HOMEOGLOBIN A1C IN DIABETES MANAGEMENT

Hemoglobin A1c is a robust and reliable measure of long-term glycemic level, and can be used to monitor glycemic control in diabetes, and also for actual diagnosis of diabetes (without need for obtaining a “fasting” blood sample) provided a clinical laboratory is equipped to do so and is not a “point-of-care” instrument. Hemoglobin A1c may be lower than expected for chronic level of glycemia in conditions associated with shortened RBC survival (hemolysis, acute blood loss and hemoglobinopathies). Hemoglobin A1c may be higher than expected for chronic level of glycemia in Blacks [Selvin et al, J. Amer. Med. Assoc., 2007]. Other causes of falsely elevated A1c include the cyanate anion derived from urea) at the N-terminal amino groups, which is “misread” as glycation of hemoglobin in certain assays, or alternatively, an increased RBC fragility in the uremic milieu may lead to lower levels of glycated adducts in CKD erythrocytes.

ALLOPURINOL: NEW KID OR JUST ANOTHER BLOCK?

The xanthine oxidase inhibitor, allopurinol, is of proven effectiveness in the treatment of hyperuricemia and gout, and now comes data suggesting that hiddens of allopurinol could improve exercise tolerance in chronic stable angina (CAD) by Awsan Noman et al, Lancet 2010. The mechanism(s) for this observation is obscure, though suggested pathways include reduction of oxidative stress (and its effects) within the vascular endothelium, uncoupling of work-energy consumption in myocardium, and possibly, coronary vasodilatation. If these findings are validated in clinical situations, allopurinol could join anti-anginal drugs (such as nitrates, beta-blockers, non-dihydropyridine calcium channel antagonists, and the K-channel activator, nicorandil), statins, ASA, anti-platelet drugs, and renin-angiotensin-aldosterone antagonists as standard treatment for CAD.

ENVIRONMENTAL TRIGGERS ARE GENETICALLY PREDISPOSED

Classic pathogenetic theory requires a genetic “predisposition” and an environmental “trigger”; the genetic “tool” being maximal in so-called single gene diseases such as sickle cell hemoglobinopathy, and the environmental “seed” predominating in common infections such as the common cold. Human immunologic defence against common infections is mediated in part by interleukin-2 signaling, which is itself controlled by the CISH protein (cytokine-induced SRC homology 2 domain protein). A case-control analysis by Chia Khor et al, J. Enlg. Med. 2010, using over 800 samples, reveal that genetic variation in the CISH protein greatly influences the response of IL-2 (a cytokine which helps govern T-cell response following an infectious exposure) to common infections, from tuberculosis to acute bacteremia, even to falciparum malaria. In other words, genes control predication to infection – how come no one appears to be surprised?

ACUTE KIDNEY INJURY FOLLOWING EXERCISE OR SEIZURES

A recent report by M-T Yan et al, Kidney International, 2010, highlights the problem of kidney failure provoked by exercise. This complication also occurs following repetitive seizures, and may be more common during hot summer months. A thorough history followed by appropriate confirmatory tests are the steps to proper diagnosis.

1. Rhabdomyolysis: classically occurs with crush injury or following severe, unaccustomed exercise, but look for pigmenturia (i.e. positive dipstick tests are the steps to proper diagnosis. In CKD, hemoglobin A1c levels might be spuriously elevated or decreased, as a result of carbamylation of hemoglobin i.e. a condensation reaction involving the cyanate anion derived from urea) at the N-terminal amino groups, which is “misread” as glycation of hemoglobin in certain assays, or alternatively, an increased RBC fragility in the uremic milieu may lead to lower levels of glycated adducts in CKD erythrocytes. Hyperuricosuria, which results in kidney stone disease and kidney failure under anerobic conditions (of exercise).

2. Hypophosphatemia, diabetic crisis, hypokalemia), myositis from viremia, bacterial infections, autoimmune disease/vasculitis), alcoholism, toxins/

3. Hypoprolactinemia: may be aggravated by NSAIAD use, ACE inhibitors/ARBs; concurrent diuretic treatment, high humidity, high ambient temperatures, high altitude and athosclerosis/peripheral artery disease.

4. Metabolic dysfunction: typically from endocrinopathy (thyroid disease, adrenal dysfunction, hypoglycemia), glycogen storage diseases, mitochondrial disorders (including MELAS, where the clue may be severe lactic acidemia) and defects in fatty oxidation pathway.

5. Sickle cell disease: the clue may be unexplained anemia with signs of marrow expansion, presenting as “bossing” of the skull

6. Hereditary renal hypouricemia: rare disorder characterized by high renal urine acid clearance, resulting in normal urine acid levels despite severe hyperuricemia, which results in kidney stone disease and kidney failure under anerobic conditions (of exercise).

H. pylori is often likened to a moving target. Management should be based on local susceptibilities and results, and not on consensus algorithms which are often ineffective (Graham & Fischbach, Gut 2010). The classic standard treatment uses 3 different drugs over 14 days: PPI + clarithromycin + amoxicillin/ metronidazole. Best results are obtained from a hybridization protocol (PPI plus amoxicillin 7 days, then PPI plus amoxicillin plus clarithromycin plus metronidazole x 7 days), with eradication rates >95%; this result is superior to sequential treatment with 4 drugs (PPI + amoxicillin x 7 days, PPI + clarithromycin + metronidazole x 7 days and concomitant treatment with 4 drugs (PPI + amoxicillin + clarithromycin + metronidazole x 14 days).
patients. Aggressive BP control <120/80 mmHg may not foster cardiovascular benefits or prevent strokes in CKD patients, but may rather worsen renal outcomes (Miletta et al, Advances in Chronic Kidney Disease, 2010). However, a recent trial demonstrates that a radio-iodine-tagged monoclonal antibody (girentuximab, marketed as Redectane) directed against carbonic anhydrase IX (an enzyme that is overexpressed in kidneys or liver, as well as non-Hodgkin’s lymphomas and myelodysplastic syndromes), medications (especially antibiotics, NSAIDs, anti-epileptics, and corticosteroids), and may present as acute pulmonary edema during an acute coronary syndrome) or angina pectoris (which simulates GERD more commonly in elderly women, and may present as acute pulmonary edema during an acute coronary syndrome) or angina pectoris (which simulates GERD more commonly in elderly women).

ALCOHOLIC LIVER DISEASE

The spectrum of alcoholic liver disease spans fatty liver disease to cirrhosis (characterized by fibrosis and nodular regenerative hyperplasia, or dyslipidemia and insulin resistance), alcohol-related cirrhosis, alcoholic hepatitis, alcoholic steatohepatitis, and alcoholic cirrhosis. Alcohol-related cirrhosis is a common cause of hepatic decompensation, and may present as acute pulmonary edema during an acute coronary syndrome or heart failure.

FOREVER OF UNKNOWN ORIGIN

Fewer are infectious and resolve spontaneously, often within 1 week, before any diagnostic tests are conclusive; those that are communicable (e.g., HIV, VIH) cannot be readily or effectively treated. New data coming from the RBY17 trial demonstrates that a radio-iodine-tagged monoclonal antibody (girentuximab, marketed as Redectane) directed against carbonic anhydrase IX (an enzyme that is overexpressed in kidneys or liver, as well as non-Hodgkin’s lymphomas and myelodysplastic syndromes), medications (especially antibiotics, NSAIDs, anti-epileptics, and corticosteroids), and may present as acute pulmonary edema during an acute coronary syndrome or heart failure.