應考同學得使用普通電子計算機或工程(商業)用電子計算機。其他電子輔助機具一律不可使用。本卷所附之統計表可供計算參考，其餘書本、筆記、講義、印刷品等，請收放於考場規定位置。

Please describe what "**healthy worker effect**" is; in addition, please give a **definite example** to explain how the effect influences the study. (25%)

2. The use of genetic biomarkers in occupational epidemiology now is a novel progress. For example, recent research has uncovered an allele that appears directly related to the risk of contracting chronic beryllium disease; other chromosomal abnormalities have been identified in association with cancer. Gene-environment interactions are thought to be critical for multifactorial diseases such as cancers, occupational asthma…etc. Please **state your opinions** on the scientific, ethical, and social implications for occupational epidemiologists and practitioners to consider, including issues involving individual risk estimation, the communication of epidemiologic results, and the translation of epidemiologic data into clinical or occupational health practice. (20%)

3. What is a case-control study? Please give **a definite example of case-control study with the statistic methods, and explain the advantage and drawback.** (25%)

4. What are the **assumptions** of a regression analysis? (10%) Meanwhile an computer output as:

Dependent Variable: Y

Model		Sum of Squares	df	Mean Square	F	P
1	Regression	49359.045	4	12339.761	44.880	< 0.001
	Residual	6598.765	24	274.949		
	Total	55957.810	28			

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	0.939(a)	0.882	0.862	16.58157

Model		Unstandardized coefficients		Standardized Coefficients	t	P
		Beta	Std. Error			
	(Constant)	-16.577	18.880		-0.878	0.389
	X1	7.839	1.234	0.727	6.350	< 0.001
	X2	-34.389	11.146	-0.380	-3.085	0.005
	X3	-7.990	8.249	-0.114	-0.969	0.342
	X4	54.930	13.524	0.584	4.062	< 0.001

Please explain what difference between R square and adjusted R square. (10%)
Please explain what difference between unstandardized coefficients and standardized coefficients. (10%)

A common symptom of otitis media in young children is the prolonged presence of fluid in the middle ear, known as middle-ear effusion. One hypothesis is that babies who are breast-fed for at least 1 month build up some immunity against the effects of the disease and have less prolonged effusion than do bottle-fed babies. A small study of 20 pairs of babies is set up, where the babies are matched on a one-to-one basis according to age, sex, socioeconomic status and type of medications taken. One member of the matched pair is a breast-fed baby whereas the other member is a bottle-fed baby. The outcome variable is the duration of middle-ear effusion after the first episode of otitis media. The results are given in the table. (15%)

Pair number	Duration of effusion in breast-fed baby (days)	Duration of effusion in bottle-fed baby (days)	Pair number	Duration of effusion in breast-fed baby (days)	Duration of effusion in bottle-fed baby (days)
1	20	18	11	12	21
2	11	35	12	30	28
3	24	182	13	15	98
4	28	33	14	7	58
5	58	223	15	65	77
6	39	57	16	10	12
7	17	76	17	7	8
8	17	186	18	19	16
9	52	39	19	34	28
10	14	15	20	32	49

Please test the hypothesis that the duration of effusion is less prolonged among breast-fed babies than among bottle-fed babies using a nonparametric test.

2. 某研究生探討一基因座多型性與疾病之關係如下表，對偶基因 A 為顯性，a 為隱性，請檢定此群體的基因分布是否達到 Hardy-Weinberg equillbrium? (15%)

基因型	有病	正常	合計
AA	121	169	290
Aa	146	117	263
aa	42	47	89

3. 有一組樣本(x_i,y_i)， x, y 皆為連續性資料，樣本數為 n, 請以最小平方法 (least squares method)求證迴歸係數 $\hat{\beta}=\frac{\sum(X-\bar{X})(Y-\bar{Y})}{\sum(X-\bar{X})^2}$ (20%)

問答題:

一、說明免疫球蛋白（immunoglobulin）基因及其蛋白質構造（protein structure）特性，及其透過那些鍵結用以中和（neutralization）抗原或毒蛋白的生物活性。 (10 %)

二、正常人和糖尿病患者如何利用脂肪酸(fatty acid)代謝成能量，二者之間生化代謝上比較有何異同，請說明之。(10%)

三、DNA replication 需那些酵素參予，及如何進行 replication 說明之。(10%)

四、說明 Vitamin 在人體內具有那些重要的生化功能? (10%)

五、有一研究者從病患取得腫瘤檢體，想瞭解此腫瘤細胞的特性，該如何設計研究步驟及進行研究? (10%)

A. Interpret the following items: (5 point for each item)

1. Western blot
2. DNA affinity precipitation assay (DAPA)
3. RT-PCR
4. TUNEL
5. Hybridoma
6. MALDI-TOF

B. Answer the following questions:

1. Write out three species and three strains of experimental animals that are commonly used for *in vivo* study (10 point).
2. Describe three kinds of methods to study protein-protein interaction (10 point).

問答題: 請自下列六大題中任選五大題作答(每題十分)

(一)試述血紅素(hemoglobin)衍生物產生的色素在體內沉積時所造成之病理變化。

(二)請依時序前後(time sequence)敘述傷口之第二期癒合(second intention healing)的病理變化。

(三)試述休克時所造成的身體各器官之形態學上的變化

(四)試舉例說明生理性增生(physiologic hyperplasia)及病理性增生(pathologic hyperplasia)。

(五)試述致癌病毒(oncogenic viruses)之致癌機轉

(六)試簡述:

a. desmoplasia
b. choristoma
c. lines of Zahn
d. labile cell
e. siderosis

A. Interpret the following items: (6 point for each item):

Genomic imprinting

2. Chromatin IP assay

3. Single-nucleotide polymorphism

4. Translational frameshifting

5. Histone deacetylase

B. Answer the following questions

Describe the molecular mechanism by which small interference RNA induces gene silencing (10 point).

2. Describe three kinds of post-translational modification that may modulate the activity of transcription factors (10 point).