

## CLINICAL CAPSULES

### Dating Violence Link to STDs

Approximately 1 in 3 girls in grades 9-12 who reported sexual activity also reported sexual or physical violence from their dating partners in a study of 1,641 girls, said Michele R. Decker of Harvard School of Public Health, Boston, and her colleagues (Pediatrics 2005;116:e272-6). A similar percentage reported being tested for an STD or HIV. Overall, girls who reported physical and sexual violence or physical violence alone were significantly more likely to be tested for an STD (odds ratio 2.4 or 1.6, respectively) than were girls who did not re-

port any violence. In addition, the odds of a positive diagnosis were significantly higher for girls reporting physical and sexual violence or physical violence alone (odds ratio 2.6 or 2.2, respectively) compared with girls who did not report any violence. The study was limited by several factors, including possible underreporting of testing behaviors, since many adolescents may not know or report their positive results.

### Predicting STI Risk in Teens

Teenagers who thought their parents would strongly disapprove of their having sex were

less likely to have developed sexually transmitted infections 6 years later, said Carol A. Ford, M.D., of the University of North Carolina at Chapel Hill, and her associates. The study included data on 11,594 adolescents from the National Longitudinal Study of Adolescent Health, a prospective cohort study initiated in 1995 when the participants were in grades 7-12 (Arch. Pediatr. Adolesc. Med. 2005;159:657-64). Approximately half (52.8%) of the subjects were female, and the mean age at follow-up was 22 years. Overall, 5.5% of adolescents who thought that their parents strongly disapproved of sex during adolescence tested positive for *Chlamydia trachomatis*, *Neisseria gonorrhoeae*,

or *Trichomonas vaginalis*, compared with 8.0% and 8.9%, respectively, of those who thought that their parents' disapproval was moderate or low. In a bivariate analysis, factors associated with an increased likelihood of sexually transmitted infections included low grade point average, a perception of looking younger than one's peers, and a higher average daily school attendance rate. However, in a stratified, multivariate analysis, family, school, and individual factors associated with prolonged virginity—such as a high grade point average or attending a parochial school—were not predictive of STI status among boys at follow-up.

### Kingella kingae Rising?

In the first reported outbreak of invasive *Kingella kingae* disease, it affected several toddlers at a day-care center in Minnesota in October 2003, said Karen M. Kiang, M.D., of the Minnesota Department of Health, Minneapolis, and the Centers for Disease Control and Prevention, Atlanta, and her colleagues (Pediatrics 2005;116:206-13). Three cases of osteomyelitis/septic arthritis due to *K. kingae* occurred: in a 21-month-old boy, a 20-month-old girl, and a 17-month-old boy. The first two cases were confirmed by culture. All three children presented with limping and fevers higher than 100° F, and all three had symptoms of upper respiratory infections prior to or concurrent with the development of their skeletal infections. They were treated with a variety of medications, including intravenous cefazolin and oral amoxicillin. The researchers collected oropharyngeal cultures from 115 of 122 children who attended the day-care center, and 28 of 29 staff members. Overall, 15 (13%) of the children showed *K. kingae* colonization, but none of the staff members or the 14 children older than 16 months showed colonization. The three infected children had spent time in the same toddler classroom, and the staff and other children in this room received a 2-day prophylactic course of rifampin. By comparison, at a control day center, 45 (38%) of 118 children of similar ages were cultured, and 7 (16%) of them showed *K. kingae* colonization.

### Hepatitis Rates Decline

The incidence of hepatitis dropped from 35% to 19% among children aged 2-18 years between a baseline period of 1990-1997 and 2003, said Annemarie Wasley, Sc.D., of the Centers for Disease Control and Prevention, Atlanta, and her colleagues. The greatest decline occurred among children aged 2-9 years (89%), followed by declines in children aged 10-18 years (83.7%) and children younger than 2 years (79.5%). Overall, 9 of the 10 states with the greatest declines in infection rates were states that had implemented hepatitis vaccination, which became widely available in 1995 (JAMA 2005;294:194-201). In an accompanying editorial, Pierre Van Damme, M.D., and Koen Van Herck, M.D., of the University of Antwerp, Belgium, said that given the proven existence of antibodies more than 10 years after vaccination, and the odds that antibodies will persist for more than 25 years after vaccination, boosters should be unnecessary for healthy people, and childhood vaccination can be reasonable for countries where hepatitis rates are declining (JAMA 2005;294:246-8).

—Heidi Splette

### Treatment of osteoporosis Postmenopausal women

In two identically designed, three-year, placebo-controlled, double-blind, multicenter studies (United States and Multinational; n=994), discontinuation of therapy due to any clinical adverse experience occurred in 4.1% of 196 patients treated with FOSAMAX® (alendronate sodium) 10 mg/day and 6.0% of 397 patients treated with placebo. In the Fracture Intervention Trial (n=6459), discontinuation of therapy due to any clinical adverse experience occurred in 9.1% of 3236 patients treated with FOSAMAX 5 mg/day for 2 years and 10 mg/day for either one or two additional years and 10.1% of 3223 patients treated with placebo. Discontinuations due to upper gastrointestinal adverse experiences were: FOSAMAX, 3.2%; placebo, 2.7%. In these study populations, 49-54% had a history of gastrointestinal disorders at baseline and 54-89% used nonsteroidal anti-inflammatory drugs or aspirin at some time during the studies. Adverse experiences from these studies considered by the investigators as possibly, probably, or definitely drug related in B1% of patients treated with either FOSAMAX or placebo are presented in the following table.

	Osteoporosis Treatment Studies in Postmenopausal Women Adverse Experiences Considered Possibly, Probably, or Definitely Drug Related by the Investigators and Reported in ≥1% of Patients			
	United States/Multinational Studies		Fracture Intervention Trial	
	FOSAMAX* % (n=196)	Placebo % (n=397)	FOSAMAX** % (n=3236)	Placebo % (n=3223)
<b>Gastrointestinal</b>				
abdominal pain	6.6	4.8	1.5	1.5
nausea	3.6	4.0	1.1	1.5
dyspepsia	3.6	3.5	1.1	1.2
constipation	3.1	1.8	0.0	0.2
diarrhea	3.1	1.8	0.6	0.3
flatulence	2.6	0.5	0.2	0.3
acid regurgitation	2.0	4.3	1.1	0.9
esophageal ulcer	1.5	0.0	0.1	0.1
vomiting	1.0	1.5	0.2	0.3
dysphagia	1.0	0.0	0.1	0.1
abdominal distention	1.0	0.8	0.0	0.0
gastritis	0.5	1.3	0.6	0.7
<b>Musculoskeletal</b>				
musculoskeletal (bone, muscle or joint) pain	4.1	2.5	0.4	0.3
muscle cramp	0.0	1.0	0.2	0.1
<b>Nervous System/Psychiatric</b>				
headache	2.6	1.5	0.2	0.2
dizziness	0.0	1.0	0.0	0.1
<b>Special Senses</b>				
taste perversion	0.5	1.0	0.1	0.0

\*10 mg/day for three years

\*\*5 mg/day for 2 years and 10 mg/day for either 1 or 2 additional years

Rarely, rash and erythema have occurred.

One patient treated with FOSAMAX (10 mg/day), who had a history of peptic ulcer disease and gastrectomy and who was taking concomitant aspirin developed an anastomotic ulcer with mild hemorrhage, which was considered drug related. Aspirin and FOSAMAX were discontinued and the patient recovered.

The adverse experience profile was similar for the 401 patients treated with either 5 or 20 mg doses of FOSAMAX in the United States and Multinational studies. The adverse experience profile for the 296 patients who received continued treatment with either 5 or 10 mg doses of FOSAMAX in the two-year extension of these studies (treatment years 4 and 5) was similar to that observed during the three-year placebo-controlled period. During the extension period, of the 151 patients treated with FOSAMAX 10 mg/day, the proportion of patients who discontinued therapy due to any clinical adverse experience was similar to that during the first three years of the study.

In a one-year, double-blind, multicenter study, the overall safety and tolerability profiles of once weekly FOSAMAX 70 mg and FOSAMAX 10 mg daily were similar. The adverse experiences considered by the investigators as possibly, probably, or definitely drug related in B1% of patients in either treatment group are presented in the following table.

	Osteoporosis Treatment Studies in Postmenopausal Women Adverse Experiences Considered Possibly, Probably, or Definitely Drug Related by the Investigators and Reported in ≥1% of Patients			
	Once Weekly FOSAMAX 70 mg		FOSAMAX 10 mg/day	
	% (n=519)	% (n=370)	% (n=519)	% (n=370)
<b>Gastrointestinal</b>				
abdominal pain	3.7	3.0	3.7	3.0
dyspepsia	2.7	2.2	2.7	2.2
acid regurgitation	1.9	2.4	1.9	2.4
nausea	1.9	2.4	1.9	2.4
abdominal distention	1.0	1.4	1.0	1.4
constipation	0.8	1.6	0.8	1.6
flatulence	0.4	1.6	0.4	1.6
gastritis	0.2	1.1	0.2	1.1
gastric ulcer	0.0	1.1	0.0	1.1
<b>Musculoskeletal</b>				
musculoskeletal (bone, muscle, joint) pain	2.9	3.2	2.9	3.2
muscle cramp	0.2	1.1	0.2	1.1

### Men

In two placebo-controlled, double-blind, multicenter studies in men (a two-year study of FOSAMAX 10 mg/day and a one-year study of once weekly FOSAMAX 70 mg) the rates of discontinuation of therapy due to any clinical adverse experience were 2.7% for FOSAMAX 10 mg/day vs. 10.5% for placebo, and 6.4% for once weekly FOSAMAX 70 mg vs. 8.6% for placebo. The adverse experiences considered by the investigators as possibly, probably, or definitely drug related in B2% of patients treated with either FOSAMAX or placebo are presented in the following table.

	Osteoporosis Studies in Men Adverse Experiences Considered Possibly, Probably, or Definitely Drug Related by the Investigators and Reported in ≥2% of Patients			
	Two-year Study		One-year Study	
	FOSAMAX 10 mg/day % (n=146)	Placebo % (n=95)	Once Weekly FOSAMAX 70 mg % (n=109)	Placebo % (n=58)
<b>Gastrointestinal</b>				
acid regurgitation	4.1	3.2	0.0	0.0
flatulence	4.1	1.1	0.0	0.0
gastroesophageal reflux disease	0.7	3.2	2.8	0.0
<b>Musculoskeletal</b>				
dyspepsia	3.4	0.0	2.8	1.7
diarrhea	1.4	1.1	2.8	0.0
abdominal pain	2.1	1.1	0.9	3.4
nausea	2.1	0.0	0.0	0.0

### Concomitant use with estrogen/hormone replacement therapy

In two studies (of one and two years' duration) of postmenopausal osteoporotic women (total n=853), the safety and tolerability profile of combined treatment with FOSAMAX 10 mg once daily and estrogen ± progestin (n=354) was consistent with those of the individual treatments.

### Other studies with FOSAMAX® (alendronate sodium)

#### Prevention of osteoporosis in postmenopausal women

The safety of FOSAMAX 5 mg/day in postmenopausal women 40-60 years of age has been evaluated in three double-blind, placebo-controlled studies involving over 1,400 patients randomized to receive FOSAMAX for either two or three years. In these studies the overall safety profiles of FOSAMAX 5 mg/day and placebo were similar. Discontinuation of therapy due to any clinical adverse experience occurred in 7.5% of 642 patients treated with FOSAMAX 5 mg/day and 5.7% of 648 patients treated with placebo.

In a one-year, double-blind, multicenter study, the overall safety and tolerability profiles of once weekly FOSAMAX 35 mg and FOSAMAX 5 mg daily were similar.

The adverse experiences from these studies considered by the investigators as possibly, probably, or definitely drug related in B1% of patients treated with either once weekly FOSAMAX 35 mg, FOSAMAX 5 mg/day or placebo are presented in the following table.

	Osteoporosis Prevention Studies in Postmenopausal Women Adverse Experiences Considered Possibly, Probably, or Definitely Drug Related by the Investigators and Reported in ≥1% of Patients			
	Two/Three-Year Studies		One-Year Study	
	FOSAMAX 5 mg/day % (n=642)	Placebo % (n=648)	FOSAMAX 5 mg/day % (n=361)	Once Weekly FOSAMAX 35 mg % (n=362)
<b>Gastrointestinal</b>				
dyspepsia	1.9	1.4	2.2	1.7
abdominal pain	1.7	3.4	4.2	2.2
acid regurgitation	1.4	2.5	4.2	4.7
nausea	1.4	1.4	2.5	1.4
diarrhea	1.1	1.7	1.1	0.6
constipation	0.9	0.5	1.7	0.3
abdominal distention	0.2	0.3	1.4	1.1
<b>Musculoskeletal</b>				
musculoskeletal (bone, muscle or joint) pain	0.8	0.9	1.9	2.2

#### Treatment of glucocorticoid-induced osteoporosis

In two, one-year, placebo-controlled, double-blind, multicenter studies in patients receiving glucocorticoid treatment, the overall safety and tolerability profiles of FOSAMAX 5 and 10 mg/day were generally similar to that of placebo. The adverse experiences considered by the investigators as possibly, probably, or definitely drug related in B1% of patients treated with either FOSAMAX 5 or 10 mg/day or placebo are presented in the following table.

	One-Year Studies in Glucocorticoid-Treated Patients Adverse Experiences Considered Possibly, Probably, or Definitely Drug Related by the Investigators and Reported in ≥1% of Patients		
	FOSAMAX 10 mg/day % (n=157)	FOSAMAX 5 mg/day % (n=161)	Placebo % (n=159)
	<b>Gastrointestinal</b>		
abdominal pain	3.2	1.9	0.0
acid regurgitation	2.5	1.9	1.3
constipation	1.3	0.6	0.0
melaena	1.3	0.0	0.0
nausea	0.6	1.2	0.6
diarrhea	0.0	0.0	1.3
<b>Nervous System/Psychiatric</b>			
headache	0.6	0.0	1.3

The overall safety and tolerability profile in the glucocorticoid-induced osteoporosis population that continued therapy for the second year of the studies (FOSAMAX: n=147) was consistent with that observed in the first year.

#### Paget's disease of bone

In clinical studies (osteoporosis and Paget's disease), adverse experiences reported in 175 patients taking FOSAMAX 40 mg/day for 3-12 months were similar to those in postmenopausal women treated with FOSAMAX 10 mg/day. However, there was an apparent increased incidence of upper gastrointestinal adverse experiences in patients taking FOSAMAX 40 mg/day (17.7% FOSAMAX vs. 10.2% placebo). One case of esophagitis and two cases of gastritis resulted in discontinuation of treatment.

Additionally, musculoskeletal (bone, muscle or joint) pain, which has been described in patients with Paget's disease treated with other bisphosphonates, was considered by the investigators as possibly, probably, or definitely drug related in approximately 6% of patients treated with FOSAMAX 40 mg/day versus approximately 1% of patients treated with placebo, but rarely resulted in discontinuation of therapy. Discontinuation of therapy due to any clinical adverse experience occurred in 6.4% of patients with Paget's disease treated with FOSAMAX 40 mg/day and 2.4% of patients treated with placebo.

#### Laboratory Test Findings

In double-blind, multicenter, controlled studies, asymptomatic, mild, and transient decreases in serum calcium and phosphate were observed in approximately 18% and 10%, respectively, of patients taking FOSAMAX versus approximately 12% and 3% of those taking placebo. However, the incidences of decreases in serum calcium to <8.0 mg/dL (2.0 mM) and serum phosphate to <2.0 mg/dL (0.65 mM) were similar in both treatment groups.

#### FOSAMAX PLUS D™ (alendronate sodium/cholecalciferol)

In a fifteen week double-blind, multinational study in osteoporotic postmenopausal women (n=682) and men (n=35), the safety profile of FOSAMAX PLUS D was similar to that of FOSAMAX once weekly 70 mg.

#### Post-Marketing Experience

The following adverse reactions have been reported in post-marketing use with alendronate:

**Body as a Whole:** hypersensitivity reactions including urticaria and rarely angioedema. Transient symptoms of myalgia, malaise and rarely, fever have been reported with alendronate, typically in association with initiation of treatment. Rarely, symptomatic hypocalcemia has occurred, generally in association with predisposing conditions.

**Gastrointestinal:** esophagitis, esophageal erosions, esophageal ulcers, rarely esophageal stricture or perforation, and oropharyngeal ulceration. Gastric or duodenal ulcers, some severe and with complications have also been reported (see WARNINGS, PRECAUTIONS, Information for Patients, and DOSAGE AND ADMINISTRATION).

**Localized osteonecrosis of the jaw,** generally associated with tooth extraction and/or local infection, often with delayed healing, has been reported rarely (see PRECAUTIONS, Dental).

**Musculoskeletal:** bone, joint, and/or muscle pain, occasionally severe, and rarely incapacitating (see PRECAUTIONS, Musculoskeletal Pain).

**Skin:** rash (occasionally with photosensitivity), pruritus, rarely severe skin reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis.

**Special Senses:** rarely uveitis, scleritis or episcleritis.

#### For more detailed information, please read the Prescribing Information.

FOSAMAX PLUS D is a trademark of Merck & Co., Inc.

FOSAMAX is a registered trademark of Merck & Co., Inc.



© 2005 Merck & Co., Inc., Whitehouse Station, NJ 08889, USA. All rights reserved.  
20504405(1)(601)-FOS