GENETICS 603
EXAM 3, Dec. 1, 2006
NAME_____

1. Retinoblastoma in humans was long considered to be a dominant trait with reduced penetrance, since not every child who inherited the gene developed the cancer. What is the actual situation as far as the inherited form of retinoblastoma is concerned?

Almost all familial cases result from a deletion on one copy of the RB gene: if the second copy of this tumor suppressor gene mutates in a developing retina cell, cell division continues and the tumor forms.

2. A recent speaker at a Genetics seminar suggested that crossovers initiated early in synapsis of homologous chromosomes play an important role in making sure that the kinetochores of the homologues find and remain attached to spindle fibers from opposing poles. Connect this observation with the relatively high frequency of trisomy-21 births seen in humans.

First, 21 is a short chromosome so there may not always be a crossover present. Meisois I begins in human females soon after conception, arrests until at least puberty and then resumes years later as each ovarian follicle matures. Since the frequency of trisomy 21 increases greatly with maternal age, perhaps the lack of crossovers (if true) permits more detachments with time. The translocation type of trisomy could also lead to problems as there may be 3 centromeres rather than 2 pairs, but these account for only a small portion of the trisomy 21 births.

3. Many species of insects are infected with *Wolbachia sp*, which are rickettsia-like bacteria that are passed through the egg. Sperm of infected males are inactivated from fertilization unless Wolbachia are present in the egg.
A) Predict the "population-genetics" effects of Wolbachia on the host species.

The theory is that since Wolbachia (W) infected females can mate with either infected or non-W males, they will be more fit (higher reproductive rate) than non-infected so that W will spread through the population (much as the P-element has spread in Drosophila. I would certainly accept other answers, such as evolving to 2 separate populations or that W makes the mosquitoes less fit, but that would then require explaining why they are so prevalent.

B) Is Wolbachia an example of cytoplasmic inheritance? Justify your answer.

It is cytoplasmically transmitted, but technically is infectious heredity since it is not one of the essential organelles that contains DNA.

C) Recently it has been shown that Wolbachia injected into *Aedes aegypti* cause the same fertility characteristics in this mosquito species. It has been suggested that Wolbachia may prove useful in preventing the spread of dengue fever from a virus carried by *Aedes aegypti*. What is the rationale for this claim, and how might a prevention plan be implemented?

The primary concept requires establishing a W+ population of *A. aegyti* and then releasing it in high dengue fever areas where it would "take over" bsed on increased fitness. The bacteria would also be engineered to prevent virus replication in the cytoplasm.

4. A trisomic Datura plant has a "Dwarf" gene D on the trisomic chromosome that is dominant even if present in only one copy. Predict the phenotypic ratios for progeny of DDd by Ddd reciprocal crosses if

a) disomic eggs are functional but not pollen

DDd female by Ddd male

Eggs\Pollen	1 D	2 d
2 Dd	2 DDd	4 Ddd
1 DD	1 DDD	2 DDd
1 d	1 Dd	2 dd
2 D	2 DD	4 Dd

1 Tall : 8 dwarf

Ddd female by DDd male

Eggs\Pollen	2 D	1 d
2 Dd	4 DDd	2 Ddd
1 dd	2 DDD	1 ddd
1 D	2 DD	1 Dd
2 d	4 Dd	2 dd

1 tall 6 dwarf

b) both disomic eggs and pollen are functional.

(Since male female gametes will make the same ratiosn, reciprical crosses will be the same)

Eggs\Pollen	1 D	2 Dd	1 dd	2 d
2 Dd	2 DDd	4 DDdd	2 Dddd	4 Ddd
1 DD	1 DDD	2 DDDd	1 DDdd	2 DDd
1 d	1 Dd	2 Ddd	1 ddd	2 dd
2 D	2 DD	4 DDd	2Ddd	4 Dd

3 of 36 (1:12) will be tall

5. The term "threshold disease" has been applied both to quantitatively and cytoplasmically inherited traits. Explain how the term applies to these 2 very different types of inheritance, and give an example of each if possible.

Thresholds in quantitative traits occur when any individual with more than a specific number of contributing alleles has an "all or none" trait (for example schizophrenia).

In cytoplasmic traits, most individuals are heteroplasmic, and since the organelles distribute by chance into daughter cells or eggs, only tissues or individuals with a "threshold" level of defective (mitochondria in the case of MERF for example) exhibit the symptoms.

6. Lebers hereditary optic neuropathy (LHON) is always associated with a point mutation in one of the 13 protein encoding genes in human mtDNA. However, not everyone with the mutation has LHON, and the disease is seen 5 times more often in males than females. Propose a model that will account for these facts.

Since all mt-coded proteins are parts of proteins that interact with nuclear components, the simplest model would be to say that the LHON mutation can be seen only in the presence of a recessive allele of a gene on the X chromosome that encodes another of the interacting components. Even if the X-linked allele is common, say in 20% of the males, it would only be homozygous in 4% of females

7. A shepherd has a random mating flock of 200 sheep (100 each sex) where ¾ of the rams have horns and ¾ of the ewes are hornless. Not realizing the mechanism of inheritance involved, but knowing that he would like to have all males with horns and hornless females, he sells off the hornless males and horned females before producing the next generation of progeny.

A) Give a legend that describes the inheritance of horns in these sheep.

Male	horns	horns	hornless
	H'H'	H'H'	HH
Female	horns	hornless	hornless

B) What are the allele and genotype frequencies in the original herd.

allele f(H') = 0.5, f(H) = 0.5, genotype: .25 H'H': 0.5 H'H: 0.25 HH

C) What will happen to the gene and genotype frequencies in the progeny generation?

		sperm		
		1/3H	2/23 H'	
eggs	2/3 H	2/9HH	4/9H'H	males 7 horns:2 non
	1/3 H'	1/9H'H	2/9H'H'	females 2 horns:7 non

D) Suppose the same selection protocol is applied the next generation. What will the male and female progeny in the following generation look like, with regard to horns?

males 151 horned : 45 hornless
females 151 polled:45 horned

8. Genetic tests of adults in a fairly large and fairly closed society in Senegal where malaria remains a problem showed 626 homozygous for Hb-β^A/ Hb-β^A, 249 heterozygous (Hb-β^A/ Hb-β^S, and 0 adults with sickle cell anemia Hb-β^S/Hb-β^S.

a) Calculate allele and expected genotype frequencies for this population.
1501/1750 = f(HbA) = 0.858; f(HbS) = 0.142
genotypes expected under HW .7357 AA : .2411 AS : .0202 SS

b) How would you test for Hardy-Weinberg equilibrium?
Chi square test for the 3 classes; sum of (observed-expected)/expected with 1 df

c) Calculate relative fitness value for each genotype:

Hb-β^A/ Hb-β^A	Hb-β^A/ Hb-β^S	Hb-β^S/Hb-β^S
0.834	1 (by definition)	0 since none survive

(for AA, 626/644 is fraction expected surviving, then divide by 1.16 to normalize the heterozygotes to 1)

d) If an anti malarial vaccine can be developed, what will happen to the gene frequencies? What would the eventual equilibrium value of the Hb-β^S allele be predicted to be?
Since the heterozygote is no longer favored but the Hb^SHb^S is still lethal, the S allelel should decline to the square root of the mutation rate (selection against recessive lethal)

e) Now suppose that that effective treatment for sickle cell anemia is also found. Predict the eventual equilibrium genotypic frequencies for the Senegal population in this case.
It should go to equilibrium immediately (no force acting other than forward and reverse mutations) ie 0.7357 AA : 0.2411 AS : 0.0202 SS