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ORIGINAL ARTICLE

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Teaching rational prescribing: a new clinical pharmacology curriculum for medical schools

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Abstract In most U.S. and Canadian medical schools, pharmacology is taught during the preclinical year 2 of the 4-year-long curriculum. This is despite the fact that medical school graduates and residency directors have identified teaching rational therapeutics as a priority. Hence, we have developed a core curriculum in clinical pharmacology for 4th-year medical students that builds on the core principles of rational therapeutics described by Nierenberg 10 years ago (Nierenberg, DW. Clin Pharmacol Ther 1990; 48:606–610). Here we report on our 3-year experience teaching this course, which addresses the following teaching objectives: to teach medical students on how to (1) critically evaluate medications; (2) obtain a complete medication history including herbal and over-the-counter medications; (3) apply pharmacokinetic principles to clinical practice; (4) recognize and report adverse drug events and interactions; (5) optimize pain management; (6) recognize and treat substance abuse and poisoning; and (7) prescribe rationally regardless of prescribing environment. Student assessment was in the form of multiple-choice and formative oral examinations, which were validated against the clinical part of the U.S. medical licensing examination. The course significantly increased the student rating of clinical pharmacology teaching measured by a national survey of U.S. medical school graduates. We conclude that this course may be useful for teaching rational prescribing to medical students. With the guidance and educational material provided by this article, a successful implementation of such a course should be possible in most medical schools.

Keywords Education · Prescribing · Medical · Pharmacology · Curriculum · Medication history

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Introduction

Changes in the practice of medicine over the past 20 years present many challenges to medical schools, perhaps none more important than the challenge of teaching physicians how to choose and prescribe drugs in a scientifically sound manner that is safe and effective. This has been emphasized recently by the Institute of Medicine report on the high incidence of medication errors and increased concern about adverse drug reactions (Committee on Quality of Health Care in America: Institute of Medicine 2000). At the same time, expectations of patients have never been higher, as evidenced by the documented concerns of the public about drug interactions and side effects (American Society of Health Systems Pharmacists 1999).

Threats to scientifically sound prescribing by physicians include pressure from the managed care industry, pressure from patients, and pressure from the pharmaceutical industry (Chew et al. 2000; Chren and Landefeld 1994; Wazana 2000). We do not routinely provide physicians-in-training with the skills to advocate for their patients in such settings. The advent of direct-to-consumer advertising via television and particularly the Internet means that doctors are frequently presented with patients who demand a specific drug (Bell et al. 1999; Scott et al. 2001; Spurgeon 1999). In addition to prescribing pres-

sures, the ever-increasing number of new medicines available leaves many practicing physicians foundering in a sea of information with nowhere to go to find objective, useful data. We should train them how to find it.

Patients' widespread use of alternative remedies (Bennett and Brown 2000; Eisenberg et al. 1998; Harnack et al. 2001) and the reluctance of patients to admit such use to their physicians (Eisenberg et al. 1998) requires that we train doctors to obtain a complete medication history – one that includes specific and careful questions about herbal and natural remedies. Complementary and alternative medicine is an area of therapeutics that is currently not a required part of formal training for most doctors in the United States; we believe it should be added to the medical school curriculum to provide context (Wetzel et al. 1998).

Many of these needs in undergraduate medical education were addressed already in a consensus document published over a decade ago (Nierenberg 1990). Teaching the core skills (e.g., how to analyze adverse drug interactions, how to utilize pharmacogenetic information) and the core attitudes (e.g., the process of rational therapeutics) of clinical pharmacology identified in the consensus document is now more important than ever. Nevertheless, a recent survey demonstrates that a clinical pharmacology core curriculum remains the exception at U.S. medical schools, with only 8% of all medical schools requiring a course or clerkship in clinical pharmacology (Rosebraugh et al. 2001b). This is despite the fact that training in rational therapeutics has been identified as a priority by residency programs (Rosebraugh et al. 2001b).

The general structure of the typical 4-year curriculum of U.S. and Canadian medical schools is as follows. The first 2 years focus primarily on the basic sciences including gross anatomy, embryology, biochemistry, physiology, neurobiology, immunology, pathology, microbiology, genetics and pharmacology, as well as exposure to statistics and ethics. The 3rd and 4th years of the undergraduate curriculum are the clinical years, with 3rd-year clerkships in surgery, family medicine, neurology, psychiatry, medicine, pediatrics and obstetrics/gynecology, and 4th-year acting internships in surgery and medicine in addition to emergency room and ambulatory care rotations as well as electives. At Georgetown University School of Medicine, the 2nd-year pharmacology course, while basic in nature, begins to address several key concepts in clinical pharmacology, including drug interactions, adverse drug reactions and pharmacokinetics. A database search using the Association of American Medical Colleges (AAMC) Curriculum Management and Information Tool (CurrMIT) confirmed that, even in 2001, only 9 out of 143 U.S. and Canadian medical schools required clinical pharmacology training during their clinical curricula. Thus, at present, teaching of clinical (applied) therapeutics, if it occurs, is largely restricted to the 2nd (preclinical) year of the typical 4-year medical school curriculum.

To address this need for clinical pharmacology and therapeutics training during the clinical curriculum, we have designed a core curriculum for 4th-year medical students. The focus is less on teaching facts than on teaching the skills and attitudes of clinical pharmacology, with emphasis on the rational use of the many information tools currently available. The course was first implemented in the academic year 1999/2000 as a required and graded part of the medical school clinical curriculum at Georgetown University School of Medicine. Here we report on our 3-year experience teaching this course.

Methods

Course objectives

We identified a set of course objectives for teaching clinical pharmacology to medical students based on the following sources: (1) the consensus document on core curricula in clinical pharmacology for medical students (Nierenberg 1990); (2) a needs assessment from the 1998 Medical School Graduation Questionnaire (AAMC 1998); and (3) a literature survey. Results are presented as the rationale for each course objective.

Course implementation

After an initial pilot program in 1999, these objectives were implemented in January of 2000 as a 1-week long full-time course. Course objectives were taught in eight core lectures, one expert panel discussion, and a number of case-based discussions, student research presentations and role-playing exercises in small groups over 4 consecutive days (see Results for details). Figure 1 outlines the organizational structure of the course.

Student assessment

On days 4 and 5, student achievement of learning objectives was measured using a written multiple-choice examination and two problem-based oral examinations ("personal formulary exercise", "triple jump"). For each learning objective, 3–4 multiple-choice questions were included in the written exam. Students were encouraged to utilize drug evaluation tools provided as part of the course (such as the P450 card; Fig. 2) during the exam. To further reinforce the 13 teaching objectives, we also designed and implemented two formative examinations described below:

Personal formulary exercise. Every physician should develop a working knowledge of therapeutics that he frequently uses, and should be able to update this knowledge on an ongoing basis. The purpose of the personal formulary exercise (Module 4) was to develop the appropriate knowledge for a particular drug of the student's choice. On the 1st day of the course, each student was asked to select a specific drug for use in his or her personal formulary. This could be for a specific type of patient, or for a

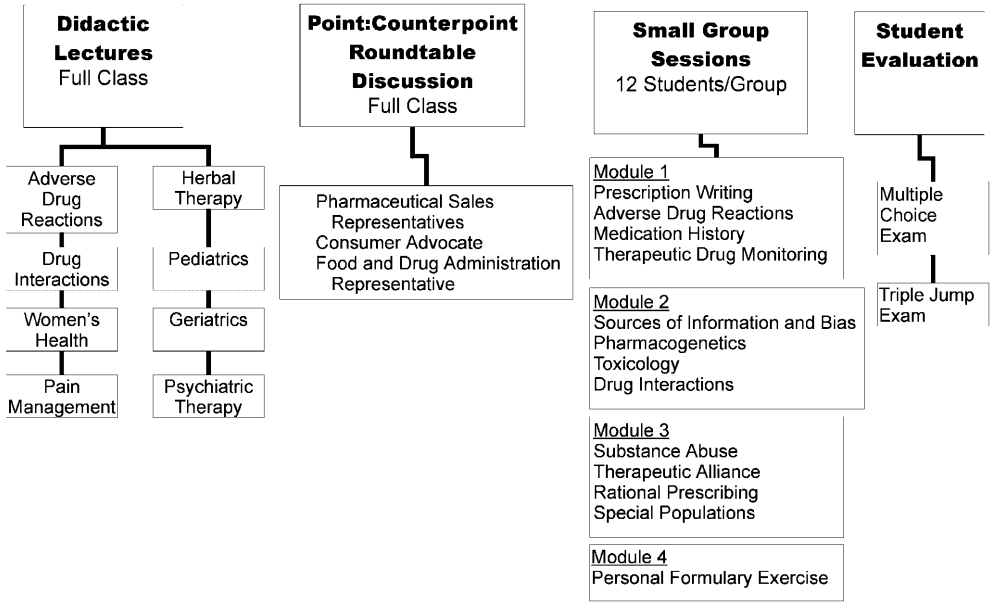

Fig. 1 Clinical pharmacology course structure. The first lecture was an organizational session that gave an overview of the course, and, importantly, provided a framework for the need to apply tools of clinical pharmacology in therapeutic decision-making. Other lectures that had been included are listed in the figure. The specific lectures chosen could be modified depending on the educational needs that have been identified. On day 4, the 3-h morning session was devoted to the roundtable discussion between representatives from the pharmaceutical industry, academia, Food and Drug Administration, and consumer advocacy groups in an attempt to reinforce objectives 2 and 11. The small group sessions were presented primarily in modular concepts, and each session lasted approximately 2 h, with the exception of the personal formulary exercise that was done on the afternoon of day 4, and lasted approximately 3 h. Students were evaluated on day 4 and 5 by two formative tests (personal formulary exercise, triple jump exam) and one multiple-choice written exam

specific indication, or for a specific drug among a class of similar drugs. During the week the student was asked to find evidence of drug efficacy taken from the primary literature, *not* reviews or editorials. The drug evaluation had to include a critical discussion on the validity of the clinical trial data, their clinical relevance, and their applicability to the specific patient. Pertinent drug interactions, cost effectiveness, and a therapeutic plan for use of the drug could be included. On the 4th day of the course, each student presented a critical evaluation of his or her formulary selection. A one-page summary was required at the time of the presentation. This 10-min presentation was followed by a 5-min discussion with the facilitator and the other students. This personal formulary exercise was a required element, but was not graded.

Triple jump examination. The *triple jump* is a formative examination that has previously been validated as a teaching instrument (Painvin et al. 1979). As performed in the present course, the triple jump was a one-on-one session with the student and a faculty facilitator. The student was presented with a clinical case, and asked to develop the differential diagnosis and a therapeutic plan. The first part of the triple jump required approximately 15 min per student. Following this session, the student was given 3 h to research the case. During this time the students were allowed to use any means available to them (data base search, medical library, textbooks etc.) to identify scientific data (or lack thereof) from the primary medical literature for their therapeutic plan. Review articles and textbooks were not acceptable. In the third part of the triple jump, the student returned to the faculty facilitator to critically discuss the scientific evidence supporting the therapeutic plan, using all of the tools discussed throughout the week to provide a rational course of therapy for the patient. This final part of the example required a 15-min meeting between the student and the faculty facilitator. The triple jump grade was based on a 5-point rating scale for *differential diagnosis*, *research* and *therapeutic plan*. Faculty facilitators were trained during two review sessions to incorporate the achievement of teaching objectives into the three elements of the triple jump score.

Course evaluation

The course was evaluated at three different levels:

1. **Validation of written and oral examination:** for each student, written and oral examination test scores were correlated with that student's test scores on the United States Medical Licensing Examination, Step 2 (USMLE 2), an extensively validated examination that is considered a gold standard for measuring medical student performance. Step 2 is administered during the last 6 months of the medical school curriculum, and assesses whether students can apply medical knowledge and understanding of clinical science essential for the provision of patient care under supervision. Most test scores fall between 160 and 240. The mean score for

Fig. 2 Listing of six major cytochrome P450 (CYP) isoforms involved in drug metabolism. This educational tool is designed to alert physicians to the possibility of important drug interactions in their patients that result from drugs metabolized by the cytochrome P450 system. Drugs metabolized by individual cytochrome P450 isoforms (CYPs) are listed in the *column* below each enzyme. Inhibitors and inducers of each enzyme are listed below the drugs metabolized. [E.g., Triazolam (Halcion) may become long-acting when its CYP3A4 metabolism is inhibited by itraconazole, and may be ineffective when co-administered with rifampin, a CYP3A4 inducer.]

Drugs Metabolized by Known P450's

1A2	2B6	2C19	2C9	2D6	3A
Clozapine	Buproprion	Amitriptyline	Celecoxib	Amitriptyline	Alprazolam
Cyclobenzaprine	Cyclophosphamide	Citalopram	Diclofenac	Carvedilol	Buspirone
Fluvoxamine	Ifosfamide	Clomipramine	Flurbiprofen	Clomipramine	Calcium Channel Blockers
Haloperidol		Diazepam	Ibuprofen	Codeine	Carbamazepine
Imipramine		Imipramine	Losartan	Desipramine	Cyclosporine
Mexiletine		Lansoprazole	Naproxen	Dextromethorphan	Efavirenz
Olanzapine		Nelfinavir	Phenytoin	Fluoxetine	Haloperidol
Tacrine		Omeprazole	Piroxicam	Metoprolol	HIV Protease Inhibitors
Theophylline		Phenytoin	Torsemide	Nortriptyline	'statins
Zileuton		Pantoprozole	Tolbutamide	Ondansetron	NOT pravastatin
Zolmitriptan			Warfarin	Oxycodone	Midazolam
				Paroxetine	Nevirapine
				Propafenone	Tacrolimus
				Risperidone	Triazolam
				Timolol	Zolpidem
INHIBITORS					
Cimetidine	Thiotepa	Cimetidine	Amiodarone	Amiodarone	Amiodarone
Ciprofloxacin		Felbamate	Fluconazole	Chlorpheniramine	Diltiazem & Verapamil
Fluvoxamine		Fluoxetine	Fluoxetine	Fluoxetine	Grapefruit Juice
Levofloxacin		Fluvoxamine	Fluvastatin	Haloperidol	HIV Protease Inhibitors
		Isoniazid	Metronidazole	Indinavir	Itraconazole
		Ketoconazole	Paroxetine	Paroxetine	Ketoconazole
		Lansoprazole	Zafirlukast	Ritonavir	Macrolide Antibiotics
		Omeprazole		Terbinafine	(NOT Azithromycin)
		Ticlopidine		Ticlopidine	Nefazadone
INDUCERS					
Carbamazepine	Phenobarbital	Carbamazepine	Phenobarbital		Carbamazepine
Char-grilled Meat	Phenytoin	Rifampin	Rifampin		Efavirenz & Nevirapine
Rifampin	Rifampin				Rifabutin & Rifampin
Tobacco					Ritonavir
					St. John's Wort
		Absent in 15-30	Absent in ~ 1%	Absent in 7 % of	
		% of Asians	of Caucasians	Caucasians	

first-time examinees from accredited medical schools in the United States is in the range of 200–220, and the standard deviation is approximately 20. Passing score is 174 (USMLE bulletin, http://www.usmle.org/bulletin/2002/scoring.htm, accessed 2/21/02).

2. **Assessment of the efficacy of didactic interventions:** as an example, we measured the effect of a 15-min lecture intervention on adverse drug event reporting. Students were randomized to either "lecture" or "no lecture". The lecture provided information on completing

a MedWatch adverse reaction report form, the standard form for voluntary submission of adverse reaction reports to the United States Food and Drug Administration (FDA). The lecture focused on completing the form using information considered by the FDA to be critical to adverse drug reaction reporting, with an emphasis on providing high quality information in the report. Afterwards, all students attended a structured patient interview by one faculty member evaluating a patient for a recognizable adverse drug reaction, and were asked to fill out an adverse event report form on this case. The quality of the adverse event report was evaluated by two FDA Safety Evaluators, who where blinded to the students' group assignment.

3. **Survey of U.S. medical school graduates prior to, and after the implementation of our clinical pharmacology course:** data on student ratings of the time devoted to instruction in clinical pharmacology, and in topics covered by our educational objectives, were obtained from the AAMC Medical School Graduation Questionnaire. Data were in form of a 3-point rating scale (inadequate, appropriate, excessive). Ratings from Georgetown University graduates were compared to ratings from all other U.S. medical school graduates from 1998 (before introduction of our course) to 2001 using a logistic regression model to predict the probability of being rated "appropriate" as a function of time (1998 vs. 2001), comparison group (Georgetown vs. all other U.S. graduates) and an interaction term that represented the extent to which the change in Georgetown's "appropriate" percentage from 1998 to 2001 differed from the corresponding change in the national group's "appropriate" percentage over that same time interval.

Results

Course objectives, practical implementation and student assessment

Based on the recommendations from the consensus document on clinical pharmacology teaching, the student needs survey and a critical review of the medical literature, we identified the following 13 teaching objectives, which were implemented and assessed as described below:

1. The student will be able to utilize the tools necessary to critically evaluate medications.
   - **Rationale:** The practicing physician must be able to compare recently approved medications with currently available therapy in terms of efficacy, safety and cost.
   - **Implementation:** This was taught using several approaches including small group discussions intended to emphasize, through practice, the critical evaluation of the design and conduct of clinical studies, statistical evaluations of data including a careful series of exercises designed to familiarize physicians with the use of "number needed to treat" as a decision-making tool. Risk considerations, and the importance of a *working* ability to evaluate sensitivity and specificity were also emphasized. The utility and appropriate uses of various sources of information were considered and the use of *primary* literature, as opposed to review articles and electronic databases in the critical evaluation of medications, was promoted.
   - **Student assessment:** Personal formulary exercise, triple jump, multiple-choice exam.
2. The student will be able to recognize potential for bias in sources of information.
   - **Rationale:** Physicians are presented with many sources of information about medications and must learn to recognize the limitations as well as advantages of the various reference sources including FDA-approved product information, pharmaceutical sales representatives, review articles and primary literature.
   - **Implementation:** This was carried out using case-based examples that allowed students to recognize the potential for bias in the medical literature. A Panel discussion with pharmaceutical sales representatives, a consumer advocate, and a representative from the Food and Drug Administration was held to highlight the potential for bias in information presented to physician.
   - **Student assessment:** Personal formulary exercise, triple jump, multiple-choice exam.
3. The student will be able to obtain a comprehensive medication history.
   - **Rationale:** Incomplete medication histories could result in co-administration of medications with potential for interaction, in failure to recognize potential sources of toxicity. Evaluation of medical records suggests that 25% of prescription drug use is *not* recorded, and that more than 60% of patients have at least one medication that has not been recorded (Lau et al. 2000). In addition, it is hard to overemphasize the value of a more extended medication history in a context where 60% of physician visits generate a prescription (Schappert 1999).
   - **Implementation:** Case-based discussions throughout the course in multiple examples and contexts allow the student to carefully consider the medication history using the "AVOID Mistakes" mnemonic, shown in Fig. 3, and to develop an appropriate approach to the patient that includes this information. This includes a history of adverse reactions to medications, over-the-counter medications including vitamins and herbal therapy, previous medications, the potential for drug interactions, substance abuse and smoking cessation, and pharmacogenetics.
   - **Student assessment:** Triple jump, multiple-choice exam.
4. The student will be able to apply pharmacokinetic principles to clinical practice.

Allergies? -- *to medications or foods*

Vitamins and Herbs? -- *and other over-the-counter medications*

Old drugs? -- *as well as current*

Interactions? -- *with medications or foods*

Dependence? -- *do you need a Contract?*

Mendel: -- *Family Hx of benefits or problems with any drugs?*

Fig. 3 Mnemonic on how to obtain a good medication history: AVOID Mistakes. This educational tool emphasizes elements that should be included in a complete medication history

- **Rationale:** Therapeutic drug monitoring is used to avoid toxicity, to achieve therapeutic efficacy, or to maintain a usually therapeutic range of plasma concentrations. It is also useful in evaluating the causes for unexpected toxicity or therapeutic failure. Pharmacokinetic principles can help guide dosing in these cases, particularly in certain disease states (e.g., impaired renal function, septic shock, extreme obesity).
- **Implementation:** Case studies provide examples of situations in which therapeutic drug monitoring may *or may not* be valuable, and provide the students the opportunity for hands-on use of pharmacokinetic principles in medication dosing. Students are provided with a pocket card with the few simple pharmacokinetic equations necessary to use therapeutic drug monitoring in clinical practice.
- **Student assessment:** Triple jump, multiple-choice exam.

5. The student will be able to recognize the differences in pharmacokinetics and pharmacodynamics of drugs in the pediatric, obstetric and geriatric population.
   - **Rationale:** Pharmacokinetics and pharmacodynamics of commonly used medications change over the continuum of age from neonatal patients to the elderly, as well as in pregnancy. Because of the relative lack of data in these populations, limitations eist in the labeling of medications when used in these populations (Kearns 2000) (Turnheim 1998).
   - **Implementation:** Didactic lectures are used to present recent research providing specific data about pharmacokinetics and pharmacodynamics in these populations. Case-based discussions in small groups reinforce the use of these concepts and encourage each prescription to be considered as an experiment.
   - **Student assessment:** Personal formulary exercise, triple jump, multiple-choice exam.
6. The student will be able to utilize tools to recognize and/or prevent adverse drug reactions and drug interactions.
   - **Rationale:** The Institutes of Medicine report "To Err is Human" (Committee on Quality of Health Care in America: Institute of Medicine 2000) estimated that 44,000 to 98,000 deaths occur annually in the United States due to medical errors. Subsequent studies also estimate that Medication errors are responsible for significant mortality, with minimal estimates of 7,000 deaths reported annually (Phillips et al. 1998). This is larger than the number of deaths due to workplace injuries in the United States (U.S. Bureau of Labor Statistics 2001a). Other studies have estimated that adverse reactions to medications are the fourth to sixth leading cause of death in the United States (Lazarou et al. 1998). A large number of adverse drug reactions are preventable, including those that are due to drug interactions.
   - **Implementation:** A core lecture on drug interactions as cause of adverse drug reactions has been used. In addition, using case-based small group discussions, students use readily available tools to assist in the prevention of drug interactions and to prevent or recognize adverse drug reactions due to other mechanisms. These tools include a pocket-sized laminated card (www.drug-interactions.com) that is useful in identifying cytochrome P450-mediated drug interactions (Fig. 2), and a table of drugs known to prolong the QT interval on the ECG or cause torsades de pointes cardiac arrhythmia (www.torsades.org). Students are also given a laminated card with pertinent equations to help with drug dosing. These tools are used throughout the cases in the course. Case-based small group discussions demonstrate the role of pharmacogenetics in drug metabolism and pharmacodynamics. Students also learn how to treat specific adverse drug reactions that are due to preventable events, overdose, or unexpected events.
   - **Student assessment:** Personal formulary exercise, triple jump, multiple-choice exam.
7. The student will be able to recognize the usage of over-the-counter and herbal medications and their implication in the practice of medicine.
   - **Rationale:** Over-the-counter and natural products may be a source of major unrecognized toxicity, either due to the product itself (Haller and Benowitz 2000; Kernan et al. 2000), or unlabeled toxic components of the preparation (Nortier et al. 2000). Adverse drug reactions, including therapeutic failure, may be due to interactions of the product with a prescription medication (Ruschitzka et al. 2000) or due to abuse of the product (Phillips 1999). As well-designed studies begin to be published, the physician should be aware of the potential role for natural products in therapeutics, and should not only be aware of increasing use of natural products among patients who may not feel comfortable discussing such use with the physician, but have the tools available to deal with it: specific questions as part of the medication history and an awareness of the significant potential for drug-herb interactions.

- **Implementation:** These issues are addressed in a core lecture on herbal therapy. The core lecture is a follow-up to an herbal therapy lecture that the students have heard in the 2nd year of the medical school pharmacology curriculum. It provides an overview of herbal therapy including regulatory issues relating to efficacy, safety and quality of herbal products, including the well-recognized variability in composition of marketed products. It also includes a review of the basic and clinical pharmacology of specific preparations. The lecture provides a basis from which physicians can rationally and openly discuss the use of natural products with their patients. The case-based discussions emphasize obtaining a complete medication history, the difficulty of obtaining accurate herbal medication histories and the use of practical quick-reference tools to identify important drug interactions.
- **Student assessment:** Triple jump, multiple-choice exam.

8. The student will be able to use the principles of pain management to optimize medication use in treating severe acute and chronic pain.
   - **Rationale:** Medical school graduates have consistently rated teaching in pain management during medical school as inadequate (AAMC 2001b). Several recent studies have evaluated attitudes of medical students as well as physicians about the management of pain, that identified attitudinal barriers to the management of pain (Breitbart et al. 1999; Weinstein et al. 2000a, 2000b). An important perception of many patients with a variety of different painful conditions has been that physicians do not know how to manage pain well, particularly in outpatient settings. Given the wide range of analgesics now available and the availability of World Health Organisation guidelines on the management of pain, the skill of rational prescribing for pain should be included in the training of physicians.
   - **Implementation:** The curriculum included a core lecture and a series of practice cases that trained students how to calculate routine dosing and equivalent doses of opiates, and that addressed rational prescribing for acute and chronic cases of severe pain of various etiologies.
   - **Student assessment:** Personal formulary exercise, triple jump, multiple-choice exam.
9. The student will be able to document and report adverse drug reactions and medication errors.
   - **Rationale:** Despite some limitations of the Food and Drug Administration's voluntary MedWatch system for reporting adverse drug reactions, the value of this program for recognizing signs of medication-associated events is apparent. This has been demonstrated in the recognition of adverse events, and eventual removal from the market for several drugs since 1998 including terfenadine, astemizole, mibefradil and cisapride. In addition, it has recently been demonstrated that a brief description of the MedWatch reporting form can improve the quality of reports.
   - **Implementation:** Students are exposed to data regarding the value of the MedWatch and medication errors reporting programs and go through an exercise in which they record an adverse event after a patient interview, and complete a MedWatch form from the same data.
   - **Student assessment:** Multiple-choice exam.
10. The student will be able to integrate medical ethics regarding prescribing.
    - **Rationale:** Physicians have become the target of heavy marketing by the pharmaceutical industry, with budgets for drug marketing exceeding that for research and development. Marketing strategies such as "seeding trials", in which the physician can become the instrument of increasing sales under the guise of participation in research, raise ethical questions.
    - **Implementation:** Small group discussions of the American Medical Association opinion on gifts to physicians from industry (American Medical Association 2001) and role-plays of "seeding trials" are used as examples of how to integrate medical ethics into prescribing.
    - **Student assessment:** Triple jump, multiple-choice exam.
11. The student will be able to prescribe rationally regardless of the prescribing environment.
    - **Rationale:** There are many pressures to prescribe irrationally. These include cost-containment in the era of managed care in a setting that may lead to adverse outcomes (ACP-ASIM Observer 2000), pressures to prescribe antibiotics inappropriately in the setting of antibiotic resistance (Scott et al. 2001) and patient pressures due to direct-to-consumer advertising (Bell et al. 1999; Spurgeon 1999). Furthermore, medical school graduates have consistently rated teaching on managed care during medical school as inadequate (AAMC 1998).
    - **Implementation:** On day 4 of the course, the 3-h morning session was devoted to a roundtable discussion between representatives from the pharmaceutical industry, academia, Food and Drug Administration, and consumer advocacy groups in an attempt to demonstrate the many pressures leading to irrational prescribing. A role-play exercise trained students on how to respond to prescribing pressures by managed care representatives. Small group discussions and case-based exercises illustrated the importance of the therapeutic alliance in rational considerations of therapeutics. Prescription-writing exercises reiterated the principles learned throughout the course. The personal formulary exercise and the triple jump required a critical review of the peer-reviewed literature in developing a therapeutic plan.
    - **Student assessment:** Personal formulary exercise, triple jump, multiple-choice exam.

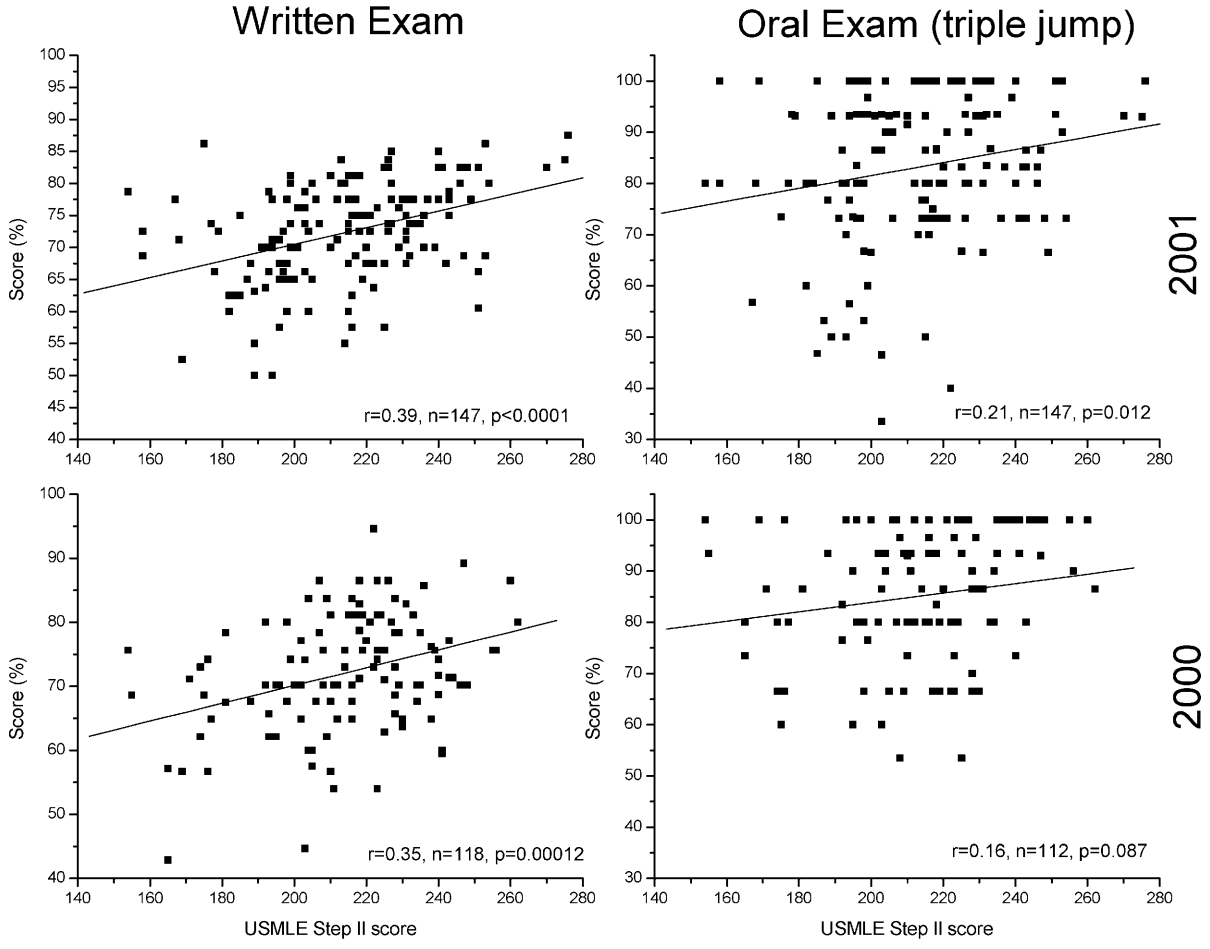

Fig. 4 Correlation between USMLE Step 2 test scores and multiple-choice examination and triple jump examination. Examination scores are plotted for medical students that graduated in 2001 (*top panels*) and in 2000 (*bottom panels*). Results of the linear regression analysis (correlation coefficient *r* and *P*-value) are indicated in each panel

12. The student will be able to recognize and treat substance abuse.
    - **Rationale:** Unrecognized substance dependence can interfere with any therapeutic plan and endanger the patient. Despite its huge importance for all clinical specialties, more than 10% of residents feel unprepared to care for patients with substance abuse (Blumenthal et al. 2001). Skills such as recognition and treatment for substance abuse are not required during clinical curricula of many U.S. medical schools, as has been recently demonstrated for smoking cessation (Ferry et al. 1999).
    - **Implementation:** Case-based small group discussions emphasize the importance of recognizing a history of substance abuse, and provide the students with tools on how to assess the degree of dependence. They also emphasize the need to establish a *therapeutic alliance* with the patient and other care-providers such as family members, nurses and pharmacists.
    - **Student assessment:** Triple jump, multiple-choice exam.
13. The student will be able to recognize and treat poisoning.
    - **Rationale:** It is important for all the students to understand the pharmacokinetic and pharmacodynamic principles that govern the diagnosis and treatment of poisoning. Included in this is the need to obtain an accurate medication history and outline a differential diagnosis.
    - **Implementation:** Case-based small group discussion emphasizes the use of information tools for rapid diagnosis, and teaches the pharmacological principles underlying the different therapeutic approaches to poisoning.
    - **Student assessment:** Multiple-choice exam.

The overall organization of the course is summarized in Fig. 1. The first lecture was an organizational session that gives an overview of the course, and, importantly, it provided a framework for the need to apply tools of clinical pharmacology in therapeutic decision-making. Other lectures that had been included are listed in Fig. 1. The specific lectures chosen could be modified depending on the educational needs that have been identified. The small group sessions were presented primarily in modular concepts, and each session lasted approximately 2 h, with the

exception of the personal formulary exercise that was done on the afternoon of day 4, and lasted approximately 3 h.

Required faculty time

For a class size of 150–160 students, 10–12 facilitators were occupied full-time for the 1-week period. This allowed teaching with groups of 12–15 students, which was also the maximum number of students that could be handled by individual facilitators during the personal formulary exercise and triple jump examination.

Course evaluation

A number of approaches were taken to evaluate individual elements and overall impact of the course. We first validated the two graded examinations (multiple-choice and triple jump) against test results from Step 2 of the USMLE examination, which is the accepted and validated standard of clinical proficiency of U.S. medical school graduates. As shown in Fig. 4, results from our written multiple-choice examination were highly significantly correlated with the USMLE 2 test scores, both in 2000 and 2001. Compared to the written test, test scores from the oral examination had a lower correlation coefficient, which was statistically significant only in 2001. Nevertheless, these results suggest that both exams are valid measures of clinical proficiency of medical students.

We next examined the efficacy of teaching adverse drug events reporting (objective no. 9). As previously reported (Rosebraugh et al. 2001a), a 15-min core lecture intervention on this topic significantly increased the quality of the adverse drug event reports submitted by the intervention group compared to the nonintervention group as judged by an expert panel of FDA representatives. Thus, even a brief intervention of this type can improve adverse reaction reporting.

The overall impact of the course was based on the results from AAMC medical school graduation questionnaires from 1998 to 2001. The annual questionnaire provides data on how U.S. Medical School Graduates rate elements of their medical school training. As illustrated in Fig. 5, the introduction of a pilot program in 1999, and the full course in 2000, appeared to be associated with an increase in ratings of teaching clinical pharmacology, pain management and managed care, three areas which were addressed by our course objectives. Logistic regression (Table 1) indicated that for all three measures there was a highly significant increase in a rating of "appropriate" over time ($P<0.001$), in both the Georgetown and the national student group. Furthermore, Georgetown students delivered a significantly higher percentage of "appropriate" pain management ratings than the national group ($P=0.044$), independent of year. There was no significant difference between Georgetown and the national group in clinical pharmacology or managed care. The group-by-year interaction term, which most directly indicates the extent to which the percentage of "appropriate" ratings by Georgetown's students increased faster than those of the national group from 1998 to 2001, was highly significant for clinical pharmacology ($P=0.013$) and for managed care ($P=0.017$), but not for pain management ($P=0.178$).

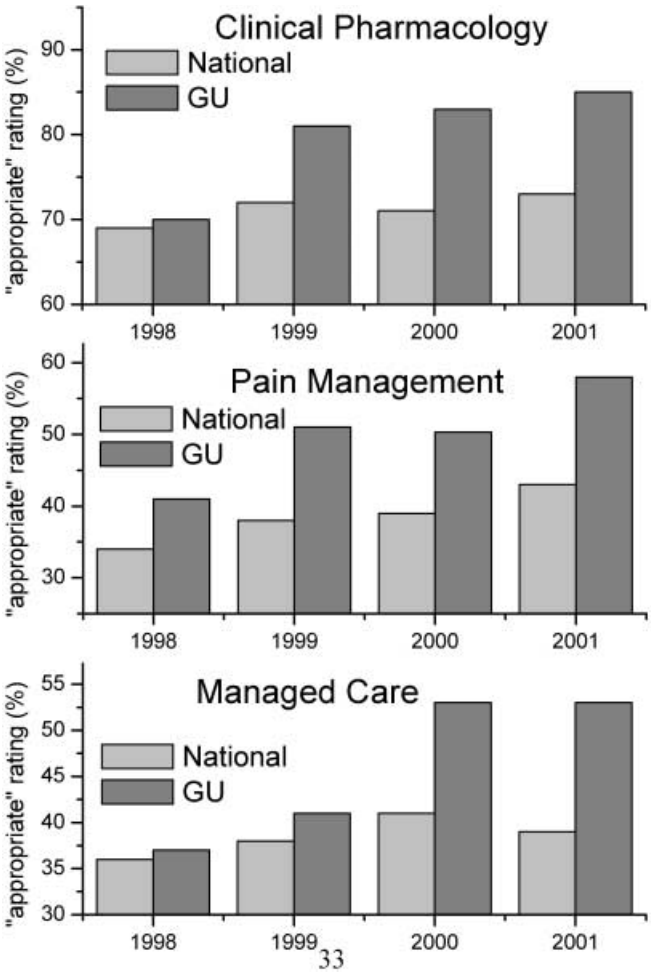

Fig. 5 Results of the AAMC Annual Medical School Graduation Questionnaire from 1998 until 2001. Graduates were asked to rate the time devoted to their instruction during medical school in different areas as inadequate, appropriate or excessive. Plotted are the percentages of appropriate instruction time provided in three areas (clinical pharmacology, pain management, managed care) that were taught as part of our course objectives. Note the significant increase in the ratings after course introduction in 1999 and 2000 (*National* all US medical school graduates, *GU* Georgetown University graduates)

Discussion

Based on our experience, a successful implementation of this core curriculum in clinical pharmacology required several key elements. First and foremost, enough physicians of various specialties trained in clinical pharmacology must be available to give the core lectures, to run the

Table 1 Results of logistic regression of "appropriate" rating as a function of year, study group, and interaction term. The interaction term represents the effect of the 4th-year course in clinical pharmacology

	Coefficient ± SE	Odds ratio (95% CI)	Significance
Clinical pharmacology			
Georgetown vs. national	0.0447±0.1581	1.046 (0.767–1.426)	*P*=0.777
2001 vs. 1998	0.1944±0.0279	1.215 (1.150–1.283)	*P*<0.001
Interaction (course effect)	0.6980±0.2809	2.010 (1.159–3.485)	*P*=0.013
Intercept	0.8001	–	–
Pain management			
Georgetown vs. national	0.2964±0.1475	1.345 (1.007–1.796)	*P*=0.044
2001 vs. 1998	0.3813±0.0260	1.464 (1.391–1.541)	*P*<0.001
Interaction (course effect)	0.3010±0.2236	1.351 (0.872–2.094)	*P*=0.178
Intercept	–0.6632	–	–
Managed care			
Georgetown vs. national	0.0341±0.1503	1.035 (0.771–1.389)	*P*=0.820
2001 vs. 1998	0.1281±0.0261	1.137 (1.080–1.196)	*P*<0.001
Interaction (course effect)	0.5358±0.2242	1.709 (1.101–2.652)	*P*=0.017
Intercept	–0.5755	–	–

small group sessions effectively, and most importantly to administer the problem-based oral examinations (personal formulary, triple-jump). The use of many small groups will be a major limiting factor for many institutions, but it is possible to include facilitators with a variety of backgrounds and levels of experience, if appropriate training sessions are conducted. Even in our situation where trained clinical pharmacology faculty members were available, training sessions for this course were conducted monthly throughout the academic year. In addition, each session of the course was outlined in a teaching notebook for the faculty that includes learning objectives, teaching points, and copies of pertinent reference materials. Secondly, medical school support to make the clinical pharmacology course a required part of the clinical curriculum has to be present. Finally, small-group cases and educational tools are necessary.

As part of our educational effort at Georgetown University, the educational material used in this course is available free of charge to any medical school or faculty member interested in administering such a course. These resources include the therapeutic tools, the small-group modules, organization, lecture outlines and teaching points themselves, a list of speakers, and the educational module for the drug interaction lecture.

Limitations

Although we have designed and implemented this clinical pharmacology curriculum with the ultimate goal to improve physicians' prescribing habits, at this time we do not know if the course made a difference in the clinical performance of our graduates. Measuring the impact of a 1-week-long course is difficult, but, to address this question, we are currently planning a survey of residency directors to assess the clinical performance of our graduates. Nevertheless, in the design of our course, we relied heavily on small group exercises, which have been shown to be the most effective intervention to change physician prescribing behavior (P. Honig, Director, Office of Postmarketing Drug Risk Assessment, Food and Drug Administration, personal communication 2002).

We have used logistic regression analysis to assess the impact of our course on ratings by medical school graduates. This analysis entails several assumptions, most notably that the logarithm of the odds of an "appropriate" rating can be modeled as the sum of "year", "group" and "interaction" terms. Equating the year × group interactive term in the model with the "course effect" assumes that no other effects specific to Georgetown during 1998–2001 could have accounted for the observed interaction.

Summary

In this article, we have developed and evaluated a core curriculum in clinical pharmacology for 4th-year medical students that builds on core principles of rational therapeutics. If the educational objectives are achieved, this course should be useful for teaching rational prescribing to senior medical students, and provide a foundation for physicians to promote life-long learning on therapeutics. With the guidance and educational material provided by this article, a successful implementation of such a course should be possible in most medical schools.

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References

American Medical Association (2001) E-8.061 gifts to physicians from industry. http://www.ama-assn.org/ama/pub/article/4001-4236.html

American Society of Health Systems Pharmacists (1999) Patient concerns national survey

Anonymous (1998) Medical School Graduation Questionnaire 1998. Association of American Medical Colleges

Anonymous (2001a) 2000 Census of Fatal Occupational Injuries. U.S. Bureau of Labor Statistics http://www.bls.gov/iif

Anonymous (2001b) Medical School Graduation Questionnaire 2001. Association of American Medical Colleges

Bell RA, Kravitz RL, Wildes MS (1999) Direct-to-consumer prescription drug advertising and the public. J Gen Intern Med 14:651–657

Bennett J, Brown CM (2000) Use of herbal remedies by patients in a health maintenance organization. J Am Pharm Assoc (Wash) 40:353–358

Blumenthal D, Gokhale M, Campbell EG, Weissman JS (2001) Preparedness for clinical practice: reports of graduating residents at academic health centers. JAMA 286:1027–1034

Boothby LA, Doering PL (2001) FDA labeling system for drugs in pregnancy. Ann Pharmacother 35:1485–1489

Breitbart W, Kaim M, Rosenfeld B (1999) Clinicians' perceptions of barriers to pain management in AIDS. J Pain Symptom Manage 18:203–212

Chew LD, O'Young TS, Hazlet TK, Bradley KA, Maynard C, Lessler DS (2000) A physician survey of the effect of drug sample availability on physicians' behavior. J Gen Intern Med 15:478–483

Chren MM, Landefeld CS (1994) Physicians' behavior and their interactions with drug companies. A controlled study of physicians who requested additions to a hospital drug formulary. JAMA 271:684–689

Committee on Quality of Health Care in America: Institute of Medicine (2000) To err is human: building a safer health system. National Academy Press, Washington, D.C.

Eisenberg DM et al. (1998) Trends in alternative medicine use in the United States, 1990–1997: results of a follow-up national survey. JAMA 280:884–886

Ferry LH, Grissino LM, Runfola PS (1999) Tobacco dependence curricula in US undergraduate medical education. JAMA 282: 825–829

Gesensway D (2000) Drug switching: lowering costs vs. adverse interactions, potential errors. ACP-ASIM Observer http://www.acponline.org/journals/news/jul-aug00/drugswitching.htm

Haller CA, Benowitz NL (2000) Adverse cardiovascular and central nervous system events associated with dietary supplements containing ephedra alkaloids. N Engl J Med 343:1833–1838

Harnack LJ, Rydell SA, Stang J (2001) Prevalence of use of herbal products by adults in the Minneapolis/St. Paul, Minn., metropolitan area. Mayo Clin Proc 76:688–694

Kearns GL (2000) Impact of developmental pharmacology on pediatric study design: overcoming the challenges. J Allergy Clin Immunol 106:S128–S138

Kernan WN et al. (2000) Phenylpropanolamine and the risk of hemorrhagic stroke. N Engl J Med 343:1826–1832

Lau HS, Florax C, Porsius AJ, De Boer A (2000) The completeness of medication histories in hospital medical records of patients admitted to general internal medicine wards. Br J Clin Pharmacol 49:597–603

Lazarou J, Pomeranz B, Corey PN (1998) Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA 279:1200–1205

Nierenberg DW (1990) Consensus for a core curriculum in clinical pharmacology for medical students. Clin Pharmacol Ther 48: 603–605

Nortier JL et al. (2000) Urothelial carcinoma associated with the use of a Chinese herb (*Aristolochia fangchi*). N Engl J Med 342:1686–1692

Painvin C, Neufeld V, Norman G, Walker I, Whelan G (1979) The "triple jump" exercise – a structured measure of problem solving and self directed learning. Annu Conf Res Med Educ 18: 73–77

Phillips DP, Christenfeld N, Glynn LM (1998) Increase in US medication-error deaths between 1983 and 1993. Lancet 351: 643–644

Phillips SF (1999) Surreptitious laxative abuse: keep it in mind. Semin Gastrointest Dis 10:132–137

Rosebraugh CJ et al. (2001a) Improving the quality of adverse drug reaction reporting by 4th year medical students with a 15-minute intervention. Clin Pharmacol Ther 69:P93

Rosebraugh CJ, Honig PK, Yasuda SU, Pezzullo JC, Woosley RL (2001b) CERTS report: survey of medication errors education during United States undergraduate and graduate medical education. Clin Pharmacol Ther 71:4–10

Ruschitzka F, Meier PJ, Turina M, Luscher TF, Noll G (2000) Acute heart transplant rejection due to Saint John's wort. Lancet 355:548–549

Schappert SM (1999) Ambulatory care visits to physician offices, hospital outpatient departments, and emergency departments: United States, 1997. (1999) Vital Health Stat 13(143):1–39

Scott JG, Cohen D, DiCicco-Bloom B, Orzano AJ, Jaen CR, Crabtree BF (2001) Antibiotic use in acute respiratory infections and the ways patients pressure physicians for a prescription. J Fam Pract 50:853–858

Spurgeon D (1999) Doctors feel pressurized by direct to consumer advertising. Br Med J 319:1321

Turnheim K (1998) Drug dosage in the elderly. Is it rational? Drugs Aging 13:357–379

Wazana A (2000) Physicians and the pharmaceutical industry: is a gift ever just a gift? JAMA 283:373–380

Weinstein SM, Laux LF, Thornby JI, Lorimor RJ, Hill CS, Thorpe DM, Merrill JM (2000) Physicians' attitudes toward pain and the use of opioid analgesics: results of a survey from the Texas Cancer Pain Initiative. South Med J 93:479–487

Weinstein SM, Laux LF, Thornby JI, Lorimor RJ, Hill CS, Thorpe DM, Merrill JM (2000) Medical students' attitudes toward pain and the use of opioid analgesics: implications for changing medical school curriculum. South Med J 93:472–478

Wetzel MS, Eisenberg DM, Kaptchuk TJ (1998) Courses involving complementary and alternative medicine at US medical schools. JAMA 280:784–787