Questions and guide to answers

Hoda Atya[a], Mohammad Aon[a] and Zaynab H. El Gammal[b]

[a]Department of Internal Medicine and [b]Medical Genom Center, Cairo University, Cairo, Egypt

Correspondence to Hoda Atya, Department of Internal Medicine, Cairo University, Cairo, Egypt
Tel: +20 122 745 6569;
e-mail: hoda.attya@yahoo.com

Egypt J Intern Med 25:108–110

1110-7782

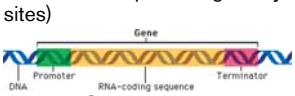
Received 10 April 2013
Accepted 27 April 2013
The Egyptian Society of Internal Medicine 2013, 25:108–110

Questions from exam

(1) Difference between regulatory and coding gene.
(2) Clinical suspicion and management of Budd–Chiari syndrome.
(3) Reversible causes of dementia in the elderly.
(4) Diagnostic modalities in intestinal vascular disorders.

Guide to answers

(1) Difference between regulatory and coding gene
A gene is any type of sequence of genomic DNA or RNA that is indispensable for a specific biological function, irrespective of whether that function requires the transcription or translation of the gene. Genes are subdivided into regulatory genes, RNA-genes, and protein-coding genes.

Regulatory	Coding
Gene encoding products involved in controlling the expression of one or more other genes [1]	The entire nucleic acid sequence that is necessary for the synthesis of a functional polypeptide [2]
These products may be RNA (as in the case of genes encoding mRNAs) or protein that binds to the regulatory sites regulating transcription of genes [1]	It is a segment of DNA containing transcribed parts (exon and introns) separated by untranscribed parts (regulatory sites)
	
Can act as an activator, turning a gene or a group of genes on so that expression can occur [1]	Exons → Synthesis of functional proteins
Are involved in the process of cell differentiation, determining what a cell will develop into. This allows organisms to have great diversity in cell types, making everything from neurons to skin cells [1]	Regulatory sites Promotor Enhancer (50 kb or more from the coding region)
Can act as repressors, turning genes off so that they cannot express by preventing RNA transcription. This type of regulatory gene may also act to suppress a harmful gene 'oncogene per example, keeping an organism healthy [1]	Sequences that specify 3′ cleavage and polyadenylation Sequences that specify splicing of primary RNA transcripts [2]

(2) Clinical suspicion and management of Budd–Chiari syndrome
(a) Definition [3]
(i) Any pathophysiologic process that results in interruption or diminution of the normal blood flow out of the liver. Budd–Chiari syndrome implies thrombosis of the hepatic veins and/or the intrahepatic or suprahepatic inferior vena cava.
(b) Predisposing factors [3]
(i) *Locally invasive tumors*: Hepatocellular carcinoma, renal, and adrenal adenocarcinoma. Also, parasitic and nonparasitic cysts and abscesses.
(ii) *Surgery or trauma*: Compression or kinking of the hepatic veins can occur following hepatic resection or transplantation. Budd–Chiari syndrome may occur following blunt abdominal trauma.
(iii) *Hypercoagulable states*: Myeloproliferative diseases, malignancy, oral contraceptives, pregnancy, factor V Leiden mutation, prothrombin gene mutation, antiphospholipid antibody syndrome, antithrombin III deficiency, protein C deficiency, protein S deficiency, paroxysmal nocturnal hemoglobinuria, JAK2 mutations, Behcet's disease, membranous webs of the inferior vena cava and/or the hepatic veins.
(iv) *Idiopathic*.
(c) Patients with acute disease usually present with severe right upper quadrant pain and hepatomegaly. Jaundice and ascites may not be apparent initially, but often develop rapidly. Variceal bleeding may also occur. Fulminant hepatic failure may occur. The subacute and chronic forms of Budd–Chiari syndrome have been present for several weeks to more than 6 months before clinical presentation. The clinical manifestations and duration of disease before presentation depend on the particular vessels that are occluded, the extent of occlusion, and the recruitment of collateral circulation. Chronic or subacute Budd–Chiari syndrome should be considered in the differential diagnosis of otherwise unexplained liver dysfunction, particularly in patients in whom ascites is a principal

 DOI: 10.7123/01.EJIM.0000431209.17447.64

feature, or in those who have a known risk factor for Budd–Chiari syndrome [4].

(d) Laboratory
  (i) Serum aminotransferases and alkaline phosphatase can be normal or increased.
  (ii) Levels of serum albumin, serum bilirubin, and prothrombin can be normal or abnormal.

(e) Imaging features [5]
  (i) Radiograph venography has been the gold standard for the evaluation of the hepatic veins. It is performed by accessing the hepatic venous circulation percutaneously.
  (ii) Doppler imaging is the most useful noninvasive diagnostic test to screen for the presence of Budd–Chiari syndrome.
  (iii) Computed tomography (CT) with failure to visualize the hepatic veins is considered suggestive of hepatic vein obstruction. Caudate lobe hypertrophy is found in about 75% of patients (separate venous drainage of this liver lobe into the inferior vena cava).
  (iv) MRI, contrast-enhanced magnetic resonance venography.

(f) Treatment [5]
  (i) Medical treatment (including supportive care, anticoagulation, thrombolysis, and medical treatment for portal hypertension).
  (ii) Radiologic procedures (such as angioplasty, TIPS, and stenting).
  (iii) Surgical intervention (including shunting procedures and liver transplantation).

(3) Reversible dementia in the elderly

(a) Definition [6]

Dementia is a disorder that is characterized by impairment of memory and at least one other cognitive domain (aphasia, apraxia, agnosia, executive function). These must represent a decline from a previous level of function and be severe enough to interfere with daily function and independence.

(b) Reversible causes [6]

Some types of dementia are reversible. This means that they can be treated and possibly cured. A treatable dementia occurs because of some other condition. The most common cause of reversible dementia is a toxic reaction to medication. The reported frequency of dementia because of potentially reversible causes varies from 0 to 23%.

The most common among these causes are
  (i) Alcohol-related and medication-related dementia.
  (ii) Depression-induced cognitive impairment.
  (iii) Surgical brain lesions such as normal pressure hydrocephalus, tumors, and chronic subdural hematomas.
  (iv) Metabolic disorders such as hypothyroidism, vitamin B_{12} deficiency.
  (v) Central nervous system infections such as neurosyphilis and HIV.
  (vi) Other less common causes such as thrombotic thrombocytopenic purpura can cause microangiopathic thromboses, producing global cerebral ischemia, resulting in an encephalopathy. Hyperviscosity syndromes from blood dyscrasias, such as polycythemia, or gammopathies, such as Waldenstrom's macroglobulinemia, can present as dementia by causing global cerebral microvessel ischemia. Also, minimal hepatic encephalopathy.
  (vii) Central nervous system vasculitis can also present as dementia.

(c) The following is a recommended panel for all patients with dementia [7]
  (i) Screening for B_{12} deficiency and hypothyroidism.
  (ii) Screening for depression in patients with dementia is recommended because depression is a common treatable comorbidity that may also masquerade as dementia.
  (iii) Structural neuroimaging with either a head CT or MRI should be considered in the initial evaluation of all patients with dementia.

(d) Other tests (according to clinical suspicion)

To rule out infections
  (i) Viral PCRs and cultures.
  (ii) Syphilis serology.
  (iii) Whipple's PCR.

To rule out autoimmune
  (i) ESR, CRP, C3, C4, ANA, RF, anti-SSA, anti-SSB, anti-dsDNA, anti-Smith, P-ANCA, C-ANCA.

To rule out toxic and metabolic causes
  (i) Serum copper and ceruloplasmin; 24 h urine copper.
  (ii) Exposure history.
  (iii) Liver function tests.

(4) Diagnostic modalities in intestinal vascular disorders

(a) Intestinal vascular disorders [7]
  (i) Acute mesenteric ischemia.
  Superior mesenteric artery embolism.
  Superior mesenteric artery thrombosis.
  Venous thrombosis.
  Focal segmental ischemia.
  (ii) Chronic mesenteric ischemia.
  (iii) Colonic ischemia.

(b) Diagnosis [8]
  (i) High index of suspicion (describe clinical features).
  (ii) Laboratory: Nonspecific: (leukocytosis and metabolic acidosis) any patient with acute abdominal pain and metabolic acidosis should be considered to have intestinal ischemia until proven otherwise.
  (iii) Radiologic:
  CT angiography: sensitive, specific.
  Mesenteric angiography remains the gold standard diagnostic study for acute arterial ischemia.
  MRI angiography.
  Plain abdominal radiographs are relatively nonspecific. Suggestive findings include the presence of an ileus with distended loops of

bowel, bowel wall thickening, and/or pneumatosis intestinalis.

(iv) Doppler (limited) (only in proximal occlusion celiac or superior mesenteric arteries).

(v) Experimental tests [9].
Glutathione S-transferase α.
Intestinal fatty acid-binding protein.

Acknowledgements

Conflicts of interest
There are no conflicts of interest.

References

1 Snustad DP. Regulation of gene expression in prokaryotes and their viruses. In: Snustad DP, editor. *Principles of genetics*. 6th ed. New York: Wiley; 2011.

2 Lodish H, Berk A, Zipursky SL, Matsudaira P, Baltimore D, Darnell J. *Molecular cell biology*. 4th ed. New York: W.H. Freeman; 2000.

3 DeLeve LD, Valla DC, Garcia Tsao G. Vascular disorders of the liver. Hepatology 2009; 49:1729–1764.

4 Menon KVN, Shah V, Kamath PS. Current concepts the Budd–Chiari syndrome. N Engl J Med 2004; 350:578–585.

5 Valla DC. The diagnosis and management of the Budd–Chiari syndrome: consensus and controversies. Hepatology 2003; 38:793–803.

6 Tripathi M, Vibha D. Reversible dementias. Indian J Psychiatry 2009; 51 (Suppl 1): S52–S55.

7 Knopman DS, DeKosky ST, Cummings JL, Chui H, Corey Bloom J Relkin N, *et al*. Practice parameter: diagnosis of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2001; 56: 1143–1153.

8 Gewertz BL, Ottinger LW, Rogers AL. American gastroenterological association medical position statement: guidelines on intestinal ischemia. Gastroenterology 2000; 118:951–953.

9 Kanda T, Fujii H, Tani T, Murakami H, Suda T, Sakai Y, *et al*. Intestinal fatty acid-binding protein is a useful diagnostic marker for mesenteric infarction in humans. Gastroenterology 1996; 110:339–343.