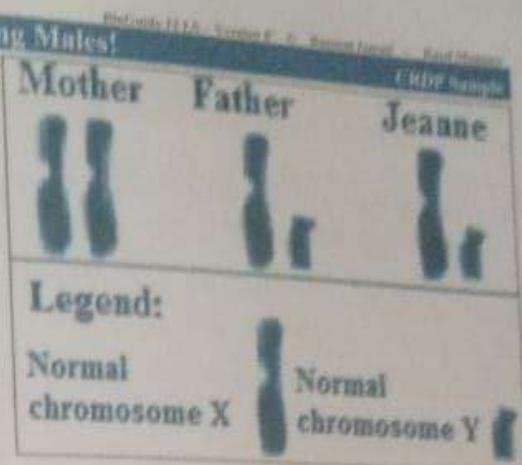


Spontaneous and Deliberate mutations are due to mutations carried by the chromosome X. The pedigree of a family where both abnormalities are expressed permits for each gene the dominant and massive allele, whilst the localizations of the 2 genes are the recombination of individuals 6, 7.

### Young Girls Becoming Males!

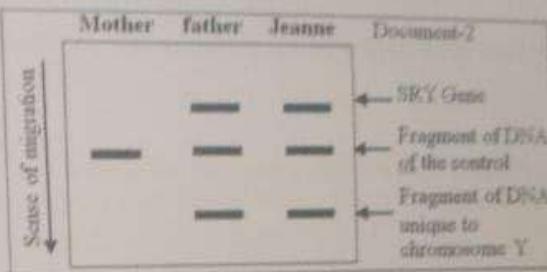
**Question 60:** Some girls in Salinas, a village in the Dominican Republic islands, become boys around the age of 12 years by developing their external genital organs. The parents of Jeanne, a 7-year-old girl from Salinas, consulted a doctor to know if their daughter will suffer from this abnormality. The doctor initially demanded a karyotype for Jeanne and her parents. The results are presented in document 1 that shows only the sex chromosomes X & Y.

- What problem is posed upon studying the karyotype of Jeanne?



Chromosome Y carries a gene named SRY which is responsible for determining the masculine phenotype. The doctor performed a DNA analysis for the family members. The obtained electropherogram is presented in document 2.

- Show that Jeanne's anomaly is not due to the absence of the SRY gene.



SRY gene codes for "TDF protein" which activates testosterone during embryonic life leading to the development of testicles in an embryo of karyotype XY.

Document 3 shows the partial sequences of amino acids of a functional TDF protein (A), a non-functional TDF protein (B) and a TDF protein (C) of Jeanne.

- Does the result of document 3 reveal the origin of Jeanne's anomaly? Justify the answer.

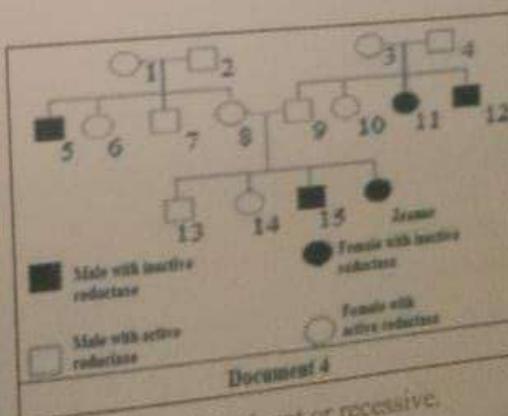
| 1                                             | 5 | 10          |
|-----------------------------------------------|---|-------------|
| A :Met-Gln-Asp-Arg-Val-Lys-Arg-Pro-Met-Asn... |   |             |
| B :Met-Gln-Asp-Arg-Val-Lys-Arg-Pro-Ile-Asn... |   |             |
| C :Met-Gln-Asp-Arg-Val-Lys-Arg-Pro-Met-Asn... |   | Document-3. |

In males, testosterone hormone favors the development of primary and secondary sexual characteristics. During embryonic life, testosterone becomes active in the presence of 5 $\alpha$  reductase enzyme.

At puberty, around the age of 12, testosterone is active without the presence of this enzyme.

The pedigree in document 4 shows the family members of Jeanne with active or inactive form of 5 $\alpha$  reductase enzyme. Individuals 5, 12 and 15 show feminine phenotype before the age of 12. Jeanne's mother 8 and the woman 11 have similar karyotypes.

- Specify if the allele that determines the inactive form of 5 $\alpha$  reductase is dominant or recessive.
- Determine the chromosomal location of the gene responsible for the synthesis of 5 $\alpha$  reductase enzyme.
- Explain why Jeanne who is born with a feminine phenotype becomes a boy at the age of 12.



**Question 61-****Albinism**

Albinism is a hereditary anomaly; it is due to the absence of substance melanin in the epidermal cells and in the cells of the hair roots.

Document 1 shows the pedigree of a Lebanese family with some of its members, represented in black, affected with the disease. In the Lebanese population, statistical studies determined that the disease affects 1/10000 persons, and the proportion of normal persons heterozygous for the disease is 1/20.

1- Specify if the allele responsible for the anomaly is dominant or recessive.

2- Determine logically the chromosomal localization of the gene of albinism.

3- Identify the possible genotypes of individuals: 3, 4, 8 and 9.

4- Calculate the genetic risk of the couples: 3-4 and 8-9 to have an albino fetus.

The synthesis of melanin requires an enzyme which catalyzes the transformation of a substance called phenylalanine into melanin.

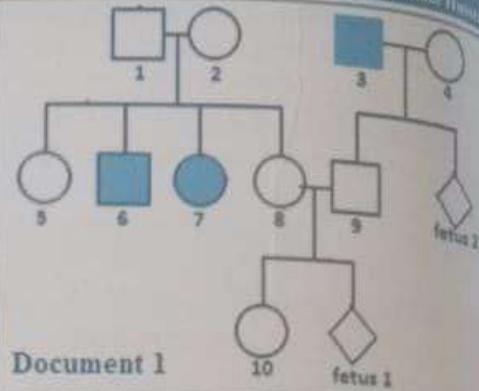
Two alleles exist for the gene that code for this enzyme: normal allele that produces an active enzyme and a mutant allele that codes for an inactive enzyme. Both alleles are extracted from epidermal cells, and then they are put in the presence of restriction enzyme that cut them into fragments. The results obtained are shown in document 2.

5- Based on the obtained results, what is the length of the gene coding for this enzyme?

Document 3 represents the DNA analysis of individuals 3, 4, 8, and 9.

6- Identify referring to results of document 3 the allele responsible for albinism.

7- Calculate according to document 3 the risk of the couple 3-4 and 8-9 to have an albino fetus.

**Document 1**

Period of a Genetics  
**Question 62:**  
There are three 1). Such enzymes called restriction produced by bacteria defend themselves microorganisms (bacteriophages)

We study two all corresponds to the a in refers to the a

1- Pick out from

2- Determine w

3- Knowing th  
Determine why

4- Indicate the  
number of DN

5- Schematize  
enzyme (s).

**Document 2**

| Size of fragment | Allele 1 | Allele 2 |
|------------------|----------|----------|
| 100pb            | —        | —        |
| 200pb            | —        | —        |
| 300pb            | —        | —        |
| 400pb            | —        | —        |
| 500pb            | —        | —        |

| Size of fragment | Document 3   |              |              |              |
|------------------|--------------|--------------|--------------|--------------|
|                  | Individual 3 | Individual 4 | Individual 8 | Individual 9 |
| 100pb            | —            | —            | —            | —            |
| 200pb            | —            | —            | —            | —            |
| 300pb            | —            | —            | —            | —            |
| 400pb            | —            | —            | —            | —            |
| 500pb            | —            | —            | —            | —            |

8- Compare the results calculated in part 7 to those calculated in part 3. What do you conclude regarding the importance of DNA analysis?

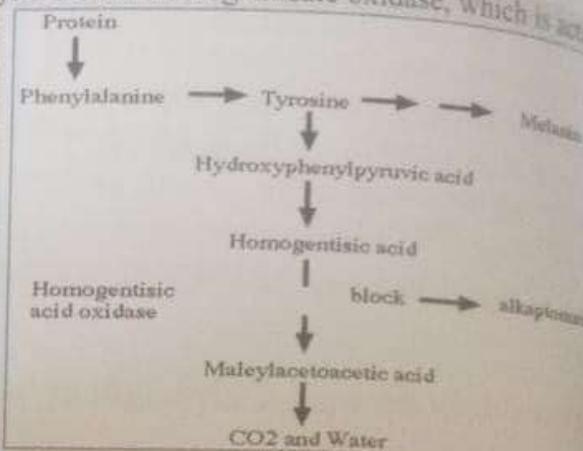
**Question-67****Alkaptonuria**

Updated from Miss Nariman Al-Harbi

Alkaptonuria, also called black urine disease, alcaptonuria, and black bone disease, is a rare inherited disorder. It occurs when your body can't produce enough of an enzyme called homogentisic dioxygenase (HGD). This enzyme is used to break down a toxic substance called homogentisic acid.

The HGD gene provides instructions for making an enzyme called homogentisate oxidase, which is active chiefly in the liver and kidneys. This enzyme participates in a step-wise process that breaks down two protein building blocks (amino acids), phenylalanine and tyrosine, when they are no longer needed or are present in excess. (Document 1) →

The buildup of homogentisic acid causes your bones and cartilage to become discolored and brittle. This typically leads to osteoarthritis, especially in your spine and large joints. Alkaptonuria can also lead to heart problems & high blood pressure. People with alkaptonuria also have urine that turns dark brown or black when it's exposed to air.



- Pick out from the text, the cause & symptoms of Alkaptonuria.

Document 2 represents the pedigree of a family whose some members show Alkaptonuria.

- Is the disease dominant or recessive? Justify your answer.
- Make a logical analysis to determine the location of the disease.
- Formulate a hypothesis to explain the origin of the disease.

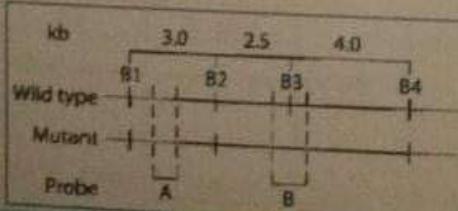
Document 3 represents a portion of the nucleotide sequence of the alleles of HGD gene in normal & affected individual.

| Codon number                                            | 1   | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9   | 10  | 11  | 12  | 13  | 14  | 15  | 16  | 17  | 18  | 19  | 20  |
|---------------------------------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Non transcribed DNA                                     | TTG | GCC | AAT | CCT | CGT | GAT | TTC | TTG | ATA | CCC | ATT | GCC | TGG | TAT | GAG | GAT | CGC | CAA | GTA | CCA |
| Strand of a normal individual:                          |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Non-Transcribed DNA strand:<br>of a diseased individual | TTG | GCC | AAT | TCT | CGT | GAT | TTC | TTG | ATA | CCC | ATT | GCC | TGG | TAT | GAG | GAT | CGC | CAA | GTA | CCA |

4. Write the amino acid sequence of HGD coded by the two DNA strands in a normal individual & in the patient.

5. Compare the DNA & amino acid sequences in both individuals. Conclude the real cause of Alkaptonuria.

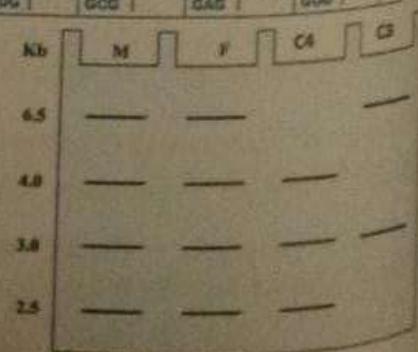
Document 4 shows the DNA restriction fragments of HGD gene obtained by the action of Hind III.



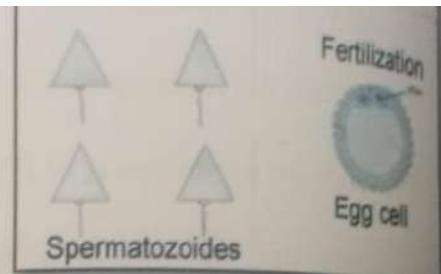
Couple III-1,2 was subjected to DNA analysis in order to determine the origin of the disease in IV-3 & IV-7. The obtained DNA restriction fragments are then separated by electrophoresis & hybridized with a radioactive probe then visualized by autoradiography. The results are presented in Document 5.

5. Specify, by referring to documents 4 & 5, the respective alleles of C3 & C4.

| Letter | Second Letter                    |                              |                              |                             |                                      |
|--------|----------------------------------|------------------------------|------------------------------|-----------------------------|--------------------------------------|
|        | U                                | C                            | A                            | G                           |                                      |
| U      | UUU Phe<br>UUC<br>UUA<br>UUG     | UCU Ser<br>UCC<br>UCA<br>UCG | UAU<br>UAC<br>UAA<br>UAG     | Tyr<br>Stop<br>Stop<br>Stop | UGU Cys<br>UGC<br>UGA Arg<br>UGG Trp |
| C      | CUU Leu<br>CUC<br>CUA<br>CUG     | CCU<br>CCC<br>CCA<br>CCG     | CAU Pro<br>CAC<br>CAA<br>CAG | His<br>Gln                  | CGU Cys<br>CUC<br>CGA Arg<br>CGG     |
| A      | AUU Ser<br>AUC<br>AAA Met<br>AUG | ACU Thr<br>ACC<br>ACA<br>ACG | AAU Asn<br>AAC<br>AAA<br>AAG | Asn<br>Lys                  | AGU Ser<br>AGC<br>AGA Arg<br>AGG     |
| G      | GUU Val<br>GUC<br>GUA<br>GUG     | GCU<br>GCC<br>GCA<br>GCG     | GAU<br>GAC<br>GAA<br>GAG     | Asp<br>Glu                  | GGU Gly<br>GGA<br>GCA<br>GCG         |



3-c. Using document 1, Indicate the types of gametes that are at the origin of individual III<sub>2</sub> and represent the chromosomal and allelic combination of the egg cells (zygotes) that result from the union of these gametes.

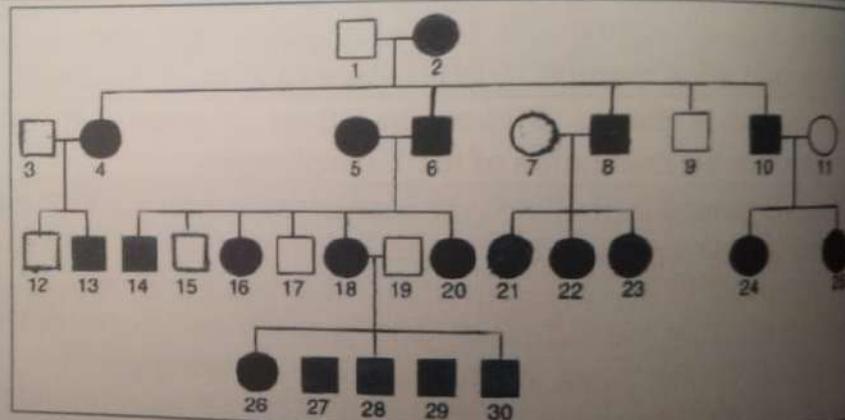


#### Question -85-

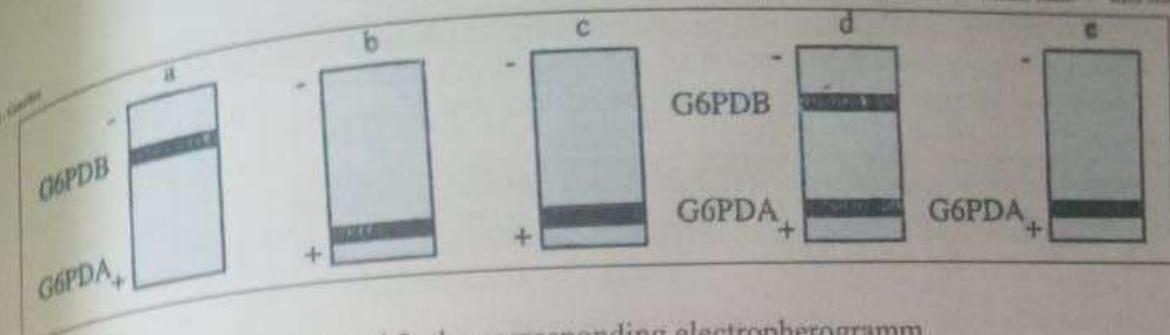
The opposite pedigree shows the transmission in a family of the vitamin-miner-resistant hypophosphatemia, a dominant sex linked hereditary disease.

1- Justify from the pedigree the characteristics of this disease.

2- Determine the chromosomal localization of the gene of this disease.



We perform tests for an enzyme; the G6PD at some members of this family, this enzyme has the gene localized on the X chromosome, and has two forms A and B. The results of these tests are indicated on the electropherograms of the document below.



Look for each one of the parents 1 and 2, the corresponding electropherogramm.

Indicate the genotypes of the tested individuals concerning the disease and the G6PD enzyme.

The individual 13 has an electropherogramme identical to that of the father 1.

How can you explain the state of the individual 13?

#### Duchene muscular dystrophy

Tn-updated

**Section 86:**  
Given the pedigree of a family (document 1) in which certain members are affected by Duchene muscular dystrophy, a disease provoking serious muscular degeneration.

Knowing that the disease was never detected in the families of individuals I2 & II4, show that:

I-1. The diseased allele is recessive.

I-2. The involved gene cannot be autosomal but it is sex-linked.

2- Find the genotypes of the two parents II3 and II4, what was the probability for this couple to have an affected child, just after their marriage? Justify your answer.

3- The couple II3 — II4 after a first affected child is waiting for a second child; to answer the worries of the parents, a prenatal diagnosis was performed by establishing the karyotypes of the parents and that of the fetus. Only the chromosomes involved in the disease are represented:

#### Extracts of karyotypes of the parents and the fetus

3- Explain why one single chromosome is represented in the father's karyotype, while there are two chromosomes in the mother's karyotype; identify this chromosome. Compare the chromosomes of the father and the mother; Find the correlation between the karyotype and the disease.

4- Determine the sex of the fetus, and using a logical reasoning, find its genotype and phenotype.

