Sickle-Cell Genetics

Believe it or not, there are 50 couples all with the same blood type and hemoglobin genotypes. They live on a small, isolated Pacific island on which very few mosquitoes have been identified. All the individuals are <u>heterozygous for type</u> A blood and have the sickle cell trait. The fifty couples have had 224 children over the years. The children were all tested for blood type and for the presence of the sickle cell allele. Here are the results:

$I^A ; S_s \times I^A ; S_s$

Blood test results	Number of Children
Type A, normal RBCs	48
Type O, normal RBCs	18
Type A, sickle cell trait	92
Type O, sickle cell trait	33
Type A, sickle cell disease	27
Type O, sickle cell disease	6

Are these data significant? Explain using a chi-squared statistical analysis test. (Use the table below if you need assistance.)

Phenotype	Observed (o)	Expected (e)	(o-e)	$(o-e)^2/e$
A, Normal	48	$\frac{3}{4} \times \frac{1}{4} = \frac{3}{16}$ 42	6	0.86
O, Normal	18	$\frac{1}{4} \times \frac{1}{4} = \frac{1}{16}$ 14	4	1.14
A, Trait	92	$\frac{3}{4} \times \frac{1}{2} = \frac{3}{8}$ 84	8	0.76
O, Trait	33	$\frac{1}{4} \times \frac{1}{2} = \frac{1}{8}$ 28	5	0.89
A, Disease	27	$\frac{3}{4} \times \frac{1}{4} = \frac{3}{16}$ 42	-15	5.36
O, Disease	6	$\frac{1}{4} \times \frac{1}{4} = \frac{1}{16}$ 14	-8	4.57

224   224

1) What is the chi-square value ($\chi 2$)? 13.58 $\chi^2 = 13.58$

2) Calculate the degrees of freedom (df). 6-1 = 5

3) Using the Critical Values Table, determine the p value. $\chi^2 > 11.07$
   $p < 0.05$ $(0.025 < p < 0.01)$

4) Interpret the p value as it relates to these data. Explain the significance.
   Reject null hypothesis, no stat. significance btw exp. + obs. There's a significance to these differences.

5) From what you know about hemoglobin, sickle cell disease, and blood type, what selection pressure is acting on this population of children causing the null hypothesis to be rejected? Explain your answer. (Hint: Look at the actual differences between the observed and expected numbers.)
   Much less people w/ disease than expected b/c they are dying of sickle cell before reproducing. They are being selected against

6) Due to the increase in global travel and the prevalence of invasive species, the *Anopheles* mosquito carrying the malaria parasite was inadvertently introduced to this isolated Pacific island. A researcher, one hundred years from the present day, decides to complete a follow-up study and monitors another 50 couples, all of whom are heterozygous for type A blood and have the sickle cell trait. These couples had 136 children. Based on the introduction of the *Anopheles* mosquito carrying the malaria parasite, predict scientifically, logical observed numbers of children for each genotype possibility and complete a chi-squared statistical analysis test.

	Phenotype	Predicted Observed (o)	Expected (e)	(o-e)	$(o-e)^2 / e$
A	Normal	19	$3/4 \times 1/4 = 3/16$ 25.5	-6.5	1.66
O	Normal	5	$1/4 \times 1/4 = 1/16$ 8.5	-3.5	1.44
A	Trait	70	$3/4 \times 1/2 = 3/8$ 51	21	8.65
O	Trait	25	$1/4 \times 1/2 = 1/8$ 17	8	3.76
A	Disease	13	$3/4 \times 1/4 = 3/16$ 25.5	-12.5	6.13
O	Disease	4	$1/4 \times 1/4 = 1/16$ 8.5	-4.5	2.38

(left margin annotations:) ↓ than expected [A, O Normal]   ↑ than expected [A, O Trait]   ↓ than expected [A, O Disease]

136                          $x^2 = 24.02$

(margin:) Should still see 3 Type A to 1 Type O Ratio

a) What is your **predicted chi-square value** ($x2$)? ___24.02___

b) Calculate the **degrees of freedom** (*df*). ___6-1 = 5___

c) Using the Critical Values Table attached, determine the **predicted p value**. ___$p < 0.01$___

d) From your predicted numbers, do you accept or reject the null hypothesis? ___reject___

e) Based on what you know about hemoglobin, sickle cell disease, blood type, and malaria, what selection pressures are acting on this population of children? Explain your answer.

— Malaria killing more normal's (Homo. Dom) than expected — Selection against them.

— Sickle cell killing more with disease (Homo Rec) than expected — selection against them.

— Heterozygotes — have an advantage and thus (more and expected. — selection for them
⟶ Their cells — not enough to cause disease, but not enough for protozoan to cause malaria