A summary of general medicine news that affects your patients, your practice, and you.

Contaminated Heparin Seized by the FDA

The US Food and Drug Administration (FDA) recently seized 11 lots of the blood-thinning drug heparin from Celsus Laboratories (Cincinnati, Ohio), according to a news release. The FDA's action followed Celsus' refusal to cooperate with the agency's two previous requests to recall contaminated lots of the drug. Celsus distributes heparin to drug and medical-device manufacturers in the United States and internationally.

In January, the FDA recalled heparin after the agency found that large amounts of Chinese heparin imported into the United Sates were contaminated with oversulfated chondroitin. Nearly 250 deaths and hundreds of severe allergic reactions were connected with the tainted batches of heparin, the news release reported.

Following the FDA's recall in January, Celsus claimed informed its customers about the contaminated heparin via a letter, but never recalled the product. The FDA discovered two of Celsus' heparin products were contaminated in April. The FDA sent a follow-up letter to the company asking for a second recall in May.

The FDA advised manufacturers who might have bought heparin from the company to contact the agency to make sure they do not have contaminated heparin in their possession. In addition, the agency has also notified Japan, Canada, Australia, the European Union and other countries to be on the watch for shipments of contaminated heparin from Celsus.

Waist Size May Predict Premature Death

Individuals with large waists (≥40.4 inches for men, ≥ 35 inches for women) are twice as likely to die prematurely than those with smaller waists, according to a study in the *New England Journal of Medicine*.

Lead author Tobias Pischon, MD, of the German Institute of Human Nutrition, and colleagues examined the association of body-mass index (BMI), waist circumference, and waist-to-hip ratio with the risk of death among 359,387 participants from nine countries in the European Prospective Investigation into Cancer and Nutrition (EPIC). Patients ranged in age from 25 to 70.

During a mean follow-up of 9.7 years,14,723 participants died. Of these participants, 4,232 of people with the largest waist died of various causes, including heart disease and cancer, compared with 2,155 deaths of smallest-waisted people. The lowest risks of death related to BMI were observed at a BMI of 25.3 inches for men and 24.3 inches for women. After adjustment for BMI, waist circumference and waist-to-hip ratio were strongly associated with the risk of death. BMI remained significantly associated with the risk of death in models that included waist circumference or waist-to-hip ratio (P<.001).

Intravenous Therapy for Multiple Sclerosis Reduces Disability, Reverses Brain Damage

A recent phase 2 study suggested that alemtuzumab (Campath; Genzyme, Cambridge, MA) was more effective than interferon beta-1a (Rebif; EMD Serono, Inc., Rockland, MA; Pfizer, Inc, New York, NY) for the treatment of early, relapsing-remitting multiple sclerosis, according to a report in the *New England Journal of Medicine*.

Patients (n=334) were randomized to receive either a 44 µm-dose of subcutaneous interferon beta-1a three times weekly or annual intravenous cycles of 12 mg or 24 mg alemtuzumab per day for 36 months. All patients were previously untreated for early, relapsing-remitting multiple sclerosis, had 3 or less on the 10-point Expanded Disability Status Scale, and had multiple sclerosis for 3 years or less.

Alasdair J. Coles, PhD, at Addenbrooke's Hospital, United Kingdom, and colleagues with the CAMMS223 Trial Investigators found that alemtuzumab significantly reduced the rate of sustained accumulation of disability (P<.001) and the rate of relapse per year (P<.001) compared with interferon beta-1a. On this scale, mean

disability improved by 0.39 points in the alemtuzumab group and deteriorated by 0.38 points in the interferon beta-1a group (*P*<.001). The lesion burden was reduced for patients treated with alemtuzumab compared with patients treated with interferon beta-1a group (*P*=.005). Also, from month 12 to month 36, researchers found that brain volume increased in the alemtuzumab group but decreased in the interferon beta-1a group (*P*=.02).

A higher percentage of patients receiving alemtuzumab experienced adverse events than those taking interferon beta-1a. Adverse events in the alemtuzumab group, as compared with the interferon beta-1a group, included autoimmunity (thyroid disorders [23% vs 3%], immune thrombocytopenic purpura [3% vs 1%]), and infections (66% vs 47%). According to investigators, no significant differences in outcomes between the 12-mg dose and the 24-mg dose of alemtuzumab were observed.

Some COPD Drugs Increase Patients' Risk of Major Adverse Cardiovascular Event

A recent study found that patients treated with inhaled anticholinergics (Atrovent, Boehringer Ingelheim Gmbh; Spiriva, Boehringer Ingelheim Gmbh and Pfizer, Inc.) for chronic obstructive pulmonary disease (COPD) are at a significantly increased risk of cardiovascular death, myocardial infarction (MI), or stroke.

The study, published in the *Journal of the American Medical Association* and conducted by Sonal Singh, MD, MPH, at Wake Forest University School of Medicine, North Carolina, and colleagues, included 14,783 patients in 17 trials randomized to receive inhaled anticholinergics (n=7,472) or control therapy (n=7,311). Follow-up ranged from 6 weeks to 5 years.

Researchers reported that cardiovascular death, MI, or stroke occurred in 135 of 7,472 patients (1.8%) receiving inhaled anticholinergics and 86 of 7,311 patients (1.2%) receiving control therapy (*P*<.001). Inhaled anticholinergics significantly increased the risk of MI (*P*=.03) and cardiovascular death (*P*=.008) without a statistically significant increase in the risk of stroke (*P*=.20). Additionally, all-cause mortality was reported in 149 of the patients treated with inhaled anticholinergics (2.0%) and 115 of the control patients (1.6%; *P*=.06).

Based on sensitivity analysis, Dr. Singh and colleagues predicted that 2.9% of patients treated with anticholinergics compared with 1.8% of the control patients were at a significantly increased risk of cardiovascular death, MI, or stroke (*P*<.001).

Correlation Found Between Gene Mutations, Lung Cancer

Researchers with the Tumor Sequencing Project (TSP) identified 26 genes that are frequently mutated in the most common form of lung cancer, lung adenocarcinoma, according to a study in *Nature*. This breakthrough could lead to new lung cancer treatments tailored to individual patients, TSP members suggested.

The TSP collected samples of lung tissue tumors from 188 patients and examined 623 genes to determine those that mutated most often. DNA sequencing of the genes revealed more than 1,000 somatic mutations across the samples with 26 genes mutating at significantly high frequencies. Researchers believe that the high frequency of mutation suggests that these genes are involved in carcinogenesis.

The genes were not mutated from birth in individuals but were genetic mistakes that accumulated in lung tissue throughout individuals' lifetimes. Smokers' tumors, for example, each had an average of about 49 gene mutations, compared with an average of five in the tumors of individuals who never smoked, the researchers reported.

In a related study published in *Cancer Research*, researchers found that nicotine, whether absorbed by smoking cigarettes or inhaling second-hand smoke, may promote tumor growth in breast cancer patients. Both breast epithelial cells and cancerous cells have nicotine receptors with the potential to increase cell growth and migration in the presence of nicotine, the study reported.

Children Need Twice As Much Vitamin D As Previously Recommended

The American Academy of Pediatrics recently recommended that all infants, children, and adolescents take a minimum of 400 IU of vitamin D per day beginning soon after birth, in a report in *Pediatrics*. This recommendation replaces the previous recommendation of a minimum daily intake of 200 IU/day beginning in the first 2 months after birth and continuing through adolescence. These revised guidelines for vitamin D intake are based on evidence from new clinical trials, the historical precedence of safely giving 400 IU of vitamin D per day to children and adolescents, and growing concern in the medical community about the possible health consequences of limited natural dietary sources of vitamin D and adequate sunshine exposure for the cutaneous synthesis of vitamin D. Lack of vitamin D is associated with rickets in infants, and new evidence

suggests a potential role for vitamin D in maintaining innate immunity and preventing diseases such as diabetes and cancer, the study stated.

Nasal Insulin Does Not Protect At-Risk Children From Diabetes

Nasally administered insulin does not prevent or delay type 1 diabetes in children susceptible to the illness, according to a study in *The Lancet*. In a double-blind trial study, Olli G. Simell, MD, PhD, at the University of Turku, Finland and colleagues randomly assigned 264 children positive for two or more diabetes-associated autoantibodies to receive short-acting human insulin (n=137) or placebo (n=127) once a day intranasally for a median of 1.8 years. Researchers reported that 56 children in the insulin group eventually developed diabetes compared with 53 children in the placebo group (*P*=.91).

Food Allergies on the Rise Among US Children

Food or digestive allergies among young people increased 18% between 1997 and 2007, according to a new report by the Centers for Disease Control and Prevention (CDC). In 2007, approximately 3 million (4%) US children and teenagers under 18 years of age were reported to have a food or digestive allergy in the previous 12 months, compared with 2.3 million (3.3%) in 1997.

Approximately 4.7% of children younger than 5 years had a reported food allergy compared with 3.7% of children and teens aged 5 to 17 years. The report found that milk, eggs, peanuts, tree nuts, fish, shellfish, soy, and wheat account for 90% of all food allergies. Allergic reactions to these foods range from a tingling sensation around the mouth and lips, to hives, and even death.

The CDC also found that children with food allergies are two to four times more likely to experience other conditions, such as asthma, eczema, and respiratory allergy. There does not appear to be a difference in the rate of allergy between boys and girls. However, Hispanic children are less likely than non-Hispanic white children or non-Hispanic black children to have food allergies, the CDC reported. ■

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