JOYCE GENERALI

Clin-Alert® 2001

A Quick Reference to Adverse Clinical Events

Clin-Alert® 2001

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A Quick Reference to Adverse Clinical Events

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Contents

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Introduction

Keeping current with the safety profiles of drug therapy is essential in optimizing decisions regarding patient health care. However, with the addition of 25 to 30 new drugs to the United States market each year, this task becomes formidable. Although all drugs are tested for safety during premarketing trials, the full scope of the safety profile and drug interactions is not realized until the drug has been on the market for several years and used in a varied population in clinical scenarios that often involve polypharmacy. Thus, attention to potential side effects and drug interactions remains an important component of effective and rational drug therapy.

Changing safety profiles are not limited only to new drugs as new information is also published regarding new adverse reactions and/or drug interactions with older products. In addition, the popularity of alternative medicines and their use with conventional medicines has created a new need for information regarding drug interactions in this area.

The *Clin-Alert* newsletter is designed to collect, summarize and report newly published information regarding significant adverse drug events and drug interactions. In the last three years, the scope of the newsletter has expanded to include information on alternative medicines and herbal therapies, and to alert health care professionals regarding FDA notifications and public health advisories. This book is the second compilation of abstracts published in *Clin-Alert* and collates the reports presented in *Clin-Alert* for the last year. The abstracts are arranged by drug class and there are six indices for easy accessibility. This year a new index has been added which highlights adverse drug events with newly marketed agents (1997–2000).

Although most of the presented abstracts are summaries of published case reports, several abstracts also review data from drug interaction studies, prospective safety trials, case series or retrospective investigations. When the information is available a *Clin-Alert* abstract data regarding the suspected adverse event, the suspected drug (dose, duration of therapy and

route of administration), concurrent therapy, onset of action of the event, management or treatment of the side effect, relevant laboratory or physical examination data, dechallenge and rechallenge information, and clinical outcome. In addition, the author's conclusion and suggested mechanism of actions are provided. Full reference citations with reprint address and author's e-mail address (if available) are provided for ease of access to further information if needed. In addition, web page citations are included for easy access to information regarding FDA notifications or online journal access via the Internet.

It should be noted that these abstracts summarize reported information and that definitive causality is difficult to assess from case report data. Patient care decisions should never be based on abstract data alone and the reader is encouraged to access the original publication when needed. Abstracts are a useful tool in keeping current with the published literature and in identifying which articles may be of particular interest for the reader.

Adverse reactions and drug interactions are a dynamic part of a drug therapy. I am hopeful that this book will be a useful addition to the reader's library.

Joyce Generali, MS, RPh, FASHP
Director, Drug Information Center
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Drug	Interacting Drug	ADR	Page Number
Androstenedione		Priapism	3
Aristolochic Acid		Nephrotoxicity	3
Averrhoa Carambola		Death in uremia^	4
Chromium picolinate		Exanthematous pustulosis*	4
Creatine	Ma Huang	Ischemic stroke*	8
Ecabalium elaterium		Uvular angioedema	5
Henna		Cutaneous reactions	6
Henna		Hemolysis	5
Herbal vitamins		Lead intoxication	6
Kampo		Epithelial keratopathy*	7
Laminaria tents		Bacteremia	7
Ma Huang	Creatine	Ischemic stroke*	8
St. John's wort	Cyclosporine	Cyclosporine concentrations decreased	10, 11
St. John's wort	Digoxin	Digoxin levels decreased	11
St. John's wort	Indinavir	Indinavir concentrations decreased	9

* = first report
^ = death
(+) = legal action

Alternative Medicines

ANDROSTENEDIONE
Priapism

A 30-year-old man developed priapism after starting androstenedione (1 pill daily) one week earlier. He did not seek medical attention until the episode had lasted for 30 hrs. There were no concurrent medications but a medication history revealed a previous episode one year earlier (duration: two to three hours) while taking the same supplement. Therapy included corpora cavernosa aspiration, normal saline irrigation and intracavernous injection with phenylephrine. Alternate etiologies were excluded. The authors suggested that androstenedione, a precursor of testosterone, increased serum testosterone levels in this patient, and possibly resulted in a hypersensitivity to erectile blood flow and an increased risk of priapism.

Kachi PN & Henderson SO (Henderson SO, Dept Emerg Med, LAC+USC Med Center, Unit #1, Room 1011, 1200 N Stone St, Los Angeles, CA 90033; e-mail: sohender@hsc.usc.edu) Priapism after androstenedione intake for athletic performance enhancement. Ann Emerg Med 35(4):391–393 (Apr) 2000

ARISTOLOCHIC ACID
Nephrotoxicity, FDA Advisory

On June 1, 2000, the FDA notified health professionals regarding potential nephrotoxicity associated with botanical products containing aristolochic acid. Although the FDA has not received similar adverse events, in July 1999, two new cases were reported in England regarding nephropathy associated with the use of Chinese botanical preparations containing this product. (See Clin Alert: 1999, 37:207) End stage renal disease cases were also reported in Belgium after ingestion of diet pills containing the same botanical. The FDA encouraged health care professionals to report adverse

events, which occur during therapy with alternative medicines or botanical products. A complete list of products containing aristolochic acid can be found at http://vm.cfsan.fda.gov/~dms/ds-bot2.html

Letter to health care professionals on FDA concern about botanical products including dietary supplements containing aristolochic acid. (Jun 1) 2000 http://vm.cfsan.fda.gov/~dms/ds-bot2. html

AVERRHOA CARAMBOLA (STAR FRUIT)
Death in Uremic Patients

Over a nine year period, 20 uremic patients (mean age: 53.8 yrs) were hospitalized with acute neurological symptoms after ingesting star fruit or juice. Symptoms included limb numbness (15), persistent hiccups (12), altered consciousness (10), decreased muscle strength (7), dyspnea (5) and skin paresthesias (1). Patients were receiving regular hemodialysis (15), peritoneal dialysis (4) or in chronic renal failure without dialysis (1). Of the eight patients who died after ingestion (mean age: 56.6 yrs), all had eaten one to two fresh fruits with subsequent symptom onset between 2.5 and 14 hours. Symptom onset was shorter in patients who died than in those who had survived (mean: 4.6 vs 8.8 hrs). Hyperkalemia was evident in only four patients. Otherwise, serum calcium and potassium were within normal ranges. Treatment included emergent or routine dialysis in 10 patients each.

The authors cautioned that renal failure patients undergoing dialysis might develop neurological complications that could potentially be fatal after ingesting star fruit. Although star fruit has a high potassium content, hyperkalemia occurred in only four patients.

Chang JM et al (Lai YH, Div Nephrology, Dept Med, Kaoshiung Med Univ, 100 Shih-Chuan 1st Rd, Kaoshiung 807, Taiwan; e-mail:jemich@cc.kmc.edu.tw) Fatal outcome after ingestion of star fruit (averrhoa carambola) in uremic patients. Am J Kidney Diseases 35(2):189–293 (Feb) 2000

CHROMIUM PICOLINATE
Exanthematous Pustulosis (First Report*)

A 32-year-old patient developed a generalized erythematous pustular rash with low-grade fever approximately four days after starting chromium picolinate (1 gram daily) for nutritional supplementation. No other prescription or nonprescription medications were taken. The eruption consisted of several nonfollicular pustules on the trunk and extremities. Laboratory tests did not indicate an infection as evidenced by normal white blood cell counts. Skin punch biopsy revealed that the pustules contained neutrophils and eosinophils without infectious origins. Treatment included an oral prednisone tapering regimen (60 mg daily) over 15 days and oral

dicloxacillin (1 gm daily) for one week. Chromium picolinate was also discontinued at this time. The eruption resolved within one week after treatment. Patch testing with chromium picolinate in various concentrations was negative. Rechallenge was not attempted due to the severity of the initial reaction. Despite negative patch testing, the authors concluded that this patient's cutaneous reaction was temporally related to chromium picolinate administration.

Young PC et al (Dermatol Service, Walter Reed Army Med Center, Washington, District of Columbia) Acute generalized exanthematous pustulosis induced by chromium picolinate. J Am Acad Dermatol 41:820–823 (Nov) 1999

ECBALIUM ELATERIUM
Uvular Angioedema

A 54-year-old woman developed dyspnea and sore throat approximately five hours after aspirating an intranasal alternative medicine (Ecbalium elaterium) for sinusitis. Upon hospitalization she was hypertensive (140/100 mmHg) and tachycardic (100 bpm) with an increased respiratory rate (34/min). In addition, the patient had severe uvular angioedema. Other medications included amoxicillin/clavulanate (1 gram twice daily) and naproxen sodium (550 mg twice daily). Gradual improvement occurred over 1.5 hours after supportive therapy was initiated, including intravenous epinephrine (0.3 mg) and prednisolone (80 mg). Further recovery was uneventful and the patient was discharged.

The authors noted that ecbalium elaterium is more commonly called "squirting cucumber" and often used as a folk medicine for sinusitis. They concluded that this patient's experience probably was a result of a local allergic reaction to a small amount of aspirated product. They also cautioned that patients who develop dyspnea after inhalation of "squirting cucumber" should seek immediate medical attention.

Eray O et al (Dept Emerg Med, Dokuz Eylul Univ, Balcova, 35340 Izmir, Turkey) Severe uvular angioedema caused by intranasal administration of ecbalium elaterium. Vet Human Toxicol 41(6):376–378 (Dec) 1999

HENNA
Acute Hemolysis

An 11-year-old patient was hospitalized for paleness, weakness and red colored urine, which occurred within 24 hours after total body henna application. A physical examination upon admission revealed reddish brown hued psoriatic lesions over the entire body surface area, predominantly on the extensor side of the extremities. Abnormal laboratory values included hemoglobin (4.5 gm/dL), hematocrit (13%), white blood cell count

(6700/mm^3), platelet count (342,000/mm^3), BUN (90 mg/dL), aspartate aminotransferase (420 IU/L), alanine aminotransferase (104 IU/L), indirect bilirubin (5.2 mg/dL), and creatine kinase (254 IU/dL). Treatment with transfusion and supportive care resulted in eventual recovery. The authors concluded that lawsone, a primary ingredient in henna, was substantially absorbed after topical application and was responsible for hemolysis in G6PD deficient red blood cells.

Soker M et al. (Dept Ped, Dicle Univ Faculty Med, Diyarbakir, Turkey; e-mail:sokerm @hotmail.com) Henna induced acute hemolysis in a G6PD deficient patient: A case report. Int Pediatrics 15(2):114–116 (Jul) 2000

HENNA
Cutaneous Reactions

In the past decade, henna induced cutaneous reactions were observed in 14 adult women (ages: 18 to 52 years) seeking medical attention at a Taiwan hospital. Six patients were successfully treated with potent topical corticosteroids and declined further study. Of the remaining eight patients who were patch tested for allergic responses, two exhibited a positive response to plain henna and six had a positive response to common additives in henna products.

The authors concluded that these findings support data that true henna allergy is a rare event. The allergens that are usually responsible for cutaneous reactions after henna application are most likely scented oils and additives, such as p-phenylenediamine.

Lestringant GG et al (Dept Dermatol, Taiwan Univ Hosp, PO Box 15258, Al Ain, United Arab Emirates; e-mail:hhlest@emirates.net.ae) Cutaneous reactions to henna and associated additives. Br J Dermatol 141:573–609 (Sep) 1999 (letter)

HERBAL VITAMINS
Lead Intoxication

A 5-year-old patient with encephalopathy, seizures and developmental delay as a result of neonatal asphyxia was noted to have an elevated lead concentration (86 mcg/dL) during an evaluation for persistent anemia. A repeated medication history revealed that the mother had been administering a Tibetan herbal vitamin three times daily for the last four years. A physical examination after hospitalization revealed a nonverbal child who was alert, but was unable to ambulate. Skeletal and abdominal x-rays did not reveal lead lines or particles, respectively. Chelation therapy with EDTA and BAL decreased the lead levels to 25.6 mcg/dL. Urinary lead excretion was 5578 mcg/24 hour urine. Analysis of the vitamin tablets revealed that the product contained lead, arsenic, cadmium, and mercury.

Lead ingestion over a four-year period was estimated at 63 grams. Repeat analysis of the 24 hour urine sample revealed the additional presence of mercury (28.64 mcg/24 hr urine) but arsenic was undetectable. Serum concentrations of mercury were undetectable and arsenic levels were 0.2 mcg/dL. Over the next four year period six additional chelation treatments were administered with succimer, resulting in the most recent lead level of 24.5 mcg/dL.

The authors concluded that this patient's lead intoxication was due to the ingestion of an herbal medicine as testing at the home site was negative for other lead sources.

Moore C & Adler R (Div Gen Pediatrics, Children's Hosp Los Angeles, Los Angeles, CA 90027) Herbal vitamins: Lead toxicity and developmental delay. Pediatrics 106(3): 600–602 (Sep) 2000

KAMPO (CHINESE HERBAL)
Epithelial Keratopathy (First Report*)

A 30-year-old patient developed bilateral photophobia during chronic therapy with an oral oriental herbal medicine, used to treat constipation, for five years. Composition of the herbal medicine included extracts from the scutellaria root, glycyrrhiza root, patycodon root, gypsum, atractylodes rhizome, rhubarb rhizome, schizopepeta spike, gardenia fruit, peony root, cridium rhizome, Japanese angelica root, mentha herb, saposhnikovia root, ephedra herb, forsythia fruit, ginger rhizome, talc, and anhydrous mirabilitum. A slit lamp examination revealed dust like opacities in the epithelial layers of both corneas and brown colored precipitates. No other concurrent medications were taken at this time. Two years prior to this event, similar ocular symptoms occurred, but reversed after withdrawal of the herbal medicine. At withdrawal of the drug this time, the corneal opacities decreased within three months and reversed completely within one year. No recurrences have been noted within four years of follow-up.

The authors concluded that this is the first case report of oriental herbal medicine induced keratopathy.

Akatsu T et al (Dept Ophthalmol, Juntendo Univ, Sch Med) Oriental herbal medicine induced epithelial keratopathy. Br J Ophthalmol 84:934 (Sep) 2000 (letter)

LAMINARIA TENTS
Bacteremia

A 26-year-old woman developed fever and shaking chills within 24 hours after laminaria tents were placed intravaginally in preparation for a planned abortion. Symptoms reversed with acetaminophen (no dosage provided) and the elective procedure was performed under sterile conditions. The

fever and chills recurred post-procedure requiring hospitalization for suspected infection. Upon admission, the patient had a fever of 104 degrees Fahrenheit and was hypotensive (100/80 mmHg). Although a physical examination was normal, the white blood cell count was 1,400/mL with 79% neutrophils. Urine cultures were negative, but blood cultures revealed K. pneumoniae and group B streptococcus. Ceftriaxone and clindamycin therapy was switched to intravenous ampicillin/sulbactam. Although a superficial venous thrombosis was noted at the catheter placement site, recovery was uneventful and the patient was discharged on oral levofloxacin.

The authors concluded that although the laminaria tents were sterile, their placement inadvertently transferred flora from the vaginal tract into the uterine cavity, thus causing an infection.

Acharya PS & Gluckman SJ (Div of Infectious Dis & Dept Internal Med, Hosp of Univ Pennslyvania, Phildelphia, PA) Bacteremia following placement of intracervical laminaria tents. Clin Infectious Diseases 29:695–696 (Sep) 1999 (letter)

MA HUANG AND CREATINE
Ischemic Stroke (First Report*)

A 33-year-old body builder developed aphasia and right sided face and arm weakness approximately six weeks after starting athletic performance enhancers, Ma Huang and creatine products. He was taking no other medications at the time. Two capsules of the Ma Huang product contained ephedra alkaloids (20 mg), caffeine (200 mg), L-carnitine (100 mg), and chromium (200 mcg). One scoop of the powdered product contained creatine monohydrate (6000 mg), taurine (100 mg), inosine (100 mg), and co-enzyme Q10 (5 mg). Prior to his stroke he ingested 40 to 60 mg ephedra alkaloids and 400 to 600 mg of caffeine daily. A CT scan of the brain revealed an extensive left middle cerebral artery infarct. However, normal results were obtained via cerebral angiography, CSF examination, cardiac examinations, and cervical ultrasound. Creatinine was high but within normal ranges (102 umol/L).

The authors concluded that the combination of high dose ephedra and creatine were most likely responsible for ischemic stroke in this patient. They also suggested that caffeine may have enhanced the cardiovascular effects of ephedrine. According to the authors this is the first case report of cerebral infarct associated with high doses of these products. They also cautioned clinicians to alert the sports community of the potential risks of energy supplements.

Vahedi K et al (Serv Neurol, Hosp Lariboisiere, 2 Rue A Pare, 75010, Paris, France; e-mail:vahedi@ccr.jussieu.fr) Ischaemic stroke in a sportsman who consumed Ma Huang extract and creatine monohydrate for body building. J Neuro Neurosurg Psychiatry 68:112–113 (Jan) 2000

ST. JOHN'S WORT AND INDINAVIR Interaction: Decreased Indinavir Concentrations, FDA Advisory

On February 10th, 2000 the FDA published a public health advisory regarding a recent NIH study which demonstrated a significant drug interaction between St. John's wort (hypericum perforatum) and indinavir. Concurrent administration resulted in decreased indinavir concentrations possibly related to cytochrome P450 isoenzyme induction. The FDA recommended that St. John's wort should not be used concurrently with any of the currently marketed protease inhibitors or nonnucleoside transcriptase inhibitor antiretrovirals as suboptimal plasma concentrations may reduce virologic response and promote resistance. The FDA is working with manufacturers of the antiretrovirals to revise product labeling to include these new recommendations.

FDA Public Health Advisory. Risk of drug interactions with St. John's wort and indinavir and other drugs. (Feb 10) 2000. http://www.fda. gov/cder/drug/advisory/stjwort.htm

ST. JOHN'S WORT AND INDINAVIR Interaction: Decreased Indinavir Concentrations

In an open label study, eight healthy male volunteers (age range: 29 to 50 yrs) received indinavir alone (800 mg) every eight hours for four doses. After monotherapy plasma concentrations were obtained, St. John's wort (300 mg three times daily) was administered with meals for 14 days. Four doses of indinavir (800 mg every eight hours on an empty stomach) therapy were administered during the last two days of St. John's wort therapy. Although time to maximum indinavir concentrations were unchanged with or without St. John's wort administration (1.1 hrs), the mean AUC at eight hours was decreased by 57% when administered with the herbal product (30.8 mcg.hr/mL vs 12.3 mcg.hr/mL). Concurrent administration also resulted in reduced indinavir concentrations at eight hours by a range of 49% to 99%. Mean maximum concentrations were also reduced (12.3 mcg/mL to 8.9 mcg/mL).

The authors concluded that indinavir plasma concentrations are significantly reduced by concurrent St. John's wort therapy most likely via CYP3A4 isoenzyme induction. Because other antiretrovirals are also metabolized by the same isoenzyme system, they recommended that these combinations be avoided until further information is available.

Piscitelli SC et al (Dept Pharmacy, Warren G Magnuson Clin Center & Lab of Immunoregulation, NIH, Bethesda, MD 20892; e-mail:spisc@nih.gov) Indinavir concentrations and St. John's wort. Lancet 355:547 (Feb 12) 2000 (letter)

ST. JOHN'S WORT AND CYCLOSPORINE
Interaction: Heart Transplant Rejection

Two cases of failed heart transplants are presented in patients who had reduced cyclosporine levels while taking the alternative medicine, St. John's Wort.

Patient #1: A 61-year-old patient previously stabilized after a heart transplant 11 months earlier was hospitalized with fatigue three weeks after starting St. John's wort (300 mg three times daily) for depression. Other chronic medications included cyclosporine (125 mg twice daily), azathioprine (100 mg daily), and corticosteroids (7.5 mg daily). Prior to St. John's wort therapy cyclosporine levels had been consistently within therapeutic range but upon admission they were decreased (95 mcg/L). Endomyocardial biopsy revealed acute cellular transplant rejection. Despite stopping St. John's wort therapy, increasing cyclosporine dosages (150 mg twice daily) and intravenous steroid dosing (1 gram/day), rejection status was unchanged. However, permanent rejection was avoided by treatment substitution with mycophenolate mofetil (1 gram twice daily) and short term intravenous anti-thymocyte globulin (1250 mg daily for 10 days). Cyclosporine levels returned to baseline levels after St. John's wort therapy was stopped.

Patient #2: A 63-year-old patient previously stabilized after a heart transplant 20 months earlier was hospitalized for elective endomyocardial biopsy three weeks after starting St. John's wort (300 mg three times daily) for anxiety and depression. Other chronic medications included cyclosporine (125 mg twice daily), azathioprine (125 mg daily), and corticosteroids (7.5 mg daily). Prior to St. John's wort therapy cyclosporine levels had been consistently within therapeutic range but upon admission they were decreased (87 mcg/L). Endomyocardial biopsy revealed acute cellular transplant rejection. Cyclosporine levels returned to therapeutic range after St. John's wort therapy was stopped and no further rejection episodes occurred during follow-up.

The authors concluded that in both patients, St. John's wort therapy was associated with a reduction in cyclosporine plasma concentrations and subsequent transplant rejection episodes. After stopping St. John's wort treatment, cyclosporine concentrations returned to therapeutic range, and rejection episodes were reversed. The authors suggested that cyclosporine levels were decreased via cytochrome P450 induction via St. John's wort. As this is an interaction with serious consequences clinicians are encouraged to avoid this combination.

Ruschitzka F et al (Division of Cardiology, Dept Internal Med, Univ Hosp, C4-8091 Zurich, Switzerland) Acute heart transplant rejection due to Saint John's wort. Lancet 355:548 (Feb 12) 2000 (letter)

ST. JOHN'S WORT AND CYCLOSPORINE
Drug Interaction: Decreased Cyclosporine Concentrations, Transplant Rejection

A 29-year-old renal/pancreatic transplant patient, previously stabilized on cyclosporine with whole blood concentrations ranging from 250 to 300 ng/mL, developed decreased levels after self medicating with St. John's wort for mood elevation. Maintenance cyclosporine therapy was 100 mg twice daily. Other medications, which were unchanged during this time, included prednisone (10 mg daily) for immunosuppression and oral clonidine (0.2 mg twice daily) for hypertension. The patient denied other new prescription drug use but did not identify herbal product use. Within 30 days after starting St. John's wort cyclosporine trough concentrations decreased to 155 ng/mL and continued to drop when repeat measurements were performed three weeks later (97 ng/mL). Serum amylase increases (314 U/L) with abdominal pain suggested acute transplant rejection, which was verified by a renal biopsy. Treatment included antithymocyte globulin (20 mg/kg/day for two weeks) and cyclosporine dosage increases (175 mg twice daily). St. John's wort use, discovered at this time, was discontinued. After two weeks at increased dosages trough concentrations increased to 510 ng/mL and eventually stabilized between 200 to 350 ng/mL at previous doses. Serum amylase concentrations did not return to baseline and the patient experienced chronic organ rejection, requiring dialysis.

The authors suggested that acute transplantation rejection occurred in this patient as a result of subtherapeutic cyclosporine levels via CYP3A4 isoenzyme induction and/or P-glycoprotein pump activity, both induced by St. John's wort. They recommended that patient medication interviews should include specific inquiries about alternative medicine and herbal product use.

Barone GW et al (Dept Surgery, Slot 520-4, Univ Arkansas Med Sciences, 4301 W. Markham St, Little Rock, AR 72205; e-mail:baronegary@exchange.uams.edu) Drug interaction between St. John's wort and cyclosporine. Ann Pharmacother 34:1013–1016 (Sep) 2000

ST JOHN'S WORT AND DIGOXIN
Interaction: Decreased Digoxin Levels

In a single blinded, placebo controlled parallel study, 25 healthy volunteers (mean age: 26 yrs) received an oral loading dose of digoxin (0.25 mg twice daily) for two days followed by once daily dosing for an additional 13 days. Steady state serum concentrations were collected on day five and patients were then allocated to receive either placebo or St. John's wort three times daily for 10 days. Each enteric-coated active treatment tablet

contained hypericin (92 mcg), pseudo hypericin (262 mcg) and hyperforin (18.37 mcg). After combination therapy for 10 days, mean half-life (42.8 vs 39.5 hrs) and median time to maximum concentrations (1 hr) were not different when compared to digoxin therapy alone. However, AUC values were decreased by 25 (17.2 vs 12.9 mcg/h/L), C_{max} was decreased by 26 (1.9 vs 1.4 mcg/L) and trough concentrations were decreased by 19 (0.58 vs 0.47 mcg/L). In contrast, the AUC values of hypericin and pseudo hypericin were unchanged when administered alone or with digoxin.

The authors concluded that St. John's wort might reduce the efficacy of digoxin via lowered AUC levels and trough concentrations. They theorized that digoxin kinetics are altered by hypericin extract induced P-glycoprotein activity.

Johne A et al (I Roots, Instit of Clin Pharmacol, Charite, Humboldt Univ of Berlin, Schumannstrasse 20/21, D-10098 Berlin, Germany) Pharmacokinetic in-teraction of digoxin with an herbal extract from St. John's wort (hypericum perforatum). Clin Pharmacol & Ther 66:338–345 (Oct) 1999

Drug	Interacting Drug	ADR	Page Number
General			
Antibiotics		Rash in pediatric patients	17
Aminoglycoside			
Gentamicin		Neurotoxicity, ototoxicity (+)	18
Antifungals			
Fluconazole		QT prolongation	19
Fluconazole		Fixed drug eruption	18
Itraconazole	Clarithromycin	Clarithromycin concentrations increased	35
Ketoconazole	Amprenavir	Increased concentrations	23
Miconazole (vaginal)	Warfarin	INR increased*	19
Antivirals			
Antiretroviral		Lipodystrophy, curly hair	20
Antiretroviral	Methylprednisolone	Immunosuppression (+)	21
Abacavir		Hypersensitivity reactions^	21
Amantadine		CNS ADRs	22
Amprenavir		Propylene glycol toxicity (potential)	23
Amprenavir	Ketoconazole	Increased concentrations	23
Indinavir	St. John's wort	Indinavir concentrations decreased	25
Indinavir		Crystalluria	24
Protease inhibitors		Hyperglycemia	27
Protease inhibitors		Hyperprolactinemia	26
Ritonavir	Meperidine	Meperidine concentrations increased	28
Ritonavir	Fentanyl	Fentanyl clearance decreased	27
Ritonavir		Hepatoxicity in hepatitis C or B	29

Drug	Interacting Drug	ADR	Page Number
Ritonavir	Methadone	Methadone effect decreased	28
Saquinavir		Hypoglycemia	29
Valacyclovir		Thrombotic thrombocytopenic purpura	30
Zanamivir		Respiratory distress	31
Cephalosporins			
Cefazolin		Fever	31
Cefdinir		Red stools	32
Cefotetan		Hemolysis	32
Ceftazidime	Vancomycin	Ocular precipitation (intravitreal)	33
Cefuroxime		Lymphomatoid hypersensitivity	34
Macrolides			
Clarithromycin	Omeprazole	Omeprazole concentrations increased	34
Clarithromycin	Itraconazole	Clarithromycin concentrations increased	35
Erythomycin		Pyloric stenosis (infantile)	36
Miscellaneous			
Bacitracin		Anaphylaxis	37
Quinupristin Dalfopristin		Hyponatremia	37
Vancomycin	Ceftazidime	Ocular precipitation (intravitreal)	33
Quinolones			
Alatrovafloxacin		Thrombocytopenia*	38
Ciprofloxacin	Warfarin	Hypothrombinemia, bleeding	41
Ciprofloxacin		Allergy	39
Ciprofloxacin		Tendon rupture	40
Ciprofloxacin		Bullous pemphigoid*	39
Ciprofloxacin	Glyburide	Hypoglycemia (resistant)	40
Levofloxacin		QT prolongation*	42
Trovafloxacin		Neurotoxicity	42
Trovafloxacin		Eosinophilic hepatitis	43
Trovafloxacin		Demylinating polyneuropathy*	43
Sulfonamides			
Trimethoprim Sulfamethoxazole		Stevens Johnson syndrome^ (+)	44
Trimethoprim Sulfamethoxazole		Hypokalemia in renal transplant patients	44

Drug	Interacting Drug	ADR	Page Number
Tetracyclines			
Minocycline		Chest pain	46
Minocycline		Hyperpigmentation (tongue)	46, 47
Tetracycline		Pseudotumor cerebri (+)	47

* = first report
^ = death
(+) = legal action

Antiinfectives

GENERAL
ANTIBIOTICS
Rash in Pediatric Patients

The frequency and severity of antibiotic rashes was investigated in a retrospective review of 5923 medical records of pediatric patients cared for in a community practice setting over a five month period. Approximately one-third (32%) of the patients did not receive antibiotics during this time period. However, antibiotic related reactions were documented in 8.6% (509) of the patients with 37 of these reactions classified as mild (e.g., gastrointestinal upset). The remaining 472 reactions were rash related. Of these reactions, there were no significant differences between the total number of boys and girls (53.8% vs 47.2%) who developed rashes, but there was a higher incidence observed in boys younger than three years of age, and in girls older than nine years. The highest incidence of reported rashes occurred in children who received cefaclor (12.3%), penicillins (7.4%), sulfonamides (8.5%), and other cephalosporins (2.6%). Urticarial type rashes (e.g., welts, hives, etc) were the most common, accounting for 45.9% (208) of the describable rashes. Thirty-one cases of serum sickness-like reactions were also observed in this patient population and were most frequently associated with cefaclor (1.9%), but also occurred in patients receiving penicillins (0.35%) and sulfonamides (0.36%). During the study period, no cases of severe rash related reactions (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis) occurred. In addition, there were no deaths or hospitalizations related to antibiotic induced rashes.

The authors concluded that antibiotic related rashes occurred in approximately 7% of the pediatric patients treated in a private pediatric practice. A significantly higher incidence of rash was associated with the use