What's New

January 2019

NEW BOOKS IN CLINICAL KEY

Biologics in Orthopedic Surgery (Mazzocca, Augustus) 1st ed;

Chronic Kidney Disease, Dialysis, and Transplantation (Himmelfarb, Jonathan) 4th ed;

Clinical Obstetrics and Gynaecology (Magowan, Brian) 4th ed;

Conn's Current Therapy 2019 (Kellerman, Rick) 1st ed;

Contact Lens Complications (Efron, Nathan) 4th ed;

Critical Heart Disease in Infants and Children (Ungerleider, Ross) 3rd ed;

Drugs for Pregnant and Lactating Women (Weiner, Carl) 3rd ed;

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Principles and Practice of Medical Genetics and Genomics (Pyeritz, Reed) 7th ed;

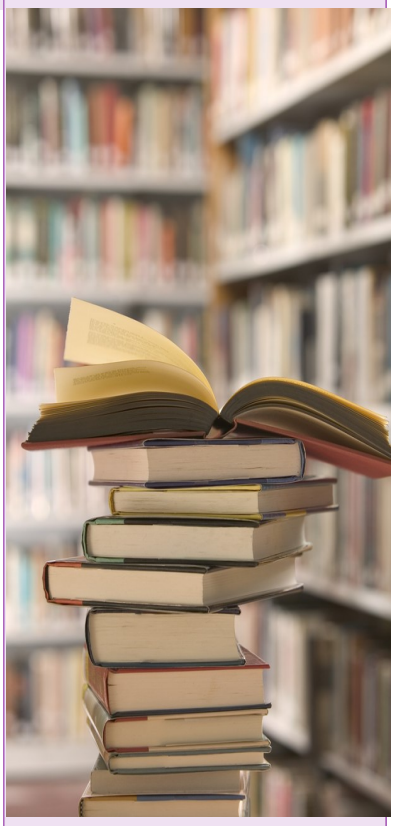
Human Embryology and Developmental Biology (Carlson, Bruce) 6th ed;

Injection Techniques in Musculoskeletal Medicine (Saunders, Stephanie) 5th ed;

Medical Pharmacology and Therapeutics (Waller, Derek) 5th ed;

Pharmacology and Physiology for Anesthesia (Hemmings, Hugh) 2nd ed;

Travel Medicine (Keystone, Jay) 4th ed;



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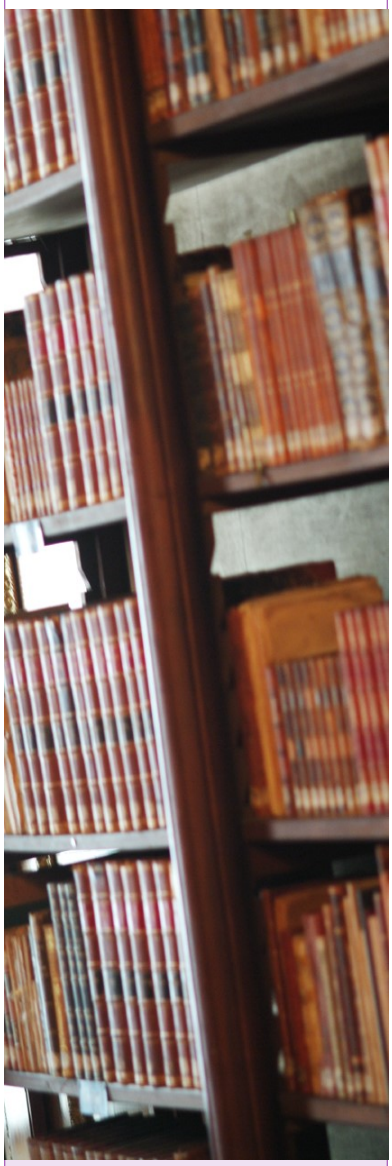

NEW AND UPDATED TOPICS IN UPTODATE

PCSK9 inhibitors after acute coronary syndromes

All patients with an acute coronary syndrome (ACS), irrespective of their baseline low density lipoprotein cholesterol (LDL-C) level, should receive statin therapy to lower the risk of subsequent cardiovascular events. Some will need further LDL-C lowering with ezetimibe. The question of whether additional LDL-C lowering with a PCSK9 inhibitor further reduces this risk was evaluated in the ODYSSEY OUTCOMES trial, which randomly assigned nearly 19,000 patients with an ACS who had an LDL-C level of at least 70 mg/dL (1.81 mmol/L) and were receiving statin therapy to the PCSK9 inhibitor alirocumab or placebo [1]. At nearly three years, the risk of death from any cause was lower for the alirocumab group. For many ACS patients with an LDL-C ≥50 mg/dL (1.29 mmol/L) while taking maximally tolerated statin plus ezetimibe, we add a PCSK9 inhibitor.

Vitamin D supplementation does not reduce incidence of cancer or cardiovascular events

In a large, randomized trial evaluating vitamin D3 supplementation (2000 international units daily) versus placebo in over 25,000 adults (mean age 67 years, mean serum 25 [OH] vitamin D 30 ng/mL [77 nmol/L]), with median follow-up of 5.3 years, there was no difference in the occurrence of the primary cardiovascular endpoint (composite of myocardial infarction, stroke, or cardiovascular death) or the primary cancer outcome (invasive cancer) [2]. The incidence of death from cancer, cardiovascular disease, or any cause did not differ significantly between the two groups. We suggest not administering vitamin D supplements above and beyond what is required for osteoporosis or fall prevention.

Oral immunotherapy for peanut allergy

Management of food allergy currently consists of strict avoidance of the food allergen and treatment of accidental

exposures, but oral immunotherapy (OIT) is under investigation as an alternative approach. In a randomized trial of almost 500 children aged 4 to 17 years with peanut allergy and dose-limiting symptoms with ≤100 mg peanut protein, more of those receiving OIT versus placebo tolerated ≥600 mg of peanut protein upon completion of maintenance therapy (67 versus 4 percent) [3]. However, rates of severe adverse events, study withdrawal due to adverse events, and epinephrine administration during the study were all higher in the treatment group. OIT may be a future option for prevention of allergic reactions due to accidental exposures, but there are still a number of limitations with this therapy.

Ibrutinib in previously untreated younger adults with CLL

Practice Changing UpDate: For most younger (eg, <70 years) patients with IGHV-unmutated chronic lymphocytic leukemia who require therapy, we suggest ibrutinib with or without rituximab rather than chemoimmunotherapy as initial therapy (Grade 2B).

Until now, fludarabine, cyclophosphamide, and rituximab (FCR) had been our preferred initial therapy for young, fit patients with previously untreated symptomatic chronic lymphocytic leukemia (CLL) without a 17p deletion/TP53 mutation. In a large randomized trial in this population (ECOG-ACRIN E1912), ibrutinib plus rituximab improved progression-free survival (PFS) and overall survival over that seen with FCR, with fewer severe adverse events [1]. In subgroup analysis, this benefit was clear in those with IGHV-unmutated CLL, but did not reach statistical significance in those with IGHV-mutated CLL. Based on this and other studies, ibrutinib-based therapy is now our preferred treatment for patients with previously untreated IGHV-unmutated CLL who require systemic therapy. Some UpToDate contributors offer ibrutinib plus rituximab as used in this trial protocol, while others prefer single agent ibrutinib based on extrapolation of data from randomized trials in older adults that have not shown a benefit with the addition of rituximab. While ibrutinib is also an option for IGHV-mutated CLL, some patients may prefer FCR if they are willing to undergo a more intensive therapy with the potential for long-term control.

Prevention of TB-associated IRIS

Practice Changing UpDate: For HIV-infected adults who have a baseline CD4 cell count ≤100 cells/microL, are being treated for active tuberculosis, and are initiating antiretroviral therapy (ART) within 30 days of starting antituberculous therapy, we suggest prophylactic administration of prednisone during the first four weeks following ART initiation (Grade 2B).

Initiation of antiretroviral therapy (ART) in HIV-infected patients with low CD4 cell counts can be complicated by the immune reconstitution inflammatory syndrome (IRIS), which presents as a paradoxical worsening of a preexisting infectious process as immune function improves. IRIS has been reported in up to half of HIV-infected individuals with underlying tuberculosis (TB) starting ART. In a randomized trial including more than 200 adults with previously untreated HIV who had a CD4 cell count ≤100 cells/microL, had recently started therapy for active TB, and were initiating ART, the incidence of TB-associated IRIS was lower among those who were assigned to receive prednisone during the first four weeks of ART compared with those in the placebo group (32 versus 47 percent) [2]. Prednisone did not increase the risk of severe infection or other serious adverse events. Based on these findings, we suggest prophylactic administration of prednisone during the first four weeks following ART initiation in patients with a CD4 cell count ≤100 cells/microL who are within 30 days of starting antituberculous therapy.

Prostate cancer and 5-alpha reductase inhibitors

The 5-alpha reductase inhibitors (5-ARIs) finasteride and dutasteride improve lower urinary tract symptoms in men with benign prostatic hyperplasia (BPH), by blocking the conversion of testosterone to the more potent androgen dihydrotestosterone. Although two randomized trials have shown a reduced risk of prostate cancer in men receiving 5-ARIs, concerns were raised about a possible increased risk of high-grade prostate cancers. In a Swedish population-based cohort study of all men over the age of 40 who had at least one prostate-specific antigen (PSA) test in Stockholm County between 2007 and 2015, men who were prescribed a 5-ARI had a decreased risk for prostate cancer and the effect was larger with longer duration of exposure [3]. The reduction was limited to prostate cancers with Gleason score 6 to 7; there was no impact on the risk of higher-grade disease (Gleason score 8 to 10). These data provide some reassurance that treatment with a 5-ARI for lower urinary tract symptoms is safe with regard to prostate cancer risk, but long-term follow-up data demonstrating improved survival are needed to determine the role of 5-ARIs as chemopreventive agents.

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