

Endocrinology

Questions

- 924. The treatment for a case of virilising adrenal hyperplasia is: (CMC 2000, JIPMER-99, AI 2000, AIIMS-99, PGI-99; AI 2005)**
- a. Estrogens
 - b. Antiandrogens
 - c. ACTH
 - d. Cortisone
- 925. A 8-years-old child presented with lethargy, mental retardation and growth retardation. He was also revealed to have delayed skeletal maturation, fragmented stippled epiphyses and wormian bones on further investigations. The most likely diagnosis is: (AIIMS Nov 2001)**
- a. Hypopituitarism
 - b. Hypothyroidism
 - c. Hypophosphatasia
 - d. Rickets
- 926. Which endocrine disorder is associated with Epiphyseal dysgenesis? (DNB-2002; AI 2003; Manipal 2003; JIPMER 2003)**
- a. Hypothyroidism
 - b. Cushing's syndrome
 - c. Addison's disease
 - d. Hypoparathyroidism
- 927. Which is not demonstrable in Cushing's syndrome? (AIIMS 1990)**
- a. Osteosclerosis
 - b. Abnormal callus formation
 - c. Osteoporosis
 - d. Pathological fractures

928. All the following are correct statements about radiological evaluation of a patient with Cushing's syndrome except: (AI 2002)

- a. Adrenal CT scan distinguishes adrenal cortical hyperplasia from an adrenal tumor
- b. MRI of the adrenals may distinguish adrenal adenoma from carcinoma
- c. MRI of the sella turcica will identify a pituitary cause for Cushing's syndrome
- d. Petrosal sinus sampling is the best way to distinguish a pituitary tumor from an ectopic ACTH-producing tumor.

929. In a patient with ectopic kidney the ADRENAL would mostly be located: (JIPMER 2003)

- a. In the pelvis
- b. In normal position
- c. On opposite side
- d. Behind liver or spleen

930. Adrenal gland enlargement is best diagnosed by: (PGI 1986)

- a. Plain X-ray
- b. CT Scan
- c. Retrograde pyelography
- d. IVP

931. Most common cause of secondaries in adrenals is from (AI 2000)

- a. Carcinoma breast
- b. Carcinoma lung
- c. Carcinoma Kidney
- d. Carcinoma Stomach

932. Which one of the following imaging modalities is most sensitive for evaluating a patient of extraadrenal pheochromocytoma? (AIIMS 2002 Nov; AIIMS may 2003)

- a. USG
- b. CT
- c. MRI
- d. MIBG scan

933. In the diagnosis of pheochromocytoma which of the following radionuclide scans is useful? (KAR 2001)

- a. MIBG scan
- b. MIDA scan
- c. DTPA scan
- d. DMSA scan

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- 934. MIBG scan is specifically used for diagnosis of: (CMC Vellore 2001)**
- a. Adrenal tumors
 - b. Pancreatic tumors
 - c. Parathyroid tumors
 - d. Thyroid tumors
 - e. Gallbladder tumor
- 935. Investigation of choice for neuroendocrinal tumors is: (AIIMS Nov 2001)**
- a. MRI
 - b. PET scan
 - c. CECT
 - d. Radionuclide scan
- 936. In secondaries of thyroid, primary is usually in: (Delhi 2002)**
- a. Breast
 - b. Lung
 - c. Kidney
 - d. Esophagus
- 937. FSH is secreted by: (PGI 2001)**
- a. Anterior adenohypophysis
 - b. Posterior adenohypophysis
 - c. Both
 - d. None
- 938. Multi-nodular goiter (MNG) secondary thyrotoxicosis is seen how much percentage of patient with MNG: (MP 2003)**
- a. 10 %
 - b. 20 %
 - c. 30 %
 - d. 40 %
- 939. Conditions associated with an increased urinary sodium concentration is/are: (PGI 91)**
- a. Diuretic therapy
 - b. Chronic Liver diseases
 - c. Adrenal insufficiency
 - d. SIADH
- 940. MEN 2A includes all the following EXCEPT: (Delhi 98)**
- a. Parathyroid adenoma
 - b. Pancreatic Islet Cell Tumors
 - c. Gastrinoma
 - d. Medullary Thyroid Carcinoma

- 941. Which of the following clinical condition may improve with pregnancy? (Maharashtra 2006)**
- Ulcerative colitis
 - Myasthenia gravis
 - Multiple sclerosis
 - Systemic lupus erythematosus
- 942. The first and the most important medication to be given in a patient of thyroid storm:**
- Methimazole
 - Propylthiouracil
 - Beta-blocker
 - Corticosteroids
- 943. Which of the following channelopathies is associated with calcium channel disorder of muscles?**
- Hypokalemic periodic paralysis
 - Episodic ataxia type 1
 - Hyperkalemic periodic paralysis
 - Paralysis Spinocerebellar ataxia 1
- 944. Hypothalamopituitary axis becomes active and functional at: (DNB 90)**
- 20th week of gestation
 - 5th year of life
 - 5th week of life
 - 5th month of life
- 945. Diffuse form of hyperpigmentation is seen in: (Maharashtra 2006)**
- Vitamin B12 deficiency
 - Ectopic ACTH secretion
 - Whipple's disease
 - All of the above
- 946. I-131 is used in the treatment of Grave's disease in the dose of:**
- 5-15 mCi
 - 15-20 mCi
 - 20-40 mCi
 - 40-60 mCi
- 947. Pancreatitis, pituitary tumor and pheochromocytoma may be associated with: (AIIM'S 2000 Dec)**
- Medullary carcinoma thyroid
 - Papillary carcinoma thyroid
 - Anaplastic carcinoma thyroid
 - Follicular carcinoma thyroid

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948. Fibrinoid necrosis may be observed in all of the following, except:

- a. Malignant hypertension
- b. Polyarteritis nodosa
- c. Diabetic glomerulosclerosis
- d. Aschoff's nodule

949. About Conn's syndrome, true is/are: (PGI 89)

- a. Is due to secondary hyperaldosteronism
- b. Can result in hypokalaemia
- c. Can result in a metabolic alkalosis
- d. Is most often due to an adrenal adenoma
- e. Can cause severe hypotension

950. A newly diagnosed type 2 diabetic patient asks for clarification about dietary management. Which of the following is correct advice?

- a. Restrict carbohydrates and eat a high-protein diet
- b. Avoid sucrose altogether
- c. Caloric intake should be very consistent from one day to another
- d. Less than 10% of caloric intake should be saturated fat

951. A 50-year-old female is evaluated for hypertension. Her blood pressure is 130/98. She complains of polyuria and of mild muscle weakness. She is on no diuretics or other blood pressure medication. On physical exam, the PMI is displaced to the sixth intercostal space. There is no sign of congestive heart failure and no edema. Laboratory values are as follows:

Na⁻: 147 meq/dL

K⁻: 2.3 meq/dL

Cl⁻: 112 meq/dL

HCO₃⁻: 27 meq/dL

The patient is on no other medication. The first step in diagnosis is:

- a. 24-h urine for cortisol
- b. Urinary metanephrine
- c. Plasma renin and aldosterone
- d. Renal angiogram

952. A 30-year-old woman is found to have a low serum thyroxine level after being evaluated for fatigue. Five years ago she was treated for Graves' disease with radioactive iodine. The diagnostic test of choice is:

- a. Serum TSH
- b. Serum T₃
- c. TRH stimulation test
- d. Radioactive iodine uptake

- 953. A 25-year-old woman is admitted for hypertensive crisis. In the hospital, blood pressure is labile and responds poorly to antihypertensive therapy. The patient complains of palpitations and apprehension. Her past medical history shows that she developed hypotension during an operation for appendicitis.**
Hematocrit: 49% (37–48)
ESR: 103 mm (4.3–10.8)
Plasma glucose: 160 mg/dL (75–115)
Plasma calcium: 11 mg/dL (9–10.5)
The most likely diagnosis is:
- Pheochromocytoma
 - Renal artery stenosis
 - Essential hypertension
 - Insulin-dependent diabetes mellitus
- 954. A 60-year-old woman comes to the emergency room in a coma. The patient's temperature is 90°F. She has bradycardia. Her thyroid gland is enlarged. There is bilateral hyporeflexia. The next step in management should be:**
- T4, TSH level assay only
 - Obtain T4, TSH; begin thyroid hormone and glucocorticoid
 - Begin rapid rewarming
 - CT scan of the head
- 955. A 19-year-old with insulin-dependent diabetes mellitus is taking 30 units of NPH insulin each morning and 15 units at night. Because of persistent morning glycosuria with some ketonuria, the evening dose is increased to 20 units. This worsens the morning glycosuria, and now moderate ketones are noted in urine. The patient complains of sweats and headaches at night. The next step in management should be:**
- Increase the evening dose of insulin
 - Increase the morning dose of insulin
 - Switch from human NPH to pork insulin
 - Obtain blood sugar levels between 2:00 and 5:00 A.M.
- 956. The Features of acromegaly is/are: (PGI 90)**
- Reduced heel pad thickness
 - Prognathism
 - Bitemporal hemianopsia
 - Intervertebral disc calcification
 - AV malformations in bone
- 957. Features of SIADH are all except: (Orissa 99)**
- Hyponatremia
 - Hypovolemia
 - Concentrated urine
 - None

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958. Which of the following is not true regarding Klinefelter syndrome? (AP 2004)

- a. XXY karyotype
- b. Infertility
- c. Small stature
- d. Gynecomastia

959. Iron overload is not seen in: (TN 1994)

- a. Alcoholic cirrhosis
- b. Hemochromatosis
- c. Alpha-1-antitrypsin deficiency
- d. Repeated blood transfusions

960. A 52-year-old man complains of impotence. On physical examination, he has an elevated jugular venous pressure, S₃ gallop, and hepatomegaly. He also appears tanned, with pigmentation along joint folds. His left knee is swollen and tender. He has hyperglycemia, and his liver enzymes are elevated. Next study to establish the diagnosis should be: (Kerala 94)

- a. Detection of nocturnal penile tumescence
- b. Determination of iron saturation
- c. Determination of serum copper
- d. Detection of hepatitis B surface antigen
- e. Echocardiography

961. The use of repeated phlebotomy in the treatment of persons with symptomatic hemochromatosis may result in:

- a. Increased skin pigmentation
- b. Improved cardiac function
- c. Return of secondary sex characteristics
- d. Decreased joint pain

962. 55-year-old woman who has a history of severe depression and who had radical mastectomy for carcinoma of the breast 1 year previously develops polyuria, nocturia, and excessive thirst. Laboratory values are as follows: (SGPGI 95)

Serum electrolytes: Na- 149 meq/L; K- 3.6 meq/L

Serum calcium: 9.5 mg/dL

Blood glucose: 110 mg/dL

Blood urea nitrogen: 30 mg/dL

Urine osmolality: 150 mOsm/kg

The most likely diagnosis is

- a. Psychogenic polydipsia
- b. Renal glycosuria
- c. Inappropriate antidiuretic hormone syndrome
- d. Diabetes insipidus

- 963. Maturity-onset diabetes of the young (MODY) is inherited as: (Bihar 2005)**
- Autosomal dominant disease
 - Autosomal recessive disease
 - X-linked dominant disease
 - X-linked recessive disease
- 964. Which of the following studies is most sensitive for detecting diabetic nephropathy? (MP 98)**
- Ultrasonography
 - Glucose tolerance test
 - Urine albumin
 - Serum creatinine level
- 965. A 30-year-old nursing student presents with confusion, sweating, hunger, and fatigue. Blood sugar is noted to be 40 mg/dL. The patient has no history of diabetes mellitus, although her sister is an insulin-dependent diabetic. The patient has had several similar episodes over the past year, all occurring just prior to reporting for work in the early morning. On this evaluation, the patient is found to have high insulin levels and a low C peptide level. The most likely diagnosis is:**
- Reactive hypoglycemia
 - Early diabetes mellitus
 - Factitious hypoglycemia
 - Insulinoma
- 966. Which of the following inhibits growth hormone secretion from the anterior pituitary gland? (JIPMER 97)**
- Somatostatin
 - Growth hormone-releasing hormone (GHRH)
 - Hypoglycemia
 - All
- 967. Insulin receptors are: (ROHTAK 98)**
- Tyrosine kinase receptors
 - Phosphodiesterase
 - Calcium- calmodulin
 - All
- 968. In terms of chemical structure, which one of the following is a tetrameric glycoprotein? (UPSC 97)**
- Insulin receptors
 - Leptins
 - Neuropeptide
 - Thyrotrophin

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969. The McCune-Albright syndrome is characterized by: (CUPGEE 2000)

- a. Cutaneous hypopigmentation, polyostotic fibrous dysplasia, and menorrhagia
- b. Cutaneous hyperpigmentation, polyostotic fibrous dysplasia, and precocious puberty
- c. Hypogonadotropic hypogonadism, precocious puberty and multiple exostosis
- d. Pseudohermaphroditism, toxic multinodular goiter and multicystic ovaries

970. Drugs that can precipitate acute attack of porphyria are all EXCEPT: (Manipal 98)

- a. Sulfonamides
- b. Alcohol
- c. Phenytoin
- d. Phenothiazines

971. A 54-year-old obese female presented with giddiness. Her fasting blood serum glucose was 220-250 mg/dL, repeated several times. She underwent a diet and exercise program, but after 6 months, she was able to decrease his weight only 5 kg. There was no significant change in his fasting serum glucose level. A test for thyroid function was normal. A fasting cholesterol level was 290 mg/dL, with low-density lipoprotein (LDL) cholesterol of 190 mg/dL. Her renal and hepatic functions are within normal limits. Which of the following oral anti-diabetic agents would be best for her?

- a. Metformin
- b. Glipizide
- c. Repaglinide
- d. Acarbose

972. A 20-year-old woman has a history of multiple fractures since childhood, kyphoscoliosis, bluish-gray teeth, and conductive hearing loss. Examination of the face reveals blue sclerae. Several relatives on her mother's side have been similarly affected. She has no history of physical abuse or abnormal serum chemistries. The most likely mechanism of the patient's disease is:

- a. Mutation in the gene for type III procollagen
- b. Inability to convert procollagen to collagen
- c. Mutation in the gene for type I procollagen
- d. Mutation in the gene for type II procollagen

Endocrinology

Answers

924. Ans. d (Cortisone)

(Ref. Harrison Medicine 15th ed. 2178; Nelson's Paediatrics 7th ed. 1912)

Congenital adrenal hyperplasia (CAH)

Features	3-Beta-OH	21-OH	11-Beta-OH	17-alpha-OH
1. Salt loss	+	+	-	-
2. Hypertension	-	-	+	+
3. Virilization	-	+	+	-
4. Ambiguous Genitalia				
a) Male	+	-	-	+
b) Female	+	+	+	-

Note: 21-hydroxylase deficiency is the most common type of CAH. Treatment:

A. During pregnancy:

Recommendations for pregnancies at risk consist of administration of dexamethasone (readily crosses the placenta); 20 microgm/kg pre-pregnancy maternal weight daily 2-3 divided doses.

This suppresses steroid selection by fetal adrenal, including secretion of adrenal and androgens.

If started by 6wk of gestation, it ameliorates virilization of external genital in affected females. (CVS are performed to determine sex and genotype of fetus; therapy is continued only if fetus is affected female).

B. After delivery:

o Hydrocortisone is used to treat these babies.

o **Thus, treatment for a case of virilising adrenal hyperplasia is cortisone.**

925. Ans: b (Hypothyroidism)

(Ref. Grainger's Diagnostic Radiology, 4th Ed., 1369, 1950, 1963)

Childhood hypothyroidism (cretinism) is characterized by:

- Delayed skeletal maturation
- Delayed dentition
- Delayed pneumatization of sinuses/mastoids
- Demineralization

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- Dense vertebral margins with bullet shaped vertebrae
- Delayed closure/open wide fontanels/sutures
- Fragmented stippled epiphyses
- Hypoplastic phalanges of 5th finger
- Hypertelorism
- Wormian skull bones

Adulthood hypothyroidism

- Calvarial thickening/sclerosis
- Coxa vara with flattened femoral head
- Wedging of dorsolumbar vertebral bodies
- Premature atherosclerosis

926. Ans: a (Hypothyroidism)

(Ref. O.P. Ghai Paediatrics, 4th ed., 371)

Features of childhood hypothyroidism (cretinism)

- Delayed skeletal maturation
- Fragmented stippled epiphyses, i.e., Epiphyseal dysgenesis
- Delayed dentition
- Delayed/decreased pneumatization of sinuses and mastoids
- Dense vertebral margins
- Demineralization
- Hypertelorism
- Hypoplastic phalanges of 5th finger
- Wide fontanels/sutures with delayed closure

Features of adulthood hypothyroidism

- Calvarial thickening/sclerosis
- Wedging of dorsolumbar vertebrae
- Coxa vara with flattened femoral head
- No skeletal changes with adult onset

927. Ans. a (Osteosclerosis)

(Ref. Grainger diagnostic radiology 4th ed. 1930)

Cushing's disease

Common findings:

- o Generalized osteopenia (fish vertebrae, wedge and compression fractures, insufficiency fractures in pelvis, mottled appearance of skull)
- o Exuberant callus formation
- o Osteonecrosis

Uncommon findings:

- o Joints infections
- o Neuropathic-like joints
- o Delayed skeletal maturation
- o Decreased osteophyte formation
- o Tendon rupture

928. Ans: c (MRI of the sella turcica will identify a pituitary cause for Cushing's syndrome)

(Ref. *CT and MR Imaging of Whole Body* by Hagga 4th ed. 1517; *Anne Osborn Neuroradiology*, 642)

Imaging of Adrenals

- 1) The initial imaging of the adrenal glands is usually performed with CT due to its superior spatial resolution and the ability to perform routine thin slice imaging.
- 2) Adrenal adenomas contain a large amount of lipid-laden cells, giving them a characteristic low density (fat density) appearance on CT scans.
- 3) The radiologic findings of adrenal carcinoma show a large mass that usually envelops much of the area surrounding the involved adrenal gland. Most masses show degenerative and cystic changes, and 33% show calcification. CT and MRI findings thus reflect these pathologic changes that occur within these tumors. CECT shows vascularity in certain areas. With MRI, masses show low signal intensity on T1-weighted images and higher signal intensity on T2-weighted images when compared with liver. Signal intensity generally increases on opposed-phase chemical shift imaging. When CT or MRI is performed, tumors should also be staged.
- 4) Adrenal gland hyperplasia secondary to pituitary or ectopic causes of Cushing's syndrome can have several imaging appearances. The most common pattern of it is diffuse bilateral enlargement without a focal mass. MRI has a secondary role in evaluation of patients with Cushing's syndrome because CT can better evaluate smaller adrenal masses. MRI signal intensity seen in adrenal hyperplasia closely follows that of the normal adrenal gland, rendering MRI less sensitive than CT in evaluating adrenal gland hyperplasia.
- 5) In some cases of Cushing's syndrome secondary to hyperplasia, when evaluation of the pituitary gland does not reveal an adenoma, petrosal venous sampling may be valuable in determining the cause finally.
- 6) 2/3rd of microadenomas of pituitary gland typically appear hypodense on dynamic, rapid sequence CECT scans, 1/3rd show "early" enhancement. Macroadenomas of pituitary gland have a variable appearance. Microadenomas are sometimes difficult to detect by MRI unless dynamic techniques are used. Macroadenomas typically parallel gray matter signal on all MR imaging sequences. Benign invasive adenomas cannot be distinguished from the rare pituitary carcinoma on imaging studies above. Microadenomas are less than 10 mm and Macroadenomas are of more than 10 mm size.

929. Ans. b (In normal position)

(Ref. Grainger radiology 4th ed. 1722)

In a patient with ectopic kidney the adrenal would mostly be located in normal position.

930. Ans. b (CT Scan)

(Ref. Sutton Radiology 7th ed. 1307)

Normal adrenals are best seen on CECT. The initial imaging of the adrenal glands is usually performed with CT due to its superior spatial resolution and the ability to perform routine thin slice imaging.

931. Ans. b (Carcinoma lung)

The adrenals are commonly involved in patients with lung and breast carcinoma on one or both sides by metastases.

Although with adrenal metastases, the primary is usually in lung and breast, melanoma, renal and gastrointestinal secondaries and secondary lymphomatous involvement are well known.

932. Ans: d (MIBG scan)

Ref. (CT and MR Imaging of Whole Body by 'Hagga 4th ed. 1520)

Pheochromocytoma

CT has been the primary method of diagnosis for intraadrenal pheochromocytoma. The accuracy of CT in detecting intraadrenal pheochromocytomas is nearly 100%. It is 93–100% sensitive for adrenal ones. MRI is also excellent for evaluating intraadrenal pheochromocytomas as these are generally larger than 5 cm size and the poorer spatial resolution of MRI is usually not a problem. Even a percentage of adrenal metastases have overlapping imaging findings. MIBG scanning can play a complementary role in evaluating intraadrenal pheochromocytomas. It is 80–90% sensitive for adrenal one.

MIBG scintigraphy is extremely valuable in imaging of extraadrenal and recurrent pheochromocytomas. MIBG is a precursor of catecholamines and therefore, is actively taken up in catecholamines producing tissues. After recurrent, metastatic or extraadrenal lesions are sensitively discovered initially via whole body MIBG scanning, CT or MRI can then be performed for more accurate specific anatomic localization of lesion to be resected.

933. Ans: a (MIBG scan)

(Ref. CT and MR Imaging of Whole Body by Hagga 4th ed. 1520)

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934. Ans. a (Adrenal tumors)

MIBG scan → Adrenal tumors and extraadrenal pheochromocytomas
 Neuroendocrine tumors of pancreas → Tc octreotide scan
 Parathyroid tumors → Sestamibi scan
 Thyroid tumors → MCT → Tc DMSA scan

935. Ans: d (Radionuclide scan)

(Ref. Sutton's textbook of diagnostic radiology-6th Ed. 660)

Neoplasms of neuroendocrine origin include:

- o Pancreatic islet cell tumors
- o Carcinoids
- o Vipomas
- o Apudomas
- o Some pituitary adenomas
- o Medullary thyroid cancers
- o Pheochromocytomas
- o Neuroblastomas
- o Paragangliomas

Radionuclide scan (somatostatin receptor scintigraphy and MIBG scan) have major role in localization of pancreatic islet cell tumors and their metastases and also investigation of gastrointestinal carcinoids, apudomas and related neuroendocrine tumors and their metastases.

936. Ans: c (Kidney)

(Ref. to Diagnostic Radiology by Grainger, 4th ed., 1376)

Metastatic tumor in thyroid is from renal cancer. Other cancers, which are known to metastasize to thyroid are melanoma and bronchogenic carcinoma.

937. Ans. a (Anterior adenohypophysis)

PITUITARY HORMONES

Name and source	Principal actions
Anterior lobe: (Hint—FLAT GP ML)	
1. Follicle-stimulating hormone (FSH)	Stimulates ovarian follicle growth in female & spermatogenesis in male
2. Luteinizing hormone (LH)	Stimulates ovulation and luteinization of ovarian follicles in female and testosterone secretion in male
3. Adrenocorticotrophic hormone (ACTH, corticotropin)	Stimulates secretion and growth of zona fasciculata and zona reticularis of adrenal cortex.
4. Thyroid-stimulating hormone (TSH, thyrotropin)	Stimulates thyroid secretion and growth of thyroid gland.

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5. Growth hormone (GH, somatotropin)	Accelerates body growth, stimulates secretion of IGF-1
6. Prolactin (PRL)	Stimulates secretion of milk and maternal behaviour
7. Melanocyte -stimulating hormone (MSH)	Stimulates melanin synthesis in melanocytes.
8. Lipotropin (LPH)	Secretes MSH and lipotropin

Intermediate lobe:**Posterior lobe:**

1. Vasopressin (Antidiuretic hormone, ADH)	Promotes water retention
2. Oxytocin	Causes milk ejection, contraction of pregnant uterus.

938. Ans. c (30 %)

(Ref. Bailey and Love 23rd ed. 715)

Many patients with nodular goiters experience transient episodes of mild hyperthyroidism, the incidence of which is difficult to estimate, but figures **as high as 30%** have been suggested.

Carcinoma, usually of **follicular type** may uncommonly develop in a nodular goiter.

939. Ans. a, c, d

ADH is a polypeptide synthesized in the supraoptic and paraventricular nuclei in the hypothalamus and is released in response to a number of stimuli. ADH is rapidly metabolized in the liver and kidneys and has a half-life of 15-20 minutes. In the kidneys, ADH acts on the principal cells of the cortical and medullary collecting tubules to increase water permeability. Other renal actions include local production of prostaglandins in a variety of renal cells, including the glomerulus and the thick ascending limb of the loop of Henle. Elsewhere, ADH causes vasoconstriction in a number of vascular beds and releases factor VIII and von Willebrand factor from vascular endothelium.

The major stimuli to ADH are hyperosmolality and effective circulating volume depletion. Normally, ADH secretion ceases when plasma osmolality falls below 275 mOsm/kg. This fall causes increased water excretion, which leads to a dilute urine with an osmolality of 40-100 mOsm/kg. In addition to the hypothalamic osmoreceptors, hypothalamic neurons secreting ADH also receive input from baroreceptors in the great vessels and the atria. This results in nonosmotic release of ADH. Other stimuli for ADH secretion include pain and nausea.

In general, the plasma sodium concentration is the primary osmotic determinant of ADH release. However, in persons with SIADH, a nonphysiologic secretion of ADH results in enhanced water reabsorption, leading to dilutional hyponatremia.

In addition to the inappropriate ADH secretion, persons with this syndrome also may have an inappropriate thirst sensation, which leads to an intake of water that is in excess of the free water excreted. This increase in water ingested may then contribute to the maintenance of hyponatremia.

Lab Studies for SIADH:

Hyponatremia combined with high serum osmolality: This indicates the presence of an osmotically active substance such as mannitol or an elevated blood glucose concentration.

Hyponatremia with normal serum osmolality: This indicates pseudohyponatremia.

Hyponatremia with serum hypoosmolality: If urine osmolality is higher than plasma osmolality, this finding excludes primary polydipsia and reset osmostat. In both these conditions, the body is able to appropriately dilute the urine to rid itself of excess free water.

In persons with SIADH, serum osmolality is generally lower than urine osmolality. In the setting of serum hypoosmolality, ADH secretion is usually suppressed to allow the excess water to be excreted, thus moving the plasma osmolality toward normal. **If ADH secretion is shut down completely, urine should have an osmolality of less than 100 mOsm.** Therefore, urine osmolality of more than 100 mOsm in the context of plasma hypoosmolality is sufficient to confirm the diagnosis of SIADH, although classic SIADH is associated with urine osmolality greater than the serum osmolality. Inappropriate water retention causes the dilutional hyponatremia.

Urine sodium concentration in persons with SIADH is usually more than 40 mEq/L because, in SIADH, sodium handling is not abnormal and the urine sodium concentration reflects sodium intake, which is generally more than 40 mEq per day (usually 50-100 mEq/d). However, the urine sodium concentration in persons with SIADH can be modulated by dietary sodium intake. On a low-sodium diet, patients with SIADH may have a urine sodium level of less than 40 mEq/L. Other conditions associated with an increased urinary sodium concentration include reset osmostat, renal sodium-wasting conditions (e.g., diuretic therapy), renal disease, and adrenal insufficiency.

940. Ans. d (Medullary Thyroid Carcinoma)

(Ref. Harrison's Principles of Medicine 16th ed. 2231, 2234)

Multiple endocrine neoplasia syndromes

MEN 1 Syndrome (Wermer's Syndrome)

- o Hyperparathyroidism 90%
- o Pancreatic Islet Cell Tumors 60%
- o Gastrinoma 60%
- o Insulinoma 10%
- o Vipoma
- o PPoma
- o Glucagonoma
- o Pituitary Tumors 5%
- o Prolactinoma
- o GH, ACTH, TSH secreting tumours
- o Thyroid adenoma
- o Adrenal adenoma
- o Carcinoid tumours

MEN 2a Syndrome (Sipple's Syndrome)

- o Medullary Thyroid Carcinoma 100%
- o Pheochromocytoma 50%
- o Hyperparathyroidism 10%

MEN 2b Syndrome

- o Medullary Thyroid Carcinoma 100%
- o Pheochromocytoma 50%
- o Multiple mucosal neuromas 100%
- o Ganglioneuromatosis of the gut 100%
- o Marfanoid appearance 100%>

941. Ans. d (Systemic lupus erythematosus)

(Ref. Harrison medicine 15th ed. 1256, 1257; 16th ed. 34, 1966; 36, 2466)

Pregnancy and Lupus

Female gender is permissive for SLE; females of many mammalian species make higher antibody response than males. Women exposed to estrogen-containing OCP or HRT have an increased risk of developing SLE (twofold). Estradiol binds to receptors on T and B cells, thus favouring prolonged immune response.

In past, SLE was considered to be a contraindication to pregnancy. With improved understanding of the effects of SLE on pregnancy, and vice versa, and improved pharmacologic methods of managing SLE, successful pregnancy outcome is likely. Previously a point of controversy, there is now increasing consensus that pregnancy and the postpartum period are times of increased lupus activity.

Currently, 50 percent of all lupus pregnancies are completely normal, and 25 percent deliver normal babies prematurely. Fetal loss, due to spontaneous abortion (miscarriage), or death of the baby

accounts for the remaining 25 percent. While not all of the problems of pregnancy with lupus have been solved, pregnancies are possible, and normal children are the rule.

While it is certainly possible for lupus patients to have children, pregnancy may not be easy. It is important to note that although many lupus pregnancies will be completely normal, all lupus pregnancies should be considered "high risk." "High risk" is a term commonly used by obstetricians to indicate that solvable problems may occur and must be anticipated. Pregnant lupus patients should be managed by obstetricians who are thoroughly familiar with high risk pregnancies and work in close concert with the woman's primary physician. Delivery should be planned at a hospital that has access to a unit specializing in the care of premature newborns. SLE mothers should not attempt home delivery, or be overly committed to "natural" childbirth, since treatable complications during delivery are frequent. However, under close observation, the risk to the mother's health is lessened, and healthy babies can be born.

Although older medical texts suggest that SLE flares are common in pregnancy, recent studies indicate that flares are uncommon and are usually easily treated. **In fact, 6-15 percent of lupus patients will actually experience an improvement in lupus symptoms during pregnancy.** Flares most often occur during the first or second trimester, or during the two months immediately after delivery. Most of the flares tend to be mild. The most common symptoms of these flares are arthritis, rashes and fatigue. Approximately 33 percent of lupus patients will have a decrease in platelet count during pregnancy, and about 20 percent will have an increase in or new occurrence of protein in the urine.

Women who conceive after 5-6 months of remission are less likely to experience a lupus flare than those who get pregnant while their lupus is active. Lupus nephritis before conception also increases the chance of experiencing a lupus flare during pregnancy.

About 20 percent of lupus patients will have a sudden increase in blood pressure, protein in the urine, or both during pregnancy. This is called toxemia of pregnancy (or pre-eclampsia, or pregnancy-induced hypertension). It is a serious condition, and will require immediate treatment and usually immediate delivery.

About 33 percent of lupus patients have antibodies that interfere with the function of the placenta **called antiphospholipid antibodies, the lupus anticoagulant or anti-cardiolipin antibodies.** These antibodies may cause blood clots, including blood clots in the placenta, which prevent the placenta from growing and functioning normally. This usually occurs during the second trimester. Since the placenta is the passageway for nourishment from the mother to the baby, the baby's growth slows. The baby can be delivered at this time and will be normal if it is big enough.

Treatment for lupus patients who have these antibodies is still being tested. Aspirin, Prednisone, Heparin and plasmapheresis have all been suggested as possible therapies. However, even with the use of such medications, these antibodies may still lead to miscarriage.

About 33 percent of lupus patients have an antibody known as **anti-Ro or anti-SSA antibody**. About 10 percent of women with Anti-Ro antibodies, or about 3 percent of all lupus women, will have a baby with a syndrome known as neonatal lupus. Neonatal lupus is not SLE. **Neonatal lupus consists of a triad of** transient rash, transient blood count abnormalities, and a special type of heart beat abnormality (complete heart block). If the heart beat abnormality occurs, which is very rare, it is treatable; but it is permanent. Neonatal lupus is the only type of congenital abnormality found in children of mothers with lupus. For babies with neonatal lupus who do not have the heart problem, there is no trace of the disease by 3-6 months of age, and it does not recur. Even babies with the heart beat abnormality problem grow normally. If a mother has had one child with neonatal lupus, there is about a 25 percent chance of having another child with the same problem.

Pregnancy with preexisting multiple sclerosis experience a gradual decrease in the risk of relapses as pregnancy progresses and, conversely, an increase in attack risk during postpartum period i.e. fewer attacks than expected during pregnancy (especially in last trimester) but more attacks than expected in the first 3 month post-partum. Beta interferons and glatiramer acetate should not be administered to pregnant MS patients, but moderate or severe relapses can be safely treated with pulse glucocorticoid therapy. Certain brain tumors, particularly pituitary adenoma, meningioma, may manifest during pregnancy due to accelerated growth, possibly driven by hormonal factors.

Ulcerative colitis is associated with disease exacerbations in first trimester and during the early postpartum period. Its medical management during pregnancy is similar to that during nonpregnant state.

942. Ans. b (Propylthiouracil)

(Ref. Harrison medicine 16th ed. 2117)

Thyroid storm/ crises

Triggering factors:

Post-operative, radioactive iodine therapy, pregnancy (during child-birth), acute iodine load, uncontrolled diabetes, trauma, acute infection, severe drug reaction, myocardial infarction

Pathophysiology:

- o There is no evidence that increased *production* of T3 or T4 causes thyroid storm.

- o Increased catecholamine receptors (increased sensitivity to catecholamines) plays a key role.
- o Decreased binding to TBG (increased free T3 or T4) may play a role
- o Thus, patients who are susceptible to thyroid storm have increased sensitivity to catecholamines; therefore, in states of stress (catecholamine excess), thyroid storm can occur.

Clinical manifestations:

- o Characterized by marked hypermetabolism and excessive adrenergic response.
- o Hyperpyrexia is the most reliable clinical finding
- o Other symptoms: flushing, sweating, tachycardia, atrial fibrillation, high pulse pressure, occasionally heart failure, CNS (marked agitation, psychosis, restlessness, delirium, coma), GI (nausea, diarrhea, jaundice)
- o Hypertension: may be present, but a normal or low BP does not rule out thyroid storm
- o Elderly patients often present atypically (apathetic thyroid storm)

Management:

All patients with thyroid storm should be managed in the ICU

Treatment includes:

- Decrease the sympathetic outflow (beta-blockers – esmolol is a great choice)
- Decrease production of thyroid hormone (PTU is anti-thyroid drug of choice); super-saturated iodine solution(SSKI) can also be used to block outflow of thyroid hormone from the thyroid gland.
- Decrease peripheral conversion of T4 T3 (PTU, beta-blockers, steroids)

943. Ans. a (Hypokalemic periodic paralysis)

(Ref. Harrison medicine 15th Edⁿ-2295, 16th ed. 2339, 2363, 2536)

1. Spinocerebellar ataxia 1 - Trinucleotide repeat (CAC) expansion in gene.
2. Episodic ataxia type 1 - K channel gene mutations.
3. Hypokalemic periodic paralysis - L-type Ca⁺⁺ channelopathy.
4. Hyperkalemic periodic paralysis - Point mutation sodium channel.
5. Malignant hyperthermia - Mutation in Ryanodine receptor gene.
6. Myotonia - Mutation in Cl⁻ channel gene.

944. Ans. a (20th week of gestation)

(Ref. Nelson's textbook of Paediatrics 17th ed. 1870)

Hypothalamic neuronal synthesize TRH by 6-8 weeks (of gestation) and TRH by 12 weeks.

Maturation of HP-thyroid axis occurs by 2nd half of gestation.
Feedback relationships by 3 months postnatally.

945. Ans. d (All of the above)

(Ref. Harrison's principles of Internal medicine 16th ed. 302)

Hyperpigmentation

It occurs when an excess of melanin, the brown pigment that produces normal skin color, forms deposits in the skin.

Types of common hyperpigmentation disorders

I. Primary cutaneous disorders

A. Localized

1. Epidermal alteration
 - a. Seborrhic keratosis
 - b. Acanthosis nigricans (obesity)
 - c. Pigmented actinic keratosis
2. Proliferation of melanocytes
 - a. Lentigo
 - b. Nevus
 - c. Melanoma
3. Increased pigment production
 - a. Ephelides (freckles)
 - b. Café au lait spots

B. Diffuse

1. Drugs

II. Systemic diseases

A. Localized

1. Epidermal alteration
 - a. Seborrhic keratosis (sign of Leser Trelat)
 - b. Acanthosis nigricans (endocrine disorders, paraneoplastic)
2. Proliferation of melanocytes
 - a. Lentigines (Peutz Jegher's syndrome, Leopard syndrome, Xeroderma pigmentosum)
 - b. Nevi (Carney complex – LAMB and NAME syndromes)
 - c. Melanoma
3. Increased pigment production
 - a. Urticaria pigmentosa
 - b. Café au lait spots (NF and McCune Albright syndrome)
4. Dermal pigmentation
 - a. Incontinenta pigmenti (stage III)
 - b. Dyskeratosis congenita

B. Diffuse

1. Endocrinopathies
 - a. Addison's disease
 - b. Nelson's syndrome
 - c. Ectopic ACTH syndrome

2. Metabolic
 - a. Porphyria cutanea tarda
 - b. Hemochromatosis
 - c. Vitamin B12, Folate deficiency
 - d. Pellagra
 - e. Malabsorption, Whipple's disease
3. Melanosis secondary to metastatic melanoma
4. Autoimmune
 - a. Biliary cirrhosis
 - b. Scleroderma
 - c. POEMS syndrome
 - d. Eosinophilia myalgia
5. Drugs and metals

946. Ans. a (5-15 mCi)

(Ref. Harrison's Principles of Medicine 16th ed. 2116)

I-131 therapy is designed to administer a sufficient radiation dose to partially destroy the thyroid parenchyma. Biologic effects of I-131 include pyknosis and necrosis of the follicular cells and, later, vascular and stromal fibrosis. The studies directed at evaluating the safety of radioiodine therapy have failed to show any significant carcinogenic, leukemogenic or teratogenic effect in doses used to treat hyperthyroidism.

Efforts to calculate an optimal dose of radioiodine that achieves euthyroidism, without a high incidence of relapse or progression to hypothyroidism, have not been successful. However following is tried:

$$\frac{\text{I-131 dose (in mCi)} \times \text{Weight of Gland (gm)} \times \text{Dose (mCi/gm)}}{\text{Uptake (\%)}}$$

A practical strategy today is to give a fixed dose based on clinical features, like the severity of thyrotoxicosis, the size of goiter, and the level of radioiodine uptake. The dose of I¹³¹ that is used for treatment of Graves' disease may range from 70 to 215 mCi/gm. However, I¹³¹ dosage generally ranges between 5 mCi to 15 mCi i.e. 185 MBq to 555 MBq.

Higher doses are associated with less relapse but will be associated with a higher incidence of hypothyroidism during the first few years following treatment. When used 85 mCi/gm (for a total thyroid dose of 7000 rads) it makes 80% of patients to a euthyroid range with 10% of patients requiring a second treatment and 10% remaining hypothyroid.

947. Ans: a (Medullary carcinoma of thyroid)

(Ref. Robbin's pathology-7th Edⁿ-1222)

MEN-1 (Wermer Syndrome)	Pituitary adenomas Parathyroid hyperplasia/adenomas Pancreatic hyperplasia/adenomas/carcinomas Adrenal cortical hyperplasia
MEN-2A (Sipple Syndrome)	Parathyroid hyperplasia Pheochromocytoma Medullary carcinoma of thyroid
MEN-2B	Pheochromocytoma Medullary carcinoma of thyroid Mucocutaneous ganglioneuromas Marfanoid habitus

948. Ans: c (Diabetic glomerulosclerosis)

(Ref. *Robbin's pathology-7th Ed*-214, 593, 990, 1007)

- The necrotic tissue and deposits of immune complexes, complement and plasma protein produce a smudgy Eosinophilic deposit that obscures the underlying cellular detail, an appearance termed fibrinoid necrosis.
- In Rheumatic Carditis, the myocardial interstitium has a circumscribed collection of mononuclear inflammatory cells, including some large histiocytes with prominent nucleoli and prominent binuclear histiocytes and central necrosis known as Aschoff bodies, the most distinctive feature.
- Systemic immune complexes diseases especially immune complex vasculitis like PAN, PSGN, serum sickness characteristically shows acute necrotizing vasculitis, with fibrinoid necrosis of vessel wall and intense neutrophilic infiltration.
- Malignant hypertension and accelerated nephrosclerosis is characterized by fibrinoid necrosis of arterioles and onion skinning of vessel walls in kidney. Diabetic glomerulosclerosis is characterized by capillary basement membrane thickening; diffuse mesangial sclerosis (**Armani Ebstein Lesions**), nodular glomerulosclerosis (**Kimmelstiel Wilson Lesions**) and fibrin caps and capsular drops.

949. Ans: b, c and d

Aldosteronism - excess secretion of aldosterone - can be:

Primary - due to primary pathology of the adrenal gland

Secondary - due to reduced plasma volume and increased angiotensin production. Secondary aldosteronism is due to cirrhosis, nephrotic syndrome or cardiac failure

Conn's syndrome

Conn's syndrome is primary hyperaldosteronism due to:

- o Aldosterone producing adrenal adenoma (50%)

- o Bilateral idiopathic adrenal hyperplasia - idiopathic hyperaldosteronism (40%)
- o Aldosterone secreting carcinoma

Pathophysiology

Aldosterone is produced by the zona glomerulosa of the adrenal cortex.

Acts on distal convoluted tubule to increase sodium reabsorption
Sodium reabsorption occurs at the expense of potassium and hydrogen ion loss

Clinical presentation

Usually occurs between 30 and 60 years

Conn's syndrome accounts for 1% of cases of hypertension

Hypertension often responds poorly to treatment

Biochemically there is usually a hypokalaemic alkalosis

NB - serum potassium may be normal

Investigation

Investigations need to:

Confirm primary hyperaldosteronism

Localise pathology

Diagnosis depend on demonstration of

Reduced serum potassium:

Increased urinary potassium excretion

Increased plasma aldosterone

CT is able to demonstrate 80% of adrenal adenomas

MRI has a similar sensitivity

Assessment of function may require isotope (NP59) scanning or renal vein sampling for aldosterone

Treatment

If adrenal adenoma demonstrated - adrenalectomy is treatment of choice

Requires preoperative spironolactone to increase serum potassium

Blood pressure returns to normal in 70% of patients

Hypertension associated with bilateral idiopathic hyperplasia is difficult to control

Spironolactone alone or with an ACE inhibitor is often useful

950. Ans. c (Caloric intake should be very consistent from one day to another)

In order to reduce plasma cholesterol and decrease the risk of vascular disease, fat intake should be moderated, with less than 10% of total caloric intake being saturated fat. Caloric distribution does not restrict or decrease carbohydrates. Use of caloric sweeteners, including sucrose, is acceptable as long as it is matched to insulin demand. Dietary protein should provide 10% to 20% of total calories. In patients with diabetic nephropathy, reducing dietary

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protein to 10% is often recommended. Caloric intake is not consistent from day to day but is matched with level of activity.

951. Ans. c (Plasma renin and aldosterone)

The patient has diastolic hypertension with associated hypokalemia. She is not taking diuretics. There is no edema on physical exam. Excessive inappropriate aldosterone production will produce a hypertension with hypokalemia syndrome. Hypersecretion of aldosterone increases distal tubular exchange of sodium for potassium with progressive depletion of body potassium. The hypertension is due to increased sodium absorption. Very low plasma renin that fails to increase with appropriate stimulus (such as volume depletion) and hypersecretion of aldosterone suggest the diagnosis of primary hyperaldosteronism. Suppressed renin activity occurs in about 25% of hypertensive patients with essential hypertension. Lack of suppression of aldosterone is also necessary to diagnose primary aldosteronism. High aldosterone levels that are not suppressed by saline loading prove that there is a primary inappropriate secretion of aldosterone. A 24-h urine for free cortisol would be used in the workup of a patient with Cushing syndrome. Urinary metanephrine is a screening test for pheochromocytoma.

952. Ans. a (Serum TSH)

TSH levels are always increased in patients with untreated hypothyroidism (from primary thyroid disease) and would be the test of choice in this patient. Serum T3 is not sensitive for hypothyroidism. The TRH stimulation test is used to assess pituitary reserve of thyroid-stimulating hormone. A decreased RAIU is of limited value because of the low value for the lower limit of normal. In goitrous hypothyroidism, the RAIU may even be increased.

953. Ans. a (Pheochromocytoma)

A hypertensive crisis in this young woman suggests a secondary cause of hypertension. In the setting of palpitations, apprehension, and hyperglycemia, pheochromocytoma should be considered. Pheochromocytomas are derived from the adrenal medulla. They are capable of producing and secreting catecholamines. Unexplained hypotension associated with surgery or trauma may also suggest the disease. Clinical symptoms are the result of catecholamine secretion. For example, the patient's hyperglycemia is a result of a catecholamine effect of insulin suppression and stimulation of hepatic glucose output. Hypercalcemia has been attributed to ectopic secretion of parathormone-related protein. Renal artery stenosis can cause severe hypertension but would not explain the systemic symptoms or laboratory abnormalities in this case.

954. Ans. b (Obtain T4, TSH; begin thyroid hormone and glucocorticoid)

The clinical concern in this patient is myxedema coma. Myxedema coma is a medical emergency. Treatment is initiated immediately; and should the lab reports do not support the diagnosis, then treatment would be stopped. An intravenous bolus of thyroxine is given (300 to 500 mg), followed by daily intravenous doses. Glucocorticoids are given concomitantly. Intravenous fluids are also needed; rewarming should be accompanied slowly, so as not to precipitate cardiac arrhythmias. If alveolar ventilation is compromised, then intubation may also be necessary.

955. Ans. d (Obtain blood sugar levels between 2:00 and 5:00 A.M.)

Episodic hypoglycemia at night is followed by rebound hyperglycemia. This condition, called the Somogyi phenomenon, develops in response to excessive insulin administration. An adrenergic response to hypoglycemia results in increased glycogenolysis, gluconeogenesis, and diminished glucose uptake by peripheral tissues. After hypoglycemia is documented, the insulin dosages are slowly reduced.

956. Ans. b, c, d

The patient suffering from acromegaly shows excessive growth of soft tissue that results in coarsening of facial features, prognathism, and frontal bossing. This growth hormone-secreting pituitary tumor will result in bitemporal hemianopsia when the tumor impinges on the optic chiasm, which lies just above the sella turcica. Intervertebral disc calcification can occur.

957. Ans. b (Hypovolemia)

Hyponatremia, normovolemia, and concentrated urine. These features are sufficient to make a diagnosis of inappropriate antidiuretic hormone secretion. Inappropriate ADH secretion occurs, in some cases, due to ectopic production by neoplastic tissue. Treatment necessitates restriction of fluid intake. A negative water balance results in a rise in serum Na⁺ and serum osmolality and symptom improvement. This syndrome can occur as a side effect of many drugs or from carcinoma, head trauma, infections, neurologic diseases, or stroke.

958. Ans. c (Small stature)

The picture of infertility, gynecomastia, and tall stature is consistent with Klinefelter syndrome and an XXY karyotype. The patient has abnormal gonadal development with hyalinized testes that result in low testosterone levels and elevated levels of gonadotropin. Turner syndrome refers to the 45X karyotype that results in abnormal sexual development in a female.

959. Ans. c (Alpha-1-antitrypsin deficiency)

(Ref. Robbins 7th Ed. – 906, 908, 911)

Classification of Iron overload: -

I. Hereditary Haemochromatosis

II. Secondary Haemochromatosis



B. Ineffective erythropoiesis - β thalassemia
Sideroblastic anemia
Pyruvate Kinase deficiency

C. Increased oral intake of iron – African iron overload (Bantu siderosis)

D. Congenital atransferrinemia

E. Chronic alcoholic liver disease, Porphyria cutanea tarda.

960. Ans. b (Determination of iron saturation)

Iron overload should be considered among patients who present with any one or a combination of the following: hepatomegaly, weakness, pigmentation, atypical arthritis, diabetes, impotence, unexplained chronic abdominal pain, or cardiomyopathy. Excessive alcohol intake increases the diagnostic probability. Diagnostic suspicions should be particularly high when the family history is positive for similar clinical findings. The most frequent cause of iron overload is a common genetic disorder known as (idiopathic) hemochromatosis. Secondary iron storage problems can occur in a variety of anemias. The most practical screening test is the determination of serum iron, transferrin saturation, and plasma ferritin. Plasma ferritin values above 300 ng/mL in males and 200 ng/mL in females suggest increased iron stores. Genetic screening is now used to assess which patients are at risk for severe fibrosis of the liver. Definitive diagnosis can be established by liver biopsy. Determination of serum copper is needed when Wilson's disease is the probable cause of hepatic abnormalities. The clinical picture here is inconsistent with that diagnosis. Nocturnal penile tumescence and echocardiogram can confirm clinical findings but will not help to establish the diagnosis.

961. Ans. b (Improved cardiac function)

In persons with symptomatic hemochromatosis, repeated phlebotomy, by removing excessive iron stores, results in marked clinical improvement. Specifically, the liver and spleen decrease in size, liver function improves, cardiac failure is reversed, and skin pigmentation ("bronzing") diminishes. Carbohydrate intolerance may abate in up to half of all affected persons. For unknown reasons, there is no improvement in the arthropathy or hypogonadism (resulting from pituitary deposition of iron) associated with hemochromatosis. The 5-year survival rate increases from 33 to 90% with treatment; prolonged survival may actually increase the risk of hepatocellular carcinoma, which affects one-third of persons treated for hemochromatosis. However, if phlebotomy is begun in the precirrhotic stage, which is possible with effective genetic screening, liver cancer will not develop.

962. Ans. d (Diabetes insipidus)

Metastatic tumors rarely cause diabetes insipidus, but of the tumors that may cause it, carcinoma of the breast is by far the most common. In this patient, the diagnosis of diabetes insipidus is suggested by hypernatremia and low urine osmolality. Psychogenic polydipsia is an unlikely diagnosis since serum sodium is usually mildly reduced in this condition. Renal glycosuria would be expected to induce a higher urine osmolality than this patient has because of the osmotic effect of glucose. While nephrocalcinosis secondary to hypercalcemia may produce polyuria, hypercalciuria does not. Finally, the findings of inappropriate antidiuretic hormone syndrome are the opposite of those observed in diabetes insipidus.

963. Ans. a (Autosomal dominant)

Although non-insulin-dependent diabetes mellitus disease (nonketogenic) is familial, the exact mode of inheritance is not known except for the specific variant known as maturity-onset diabetes of the young (MODY), which is manifested by mild hyperglycemia without ketosis. On the basis of family studies, this disease is inherited in an autosomal dominant fashion with almost complete penetrance. Therefore, 50% of the children of a diabetic parent with MODY will develop the disease. There is linkage between MODY and mutations in the glucokinase gene on the short arm of chromosome 7. This abnormality is not present in ordinary nonketotic diabetics. Unlike the case in insulin-dependent diabetes, no HLA relationships have been identified. Moreover, an autoimmune etiology for the disease is not felt to be important; this is also a distinctive feature compared with typical juvenile-onset insulin-dependent diabetes.

964. Ans. c (Urine albumin)

Nephropathy is leading cause of death in diabetic patients. Diabetic nephropathy may be functionally silent for 10 to 15 years. Clinically detectable diabetic nephropathy begins with the development of microalbuminuria (30 to 300 mg of albumin per 24 h). The glomerular filtration rate actually may be elevated at this stage. Only after the passage of additional time will the proteinuria be overt enough (0.5 g/L) to be detectable on standard urine dipsticks. Microalbuminuria precedes nephropathy in patients with both non-insulin-dependent and insulin-dependent diabetes. An increase in kidney size also may accompany the initial hyperfiltration stage. Once the proteinuria becomes significant enough to be detected by dipstick, a steady decline in renal function occurs, with the glomerular filtration rate falling an average of 1 mL per minute per month. Therefore, azotemia begins about 12 years after the diagnosis of diabetes. Hypertension clearly is an exacerbating factor for diabetic nephropathy.

965. Ans. c (Factitious hypoglycemia)

This clinical picture and laboratory results suggest factitious hypoglycemia caused by self-administration of insulin. The diagnosis should be suspected in health care workers, patients or family members with diabetes, and others who have a history of malingering. Patients present with symptoms of hypoglycemia and low plasma glucose levels. Insulin levels will be high, but without a concomitant rise in C peptide. Endogenous hyperinsulinism, such as would be seen with an insulinoma, would result in elevated plasma insulin concentrations (>36 pmol/L) and elevated C peptide levels (>0.2 mmol/L).

C peptide is derived from the breakdown of proinsulin, which is produced endogenously; thus C peptide will not rise in the patient who develops hypoglycemia from exogenous insulin. Reactive hypoglycemia occurs after meals and is self-limited. A rapid postprandial rise in glucose may induce a brisk insulin response that causes transient hypoglycemia hours later. It may be associated with gastric or intestinal surgery.

966. Ans. a (Somatostatin)

Growth hormone, also known as somatotropin, is secreted by somatotroph cells, which account for 50% of the anterior pituitary glands. The release of growth hormone from the anterior pituitary is pulsatile in nature, increasing after meals, with exercise, and during slow-wave sleep. Growth hormone, which is necessary for normal growth, exerts its effects through mediators such as somatomedins and insulin-like growth factors. In addition to its involvement in growth, somatotropin is involved in stimulating the

incorporation of amino acids into protein and inhibiting glucose uptake by tissues. By the latter effect, growth hormone helps restore low blood sugars to normal and is therefore a counterregulatory hormone to insulin. Both hypoglycemia and insulin stimulate growth hormone release, as does the presence of free amino acids such as arginine. Hypothalamic secretagogues also control growth hormone release. These molecules include the stimulatory hormone GHRH and the inhibitory hormone somatostatin (somatotropin release-inhibitory factor). The former is probably more important, since sectioning of the pathways between the hypothalamus and the anterior pituitary results in inhibition of growth hormone release. Other neurotransmitters influence growth hormone release, including hypothalamus-derived dopamine, which stimulates GHRH. -Adrenergic agonists stimulate growth hormone release, and -adrenergic blockers inhibit growth hormone increases. Serotonin agonists stimulate growth hormone release; this perhaps accounts for the nocturnal surge in growth hormone secretion.

967. Ans. a (Tyrosine kinase receptors)

(Ref. Ganong 18th Ed. - 317)

Insulin Receptor:

Mol. Wt. – 340,000

Tetramers (2 α and 2 β glycoprotein subunits)

The gene is located on chromosome 19

α -subunits are extra cellular and binds to insulin where as β -subunits span the membrane and their intracellular portion has Tyrosine kinase activity + Autophosphorylation

Insulin Receptor has t $\frac{1}{2}$ - 7hours

Number of Rs. \rightarrow increases on exposure of (insulin)

o Number of Rs. \rightarrow increases in obesity and Acromegaly, excess glucocorticoids

o Number of Rs. \rightarrow increases in starvation, in adrenal insufficiency

o Tyrosine Kinase Rs. \rightarrow Also for EGF, PDGF

968. Ans. a (Insulin)

(Ref. Ganong 18th Ed. – 223, 305 and 317)

• **Insulin receptor:** Mol. Wt-340, 000 is a Tetramere, made up 2 α and 2 β glycoprotein subunits. The gene for insulin receptor has 22 exons and is located on chromosome 19. The α -subunits binds with Insulin and are extra-cellular, while β -subunits across the cell membrane and their intracellular parts have Tyrosine Kinase activity.

• **Leptin:** Contain 167 amino acids, acts on leptin receptors present in choroid plexuses and hypothalamus (Arcuate nuclei). Leptin receptor is a single membrane-spanning protein that resemble

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the single – transducing component of IL-6. When Leptin Receptors are stimulated by leptin decrease food intake and increase energy output.

- **Neuropeptide Y:** Increase food intake, is only part of the efferent appetite regulating pathway.

- **Thyrotropin, TSH** i.e. thyroid – stimulating – hormone.

a) Secreted from anterior pituitary

b) TSH is a glycoprotein contain 211 amino acids, plus hexoses, hexosamines and sialic acid, made up of α and β subunits.

c) The TSH receptor (Glycoprotein) is a typical serpentine receptor that activate adenylyl cyclase through Gs. Serpentine Receptor means that span the membrane seven times.

969. Ans. b (Cutaneous hyperpigmentation, polyostotic fibrous dysplasia, and precocious puberty)

The McCune-Albright syndrome is characterized by patchy cutaneous hyperpigmentation, polyostotic fibrous dysplasia, and several endocrine disorders including toxic multinodular goiter. Patients often have amenorrhea and galactorrhea, Cushing's syndrome, as well as the development of precocious puberty. The precocious puberty is gonadotropin-independent, and the defect lies within a constitutively active G protein. Kallmann's syndrome is an X-linked disorder characterized by hypogonadotropic hypogonadism, which is associated with anosmia. This disorder more commonly affects men than women.

970. Ans. d (Phenothiazines)

Acute attacks of abdominal pain that are often precipitated by diet or drugs such as barbiturates, sulfonamides, anticonvulsants, and alcohol and that have no clear-cut etiology despite an aggressive diagnostic workup may be due to acute intermittent porphyria. The porphyrias are inherited or acquired disorders of heme biosynthesis. Acute intermittent porphyria, which is caused by an autosomal dominant mutation, is characterized by a half-normal level of HMB synthase (the enzyme that catalyzes the condensation of four pyrrole porphobilinogen molecules to form the linear tetrapyrrole hydroxymethylbilane, which ultimately undergoes cyclization). Heterozygotes are prone to a host of sympathomimetic symptoms and psychological problems in addition to recurrent abdominal pain. Peripheral neuropathy, which is due to axonal degeneration of motor neurons, also may occur. The diagnostic test of choice is demonstration of increased urinary pyrrole porphobilinogen excretion as well as increased levels of urinary δ -aminolevulinic acid. Usually there is no skin disease, even after sun exposure. During acute attacks, narcotics may be given without fear of exacerbation of the attack; phenothiazines also may be administered safely. Heme therapy,

presumably by including feedback inhibition of early heme biosynthesis, can abort attacks. However, recovery from the severe motor neuropathy may take years.

971. Ans. a (Metformin)

Type 2 diabetes mellitus is a progressive disorder that can be treated initially with oral agent monotherapy. Eventually, however, the addition of other oral agents or, in many patients, insulin therapy will be needed in order to achieve the targeted glycemic level. Approximately 25% of patients treated with sulfonylureas will achieve a target fasting plasma glucose level. Therefore, 75% of patients will require the addition of a second agent. The high secondary failure rate was also observed with metformin monotherapy. There seems to be no demonstrable superiority of one sulfonylurea over another. In most studies, sulfonylureas have neutral or only slightly beneficial effects on plasma lipid levels. In addition, sulfonylurea therapy is usually associated with a modest weight gain. This has been implicated as a cause of secondary drug failure. Metformin shows similar efficacy when compared to sulfonylurea monotherapy. In addition, however, the use of metformin is associated with significant decreases in plasma triglyceride and LDL cholesterol levels, and patients treated with metformin show modest weight loss during the first 6 months of treatment; therefore metformin should be recommended in obese patients with elevated serum cholesterol levels. The clinical efficacy of acarbose is less than that of sulfonylureas or metformin. In limited studies repaglinide, a non-sulfonylurea insulin secretagogue, showed similar efficacy when compared to sulfonylurea monotherapy. Repaglinide has no significant effect on plasma lipid levels. In drug-naive patients treated with repaglinide, body weight increased by ~3%.

972. Ans. b (Inability to convert procollagen to collagen)

Osteogenesis imperfecta, which is usually transmitted in an autosomal dominant fashion, results in brittle bones because of a generalized decrease in bone mass. Although the clinical course is variable, some patients have multiple fractures in childhood, undergo some remission during puberty, and begin to suffer fractures again later in life. Associated abnormalities include blue sclerae, brown or translucent bluish-gray discoloration of the teeth, and progressive hearing loss. The family history is usually positive. The most common molecular defect is a mutation in one of the two genes coding for type I procollagen. Some mutations result in a decreased synthesis of pro- I collagen genes, whereas other mutations result in the synthesis of structurally abnormal procollagen alpha chains. Most patients with Ehlers-Danlos

syndrome have a defect in the synthesis of type III procollagen, and those with chondrodysplasia have a defect in the gene for type II procollagen.

Type I collagen is the most abundant of the 18 different collagens identified thus far. It is composed of two identical chains: alpha I and alpha II. After procollagen chains are translated from messenger RNA in ribosomes, they pass into the rough endoplasmic reticulum, where hydrophobic signal peptides at the N terminus are cleaved (resulting in up to a 50% reduction of protein mass). Additional posttranslational modification includes conversion of proline residues to hydroxyproline and hydroxylation of lysine residues. After the requisite number of posttranslational conversions, the protein can fold into its native triple-helical conformation.