1. Anti-tTg testing reliable?

How reliable is anti-tTg testing in diagnosing celiac disease?

Submitted by:
Deirdre Ashton, MD
Edmonton, Albera

A positive anti-transglutaminase antibody (anti-tTg) test using human recombinant tissue glutaminase in a patient with normal immunoglobin A is highly suggestive of celiac disease. It has a specificity of 95% to 100% and a sensitivity of 93% to 96%. This is similar to anti-endomysial antibody. Unlike anti-endomysial antibody, anti-tTg antibody may be positive in ulcerative colitis, Crohn's disease and chronic liver disease. A positive test should also be confirmed by a small bowel biopsy. Anti-tTg antibody can also be used to follow dietary compliance, since it clears in patients with a strict diet.

Answered by:
Flavio Habal, MD, PhD, FRCP
Associate Professor of Medicine
University of Toronto
University Health Network
Toronto, Ontario

The anti-tTg test has a specificity of 95% to 100% and a sensitivity of 93% to 96%.

This month's topics:

2. New chemo treatments

Are there any new chemotherapy treatments for esophageal or pancreatic cancers?

Submitted by:
Greag Karaguesian, MD
Haliburton, Ontario

For esophageal cancers, cisplatin and 5-fluorouracil remain the standard options. New agents, including, irinotecan, epirubicin and docetaxel may have activity and, thus, combination regimens with epirubicin, cisplatin and 5-fluorouracil or irinotecan and 5-fluorouracil have been explored for metastatic disease.

For pancreatic cancer, the challenge to identify active chemotherapy has been significant. Multiple trials of gemcitabine in combination with other chemotherapy agents have failed to demonstrate superior results when compared to gemcitabine alone. Gemcitabine with erlotinib, a targeted therapy against the epidermal growth factor receptor, appears to be modestly more efficacious. Current trials are exploring combinations of chemotherapy and targeted or biologic therapies to improve outcomes for patients with pancreatic cancer.

Answered by:
Sharlene Gill, MD, MPH, FRCPC
Assistant Professor of Medicine
British Columbia Cancer Agency
University of British Columbia
Vancouver, British Columbia

3. Should low-grade infant fevers be treated?

Should a mild fever of less than 100 F be treated in infants with an upper respiratory tract infection?

Submitted by:
S. Chaudhry, MD
Toronto, Ontario

Fever in infants is a marker of infection and does not require fever control medication if the infant is feeding well, remains socially interactive and visually attentive. Antipyretic therapy is not indicated for a temperature of 100 F or less, including cases where there are clinical features of a respiratory tract infection.

Infants with or without fever who are listless, lethargic, feeding poorly or are having difficulty breathing require urgent medical care.

Answered by:
Paul Korn, MD, DABPed
Clinical Associate Professor
University of British Columbia
Staff
Children's & Women's Health Centre of British Columbia
Vancouver, British Columbia

Fever in infants is a frequent marker of infection and does not require fever control medication if the infant is feeding well, remains socially interactive and visually attentive.

4. Making preliminary RA diagnoses

How can we make a preliminary diagnosis of rheumatoid arthritis? What laboratory tests are needed?

Submitted by:
Gaéan Y. Lavoie, MD
Ste-Félicité, Quebec

The American College of Rheumatology has defined the following criteria useful for the diagnosis of rheumatoid arthritis (RA). The patient has RA if they satisfy four of the seven criteria and if criteria one to four have been present for six weeks (Table 1). The following baseline evaluation is recommended: erythrocyte sedimentation rate/C-reactive protein, rheumatoid factor, complete blood cell count, creatinine, hepatic pane, urinalysis, synovial fluid analysis (when possible) and baseline radiography.

Answered by:
Monique Camerlain, MD, FRCPC
Consultant Member, Service de Rhumatologie
Centre Hospitalier Universitaire de Sherbrooke
Sherbrooke, Quebec

Table 1

ACR criteria for the classification of rheumatoid arthritis

Criterion	Definition
Morning stiffness	Morning stiffness in and around the joints, lasting at least an hour before maximal improvement
Arthritis of three or more joint areas	At least three joint areas have had soft tissue swelling or fluid (not bony overgrowth alone) observed simultaneously by a physician. The 14 possible areas are the right or left PIP, MCP, wrist, elbow, knee, ankle and MTP joints
Arthritis of hand joints	At least one swollen area (as defined above) in the wrist, MCP or PIP joint.
Symmetric arthritis	Simultaneous involvement of the same joint areas (as defined above) on both sides of the body (bilateral involvement of PIPs, MCPs or MTPs is acceptable without absolute symmetry)
Rheumatoid nodules	Subcutaneous nodules, over bony prominences, extensor surfaces or in juxta-articular regions, observed by a physician
Serum rheumatoid factor	Demonstration of abnormal amounts of serum rheumatoid factor by any method for which the result has been positive in < 5% of normal control subjects
Radiographic changes	Radiographic changes typical of rheumatoid arthritis on posteroanterior hand and wrist radiographs, which must include erosions or unequivocal bony decalcification localized in or most marked adjacent to the involved joints (osteoarthritis changes alone do not qualify)

PIP: Proximal interphalangeal
MCP: Metacarpophalangeal
MTP: Metatarsophalangeal

5. Should I stop warfarin?

A patient is on warfarin for atrial fibrillation and has an international normalized ratio of 15. He is not bleeding. Would you stop the warfarin?

Submitted by:
Greg Karagesian, MD
Haliburton, Ontario

Fortunately, clinical practice guidelines exist to help us in this situation.[1] For international normalized ratios (INRs) of nine to 19.9 without bleeding, hold warfarin, give oral vitamin K_1, 3 mg to 10 mg, and monitor the INR daily. If the INR remains above the therapeutic range for 48 hours, give another dose of vitamin K_1. When the INR is therapeutic, resume warfarin at a lower dose. The more vitamin K_1 the patient receives, the longer regaining a therapeutic INR will take. If bleeding occurs, give vitamin K_1 intravenously, as well as prothrombin complex concentrate or fresh frozen plasma. Finally, ask "Why did this patient's INR go so high?" Remember the myriad of drug/drug and drug/food interactions with warfarin.

Reference
1. Ansell J, Hirsh J, Poller L, et al: The pharmacology and management of the vitamin K antagonists: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004; 126(3 Suppl):204S-33S.

Answered by:
Thomas Wilson, MD
Head
Department of Medicine
Professor
University of Saskatchewan
Saskatoon Health Region
Saskatoon, Saskatchewan

For INRs of nine to 19.9 without bleeding, hold warfarin, give oral vitamin K_1, 3 mg to 10 mg, and monitor the INR daily.

6. Concerned about ovarian cancer

What screening technique can be used successfully for asymptomatic patients concerned about ovarian cancer?

Submitted by:
Anne S. MacCara, MD
Picton, Nova Scotia

Unfortunately, there is no evidence that the current screening modalities of Ca 125 and transvaginal ultrasonography are effective in reducing mortality from ovarian cancer.

Women who are at increased risk of developing ovarian cancer because they have hereditary risk factors (*i.e.,* breast cancer screening 1 and 2 gene positive) are advised to consider risk-reducing surgery when they are 35-years-old or have completed their childbearing. Complete removal of the fallopian tubes and ovaries is recommended to prevent the development of ovarian cancer in this high-risk population.

Answered by:
David Popkin, BSc, MD, CM, FRCSC
Gynecologic Oncologist
Head, Division of Oncology
College of Medicine
University of Saskatchewan,
Saskatoon, Saskatchewan

There is no evidence that the current screening modalities of Ca 125 and transvaginal ultrasonography are effective in reducing mortality from ovarian cancer.

7. Q-wave or ST-elevation?

Why do we still hear and read the terms Q-wave and non-Q-wave MI? Should it be ST-elevation and non-ST-elevation?

Submitted by:
SW Verster, MD
Lestock, Saskatchewan

I still see non-Q-wave infarction with corresponding cardiac enzyme marker increases. ST-elevation could be symptomatic or indicative of other conditions (*e.g.,* pericarditis or early repolarization or medication effect). Reciprocal leads will also be reflective of ST-depression from other cases.

Answered by:
Stephen Coyle
Assistant Lecturer
Department of Family Medicine
University of Manitoba
Chief Medical Officer
Misericordia Health Centre
Winnipeg, Manitoba

I still see non-Q-wave infarction with corresponding cardiac enzyme marker increases.

8. Strategies for ascites

What are the current management and investigation strategies for ascites?

Submitted by:
Philip Fingrut, MD
Toronto, Ontario

Table 1
Ascite etiology

Cirrhosis: 81%
Cancer: 10%
CHF: 3%
Tuberculosis: 2%
Dialysis: 1%
Pancreatic disease: 1%
Other: 2%

CHF: Congestive heart failure

Answered by:
Robert Bailey, MD, FRCPC
Clinical Professor
University of Alberta
Head
Gastroenterology
Royal Alexandra Hospital
Edmonton, Alberta

Christopher Szeto, MD
Department of Surgery
University of Alberta
Edmonton, Alberta

Successful treatment of ascites depends on the accurate diagnosis of the etiology (Table 1). Patients should have an ultrasound to confirm or refute the presence of ascites. It is an easy, sensitive and cost-effective imaging study.

Abdominal paracentesis with appropriate ascitic fluid analysis is the most efficient way to confirm the presence of ascites, diagnose their cause and, most importantly, to determine if the fluid is infected.

There are many tests to perform on peritoneal fluid, but the most important ones include:

- white blood cell count and differential (polymorphonuclear neutrophils > 250 cells/ml is highly suggestive of bacterial peritonitis) and
- serum ascites-albumin gradient is the best single test for classifying ascites.

The initial management of non-infective ascites consists of sodium restriction and diuretic therapy. A diet of no added salt to meals or cooking is usually sufficient. Furosemide and spironolactone are effective in 95% of patients. A relation of spironolactone, 100 mg, daily, and furosemide, 40 mg, daily, is a good start. Men tend to develop gynecomastia, as spironolactone is a known anti-androgen. Amiloride, 10 mg, daily, is a good substitution.

One must be mindful of electrolyte imbalances and renal comprise while on diuretics. Therapeutic paracentesis for symptom relief should be followed by intravenous albumin, 5 g, for each litre of ascites removed. Repeated paracentesis or TIPS may be required for diuretic refractory ascites (defined as the need for > 400 mg, daily, of spironolactone and 160 mg, daily, of furosemide).

9. Endometriosis: Causes & treatment

What causes endometriosis? What is the best way to surgically treat it?

Submitted by:
Marichal Binns, MD
Edmonton, Alberta

Endometriosis is caused by retrograde menstruation. In susceptible women, the stroma and glands remain in the peritoneal cavity and infiltrate.

Surgical therapy should include:

- removal (by excision) or destruction (by electrocautery desiccation or laser ablation) of any visible endometriosis,
- lysis of adhesions and
- removal of endometriomas (chocolate cysts).

No method has proven superior to another.[1] Conservative therapy by laparoscopy is aimed at restoring normal anatomy and maintaining fertility. Rarely should a hysterectomy and bilateral salpingo-opherectomy be contemplated.

Reference
1. Wright J, Lotfallah H, Jones K, et al: A randomized trial of excision versus ablation for mild endometriosis. Fertil Steril 2005; 83(6):1830-6.

Answered by:
Magali Robert, MD
Clinical Associate Professor
University of Calgary
Calgary, Alberta

10. Blood BNP and CHF

What is the role of blood BNP levels in the management of CHF?

Submitted by:
Monique Belanger, MD
Sudbury, Ontario

BNP (B-type natriuretic peptide) is secreted by the ventricles in response to volume and pressure overload (stretch), as occurs in decompensated congestive heart failure (CHF). It is a natriuretic, diuretic and vasodilator.

In recent trials, blood BNP level was found to be useful in distinguishing cardiac causes from non-cardiac causes of dyspnea in patients presenting to the emergency department (ED). A cutoff level of > 100 pg/mL has a high negative predictive value and good specificity in diagnosing CHF. Slightly elevated levels (100 pg/mL to 400 pg/mL) may also be found in certain lung conditions (*e.g.,* pulmonary embolism) and renal failure, but levels > 400 pg/mL almost always indicates CHF. BNP is more predictive than clinical examination or other laboratory studies.[1]

Besides being an initial diagnostic tool, BNP may also be useful in following the response to treatment of CHF.[2] The level of BNP seems to correlate with the severity of CHF and with survival.[3,4] A recent study showed that the BNP assay used in the ED is effective, safe and decreases unnecessary hospitalizations for suspected CHF.[5] Some very preliminary studies have shown that BNP may also be useful for screening asymptomatic people, but this definitely requires further study.[6]

The BNP assay is not meant to replace, but rather to supplement, the clinical history and exam and chest X-ray. It is increasing in popularity in the US and Europe for the diagnosis of CHF and is recommended in the recent European CHF guidelines. Rapid diagnostic kits and laboratory assays are available. In Canada, we may be seeing a gradual increase in the use of BNP levels, but guidelines regarding its use have not been published. Dx

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2. Cheng V, Kazanagra R, Garcia A, et al: A rapid bedside test for B-type peptide predicts treatment outcomes in patients admitted for decompensated heart failure: A pilot study. J Am Coll Cardiol 2001; 37(2):386-91.
3. Harrison A, Morrison LK, Krishnaswamy P, et al: B-type natriuretic peptide predicts future cardiac events in patients presenting to the emergency department with dyspnea. Ann Emerg Med. 2002; 39(2):131-8.
4. Berger R, Huelsman M, Strecker K, et al: B-type natriuretic peptide predicts sudden death in patients with chronic heart failure. Circulation 2002; 105(20):2392-7.
5. Mueller C, Scholer A, Laule-Kilian K, et al: Use of B-type natriuretic peptide in the evaluation and management of acute dyspnea. N Engl J Med 2004; 350(7):647-54.
6. Wang TJ, Larson MG, Levy D, et al: Plasma natriuretic peptide levels and the risk of cardiovascular events and death. N Engl J Med 2004; 350(7):655-63.

Answered by:
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