

Module no. 15 Endocrinology

Learning objectives

At the end of this module, the non- specialist medical officer will be able to :

1. Know the typical clinical features of hyperthyroidism, hypothyroidism and diabetes mellitus.
2. Recognize that elderly patients do not present with typical symptoms
3. Interpret appropriate investigations
4. Plan the management in the elderly patient
Decide on the need for early referral to a specialist

Hyperthyroidism (Graves' disease)

Introduction

It is a relatively common endocrine disorder, especially in younger females, having a striking clinical presentation which is easy to recognize. However, in the elderly it may lack the typical clinical features and represents a diagnostic challenge.

Definition:

- Thyroid hormone excess due to any cause and the hyper-metabolic state produced by it is called **thyrotoxicosis**.
- When this is a result of excessive thyroid gland function it is termed **hyperthyroidism**. It is the
- Most common cause of thyroid hormone excess and is usually due to Graves' disease.

Clinical features:

Typical Clinical Features in all ages:

Symptoms	Signs
Anxiety	Resting Tachycardia
Palpitation	High-volume pulse
heat intolerance	Systolic hypertension
Sweating	Tremors
Fatigue	Hyperreflexia
weight loss with increased appetite	Warm and moist hands
Diarrhea	Muscle weakness (especially bulbar myopathy),
Irritability	Graves' ophthalmopathy (stare, proptosis, lid-retraction, lid-lag, peri-orbital oedema, diplopia, corneal involvement, lacrimation, grittiness of eyes and visual loss),
Emotional lability	Pre-tibial myxoedema
Tremulousness	Clubbing of the fingers
Dyspnoea	Goitre: enlarged thyroid with or without bruit

Clinical features in elderly including atypical presentations:

Depression, lethargy, apathy, weight loss with decreased appetite, agitation, confusion, atrial fibrillation, angina pectoris, heart failure and osteoporosis.

Apathetic Thyrotoxicosis: elderly patients presenting with lethargy, depression and weight loss, some of these features are like hypothyroidism.

Clinical Features that are similar to age-related changes:

Fatigue, lethargy, weakness, agitation, confusion, apathy, dementia, myopathy

Differential Diagnosis:

1. Anxiety state
2. Panic attacks
3. Mania
4. Heart failure
5. Malignancy
6. Pheochromocytoma

Key Investigations

- Serum Thyroid stimulating hormone (TSH) - extremely low
- T3 and T4 - Elevated
- Elevated Free T3 and Free T4 are better indicators for hyperthyroidism.
- Rarely, the T4 is in the high normal range but T3 is elevated (T3 toxicosis)
- The ultrasound of neck and thyroid scintigraphy to be done in higher centres

SUBCLINICAL HYPERTHYROIDISM

Refers to low TSH with normal T3 and T4 levels

Management:

- A. The symptomatic treatment of hyperthyroidism is:
Non-selective beta-blockers: Propranolol 40-80 mg 8-12 hourly (Maximum dose of 160 mg / day) or Nadolol (40-80 mg / day).
- B. The definitive treatment of hyperthyroidism is :
 1. **Anti-thyroid medication:** The usual drugs are
 - a. Carbimazole
 - b. Methimazole
 - c. Propylthiouracil (PTU)

Monitor – T4 and TSH

Complete blood count and Liver function tests.

2. Radioactive Iodine (RAI) ablation

3. **Thyroid surgery:** According to medical advice at higher centre

Indications for referral:

The following patients should be considered for referral to a specialist:

1. For initiation / non availability of anti-thyroid medications
2. Those with abnormal thyroid function tests results that are difficult to interpret.
3. Those with cardiac presentation (Angina, Arrhythmias, Heart failure) and thyrotoxicosis
4. Patients needing radioactive treatment or surgery of the thyroid
5. Patients with side effects of anti-thyroid drugs and drug-induced hyperthyroidism.

Complications

1. **Cardiac:** palpitations, atrial fibrillation, high cardiac output state and heart failure.
2. **Neurologic:** Agitation, confusion, delirium.
3. **Osteoporosis:** in elderly females, thyrotoxicosis may lead to increased osteoporosis.
4. **Thyroid Eye disease:** This may produce major visual loss by raised intra-orbital pressure and compression of the optic nerve.
5. **Thyroid Storm or Thyrotoxic crisis:** This is an emergency with high mortality but is less common in elderly. Due to excessive high levels of thyroid hormone, there is hyper- metabolism, fever, neuropsychiatric presentation and heart failure. It is usually precipitated by infection, surgery (especially if preparation for sub-total thyroidectomy is not optimal), radioactive iodine. There is a need to immediately stop the release of thyroid hormone from the gland.
6. Stabilize and rehydrate the patient and administer Intravenous Hydrocortisone 100 mg 8 hourly or Dexamethasone 2 mg 6 hourly and refer to higher centre for further management

Resources and Additional Reading

1. Davidson's Principles and Practice of Medicine, 21st Edition
2. Kumar and Clark Clinical Medicine, 6th Edition
3. Harrison's Principles of Internal Medicine, 19th Edition
4. Brocklehurst Textbook of Gerontology and Geriatric Medicine.
5. Ajish TP, Jayakumar RV. Geriatric thyroidology: an update. Indian J Endocrinol Metab. 2012; 16: 542-7.
6. Mariotti S, Franceschi C, Cossarizza A, Pinchera A. The aging thyroid. Endocr Rev. 1995; 16: 686-715.
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9. Diez JJ. Hyperthyroidism in patients older than 55 years: an analysis of aetiology and management. Gerontology 2003; 49: 316-23.

HYPOTHYROIDISM

Introduction

Hypothyroidism is a common endocrine condition which affects 1% of the general population and up to 10% of those over 60 years of age. While it may be easily recognized by its typical presentation in the younger patients, it may be more difficult to identify in the elderly who have a more atypical and subtle presentation.

Definition: Hypothyroidism is a failure of the thyroid gland in producing thyroid hormone (it mainly produces T4 and smaller amount of T3, an active form of the hormone; T4 converts to the active form T3). The thyroid hormone is vital for the body metabolism and failure of the gland results in a hypo-metabolic state.

Primary hypothyroidism is due to failure of the thyroid gland

- autoimmune process - Hashimoto's Thyroiditis;
- fibrosis or atrophy
- radio-iodine induced thyroid failure
- post-irradiation (external neck radiation for cancer)
- post-thyroid surgery (for treating Graves' disease, goiter or thyroid cancer)
- Iodine deficiency goiter

Secondary hypothyroidism is due to pituitary or hypothalamic disorders and is very uncommon.

Drug-induced hypothyroidism:

- Amiodarone
- Lithium

Overt hypothyroidism: The typical symptomatic patient presents with an elevated TSH (usually > 10 uIU/L) and low FT4 levels. In this case, the diagnosis is clear and straightforward.

Subclinical hypothyroidism: This group comprises of those cases, especially the elderly, where the clinical presentation may be vague, the TSH is elevated (but usually < 10 uIU / L) but the FT4 is within normal limits. It is observed in 5-15% elderly patients. It may convert to overt hypothyroidism over time.

Clinical features:

Symptoms	Signs
Aches and pains	Moderate obesity
weight gain with poor appetite	puffy face, hands and feet,
Constipation	peri-orbital and peripheral oedema
cold intolerance	hoarse voice
Fatigue	coarse and dry skin
Tiredness	alopecia
Somnolence	delayed relaxation of tendon jerks especially the ankle jerk
Dry skin and hair	
Paraesthesias, carpal tunnel syndrome	
Difficulty in concentration	
Depression, psychosis	

HYPOTHYROIDISM



Clinical features that overlap with other disorders in the elderly:

- 1. Those that may be considered a part of old age:** Tiredness, fatigue, dry skin, arthralgia, myalgia, constipation, cramps and cold intolerance.
- 2. Those suggestive of depression or dementia:** apathy, poor appetite, lack of will, memory defects and low concentration.
- 3. Those suggestive of anemia in the elderly:** Pallor, mild icterus, tiredness, fatigue, breathlessness.

Uncommon clinical features :

Cerebellar dysfunction, neuropathy, macrocytic anemia, parasthesias.

The thyroid gland is often enlarged and palpable (goitre) but may be atrophic and not palpable.

Some of the important clinical situations to consider are:

Myxoedema coma: this is a medical emergency and patients present with confusion, loss of consciousness, seizures, respiratory depression and also have hypothermia, bradycardia and hypoglycemia. The condition is life-threatening and has a high mortality of 40-50% if not diagnosed and effectively treated early.

Neurologic presentations ,cognitive impairment and depression: Several cognitive domains are affected and some cases may mimic dementia depression or neuropsychiatric conditions. . Some may have cerebellar ataxia. Identification of hypothyroidism and its treatment will result in improvement of the clinical state.

Cardiovascular effects: There is an increased risk of atherosclerosis, increased arterial stiffness, marked bradycardia, and lipid abnormalities which should be identified and treated. Treatment of hypothyroidism will reduce cardiovascular risk. The ECG has a low-voltage with bradycardia. Chest X-ray may show cardiomegaly and echocardiography may reveal pericardial effusions.

Differential Diagnosis:

1. Symptoms and Signs of Ageing
2. Depression
3. Dementia

Key Investigations

The most important investigation is the T4 (A Free T4 is preferred)

To be done at higher centre:-

- The presence of anti-thyroid antibodies (Anti-TPO antibodies) indicates that the cause of hypothyroidism is autoimmune (Hashimoto's thyroiditis).
- Ultrasound Neck

Management:

- Thyroid hormone replacement therapy is with tablet Levo-thyroxine once a day, taken 30 minutes before breakfast on an empty stomach to improve absorption. The treatment is life-long.
- The initial dose is usually lower in the elderly (25ug/day) and it is stepped up at periods of 3-6 weeks by 25 ug increments.

- Repeat testing of TSH should be done after a period of 6-8 weeks on a stable dose of Levo-thyroxine.
- Once the TSH values are stable, repeat testing may be done once a year.
- Symptoms usually begin to resolve by 3-6 weeks but some symptoms may take 6 months.

Special situations:

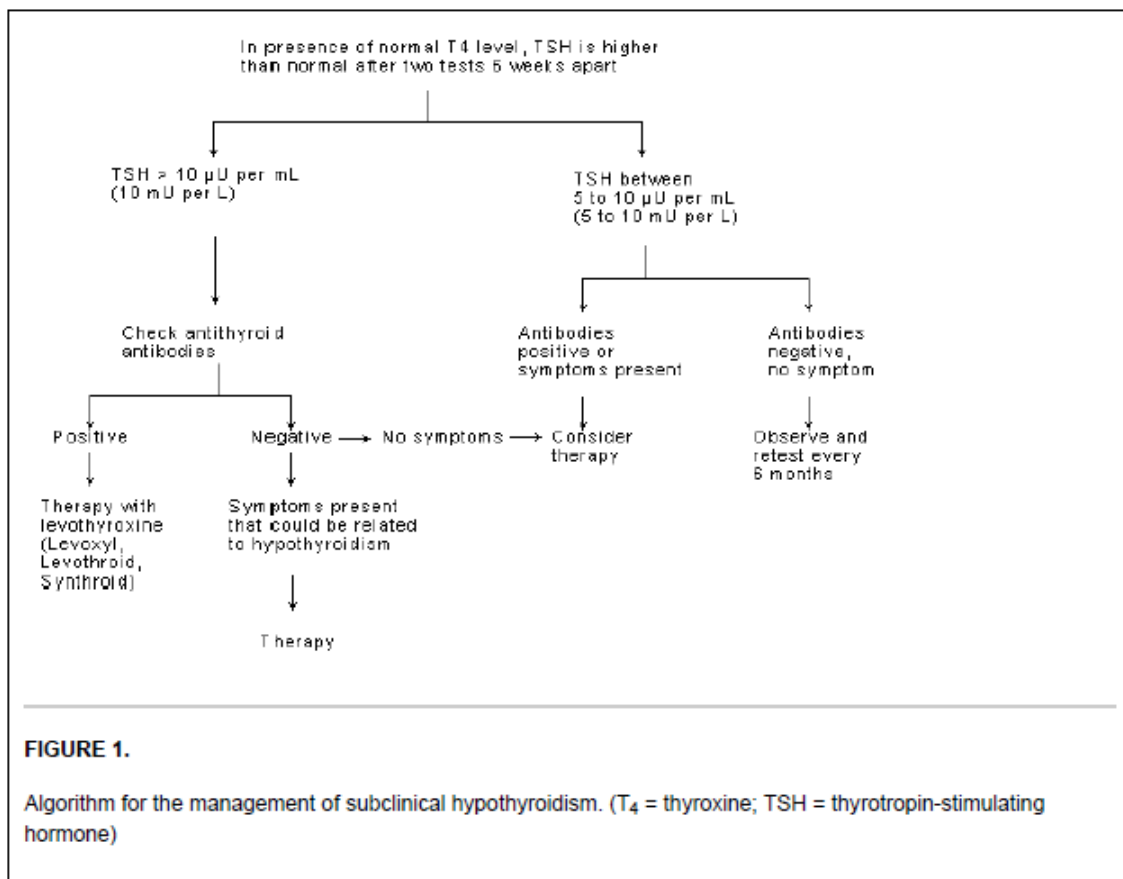
Elderly patients with ischemic heart disease: The starting dose of Levo-thyroxine should be lower (12.5 ug / day) and the 6 weekly step-up increments should be 12.5 ug.

The patients should be closely monitored for angina or other cardiac symptoms.

Subclinical hypothyroidism:

Indications for treatment:-

Subclinical Hypothyroidism: Deciding When to Treat



Indications for referral:

1. A patient with unexplainable TSH and FT4 levels.
2. Subclinical hypothyroidism where decision to treat or not treat needs to be taken.
3. Myxoedema coma
4. Suspicious thyroid nodule.
5. Multi-morbidity, especially cardiac disease with hypothyroidism.

Complications:

Myxoedema Coma: This is a rare but serious condition. The patient is unconscious, or drowsy and having generalized edema. The heart rate and breathing are slow. Seizures may occur and the body temperature is also low (hypothermia). Patient should be promptly referred to higher centre.

Interpretation of thyroid function tests

TSH	FREE T ₄	FREE T ₃	DISEASE
Normal	Normal	Normal	None
Low	High	High	Hyperthyroidism
Low	Normal	Normal	Subclinical hyperthyroidism
Low	Normal	High	T ₃ toxicosis
Low	High	Normal	Thyroiditis, T ₄ ingestion, hyperthyroidism in the elderly or with comorbid illness
Low	Low	Low	Euthyroid sick syndrome; central hypothyroidism
High	Normal	Normal	Subclinical hypothyroidism; recovery from euthyroid sick syndrome

Case Scenario:

A 72 year old man presents with hoarse voice, constipation, weight gain and cold intolerance. He has history of coronary artery disease for 2 years and has been on tablet Ecosprin 75 mg daily, Tablet Atorvastatin 20 mg daily, Tablet Amiodarone 200 mg daily, Tablet Metoprolol 50 mg twice daily.

Critical Thinking: Use the clinical situation to think of whether the changes are age related or indicate hypothyroidism.

Summary

Hypothyroidism is a common endocrine disorder in elderly, and clinicians may mistake the clinical symptoms and signs to be due to old age, dementia, depression or anemia. This disorder should be identified early in the elderly as it is easily treatable with thyroid hormone replacement therapy. The rule is to start slowly with low-doses and build up the drug doses gradually.

Resources and Additional Reading

1. Davidson's Principles and Practice of Medicine, 21st Edition
2. Kumar and Clark Clinical Medicine, 6th Edition
3. Harrison's Principles of Internal Medicine, 19th Edition
4. Brocklehurst Textbook of Gerontology and Geriatric Medicine.
5. Bensenor IM, Olmos RD, Lotufo PA. Hypothyroidism in the elderly: diagnosis and management Clinical Interventions in Aging 2012; 7: 97-111.
6. Mokshagundam S, Barzel US. Thyroid disease in the elderly. J Am Geriatr Soc. 1993; 41: 1361-9.
7. Tachman ML, Guthrie GP. Hypothyroidism: Diversity of presentation. Endocr Rev. 1984; 5: 456-65.
8. Papaleontiou M, Haymart MR. Approach to and Treatment of Thyroid Disorders in the Elderly. Med Clin North Am. 2012; 96: 297-301.

DIABETES MELLITUS IN ELDERLY

Introduction

The prevalence of Diabetes mellitus is increasing worldwide especially in India. Elderly patient may not present with classical symptoms.

Definition:

The American Diabetes Association (ADA) criteria for diagnosis of diabetes are: HbA1C 6.5% or two fasting plasma glucose levels ≥ 126 mg/dl on two separate occasions, a random plasma glucose ≥ 200 mg/dl with classic symptoms of hyperglycemia or hyperglycemic crisis, or a 2-h oral glucose tolerance test (OGTT) ≥ 200 mg/dl.

Content

Table 2 – American Diabetes Association diagnostic criteria for diabetes¹⁸

Test ^a	Threshold	Qualifier
Hemoglobin A _{1c} or	$\geq 6.5\%$	Lab NGSP-certified, standardized DCCT assay
Fasting glucose or	≥ 126 mg/dL (7.0 mmol/L)	No caloric intake for at least 8 hours
2-hour glucose or	≥ 200 mg/dL (11.1 mmol/L)	After 75 g of anhydrous glucose
Random glucose	≥ 200 mg/dL (11.1 mmol/L)	Plus classic hyperglycemia symptoms or crisis

NGSP, National Glycohemoglobin Standardization Program; DCCT, Diabetes Control and Complications Trial.

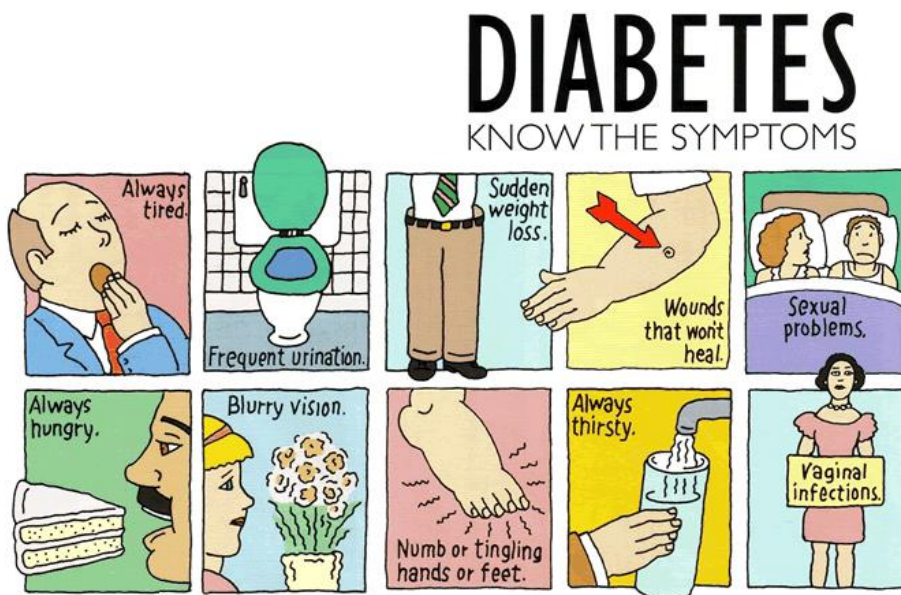
^a Results must be confirmed by repeated testing.

Types: T2DM in elderly manifest in two ways:

- a. Diabetes of middle-age onset: pre-existing diabetes (onset in adulthood or middle age) carried on to old age
- b. Diabetes of new-onset in old age: Incident diabetes mellitus occurring for the first time in geriatric age, and very rarely exceptional cases of T1DM or other rare variety

Clinical features:

The diagnosis may be made for the first time in an asymptomatic older patient during routine investigations.



Complication may be the first presenting feature like Diabetic ketoacidosis, hyperosmolar coma, hypoglycemia, visual impairment, neuropathy, acute coronary syndrome, peripheral vascular disease/ non healing foot ulcer,

Key Investigations

The most common investigations include but are not limited to:

- Anthropometric measurements: Weight, Height, BMI, waist circumference
- Vital Signs: Blood pressure, Pulse, Postural fall of BP
- Laboratory Tests: Blood glucose, (Fasting , Post-prandial), HbA1c, Lipid levels, S. creatinine
- Urine routine examination: look for albuminuria, UTI.

Refer to higher centre for baseline fundoscopic examination for retinopathy

Management Principles:

The goals of treatment are tailored to the requirement of the individual patient and not based on rigid protocols. The general rule is to “individualize treatment” and to “go slow” specially in elderly taking care to avoid hypoglycemia.

The management needs to be tailored for different elderly patients and drug treatment and goals are constantly changing with newer developments, complications, preferences and social support.

For convenience, three broad subgroups have been visualized to guide treatment:

The main groups of patients and reasonable goals are

1. The functionally and cognitively independent elderly patient with few or no co-morbidities:

The reasonable goals are: Fasting BG is 90-130 mg/dL and bedtime is 90-150 mg /dL, **HBA1C of < 7.5%.**

The treatment is similar to the younger DM patient with regular screening for complications and avoidance of hypoglycemia.

2. Complex/ Multiple coexisting illnesses, 2+ IADL impairments, mild-moderate cognitive impairment

The reasonable goals are: Fasting BG is 90-150 mg /dL and bedtime is 100-180 mg / dL, **HBA1C <8.0 %.**

The treatment needs to be balanced between avoiding hypoglycemic episodes and also not letting the glucose to be so uncontrolled as to result in acute complications like Hyperosmolar coma, dehydration, poor wound healing.

3. Very complex / Severe cognitive impairment, 2+ ADL impairments

The reasonable goals are: Fasting BG is 100-180 mg/dL and bedtime is 110-200 mg/dL, **HBA1C < 8.5%.**

Non-Pharmacological interventions:

Nutrition – individualise diabetic diet chart for every patient based on their occupation, economic status and cultural background

- Calculate calorie intake based on BMI and physical activity.
- Small frequent meals with inter-meal snacks.
- Advise complex carbohydrates
- Avoid refined foods

Glycemic index definition: The Glycemic Index (GI) is a relative ranking of carbohydrate in foods according to how they affect blood glucose levels.

Carbohydrates with a low GI value (55 or less) are more slowly digested, absorbed and metabolised and cause a lower and slower rise in blood glucose and, therefore usually, insulin levels.

Glycemic Index (GI) of Common Foods

Sl. No.	Name of the foods	Glycemic Index	Sl. No.	Name of the foods	Glycemic Index
1	White wheat bread	75 ± 2	17	Mango (raw)	51 ± 5
2	Whole wheat bread	74 ± 2	18	Watermelon (raw)	76 ± 4
3	Wheat roti	62 ± 3	19	Potato (boiled)	78 ± 4
4	Chappathi	52 ± 4	20	French fries (potato)	63 ± 5
5	White boiled rice	73 ± 4	21	Carrots (boiled)	39 ± 4
6	Brown boiled rice	68 ± 4	22	Milk (full fat)	39 ± 3
7	Barley	28 ± 2	23	Milk (skim)	37 ± 4
8	Instant oat porridge	79 ± 3	24	Ice cream	51 ± 3
9	Rice porridge /congee	78 ± 9	25	Chick peas	28 ± 9
10	Millet porridge	67 ± 5	26	Soya beans	16 ± 1
11	Sweet corn	52 ± 5	27	Lentils	32 ± 5
12	Cornflakes	81 ± 6	28	Chocolate	40 ± 3
13	Apple (raw)	36 ± 2	29	Popcorn	65 ± 5
14	Orange	43 ± 3	30	Soft drinks/soda	59 ± 3
15	Banana	51 ± 3	31	Honey	61 ± 3
16	Pineapple	59 ± 8	32	Glucose	103 ± 3

Source: Diabetes care, Vol: 31, Number 12, December 2008

Exercise and Habits:

Aerobic exercises (brisk walking) 30 minutes per day for at least 5 days a week.

Pharmacological interventions

Oral drugs are the cornerstone of therapy when lifestyle interventions alone are unable to maintain BG control at target level.

Sulfonylureas (SU):

Mechanism – Stimulate insulin secretion from pancreas

	Dose	Dosage/Day
(a)		
Sulphonylureas		
Gliclazide	40–320 mg	Once daily (but divided higher doses)
Glimepiride	1–4 mg	Once daily
Glipizide	2.5–20 mg	1–2 times daily
Biguanides		
Metformin	0.5–2 g	2–3 times daily

Drugs –

Starting dose of a SU should be half of that used for younger diabetic.

Side effects include

- hypoglycemia
- weight gain
- Gliclazide modified release can be used with caution in renal disease.
- Glibenclamide (Daonil) is contraindicated in the elderly.

Biguanides: Metformin is one of the most popular first line anti-diabetic drug.

Mechanism

- It decreases hepatic glucose.
- It is a low-cost drug.
- There is no hypoglycemia when used as monotherapy.
- The renal and liver functions should be evaluated before initiation of the medication.

Side effects include

- abdominal discomfort
- weight loss
- diarrhea
- rarely lactic acidosis
- B12 malabsorption

Avoid when S. creatinine is elevated. (Calculate GFR and adjust dose)

The dose should be reduced (by 50% or to half-maximal dose) with a GFR 30 to 45 mL/min/ 1.73 m², monitored at 3-month interval and stopped for an eGFR<30 ml/min/1.73 m².

In addition, it should be used with caution in cases with

- hepatic disease
- alcoholism
- severe HF
- COPD
- severe PVD

To be discontinued prior to parenteral contrast administration for CT scans. In elderly diabetics, the dose of metformin should not exceed 1500 mg/day.

Other Drugs:- Tables from ADA 2018 – pg S77, S79, S80

Combination therapy: Two or more drugs with different mechanisms of action are combined to achieve the desired result. The side effect of one drug may be obviated by the added drug, and final dosage can be minimized and may help in improving adherence.

Rational combinations of OHA include: Metformin + sulphonylurea;

Metformin + pioglitazone;

Metformin + Sulphonyluria + pioglitazone;

Metformin + DPP4 inhibitors.

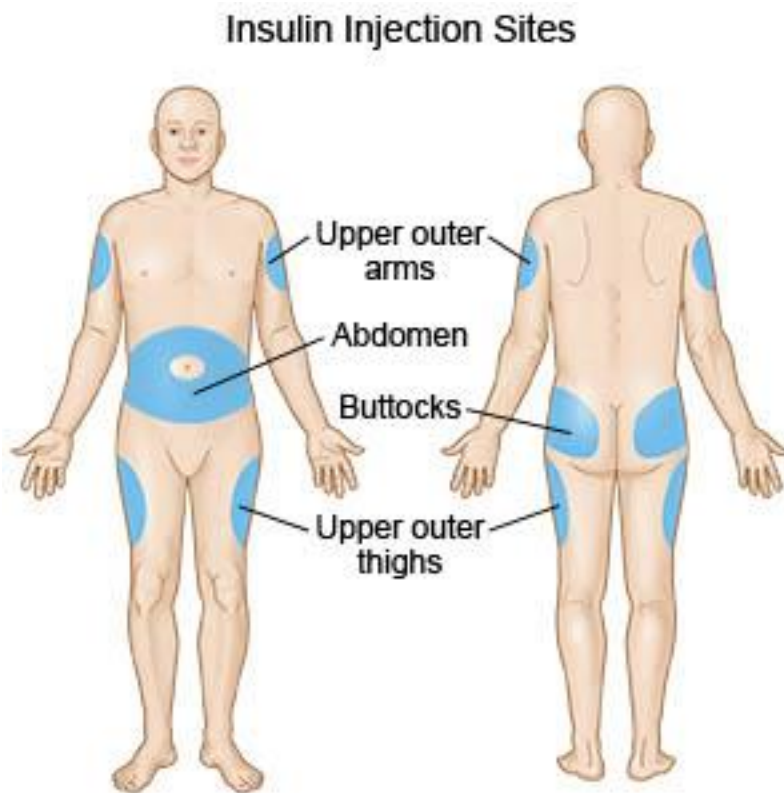
INDICATION FOR INSULIN THERAPY IN TYPE 2 DIABETES

- Acute metabolic complications
- Acute illness
- Severe infection
- Pregnancy and lactation
- Fasting plasma glucose >300 mg/dl
- Failure of oral anti-diabetic agent

Types of Insulin

TYPE	BRAND NAME(S)	ONSET Time until reaches bloodstream	PEAK Time when most effective	DURATION How long works
Rapid-acting	Humalog Novolog Apidra	10 to 30 minutes	30 minutes to 3 hours	3 to 5 hours
Short-acting	Regular (R)	10 to 30 minutes	2 to 5 hours	Up to 12 hours
Intermediate-acting	NPG (N)	1.5 to 4 hours	4 to 12 hours	Up to 24 hours
Long-acting	Lantus Levemir	0.8 to 4 hours	Minimal peak	Up to 24 hours

Sites of administration



Beyond glycemic control: Most elderly patients may also require prescription for an antihypertensive agent, statin therapy and aspirin in addition to the anti-diabetic regime.

Table 8.2—Pharmacology of available glucose-lowering agents in the U.S. for the treatment of type 2 diabetes

Class	Compound(s)	Cellular mechanism(s)	Primary physiological action(s)	Renal dosing recommendations (63–66)*
Biguanides	• Metformin	Activates AMP kinase (? other)	↓ Hepatic glucose production	• No dose adjustment if eGFR >45; do not initiate OR assess risk/benefit if currently on metformin if eGFR 30–45; discontinue if eGFR <30
Sulfonylureas (2nd generation)	• Glyburide • Glipizide • Glimepiride	Closes K_{ATP} channels on β -cell plasma membranes	↑ Insulin secretion	• Avoid use in patients with renal impairment • Initiate conservatively at 2.5 mg daily to avoid hypoglycemia • Initiate conservatively at 1 mg daily to avoid hypoglycemia
Meglitinides (glinides)	• Repaglinide • Nateglinide	Closes K_{ATP} channels on β -cell plasma membranes	↑ Insulin secretion	• Initiate conservatively at 0.5 mg with meals if eGFR <30 • Initiate conservatively at 60 mg with meals if eGFR <30
Thiazolidinediones	• Pioglitazone • Rosiglitazone [§]	Activates the nuclear transcription factor PPAR- γ	↑ Insulin sensitivity	• No dose adjustment required • No dose adjustment required
α -Glucosidase inhibitors	• Acarbose • Miglitol	Inhibits intestinal α -glucosidase	Slows intestinal carbohydrate digestion/absorption	• Avoid if eGFR <30 • Avoid if eGFR <25
DPP-4 inhibitors	• Sitagliptin • Saxagliptin • Linagliptin • Alogliptin	Inhibits DPP-4 activity, increasing postprandial incretin (GLP-1, GIP) concentrations	↑ Insulin secretion (glucose dependent); ↓ Glucagon secretion (glucose dependent)	• 100 mg daily if eGFR >50; 50 mg daily if eGFR 30–50; 25 mg daily if eGFR <30 • 5 mg daily if eGFR >50; 2.5 mg daily if eGFR \leq 50 • No dose adjustment required • 25 mg daily if eGFR >60; 12.5 mg daily if eGFR 30–60; 6.25 mg daily if eGFR <30
Bile acid sequestrants	• Colesevelam	Binds bile acids in intestinal tract, increasing hepatic bile acid production	? ↓ Hepatic glucose production; ? ↑ Incretin levels	• No specific dose adjustment recommended by manufacturer
Dopamine-2 agonists	• Bromocriptine (quick release) [§]	Activates dopaminergic receptors	Modulates hypothalamic regulation of metabolism; ↑ Insulin sensitivity	• No specific dose adjustment recommended by manufacturer
SGLT2 inhibitors	• Canagliflozin • Dapagliflozin • Empagliflozin	Inhibits SGLT2 in the proximal nephron	Blocks glucose reabsorption by the kidney, increasing glucosuria	• No dose adjustment required if eGFR \geq 60; 100 mg daily if eGFR 45–59; avoid use and discontinue in patients with eGFR persistently <45 • Avoid initiating if eGFR <60; not recommended with eGFR 30–60; contraindicated with eGFR <30 • Contraindicated with eGFR <30
GLP-1 receptor agonists	• Exenatide • Exenatide extended release	Activates GLP-1 receptors	↑ Insulin secretion (glucose dependent)	• Not recommended with eGFR <30 • Not recommended with eGFR <30

Continued on p. 580

Table 8.2—Continued

Class	Compound(s)	Cellular mechanism(s)	Primary physiological action(s)	Renal dosing recommendations (63–66)*
Amylin mimetics	• Liraglutide		↓ Glucagon secretion (glucose dependent); Slows gastric emptying; ↑ Satiety	<ul style="list-style-type: none"> • No specific dose adjustment recommended by the manufacturer; limited experience in patients with severe renal impairment • No dose adjustment required for eGFR 15–89 per manufacturer; limited experience in patients with severe renal impairment • No dose adjustment required for eGFR 60–89; no dose adjustment required for eGFR 30–59, but patients should be monitored for adverse effects and changes in kidney function; clinical experience is limited with eGFR 15–29; patients should be monitored for adverse effects and changes in kidney function; avoid if eGFR <15 • No specific dose adjustment recommended by the manufacturer; limited experience in patients with severe renal impairment
	• Albiglutide			
	• Lixisenatide			
	• Dulaglutide			
Amylin mimetics	• Pramlintide§	Activates amylin receptors	↓ Glucagon secretion; Slows gastric emptying; ↑ Satiety	• No specific dose adjustment recommended by manufacturer
Insulins	• Rapid-acting analogs	Activates insulin receptors	↑ Glucose disposal; ↓ Hepatic glucose production; Suppresses ketogenesis	• Lower insulin doses required with a decrease in eGFR; titrate per clinical response
	Lispro			
	Aspart			
	Glulisine			
	Inhaled insulin			
	• Short-acting analogs			
	Human Regular			
	• Intermediate-acting analogs			
	Human NPH			
	• Basal insulin analogs			
	Glargine			
	Detemir			
	Degludec			
• Premixed insulin products				
NPH/Regular 70/30				
70/30 aspart mix				
75/25 lispro mix				
50/50 lispro mix				

*eGFR is given in mL/min/1.73 m². §Not licensed in Europe for type 2 diabetes. GIP, glucose-dependent insulinotropic peptide; PPAR-γ, peroxisome proliferator-activated receptor γ.

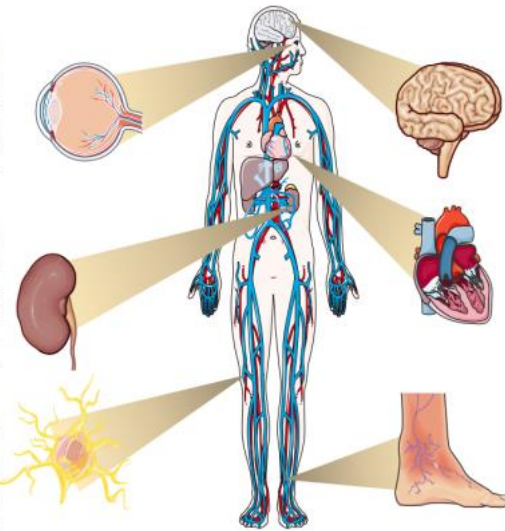
Major Complications of Diabetes

Microvascular

Eye
High blood glucose and high blood pressure can damage eye blood vessels, causing retinopathy, cataracts and glaucoma

Kidney
High blood pressure damages small blood vessels and excess blood glucose overworks the kidneys, resulting in nephropathy.

Neuropathy
Hyperglycemia damages nerves in the peripheral nervous system. This may result in pain and/or numbness. Feet wounds may go undetected, get infected and lead to gangrene.



Macrovascular

Brain
Increased risk of stroke and cerebrovascular disease, including transient ischemic attack, cognitive impairment, etc.

Heart
High blood pressure and insulin resistance increase risk of coronary heart disease

Extremities
Peripheral vascular disease results from narrowing of blood vessels increasing the risk for reduced or lack of blood flow in legs. Feet wounds are likely to heal slowly contributing to gangrene and other complications.

Indications for referral:

All patients will need referral for :

- a. Regular ophthalmological assessments
- b. Regular neurological assessment for neuropathy
- c. Regular evaluation for nephropathy
- d. Cardiovascular disorders : Stroke and Coronary artery disease
- e. Acute complications: hyperglycemia (DKA, HHS), hypoglycemia
- f. Diabetic foot problems
- g. Elective or emergency surgery

Key Messages

1. While thyrotoxicosis is uncommon, it should be considered in elderly patients who present with heart failure, atrial fibrillation or neuropsychiatric disorders.
2. Need for close monitoring of adverse effects of anti – thyroid medication
3. To rule out hypothyroidism in patients who present with vague musculoskeletal symptoms, arthralgias, memory and neuropsychiatric disorders.

4 Stringent glycemic control need not be advised for elderly patients with multiple co-morbidities.

Case Scenarios for critical thinking and reasoning:

1. 67-year-old woman with obesity, hypertension, and coronary artery disease (CAD) is recently diagnosed with diabetes. Her HbA1C is 11% and she has non-proliferative diabetic retinopathy. What regime should one follow?

2. A 70 year old male diabetic on OHA's (metformin and sulfonylureas) presents to the casualty in unconscious state. Patient has skipped the morning breakfast because of nausea and vomiting but had used OHA's. What do you suspect and how do you manage the patient?

Resources and Additional Reading

1. Davidson's Principles and Practice of Medicine, 21st Edition
2. Kumar and Clark Clinical Medicine, 6th Edition
3. Harrison's Principles of Internal Medicine, 19th Edition
4. Brocklehurst Textbook of Gerontology and Geriatric Medicine

NUTRITION IN ELDERLY

Introduction

Nutrition is an important aspect in geriatric age which is often neglected.

The age related physiological and metabolic changes increase nutritional risk. Older adults are at risk for malnutrition due to multiple co-morbidities, poly-pharmacy, psychosocial, economic, food accessibility, and environmental factors.

Normal aging is associated with a decline in food intake due to loss of taste, reduction in stomach compliance, hormonal changes, and a decline in energy demand as a consequence of lower physical activity, reduction in lean body mass, and slower rate of protein turnover.

The physician plays a key role in identifying malnutrition, intervening early to prevent its progression and providing nutritional advice to the elderly in the community.

Definition: Malnutrition is considered a geriatric syndrome as it results partly from the aging process. It is a state of being poorly nourished, either through a lack or an excess of nutrients. Therefore, malnourished older persons can be underweight, overweight or obese.

Causes of under-nutrition in elderly:

- Swallowing difficulty due to neurologic problems

- Dental problems
- Depression,
- Dementia,
- Polypharmacy
- Malabsorption
- Detrimental oral changes and defective taste and olfaction may decrease the quality of food intake
- Alcoholism
- Social issues like Problems in shopping and preparing meals,
- Financial constraints

Clinical features of undernutrition–TABLE

Classification of Clinical signs

Group 1 - Potentially Nutritionally Significant

(Signs 'strongly

suggestive' of dietary deficiency or excess)

Ex:

Deficiency Sign	Suggested nutrient abnormality
Pale conjunctiva	Iron
Bitot's spots	Vitamin A
Angular stomatitis	Riboflavin
Spongy, bleeding gums	Vitamin C
Bilateral edema (young children)	PEM
Thyroid enlargement	Iodine
Bilateral epiphyseal enlargement of wrists	Vitamin D
<i>Sign of Excess</i>	<i>Suggested nutrient abnormality</i>
Mottled enamel	Fluoride
Dental caries	Sugar

Saturday, April 10, 2010

10:00, 1962

Weight loss over a period of time which leads to protein energy malnutrition resulting in:

- Weakness, fatigue, oedema, falls, hip fractures, pressure ulcers, cognitive abnormalities, infections.
- In addition, specific single micronutrient deficiency may result in a combination of diarrhoea, constipation, keratitis, blindness, petechiae, bleeding, dermatitis, paraesthesias, dementia, and heart failure.

Assessment of malnutrition:

A comprehensive history

Clinical examination

- Indications to initiate formal assessment and includes 5% of usual body weight loss in 30 days or 10% in 180 days.
- One should proceed to a formal assessment by standard anthropometric measurements and nutrition assessment instruments:

Diet history

Anthropometric measures include measurements of

- height
- weight
- body mass index (BMI)

$$\text{BMI} = \frac{\text{weight (kg)}}{\text{height}^2 \text{ (m}^2\text{)}} \quad (\text{metric})$$

Nutritional Status	WHO criteria BMI cut-off	"Asian criteria" BMI cut-off
Underweight	<18.5	<18.5
Normal	18.5 – 24.9	18.5 – 22.9
Overweight	25 – 29.9	23 – 24.9
Pre-Obese	-	25 – 29.9
Obese	≥30	≥30
Obese Type 1 (obese)	30 – 40	30 – 40
Obese Type 2 (morbid obese)	40.1 – 50	40.1 – 50
Obese Type 3 (super obese)	>50	>50

- Body fat measurement (skin fold thickness)
- Mid arm muscle circumference or calf circumference.

Body composition– assessed by tests like DEXA (available only in higher centres)

The **Mini Nutritional Assessment (MNA)** is a basic screening tool validated in a variety of settings.

The **Simplified Nutrition Assessment Questionnaire (SNAQ)** can detect weight loss over the next 6 months.

The **Malnutrition Universal Screening Tool (MUST)** predicts mortality and length of hospital stay in acutely hospitalized persons.

Key Investigations:

- Complete blood count for anemia
- The biochemical estimation should include: serum proteins & serum albumin
- **To be done at higher centre:-**
- Peripheral smear.
- The serum ferritin, folic acid and vitamin B12 levels (if available)
- The thyroid function test may identify apathetic hyperthyroidism.
- Vitamin D levels may be estimated as low values are observed in many older persons.

Depending on the clinical situation, Chest radiograph, Ultrasound abdomen or other investigations may be ordered.

Management: **ENERGY** requirement picture

- Energy requirement that are recommended by WHO and ICMR are approximately 1500-2000 kcal for sedentary elderly person.
- The protein intake should be 0.9-1.1g/kg body weight per day to avoid depletion of muscle mass and development of sarcopenia.
- Carbohydrate should provide 45-60% of the total calories. 25-30% of the energy should come from fats which should be predominantly polyunsaturated and monounsaturated fatty acid sources. Saturated fats should not exceed 8% of the total energy.

Mineral supplementation

Iron deficiency is responsible for 20% of anemias in elderly. It is easy to treat with iron supplements.

However, it is important to look for blood loss (hemorrhoids, hookworm infestation and rarely colon cancer), or medications interfering with iron absorption or hypochlorhydria. The dosage of elemental iron required to treat iron deficiency anemia in adults is 120 mg per day for three months.

In case of poor response, patient needs further evaluation and management at higher centre.

Calcium intake in the range of 800-1200mg/day (WHO) in the presence of adequate vitamin D levels can prevent loss of bone mineral density and reduce the risk of fracture.

Vitamin D - if the serum 25-OH D levels are lower than 30 nmol / L, patient will require supplementation if available.

Anemia may be related to **Vitamin B₁₂ deficiency** due to a variety of causes including atrophic gastritis, H pylori infection, and prolonged use of proton pump inhibitors. These patients may need monthly injections or daily oral Vitamin B₁₂.

Folic acid and **Vitamin B6** (pyridoxine) deficiency should be sought and corrected by supplementation.

Micronutrient Supplementation: The use of vitamin and mineral supplements may be indicated in documented deficiencies or for preservation of health out of choice. Nutrients with anti-oxidant activity including Vitamin A, C, E and Beta-carotene have not been proven to be of benefit in cardiovascular disease and cancer prevention. A liberal intake of green leafy vegetables can provide a substantial amount of vitamin E, C, Carotenoids, Flavenoids and Selenium to prevent free radical damage.

Supplementations of magnesium, copper, chromium are also advocated for elderly.

Low Vitamin E may compromise the ability to fight oxidative stress but intake of Vitamin E > 400 IU is not likely to be of benefit and may increase risk of hemorrhagic stroke.

Requirements of Vitamin K may be adequate due to generous intake of vegetables.

However, sometimes, intake of Vitamin K supplements may interfere with efficacy of oral-anticoagulants.

Zinc deficiency may be related to a decline in immune function, resistance to infection, and response to immunizations. Zinc supplementation has a role in reducing the number of infections.

Drugs for stimulation of appetite:

Megestrol acetate and dronabinol have been advocated for appetite stimulation. The former has major side effects of deep vein thrombosis and is not recommended in patients confined to bed or for more than 3 months. Dronabinol is also useful in a palliative care setting but has serious side effects.

Feeding assistance and tube feeding

If a patient cannot feed himself, assisted feeding may be used. While tube feeding is a more convenient method, it should be a last resort.

Tube feeding is lifesaving in patients who cannot swallow for any reason but it should not be advocated for patients with late stages of dementia.

Indications for referral:

The following group of patients may constitute a broad category needing specialist referral :

- A documented weight loss of 5% of usual body weight in 30 days or 10% in 180 days.

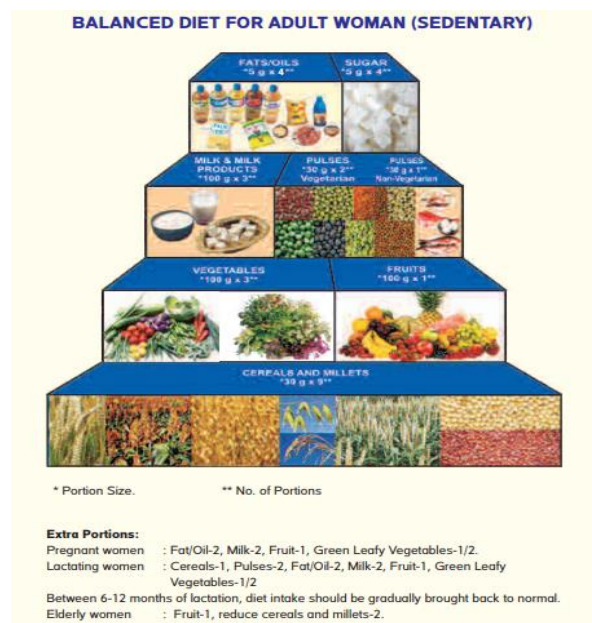
Complications

Falls and fractures
Increased risk of infections and hospitalizations
Increased dependency and mortality

Prevention and Control

The general nutritional advice for all community living elders is to balance food intake to your physical activity and more physically active will need more food.

BALANCED DIET CHART



Take adequate exercise: Be physically active for at least 30 minutes daily.

Key Messages

Subtle changes in the elderly usually tilt them towards under-nutrition and its adverse consequences. Therefore, the clinician should be alert to the symptoms and signs indicating any form of malnutrition and intervene early to prevent the adverse outcomes. This is especially important in the patients who have been recently hospitalized and are on multiple medications, socially isolated, economically backward, depressed and with limitations in ADL.

Case Scenario

Rani is a 72 year old widow, who was a daily wager in rural Bihar. She is now living in Patna city in a two room quarter with her daughter, her husband and their two children aged 6 and 4 years. Both husband is a taxi driver and wife works as a housemaid. Rani has diabetes, hypertension and mild renal insufficiency. She says that ever since she has come to Patna, she has loss of appetite and also seems to have lost some weight. She fell down in the market 5 days ago while accompanying the children to buy some groceries.

Critical thinking: Identify family support, dependence on her daughter, depression over the loss of her husband, frailty, sarcopenia or age or disease related symptoms ?

Audio-Visual / Power point: will be prepared

Resources and Additional Reading

1. Davidson's Principles and Practice of Medicine, 21st Edition
2. Kumar and Clark Clinical Medicine, 6th Edition
3. Harrison's Principles of Internal Medicine, 19th Edition
4. Brocklehurst Textbook of Gerontology and Geriatric Medicine
5. Current Medical Diagnosis and Treatment 2015. Papadakis MA, McPhee SJ eds. McGraw Hill Education.
6. Bales CW and Johnson MA. Chapter 56. Nutrition in older Adults. In Ross CA, Caballero B, Cousins RJ, Tucker KL, Ziegler TR Eds. Modern Nutrition in Health and Disease. 11th Edition. Wolters Kluwer/ Lippincott Williams and Wilkins. Philadelphia. 2014. p 744-756.
7. Morley JE. Under-nutrition in older adults. Family practice 2012; 29:i89-i93.
8. Bennett AM. Updated in May 2016. Irish Nutrition + Dietetic Institute Factsheet Good Nutrition for the Older Person. 2016 Irish Nutrition and Dietetics Institute
9. Thomas DR. NutrClinPract 2008; 23: 383-387.

Evaluation Questions: A set of 10 MCQs

