1. Too much HDL?

Can you have too much high-density lipoprotein (HDL)?

Submitted by:
Alexander Juvshik, MD, CCFP
Thunder Bay, Ontario

This is one occasion where it is alright to have too much of a good thing!

HDL is also known as the "good" cholesterol. Plasma levels of HDL generally correlate inversely with the presence of coronary artery disease or other vascular diseases. This means, all other risks being equal, the higher the measured HDL, the lower the cardiovascular risk.

One mechanism to explain this antiatherogenic effect is reverse cholesterol transport. Nascent HDL particles contain little cholesterol and, thus, capture membrane-associated cholesterol onto other HDL particles.

Another proposed mechanism is that HDL limits lipoprotien oxidation.

Finally, HDL particles act as shuttles between tissue cholesterol and the liver (where it is stored).

All in all, normal HDL levels are good; high HDL levels are better.

Answered by:
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This month's topics:

2. The biochemical basis of PSA

What is the biochemical basis of free/total prostate-specific antigen?

Submitted by:
Michael De Roode, MD, CCFP
Burks Falls, Ontario

Small amounts of enzymatically active PSA leak into the serum (more so when cancer is present). Upon reaching the serum, PSA's proteolytic activity is neutralized by antichymotrypsin (ACT) or a-2-macroglobulin. We are only able to measure the PSA that is bound to ACT using anti-PSA antibodies. This complexed component is the major portion of PSA in serum, while a small amount is in a non-complexed form (free or fPSA).

Free to total serum PSA ratio (%fPSA) is higher in men with benign prostatic hyperplasia (BPH) than in men with prostate cancer. The molecular basis for the differences in PSA binding to ACT between BPH and cancer is unclear.

By using a %fPSA cutoff of 25% the specifity of PSA screening improves. In the PSA range of four to 10, approximately 20% of biopsies can be avoided, while keeping the sensitivity to detect cancer at 95%. In younger men, this may be important since PSA cutoffs are being lowered to 2.5 in many centres (which leads to better detection of cancer, but also more unnecessary biopsies).

Several other PSA variation markers are being investigated. The bottom line is to find ways to improve on the specificity of PSA, which remains an excellent tool in prostate cancer detection.

Answered by:
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3. Managing CV risks

How aggressively should cardiovascular risk factors be managed in patients with impaired fasting glucose compared to patients with diabetes and those with low-risk factors?

Submitted by:
George Michaels, MD, CCFP, FCFP
Montreal, Quebec

Although we are awaiting long-term trials, the cardiovascular risk posed by impaired glucose tolerance is likely somewhat less than that of frank diabetes, but significantly higher than that of the normal population. Recall also that a large percentage of patients with impaired fasting glucose will go on to develop frank diabetes. (Some refer to it as pre-diabetes.)

You may want to ensure the patient actually does not have overt diabetes by doing a two-hour (2h) oral glucose tolerance glucose level test (> 11 mmol/L is also diagnostic for Type 2 diabetes). This test may identify as many as 20% to 30% more cases of diabetes than fasting glucose alone.

The Diabetes Epidemiology: Collaborative Analysis Of Diagnostic criteria in Europe (DECODE) trial 1 looked at the cardiovascular risk posed by postprandial hyperglycemia and compared it with the risk from fasting hyperglycemia. The trial found that the 2h pc glucose level provided a much better correlation with cardiovascular risk.

I'd suggest erring on the side of caution by aggressively addressing lifestyle issues, including weight loss and exercise. This should be done not only to manage cardiovascular risk, but to help avoid progression to frank diabetes as well. However, assuming no other risk factors are present, current guidelines still suggest treating to a blood pressure target of 140/90 mmHg (instead of 130/80 mmHg in "true" diabetes), a low-density lipoprotein cholesterol level of < 4.5, and a cholesterol ratio of < 6.0 (assuming low risk by Framingham).

Retesting with a 2h pc glucose level may actually identify a patient as having diabetes, thus, clarifying your targets.

Reference
1. DECODE Study Group: Glucose tolerance and cardiovascular mortality: Comparison of fasting and 2-hour diagnostic criteria. Arch Intern Med 2001; 161(3):397-405.

Answered by:
Steve Wong, MD, FRCPC
Program director
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Vancouver, British Columbia

4. How is urticaria diagnosed?

What is the current recommended workup for urticaria?

Submitted by:
Karen Edstrom, MD, FRCPC
Hamilton, Ontario

Urticaria is classified as acute (< six weeks duration) or chronic (> six weeks duration). Acute urticaria is often etiologically related to infections or medications and is, therefore, self-limited. If an episode of urticaria lasts longer than one to two weeks without an evident cause, investigations are warranted.

History and physical exam are important to identify the physical urticarias (hives induced by pressure, vibration, cold, heat, light, water, stress, exercise). Directed provocative challenges to elicit urticaria are also an integral part of the investigation. Initial screening tests include a complete blood count with differential analysis, C-reactive protein, blood chemistry profile, and urinalysis.

Eosinophilia would suggest parasitic infection (therefore, a need for stool exam for ova and parasites), allergic reactions, or a drug-related etiology.

Elevated C-reactive protein and an active urinary sediment suggest the possibility of vasculitis, which requires complement and immune complex determinations, plus a skin biopsy to rule out urticarial vasculitis.

Abnormal liver function tests suggest the need for hepatitis B and C serology.

Cryoproteins should be requested in patients with cold-induced urticaria.

Other screening tests include thyroid-stimulating hormone and antithyroid antibodies (to rule out contributing thyroid disease), and fluorescent antinuclear antibody (to uncover systemic lupus erythematosus).

Any further investigations would be dictated by findings on history, physical exam, and screening tests.

Answered by:
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5. Oral bisphosphonates and cancer

? Is there a role for oral bisphosphonates in metastatic bone cancer?

Submitted by:
Diane Zatelny, MD
Barrie, Ontario

Oral bisphosphonates do have a role in the management of bone-related complications of metastatic cancer. While intravenous bisphosphonates, such as pamidronate or zoledronate, are used more frequently, oral etidronate and clodronate have also been tried.

Typically, the patients studied had either breast cancer, prostate cancer, or multiple myeloma. Potential benefits of bisphosphonates include treatment of hypercalcemia, prevention of new bone metastases, prevention of pathologic fractures, and reduction in bone pain. Clodronate, 1,600 mg daily, is the most frequently used oral dose.

A recent Canadian meta-analysis found that bisphosphonates, including oral clodronate, were moderately effective in relieving pain from bone metastases after 12 weeks of therapy, compared to placebo. A two-year, randomized, controlled trial of clodronate, 1,600 mg once daily, versus placebo in patients with breast cancer, showed that clodronate-treated patients benefited. These patients showed a 50% reduction in the risk of new bony metastases and the number of bony metastases which developed over three years of followup. Mortality was also reduced in the clodronate-treated group.[1]

Reference
1. Diel IJ, Solomayer EF, Costa SD, et al: Reduction in new metastases in breast cancer with adjuvant clodronate treatment. N Engl J Med 1998; 339(6):357-63.

Answered by:
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6. Treating plantar warts

What is the most successful treatment for plantar warts?

Submitted by:
Francois Dippenaar, MB ChB
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Most plantar warts can be effectively treated with over-the-counter salicylic acid preparations, applied as a liquid or a plaster. However, this treatment is slow and usually needs to be continued for 12 weeks. Doctor-administered cryotherapy with liquid nitrogen can result in 50% of all lesions being cured after a single treatment, but can also result in local pain and blistering. Multiple treatments with cryotherapy may be required to eliminate the lesion.

Laser therapy, such as with carbon dioxide laser, is probably the most effective, but also the most expensive therapy. It reduces the post-operative pain associated with treatment and also reduces the recurrence rate to 10%.

Some recalcitrant lesions require specialist referral to be treated with intralesional injections of bleomycin.

The use of imiquimod in the treatment of some cases of plantar warts looks promising in combination with other, more commonly used, therapies.

Answered by:
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7. Prostatic calcifications on ultrasound

What is the clinical significance of prostatic calcifications on ultrasound?

Submitted by:
Hany Aeta, MD, CCFP
Orleans, Ontario

Most prostatic calcifications are prostatic calculi, formed by the deposition of calcareous material in the tissues or acini of the prostate gland. They are composed of calcium phosphate.

It is generally believed that the formation of prostatic calculi comes with aging and typically has no clinical significance. Infection may also contribute to the formation of some prostatic calculi.

On ultrasound, prostatic calcifications are highly echogenic with the presence of shadowing. They may be found in association with benign prostatic hyperplasia and in cancer patients. They may also be associated with acute and chronic prostatitis.

Prostatic calcifications are reported when they are found on ultrasonography. Although these calcifications have no clinical meaning, a prostatic nodule felt on rectal exam may, in some cases, correspond with a well-identified prostatic calcification. Such a finding may help the doctor decide if futher biopsies are required and may help reassure the patient that his prostate nodule is not a tumour. Dx

Answered by:
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