

الاسم:  
الرقم:

مسابقة في مادة علوم الحياة  
المدة: ثلاث ساعات

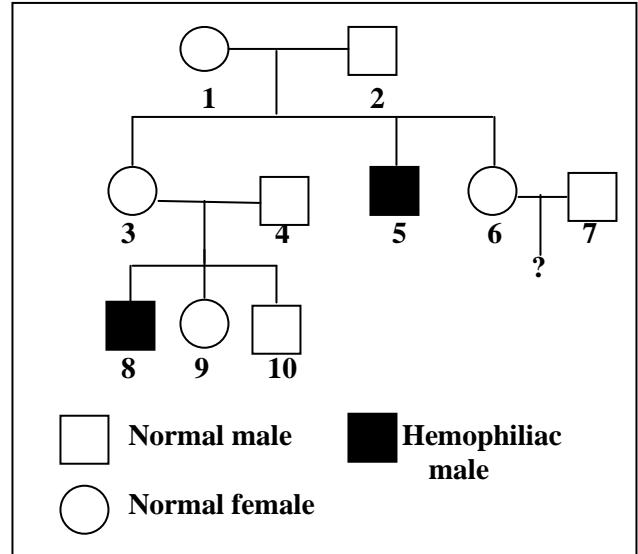
**Answer the following questions.**

**Question I (5 ½ pts)**

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.

- a- Indicate the genotypes of persons 6 and 7. Justify the choice.
- b- Show by logical reasoning, that this pedigree does not permit a sure diagnosis concerning the fetus.
- c- Determine the genetic risk of this child to be hemophiliac.



*Document 1*

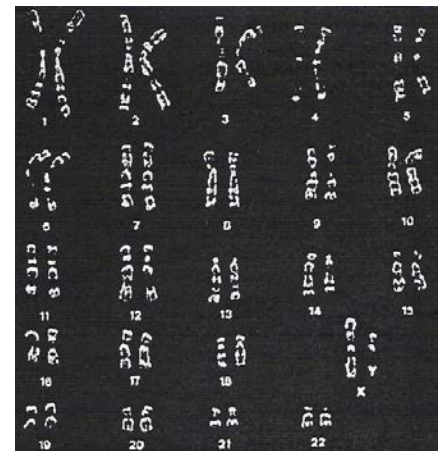
To clarify the diagnostic problem of hemophilia in the fetus, two tests were done. The first test is a karyotype of the fetus, document 2.

- d- 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, 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.



*Document 2*

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

	Mother	Fetus	Person 8
Allele 3	■	■	
Allele 5			

*Document 3*

**Question II (5pts)**

In the framework of studying immune responses, we do the following experiments.

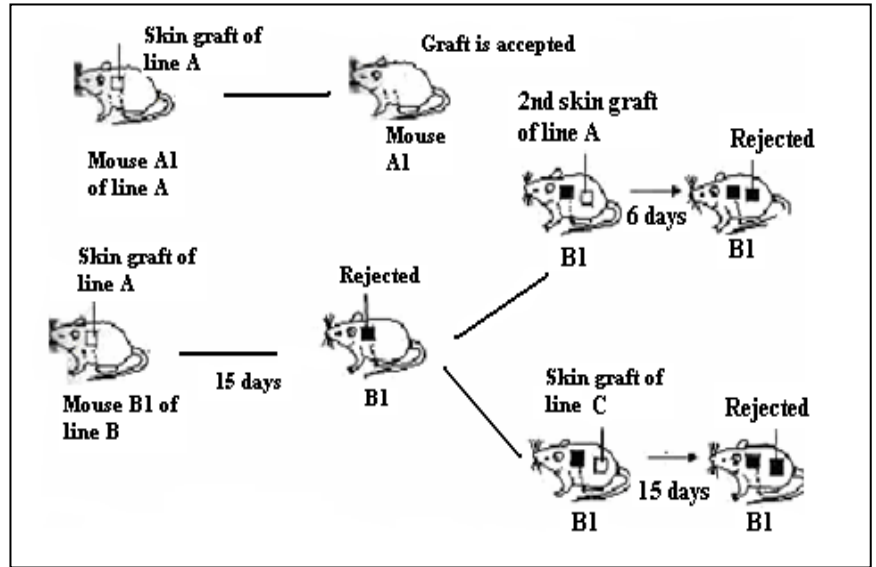
**1<sup>st</sup> Series of experiments:** We perform skin graft between mice A, B, and C of different lines, document 1.

- a- Interpret these experiments.
- b- Indicate two characteristics of the immune system revealed by these experiments.

**2<sup>nd</sup> Series of experiments:** We graft skin of mouse A into mouse B under different conditions. The experiments done and the obtained results are shown in document 2.

- c- Starting from the analysis of document 2, specify the organs involved in graft rejection.

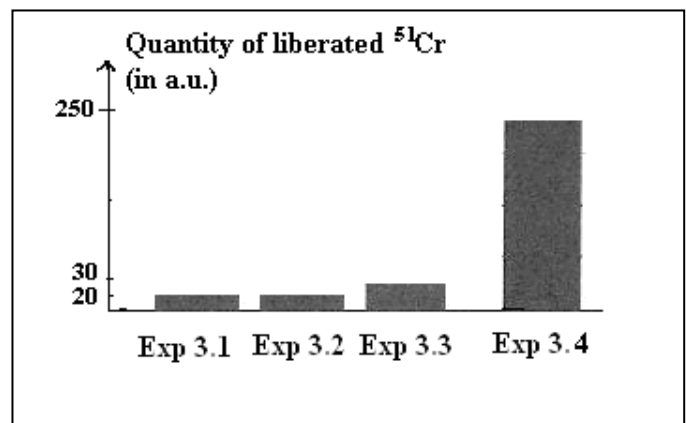
**3<sup>rd</sup> Series of experiments:** We remove cells infected by virus X from a mouse of line A. We incubate the cells with radioactive chromium <sup>51</sup>Cr. This <sup>51</sup>Cr is absorbed and binds to proteins in the cells. After incubation, we wash these cells and culture them with different effector cells obtained from the same mouse A. The supernatants are then collected for measuring the quantity of <sup>51</sup>Cr released by the lysed target cells. Document 3a shows the experiments that are carried out, and document 3b shows the obtained results.



*Document 1*

N <sup>o</sup> of experiment	Experimental conditions	Results
1	Control mouse B	Graft is rejected
2	Mouse B deprived of its thymus	Graft is accepted
3	Irradiated mouse B (destruction of bone marrow)	Graft is accepted

*Document 2*



*Document 3b*

N <sup>o</sup> of experiment	Effector cells of mouse A
3.1	None
3.2	Macrophages
3.3	LT4 + LT8
3.4	LT4 + LT8 + macrophages

*Document 3a*

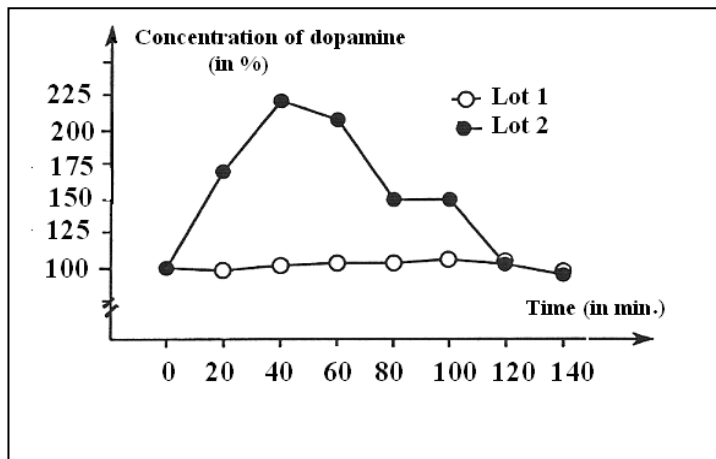
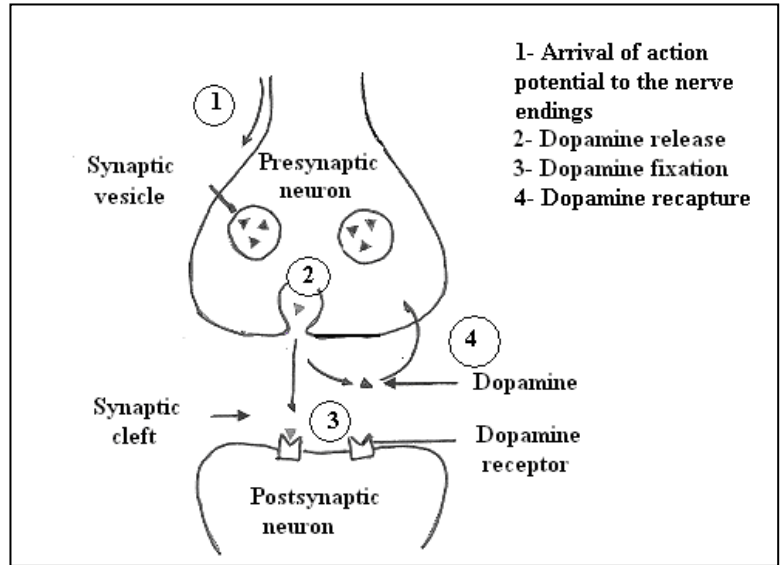
- d- Interpret the obtained results.
- e- By referring to the acquired knowledge, explain how the effector cells of document 3a intervene in the lysis of infected cells.

**Question III (4 ½ pts)**

Studies are done to show the mode of action of cocaine at the level of the dopamine synapse. Dopamine is a cerebral neurotransmitter. Document 1 reveals the functional diagram of the dopamine synapse.

- a- Write a short text describing the mode of action of this synapse.

We measure the concentration of dopamine in the synaptic cleft in two lots of rats. The rats of lot 1 are kept as a control and those of lot 2 received an injection of cocaine at time t = 0 minute. The results are shown in document 2.



*Document 2*

- b- Interpret the obtained results.
- c- Based on documents 1 and 2, propose two hypotheses that explain the mode of action of cocaine at the level of this synapse.

Document 3 indicates the effects of cocaine on the nervous system.

- d- Which of the two proposed hypotheses is validated in document 3? Justify the answer.
- e- Pick out from the text the statements that indicate that cocaine consumption leads to tolerance.

*Document 1*

Cocaine disrupts the fragile balance that allows the few billions of neurons of our brain to function... In the brain, the privileged target of cocaine, are the neurons that secrete dopamine. Normally, the neurotransmitter substances are liberated by a neuron and passes into the synaptic cleft to fix on receptors of the next neuron. Some are recaptured by a specific pump to be liberated later when needed. Cocaine blocks this pump of dopamine recapture. As a consequence: the neurotransmitter stimulates the neighboring neurons permanently. Under the repeated effects of cocaine, the neurons adapt to the abnormally elevated concentration of this substance. The brain is thus, forced to maintain an increased production of this neurotransmitter. This production can only be maintained by the frequent consumption of the drug. This leads to the anxious behavior of cocaine addict in constantly searching for the drug.

*Document 3*

**Question IV (5 pts)**

In the framework of studying birth control, two women A and B use two different types of pills. Mrs. A uses pill of type X. We measure the concentration of progesterone in this woman before and after taking pill X. The results are presented in documents 1 and 2.

**Without pill X**

**N.B. Progesterone concentration is more than 20 ng/mL during the second half of the cycle, which indicates that ovulation took place**

**With pill X**

*Document 1*

- a- Construct a table that includes the variations of the concentration of progesterone of Mrs. A, before and after taking pill X.
- b- Compare the variations of the concentration of progesterone, before and after this woman takes pill X. What can you deduce concerning the effect of pill X?

Mrs. B uses another pill Y to interrupt her early pregnancy. To understand the effect of pill Y, we perform experiments on three lots of rabbits that did not reach puberty. Document 3 shows the experimental conditions and the obtained results.

- c- Draw out from document 3 the target organ and the effect of pill Y. Justify the answer.
- d- Name the birth control method that corresponds to each of the two pills used.

*Document 2*

	<b>Lot 1</b>	<b>Lot 2</b>	<b>Lot 3</b>
<b>Injection of estradiol</b>	+	+	+
<b>Injection of progesterone</b>	-	+	+
<b>Intake of a appropriate dose of pill Y</b>	-	-	+
<b>Results</b>	Thickening of the endometrium, no formation of uterine lace	Thickening of the endometrium, no formation of uterine lace	Thickening of the endometrium, no formation of uterine lace

**(+) presence**

**(-) absence**

*Document 3*

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أسس التصحيح**Question I (5 ½ pts)**

- a- Woman 6 : Normal woman but having a hemophiliac brother, she can be either homozygous  $X^N X^N$  or heterozygous  $X^N X^h$ . ( ¾ pt)  
Man 7:  $X^N Y$ ; normal man and having only one X, thus he carries the normal allele. (½ pt)
- b- The child to be born can be either a girl or a boy. If it was a girl, this pedigree permits a sure diagnosis; she will be normal because her father can give her only  $X^N$ . But if he was a boy, the diagnosis is sure if the mother was homozygous and he will be normal, but if the mother is heterozygous we cannot determine whether the boy is normal or hemophiliac because his mother can give him either  $X^N$  or  $X^h$ . (1pt)
- c- If this child was a girl, the risk is null.  
If this child was a boy, its phenotype depends on the allele provided by his mother. The possibility of the mother of being heterozygote is ½. If she was heterozygous there is a possibility of ½ for giving him  $X^h$  and since we do not know the sex of the fetus there is a chance of ½ to be a boy. Hence the genetic risk becomes  $\frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} = 1/8$ . (1pt)  
Or  
The probability of the mother to be heterozygous is ½, in this case ¼ of her children will be hemophiliac. Hence, the genetic risk =  $\frac{1}{2} \times \frac{1}{4} = 1/8$
- d- No, because the karyotype reveals that it is a boy. If it was a girl the problem would have been solved. (½ pt)
- c- Person 8, has only allele 5. Being hemophiliac, we can say that allele 5 is linked with allele h that codes for hemophilia.  
Mother 6, who is normal, has the two alleles 3 and 5 each one is on an X chromosome. Since allele 5 is linked with allele h, then allele 3 must be linked with the normal allele N. She is thus, healthy but has the allele h, her genotype is  $X^N X^h$ . (¾ pt)  
The fetus has only allele 3, thus he received  $X^N$  from his mother and Y from his father, thus, he will be normal of genotype  $X^N Y$ . (½ pt)
- f- No, because there is a possibility of crossing over between the polymorphic zone and the gene.  
Non-sister chromatids of the two homologous X chromosomes will exchange segments leading to the formation of a chromosome X on which allele 5 is linked with the normal allele N and another chromosome X on which allele 3 is linked with the hemophiliac allele h. Thus, the fetus will be hemophiliac even if his autoradiogram shows the presence of allele 3. (½ pt)

## Question II (5pts)

- a- The skin graft of mouse A received by mouse A<sub>1</sub> of the same line is accepted while the skin graft of a mouse A received by mouse B<sub>1</sub> of line B different from A, is rejected after 15 days. This same mouse rejects a second graft of A, 6 days after grafting, on the other hand it takes 15 days to reject the graft received from a mouse of line C.  
Therefore, the graft succeeds only between mice of the same line and the rejection of the graft is faster upon second recognition. **(1pt)**
- b- Recognition of the non-self by the immune system, the presence of an immune memory, and specificity of the immune response **(½ pt)**
- c- Skin graft taken from a mouse of line A to mouse B (control) leads to the rejection of the graft. On the other hand, the graft is accepted when it is done on mouse B that is deprived of its thymus (experiment 2) or on mouse B that is subjected to the irradiation of the bone marrow (experiment 3).  
Therefore, the thymus and the bone marrow are involved in graft rejection. **(1pt)**
- d- The quantity of <sup>51</sup>Cr released by the cells lysed in a medium deprived of effector cells of mouse of line A and in a medium containing macrophages is 20 a.u. This quantity increases to become 30 a.u. in a medium containing LT4 and LT8 and reaches 250 a.u. in a medium containing LT4, LT8 and macrophages.  
Hence, graft rejection requires the co-operation between these three types of immune cells. **(1pt)**
- e- The macrophages digest the free virus, recognized as non-self, and transform them into peptides and present them on HLA molecules of class II. These macrophages are thus, antigen presenting cells (APC). These latter migrate towards the lymphatic ganglia where they activate the LT4 (LT<sub>H</sub>) that secrete IL-2.  
IL-2 activates the LT8 (LT<sub>C</sub>), which adheres to the membrane of the target cell and releases perforin and granzymes that perforate the membrane and degrades the DNA of the target cell leading to its lysis. **(1½ Pt)**

**Question III (4 ½ pts)**

a- The arrival of action potential to the nerve endings of the presynaptic neuron allows the release of dopamine in the synaptic cleft. Dopamine binds on its postsynaptic receptors, then it is recaptured by the presynaptic neuron. **(1 ½ pt)**

b- At the beginning of the experiment, the percentage of dopamine concentration in the two lots of rats is 100%. This percentage remains almost constant in the control rats of lot 1, while after the injection of cocaine at time  $t = 0$  min. it increases in the rats of lot 2, to become more than twice (225%) after 40 minutes. This percentage starts to decrease to become normal again 100% after 120 minutes.

Therefore, cocaine permits the increase, for a certain time, the quantity of dopamine in the synaptic cleft. **(1pt)**

c- Cocaine increases the release of dopamine in the synaptic cleft.  
Cocaine prevents or decreases the recapture of dopamine by the presynaptic neuron. **( ½ pt)**

d- The validated hypothesis that cocaine prevents the recapture of dopamine because it blocks the pump that allows its recapture. **( ½ pt)**

e- Under the repeated effects of cocaine, the neurons adapt to the abnormally elevated concentration of this substance. The brain is thus, forced to maintain an increased production of this neurotransmitter. This production can only be maintained by the frequent consumption of the drug. **( ½ pt)**

**Question IV (5 pts)**

a- (1 ½ pts)

<b>Time in days</b>	<b>0</b>	<b>4</b>	<b>12</b>	<b>16</b>	<b>18</b>	<b>20</b>	<b>22</b>	<b>28</b>
<b>Concentration of progesterone without pill X (in ng/mL)</b>	0	0	0	5	25	30	30	0
<b>Concentration of progesterone with pill X (in ng/mL)</b>	0	0	0	0	5	10	5	0

*Variations of the concentration of progesterone as a function of time with or without the pill*

- b- Mrs. A with or without taking pill X, the concentration of progesterone is the same, almost null (0.2 ng/mL) from day 1 until day 12. Without pill X, this concentration in a cycle begins to increase to reach 30 ng/mL (> 20 ng/mL) on day 20, indicating that ovulation has taken place. On the other hand, in the cycle with the pill X, the concentration of progesterone increases slightly from 0 - 8 ng/mL (< 20 ng/mL) from day 14 to day 24 of the cycle, which indicates that ovulation did not take place. This concentration starts to decrease from day 24 in a cycle without the pill X and from day 20 in a cycle with the pill to become null, in both cases, on day 28. Therefore, in the presence of pill X, the concentration of progesterone does not reach a high concentration, but remains less than the value that induces ovulation and decreases rapidly. Hence, pill X has an effect of preventing ovulation. (1 ½ pts)
- c- The target organ is the uterus and the effect of this pill is to inhibit the development of the uterine lace, because in the presence of injections of estrogen and progesterone (lot 2) there is a thickening of the endometrium and a development of the uterine lace. On the other hand, the injection of estrogen alone (lot 1) there is only a thickening of the endometrium. This indicates that progesterone acts on the development of the uterine lace. When we add to the injections of estrogen and progesterone the intake of pill Y (lot 3), the uterine lace did not develop. This indicates that pill Y has blocked the action of progesterone on the development of the uterine lace. (1 ½ pts)
- d- Pill X corresponds to a contraceptive method  
Pill Y corresponds to a contragestive method. (½ pt)