一、 以下期刊論文之摘要，係兩項口服抗凝血藥物之安全性比較，請仔細閱讀後回答下列問題： （共計 20 分）

(一) 以中文簡要敘述此研究之方法與結果。 （5 分）

(二) Dabigatran 與 warfarin 的作用機轉各是什麼？若導致嚴重出血時，應如何處理？（8 分）

(三) 一般而言，進行侵入性醫療處置前多久應停止服用 warfarin？理由為何？（2 分）

(四) 試就療效與安全性的觀點，分析門診病人長期服用 dabigatran 或 warfarin 的優缺點分別是什麼？ （5 分）

Periprocedural Bleeding and Thromboembolic Events With Dabigatran Compared With Warfarin: Results From the Randomized Evaluation of Long-Term Anticoagulation Tnerapy (RE-LY) Randomized Trial

Background. Dabigatran reduces ischemic stroke in comparison with warfarin; however, given the lack of antidote, there is concern that it might increase bleeding when surgery or invasive procedures are required.

Methods. The current analysis was undertaken to compare the periprocedural bleeding risk of patients in the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) trial treated with dabigatran and warfarin. Bleeding rates were evaluated from 7 days before until 30 days after invasive procedures, considering only the first procedure for each patient.

Results. A total of 4591 patients underwent at least 1 invasive procedure: 24.7% of patients received dabigatran 110 mg, 25.4% received dabigatran 150 mg, and 25.9% received warfarin, P = 0.34. Procedures included: pacemaker/defibrillator insertion (10.3%), dental procedures (10.0%), diagnostic procedures (10.0%), cataract removal (9.3%), colonoscopy (8.6%), and joint replacement (6.2%). Among patients assigned to either dabigatran dose, the last dose of study drug was given 49 (35– 85) hours before the procedure on comparison with 114 (87–144) hours in patients receiving warfarin, P < 0.001. There was no significant difference in the rates of periprocedural major bleeding between patients receiving dabigatran 110 mg (3.8%) or dabigatran 150 mg (5.1%) or warfarin (4.6%); dabigatran 110 mg versus warfarin: relative risk, 0.83; 95% CI, 0.59 to 1.17; P = 0.28; dabigatran 150 mg versus warfarin: relative risk, 1.09; 95% CI, 0.80 to 1.49; P = 0.58. Among patients having urgent surgery, major bleeding occurred in 17.8% with dabigatran 110 mg, 17.7% with dabigatran 150 mg, and 21.6% with warfarin: dabigatran 110 mg; relative risk, 0.82; 95% CI, 0.48 to 1.41; P = 0.47; dabigatran 150 mg: relative risk, 0.82; 95% CI, 0.50 to 1.35; P = 0.44.

Conclusions. Dabigatran and warfarin were associated with similar rates of periprocedural bleeding, including patients having urgent surgery. Dabigatran facilitated a shorter interruption of oral anticoagulation.

Circulation 2012;126:343–348.

見背面

二、 請針對下列五種致病菌，分別列出治療的首選藥物（若只列出抗生素的種類，每題各得 1 分；若列舉出藥品學名，每題各得 3 分）與選用的理由（每題1分）。（共計 20 分）

(一) Methicillin-susceptible *Staphylococcus aureus*

(二) Penicillin-resistant *Streptococcus pneumoniae*

(三) Vancomycin-resistant *Enterococcus* (VRE)

(四) Extended-spectrum beta-lactamase-producing (ESBL) *Klebsiella pneumoniae*

(五) AmpC-producing *Enterobacter cloacae*

三、 請閱讀以下短文： （20 分）

When the Exception Breaks the Rule: Charitable Use of Outdated Drugs

Dr. C.A. Lien, a physician, is scheduled to depart on a mission to Burkina Faso, a country in west Africa, with the Project Assist. Medications are in very short supply in Burkina Faso, and Dr. Lien whould like to take some with him.

Dr. Lien asks Harold Deng, director of pharmacy at the local hospital if he will donate any expired or soon-to-expire products to the Project Assist. Dr. Lien explains that he believes that any medications, even those that are not fully potent, could be used. Pharmacist Deng reminds Dr. Lien that hospital procedures may prevent the pharmacy from donating medication. For example, current hospital policy is to return all eligible medication for partial credit and to incinerate all others. Pharmacist Deng explains that the health authority also prohibits the distribution of expired medications. Nevertheless, pharmacist Deng also believes that the soon-to-expire medications he has should be given to Dr. Lien.

Should pharmacist Deng follow his conscience and give the soon-to-expire drugs to Dr. Lien, even if that means he has to get around the hospital's policy?

Modified from: Veatch RM, Haddad A. *Case studies in pharmacy ethics*. 2nd ed. Oxford: Oxford University Press; 2008.

(一) 請簡述短文重點。

(二) 如果你（妳）是短文中之「pharmacist Deng」，面對 Dr. Lien 之提問，你（妳）會如何處理（並請說明理由）？

接次頁

四、 Please read the following article and answer questions. （共計 40 分）

(Total 40%, 8% for each number of questions 1-5)

Background Whether sequential treatment can replace triple therapy as the standard treatment for *Helicobacter pylori* infection is unknown. We compared the efficacy of sequential treatment for 10 days and 14 days with triple therapy for 14 days in first-line treatment.

Methods For this multicentre, open-label, randomised trial, we recruited patients (≥20 years of age) with *H pylori* infection from six centres in Taiwan. Using a computer-generated randomisation sequence, we randomly allocated patients (1:1:1; block sizes of six) to either sequential treatment (lansoprazole 30 mg and amoxicillin 1 g for the first 7 days, followed by lansoprazole 30 mg, clarithromycin 500 mg, and metronidazole 500 mg for another 7 days; with all drugs given twice daily) for either 10 days (S-10) or 14 days (S-14), of 14 days of triple therapy (T-14; lansoprazole 30 mg, amoxicillin 1 g, and clarithromycin 500 mg for 14 days; with all drugs given twice daily). Investigators were masked to treatment allocation. Our primary outcome was the eradication rate in first-line treatment by intention-to-treat (ITT) and per-protocol (PP) analyses. This trial is registered with ClinicalTrials.gov, number NCT01042184.

Findings Between Dec 28, 2009, and Sept 24, 2011, we enrolled 900 patients: 300 to each group. The eradication rate was 90·7% (95% CI 87·4–94·0; 272 of 300 patients) in the S-14 group, 87·0% (83·2–90·8; 261 of 300 patients) in the S-10 group, and 82·3% (78·0–86·6; 247 of 300 patients) in the T-14 group. Treatment efficacy was better in the S-14 group than it was in the T-14 group in both the ITT analysis (number needed to treat of 12·0 [95% CI 7·2–34·5]; p=0·003) and PP analyses (13·7 [8·3–40], p=0·003). We recorded no significant difference in the occurrence of adverse effects or in compliance between the three groups.

Lancet 2013;381:205–213.

(一) What is the disease caused by *Helicobacter pylori* in the article? What are the common symptoms of this disease?

(二) What is the pharmacological effect of each drug in the regimens?

(三) What are the most and least effective regimens of the eradication of *Helicobacter pylori*, respectively, according to the results of this study?

(四) What are the factors which may contribute to the outcome of the eradication rate of *Helicobacter pylori*? Could you please propose the potential mechanism of each factor influencing the eradication rate?

(五) What is the meaning of 「the number needed to treat of 12」 in the Findings? What is the difference between the analyses of intention-to-treat (ITT) and per-protocol (PP)?

試題隨卷繳回