一、配合題

當使用下列5種藥品時，經常可能發生哪些嚴重副作用？因此臨床上會追蹤哪些檢驗項目？並且使用哪些藥品以避免或治療此副作用？請將副作用、檢驗項目、及預防治療方式填寫於答案卷上。請注意每題答案可能不只一個，但每個錯誤答案倒扣一分。(20%)

題號	藥品	副作用	檢驗項目	預防治療方式
1	Insulin drip			
2	Warfarin			
3	Gentamicin			
4	Methotrexate (high dose)			
5	Contrast dye			

二、簡答題

1. 一名藥學生以SOAP分析並計畫一位62歲女性高血壓病人的藥物治療，其中至少有五項重要錯誤，請指出並更正之。(15%)

Subjective: Height 152 cm, Weight 65 kg.

Objective: Systolic BP 148 mmHg, diastolic BP 94 mmHg, heart rate 65 beats/min. BUN 28 mg/dL, serum creatinine 2 mg/dL, serum potassium 3.5 mEq/L, uric acid 7.8 mg/dL, fasting glucose 92 mg/dL. thirsty, frequent urination at night. Current medications include trichlormethiazide 2 mg bid oral pc and over-the-counter calcium with vitamin D daily.

Assessment: (1) Thiazide diuretics are usually not the drugs of choice for hypertension. The patient already experienced severe hypokalemia due to trichlormethiazide and blood pressure is not well controlled, so her physician should add a beta blocker to her current antihypertensive regimen.

(2) Trichlormethiazide may cause hypokalemia and increase uric acid. The physician should add potassium-sparing diuretics, spironolactone, to minimize these side effects.

Plan: (1) Add a beta blocker and spironolactone, and continue trichlormethiazide.

(2) Monitor BP, BUN, serum creatinine, uric acid, serum potassium.

(3) Patient education: Teach patient the importance of medication adherence. As long as she takes current medications regularly, her blood pressure should be under control, and end organ damages will be prevented.

見背面

2. 請閱讀以下研究論文摘要並回答問題：(15%)

A. 一般而言，darbepoetin alfa 在臨床治療上的角色與治療原則是什麼？

B. 此論文之研究設計是什麼（請用中文作答）？是否符合 darbepoetin alfa 的一般治療原則？

C. 這篇研究報告的主要結果是什麼？你認為這對臨床上使用 darbepoetin alfa 有何衝擊？

A trial of darbepoetin alfa in type 2 diabetes and chronic kidney disease.
Pfeffer MA, Burdmann EA, Chen CY, Cooper ME, de Zeeuw D, Eckardt KU, Feyzi JM, Ivanovich P, Kewalramani R, Levey AS, Lewis EF, McGill JB, McMurray JJ, Parfrey P, Parving HH, Remuzzi G, Singh AK, Solomon SD, Toto R; TREAT Investigators N Engl J Med 2009 Nov 19;361(21):2019-32.

Background
Anemia is associated with an increased risk of cardiovascular and renal events among patients with type 2 diabetes and chronic kidney disease. Although darbepoetin alfa can effectively increase hemoglobin levels, its effect on clinical outcomes in these patients has not been adequately tested.

Methods
In this study involving 4038 patients with diabetes, chronic kidney disease, and anemia, we randomly assigned 2012 patients to darbepoetin alfa to achieve a hemoglobin level of approximately 13 g per deciliter and 2026 patients to placebo, with rescue darbepoetin alfa when the hemoglobin level was less than 9.0 g per deciliter. The primary end points were the composite outcomes of death or a cardiovascular event (nonfatal myocardial infarction, congestive heart failure, stroke, or hospitalization for myocardial ischemia) and of death or end-stage renal disease.

Results
Death or a cardiovascular event occurred in 632 patients assigned to darbepoetin alfa and 602 patients assigned to placebo (hazard ratio for darbepoetin alfa vs. placebo, 1.05; 95% confidence interval [CI], 0.94 to 1.17; P=0.41). Death or end-stage renal disease occurred in 652 patients assigned to darbepoetin alfa and 618 patients assigned to placebo (hazard ratio, 1.06; 95% CI, 0.95 to 1.19; P=0.29). Fatal or nonfatal stroke occurred in 101 patients assigned to darbepoetin alfa and 53 patients assigned to placebo (hazard ratio, 1.92; 95% CI, 1.38 to 2.68; P<0.001). Red-cell transfusions were administered to 297 patients assigned to darbepoetin alfa and 496 patients assigned to placebo (P<0.001). There was only a modest improvement in patient-reported fatigue in the darbepoetin alfa group as compared with the placebo group.

Conclusions
The use of darbepoetin alfa in patients with diabetes, chronic kidney disease, and moderate anemia who were not undergoing dialysis did not reduce the risk of either of the two primary composite outcomes (either death or a cardiovascular event or death or a renal event) and was associated with an increased risk of stroke. For many persons involved in clinical decision making, this risk will outweigh the potential benefits.

接次頁

三、請研讀以下短文並回答問題（50%）：

The term "pharmacogenetics" was first coined by Friedrich Vogel in 1959, who defined it as the "study of the role of genetics in drug response." It is one of the most rapidly growing areas and is becoming increasingly important in clinical pharmacy. The pharmacogenetics of drug-metabolizing enzymes is a prominent focus of this field, because genetic makeup is responsible for a significant portion of drug-induced toxicity; many drugs are metabolized by enzymes that are encoded by polymorphically expressed genes. Genotype analysis can be used to identify DNA changes in specific metabolic pathways that produce aberrant phenotypes. Hence, patients can be classified as extensive, intermediate, or poor metabolizers according to their ability to metabolize certain drugs. This classification can differentiate interpatient and intrapatient pharmacokinetic and pharmacodynamic variability; however, not all genetic polymorphisms of drug-metabolizing enzymes are clinically relevant. The potential for a clinically significant event is enhanced if the drug is widely used and has a narrow therapeutic range, if the enzyme pathway plays a major role in the elimination of the drug, or if the number of therapeutic alternatives is limited. With increasing pharmacogenetic evidence, interindividual differences in drug-related toxicity and therapeutic response are no longer idiosyncratic. Although much work is needed to develop applications of pharmacogenetic information for daily patient care, many success stories illustrate how pharmacogenetics can be used to guide therapy. Eventually, pharmacogenetic information may become a routine tool for providing rational individualized therapeutics and patient care.

From: Ma MK, Woo MH, McLeod HL. Genetic basis of drug metabolism. *Am J Health-Syst Pharm* 2002;59:2061–2069.

1. 以上短文請逐句譯成中文。
2. 字詞闡釋：
   A. 請說明你（妳）對「drug-metabolizing enzymes」的認識。
   B. 何謂「interpatient and intrapatient pharmacokinetic and pharmacodynamic variability」？
   C. 請闡述「genetic polymorphisms」意義，其於臨床用藥有何重要性？
3. 基於安全用藥考量，臨床已知某些藥品易受到 genetic polymorphism 影響，試列舉藥品例（至少三例），並逐一說明藥品之用途、藥動學/藥效學特性與使用注意事項。

試題隨卷繳回