

Auburn Healthlink

A Newsletter of the Auburn University School of Pharmacy

Drug Information News

ANTIBIOTIC RESISTANCE: WHAT IS THE ANSWER?

The enthusiasm sparked by advances in antimicrobial therapy over the past half century has dimmed somewhat by the emergence and spread of resistant microorganisms. Antimicrobial resistance has become a worldwide phenomenon resulting in untreatable infections in both hospital and community settings. A major cause of the current crisis has been identified as the uncontrolled and inappropriate use of broad-spectrum antibiotics. As evidence, the rise in antibiotic resistance has paralleled increases in antibiotic use. Although some refuse to acknowledge this as a problem, the recent evidence of four *Staphylococcus aureus* strains harboring resistance to vancomycin should bring unprecedented fear to the healthcare community. In an effort to control this alarming trend, society must take responsibility for the prudent use of our existing antibiotic armamentarium.

Unfortunately, factors that brought about this crisis do not appear to be resolving. First, as mentioned previously, antibiotics are inappropriately used in humans. Researchers at the Centers for Disease Control and Prevention have

estimated approximately 50 million of the 150 million outpatient prescriptions written for antibiotics every year are unnecessary.¹ As well, antibiotics are exploited in animal husbandry and agriculture. In the United States, 48% of all available antibiotics are given to animals, of which, 90% are used for growth promoters.² An additional contributor to

“Approximately 50 million of the 150 million outpatient prescriptions written for antibiotics every year are unnecessary”

antibiotic resistance is the availability of over-the-counter systemic antibiotics. Even though the Food and Drug Administration has appropriately prohibited this practice in the United States, resilience of resistant microorganisms from other countries will result in their emergence within our communities. Finally, a large part of the blame falls directly on

the healthcare profession. As healthcare providers we have failed to educate our patients about appropriate use of antibiotics. Some physicians overprescribe antibiotics because of unrealistic patient expectations, insufficient time to discuss with patients why antibiotics are not needed, and concern over litigation involving a misdiagnosis or lack of treatment.³ Overall, the net result is patients expecting and demanding antibiotics each time they visit the doctor's office with complaints of the common cold.

Consequences of antimicrobial resistance include prolonged hospital stays, increased morbidity, prolonged periods during which individuals are infectious, and greater opportunities for infections to spread to other patients.⁴ The highest rates of resistance are seen in intensive care units but are increasing among stabilized patients in the hospital and community. The economic impact of antibiotic resistance is overwhelming. In the United States, it is estimated that antibiotic resistance results in direct and indirect costs totaling between \$100 million and \$30 billion. In one study, the authors concluded resistant infections

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Herbal Connection

ANXIOUS ABOUT KAVA-KAVA

JR complains that he has not had any sleep for the past six months. He has begun to have problems with his job because he just cannot seem to concentrate. JR is very worried and states that his nerves are just “shot.” He inquires as to whether there is something over-the-counter that he can take because he does not like to take “real medicine.”

The National Comorbidity Survey (NCS) report a 12 month prevalence rate

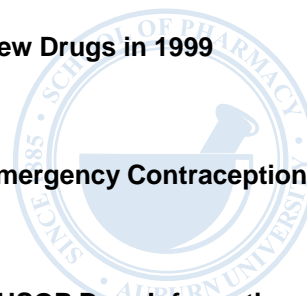
for anxiety disorders of 17.2% and a lifetime rate of 24.9%.¹ Anxiety is characterized by a subjective sense of unease or dread and may either indicate a primary psychiatric condition or another underlying medical disorder. Anxiety symptoms are common in patients with mood disorders, schizophrenia, organic mental syndromes, and substance abuse disorders. Anxiety disorders are generally chronic in

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Inside . . .

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NOTHING IN LIFE IS FREE — HOW ABOUT DRUG INFORMATION?

Have you ever had a patient ask you about an herbal product that you weren't familiar with? Perhaps a new drug was introduced to the market and your patients are asking questions before you were even detailed on it. Oftentimes, resources to answer these questions are unavailable in a physician's practice. There is now a valuable resource at the Auburn University School of Pharmacy (AUSOP) to assist physicians in these situations.

The Drug Information & Learning Resources Center (DILRC) has been created to serve the drug information needs of physicians, pharmacists, and other health care professionals in the state of Alabama. The DILRC staff is composed of the Director, Shauna Buring, PharmD, a post-doctoral Drug Information Specialty Resident, and Doctor of Pharmacy students. The service not only provides important medical and drug information but also serves as a practical experience for Doctor of Pharmacy students to develop skills and competency in the retrieval and interpretation of drug information.

The staff of the DILRC answer questions on a wide array of topics including herbal products, drug identification, therapeutic drug selection, newly approved therapies, pharmacokinetics, and many more. Although the DILRC is not a primary literature retrieval service, the staff routinely evaluates the primary literature in answering drug information questions.

The DILRC is located at the AUSOP and contains over \$25,000 worth of resources including state of the art technology resources, electronic drug information databases, over 200 journals, and tertiary references. Hours of operation are 8:00 am to 4:30 pm, Monday through Friday with voice mail service during non-operating hours. Questions may also be submitted by email at druginf@auburn.edu or via the web at <http://pharmacy.auburn.edu/DILRC/index>.

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nature, but can usually be treated effectively with long term therapy.

Kava, also termed "kava-kava", is an herb that comes from dried roots of the plant *piper methysticum*, which also means "intoxicating pepper." The kava plant is indigenous to the South Pacific islands where it is most commonly made into a drink and used for either ceremonial purposes or for its intoxicating effects. Kava is marketed as a mild anxiolytic in European countries. The herb is sold in the U.S. as a liquid tincture or as a dried-root capsule and is used as a natural alternative to anxiolytic drugs and sleeping pills. Kava is thought to produce psychological and physical relaxation via a non-opiate pathway and has been found to exert weak effects on GABA pathways in the central nervous system. Additive effects may exist with benzodiazepines given that they act on the same receptor pathways. Because of the agonism at the benzodiazepine-GABA receptor complex, kava may have some efficacy in reducing the effects of benzodiazepine drug withdrawal. Dopamine antagonism has also been proposed to play a role in the sedative effects of kava.

Side effects are minimal at the recommended daily dosage of 60 to 120 mg. Chronic ingestion may lead to dry, flaky, yellowed skin; red, puffy eyes; and muscle weakness. Abstinence from the herb for 2 to 3 weeks usually cures this syndrome. Some patients have experienced extrapyramidal side effects, including dystonic reactions and dyskinesia, perhaps due to dopamine antagonism; therefore, patients suffering from Parkinson's disease should avoid kava. Patients who are taking benzodiazepines should not take kava because of the potential additive effects mentioned earlier. Alcohol should be avoided while taking kava because it may increase the effects of the herb as well.

Although there have been no American studies done on kava to this date, clinical data does exist from studies

conducted in other countries. A 25-week, multicenter, randomized, placebo-controlled, double-blind trial took place in Germany involving 101 patients. Patients were categorized by the DSM-III-R diagnostic criteria as having either agoraphobia, specific phobia, social phobia, generalized anxiety disorder, or adjustment disorder with anxiety. The HAMA (Hamilton Anxiety Scale) score was used as the primary outcome variable. Kava was found to be superior at weeks 8 ($p = 0.02$), 12 ($p = 0.002$), 16, 20, and 24 ($p < 0.001$).²

However, no difference was seen between kava and placebo up until week 8 of the trial. A similar trial conducted compared kava to oxazepam, but no difference was seen between the two groups.

"Unlike prescription and OTC medications, herbal products are not required to demonstrate efficacy, safety, or quality."

Because herbal products are promoted as being safe and natural, some patients believe the product can be taken without concern of adverse effects or that the product is better for the body than traditional Western medicine. Unlike prescription and OTC medications, herbal products are not required to demonstrate efficacy, safety, or quality. Therefore, patients should be evaluated closely by health care providers in order to detect adverse effects, allergic reactions, and drug interactions that may occur while one is taking an herbal product. It is imperative that patient care providers access scientifically and clinically proven data when it is available in order to advise patients on the proper use of herbal medication.

by K. Kelley Rutledge, PharmD

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FDA Update NEW DRUG APPROVALS IN 1999

The Food and Drug Administration approved 12 new molecular entities (NME) in the first 7 months of 1999 (see table).¹ This was down from 19 approvals during the same time period in 1998.

Ten of these newly approved agents appeared to represent an advance over available therapy and were given priority review. Cilostazol (Pletal®) and doxercalciferol (Hectorol®) were deemed to have therapeutic qualities similar to those of drugs already marketed, thus receiving a standard review.

Two new thiazolidinediones, pioglitazone (Actos®) and rosiglitazone (Avandia®) were approved. Neither of these agents are expected to cause the

Drug	Trade Name	Indication
Alitretinoin	Panretin	AIDS-related Kaposi's sarcoma
Amprenavir	Agenerase	Protease inhibitor for HIV
Cilostazol	Pletal	Intermittent claudication
Doxercalciferol	Hectorol	Secondary hyperparathyroidism
Ganirelix acetate	Antagon	LH surge inhibition
Ketotifen fumarate	Zaditor	Allergic conjunctivitis
Orlistat	Xenical	Obesity management
Pioglitazone	Actos	Type II diabetes
Rofecoxib	Vioxx	Osteoarthritis, acute pain
Ferric gluconate complex	Ferrlicit	Iron deficiency anemia
Rosiglitazone	Avandia	Type II diabetes
Zanamivir	Relenza	Uncomplicated influenza virus

liver toxicity problems seen with troglitazone. However, post-marketing surveillance is needed to further clarify this issue.

Orlistat (Xenical®) a non-systemic inhibitor of gastrointestinal lipases was approved for the management of obesity. This includes weight loss and weight maintenance when used in conjunction

with a reduced-calorie diet. Since orlistat has been shown to reduce the absorption of fat-soluble vitamins and beta-carotene, patients may benefit from a multivitamin containing fat-soluble vitamins to insure adequate nutrition.

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Therapeutic Issues

EMERGENCY CONTRACEPTION: A CALL FOR AWARENESS

Emergency contraception involves preventing pregnancy after sexual intercourse by means of a drug or device. Approximately 48% of all pregnancies in the United States are unintended with 47% of these resulting in abortion. Aside from medical and ethical concerns over abortion, these numbers translate into a growing epidemic in our nation. Unwanted pregnancy serves as an origin of many social problems including single parenthood, teenage pregnancy, welfare dependency and the continuation of poverty.¹ One strategy for curtailing this vicious cycle involves a national campaign to increase emergency contraception awareness.

Emergency contraceptive pills (ECP) provide a short burst of hormone exposure. Depending on the stage of the menstrual cycle and the timing of unprotected intercourse, ECPs may prevent ovulation, disrupt fertilization, or inhibit implantation of a fertilized egg in the uterus. Traditionally, emergency contraception regimens consisted of 2

tablets, each containing 0.05 mg of ethinyl estradiol and 0.50 mg of norgestrel.² In 1996, a meta-analysis compiling data from 10 published clinical trials using this regimen, defined effectiveness as the percent reduction in the likelihood of pregnancy occurring.²

“...the prevention of pregnancy before implantation is defined as contraception and not abortion”

Results demonstrated effectiveness between 55.3% and 94.2%, with an average effectiveness of 74%.

About half of women taking ECPs have temporary nausea and 20% experience an emetic episode. Otherwise, there have been no serious adverse reports associated with emergency contraceptive use.

Although emergency contraception works mainly by interfering with ovula-

tion, it is regarded by many as an abortifacient because it is taken after, rather than before, intercourse. However, the prevention of pregnancy before implantation is defined as contraception and not abortion. Medical organizations and the federal government define the beginning of pregnancy as implantation of a fertilized egg in the lining of a woman's uterus.³ Thus, intervention within 72 hours after intercourse is not abortion, because implantation is not achieved until at least 5 to 7 days after ovulation.

Physicians, along with other health care professionals, play a significant role in the education and availability of emergency contraception. It is an important role in reducing unintended pregnancies and the need for induced abortion. For providers and users alike, increased understanding of contraception versus abortion could increase acceptance of emergency contraception. The FDA recently approved two products for emergency contraception. Preven® Emergency Kit is composed of

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The *Auburn HealthLink* is a service of the Auburn University School of Pharmacy. Its purpose is to disseminate information on drug therapy, current excerpts from the literature regarding drug usage, FDA warnings, and adverse reaction. The inclusion of a product name in this publication, or information on a products should not be construed as an endorsement of that product. Material in this publication may not be reprinted without written permission of the Auburn University School of Pharmacy.

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(ANTIBIOTIC RESISTANCE, Continued from page 1)

were twice as costly, in time and dollars, as a susceptible infection.² Currently, as we strive to cut down costs throughout the healthcare system, antibiotic resistance represents an area where we can make a difference. When possible, inexpensive narrow-spectrum antibiotics (ie, those that target a limited number of bacteria) should be prescribed in place of costly, extended-spectrum agents.

It is easy to understand how empirical use of new broad-spectrum antibiotics is attractive. Because infectious disease are difficult to diagnose and untreated infections can be disastrous, broad-spectrum antibiotics promise to cover errors of omission.⁵ For this reason, physicians well trained in infectious diseases and antimicrobial therapy often succumb to the pressure of overusing new antibiotics.

As seen in the past, resistance will inevitably emerge to new antibiotics; therefore, their effective life can be pro-

longed only if used appropriately. In the end, there is not a "magic bullet" for this dilemma, but through judicious use of existing antibiotics and prudent prescribing of upcoming, novel antibiotics, a major step towards avoiding the "post-antibiotic era" can be taken.

By J. Bryan Walker, PharmD

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(CONTRACEPTION, Continued from page 3)

a "Patient Information Book", a pregnancy test, and four birth control pills containing 0.25 mg levonorgestrel and 0.05 mg ethinyl estradiol. Plan B® is a progestin only emergency contraceptive containing two tablets of levonorgestrel 0.75 mgs, one to be taken within 72 hours of unprotected intercourse followed by the second tablet 12 hours later. The Reproductive Health Technologies Project has established a hotline number (1-800-585-9911) to answer questions concerning emergency contraception in your area.

By J. Bryan Walker, PharmD

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