ENDOCRINE

THYROID

1. **Classify goiter. How will you investigate and treat a 50 years old man with clinically discrete nodule of 3 cm diameter in right lobe of thyroid. 5+5+5 = 15 [The West Bengal University of Health Sciences, Paper – II of 2015]**
2. **Classify thyroid neoplasm. Discuss the management of solitary thyroid nodule 3cm of size of a 30 year old female. 5+10 [The West Bengal University of Health Sciences, Paper – II of 2018]**
3. **A 35 year old lady presents with a Solitary nodule in right lobe. How would you come to a diagnosis and manage such a patient? 8+7 = 15 [The West Bengal University of Health Sciences, Paper – II of 2009]**
4. **How do you classify goiter? Give an outline of investigations and management of a solitary nodular goiter. 5+5+5=15 [The West Bengal University of Health Sciences, Paper – II of 2013]**
5. **A 30 year old lady presents with 3cm solitary nodule on right thyroid lobe. Give the differential diagnosis. How will you manage such patient? 5+10 [The West Bengal University of Health Sciences, Paper – II of 2020]**

Answer.

Classification of thyroid swellings

Simple goitre (euthyroid)	Diffuse hyperplastic	Physiological Pubertal Pregnancy
	Multinodular goitre	
Toxic	Diffuse (Graves' disease)	
	Multinodular	
	Toxic adenoma	
Neoplastic	Benign	
	Malignant	
Inflammatory	Autoimmune	Chronic lymphocytic thyroiditis
		Hashimoto's disease
	Granulomatous	De Quervain's thyroiditis
	Fibrosing	Riedel's thyroiditis
	Infective	Acute (bacterial thyroiditis, viral thyroiditis, 'subacute thyroiditis')
		Chronic (tuberculous, syphilitic)
	Other	Amyloid

The solitary thyroid nodule is defined as a discrete palpable swelling in an otherwise impalpable gland.

It is a clinical diagnosis. Many of these cases prove to be multinodular but presenting as a single thyroid nodule.

Differential diagnosis of apparent solitary thyroid nodules:

1) Benign thyroid neoplasms		**2) Malignant thyroid neoplasms**	**3) Other thyroid abnormalities**	**4) Nonthyroid lesions**
a) Follicular adenoma **i) Colloid**	**b) Papillary adenoma**	**a) Papillary carcinoma** **b) Follicular**	**a) Thyroiditis** **b) Thyroid cyst** **c) Infections**	**a) Lymphadenopathy** **b) Thyroglossal duct cyst**

ii) Simple iii) Foetal iv) Embryonal v) Hurthle cell	**c) Teratoma** **d) Lipoma** **e) Dermoid cyst**	**Carcinoma c) Medullary carcinoma d) Anaplastic carcinoma e) Metastatic cancer f) Sarcoma g) Lymphoma**	**d) Granulomatous disease (e.g., sarcoidosis)**	**c) Parathyroid adenoma d) Laryngocele**

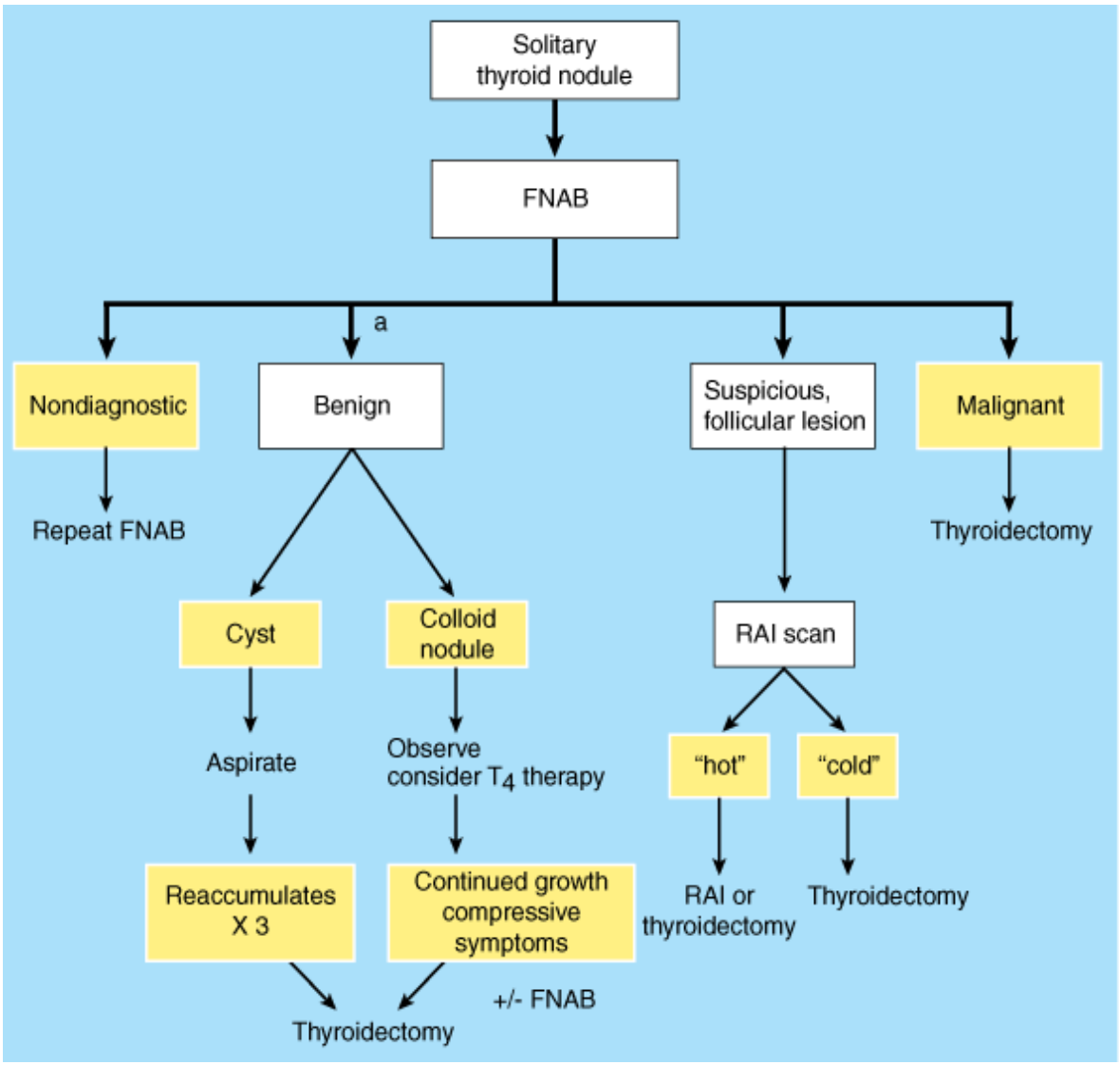
Diagnostic Tools of Solitary Thyroid Nodule:

Clinical examination **Laboratory studies: T3,T4,TSH**	**Radiological studies:** • **Neck ultrasonography** • **Isotope scanning of the thyroid** • **CT scan**	**Histopathological studies:** • **Fine needle aspiration cytology** • **Frozen section .** • **Final histopathological examination.**

Treatment of the Solitary Cold Thyroid Nodule:

Non-Surgical:	**Surgical:**
-No treatment, just follow-up by FNAC -Hormone suppressive therapy -Aspiration of a cyst -Ethanol injection -Recently, Laser photocoagulation	**-Isthmo-lobectomy -Near total thyroidectomy -Total thyroidectomy**

Workup of a solitary thyroid nodule:



6. Retrosternal goiter. 5 [The West Bengal University of Health Sciences, Paper – II of 2011]

Answer.

Introduction:
A retrosternal goitre occurs when the thyroid enlarges downwards into the chest.Although the great majority of retrosternal goitres are extensions from the neck, pure intrathoracic goitres do occur. Retrosternal goitres are more likely to be left sided.

Classification:

Primary (0.2-3%)	Intrathoracic goiters arising from ectopic mediastinal thyroid tissue and having blood supply from intrathoracic vessels.
Secondary	Intrathoracic goiters descended from neck and having blood supply from inferior thyroid artery.

Higgins sub classified intrathoracic goiters by extent-

Completely intrathoracic	More than 80 % intrathoracic with barely detectable or no cervical component.
Partially intrathoracic	More than 50 % intrathoracic
Substernal	Both cervical and mediastinal component, more than 50% in neck

Shahian classified substernal goiters as follows-

Type	**Location**	**Anatomy**	**Prevalence**	**Approach, remarks**
I	Anterior mediastinum	Anterior to great vessels, trachea, RLN	85%	Transcervical(sternotomy only if intrathoracic goiter diameter > thoracic inlet diameter)
II	Posterior mediastinum	Posterior to great vessels, trachea, RLN	15%	As above, sternotomy / right posterolateral Thoracotomy if type IIb
IIA	Ipsilateral extension			
IIB Contralateral extension B1-posterior to trachea and esophagus B2-between trachea and esophagus				
III	Isolated mediastinal goiter	No connection to orthotopic gland, mediastinal blood supply	<1%	Transcervical/ sternotomy

Clinical manifestations;

- **They are related to compression or displacement of aero digestive tract and mediastinal great vessels.**
- **Most present with palpable neck mass with lower border not reachable even on deglutition. Rarely, goiter — "Plongeont" is present in which neck mass disappears into thoracic cavity and appears again on swallowing or coughing.**
- **Early tracheal compression may manifest as nocturnal choking, cough, dyspnea, asthma or obstructive pulmonary disease.**
- **Acute airway obstruction may occur due to hemorrhage within tumor which may even need emergency tracheostomy.**
- **There is higher incidence of vocal cord palsy due to stretching and ischemia of recurrent laryngeal nerve. Extrinsic compression of esophagus may result in dysphagia.**
- ***Pemberton's sign* is described as development of head and neck venous engorgement with facial congestion, plethora and venous distension when both arms are raised over the head.**
- **Obstruction to superior vena cava or subclavian vein may result in development of collateral venous drainage leading to facial flushing/edema and dilated neck and upper thoracic veins.**
- **The downhill esophageal varices secondary to superior vena cava obstruction may lead to gastrointestinal tract bleeding in absence of other signs of portal hypertension.**
- **Cervical cutaneous nerves may be pressed resulting in pain in head, neck chest and shoulders.**
- **Compression of sympathetic plexus may lead to Horner's syndrome.**
- **Thoracic duct occlusion may lead to chylothorax. In some cases symptoms may be positional and occurring when patient turns neck to the side of goiter or raises arms.**
- **Majority of Retrosternal goiters are euthyroid with 20 % developing thyrotoxicosis in long standing goiters.**

Imaging:

Chest x-ray	Soft tissue shadow, calcification, tracheal deviation/ compression
CECT Scan	Look for continuity of cervical goiter, extent of goiter, calcification(punctate/coarse/ring like), relation of goiter to adjoining structures- trachea, esophagus, larynx, pharynx, major vessels, lymphadenopathy

Treatment: Surgery is the treatment of choice for retrosternal goiters. The various reasons for surgery include compressive symptoms, ineffectiveness of suppressive therapy, or risk of malignancy.

7. Discuss the pathogenesis of Multinodular goiter. Mention the complications of such a Goitre. How do you manage such a patient? 5+5+5 =15
8. Outline the etiopathogenesis of multinodular goiter. Describe its management. 5+10[The West Bengal University of Health Sciences, Supplementary Paper – II of 2018]

Answer.

Factors that may be involved in the evolution of Muitinodular Goiter.

- **Primary factors**

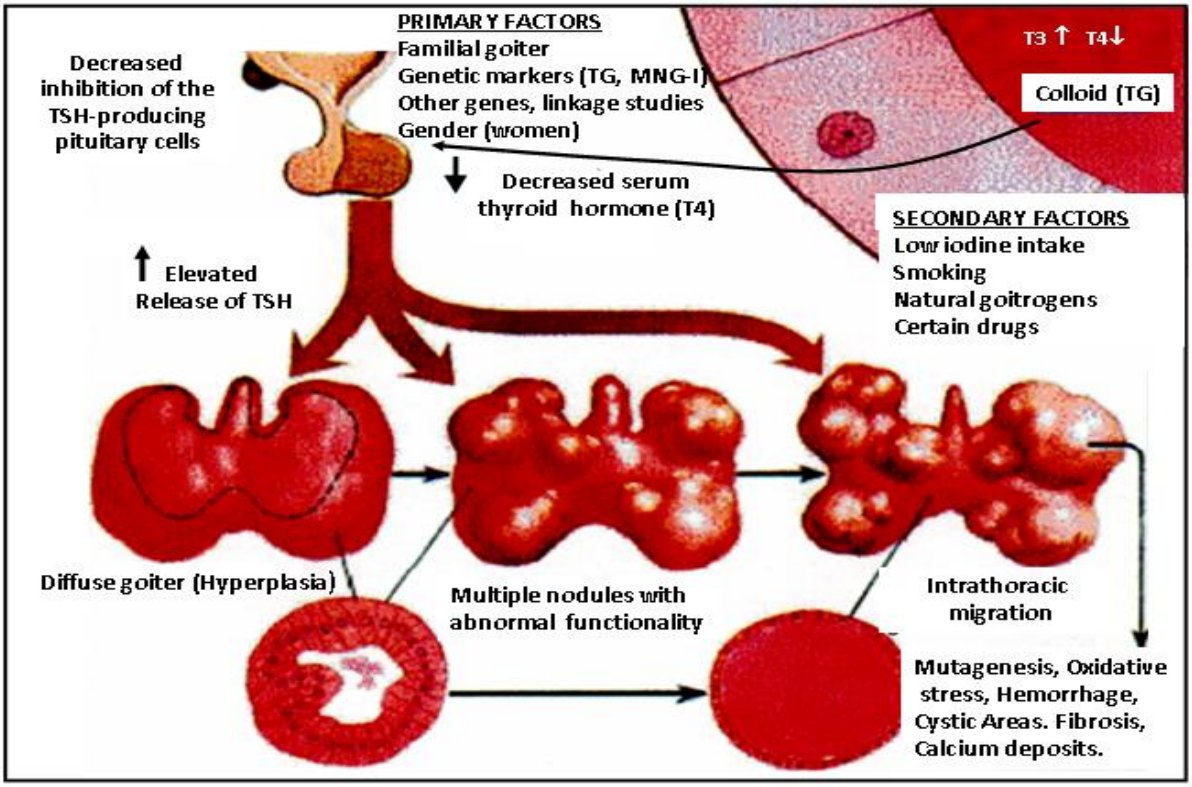
- **Functional heterogeneity of normal follicular cells, cause unknown, possibly genetic and acquisition of new inheritable qualities by replicating epithelial cells**
- **Subsequent functional and structural abnormalities in growing goiters**

❖ **Secondary factors (Stimuli to New Follicle Generation)**

- **TSH (induced by, e.g., iodine deficiency, goitrogens, inborn errors of thyroid hormone synthesis)**
- **Other thyroid-stimulating factors**

Pathogenesis:

- **Reflects impaired synthesis of thyroid hormone most often caused by iodine deficiency**
- **Impairment leads to compensatory ↑ in TSH levels → hypertrophy and hyperplasia of follicular cells → gross enlargement of gland**
- **Euthyroid metabolic state**
- **Degree of enlargement is proportional to level and duration.**
- **The pathogenesis of MNG encompasses processes of diffuse follicular hyperplasia, focal nodular proliferation and eventual acquisition of functional automaticity. The development of MNG is a result of long-term exposure of the thyroid gland to proliferative stimuli, such as iodine deficiency, goitrogens and inborn error of thyroid hormone synthesis. All of the above results in insufficient thyroid hormone production and stimulate pituitary secretion of thyroid stimulating hormone (TSH).**



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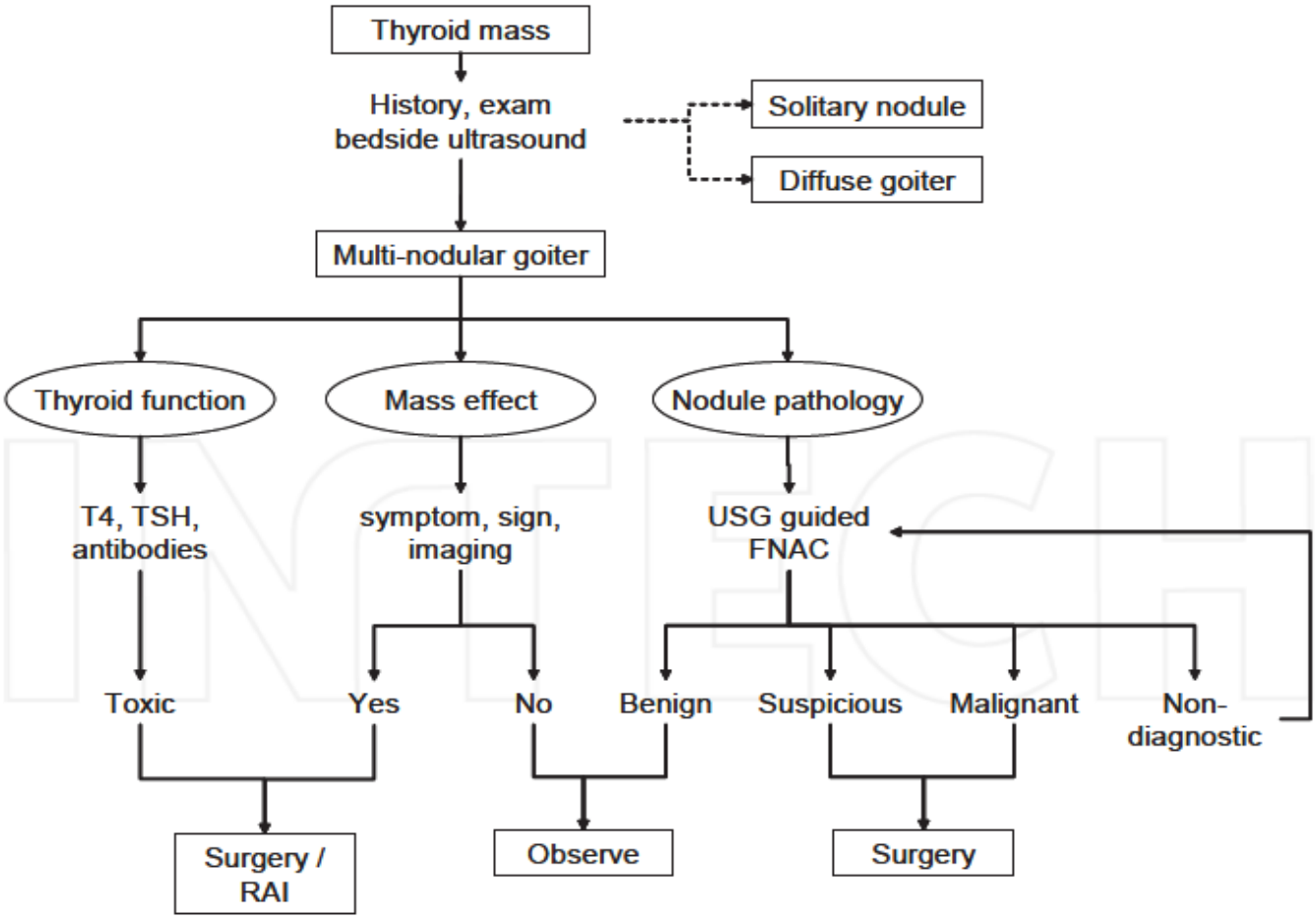
All of the above results in insufficient thyroid hormone production and stimulate pituitary secretion of thyroid.}

Complications of MNG:

- **Neck pain or dragging sensation,**
- **Cosmetic problems,**
- **Pressure symptoms like dysphagia / dyspnea**
- **Hypo or hyperthyroidism.**
- **Symptoms of toxicity.**
- **High risk of thyroid cancer in patients with multinodular goiter**

Management of multinodular goiter:



Investigations:

The investigative workup of a patient with MNG includes

- **T4 and TSH levels to evaluate thyroid function.**
- **High resolution USG and FNA should be used for suspicious or dominant nodules where malignancy is suspected. Predominantly solid nodules especially when they are hypoechoic or display a sonoluscent rim surrounding the lesion(—halo sign‖) should be evaluated by FNAC.**
- **X ray Neck AP and Lateral views to assess tracheal position, retro tracheal extension or incipient compression.**
- **Chest X ray to evaluate for any features of retrosternal extension.**
- **CT/MRI are useful in select cases where a retrosternal extension is suspected. It provides accurate delineation of the depth of goiter extension into the chest and its relation to the trachea, esophagus and great veins.**
- **Thyroid scintigraphy is another option to confirm the extent and functional status of the gland but it is not needed routinely.**

❖ **The indications for treatment are as following**

Strong

- **Compressive symptoms**
- **Hyperthyroidism**
- **Suspected malignancy**

Relative

- **Cosmesis**
- **Potential for Tracheo-esophageal compression**

The various therapeutic options include

· Suppressive levothyroxine therapy
· Surgical
· Radioactive iodine therapy.

- **Suppressive Levothyroxine Therapy:**
  - **The results of T4 suppressive therapy are inconsistent and marginal. This therapy has a limited role in management of patients with MNG. The aim of such therapy is to consistently suppress TSH levels to <0.5 mu/l. The problem of this therapy is that a significant number of patients become hyperthyroid with time. Only small goiter would respond and that too partially. Goitres that respond do so within a period of 6 months**
- **Radioactive Iodine Therapy:**
  - **It is of limited value and is useful in only two classes of patients:**
    - **Those with small goiters may benefit.**
    - **For patients with substantially increased perioperative risk and reasonable thyroid gland function.**
  - **RAI therapy is of no value in large multinodular goiters with poorly functioning nodules as the efficacy of RAI therapy depends on the presence of reasonable gland activity all over the thyroid.**
- **Surgery:**
  - **Surgical treatment is the modality of choice in the management of patients with multinodular goitre.**
  - **The results of surgery are immediate and tissue is available for histological confirmation of the diagnosis and evaluation for any malignant change.**
  - **Surgery is the only treatment option in those with compressive symptoms or those with suspected malignancy.**

- **Surgical treatment options are between Subtotal and Total thyroidectomy.**

9. Describe the management of a lady of 35 years presenting with Toxic multinodular goiter. 6+9 [The West Bengal University of Health Sciences, Supplrmentary Paper – II of 2011]

Answer:

This patient should be investigated as follow:

- **T4 and TSH levels to evaluate thyroid function.**
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The indications for treatment in multinodular goiter are:

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- **Compressive symptoms**
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- **The aim of such therapy is to consistently suppress TSH levels to <0.5 mU/l. The problem of this therapy is that a significant number of patients become hyperthyroid with time.**

- **The overall poor response to T4 supression therapy is because large amounts of thyroid tissue is likely to be hormone insensitive. Another factor for inconsistent response is the variable TSH dependencyof thyrocytes.**
- **Only small goiter would respond and that too partially.**
- **Goitres that respond do so within a period of 6 months**

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It is of limited value and is useful in only two classes of patients.

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function.

{Several groups have reported successful RAI therapy with I131 with reduction of thyroid volume by 40% at 1 year and 50-60% at 3-5 years. Whereas, radiation induced auto immune thyroiditis develops in a few patients, a significant number of patients develop hypothyroidism.
RAI therapy is of no value in large multinodular goiters with poorly functioning nodules as are commonly seen in India and other iodine deficient areas as the efficacy of RAI therapy depends on the presence of reasonable gland activity all over the thyroid.}

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Preoperative preparation:

Antithyroid medications are generally administered in preparation for radioactive iodine ablation or surgery. The medications commonly used are propylthiouracil (PTU, 100 to 300 mg three times daily) and methimazole (10 to 30 mg three times daily).

Both drugs reduce thyroid hormone production by inhibiting the organic binding of iodine and the coupling of iodotyrosines (mediated by thyroid peroxidase). In addition, PTU also inhibits the peripheral conversion of T_4 to T_3, making it useful for the treatment of thyroid storm. (Both drugs can cross the placenta, inhibiting fetal thyroid function, and are excreted in breast milk) Side effects of treatment include reversible granulocytopenia, skin rashes, fever, peripheral neuritis, polyarteritis, vasculitis, and, rarely, agranulocytosis and aplastic anemia.

Surgery should be postponed until the granulocyte count reaches 1000 cells/m^3.

The catecholamine response of thyrotoxicosis can be alleviated by administering beta-blocking agents. These drugs have the added effect of decreasing the peripheral conversion of T_4 to T_3. Propranolol is the most commonly prescribed medication in doses of about 20 to 40 mg four times daily. Higher doses are sometimes required because of increased clearance of the medication.

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11. Discuss the clinical features, investigations and treatment of Thyrotoxicosis. 5+5+5 = 15
[The West Bengal University of Health Sciences, Paper – II of 2014]

Answer:

For reading

- **Causes and pathological features**
- TSH secreting pituitary adenoma.
- Autoimmune stimulation (Graves's disease).
  - Thyroid stimulating antibodies (IgG) bind to TSH receptors and stimulate the thyroid cells to produce and secrete excessive amounts of thyroid hormones.
  - Thyroid gland hypertrophies and becomes diffusely enlarged.
  - The autoimmune process leads to mucopolysaccharide infiltration of the extra-ocular muscles and may lead to exophthalmus.
- T_3, T_4 secreting site in the thyroid.
  - Nodule in a multinodular goitre (Plummer's syndrome).
  - Adenoma or (very rarely) carcinoma.
- Thyroiditis (large amount of preformed hormones are released after the destruction of follicles, with transient thyrotoxicosis).
- Exogenous intake of thyroid hormones (factitious thyrotoxicosis).

Clinical features:

- **Weight loss, heat intolerance, sweating (due to stimulated metabolism and heat production).**
- **Tremor, nervousness, irritability, emotional disturbance, tiredness, and lethargy (due to CNS overactivity).**
- **Cardiac features are caused by beta-adrenergic sympathetic activity:**
  - **palpitations, tachycardia, and arrhythmias.**
- **Eye signs can be:**
  - **minimal/mild (soft tissue oedema, chemosis);**
  - **very prominent (severe exophthalmus, corneal ulcers, diplopia);**
  - **ophthalmopathy is usually bilateral but may only involve one eye.**

- **Pretibial myxoedema, thyroid acropachy, vitiligo, and alopecia are rare.**

Primary thyrotoxicosis	Secondary thyrotoxicosis
Eye signs:exopthalmos – more prominent. **CNS signs: tremor – more prominent.** **Cardiac signs - tachycardia**	**CNS signs: tremor – less prominent.** **Cardiac signs – tachycardia** **Cardiomegaly.CCF** **Cardiac signs are more prominent.**

Thyroid storm (thyrotoxic crisis):

- **Rare presentation of extreme signs of thyrotoxicosis and severe metabolic disturbances.**
- **Precipitated by non-thyroid surgery, major trauma, infection, imaging studies with iodinated contrast medium in patients with unrecognized thyrotoxicosis.**
- **Features are insomnia, anorexia, vomiting, diarrhoea, marked sweating, fever, marked tachycardia.**
- **Early clinical diagnosis of the condition and immediate treatment decrease the risk of fatal outcome.**

Investigations:

- **Thyroid function test: TSH level; free T_4 and free T_3 (in all causes but pituitary) - T3 thyrotoxicosis is diagnosed by estimating the free T3. It should be suspected if the clinical picture is suggestive but routine tests of thyroid function reveal a normal T4 but suppressed TSH.**
- **Positive serology for thyroid autoantibodies.**
- **Radioactive iodine scan (or technetium scan): helpful in distinguishing the diagnosis of Graves's disease, thyroiditis, toxic nodule (unilateral uptake with negative scan on the contralateral side), or toxic mutinodular goitre.**

<u>Note: Thyrotoxicosis should always be considered in:</u>

- **Children with a growth spurt, behaviour problems or myopathy**
- **Tachycardia or arrhythmia in the elderly**
- **Unexplained diarrhoea**
- **Loss of weight.**

Treatment:
Principles of treatment of thyrotoxicosis: Non-specific measures are rest and sedation and in established thyrotoxicosis should be used only in conjunction with specific measures.

- **Medical treatment:**

- **Antithyroid drugs block hormone synthesis.**
  - **Carbimazole 20mg bd, then reducing dose**
  - **Propylthiouracil 200mg bd: blocks the peripheral conversion of T_4 to T_3.**

- **Beta-blockers (propranolol 40-120mg/day, carvedilol) are used to control tachycardia and tremor.**

- **Radioactive iodine (I^{131})-**

  - **Contraindicated in severe eye disease (could worsen after I^{131} treatment),**
  - **Young women (risk of teratogenicity in pregnancy),**
  - **Patients who are main carers of small children.**

Surgical treatment

- **Total thyroidectomy (for Graves's disease). Indicated in patients who are not candidates for I^{131} therapy. It is the treatment of choice in those with eye disease and patients where control of symptoms has been difficult on medication.**
  - **Slightly higher risk of RLN injury and hypoparathyroidism (due to increased vascularity of the gland and the local fibrosis).**
- **Thyroid lobectomy: for isolated nodules or adenomas.**

Treatment options	Advantage	Disadvantage
Antithyroid drugs	No surgery and no use of radioactive materials.	○ Treatment is prolonged and the failure rate is at least 50 per cent. The duration of treatment may be tailored to the severity of the toxicity with milder cases being treated for only six months and severe for two years before stopping therapy.
Surgery	The goitre is removed, the cure is rapid, and the cure rate is high if surgery has been adequate.	○ Recurrence of thyrotoxicosis occurs in approximately 5 per cent of cases when Subtotal Thyroidectomy is carried out. ○ There is a risk of permanent hypoparathyroidism and nerve injury. ○ Young women tend to have a poorer cosmetic result from the scar.

12. Describe the clinical features and management of primary thyrotoxicosis. 5+10 [The West Bengal University of Health Sciences, Supplementary Paper – II of 2016]

13. Describe the clinical features and management of thyrotoxicosis. 8+7 [The West Bengal University of Health Sciences, Supplementary Paper – II of 2020]

Answer.

Primary thyrotoxicosis refers to excessive thyroxine (T4) and/or triiodothyronine (T3) secretion secondary to abnormal thyroid stimulation, thyroid hyperfunctioning nodules, or ectopic malignant thyroxine secretion. Secondary hyperthyroidism is the result of abnormal, excessive thyroid stimulating hormone (TSH) release and stimulation of the thyroid resulting in excessive T4 release. Excessive TSH production may be secondary to pituitary pathology or hypothalamic pathology resulting in excess thyrotropin releasing hormone (TRH) production, which will stimulate the pituitary gland to secrete excessive amounts of TSH. Overtreatment of hypothyroidism, either by physician or patient abuse, results in iatrogenic disease. The antiarrythmic agent amiodarone may also cause hyperthyroidism.

Symptoms of hyperthyroidism include heat intolerance, irritability, weight loss, frequent bowel movements, proximal muscle weakness, tremulousness, anxiety, fever, and fatigue. Menstruating females often suffer oligomenorrhea.

Physical findings include tachycardia, a widened pulse pressure, eye findings (lid lag, exophthalmos), goiter, thyroid bruit upon auscultation, a thrill with palpation of the thyroid, brisk reflexes, pretibial myxedema, and a systolic murmur.

Patients afflicted with this disorder may exhibit electrocardiographic abnormalities to include sinus tachycardia and atrial fibrillation. In fact, hyperthyroidism should be ruled out in all patients with new onset atrial fibrillation.

Apathetic hyperthyroidism refers to hyperthyroidism that is asymptomatic except for cardiac findings and occurs in the elderly. Cardiac symptoms may include congestive heart failure, which is often refractory to therapy, tachycardia, and a widened pulse pressure.

Associated lab abnormalities include an extremely depressed TSH level, an elevated free T4 and/or free T3 which are characteristic of primary hyperthyroidism. Secondary hyperthyroidism is characterized by elevated levels of TSH, freeT4 and/or free T3 levels. If the free T4 level is normal but symptoms of hyperthyroidism are present along with a suppressed TSH, T3 toxicosis should be considered and a serum free T3 level should be determined if not ordered initially. The profile of a low TSH with normal free T4 and free T3 levels is consistent with subclinical hyperthyroidism. In acutely ill patients, euthyroid sick syndrome may manifest as a low to low normal TSH, low T3, and a normal T4 level. Medications associated with low TSH levels include glucocorticoids, octreotide, dopamine, dobutamine, and amiodarone.

Hypercalcemia may result from hyperthyroidism-associated bone disease, and osteoporosis is a potential long-term complication if effective therapy is not administered. Hyperthyroid-induced hepatosteatosis may result in elevation of liver function tests to include the alkaline phosphatase, ALT and AST values.

Primary thyrotoxicosis may be secondary to one of several different pathologies, which are listed in order of decreasing frequency:

Grave's disease: This is the most common form of hyperthyroidism and is characterized by the triad of exophthalmos, diffuse goiter, and hyperthyroidism. This is an autoimmune disorder, and

diagnosis is confirmed by finding the above triad plus the presence of serum antibodies (TSH receptor antibodies composed of thyroid-stimulating immunoglobulin and the TSH receptor-blocking antibodies) or the characteristic elevated diffuse uptake of iodine 123 on uptake testing. The presence of pretibial myxedema is also indicative of Grave's disease as the underlying cause of hyperthyroidism.

Toxic nodular goiter (toxic adenoma and toxic multinodular goiter): This form of hyperthyroidism may be the result of a single or multiple autonomously hyperfunctioning nodules. This disorder usually occurs in thyroid glands that have been enlarged for prolonged periods of time. These nodules are benign. When patients with this condition are exposed to iodine (radiocontrast, amiodarone), they may suffer clinical worsening of their disease (jodbasedow effect).

Thyroiditis:These are transient forms of hyperthyroidism (subacute ,painless and postpartum). Subacute thyroiditis is a painful condition that often follows a respiratory illness and is secondary to thyroid follicle disruption with release of stored thyroid hormone. Postpartum disease is generally painless and lasts approximately one to three months. Because this disorder is transient, antithyroid agents (methimazole or propylthiouracil) are unnecessary and are ineffective. Aspirin 650 mg PO QID may relieve the pain, and if aspirin is ineffective, prednisone 20-40 mg PO QD may offer relief. Symptoms of hyperthyroidism may be controlled with propranolol 20-40 mg PO QID, but the medication should be discontinued after a few weeks and the patient monitored for signs of hyperthyroidism.

Thyrotoxicosis Factitia: This is hyperthyroidism that occurs secondary to ingestion of exogenous thyroxine preparations. In persons ingesting exogenous thyroxine, the serum thyroglobulin level will be extremely low.

Trophoblastic tumors(rare): Hyperthyroidism results when trophoblastic tumors secrete excessive amounts of beta hCG greater than 100,00mIU/mL. Hyperthyroidism occurs because beta hCG has a similar alpha subunit to that of TSH and binds to TSH receptors on thyroid follicular cells.

Struma Ovarii (rare): This uncommon disorder occurs when thyroid rests within the ovary become hyperplastic. This disorder is characterized by a low TSH, an elevated T4, low thyroid radioisotope uptake on thyroid scanning, and detection of pelvic radioisotope uptake when the gamma scanner is directed at the pelvis during thyroid scanning.

Thyroid radioiodine uptake may be helpful in establishing the cause of hyperthyroidism. Radioiodine uptake will be elevated in Grave's disease (homogeneous uptake of 35-100%), toxic nodular goiter (heterogeneous uptake 20-60%), toxic adenoma (increased uptake of 20-60% in area of nodule). Conversely, the uptake of radioiodine will be low in cases of subacute thyroiditis, postpartum thyroiditis, strumaovarii, and overdosing of exogenous thyroid hormone (iatrogenic or factitious hyperthyroidism). Radioiodine uptake testing should not be performed within 8 weeks of the patient receiving intravenous iodinated contrast medium for other radiographic testing as the prior iodine-containing contrast will saturate the thyroid and prevent uptake of the iodine 123 even if the thyroid is hyperactive. Pregnancy is a definite contraindication to iodine 123 uptake testing.

Thyroid storm is a life-threatening form of hyperthyroidism, and this disorder is characterized by signs and symptoms or a history of hyperthyroidism plus fever and a change in mental status. Therapy includes propylthiouracil (150 mg PO STAT followed by 100-150 mg PO TID) and iodides to block thyroid hormone release (SSKI 10 drops QD or sodium iodide 0. 5 grams by slow

intravenous drip Q 6-8 hours). Iodine should only be administered 1-2 hours after thyroid-blocking agents (propylthiouracil) have been given. Decadron (4 mg intravenously Q 6 hours) reduces serum T3 levels. Beta blockade with propranolol (30-60 mg PO Q 8 hours) or intravenous esmolol will help control heart rate. Supportive measures include fluids and determining the cause (infection, trauma). Fever should not be treated with cooling mattresses, and Tylenol is ineffective. Fever may be controlled with Demerol (25-50 mg intravenously Q 6 hours) and chlorpromazine (25-50 mg intravenously Q 6 hours).

Therapy for hyperthyroidism depends on the etiology. Commonly used therapies for Grave's disease include radioablation or medical therapy with propylthiouracil (50-150 mg PO TID/QID) or methimazole (5-20 mg PO BID/TID) plus beta blockade for symptom control. Therapy may be continued for a period of approximately 6 months to two years and then discontinued to see if remission has occurred. If hyperthyroidism persists, therapy may be continued indefinitely or radioablation of the thyroid may be offered to the patient. Patients should be monitored post ablation for the development of a hypothyroid state. Thyroidectomy is a uncommon form of therapy in appropriate cases.

12 Answer. Thyrotoxicosis is the clinical manifestation of excess thyroid hormone action at the tissue level due to inappropriately high circulating thyroid hormone concentrations. Hyperthyroidism, a subset of thyrotoxicosis, refers specifically to excess thyroid hormone synthesis and secretion by the thyroid gland.

Primary thyrotoxicosis is common; it is due to disease in the thyroid, and thyroid-stimulating hormone (TSH) levels are high. Secondary thyrotoxicosis is less common; it is due to pituitary or hypothalamic disease, and TSH levels are low.

Signs and symptoms

Common symptoms of hyperthyroidism and thyrotoxicosis include the following:

- **Nervousness**
- **Anxiety**
- **Increased perspiration**
- **Heat intolerance**
- **Hyperactivity**
- **Palpitations**

Common signs of hyperthyroidism and thyrotoxicosis include the following:

- **Tachycardia or atrial arrhythmia**
- **Systolic hypertension with wide pulse pressure**
- **Warm, moist, smooth skin**
- **Lid lag**
- **Stare**
- **Hand tremor**
- **Muscle weakness**
- **Weight loss despite increased appetite (although a few patients may gain weight, if excessive intake outstrips weight loss)**
- **Reduction in menstrual flow or oligomenorrhea**

Presentation of thyrotoxicosis varies, as follows :

- **Younger patients tend to exhibit symptoms of sympathetic activation (eg, anxiety, hyperactivity, tremor)**
- **Older patients have more cardiovascular symptoms (eg, dyspnea, atrial fibrillation) and unexplained weight loss**

- **Patients with Graves disease often have more marked symptoms than patients with thyrotoxicosis from other causes**
- **Ophthalmopathy (eg, periorbital edema, diplopia, or proptosis) and pretibial myxedema dermopathy specifically occur with Graves disease**
- **Elevated thyroid hormone levels associated with subacute thyroiditis may occur as part of a postviral syndrome (subacute granulomatous thyroiditis) or within a year of the end of a pregnancy (postpartum subacute thyroiditis)**

Diagnosis

Thyroid function tests for hyperthyroidism and thyrotoxicosis are as follows:
- **Thyroid-stimulating hormone (TSH)**
- **Free thyroxine (FT4) or free thyroxine index (FTI—total T4 multiplied by the correction for thyroid hormone binding)**
- **Total triiodothyronine (T3)**

Thyroid function study results in hyperthyroidism and thyrotoxicosis are as follows:
- **Hyperthyroidism and thyrotoxicosis are marked by suppressed TSH levels and elevated T3 and T4 levels**
- **Patients with milder hyperthyroidism may have elevation of T3 levels only with a suppressed TSH level**
- **Subclinical hyperthyroidism features decreased TSH and normal T3 and T4 levels**

Autoantibody tests for hyperthyroidism are as follows:
- **Anti–thyroid peroxidase (anti-TPO) antibody - Elevation with autoimmune thyroid disease found in 85% of Graves patients**
- **Thyroid-stimulating antibody (TSab) - Also known as thyroid-stimulating immunoglobulin (TSI), long-acting thyroid stimulator (LATS), or TSH-receptor antibody (TRab); found in 63-81% of Graves disease; a positive test is diagnostic and specific for Graves disease**

Autoantibody titers in hyperthyroidism and thyrotoxicosis are as follows:
- **Graves disease - Significantly elevated anti-TPO, elevated TSI ab**
- **Toxic multinodular goiter - Low or absent anti-TPO and negative TSI ab**
- **Toxic adenoma - Low or absent anti-TPO and negative TSI ab**
- **Patients without active thyroid disease may have mildly positive anti-TPO and TSI ab**
- **Subacute thyroiditis - Low or absent anti-TPO and negative TSI ab**

If the etiology of elevated thyroid hormone levels is not clear after physical examination and other laboratory tests, it can be confirmed by scintigraphy: the degree and pattern of isotope uptake indicate the type of thyroid disorder. Findings are as follows:
- **Graves disease – Diffuse enlargement of both thyroid lobes, with uniform uptake of isotope and elevated radioactive iodine uptake**
- **Toxic multinodular goiter -- Irregular areas of relatively diminished and occasionally increased uptake; overall radioactive iodine uptake is mildly to moderately increased**
- **Subacute thyroiditis – Very low radioactive iodine uptake, either with a painful thyroid (subacute granulomatous thyroiditis) or occurring within a year of pregnancy (postpartum subacute thyroiditis)**

Management:

Treatment of hyperthyroidism and thyrotoxicosis includes symptom relief, while hyperthyroidism also requires therapy with antithyroid medications, radioactive iodine-131 (^{131}I), or thyroidectomy. Symptomatic treatment is as follows:
- **Oral rehydration for dehydrated patients**

- **Beta-blockers for relief of neurologic and cardiovascular symptoms**
- **For mild ophthalmopathy, saline eye drops as needed and tight-fitting sunglasses for outdoors**
- **For vision-threatening ophthalmopathy, high-dose glucocorticoids, with consideration of orbital decompression surgery, ocular radiation therapy, or a recently approved treatment from the US Food and Drug Administration (FDA), teprotumumab-trbw, a monoclonal antibody that blocks the insulin-like growth factor-1 receptor (IGF-1R) and ameliorates proptosis by reducing inflammation and preventing muscle and fat-tissue remodeling in the orbit**

Antithyroid drug treatment is as follows:

- **Used for long-term control of hyperthyroidism in children, adolescents, and pregnant women**
- **In adult men and nonpregnant women, used to control hyperthyroidism before definitive therapy with radioactive iodine**
- **Methimazole is more potent and longer-acting than propylthiouracil**
- **Propylthiouracil is reserved for use in thyroid storm, first trimester of pregnancy, and methimazole allergy or intolerance**
- **Antithyroid drug doses are titrated every 4 weeks until thyroid functions normalize**
- **Patients with Graves disease may experience remission after treatment for 12-18 months, but recurrences are common within the following year**
- **Toxic multinodular goiter and toxic adenoma will not go into remission**

Radioactive iodine treatment is as follows:

- **Preferred therapy for hyperthyroidism**
- **Administered orally as a single dose in capsule or liquid form**
- **Causes fibrosis and destruction of the thyroid over weeks to many months**
- **Hypothyroidism is expected**
- **Pregnancy, breast feeding, and recent lactation are contraindications**
- **Radioactive iodine should be avoided in children younger than 5 years**
- **Radioactive iodine is usually not given to patients with severe ophthalmopathy**
- **Radioactive iodine is usually not given to patients who cannot comply with physician restrictions for avoidance of radiation exposure to others**

Thyroidectomy is reserved for special circumstances, including the following:

- **Severe hyperthyroidism in children**
- **Pregnant women who are noncompliant with or intolerant of antithyroid medication**
- **Patients with very large goiters or severe ophthalmopathy**
- **Patients who refuse radioactive iodine therapy**
- **Refractory amiodarone-induced hyperthyroidism**
- **Patients who require normalization of thyroid functions quickly, such as pregnant women, women who desire pregnancy in the next 6 months, or patients with unstable cardiac conditions**

14. Thyroid storm: 5 [The West Bengal University of Health Sciences, Paper – II of 2018]

Answer. Thyroid storm or thyrotoxic crisis is a rare but severe and potentially life-threatening complication of hyperthyroidism (over activity of the thyroid gland). It is characterized by a high fever (temperatures often above 40 °C/104 °F), fast and often irregular heart beat, vomiting, diarrhea, and agitation. Hypertension with a wide pulse pressure occurs in early to mid crisis, with hypotension accompanying shock occurring in the late stage. Heart failure and heart attack may occur. Death may occur despite treatment. Most episodes occur either in those with known

hyperthyroidism whose treatment has been stopped or become ineffective, or in those with untreated mild hyperthyroidism who have developed an intercurrent illness (such as an infection)

Thyroid storm is characterized by an acute onset of symptoms of hyperthyroidism (fast heart rate, restlessness, agitation) accompanied by other features such as fever (temperatures often above 40 °C/104 °F), hypertension, mental status changes, diarrhea, and vomiting.

Individuals can exhibit varying signs of organ dysfunction. Patients may experience liver dysfunction, and yellow discoloration of the skin is considered a poor prognostic sign. Heart (cardiac) symptoms include abnormal heart rhythms, decreased blood flow to the heart and heart attacks, and congestive heart failure, which may lead to cardiovascular collapse. Mortality can be as high as 20-30%.

In some situations, individuals may not experience the classic signs of restlessness and agitation, but instead present with apathetic signs of weakness and confusion

Causes: The transition from hyperthyroidism to thyroid storm is typically triggered by a non-thyroidal insult including, but not limited to fever, sepsis, dehydration, myocardial infarction, and psychiatric diseases. Individuals are at higher risk of thyroid storm if their hyperthyroidism is incompletely treated or if their anti-thyroid drugs are discontinued. Many of these individuals have underlying primary causes of hyperthyroidism (Graves disease, toxic multi-nodular goiter, solitary toxic adenoma). However, thyroid storm can occur in individuals with unrecognized thyrotoxicosis experiencing non-thyroid surgery, labor, infection, or exposure to certain medications and radiocontrast dyes.

Precipitating factors for thyroid storm

Severe infection

Diabetic ketoacidosis

Hypoglycemia

Thyroid surgery

Non-thyroid surgery

Parturition

Struma ovarii

Molar pregnancy

Trauma (i.e. hip fracture)

Burns

Myocardial infarction

Pulmonary embolism

Stroke

Heart failure

Radioactive iodine treatment

Medication side effect (anesthetics, salicylate, pseudoephedrine, amiodarone)

Exposure to iodinated contrast

Withdrawal of antithyroid treatment

Emotional stress

Intense exercise

Laboratory findings

As with hyperthyroidism, TSH is suppressed. Both free and serum (or total) T3 and T4 are elevated. An elevation in thyroid hormone levels is suggestive of thyroid storm when accompanied by signs of severe hyperthyroidism but is not diagnostic as it may also correlate with uncomplicated hyperthyroidism. Moreover, serum T3 may be normal in critically ill patients due to decreased conversion of T4 to T3. Other potential abnormalities include the following:

- **Hyperglycemia likely due to catecholamine-mediated effects on insulin release and metabolism as well as increased glycogenolysis, evolving into hypoglycemia when glycogen stores are depleted**
- **Elevated aspartate aminotransferase (AST), bilirubin and lactate dehydrogenase (LDH)**
- **Hypercalcemia and elevated alkaline phosphatase due to increased bone resorption**
- **Elevated white blood cell count**

Management:

The main strategies for the management of thyroid storm are reducing production and release of thyroid hormone, reducing the effects of thyroid hormone on tissues, replacing fluid losses, and controlling temperature.[3] Thyroid storm requires prompt treatment and hospitalization. Often, admission to the intensive care unit is needed.

Iodine

Aministration of inorganic iodide (potassium iodide or Lugol's iodine to reduce the synthesis and release of thyroid hormone. Iodine reduces the synthesis of thyroid hormone via the Wolf-Chaikoff effect. Antithyroid Medications

Antithyroid drugs (propylthiouracil or methimazole) are used to reduce the synthesis and release of thyroid hormone. Propylthiouracil is preferred over methimazole due to its additional effects on reducing peripheral conversion of T4 to T3, however both are commonly used.

Beta Blockers

The administration of beta-1-selective beta blockers (e.g. metoprolol) is recommended to reduce the effect of circulating thyroid hormone on end organs.In addition, propanolol at high doses also reduces peripheral conversion of T4 to T3, which is the more active form of thyroid hormone. Although previously unselective beta blockers (e.g., propranolol) have been suggested to be beneficial due to their inhibitory effects on peripheral deiodinases recent research suggests them to be associated with increased mortality. Therefore, cardioselective beta blockers may be favourable.

Corticosteroids

High levels of thyroid hormone result in a hypermetabolic state, which can result in increased breakdown of cortisol, a hormone produced by the adrenal gland. This results in a state of relative adrenal insufficiency, in which the amount of cortisol is not sufficient. Guidelines recommend that corticosteroids (hydrocortisone and dexamethasone are preferred over prednisolone or methylprednisolone) be administered to all patients with thyroid storm.

Supportive Measures

In high fever, temperature control is achieved with fever reducers such as paracetamol/acetaminophen and external cooling measures (cool blankets, ice packs). Dehydration, which occurs due to fluid loss from sweating, diarrhea, and vomiting, is treated with frequent fluid replacement. In severe cases, mechanical ventilation may be necessary. Any suspected underlying cause is also addressed.

15. Define thyrotoxicosis. Enumerate the grade-wise presentation of the eye signs in thyrotoxicosis. Give the brief outline of the diagnosis and options of management of Graves Disease. 2+3+5+5 [The West Bengal University of Health Sciences, Paper – II of 2019]

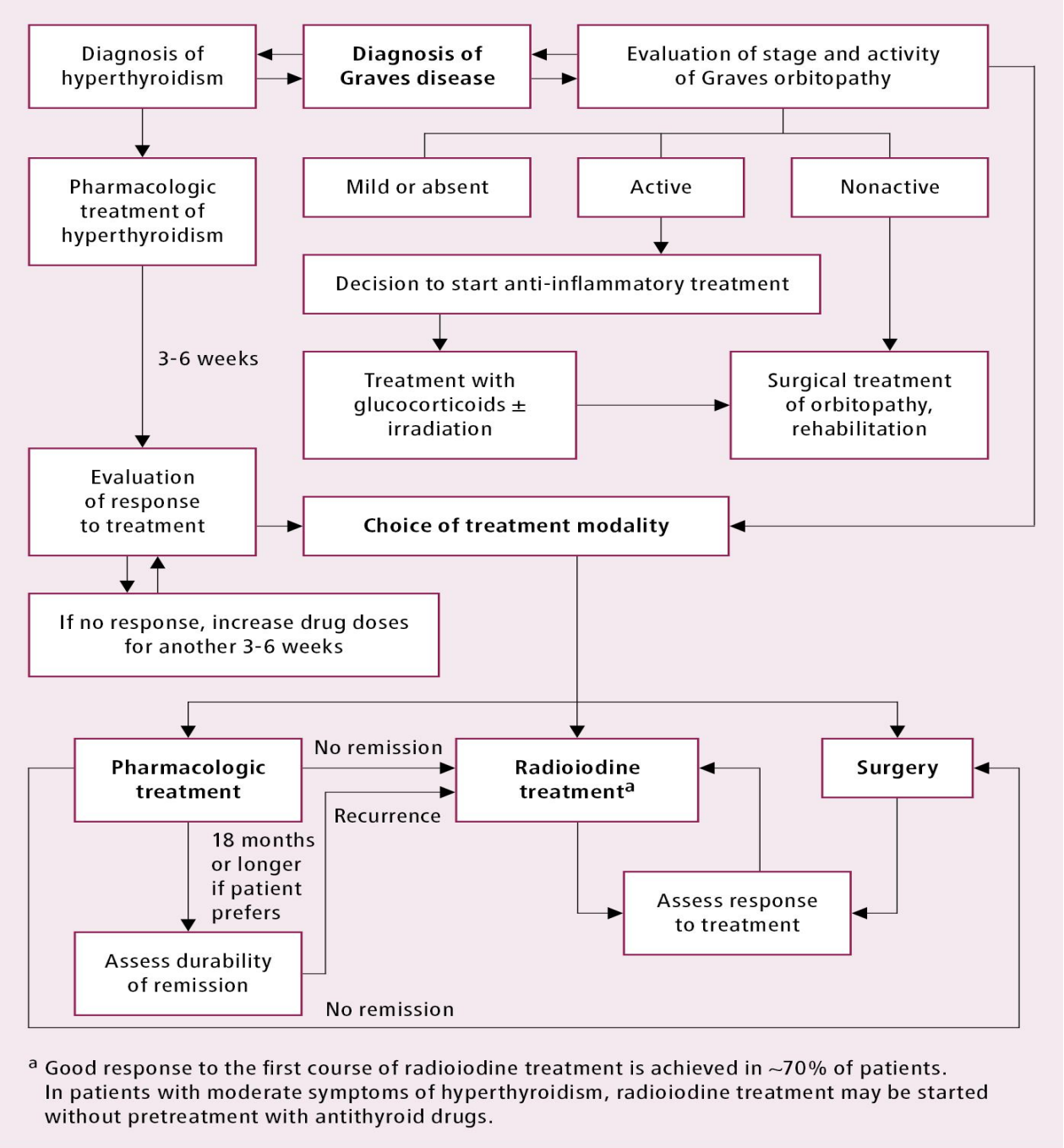
Answer.

Hyperthyroidism is the condition that occurs due to excessive production of thyroid hormone by the thyroid gland. Thyrotoxicosis is the condition that occurs due to excessive thyroid hormone of any cause and therefore includes hyperthyroidism.

Eye signs of thyrotoxicosis according to grade:

Class	Description
Class 0	No signs or symptoms
Class 1	Only signs (limited to upper lid retraction and stare, with or without lid lag)
Class 2	Soft tissue involvement (oedema of conjunctivae and lids, conjunctival injection, etc.)
Class 3	Proptosis
Class 4	Extraocular muscle involvement (usually with diplopia)
Class 5	Corneal involvement (primarily due to lagophthalmos)
Class 6	Sight loss (due to optic nerve involvement)

Algorithm of treatment of Graves disease



[a] Good response to the first course of radioiodine treatment is achieved in ~70% of patients. In patients with moderate symptoms of hyperthyroidism, radioiodine treatment may be started without pretreatment with antithyroid drugs.

16. **Classify thyroid cancer. Discuss the management of F.N.A.C proved follicular neoplasm of (R) lobe of thyroid in a lady of 45 years. 5+5+5 = 15 [The West Bengal University of Health Sciences, Paper – II of 2016]**
17. **Describe the pathology, investigations and treatment of differentiated Thyroid Carcinoma. 4+3+8 = 15 [The West Bengal University of Health Sciences, Supplementary Paper – II of 2015]**
18. **Classify thyroid malignancies. How will you manage a case of Follicular carcinoma thyroid? 5+10 = 15 [The West Bengal University of Health Sciences, Supplementary Paper – II of 2010]**

19. Classify thyroid cancer. Discuss the management of F.N.A.C proved follicular neoplasm of (R) lobe of thyroid in a lady of 45 years. 5+5+5 = 15 [The West Bengal University of Health Sciences, Paper – II of 2016]

20. Classify Thyroid Neoplasms. Write clinical features, investigations and management of papillary carcinoma of the thyroid gland (a lady of 25 years old). 3+4+3+5=15 [The West Bengal University of Health Sciences, Paper – II of 2012]

Answer.

Classification of thyroid neoplasms

Benign **- Follicular adenoma**

Malignant **- Primary**

- **Follicular epithelium –differentiated**
  - **Follicular**
  - **Papillary**
- **Follicular epithelium –undifferentiated**
  - **Anaplastic**
- **Parafollicular cells**
  - **Medullary**
- **Lymphoid cells**

  Lymphoma

  Secondary
- **Metastatic**

Local infiltration

Pathology

❖ ***Papillary carcinoma:***

On gross pathologic examination, papillary carcinomas are whitish invasive neoplasms with ill-defined margins. Under microscopy, the tumors are unencapsulated neoplasms that characteristically grow with papillae consisting of neoplastic epithelium overlying fibrovascular stalks. Very differentiated tumors can have a complex arborizing pattern. Nuclei have an empty ground-glass appearance with characteristic nuclear grooves and pseudoinclusions. Mitoses are rare.

Another histologic feature is the presence of psammoma bodies, which occur in 50% of papillary carcinomas. Psammoma bodies are calcific concretions that have a circular laminated appearance. They are found in the stroma of the tumor. In addition, many papillary carcinomas contain areas that show a follicular growth pattern. However, when the nuclear features in follicular areas are the same as those in papillary areas, the tumor behaves like a classic papillary carcinoma and should be designated as such. Papillary carcinoma may be multicentric, with foci present in both the ipsilateral and contralateral lobes

❖ ***Follicular carcinoma:***

On gross pathology, the tumors appear as round, encapsulated, light brown neoplasms. Fibrosis, hemorrhage, and cystic changes are found in the lesions. Under microscopy, the tumors contain neoplastic follicular cells, which overall can have a solid, trabecular, or follicular growth pattern (that usually produces microfollicles). The follicular cells in these tumors do not have characteristic features like papillary carcinoma cells.

Follicular carcinomas are differentiated from benign follicular adenomas by tumor capsule invasion and/or vascular invasion. For this reason, differentiating follicular adenomas from follicular carcinomas is extremely difficult with FNAB cytology and frozen section analysis. The tumors are divided into minimally invasive and widely invasive lesions depending on the histologic evidence of capsule and vascular invasion. Immunohistochemical staining for thyroglobulin and cytokeratins is nearly always positive.

- **Hürthle cell carcinoma:**

On pathologic examination, Hürthle cell carcinoma, like follicular carcinoma, is differentiated from Hürthle cell adenoma by the presence of capsular invasion, vascular invasion, or both. On gross evaluation, Hürthle cell carcinomas appear brown and solid. Most have an appreciable capsule. Under microscopy, the tumors have a solid or trabecular growth pattern of large, granular, polygonal Hürthle cells.

Because malignant tumors are difficult to identify on the basis of cellular elements alone, Hürthle cell tumors identified on FNAB findings cannot be categorized as malignant or benign. Therefore, when FNAB results suggest a Hürthle cell neoplasm, a surgically obtained specimen is required.

- **Medullary carcinoma:**

On gross examination, MTCs are fairly well circumscribed, though they are unencapsulated. They are typically tannish pink and often contain yellow granular regions, which represent focal calcification. Most tumors arise in the middle and upper third of the thyroid lobes, commensurate with the location of the parafollicular C cells in the thyroid gland. Sporadic tumors are unilateral, and inherited forms usually involve both thyroid lobes.

MTCs can have a varied microscopic appearance. The tumors typically have a lobular, trabecular, insular, or sheet like growth pattern. Some tumors have a fibrotic character. Malignant cells may appear round, polygonal, or spindle shaped. The cytoplasm is eosinophilic and finely granular. In the stroma, characteristic deposits of amyloid are commonly observed. This amyloid has typical green birefringence on Congo red staining, and this is a feature unique to MTC among thyroid malignancies. Immunohistochemical stains for calcitonin and carcinoembryonic antigen are microscopically useful for differentiating MTC from other tumors.

A unique feature to the familial cases of MTC is the finding of C-cell hyperplasia, which can help in distinguishing familial cases from sporadic ones. C-cell hyperplasia is considered a precursor to MTC and is usually adjacent to foci of MTC. The finding of C-cell hyperplasia with MTC should raise the suspicion for familial disease.

- **Anaplastic carcinoma:**

On gross examination, anaplastic thyroid carcinoma is a large and invasive tumor. Areas of focal necrosis and hemorrhage may be present throughout the tumor, giving a highly variable appearance. The tumor often extends through the capsule of the thyroid gland itself. Areas of well-differentiated thyroid carcinoma are often found concomitantly, and anaplastic thyroid carcinoma is believed to arise from a preexisting, well-differentiated thyroid carcinoma.

On microscopic evaluation, squamoid, spindle cell, and giant cell variants are observed. All 3 histologic variants show high mitotic activity, large foci of necrosis, and notable infiltration. Immunohistochemical stains are often positive for low-molecular-weight keratins and occasionally positive for thyroglobulin. Regarding their ultrastructure, the neoplasms have epithelial features (eg, desmosomes, tight junctions) that are helpful for differentiating them from sarcomas. Small cell carcinomas, which usually represent lymphomas, may be confused with anaplastic thyroid carcinoma.

Clinical features of papillary carcinoma thyroid:

i. **Papillary thyroid carcinoma (PTC) represents 85% of thyroid carcinomas. PTC is often multifocal.**
ii. **The most common presenting symptom is a thyroid swelling.**
iii. **Papillary cancer tends to spread via the lymphatics with a known propensity for involvement of the mid- and lower-anterior cervical lymph nodes.**
iv. **Enlarged cervical lymph nodes may be the presentation of papillary carcinoma.**
v. **Invasion of adjacent structures and distant metastases at the time of presentation are uncommon.**
vi. **Recurrent laryngeal nerve paralysis is very suggestive of locally advanced disease.**

Diagnosis: Essentials of Diagnosis

- **History of irradiation to the neck in some patients.**
- **Painless or enlarging nodule, dysphagia, or hoarseness.**
- **Firm or hard, fixed thyroid nodule; ipsilateral cervical lymphadenopathy.**
- **Normal thyroid function; nodule stippled with microcalcifications and solid (ultrasound), cold (radioiodine scan); positive or suspicious cytology.**
- **Family history of thyroid cancer.**

Investigations:

- **Thyroid function test**
- **USG guided FNAC: Ultrasonography and radionuclide thyroid scans cannot distinguish benign from malignant nodules and therefore are not essential in the workup of a thyroid nodule. Ultrasonography is commonly used to direct FNA biopsy and is a sensitive method for determining whether a lesion is solid or cystic.**
- **CT/USG of neck.**
- **Indirect laryngoscopy.**

Pathology:

- **Microscopically, it is composed of papillary projections of columnar epithelium.**
- **Psammoma bodies are present in about 60% of cases.**

- **Mixed papillary-follicular, follicular variants of papillary carcinoma, and poorly differentiated cancers including tall cell and columnar cell papillary thyroid cancers are sometimes found.**
- **The rate of growth may be stimulated by TSH.**
- **A *BRAF* mutation is the most common mutation in papillary thyroid cancer and is associated with lymph node metastases and a higher recurrence rate.**

Treatment: Low-Versus High-Risk Criteria in Papillary Thyroid Cancer

Low risk	High risk
1. Women < 50 years 2. Men < 40 years 3. Well-or moderately differentiated tumors 4. Tumor < 4 cm in diameter 5. Tumor confined to the thyroid gland 6. No distant metastases	1. Women ≥ 50 yr 2. Men ≥ 40 yr 3. Poorly differentiated tumors, tall-cell, columnar cell, or oxyphilic variants. 4. Tumor ≥ 4 cm in diameter 5. Local invasion 6. Distant metastases

Surgical treatment:

- **A lobectomy and isthmusectomy is satisfactory for papillary cancers less than 1.0 cm in size without lymphatic or systemic metastases.**
- **Lobectomy with isthmusectomy - for patients with papillary cancers that are greater than 1.0 cm when patients are categorized as low risk for recurrence or mortality.**
- **Total thyroidectomy is uniformly accepted for treatment of high-risk papillary carcinoma.**
- **In addition, patients with a history of head and neck irradiation should undergo total thyroidectomy due to the high incidence of carcinoma at sites other than the nodule and their increased lifetime risk of developing thyroid cancer in the remaining thyroid gland.**

Role of post operative remnant ablation:

Indications:

• Stage III and IV disease
• All patients with stage II disease younger than age 45 years
• Most patients with stage II disease 45 years or older
• Selected patients with stage I disease - especially those with multifocal disease, nodal metastases, extra-thyroidal or vascular invasion, and/or more aggressive histologies.

Protocol of thyroid hormone withdrawal for remnant ablation

Aim: Achieve TSH of more than 30 mU/L

- **Single-dose exogenous rTSH results in TSH levels between 51–82 mU/L**
- **Endogenous TSH elevation can be achieved by**
  - **Stopping levothyroxine (LT4) and switching to levo-triiodothyronine (LT3) for 2–4 weeks followed by withdrawal of triiodothyronine (T3) for 2 weeks**
  - **Discontinuation of LT4 for 3 weeks without use of T3**
  - **rTSH stimulation can be used for remnant ablation.**

Role of post operative diagnostic RAIU scan:

• Indication:

– When the extent of thyroid remnant cannot be assessed from the surgical report/ USG
– If the result is likely to alter the subsequent management
– If the result is likely to alter the dose of RAI treatment
• If used, low dose I 131 (1-3mCi)/ I123 scan recommended
– Low iodine diet (50microgram/day for 1-2 weeks) is recommended prior to scan
• Post therapy scan:
- **Detects additional foci in 10-26% cases, alters the stage in 10%**
- **Done 1 week post radio-iodine therapy.**

Role of TSH suppression therapy:
Mechanism of action:
- **Decreases the expression of thyroid specific proteins**
- **Decreases the rate of cell growth**

- **High risk pts:**
  - **Keep TSH < 0.1mIU/L**
  - **After remission continue suppressive therapy x 3-5 yrs**
- **Low risk patients**
  - **TSH= 0.1-0.5 mIU/L**
  - **After remission keep it between 0.5-1mIU/mL**

There is no role for routine adjunctive chemotherapy.

Follicular cell malignancies can be clinicopathologically divided into
Differentiated (DTC)
Papillary & variants
Follicular & variants
Hürthle cell
Undifferentiated
Anaplastic
The presentation may be:
- **With thyroid swelling, goitre which can be nodular (solitary or multiple) or diffuse.**
- **Goitre with local pressure / infiltration effects viz hoarseness of voice, dysphagia, and superior mediastinal syndrome.**
- **Manifestations due to secondaries, primary are small enough as not to be complaint of patient or occult.**
- **Dysfunction: both hypo and hyperthyroidism. Development of malignancy in a nodule of toxic goitre is well documented.**
- **Malignant change in a pre-existing goitre indicated by rapid increase in size or local pressure effects.**
- **Histological surprise: Solitary thyroid nodule has 30% chances of being malignant. Radionuclide scan is helpful in planning management. Cold nodule must vigorously be pursued to rule out malignancy.**

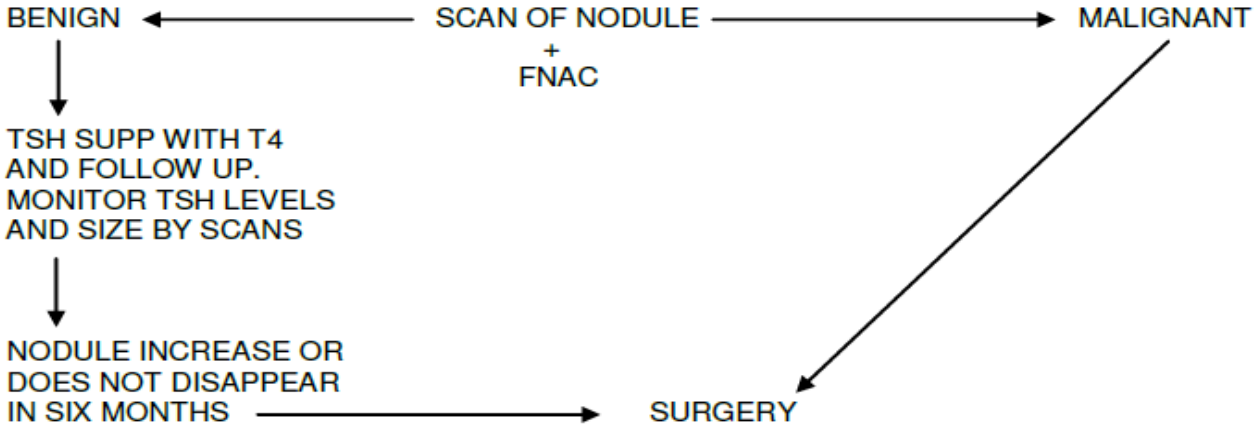
The work up includes:
- **History - short history (not necessary in WDTC) and recent rapid increase in size.**
- **Symptoms of local involvement viz change n voice, respiratory difficulty, dysphagia.**

- **Physical examination- hard consistency, local limitation of mobility, involvement of strap muscles, and obliteration of carotid pulse all suggests malignancy. Pizello's method, Lahey's method and Berry's sign are all contributory.**
- **Evidence of metastases in bones, lungs and liver besides cervical lymph nodes.**
- **Dysfunction of Thyroid, Functioning tumours are known to produce clinical hyperthyroidism in 5% cases.**

Investigations:

- **High Resolution Ultrasound: Halo sign, commet tail sign, and type 3 intranodular vascularity of malignancy are helpful. Involvement of trachea, vessels, strap muscles can be made out.**
- **Fine Needle Aspiration Cytology: Cellular diagnosis of DTC is now feasible; ultrastructural study and histo/histocytochemistry are a great help.'**
- **Trucut Biopsy: Selected indication is in inoperable cases to plan out management. Also to differentiate lymphoma from anaplastic carcinoma.**
- **Monoclonal antibodies for lymphoma: This can differentiate anaplastic carcinoma from lymphoma.**
- **Imprint smear: Better interpretation than FNAC/ Frozen section.**
- **CT/MRI: Specific indication is to know extent of tumour spread and local tissue plane infiltration.**
- **Scinti scan: Presently limited use. Cold nodule classically in malignancy. Still helpful in solitary nodule thyroid.**
- **Tumor markers: Very significant is TGB which if done before and after management helps in follow up and can indicate recurrence/ mets. CEA, CD-34, MVD, p 53 protein have also correlation.**
- **X-ray Chest and X-ray of bone met site: Demonstrates local secondary deposit.**
- **Ultrasound Liver: Done to detect liver metastases wherever suspected.**
- **Skeletal survey: Done by radionuclide scan (Gamma camera) wherever indicated can alter the clinical staging of the disease.**

Flow chart:



Surgery for Follicular Carcinoma:

- **From clinicopathological stand point these carcinomas are divided into low risk and high risk.**
- **Three important risk factors viz vascular invasion, metastases and age greater than 45 years.**

- **The result of cytological and frozen section histology in this tumour is high in accuracy of both in interpretation.**
  - **In low risk patient with intrathyroidal (non invasive) lesion less than 2.5 cm in size (determined on scan) a hemithyroidectomy with isthumusectomy suffices.**
  - **Completion thyroidectomy is indicated if histology reveals a more invasive form of carcinoma postoperatively.**
  - **In all other follicular carcinoma, a total or near total thyroidectomy is indicated. This is recommended in presence of even metastases (the incidence of which is fairly high with this carcinoma) as it facilitates adjuvant treatment with I -131.**
- **If nodes are involved, ipsilateral functional block dissection with central compartment clearance is to be undertaken.**

One point to note that F.N.A.C cannot distinguish between follicular adenoma and carcinoma. So we have to go for right subtotal thyroidectomy and send the specimen for HP examination to find out the final diagnosis and treat accordingly.

Hürthle Cell Tumors:

- **Hürthle cell, though modified follicular cell is now considered a separate tumor altogether, contrary to earlier belief, majority HCN are benign.**
- **Capsular and vascular invasion on histology and metastases clinically characterize malignant HCN.**
- **There is an indeterminate form also. The potential incidence of indeterminate forms creates controversy regarding extent of surgery.**
- **The undisputed benign forms are best treated by hemithyroidectomy.**
- **For aggressive benign type, indeterminate type and frankly malignant HCN, a total or near thyroidectomy is the standard.**
- **If malignancy is found on post operative histology in a pre operative diagnosed benign lesion, a completion thyroidectomy is then indicated.**
- **The approach to lymph nodes is same as in follicular carcinoma; if nodes are involved, ipsilateral functional block dissection with central compartment clearance is to be undertaken.**

- **The initial treatment for cancer of the thyroid is surgical. The exact nature of the surgical procedure to be performed depends for the most part on the extent of the local disease. A consensus approach might be to perform a total thyroidectomy if the primary tumor is larger than 1 cm in diameter or if there is extrathyroidal involvement or distant metastases. Clinically evident lymphadenopathy should be removed with a neck dissection. If the primary tumor is less than 1 cm in diameter, a unilateral lobectomy might be considered.**
- **Current National Comprehensive Cancer Network (NCCN) guidelines recommend lobectomy plus isthmusectomy as the initial surgery for patients with follicular neoplasms, with prompt completion of thyroidectomy if invasive follicular thyroid carcinoma (FTC) is found on the final histologic section. Therapeutic neck dissection of involved compartments is recommended for clinically apparent/biopsy-proven disease.**

PARATHYROID

21. What are the functions of parathormone? Write in detail about clinical, feature, investigations and management of hyperparathyroidism. 3+4+4+4 = 15 [The West Bengal University of Health Sciences, Paper –II of 2010]

22. What are the clinical features of primary hyperparathyroidism? Discuss the investigation and management of primary hyperparathyroidism. 6+5+4 = 15 [The West Bengal University of Health Sciences, Supplementary Paper –II of 2014]

23. Primary hyperparathyroidism. 5 [The West Bengal University of Health Sciences, Supplementary Paper –II of 2010]

Answer.

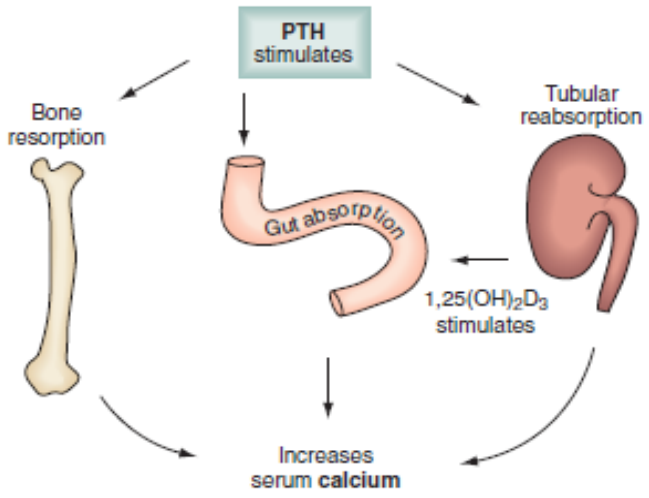
Functions of parathormone:

- **Calcium regulation:**

Actions of Major Calcium-Regulating Hormones:

HORMONE	BONE	KIDNEY	INTESTINE
Parathyroid hormone	Stimulates resorption of calcium and phosphate	Stimulates resorption of calcium and conversion of $25(OH)D_3$; inhibits resorption of phosphate and bicarbonate	No direct effects
Vitamin D	Stimulates transport of calcium	Inhibits resorption of calcium	Stimulates calcium and phosphate absorption
Calcitonin	Inhibits resorption of calcium and phosphate	Inhibits resorption of calcium and phosphate	No direct effects

Calcium homeostasis and PTH:



Hyperparathyroidism

Introduction:

- **Primary hyperparathyroidism (PHPT) is a common endocrine disease.**
- **Prevalence is highest among postmenopausal women, with 1:500 possibly being affected.**
- **Most patients are identified by an incidental finding of raised serum calcium during investigations for another condition.**

Causes:

- **The most common cause of primary hyperparathyroidism is a sporadic, single parathyroid adenoma.**
- **Less common are parathyroid hyperplasia, parathyroid carcinoma (malignant tumor), and adenomas in more than one gland.**

Familial syndromes associated with primary hyperparathyroidism:

Name	Features	Gene involved
MEN 1 (Wermer's) syndrome	PHPT Entero-pancreatic tumors Anterior pituitary tumors	MEN 1 gene on 11q13
MEN 2a syndrome	Medullary thyroid carcinoma Pheochromocytoma PHPT	RET proto-oncogene on chromosome 10
Hyperparathyroidism- Jaw tumor syndrome	PHPT (especially carcinomas) Jaw tumors	HRPT2 on 1q24-32
Familial isolated hyperparathyroidism	PHPT	

Clinical features:

- **Classical symptoms are described as:**
  - **Moans - psychological/psychiatric symptoms (lethargy, depressed mood);**
  - **Groans - non-specific gastrointestinal symptoms (abdominal pain, constipation);**
  - **Bones - aches/pains localized in large joints;**
  - **Stones - calcium based renal stones.**

Symptoms and signs of primary hyperparathyroidism:

Musculoskeletal	Renal	Neuropsychiatric
Muscle weakness	Renal calculi/renal colic	Impaired concentration
Myalgia	Nephrocalcinosis	Memory loss
Bone aches/pains	Thirst/dehydration	Anxiety
Osteoporosis	Polyuria/oliguria/anuria	Depression
Osteitis fibrosa cystica	Renal failure	Confusion
Brown's tumors		Dementia/paranoia
		Ataxia
		Hyporeflexia
		Coma
Gastrointestinal	**Cardiovascular**	**Other**
Nausea/vomiting	Hypertension	Visual changes
Abdominal pain	Vascular calcification	Band keratopathy (corneal calcification)
Anorexia	Shortened Q-T interval	Conjunctivitis
Peptic ulcer disease	Bradycardia	Pruritus
Pancreatitis	Heart block	
Constipation	Lethal arrhythmias	
Weight loss		

Investigations Diagnosis:

- **The diagnosis of primary hyperparathyroidism is made by blood tests. Serum calcium levels are elevated, and the parathyroid hormone level is abnormally high compared with an expected low level in response to the high calcium.**
- **Serum parathyroid hormone concentration (PTH) in the presence of hypercalcaemia confirms the diagnosis [e.g. bone metastases (breast, renal, thyroid carcinoma) have a low (i.e. inhibited) PTH concentration].**
- **Corrected serum calcium is highly suggestive if unexplained but not diagnostic.**
- **Urinary cAMP is occasionally measured; this is generally elevated.**
- **High-resolution neck ultrasound may identify tumours.**

- **Sestamibi (radioisotope) scanning used to localize adenomas (accurate in 50%) and allows a focused approach (minimally invasive parathyroidectomy).**
- **The most frequently applied approach is preoperative sestamibi scanning, followed by direct excision of the identified gland and confirmation of cure by intraoperative PTH measurement.**

Preoperative imaging in patients with primary hyperparathyroidism:

IMAGING MODALITY	SENSITIVITY	SPECIFICITY	COST	SAFETY
Noninvasive				
Sestamibi	Moderate	Moderate	Moderate	Safe
Sestamibi SPECT	High	High	Moderate	Safe
Ultrasound	Moderate	Moderate	Low	Safe
4D-CT	High	High	High	Radiation
MRI	Low	Moderate	Moderate	Safe
PET-CT	?	?	High	Radiation
Invasive				
Angiography	Moderate	Moderate	Very high	Hematoma, CVA, nephropathy*
Venous localization	High	High	Very high	Hematoma, nephropathy*
Ultrasound, biopsy	High	High	Moderate	Hematoma, infection

4D-CT, Four-dimensional CT; *CVA*, cerebrovascular accident (stroke); *PET*, positron emission tomography; *SPECT*, single-photon emission CT.

*IV contrast nephropathy.

Treatment:

Medical treatment

- **Hypercalcaemic crisis needs aggressive rehydration.**
- **Establish large calibre IV access. Give 1L in first hour, further 4-6L in first 24h.**
- **Monitor urine output and central venous pressure until normalized.**
- **Frusemide can be added to increase urinary excretion of calcium once rehydration is adequate.**
- **Bisphosphonates (e.g. IV pamidronate) should be avoided in PHPT when parathyroidectomy is anticipated, since they impair the ability to maintain normocalcaemia after the excision of an overactive parathyroid adenoma.**

Medical management of hypercalcemic crisis

Group	Drug	Side effects
Diuretic	Normal Saline	
	Furosemide	Hypokalemia
Antiresorptive	Bisphosphonates	Osteonecrosis of jaw
	Calcitonin	Diarrhea
	Plicamycin	Hepatotoxic Nephrotoxic Thrombocytopenia
Decrease calcium absorption	Glucocorticoids	Systemic
	i.v. Phosphate	Extraskeletal calcium deposition
Extractive	Hemodialysis	

Surgical treatment:

Indications for parathyroidectomy in primaryhyperparathyroidism.

- **Urinary tract calculi**
- **Reduced bone density**
- **High serum calcium**
- **? All in younger age group <50 years**
- **Deteriorating renal function**
- **Symptomatic hypercalcaemia**

Operation:

- **Bilateral neck exploration, visualization of all four parathyroid glands with excision of the enlarged one(s), has for many years been the standard treatment. It remains the treatment for those with negative localization scans.**
- **When imaging studies identify reliably the position of the adenoma, patients can undergo minimally invasive parathyroidectomy (MIP). This is a focused neck exploration through a lateral cervical scar aiming to remove the adenoma visualized on scanning and not to explore the other parathyroid glands.**

Secondary Hyperparathyroidism in Renal Failure

- **Renal osteodystrophy- osteitis fibrosa cystica, osteomalacia, and adynamic bone disease.**
- **It is associated with osteopenia, bone cysts, brown tumors, and decreased bone strength resulting in long bone fractures because of dystrophic bone formation.**
- **Osteomalacia is characterized by lower bone turnover, mineralization deficiency, and accumulation of unmineralized osteoid.**

- **Adynamic bone disease is characterized by hypocellular bone surfaces with little or no evidence of remodeling, and it is common in patients with normal or low PTH or severe diabetes and aluminum intoxication. It has been associated with long-term peritoneal dialysis. It can cause fractures and microfractures leading to bone pain.**

Treatment:

- **Treat renal failure.**
- **Surgery: Subtotal parathyroidectomy seems to be the preferred surgical approach in most, but not all patients.**
- **The residual parathyroid tissue in the neck or forearm will grow and cause recurrent disease if survival is prolonged and patients do not receive a renal transplant.**
- **Nodular proliferation in glands seems to predispose to recurrence more often than homogeneous gland hyperplasia does.**
- **Cryopreservation of excised tissue (if available) is a good strategy when total parathyroidectomy with autotransplantation is planned in the event that the autograft is nonfunctional.**

Tertiary HPT occurs in two settings

- **The first is in a subset of patients with secondary HPT in which the parathyroid glands become autonomous and hypercalcemia develops.**
- **The second was first recognized by St. Goar, who described how secondary HPT can persist even after patients underwent renal transplantation; he postulated that the parathyroids became autonomous.**
  - **Theoretically, reversal of parathyroid hyperplasia should be expected after successful renal transplantation. Of these, less than 1% require parathyroidectomy for tertiary HPT.**
  - **Transplant patients may have additional factors that can contribute to persistent tertiary HPT; glucocorticoids, cyclosporine, thiazide diuretics, and alterations in the glomerular filtration rate as a result of tubular injury or rejection episodes can influence parathyroid function and bone response.**
  - **Accordingly, patients with severe secondary HPT should not undergo renal transplantation until their secondary HPT has been treated.**
  - **Surgical treatment of tertiary HPT after renal transplantation is not common and is reserved for patients without resolution of symptoms, patients with hormonal and chemical abnormalities such as elevated or increasing iPTH levels and an increase in serum calcium to greater than 12.0 mg/dL that persists more than 1 year after transplantation, and patients with acute hypercalcemia (calcium level >12.5 mg/dL) in the immediate post-transplant period.**

24. Tetany. 5 [The West Bengal University of Health Sciences, Paper –II of 2008]

Answer.

Introduction: Tetany is a medical sign consisting of the involuntary contraction of muscles, which may be caused by disease or other conditions that increase the action potential frequency of muscle cells or the nerves that innervate them. Muscle cramps which are caused by the disease tetanus are not classified as tetany; rather, they are due to a lack of inhibition to the neurons that supply muscles.

Pathophysiology:

<u>Hypocalcemia:</u> It is the primary cause of tetany. Low ionized calcium levels in the extracellular fluid increase the permeability of neuronal membranes to sodium ions, causing a progressive depolarization, which increases the possibility of action potentials. This occurs because calcium ions interact with the exterior surface of sodium channels in the plasma membrane of nerve cells. When calcium ions are absent the voltage level required to open voltage gated sodium channels is significantly altered (less excitation is required). If the plasma Ca^{2+} decreases to less than 50% of the normal value of 9.4 mg/dl, action potentials may be spontaneously generated, causing contraction of peripheral skeletal muscles. Hypocalcemia is not a term for tetany but is rather a cause of tetany.

Causes:

- **Diarrhea**
- **Kidney disease**
- **Thyroid or pancreas problems**
- **Pregnancy and breast feeding**
- **Malnutrition**
- **Vitamin D deficiency**
- **Some medications**
- **Calcium deficiency**

Clinical features:

<u>Symptoms:</u>

Severe	Non severe
• Abdominal pain • Chronic diarrhea • Muscle pain • Tingling in hands or feet • Twitching fingers	• Loss of muscle coordination • Loss/change in vision • Paralysis • Seizures • Slurred speech • Sudden difficulty with memory, thinking, talking, writing or reading • Sudden weakness or numbness on one side

Diagnosis:

- **Trousseau sign: occlusion of the brachial artery by squeezing triggers cramps in the fingers.**
- **Chvostek sign: tetany can be demonstrated by tapping anterior to the ear, at the emergence of the facial nerve. A resultant twitch of the nose or lips suggests low calcium levels.**
- **Tetany is characterized by contraction of distal muscles of the hands (carpal spasm with extension of interphalangeal joints and adduction and flexion of the metacarpophalangeal joints) and feet (pedal spasm) and is associated with tingling around the mouth and distally in the limbs.**
- **EMG studies reveal single or often grouped motor unit discharges at low discharge frequency during tetany episodes.**

Treatment:

- **Detection of low calcium levels is important. Tetany can be fatal if it involves laryngeal or pharyngeal muscles; which blocks the airway.**
- **IV Treatment:**
  - **Calcium carbonate is used in the initial stage of Hypocalcemia.**
  - **Calcium gluconate is used for muscle cramps or nerve weakness.**
  - **Calcium chloride is for patients in serious condition.**

ADRENAL

25. M.E.N syndrome. 5 [The West Bengal University of Health Sciences, Paper –II of 2009, 2016]

Answer.

Introduction:

- **Multiple Endocrine Neoplasia (MEN) syndromes are familial conditions characterized by the occurrence of tumors involving two or more endocrine glands in a patient and family members.**
- **There are two major forms of MEN, namely MEN-type 1 (MEN1, →Wermer's syndrome) and MEN-type 2(MEN2, Sipple's syndrome); each form is characterized by the development of tumors of specific endocrine glands.**
- **The MEN syndromes are uncommon, but because they are inherited as autosomal dominant disorders, the finding of MEN in a patient has important implications for other family members. First degree relatives of a patient with known MEN have about a 50% risk of developing the disease.**
- **Occasionally, the MEN syndromes may arise sporadically (*i.e.* without a family history).**

MEN 1:

- **Autosomal dominant.**
- **The MEN1 gene was originally mapped to chromosome 11q13 by a combination of genetic linkage studies and tumor deletion mapping. It encodes a protein merlin.**
- **The MEN1 gene consists of 10 exons spanning 9 kb of genomic DNA and encodes a 610–amino acid protein product termed menin.**

Features of MEN 1

Major disease components	Associated tumors
• Primary hyperparathyroidism • Pancreatic endocrine tumors (PET) • Anterior pituitary tumor	• Facial angiofibroma • Collagenoma • Adrenal cortical tumor • Lipoma • Foregut carcinoid

Components of MEN-1 with estimated penetrance (in parentheses) at age 40 year:

Endocrine features	Non-endocrine features
PHPT- Parathyroid hyperplasia (90%)	Lipomas (30%)
Entero-pancreatic tumor 1. **Gastrinoma** (40%) 2. Insulinoma (10%) 3. Non-functioning (**NF**) including **pancreatic polypeptide** (20%) 4. Other rare types: (2%) **glucagonoma** **VIPoma** **somatostatinoma** *etc.*	Facial angiofibromas (85%) Collagenomas (70%) Ependymoma (1%)
Foregut carcinoid **Thymic carcinoid** NF (2%) **Bronchial carcinoid** NF (2%)	
Gastric entero-chromaffin-like tumor NF (10%)	
Anterior pituitary tumor Prolactinoma (20%) Other: GH + PRL, GH, NF (each 5%) ACTH (2%), TSH (rare)	
Adrenal cortex NF (25%)	
Pheochromocytoma (<1%)	

- **Parathyroid gland tumours. By age 40, 95% of patients have hypercalcaemia which is the commonest manifestation.**
- **Pancreatic islet cell tumours.**
  - **Prevalence of 30-75%.**
  - **Usually multicentric, slow-growing.**
  - **Secrete multiple polypeptides (insulin and gastrin commonest).**
  - **Gastrinoma leads to Zollinger-Ellison syndrome (recurrent and multiple peptic ulcers, severe reflux oesophagitis, and diarrhoea).**
  - **Rarer tumours are VIPoma, glucagonoma, somatostatinoma.**
- **Anterior pituitary tumours.**
  - **Detected in 15-40%.**
  - **Commonest is prolactinoma.**
  - **Rarer are GH- (causes acromegaly) or ACTH- (causes Cushing's disease) secreting tumours.**

Carcinoid tumours (thymus, lungs, foregut), adrenal tumours, lipomas, and pinealomas have also been reported to appear in MEN-1 patients.

MEN 2A	MEN2B
Medullary thyroid carcinoma	**Medullary thyroid carcinoma**
Pheochromocytoma	**Pheochromocytoma**
Hyperparathyroidism	**Marfanoid body habitus**

Lichen planus amyloidosis	**Mucosal neuromas**
Hirschsprung's disease	**Ganglioneuromatosis of the gastrointestinal tract**

MEN 2:
Clinical Features of Sporadic MTC, MEN 2A, MEN 2B, and FMTC:

CLINICAL SETTING	FEATURES OF MTC	INHERITANCE PATTERN	ASSOCIATED ABNORMALITIES	GENETIC DEFECT
Sporadic MTC	**Unifocal**	**None**	**None**	**Somatic *RET* mutations in >20% of tumors**
MEN 2A	**Multifocal, bilateral**	**Autosomal dominant**	**Pheochromocytomas, hyperparathyroidism**	**Germline missense mutations in extracellular cysteine codons of *RET***
MEN 2B	**Multifocal, bilateral**	**Autosomal dominant**	**Pheochromocytomas, mucosal neuromas, megacolon, skeletal abnormalities**	**Germline missense mutation in tyrosine kinase domain of *RET***
FMTC	**Multifocal, bilateral**	**Autosomal dominant**	**None**	**Germline missense mutations in extracellular or intracellular cysteine codons of *RET***

Treatment:
Surgical treatment:
MEN-1

- **Parathyroidectomy.**
- **Pancreatic tumours: enucleation of individual tumours in the head of the pancreas and distal pancreatectomy for tumours in the tail/body.**
- **Hypophysectomy and external beam irradiation are considered for pituitary tumours.**

MEN-2

- **Total thyroidectomy (TT) indicated in patients identified by genetic screening. Symptomatic patients need TT and cervical nodal dissection for the lymph nodes on the involved side.**
- **Laparoscopic adrenalectomy for phaeochromocytoma.**
- **Parathyroidectomy for MTC in patients belonging to families in which hyperparathyroidism is frequently associated.**

Medical treatment:

MEN-1 Prolactinomas can be treated with dopamine agonists (bromocriptine/cabergoline).

26. Discuss the clinical features, investigations and management of Pheochromocytoma. 4+5+6 = 15 [The West Bengal University of Health Sciences, Paper –II of 2017]

27. Discuss the clinical features of pheochromocytoma. How will you diagnose this condition? Give an outline of management. 5+5+5 = 15 [The West Bengal University of Health Sciences, Paper – II of 2013]

28. Pheochromocytoma. 5 [The West Bengal University of Health Sciences, Supplementary Paper – I of 2014]

Answer.

Pheochromocytoma is said to follow the rule of ten:

- **10% are multifocal;**
- **10% are bilateral;**
- **10% are extra-adrenal;**
- **10& are malignant;**
- **10% occur in children.**

Clinical features: Symptoms and signs are caused by catecholamine excess and are typically intermittent.

- **Excess catecholamine secretion leads to characteristic episodes of;**

Headache;	Sweating;	Palpitations

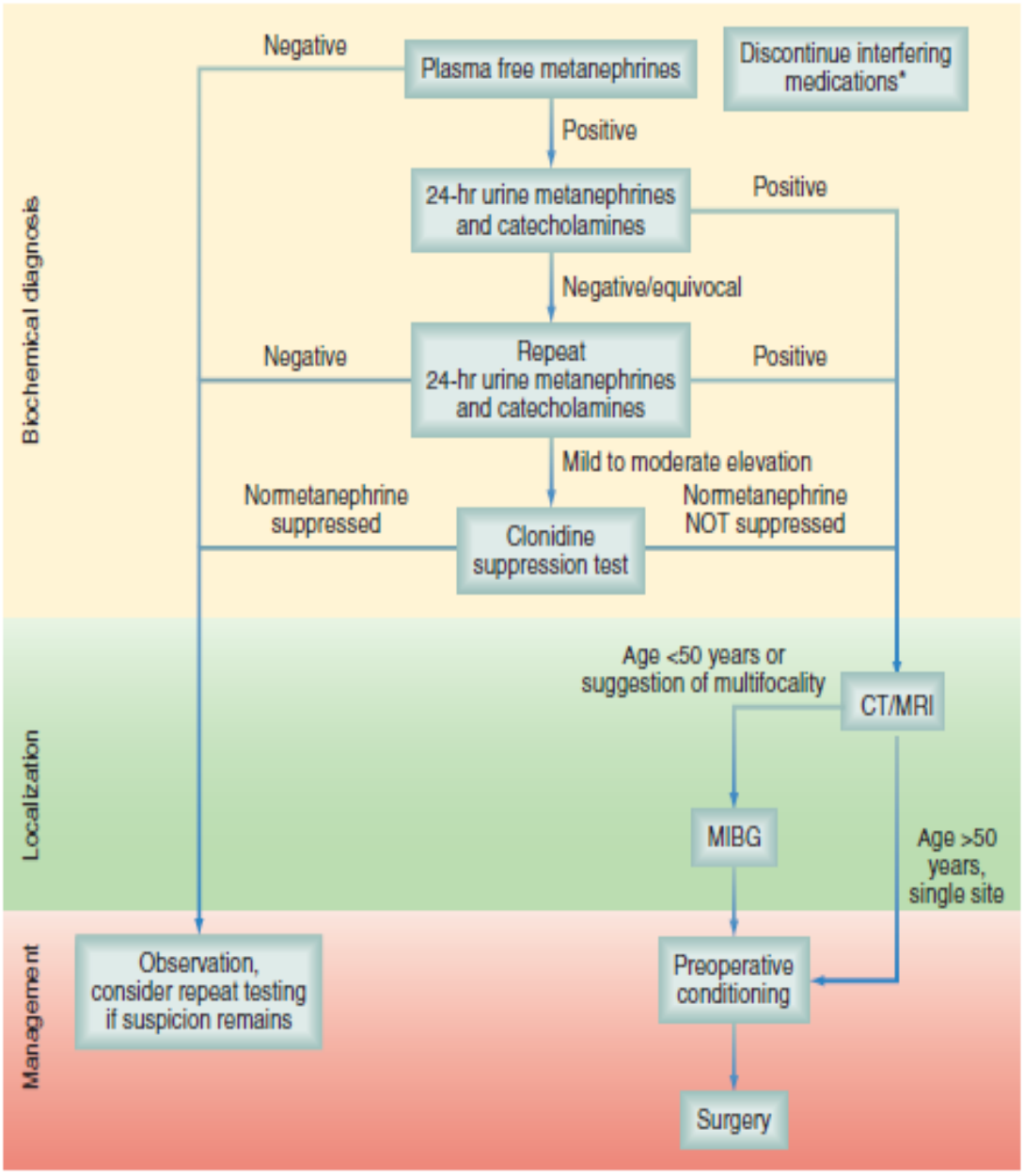
- **Paroxysmal hypertension, tachydysrhythmias, and a feeling of impending doom or death may also occur.**

- **Attacks can be triggered by activities causing mechanical pressure on the tumour (e.g. physical exercise, defecation, intercourse), by ingestion of alcohol, labour, general anaesthesia, and surgical procedures.**
- **Only 50% of patients have persistent hypertension. The other 50% have normal blood pressure or are hypotensive between the acute episodes.**

Clinical signs of phaeochromocytoma:

• **Hypertension** ○ **Paroxysmal** ○ **Continuous**	• **Headache**	• **Palpitation**	• **Weight loss**	• **Nausea**
	• **Sweating**	• **Pallor**	• **Hyperglycaemia**	• **Psychological effects**

Algorithm for the diagnosis, localization, and management of pheochromocytoma:



*Including sympathomimetics, phenoxybenzamine, acetaminophen, many psychotropic drugs.

Diagnosis and investigations: Consider the diagnosis in patients with characteristic paroxysmal episodes, in those with unusually labile or intermitted hypertension, in those with a family history of phaeochromocytoma or related conditions (see MEN syndromes), and in hypertensive children.

- **24h urine collection and assessment for VMA and NorAd is most accurate for diagnosis.**
- **Clonidine suppression test (failure of urine levels to fall after clonidine dose) confirms the diagnosis where urine levels are border line.**

- **Provocative testing (e.g. stimulation with bolus IV glucagons) is rarely necessary and risky.**

Localizing studies:

- **Thoraco-abdominal CT or MRI scanning: first-line test especially for adrenal and sympathetic chain tumours.**
- **MIBG (meta-iodo-benzyl-guanidine) scanning localizes extra-adrenal sites not seen on CT or MRI.**

Treatment:

Medical treatment:

- **It is imperative to control the blood pressure prior to any surgery**
- **Alpha-blockers are given(e.g. phenoxybenzamine 10mg bd/tds up to the maximum dose tolerated) until hypertension controlled.**
- **Beta-blockade (e.g. propranolol) can be added after hypertension is controlled to control the beta-adrenergic effects (tachycardia).**
- **Alternative treatments with doxazosin (alpha/beta blocker) or calcium channel blockers have been described but are not widely used.**

Surgical treatment:

- **The principle of surgery is complete resection of the tumour (with clear negative margins if suspected of malignancy).**
- **Laparoscopic adrenalectomy is the treatment of choice for smaller adrenal tumours (< 8-10cm); open adrenalectomy for larger tumours.**
- **Local or radical excision are appropriate for extra-adrenal tumours.**

Postoperative management:

- **Patients should be observed for 24 hours in the intensive care or high dependency unit as hypovolaemia and hypoglycaemia may occur.**
- **Lifelong yearly biochemical tests should be performed to identify recurrent, metastatic or metachronous phaeochromocytoma.**

29. Classify adrenal tumours. Describe the investigation and treatment of Adrenal incidentaloma. 5+10 [The West Bengal University of Health Sciences, Supplementary Paper –II of 2016]

Answer.

WHO histological classification of adrenal gland tumours

Adrenal cortical tumours

- **Adrenal cortical carcinoma**
- **Adrenal cortical adenoma**

Adrenal medullary tumours

- **Malignant phaeochromocytoma**

- **Benign phaeochromocytoma**
- **Composite phaeochromocytoma/paraganglioma**

Extra-adrenal paraganglioma

- **Carotid body**
- **Jugulotympanic**
- **Vagal**
- **Laryngeal**
- **Aortico-pulmonary**
- **Gangliocytic**
- **Caudaequine**
- **Orbital Nasopharyngeal**

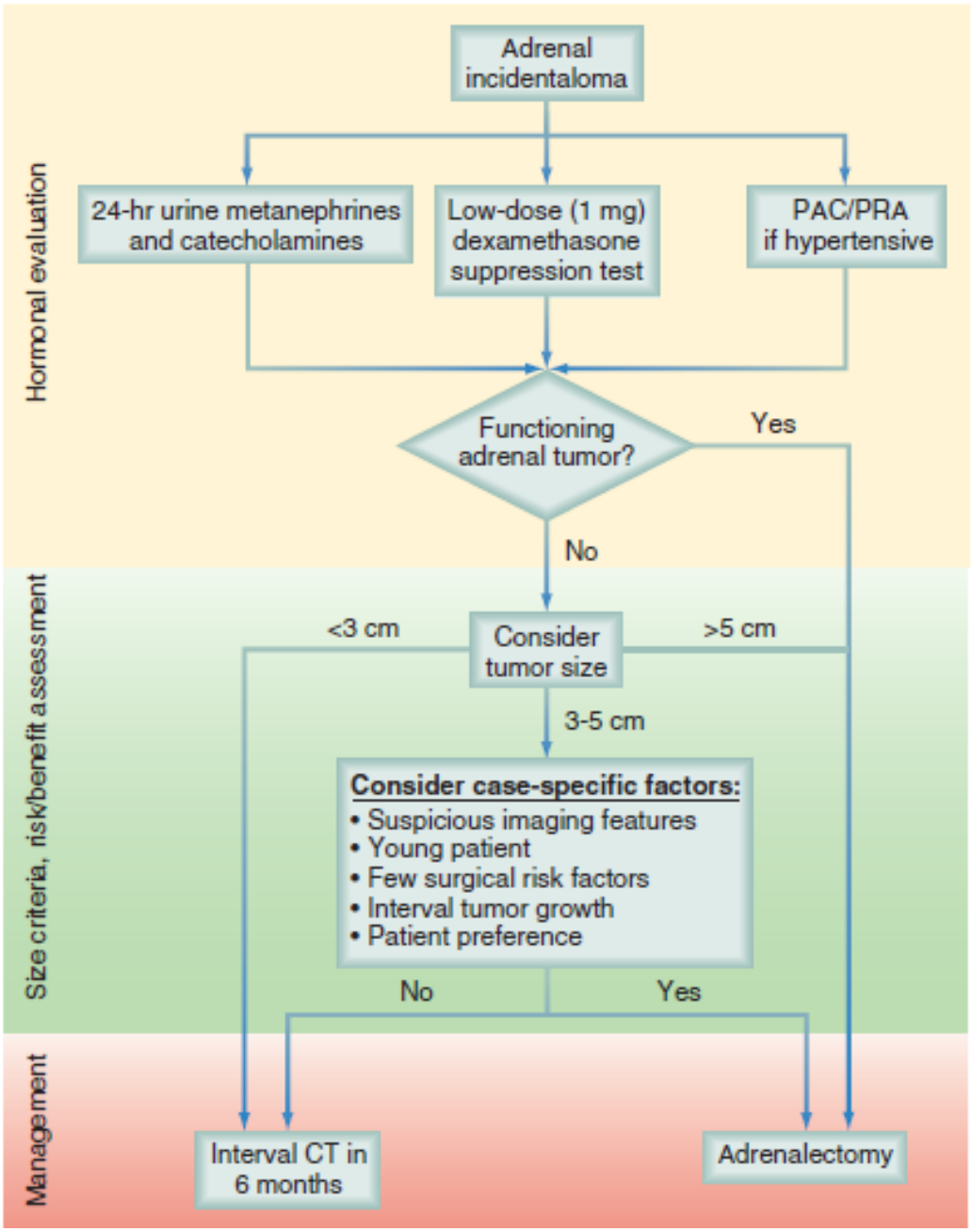
Extra-adrenal sympathetic paraganglioma

- **Superior and inferior para-aortic paraganglioma**
- **Urinary bladder**
- **Intrathoracic and cervical paravertebral**

Other adrenal tumours

- **Adenomatoidtumour**
- **Sex-cord stromal tumour**
- **Soft tissue and germ cell tumours**
- **Myelolipoma**
- **Teratoma**
- **Schwannoma**
- **Ganglioneuroma**
- **Angiosarcoma**

Secondary tumours



Algorithm for the management of an adrenal incidentaloma. Adrenalectomy is recommended for all patients with functional tumors. For nonfunctioning tumors, the risk for malignancy is assessed according to size. Tumors larger than 5 cm on CT carry a >25% risk for malignancy and need to be removed. Those <3 cm can be safely observed.

Case-specific factors must be considered for intermediate sized tumors. PAC, Plasma aldosterone concentration, in ng/ dL; PRA, plasma renin activity, in ng/(mL/ hr).

ENDOCRINE PANCREAS

30. Gastrinoma (ZES syndrome). 5 [The West Bengal University of Health Sciences, Paper –I of 2017]

Answer. Gastrinomas:

- **75% sporadic**
- **25% MEN-1: ZES usually occurs after the onset of hyperparathyroidism in MEN-1 and occurs 50% of the time.**
- **2nd most common islet cell tumor**
- **50% in duodenum**
- **Hypergastrinemia with increased acid output: Hypergastrinemiais responsible for hypertrophy of the gastric mucosa,including the gastric enterochromaffin cells, which in turn increases the number of parietal cells. This increase causes a greater maximal gastric acid output. A secondary action of hypergastrinemia is the stimulation of acid secretion resulting in increased basal acid secretion.**

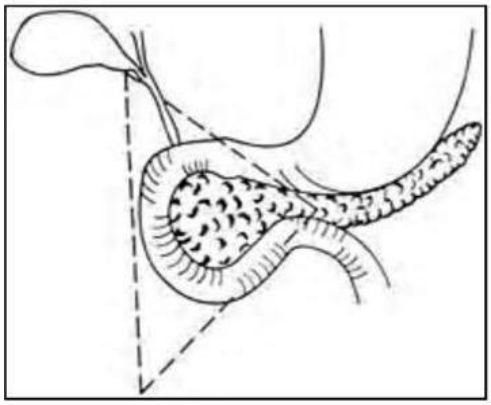
Location

- 1. Gastrinoma triangle 90%

Investigations :

- 2. Somatostatin receptor scintigraphy
- 3. Ultrasound, CT, MRI unreliable
- 4. Endoscopic ultrasound adjunct at surgery

- **Passaro's Triangle.** In 70% to 90% of patients, the primary gastrinoma is found in Passaro's triangle, an area defined by a triangle with points located at the junction of the cystic duct and common bile duct, the second and third portion of the duodenum, and the neck and body of the pancreas.



Presentation

- 1. Abdominal pain
- 2. Ulcer on EGD
- 3. Secretory diarrhea
- 4. calcium, PTH or pituitary tumor with MEN-1
- 5. Recurrence of ulcer despite adequate treatment.

- 1. Ulcers in atypical locations.
- 2. Multiple ulcers
- 3. Ulcers that fail to respond to conventional treatment
- 4. Ulcers that recur after conventional treatment
- 5. Peptic ulcer disease in association with diarrhea
- 6. Ulcers in association with hyperparathyroidism.

Clinical Presentation: Many patients with ZES present with abdominal pain, peptic ulcer disease, and severe esophagitis.

Aspects of Peptic Ulcer Disease That Raise Suspicion for Zollinger-Ellison Syndrome

1. Ulcers in atypical locations.
2. Multiple ulcers
3. Ulcers that fail to respond to conventional treatment
4. Ulcers that recur after conventional treatment
5. Peptic ulcer disease in association with diarrhea
6. Ulcers in association with hyperparathyroidism

Investigations:

- **The diagnosis of ZES is made by measuring the serum gastrin level. It is important that patients stop taking proton pump inhibitors for this test. In most patients with gastrinomas, the level is greater than 1000 pg/ml, but it can be in the 150 to 1000 pg/ml range or even normal.**
- **In equivocal cases, when the gastrin level is not markedly elevated, a secretin stimulation test is helpful. A rise of more than 200 pg/ml confirms the diagnosis of gastrinoma.**

Tumor Localization:

- **The next step is to localize the gastrinoma(s) and to determine if metastases are present. This is best accomplished preoperatively if possible. In 70% to 90% of patients, the primary gastrinoma is found in Passaro's triangle; an area defined by a triangle with points located at the junction of the cystic duct and common bile duct, the second and third portion of the duodenum, and the neck and body of the pancreas.**
- **The test of choice is somatostatin receptor scintigraphy in combination with computed tomography (CT).**
- **Endoscopic ultrasound (EUS) is another new modality that assists in the preoperative localization of gastrinomas. It is particularly helpful in localizing tumors in the pancreatic head or duodenal wall where gastrinomas are usually less than 1 cm. A combination of octreoscan and EUS detects more than 90% of gastrinomas.**

Surgery

Pharmacologic control of acid secretion has rendered total gastrectomy unnecessary. Omeprazole therapy is so effective that every patient with ZES is a candidate for a tumor removal operation until proved otherwise because of systemic illness or widespread metastases. Although gastrinomas have a high rate of malignancy, efforts at surgical cure are clearly justified.

Every attempt is made to localize the tumor before surgery, and CT and MRI are effective with larger tumors and especially with hepatic metastases. Gastric secretion is controlled during the perioperative period with either oral or parenteral proton pump inhibitors.

Intraoperative ultrasonography plus palpation is effective in localizing 90% to 98% of pancreatic gastrinomas.

Tumors within the pancreas are enucleated if at all possible.

Treatment of metastatic disease has undergone serial changes but is still unsatisfactory. Radiation therapy and chemotherapy are largely ineffective. The combination of doxorubicin, streptozotocin, and 5-fluorouracil has a low, temporary response rate, but it is highly toxic and has no impact on survival.

MISCELLANEOUS

31. Carotid body tumour. 5 [The West Bengal University of Health Sciences, Paper –I of 2010]
32. Potato tumour. 5 [Rjasthan, 2017]

Potato tumour is synonymous with carotid body tumour.

Answer. Introduction:

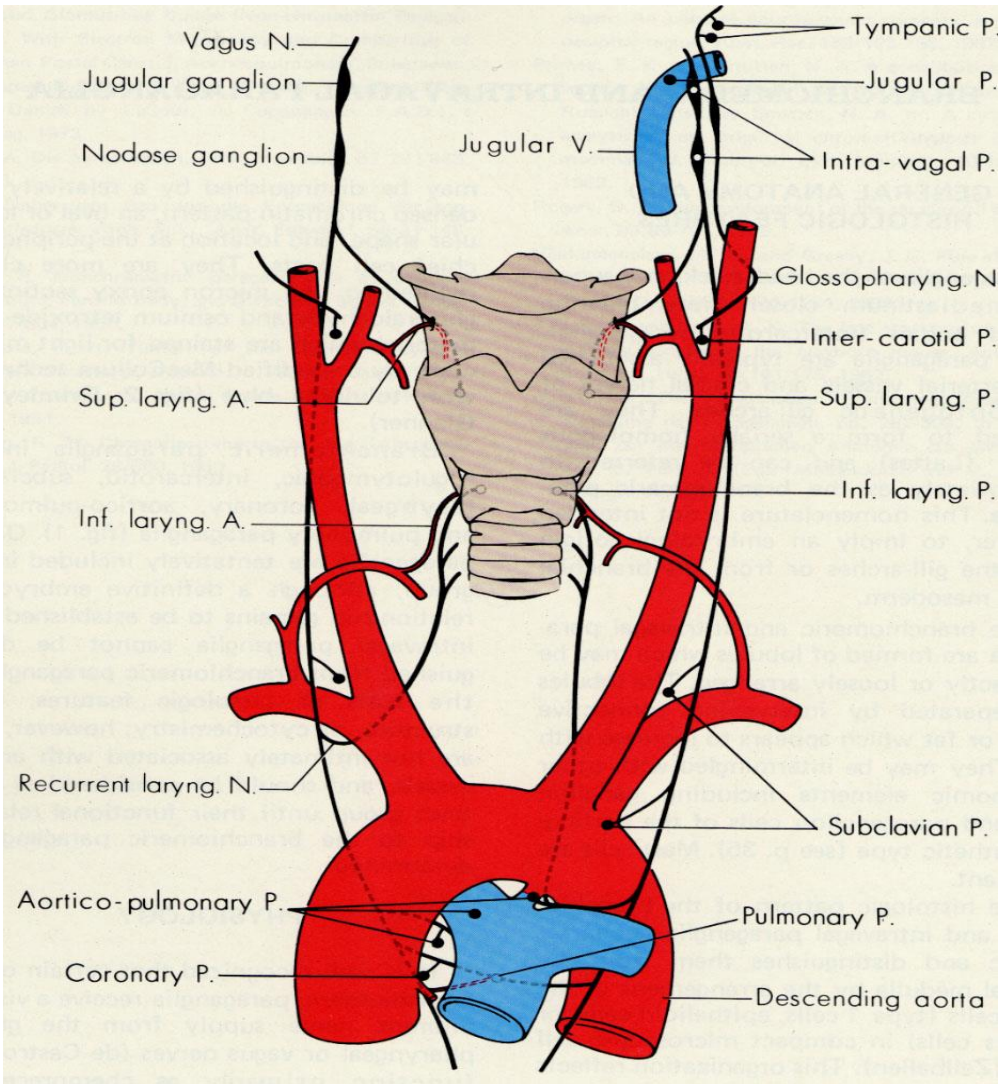
- **Also known as paraganglioma**
- **Rare tumors that arise from specialized neural crest cells associated with autonomic ganglia.**

Four extradrenal locations

- **Group I: Great vessels of chest and neck**
- **Group II: Vagus nerve**
- **Group III: Aorticosympathetic chain**
- **Group IV: Visceral organs**

Head and Neck

- **Carotid body paraganglioma**
- **Vagal paraganglioma (nodose ganglia)**
- **Glomus tympanicum - middle ear along tympanic plexus**
- **Glomus jugulare - jugular bulb**



Aetiopathology:

- **1/30,000 head & neck tumors are paragangliomas**
- **2-3% head/neck paragangliomas have functional hormone secretion**
- **Usually benign- 6% CBTs reported to be malignant**
- **Familial form (10-25%) – present younger and with multiple tumors**

Presentation:

- **Average age = 45**
- **Slow growing**
- **Asymptomatic or mass-related effects**
- **10% present with CN palsy**

Imaging studies:

CT	MRI	MRA	USG	Angiography
• Thin section	• Aids in lesion	• Noninvasive	• Delineates	• Demonstrates

scanning from thoracic inlet to skull base in patients with CB or vagal paragangliomas or other palpable neck mass • **Examines integrity of associated soft tissues** • **Detection of multiple lesions** • **3D reconstruction visualizes associated vasculature**	**diagnosis and localization** • **Differentiates mass from surrounding inflammatory changes, fluid or vascular structures** • **More sensitive for delineating encroachment and encasement of vessels** • **Images middle ear structures and bony erosions** • **Coronal sequences**	• **Delineates displacement of vasculature** • **Demonstrates tumor vascular supply.**	**tumor margins, size and location** • **Doppler: demonstrates hypervascularity of paragangliomas** • **Surveys neck for other lesions** • **Differentiates CBTs from vascular anomalies and pseudoaneurysms** • **Can obtain US guided fine needle aspiration**	**the primary arterial supply and collateral vessels of tumor** • **Reveals relationships with neck blood vessels** • **Presurgery transcatheter arterial embolization**

Radionuclide imaging:
Pentetreotide = octreotide radiolabelled with 111 indium-DTPA binds somatostatin type 2 receptors in paragangliomas

- **Uses: follow recurrent disease, locates multiple lesions, detects familial paragangliomas**

Treatment:
The main treatment modalities are surgery, embolization and radiotherapy