P.O.L. Insight

Issue 50

A Continuing Education Publication for the Physician Office Laboratory

2007-C

www.aafp.org/pt

In This Issue:

AAFPPT
The Physician's Proficiency Testing Program

Accreditation Statements

AAFP Physician's Proficiency Testing Program has been reviewed and is acceptable for up to 12 Prescribed credits by the American Academy of Family Physicians. AAFP accreditation begins 3/5/07. Term of approval covers three events offered within one year from this date with option for yearly renewal.

The American Academy of Family Physicians is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

The American Academy of Family Physicians designates this educational activity for a maximum of 12 *AMA PRA Catefory 1 Credit(s)™.* Physicians should only claim credit commensurate with the extent of their participation in the activity.

Credit may be claimed for one year from the date of this event.

AAFP-PT is approved as a Provider of continuing education programs in the clinical laboratory sciences by the ASCLS P.A.C.E.® Program. AAFP-PT is also an approved provider for California clinical laboratory licensees under the P.A.C.E.® Program. The level of instruction for this event is basic. This event is worth 4 P.A.C.E.® Contact Hours.

Published by the American Academy of Family Physicians, 11400 Tomahawk Creek Parkway, Leawood, KS 66211-2672.

Editor and Writer:
Cheryl Murray, MPA, MT(ASCP)SM

Authors:
Amitava Dasgupta, PhD, DABCC
George Fritsma, MS, MT (ASCP)
Terry Jo Gile, MT (ASCP) MA Ed.
Bernadette F. Rodak, MS, CLSSpH(NCA)

American Academy of Family Physicians

AAFP-PT Staff

Barbara Mitchell
Program Manager
e-mail bmitchel@aafp.org

Lisa Henderson
Manager, Operations
e-mail lhenders@aafp.org

Chris Hodges
Manager, Client Services
e-mail chodges@aafp.org

Cheryl Murray
Manager, Education & Technical Assistance
e-mail cmurray@aafp.org

Shaurna Williams
Program Coordinator
e-mail swilliam@aafp.org

Karen Bergman
Program Coordinator
e-mail kbergman@aafp.org

AAFP-PT FAX
913-906-6079

Visit our Web site for information about the PT program, our *POL Topics* information and continuing education material
http://www.aafp.org/pt

The PT Department is staffed from 8:30 AM to 5:00 PM, CST. Please feel free to call us during these hours . . . or use our voice mail system and we will gladly return your call . . . or send one of us an e-mail !

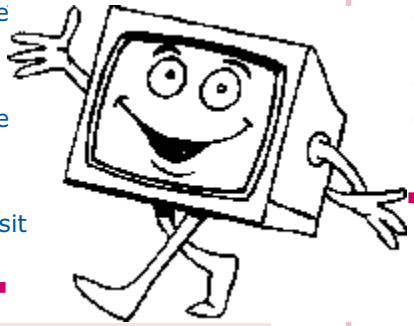
Table Of Contents

Plug in to PT Central in 2008!!

AAFP-PT is pleased to introduce our brand new Online Access System.

This easy-to-use, state-of-the-art system will be available in March 2008.

For more information, visit ***www.aafp.org/pt***.



2007-C CME Answers

1.	B	13.	D	25.	B
2.	D	14.	C	26.	C
3.	B	15.	B	27.	A
4.	A	16.	D	28.	B
5.	B	17.	A	29.	A
6.	B	18.	D	30.	A
7.	A	19.	A	31.	C
8.	A	20.	C	32.	D
9.	A	21.	B	33.	A
10.	B	22.	D	34.	D
11.	A	23.	A		
12.	B	24.	A		

To earn the CME, answer the questions included with this issue of the *Insight*, using the form included, or submit the test online at **www.aafp.org/pt** – click on Continuing Medical Education.

CME Learning Objectives

Following completion of the self-instructional material, the participant will be able to:

1. Describe the action of warfarin, understand the purpose of PT & INR results, explain the management of specimens collected for prothrombin time tests, and identify dietary & medication changes that may affect the effects of warfarin.

2. Develop a laboratory training program that will engage employees and meet regulatory requirements.

3. Identify common herbal remedies that may affect laboratory results, describe the tests most likely to be affected by herbal medicines, and list potential herbal/theraputic drug interactions.

ATTENTION PHYSICIANS AND LABORATORY PERSONNEL
P.A.C.E.® Approved For Laboratory Personnel !

Need Documentation of CME Credits?

AAFP member physicians may contact AAFP's CMER Department (800-274-8043) and request a complete transcript of their CME. Transcripts for non-Academy member physicians are mailed at the end of each year and are available upon request at 800-274-7911.

Verification of CME hours earned for laboratory personnel is mailed in January and July each year. Laboratory personnel are mailed P.A.C.E.® certificates at the end of the year (January 2008). Verification is also available upon request (swilliam@aafp.org or 800-274-7911, extension 4145). Allow 7-10 business days for requested transcripts.

P.A.C.E.® Due Dates and Course Codes

Event 2007-A ..... February 28, 2008 254-001-07
Event 2007-B ..... May 31, 2008 254-002-07
Event 2007-C ..... September 30, 2008 254-003-07

Monitoring Warfarin Therapy

By George A. Fritsma, MS MT(ASCP), Associate Professor, Laboratory Medicine, University of Alabama at Birmingham & Bernadette Rodak, MS, CLSpH(NCA), Professor Pathology & Laboratory Medicine, Indiana University.

A 61 year old man experienced severe upper leg pain after a seven-hour airplane flight. He went immediately to his physician who saw that his left leg was swollen, reddened, and warm to the touch. The diagnosis of deep venous thrombosis, a clot blocking a large vein in the upper leg was confirmed by ultrasound.

Warfarin

The patient was at risk for pulmonary embolism. The physician immediately started her patient on warfarin (warfarin sodium, Coumadin®) therapy at 5 mg/day.

The standard starting warfarin dosage is 5-10 mg/day or 2 mg/day for patients over 70. Warfarin is one of the top twenty most prescribed drugs in the US[1]. It is an antithrombotic (anticoagulant), one of a class of drugs called "blood thinners" though they do not actually thin the blood. Antithrombotics, which also include heparin, low molecular weight heparin (enoxaparin, Lovenox®), and argatroban (Novostan®) do not dissolve clots but prevent further clot growth and allow the body to resolve the clot naturally[2,3].

Warfarin acts by reducing the activity of several coagulation (clotting) factors[4]. It has saved thousands of lives and prevented a great deal of suffering, but it is dangerous. Warfarin overdose is the single most common bleeding problem seen in the emergency department[5]. Further, if the dose is too low, the patient risks another clot, pulmonary embolism, or stroke. Laboratory monitoring is essential[6].

Prothrombin Time (PT)

The test used to monitor warfarin is the prothrombin time (protime, PT). A sample of the patient's plasma, prepared by centrifugation, is mixed with the PT reagent called thromboplastin, a timer is started, and the interval to clotting is recorded. In normal healthy people, the clot forms in 11.5 to 13.5 seconds; in people taking warfarin the time may be 20 to 30 seconds. The PT is a moderately complex test performed using a semiautomated or automated *coagulometer* (Table 1). The coagulometer reports both the PT in seconds and an additional number, the international normalized ratio (INR).

TABLE 1

Instrument	Manufacturer
CD 2000 and Coalab	American Labor/Lab A.M.C. Inc
Coag-a-mate Max, MTX II & XM	bioMérieux Inc.
BFT II, Sysmex CA-560 & 1500	Dade Behring, Inc
STA Compact CT & Start-4	Diagnostica Stago Inc.
Thromboscreen 200, 400, & 1000	Fisher Diagnositcs
Cascade M, M-4, AggRAM	Helena Laboratories
ACT 100, 1000, 7000	International Laboratory/Beckman-Coulter Inc.
Amax Destiny & Destiny Plus, KC1 & KC4 delta	Trinity Biotech

Semi-automated moderate complexity desktop coagulometers designed for plasma coagulation testing in physician office and small laboratories[12]

International Normalized Ratio (INR)

In 1982, Dr. Leon Poller tackled the problem of PT variation. Laboratories use different brands of thromboplastin, some sensitive, others insensitive. As long as a patient always went to the same lab and the lab always used the same thromboplastin and coagulometer, there was no problem, but PT results were not normalized from lab to lab nor even within a lab over time. Poller devised the INR, which is computed:

$$INR = (PT_{patient}/PT_{MNR})^{ISI}$$

$PT_{patient}$ is the patient PT in seconds; PT_{MNR} is the mean (average) PT of the laboratory's normal range, usually around 12.5 seconds; and **ISI** is the *international sensitivity index*, assigned by the thromboplastin manufacturer after careful factory testing. The INR is now used everywhere in the world, and patients may trust, *within limits*, that all INRs are comparable.

The INR is provided automatically by coagulometers, and is reliable when the operator ensures the correct ISI has been recorded in the instrument's memory. There was an instance in 2002 when a U.S. lab inadvertently used the wrong ISI for a month, reporting erroneously low INRs and causing physicians to increase warfarin dosages for scores of patients, two of whom bled to death. The normal INR is 1.0 to 1.2 and the target therapeutic range for warfarin is 2.0 to 3.0. Most labs regard an INR of 5.0 as a signal for bleeding risk, so personnel are careful to immediately notify the physician who may modify the patient's dosage.

Applying the PT/INR

The physician instructed her patient to have his first PT/INR performed within 48 hours of his first pill and each day following until two consecutive INRs were in the therapeutic range. This takes 5-7 days of daily PTs provided the starting dose is effective. Subsequent PTs are required once a week until stability is assured. Dosage is individual, however, and is likely to require adjustment; so many patients return weekly for 4-6 weeks until their dosage regimen is established. This patient's dosage schedule was:

Day After Start	Dosage	INR
Day 3	5 mg/day	1.5
Day 4	5 mg/day	1.7
Day 5	5 mg/day	1.8
Day 6 (raised dosage)	5 mg/day	1.8
Day 13	7.5 mg/day	2.1
Day 20	7.5 mg/day	2.2
Day 27	7.5 mg/day	2.2

Once his dosage was established, the doctor instructed him to return to the laboratory every four weeks for follow-up PTs. Monthly PTs are required for as long as warfarin therapy continues.

Managing PT Specimens

The day the patient came to the laboratory, the phlebotomist collected venous whole blood into a blue-stoppered siliconized or plastic evacuated (Vacutainer♁) tube. If specimens are needed for other tests, for example, a lavender-stoppered tube for a complete blood count (CBC), the blue-stoppered tube must be collected *first* to avoid crossover contamination. The blue-stopper tube contains liquid 3.2% sodium citrate anticoagulant, which must be thoroughly but gently mixed with the blood within seconds after the phlebotomist completes the venipuncture. Failure to mix causes the blood to clot, irreparably compromising PT/INR results. The phlebotomist must also be certain the tube fills completely, as the vacuum is calibrated to collect a precise volume. A "short draw" also compromises PT/INR results. Both these and hemolysis, evidenced by pink supernatant plasma, necessitate a redraw. A needle smaller than the standard 21-gauge, a partially plugged needle or excessive shaking causes hemolysis.

If the blood specimen is meant for only a PT, it may be stored with the stopper on at room temperature, 18-24°C (65-75° F) upright for up to 24 hours. Before testing the specimen is centrifuged at 1500 RCF (relative centrifugal force) for 15 minutes to separate the cells from the plasma. Centrifugation at a lower force or for a shorter time leaves too many platelets in the supernatant plasma, falsely shortening the PT.

After centrifugation, the operator carefully pipettes supernatant plasma to a second tube for storage or testing. The remaining red cell layer is discarded in a biohazard container. Pipettes and storage tubes must be of polypropylene plastic to avoid activating the plasma coagulation mechanism. A sample is further pipetted from the plasma and placed on the coagulometer for testing as described above.

Continues on next page.

WHERE'S PART 2??

Due to space limitations, we regret that we are unable to print Dr. Nils Person's second article in the QC Myths series. Please visit our website, www.aafp.org/pt, and click the "CME" link for a downloadable copy of this article.

Point of Care Anticoagulation Clinic or Physician Office Laboratory Instruments

In 2001, coagulation equipment manufacturers began offering instruments that report PT/INRs on fresh whole venous or capillary blood (Table 2). These point of care (POC) devices bypass the need for centrifugation and plasma management, leading to rapid turn-around times and patient convenience[7]. They are more easily operated and maintained than plasma-based coagulometers, and most are categorized as waived procedures by laboratory regulating agencies, reducing operator restrictions[8].

TABLE 2

Instrument	Manufacturer
I Stat & I-Stat 1	Abbott Point of Care
Actalyke XL & Actalyke Mini-II	Helena Point of Care
INRatio PT/INR	Hemosense, Inc
Gem PCL Plus	Instrumentation Laboratory
ProTime Microcoagulation System, Hemochron Jr Signature, Hemochron Response, Hemochron Signature	International Technidyne Corp
HMS Plus & ACT Plus	Medtronic Cardiac Surgery
Coaguchek S	Roche Diagnositics Corp

Point of care (POC) physician office laboratory, anticoagulation clinic, and self-monitoring fresh venous & capillary whole blood PT/INR instruments[13]

POC instruments are designed for physician offices and anticoagulation clinics. Patients learn their results and receive immediate dosage change instructions during a single short visit. Although plasma-based coagulometers offer greater precision, the convenience of POC instruments encourage patient compliance and improve time "in control." At least one such instrument, the Hemosense, Inc INRatio PT/INR◊ is cleared for home self-monitoring. Long-term warfarin patients with atrial fibrillation or mechanical heart valves may apply for self-monitoring third-party reimbursement. Although self-monitoring is encouraged among compliant patients, self-dosing is discouraged in the US. Self-monitoring patients communicate PT/INR results to their physician and await dosage instructions. The key to accurate POC testing is to collect capillary blood from a free-flowing puncture and to fill the collection device completely.

Warfarin Limitations and Precautions

The patient's INR remained therapeutic for three months, but in the fourth month it dropped to 1.7. It was May and the patient had begun eating more fresh green vegetables, salads, and guacamole. His physician encouraged him to enjoy greens but to eat approximately the same amount each day, and to moderate his guacamole[9]. She raised his dosage to 10 mg/day on Monday, Wednesday, Friday, and 7.5 mg on Tuesday, Thursday, Saturday, and Sunday and resumed weekly PT/INRs. After four weeks his INR reach 2.4 on two consecutive weeks and he was able to resume his monthly schedule.

Green leafy vegetables, avocados (in particular), dietary supplements, and liver provide high concentrations of vitamin K that neutralize warfarin. Conversely, fasting, fad diets, or long-term antibiotics that destroy intestinal organisms reduce vitamin K and raise warfarin effectiveness, often to dangerous levels. At least 80 drugs reduce or raise warfarin efficacy, as does alcohol, particularly binge drinking.

About 10% of us are warfarin resistant and may need doses of 25 mg/day to reach a therapeutic INR. Nearly 20% of the population metabolize warfarin slowly and achieve therapeutic INRs on about 2 mg/day. These include in particular people over 70 and people with inherited warfarin sensitivity polymorphisms (genes) called CYP2C9 and CYP2C19[10,11]. Otherwise normal warfarin doses become a hemorrhagic threat.

When the INR exceeds the critical level, 5.0 for most institutions, the physician immediately counters by lowering the dose or by temporarily discontinuing warfarin, then resuming at a lower dose. If the patient is bleeding, the patient is admitted and 10 mg of vitamin K may be given orally, subcutaneously, or intra-

venously. It the bleeding is acute, the physician may rescue the patient with coagulation products such as frozen plasma or coagulation factor concentrates. Any change in warfarin dosage requires weekly or daily PT/INRs.

The patient's deep venous thrombosis symptoms resolved and his physician recommended he discontinue warfarin therapy after six months and avoid lengthy immobilization.

Warfarin is a staple of everyday medicine. It saves lives and prevents life-altering strokes and pulmonary emboli. Nevertheless, warfarin has a narrow therapeutic range and causes dangerous bleeding, and must be carefully monitored. The physician office laboratory, anticoagulation clinic, or judicious home monitoring using well maintained and carefully operated instrumentation, provides the patient's best opportunity to maintain therapeutic control.

Resources:

1. Kresge N, Simoni RD, Hill RL: Hemorrhagic sweet clover disease, dicumarol, and warfarin: the work of Karl Paul Link. J Biol Chem 2005;280:5-15.
2. Francis CW, Berkowitz SD: Antithrombotic and thrombolytic agents. In Kitchens CS, Alving BM, Kessler CM (eds): Consultative Hemostasis and Thrombosis. Philadelphia: Saunders, 2002:375-93.
3. Hirsch J, Raschke R: Heparin and low-molecular-weight heparin: the seventh ACCP conference on antithrombotic and thrombolytic therapy. Chest 2004;126:188S-203S.
4. Poller L: Laboratory control of anticoagulant therapy. Semin Thromb Hemost 1986;12:13-19.
5. Levine MN, Raskob G, Beyth RJ, et al: Hemorrhagic complications of anticoagulant treatment: the seventh ACCP conference on antithrombotic and thrombolytic therapy. Chest 2004;126:287S-310S.
6. Ansell J, Hirsh J, Poller L, et al: The pharmacology and management of the vitamin K antagonists: the seventh ACCP conference on antithrombotic and thrombolytic therapy. Chest 2004;126:204S-33S.
7. Wittkowsky AK, Nutescu EA, Blackburn J, et al. Outcomes of oral anticoagulant therapy managed by telephone vs in-office visits in an anticoagulation clinic setting. Chest. 2006;130:1385-9.
8. Hill J, Perreault S, Dorval M. Validity of CoaguChek S for home monitoring of anticoagulant therapy in pediatrics. Can J Cardiol. 2007;23:47-50.
9. Fritsma GA. Chapter 46, Monitoring Anticoagulant Therapy, In Rodak BF, Fritsma GA, Doig K. Hematology: Clinical Principles and Applications, 3rd Ed. 2007. Elsevier, St. Louis.
10. O'Reilly RA. Warfarin metabolism and drug-drug interactions. In WesslerS, Vecher CG, Nemerson Y, eds. The new dimensions of warfarin prophylaxis: advances in experimental medicine and biology. New York, NY: Plenum, 1986:214:205-12.
11. Schalekamp T, Brasse BP, Roijers JF, et al: VKORC1 and CYP2C9 genotypes and acenocoumarol anticoagulation status: interaction between both genotypes affects over-anticoagulation. Clin Pharmacol Ther 2006;80:13-22.
12. Coagulation Analyzers. CAP Today, February 2006, accessed 6/8/07 http://www.cap.org/apps/docs/cap_today/surveys/0206Coag.pdf
13. Coagulation Analyzers, Point of Care, Self-Monitoring. CAP Today, May 2006, accessed 6/8/07 http://www.cap.org/apps/docs/cap_today/surveys/0506Coagsurvey.pdf

Safety Training for the POL

By Terry Jo Gile, MT(ASC)MA Ed.
The Safety Lady™, www.safetylady.com

Tracy was a technologist who worked in the Southwest Medical Clinic Laboratory. The office had 13 physicians and a large payroll. Dr. Smith asked Tracy to serve as the safety trainer for all of the clinic's employees. Her responsibilities included new employee orientation and preparing a monthly safety inservice. Tracy knew that safety was a boring topic but the accreditation agencies as well as OSHA mandated that each employee receive the training and it be documented that they understand the material. The same old videos were shown year after year and sometimes employees would fall asleep during the presentation.

Does this scenario sound familiar? Are your employees bored with the same old safety program year after year? Regardless of the size of your practice, safety training must be a part of orientation and annual employee competency. What can Tracy do to put life into the safety inservices?

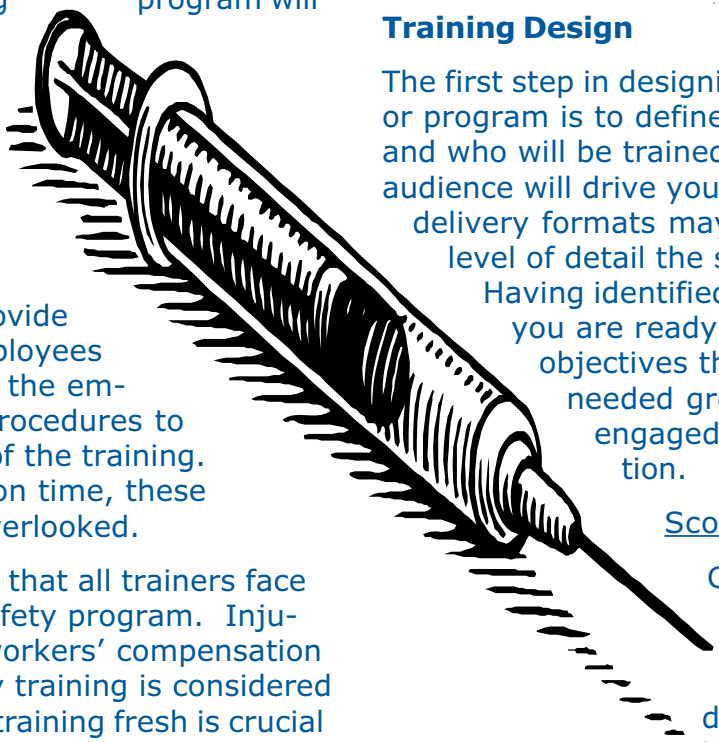
For starters, Tracy could tape $1 bills to two or three chairs in the front row. Halfway through the presentation, Tracy could stop and tell everyone that there is money to be found for keeping awake during the presentation. Employees would then have to get up and move their chairs around to see if they were the lucky winner.

Another way to move people around for discussion is to buy an assortment of miniature candy bars making sure to have an equal amount for the number of employees. Pass the container of candy bars around and ask each person to select their favorite from those that are offered. Tell them they can eat the

candy bar anytime during the presentation but to save the wrapper. During the presentation, ask the employees to group themselves according to the candy bar they selected. For example, Hershey in one corner, Snickers, in another corner, etc. This breaks up cliques into different groups and creates an opportunity to interact with others besides friends. Then ask the candy bar groups to discuss the topic and report their findings to the whole group.

Overview

OSHA's Guidelines for Employer Compliance (CFR1910.1200 Appendix E) says a properly conducted training program will ensure comprehension and understanding. This means it is not enough to read the information to employees or hand them material to read. To be compliant with OSHA, training must provide the opportunity for employees to ask questions. Also, the employer must establish procedures to evaluate effectiveness of the training. When practice is short on time, these requirements can be overlooked.



Stagnation is a problem that all trainers face in the course of their safety program. Injuries may be reduced, workers' compensation rates are low and safety training is considered boring. Keeping safety training fresh is crucial to compliance. Bookmark safety websites and sign up for safety ezines that will keep you informed of the latest information. Public health associations such as the American Red Cross and the National Safety Council often run national safety awareness campaigns that you can leverage to make your training more effective. Take advantage of national campaigns and schedule sessions focused on particular topics such as these:

- January – Specimen Transport
- February – Hoods and Environmental Issues
- March – Personal Protective Equipment
- April – Ergonomics
- May – Bloodborne Pathogens
- June – General Safety (National Safety Month)
- July – Compressed Gases
- August – Safe Work Practices
- September – Chemical Hygiene
- October – Fire Safety (National Fire Safety Month)
- November – Electrical Safety
- December – Waste Management

Start a file for each subject either on your computer or in hard copy in a drawer so when September rolls around you won't have to frantically search for information on Chemical Hygiene.

Training Design

The first step in designing any training session or program is to define what will be covered and who will be trained. Knowledge about the audience will drive your decisions about what delivery formats may work best and what level of detail the sessions should provide. Having identified content and audience, you are ready to create learning objectives that will cover the needed ground, keep employees engaged, and maximize retention.

Scope

Create an outline of what you plan to cover. Factual information that may be mandatory includes the following:

• An overview of the regulation. Who is covered? What are the main requirements? Is the regulation effective now (or when will it take effect)? What are the penalties or other risks from noncompliance?

• Potential health hazards. Summarize the dangerous properties of chemicals or equipment, types of potential injuries, routes of entry or infection, etc.

• Engineering controls. What safety equipment or physical safeguards does the practice have in place? What must employees do to take full advantage of the safeguards?

• Safe work practices. What are your lab's standard operating procedures to minimize risk in the relevant area?

• Personal protective equipment (PPE). In addition to the standard lab coat, what other PPE items, such as eye protection, respirators, special gloves, etc., must be used for the specific task(s) covered in the training?

• Handling accidents and recovery. As appropriate, the session should cover the emergency, cleanup, and medical treatment procedures spelled out in your practice's written safety manual for the relevant procedures or risks.

Audience

Your practice may have employees ranging in age from 18 to 70 or older. An employee's age can play an important role in what method of training is successful. Consider the following examples:

• Staff over the age of 70 have a wealth of knowledge but are slow to change and prefer to have a live speaker give the information in a small group, as opposed to working with a computer or other technology.

• Staff aged 56–69 work well under deadlines but need additional time to adjust to any changes required. Training for this group is best done with an in-person speaker or using a video.

• Staff aged 36–55 are usually computer literate and prefer their training via video or online. They like hands-on learning as well. They value continuing education and like to attend seminars and conventions.

• Staff aged 24–35 are computer savvy and expect training to be fun. Online training at an interesting site will keep them engaged.

Learning Objectives

Specific learning objectives spell out what employees should be able to do after completing the training, and define what constitutes acceptable performance or competence. Each objective completes a sentence starting with, "After completing this training, you will be able to . . ."

• Knowledge—of terminology, specific facts, and ways and means of dealing with specific criteria or methods. Knowledge enables the employee to remember the safety requirements of each task and relate them to previously learned information. Learning objectives based on knowledge might be worded as follows:

– Describe the acronym PASS
– Label the parts of the fire extinguisher

Other verbs that could be used for knowledge objectives include define, describe, identify, label, list, select, state, or view.

• Comprehension—understanding the meaning of information so that the learner is able to perform a task that depends on it, such as using PPE or ergonomic equipment as instructed. Learning objectives based on comprehension might be worded as follows:

– Explain the proper way to put on and remove a lab coat

– Summarize the proper way to adjust a task chair

Other verbs that might introduce learning objectives based on comprehension include describe, discuss, explain, give examples, summarize, or understand.

• Application—the use of previously learned information in new concrete situations to solve problems that have single or best answers. Learning objectives based on application might be worded as follows:

– Instruct a co-worker on how to aseptically remove gloves

– Prepare a 10% solution of bleach using appropriate PPE

Other verbs used for application include assess, chart, collect, construct, determine, develop, discover, establish, implement, inform, instruct, prepare, provide, report, show, solve, teach, or use.

Format

Format options include live presentations to small or large groups, audiotapes, videotapes, print- or computer-based self-study, or online courses. Well-designed games can also be effective in teaching some skills or in reminding staff to remain compliant with procedures they already know.

Measuring Effectiveness

The most obvious criterion for effectiveness is on-the-job results. If a safety training program is effective, employees have few or no injuries due to unsafe acts. You should review accident and injury reports at least quarterly to determine how effective training has been and to identify areas where additional training may be needed.

Update and Refresher Training

Deliver update training as quickly as possible after a new law or regulation comes out.

Build all refresher and reminder training programs around the basic safe work standards that never change and on potential problems identified by your quarterly review of accidents and injuries as well as day-to-day observation. Use games, posters, contests, and similar devices to boost motivation and keep safety awareness at a high level.

Documentation of Training

Whether you use a manual method, an Excel® spreadsheet, or another tracking system, documentation of training is essential. Regulatory and accreditation agencies take the view that if it was not written down and kept on record, it did not happen. Therefore, it is important to record the following information for each training session:

- Title of topic presented
- Name, title, and credentials of instructor
- Date of presentation(s)
- Time presentation started and ended
- Special audiovisuals used (e.g., video, CD ROM, books, online course, etc.)
- Continuing education units (CEUs) offered, if applicable
- List of attendees, including each attendee's
  - Full name
  - Facility ID or Social Security number
  - Exam scores, if applicable

Keep individual training records in employees' personnel files. Keep delivery records and copies of all materials in a central laboratory location. Remember to retain all individual training records for three years.

Resources

1. Bloom's Taxonomy: www.coun.uvic.ca/learn/program/handouts/bloom.html.
2. Games and puzzles: http://puzzlemaker.school.discovery.com/.
3. Gile, TJ. *Lab Safety Training Made Simple*, HCPro, 2006: http://www.hcmarketplace.com/prod.cfm?id=4484&CFID=3863672&CFTOKEN=25124785

Impact of Herbal Medicines on Clinical Laboratory Testing

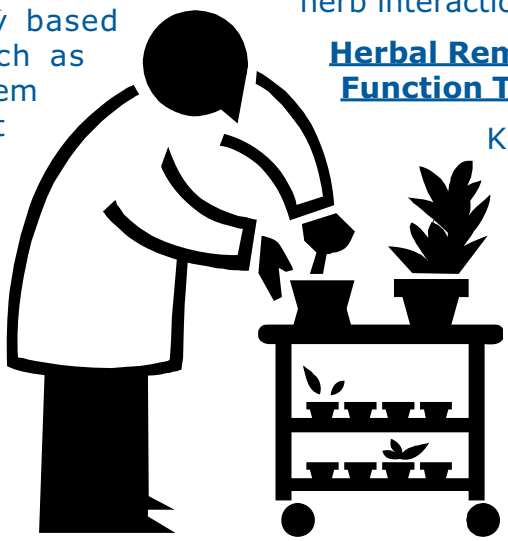
By Amitava Dasgupta, PhD, DABCC
Department of Pathology & Laboratory Medicine, University of Texas-Houston Medical School

Herbal medicines are readily available worldwide from stores without prescriptions. The majority of population who use herbal medicines in the U.S. has a college degree and falls in the age group of 25-49 years. In one study, 65% people thought that herbal medicines are safe[1]. Most herbal products are sold in the United States under "Dietary Supplement Health and Education act of 1994 and not regulated. An herbal medicine can affect laboratory test results by one of the four mechanisms.

1. Direct assay interference most commonly with the immunoassays due to cross-reactivity of a component present in the preparation. For example, falsely elevated digoxin levels may be observed using the fluorescence polarization immunoassay (FPIA) for digoxin due to ingestion of Chinese medicine Chan Su, Lu-Shen-Wan or DanShen.
2. Drug-herb interactions leading to unexpected levels of a therapeutic drug. Example, low cyclosporine level due to initiation of self-therapy with St. John's wort.
3. Unexpected laboratory test results due to toxicity of a herbal products. For example, Kava-Kava causes liver toxicity and elevated ALT, AST and bilirubin concentrations in healthy individuals.
4. A herbal product may contain undisclosed drugs or may contain heavy metals.

Herbal Remedies and Interferences with Assays for Therapeutic Drug Monitoring

So far the currently published reports indicate that only certain digoxin immunoassays are affected by herbal medicines. Chinese medicines such as Chan Su, Dan Shen, Ginsengs, and Oleander containing herbal products interfere with various digoxin immunoassays. Indian Ayurvedic medicine Ashwagandha also demonstrates moderate interference with the fluorescence polarization immunoassay (FPIA, Abbott Laboratories) for digoxin[2]. Usually Chan Su, Lu-Shen Wan and Oleander containing herbal products cause significant interferences with both polyclonal and monoclonal antibody based digoxin immunoassays. However, magnitude of interference is significantly less with monoclonal antibody based digoxin assays compared to polyclonal antibody based immunoassay. Panesar reported an apparent digoxin concentration of 1124 pmol/L (0.88 ng/ml) in healthy volunteers who ingested Lu-Shen-Wan (LSW) pills that contain Chan Su[3]. Osterloh et al reported an apparent digoxin level of 5.8 ng/ml using FPIA digoxin assay after suicidal ingestion of oleander tea in a patient with no history of taking any digoxin. The person eventually died from oleander toxicity[4]. Eddleston et al reported a mean apparent serum digoxin concentration of 1.49 nmol/L (1.16 ng/ml) in patients who were poisoned with oleander but eventually discharged from the hospital. Severe toxicity from oleander resulted in a mean apparent serum digoxin concentration of 2.83 nmol/L (2.21 ng/mL) as measured by the FPIA digoxin assay[5]. In contrast, Chinese medicine DanShen and Ginseng only caused modest interference with polyclonal antibody based digoxin immunoassays such as FPIA. Other monoclonal antibody based digoxin immunoassays such as EMIT 2000, Synchron LX system (Beckman), Tina-quant (Roche Diagnostics) and turbidimetric (Bayer Diagnostics) are free from such interferences.



Unexpected Low Levels of Therapeutic: Interactions of St. John's Wort with Drugs

Unexpectedly low levels of therapeutic drug in a patient who showed therapeutic levels before may be due to initiation of self therapy with St. John's wort. St. John's wort is an herbal antidepressant prepared from hypericum, a perennial herb. CYP3A4 is the most abundant isoenzyme of Cytochrome P450 responsible for metabolism of more than 73 drugs and numerous endogenous compounds. The active components of St. John's wort, especially hyperforin induce CYP3A4 and CYP2B6 probably through activation of a nuclear steroid/pregnane and xenobiotic receptor[6]. St. John's Wort also induces P-glycoprotein drug transporter and may reduce efficacy of drugs where hepatic metabolism may not be the major pathway of clearance. The component, hypericin, may be the active ingredient that modulates P-glycoprotein[7].

Self-medication with St. John's wort may cause treatment failures due to significant reductions in plasma drug concentrations because of increases in clearance of drugs. Published reports indicate that St. John's wort significantly reduces steady state plasma concentrations of cyclosporine, tacrolimus, amitriptyline, digoxin, fexofenadine, indinavir, methadone, midazolam, nevirapine, phenprocoumon, saquinavir, simvastatin, theophylline and warfarin[8,9]. Increased clearance of oral contraceptives has also been reported. Moreover, herbal remedies are not prepared by using rigorous standards and concentrations of active ingredients may vary widely. St. John's wort containing low concentrations of hyperforin (<1%) may not cause interactions with Western drugs[10]. Important drug-herb interactions are summarized in Table 1.

Herbal Remedies and Abnormal Liver Function Tests

Kava-Kava a herbal remedy taken for anxiety can cause severe hepatotoxicity[11]. Heavy consumption of kava has been associated with increased concentrations of gamma glutamyltransferase (GGT) suggesting potential hepatotoxicity. Escher et al described a case in where a 50-year-old man took three to four kava capsules daily for two months. Liver function tests

showed 60-70 fold increases in AST and ALT but tests for viral hepatitis (HAV, HBV and HCV) were all negative as were tests for CMV and HIV. The patient eventually received a liver transplant[12]. In January 2003, kava extracts were banned in the entire European Union and Canada and also in the USA, the FDA strongly cautioned against using kava. There are at least 11 cases of serious hepatic failure and four deaths directly linked to kava extract consumption and there are also 23 reports indirectly linking kava with hepatotoxicity[13].

Chaparral, another herbal supplement used as an antioxidant and anti-cancer product also causes severe hepatotoxicity. Gordon et al reported a case where a 60 year old woman took Chaparral for 10 months and developed severe hepatitis for which no other cause was found. On admission her bilirubin was 12.4 mg/dl, ALT 341 U/L, AST 1191 U/L and alkaline phosphatase 186 U/L. All tests for viral hepatitis were negative. Eventually she received a liver transplant[14].

Germander has been used as a remedy for weight loss and as a general tonic. Several cases of liver toxicity have been reported in Europe due to ingestion of germander. A 55-year-old woman taking 1600 mg per day of germander became jaundiced after six months. Her bilirubin was 13.9 mg/dL, AST 1180 U/L, ALT 1500 U/L, ALP 164 U/L. Serological tests for all hepatitis was negative. Liver biopsy suggested drug induced hepatitis. Germander therapy was discontinued and hepatitis resolved in two months[15].

Ginkgo and Bleeding

Ginkgo biolba is used mainly to sharpen mental focus and to improve diabetes related circulatory disorder. One common reported adverse effect of ginkgo is bleeding. Spontaneous intracerebral hemorrhage occurred in a 72-year-old woman who was taking ginkgo 50 mg three times a day for six months[16]. Fessenden et al reported a case of postoperative bleeding after laparoscopic cholecystectomy[17]. Concurrent use of ginkgo and NSAIDs as well as anticoagulants should be avoided because ginkgolide B is a potent inhibitor of platelet activating factor.

Chromium, Oral Anticoagulants and Herbs

Athletes and body builders use chromium which has effect on glucose/insulin system and can cause hypoglycemia even in diabetics. Ginseng has been associated with hypoglycemic properties. Fenugreek, ginger, nettle, sage, devil's claw can affect glucose levels also. Ginseng, Danshen, Garlic, Ginkgo Biloba, Ginger, Devil's Claw, Red Clover, Dong Qui and Horse-Chestnut increase warfarin's action[18].

Concluding Remarks

Heavy metal contamination, adulteration with Western pharmaceuticals and prohibited animal and plant ingredients are regularly reported in herbal remedies[19]. Lead, mercury, and arsenic intoxication have been reported with the use of Ayurvedic medicines. Saper et al reported that out of 70 Ayurvedic medicines tested 13 preparations contained lead (range: 5.0-37,000 mg/g), 6 contained mercury (range: 28.0-104,000 g/g) and or arsenic (range: 37-8130 mg/g)[20]. Therefore, physicians need to be aware of the potential use of such herbal medicines by their patients and abnormal laboratory tests may serve as a clue to the clinician for relevant lines of investigation in their patients where symptoms may be related to the use of herbal products.

Resources

1. Mahady GB. *Global harmonization of herbal health claims*. J Nutr 2001; 131: 1120 S-1123S
2. Dasgupta A, Bernard DW. *Complementary and alternative medicines: Effects on clinical laboratory tests*. Arch Pathol Lab Med 130: 521-528, 2006.
3. Venkataraman R, Komoroski B, Strom S. *In vitro and in vivo assessment of herb-drug interactions.* Life Sci 2006; 78: 2105-2115.
4. Hu Z, Yang X, Ho PC, Chan SY, et al. *Herb-drug interactions: a literature review.* Drugs 2005; 65: 1239-1282.
5. Williamson EM. *Interactions between herbal and conventional medicines.* Expert Opin Drug Saf 2005; 4; 355-378.
6. Escher M, Desmeules J. *Hepatitis associated with kava, a herbal remedy.* Br Med J 2001; 322: 139.
7. Clouatre DL. *Kava Kava: examining new reports of toxicity.* Toxicol Lett 2004; 150: 85-96.
8. Anke J, Ramzan I. *Kava hepatotoxicity: Are we closed to the truth?* Planta Med 2004; 70: 193-196.
9. Gordon DW, Rosenthal G, Hart J, Sirota R, Baker AL. Chaparral ingestion. *The broadening spectrum of liver injury caused by herbal medications.* JAMA 1995; 273: 489-490.
10. Laliberte L, Villeneuve JP. *Hepatitis after use of germander, a herbal remedy.* CMAJ 1996;154: 1689-1692.
11. Miller LG. *Herbal medicinals: selected clinical considerations focusing on known or potential drug-herb interactions*. Arch Intern Med 1998; 158: 2200-2211.
12. Corns CM. *Herbal remedies and clinical biochemistry.* Ann Clin Biochem 2003; 40: 489-507.

2007-C CME Questions

The material necessary to review to answer the following questions may be found in this issue of the *P.O.L. Insight* and the AAFP-PT *Handbook* or on the AAFP-PT website (http://www.aafp.org/pt and click on Continuing Medical Education). The Test Sheet may be found on page 16 of the *P.O.L. Insight.* The Accreditation information may be found on the inside cover of this issue.

1. True or False: Standard starting dosing of warfarin for patients over 70 years old is 5-10 mg/day.
   A. True
   B. False
2. Alternative anticoagulant drugs include:
   A. Heparin
   B. Low molecular weight heparin
   C. Argatroban
   D. All of the above
3. True or False: Anticoagulant drugs work by thinning the blood.
   A. True
   B. False
4. True or False: The protime test (PT) is used to monitor warfarin therapy.
   A. True
   B. False
5. Normal PT results in healthy people are in the _____ second range.
   A. 8-10
   B. 11.5-13.5
   C. 15.2-18.3
   D. 20-30
6. True or False: PT results are not affected by changed in thromboplastin reagent or instrument.
   A. True
   B. False
7. True or False: The INR is a standardized result & allows comparison between laboratories.
   A. True
   B. False
8. True or False: Using the correct ISI value is critical in determining INR results.
   A. True
   B. False
9. True or False: PT results should be monitored daily until a theraputic range is maintained for at least 2 days.
   A. True
   B. False
10. An INR value greater than _____ signals a potential bleeding risk.
    A. 2
    B. 5
    C. 7
    D. 11
11. Samples for PT testing are collected in a:
    A. Blue stoppered tube
    B. Purple top tube
    C. Red top tube
    D. Green top tube

12. True or False: The order of drawing blood samples for PT testing is not critical.
    A. True
    B. False
13. Which of the following can affect PT results:
    A. "Short draw"
    B. Hemolyzed sample
    C. Insufficient mixing
    D. All the above
14. What percent of the population is warfarin resistant?
    A. Approximately 2%
    B. Approximately 6%
    C. Approximately 10%
    D. Approximately 20%
15. True or False: The effectiveness of warfarin is not affected by diet, alcohol consumption or long-term antibiotic use.
    A. True
    B. False
16. If a patient's INR exceeds the critical level, the physican may respond by:
    A. Discontinuing warfarin therapy or modifying dosage
    B. Administrating Vitamin K
    C. Using frozen plasma or coagulation factor concentrates.
    D. Any of the above, depending on the severity of the patient's situation.
17. True or False: Laboratory safety training for new & existing employees is mandated by OSHA and accreditation agencies.
    A. True
    B. False
18. To be in compliance with OSHA mandates, safety training must include:
    A. Providing safety information to employee
    B. Providing the employee an opportunity to ask questions about the material
    C. An evaluation of effectiveness of the training
    D. All of the above
19. True or False: Taking advantage of national awareness campaigns is a good way to present fresh safety topics each month.
    A. True
    B. False
20. Before designing safety training, you should consider which of the following:
    A. Scope of training
    B. Your audience
    C. A & B above
    D. None of the above
21. True or False: On-line, computer-based training is most appropriate for employees in the 56-69 year old age group.
    A. True
    B. False
22. Learning objectives may focus on the employee's:
    A. Knowledge
    B. Comprehension
    C. Application
    D. Any of the above

23. True or False: Games can be an effective means of teaching safety skills or reinforcing training.
    A. True
    B. False
24. True or False: If safety training is effective, employees should have few to no injuries due to unsafe acts.
    A. True
    B. False
25. True or False: An annual update on new safety regulations is adequate.
    A. True
    B. False
26. Laboratory safety records and incident reports should be reviewed:
    A. Weekly
    B. Monthly
    C. Quarterly
    D. Annually
27. True or False: Documenting and tracking employee safety training is essential for regulatory compliance.
    A. True
    B. False
28. True or False: All documentation of employee safety training must be keep for seven years.
    A. True
    B. False
29. True or False: The majority of people think herbal medicines are safe.
    A. True
    B. False
30. True or False: The typical user of herbal medicines is under 50 years old and well educated.
    A. True
    B. False
31. Sales of herbal medicines and supplements is regulated by:
    A. CDC
    B. FDA
    C. No one
    D. NIH
32. Consumption of herbal medicines can cause unexpected laboratory results due to:
    A. Drug-herb interactions
    B. Organ toxicity
    C. Presence of undisclosed ingredients, such as heavy metals
    D. All of the above
33. True or False: Self-medication with St. John's Wort may reduce plasma concentrations of numerous drugs, including oral contraceptives.
    A. True
    B. False
34. Herbal medicines with known liver toxicity include:
    A. Chamomile
    B. Kava-Kava
    C. Germander
    D. "B" & "C" only

AAFP-PT CME Test Answer Sheet

ALL INFORMATION MUST BE COMPLETED TO OBTAIN CREDIT

❑ **2007-C** (submit by September 30, 2008 to obtain credit)

Please print:

Individual AAFP #: ____ ____ ____ ____ ____ ____ _____

(All participants in the AAFP-PT are now assigned a 7-digit AAFP number; AAFP-member physicians should use their AAFP-ID number; non-member physicians and laboratory personnel are assigned an ID number the first time CME is submitted)

Lab AAFP #: ____ ____ ____ ____ ____ ____ _____

(All labs enrolled in AAFP-PT are assigned a 7-digit AAFP number. The Lab ID number may be found on the Order Confirmation and on evaluations.)

Name (Last) (First) (Initial)

Street

City / State/ Zip Code

Fax Number

❑ Address or Fax change ❑ Name change

Select one if you are a physician:

❑ FP ❑ IM
❑ PED ❑ OB/GYN
❑ Other

Select one if you are laboratory personnel:

❑ MT ❑ MLT ❑ Nurse Practitioner
❑ RN ❑ LPN ❑ Physician Assistant
❑ Med. Assist. ❑ Laboratory Manager
❑ Laboratory Consultant ❑ Other

Evaluation: please fill in bubble between 1 & 5 – 1 denotes poor, 5 denotes excellent:

1. To what extent were the objectives achieved?
   poor ① ② ③ ④ ⑤ *excellent*
2. To what extent did the AAFP-PT education program *content* relate to the program's objectives?
   poor ① ② ③ ④ ⑤ *excellent*
3. Rate your overall degree of satisfaction with this education program.
   poor ① ② ③ ④ ⑤ *excellent*
4. In what general area of laboratory practice would you like to receive educational materials? (please mark all that apply).
   - ❑ CLIA and/or regulatory. requirements
   - ❑ Good laboratory practices
   - ❑ Test Procedures
   - ❑ Technical Subjects
   - ❑ Business/Financial Aspects
   - ❑ Other, please specify

   _____

Fill in the circles for the correct answers:

	A	B	C	D
1.	❍	❍	❍	❍
2.	❍	❍	❍	❍
3.	❍	❍	❍	❍
4.	❍	❍	❍	❍
5.	❍	❍	❍	❍
6.	❍	❍	❍	❍
7.	❍	❍	❍	❍
8.	❍	❍	❍	❍
9.	❍	❍	❍	❍
10.	❍	❍	❍	❍
11.	❍	❍	❍	❍
12.	❍	❍	❍	❍
13.	❍	❍	❍	❍
14.	❍	❍	❍	❍
15.	❍	❍	❍	❍
16.	❍	❍	❍	❍
17.	❍	❍	❍	❍
18.	❍	❍	❍	❍
19.	❍	❍	❍	❍
20.	❍	❍	❍	❍
21.	❍	❍	❍	❍
22.	❍	❍	❍	❍
23.	❍	❍	❍	❍
24.	❍	❍	❍	❍
25.	❍	❍	❍	❍
26.	❍	❍	❍	❍
27.	❍	❍	❍	❍
28.	❍	❍	❍	❍
29.	❍	❍	❍	❍
30.	❍	❍	❍	❍
31.	❍	❍	❍	❍
32.	❍	❍	❍	❍
33.	❍	❍	❍	❍

AAFPPT
The Physician's Proficiency Testing Program

Return to: AAFP-PT Education Program
11400 Tomahawk Creek Parkway
Leawood, KS 66211-2672
or Fax to 913-906-6079

Important: Keep a copy of the completed form for your records. Documentation of CME hours earned is mailed to lab personnel in July and January. Allow 7-10 business days for requested transcripts.