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| SAQ 2 | **Examiner Use Only** |
| Explain why haemophilia is an attractive target for gene therapy. | 4 Marks |
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| Haemophilia A and B are both single gene disorders. Genes for the missing factors (VIII and Factor IX) have been cloned and are therefore available for use in gene therapy. Because the disease is caused by a simple deficiency of the factor in plasma there is no need for tissue specific expression as long as it is secreted into blood and no need for precise regulation of production. Even a small amount of FVIII or FIX is very effective in correcting the phenotype and so even low levels of expression would be of significant benefit.  |  |
|  | Mark |
| Explain briefly why a carrier (heterozygote) for haemophilia A may have a normal Factor VIII level. What is the probability of a male child being affected? | 3 Marks |
| Carriers or heterozygotes for haemophilia are always women because the gene for Factor VIII is on the X chromosome and females have 2 X chromosomes and men only one. In a carrier, one X carries an inactive Factor VIII gene but the other X produces normal amounts of Factor VIII. However as a result of X chromosome inactivation (XCI) only one X is active in each female cell. The inactivation process is random and may be skewed in favour of one X or the other. If a greater number of cells have inactivated the X with the non-expressing FVIII gene then the carrier’s Factor VIII level will be in the normal range. A carrier may give either of her 2 X chromosomes to a male child with equal probability. Therefore if the child is male, then the probability that he is affected is 0.5.  |  |
|  | Mark |
| Explain why low molecular weight heparins have proved a popular replacement for unfractionated heparin  | 3 Marks |
| In most circumstances LMWH have a much more reliable dose response relationship than that for UFH. As a consequence they do not usually require monitoring. They can be given as a once daily sub cutaneous injection. The LMWH are associated with a lower risk of heparin induced thrombocytopenia. (HIT) |  |
|  | Mark |
|  | TOTAL |