※ 注意：請於試卷上「非選擇題作答區」內依序作答，並應註明作答之部份及其題號。

一、 請翻譯以下文章（20 分）：

Fungal Infections Associated with Contaminated Methylprednisolone Injections

Background

Fungal infections are rare complications of injections for treatment of chronic pain. In September 2012, we initiated an investigation into fungal infections associated with injections of preservative-free methylprednisolone acetate that was purchased from a single compounding pharmacy.

Methods

Three lots of methylprednisolone acetate were recalled by the pharmacy; examination of unopened vials later revealed fungus. Notification of all persons potentially exposed to implicated methylprednisolone acetate was conducted by federal, state, and local public health officials and by staff at clinical facilities that administered the drug. We collected clinical data on standardized case-report forms, and we tested for the presence of fungi in isolates and specimens by examining cultures and performing polymerase-chain-reaction assays and histopathological and immunohistochemical testing.

Results

By October 19, 2012, more than 99% of 13,534 potentially exposed persons had been contacted. As of July 1, 2013, there were 749 reported cases of infection in 20 states, with 61 deaths (8%). Laboratory evidence of *Exserohilum rostratum* was present in specimens from 153 case patients (20%). Additional data were available for 728 case patients (97%); 229 of these patients (31%) had meningitis with no other documented infection. Case patients had received a median of 1 injection (range, 1 to 6) of implicated methylprednisolone acetate. The median age of the patients was 64 years (range, 15 to 97), and the median incubation period (the number of days from the last injection to the date of the first diagnosis) was 47 days (range, 0 to 249); 40 patients (5%) had a stroke.

Conclusions

Analysis of data from a large, multistate outbreak of fungal infections showed substantial morbidity and mortality. The infections were associated with injection of a contaminated glucocorticoid medication from a single compounding pharmacy. Rapid public health actions included prompt recall of the implicated product, notification of exposed persons, and early outreach to clinicians.

摘自：Smith RM, *et al. N Engl J Med* 2013;369;17:1598.

見背面

二、 請依據第一題文章與下列框線中之文章回答下列問題（共計 20 分）：

(一) President Obama 因為怎樣的事件，在何時簽屬甚麼法案？（4 分）

(二) 此事件和法案與甚麼樣的藥事作業有關？（3 分）

(三) 甚麼是 outsourcing facilities？此法案對此 facilities 有何規定？（6 分）

(四) 此法有何漏洞，有何機制可以補強？（7 分）

President Signs Compounding Law

A year after Congress began investigating deadly fungal infections linked to tainted medications prepared by a Massachusetts compounding pharmacy, a new law to improve the safety and quality of compounded sterile products is now on the books.

President Obama signed into law the Drug Quality and Security Act on November 27. The law was supported by ASHP, the American Pharmacists Association, the National Community Pharmacists Association, and the National Association of Chain Drug Stores….

Outsourcing facilities. The act defines outsourcing facilities as entities where sterile products are compounded by or under the supervision of a licensed pharmacist. Official outsourcing facilities must register with FDA and comply with requirements set forth in the act, such as the payment of user fees, reporting of data to FDA, and submitting to FDA inspections. Outsourcing facilities do not need to obtain product-marketing approval from FDA. The facilities do not need to be licensed as pharmacies, and they may or may not process patient-specific prescriptions.

FDA is required to post on its website a list of the names and locations of registered outsourcing facilities. The list must indicate whether these entities compound products from bulk substances and if any bulk substances are used to produce sterile or nonsterile final products.

FDA Commissioner Margaret Hamburg acknowledged that nothing in the law prevents entities that don't register as outsourcing facilities from preparing and selling compounded sterile products to hospitals and physicians. But she said that marketplace dynamics may limit the appeal of products made by such businesses.

Hamburg said she hopes that outsourcing facilities "will be the standard of practice in terms of where providers will seek these kinds of products for their patients.

Hill said hospitals have been reevaluating their use of outsourcers since the 2012 outbreak of fungal infections, and the advent of outsourcing facilities may add a new layer of assurance to hospitals that purchase compounded sterile products. He said that products sold by registered outsourcing facilities could potentially cost more than medications obtained from unregistered compounding pharmacies. But ASHP members have said that they typically use outsourcers when they need a medication that can't be compounded inhouse.

摘自：*Am J Health-Syst Pharm* 2014;71:7–8.

接次頁

三、 最新的高血壓治療指引（guideline）JNC 8 於 2013 年底正式發表，茲摘要如下；請依序回答下列三子題（共計 20 分）：

(一) 以中文翻譯畫底線的部份。(4 分)

(二) 列舉 JNC 8 與先前治療指引的相異處。(6 分)

(三) 依據 JNC 8，治療國人高血壓的首選起始藥品有哪些選擇？請列出其藥理分類、各類至少列舉一藥品之學名、以及一項最需注意的副作用。(10 分)

There is strong evidence to support treating hypertensive persons aged 60 years or older to a BP goal of less than 150/90 mmHg and hypertensive persons 30 through 59 years of age to a diastolic goal of less than 90 mmHg; however, there is insufficient evidence in hypertensive persons younger than 60 years for a systolic goal, or in those younger than 30 years for a diastolic goal, so the panel recommends a BP of less than 140/90 mmHg for those groups based on expert opinion. The same thresholds and goals are recommended for hypertensive adults with diabetes or nondiabetic chronic kidney disease (CKD) as for the general hypertensive population younger than 60 years. There is moderate evidence to support initiating drug treatment with an angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, calcium channel blocker, or thiazide-type diuretic in the nonblack hypertensive population, including those with diabetes. In the black hypertensive population, including those with diabetes, a calcium channel blocker or thiazide-type diuretic is recommended as initial therapy. There is moderate evidence to support initial or add-on antihypertensive therapy with an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker in persons with CKD to improve kidney outcomes.

摘自：*JAMA* 2014;311:507–520.

見背面

四、 請閱讀以下期刊論文，依序回答下列三子題（共計 20 分）：

(一) 以中文簡要敘述此研究。(4 分)

(二) 詳述治療 mania 的常用藥品與其治療地位。(6 分)

(三) 簡述 US FDA 制定之懷孕用藥安全分級有哪五種等級，並詳述各分級之定義。(10 分)

Valnoctamide as a Valproate Substitute with Low Teratogenic Potential in Mania: a Double-Blind, Controlled, Add-on Clinical Trial

Objectives

Valproic acid's well-known teratogenicity limits its use in women of childbearing age. Valnoctamide is an analog of valproate that does not undergo biotransformation to the corresponding free acid. In mice, valnoctamide has been shown to be distinctly less teratogenic than valproate. Valnoctamide is an anticonvulsant, and we hypothesized that valnoctamide is antimanic.

Methods

We performed a double-blind, five-week, add-on, controlled trial of valnoctamide in mania. Patients were treated with risperidone at doses of the physician's discretion. Valnoctamide or placebo was begun at doses of 600 mg/day and increased to 1200 mg after four days. Weekly ratings by a psychiatrist blind to the study drug were conducted using the Brief Psychiatric Rating Scale (BPRS), the Young Mania Rating Scale (YMRS), and the Clinical Global Impression (CGI).

Results

Fifteen valnoctamide patients and 17 placebo patients completed at least one post-baseline week and were included in data analysis. In all efficacy measures valnoctamide was more effective than placebo as an add-on to risperidone, using two-way analysis of variance (ANOVA) with time as the within-subject factor. Two-way ANOVA showed a significant effect of time ($p < 0.001$) and significant interaction between treatment and time (YMRS: $p = 0.012$; BPRS: $p = 0.007$; CGI: $p = 0.003$). Differences between valnoctamide and placebo were significant from week 3 to week 5.

Conclusion

Valnoctamide could be an important valproate substitute for women of childbearing age with bipolar disorder who may become pregnant.

摘自：*Bipolar Disord* 2010: 12: 376–382.

接次頁

五、 請閱讀下列短文並回答問題（共計 20 分）：

(一) 試簡述短文重點。(5 分)

(二) 如果你（妳）是該機構之 pharmacist，於藥事委員會或相關小組中協助負責此案之專業文獻蒐集、彙整與初步評估事務。(15 分)

1. 在接手此案時你（妳）會如何處理（請述明進行步驟並分析理由）？
2. 你（妳）會涉獵那些專業文獻（試具體列出類別及名稱）。
3. 你(妳)預期對此案之綜合結論立場為何？ 又，為何持此立場(觀點)？

Marginal Benefit from an Additional Antiemetic Agent

Jerome Lin, Pharm.D., worked in a large county hospital and clinic in a major urban center. Because of the location of the hospital, most of the patients were indigent. Therefore, most of the funding and reimbursement came from county and state welfare programs.

Recently the American Society of Clinical Oncology (ASCO) had updated its antiemetic guidelines that previously had been approved in 1999. The 1999 guidelines for preventing high emetic risk included two drugs: 5-HT_3 serotonin receptor antagonists, such as granisetron or ondansetron, and dexamethasone. The 2006 guidelines added aprepitant to the 5-HT_3 serotonin receptor and dexamethasone. The three-drug combination is recommended for patients receiving chemotherapeutic agents of high emetic risk. By adding the aprepitant, the const of the regimen increased by approximately $329 (US dollar).

At the formulary committee, this change in the ASCO guidelines caused quite a bit of discussion, particularly among the pharmacists and physicians who worked with oncology patients. Dr. Lin summarized their main concerns, "The primary benefit of aprepitant, based on data from randomized controlled trials, is that it increased the complete response rate, which is defined as no emetic episode and no use of rescue therapy in patients receiving highly emetogenic chemotherapy. The absolute benefit, that is, no nausea or vomiting, is about 20%, or to put it simply, about 1 in 5 patients will benefit from the addition of aprepitant. However, because 5-HT3 serotonin antagonist plus desamethasone remains a very effective regimen and because of the high cost of the aprepitant, I recommend that the standard of care here should be to reserve aprepitant for selected patients, those who fail the 5-HT3 serotonin antagonist plus dexamethasone regimen." The unspoken message was that the hospital could not afford to offer the top recommended guideline treatment.

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

試題隨卷繳回