Paraneoplastic syndromes

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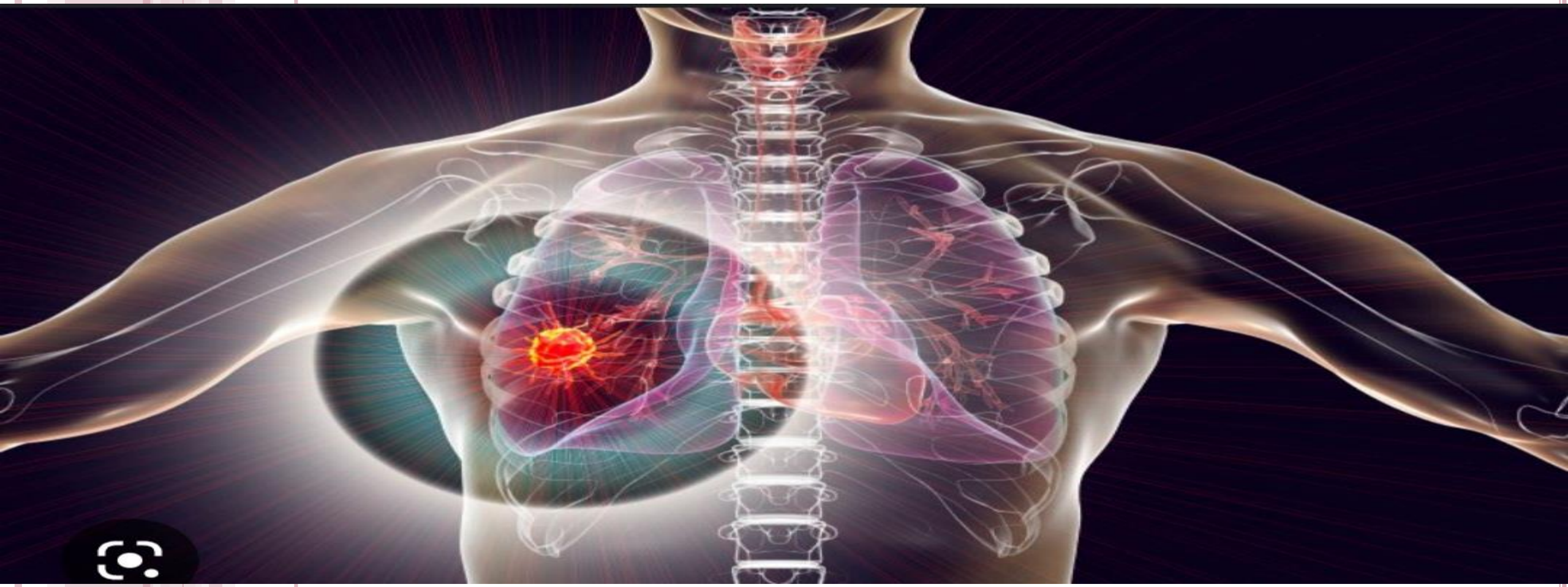
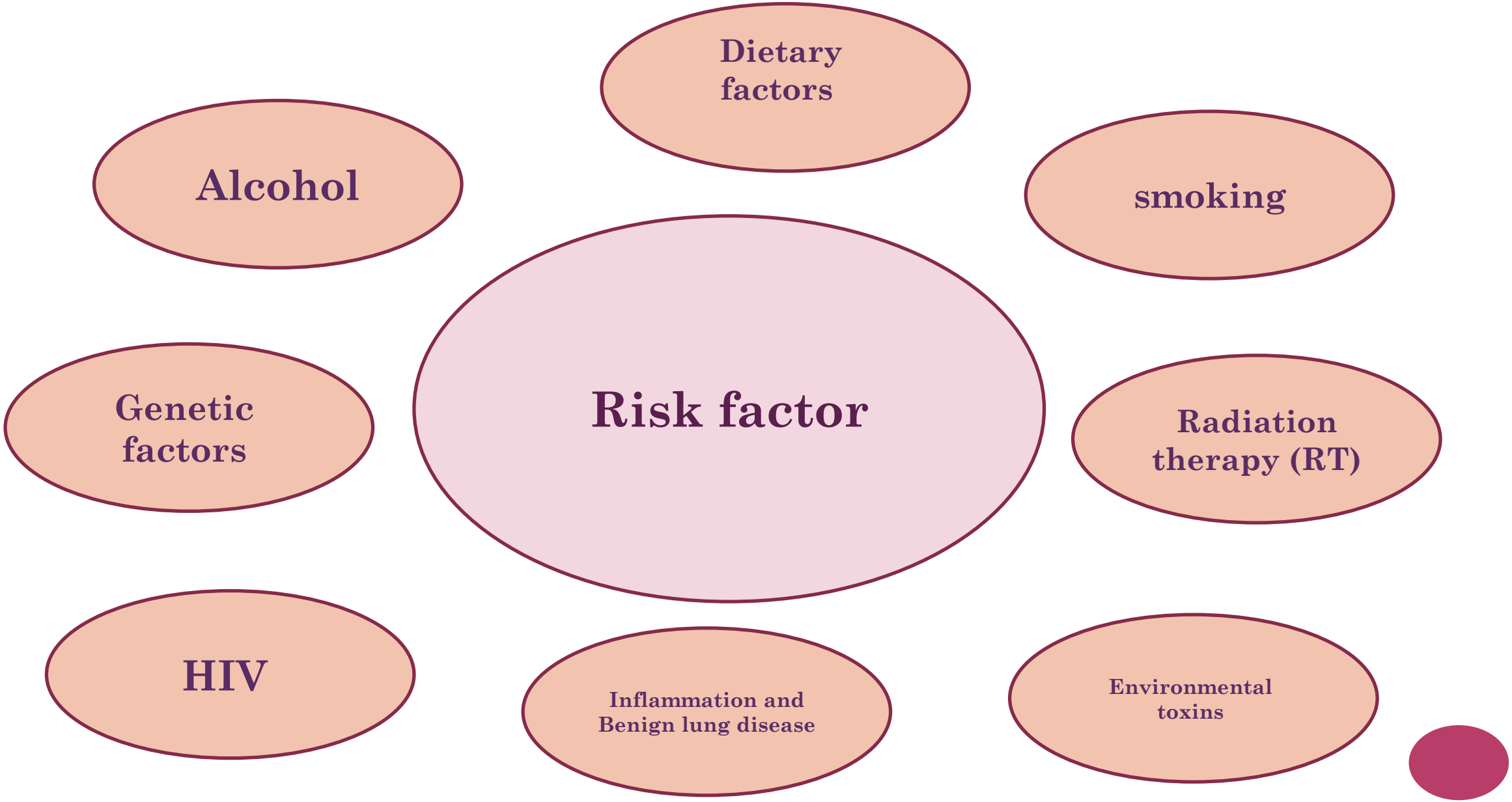
LUNG CANCER

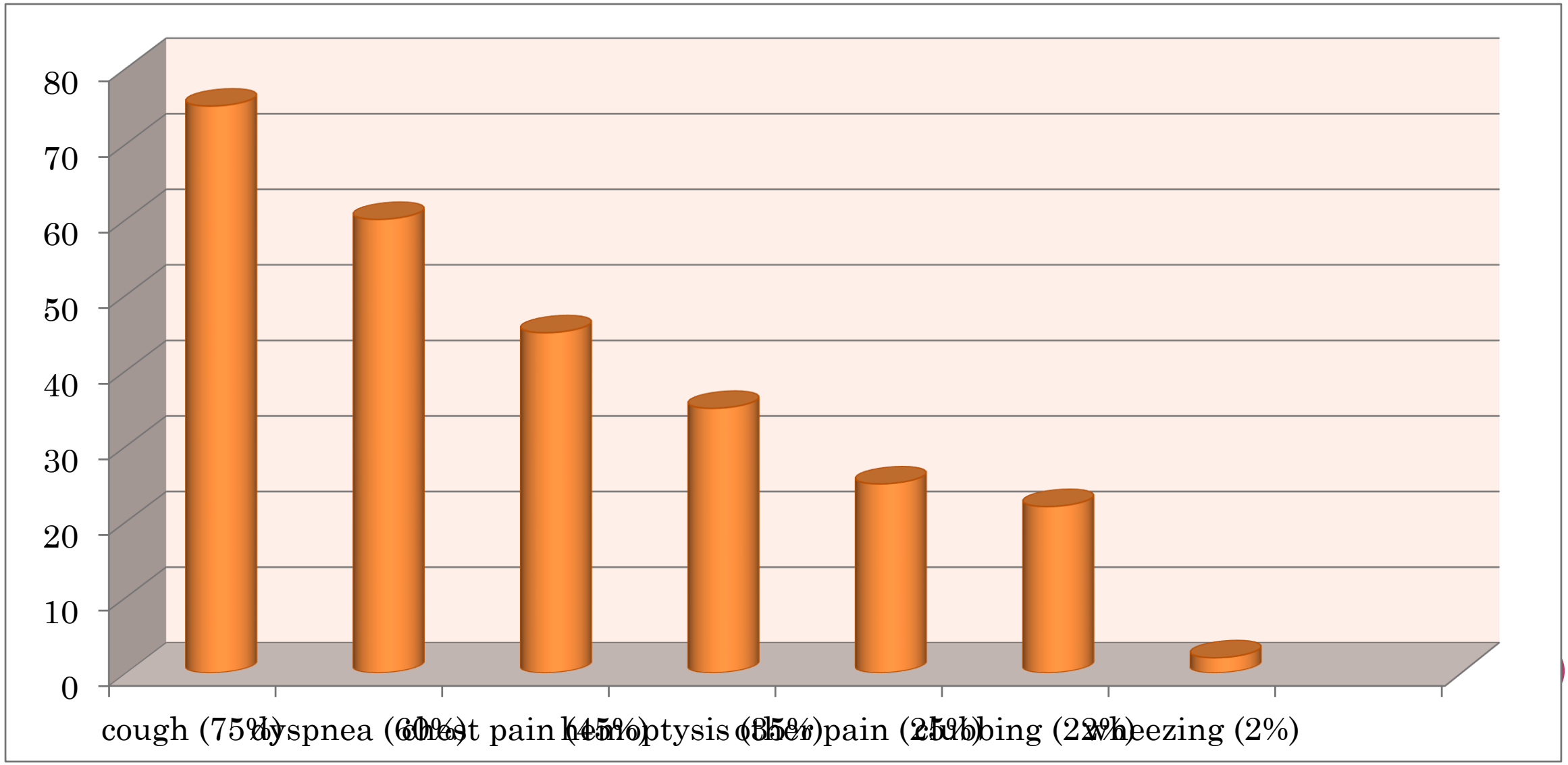


- lung cancer became the most common cause of cancer deaths in men and women

- Approximately **95 %** of all lung cancers are classified as either small cell lung cancer **(SCLC)** or non-small cell lung cancer **(NSCLC)**


Dietary factors
Alcohol
smoking
Risk factor
Genetic factors
Radiation therapy (RT)
HIV
Inflammation and Benign lung disease
Environmental toxins

THE MOST COMMON SYMPTOMS



Classification of Lung Cancer

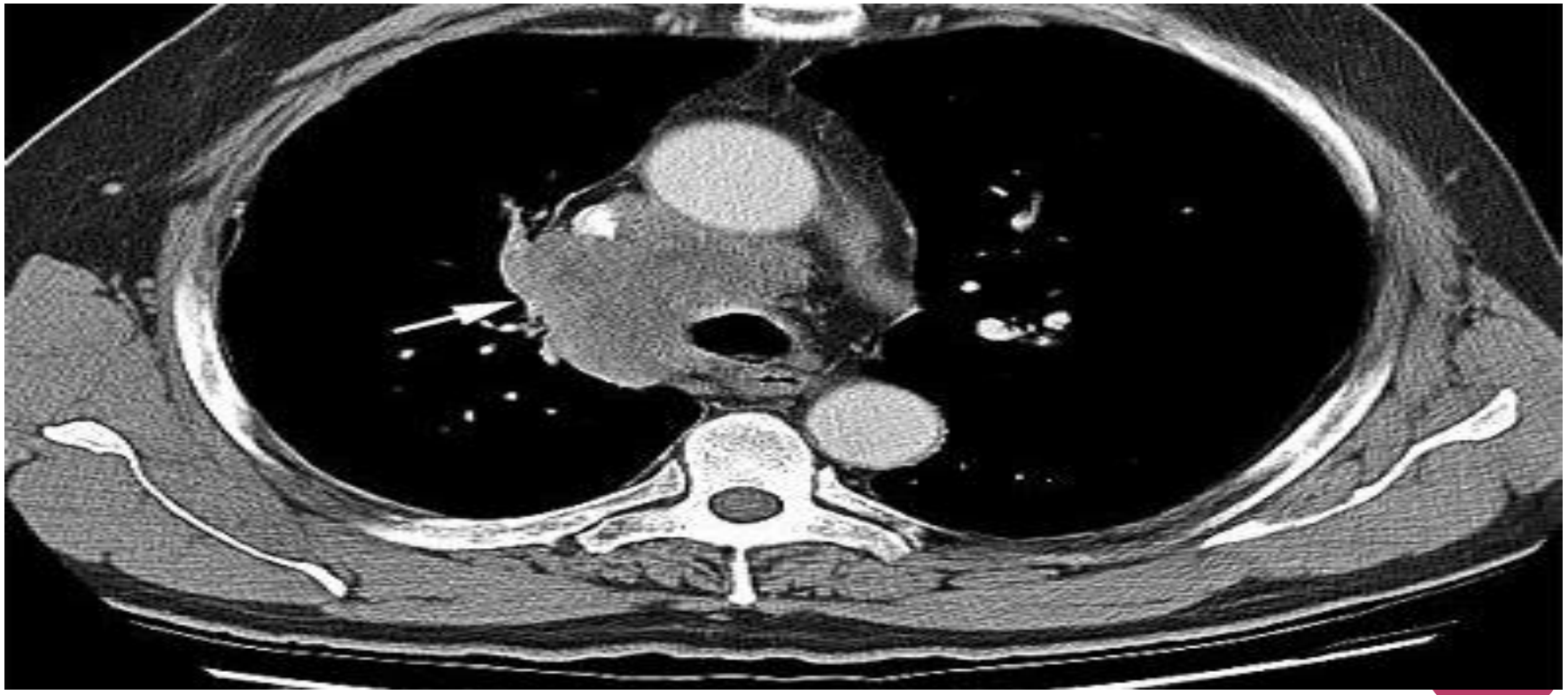
World Health Organization Histologic Class

Small cell lung cancer	Non-small cell bronchogenic carcinomas
• (15 to 18% of all lung cancers)	• (82 to 85%)

Approximately 10% of SCLCs are combined with non-small cell lung cancer (NSCLC) components

SMALL CELL CARCINOMA

- SCLC is so strongly associated with **cigarette smoking [98%]**
- Most commonly **centrally**



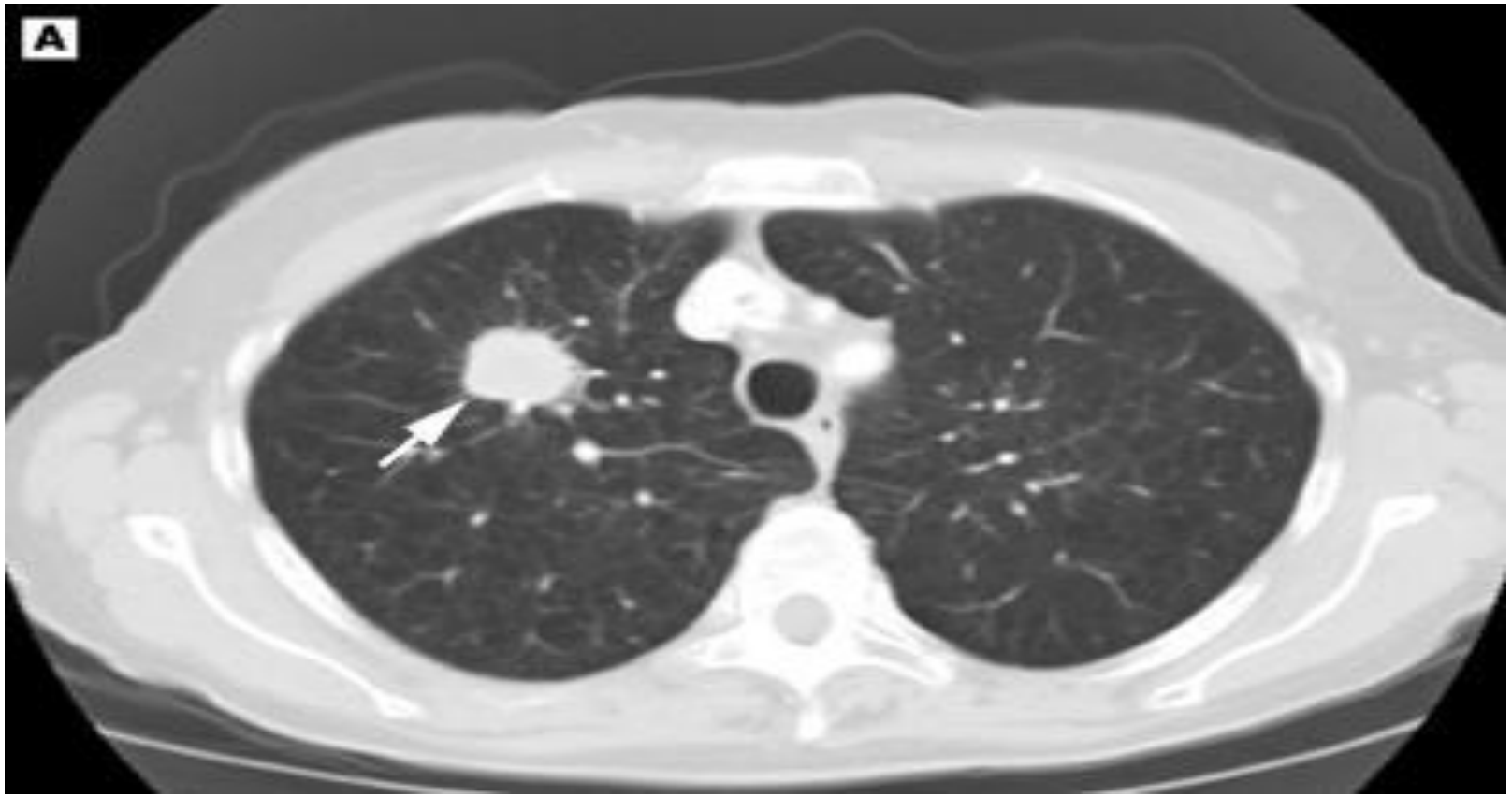
BULKY CENTRAL MASS WITH ADENOPATHY

NONSMALL CELL CARCINOMAS

Adenocarcinoma	• including bronchioloalveolar cell carcinoma (32% of the total)
squamous cell carcinoma	• (29% of the total)
large-cell carcinoma	• (9% of the total)
undifferentiated	• (11% of total)

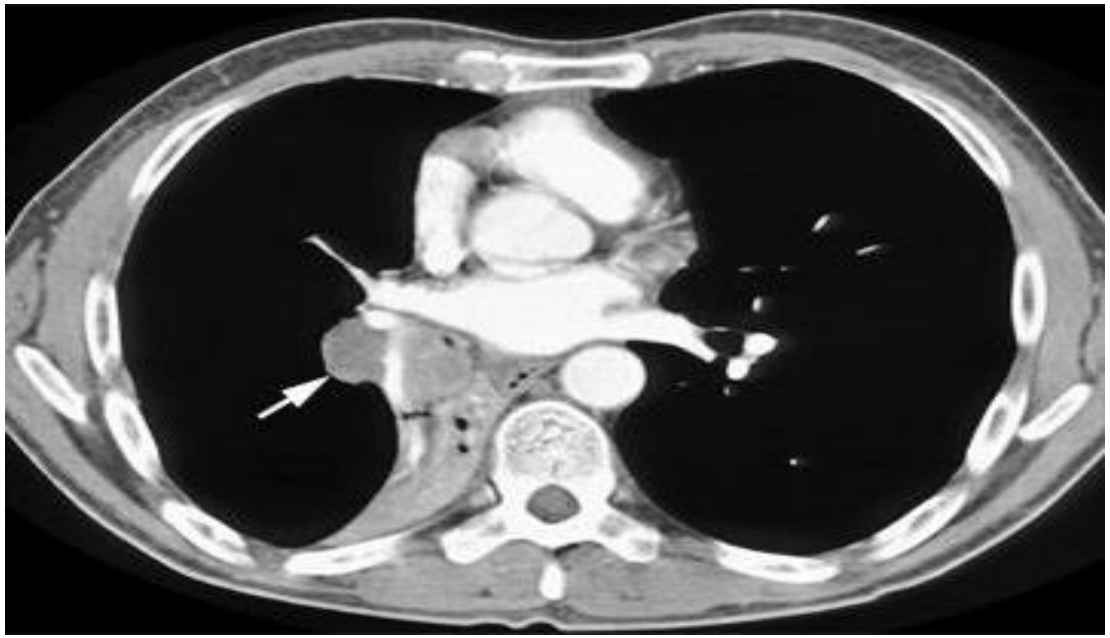
ADENOCARCINOMAS

- most commonly **periphery**



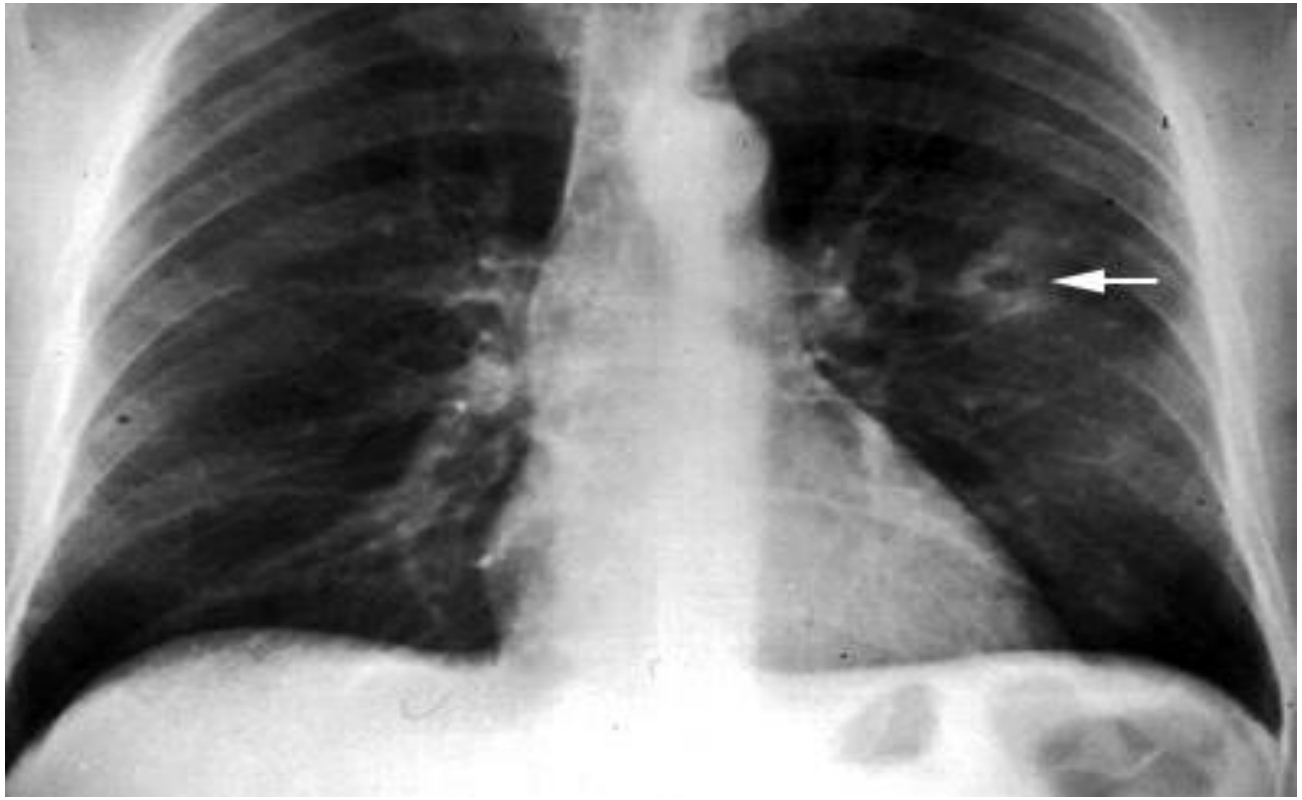
SQUAMOUS CELL CARCINOMA

- 95% of patients are **smokers**
- **centrally**, with involvement of the main stem, lobar, or segmental bronchi.
- It is more commonly associated with **cavitation**, **Pancoast syndrome**, and **hypercalcemia**.



Large cell carcinoma

- Periphery
- Smokers
- Necrosis



International Staging System for Lung Cancer

The **TNM** system

used as a guide to estimate prognosis, to select treatment options, and to report outcomes

T: Primary tumor	
Tx	Primary tumor cannot be assessed or tumor proven by presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor ≤3 cm in greatest dimension surrounded by lung or visceral pleura without bronchoscopic evidence of invasion more proximal than the lobar bronchus (ie, not in the main bronchus)*
T1a(mi)	**Minimally invasive adenocarcinoma†**
T1a	**Tumor ≤1 cm in greatest dimension***
T1b	**Tumor >1 cm but ≤2 cm in greatest dimension***
T1c	**Tumor >2 cm but ≤3 cm in greatest dimension***

T2	Tumor >3 cm **but ≤5 cm** or tumor with any of the following features:[Δ] ▪ **Involves main bronchus regardless of distance from the carina but without involvement of the carina** ▪ Invades visceral pleura ▪ **Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, involving part or all of the lung**
T2a	**Tumor >3 cm but ≤4 cm in greatest dimension**
T2b	**Tumor >4 cm but ≤5 cm in greatest dimension**
T3	**Tumor >5 cm but ≤7 cm in greatest dimension** or associated with separate tumor nodule(s) in the same lobe as the primary tumor or directly invades any of the following structures: chest wall (including the parietal pleura and superior sulcus tumors), phrenic nerve, parietal pericardium
T4	**Tumor >7 cm in greatest dimension** or associated with separate tumor nodule(s) in a different ipsilateral lobe than that of the primary tumor or invades any of the following structures: **diaphragm**, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, and carina

N: Regional lymph node involvement	
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2	Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

M: Distant metastasis	
M0	No distant metastasis
M1	Distant metastasis present
M1a	Separate tumor nodule(s) in a contralateral lobe; tumor with pleural or pericardial nodule(s) or malignant pleural or pericardial effusion[¶]
M1b	**Single extrathoracic metastasis[§]**
M1c	**Multiple extrathoracic metastases in one or more organs**

Stage groupings			
Occult carcinoma	TX	N0	M0
Stage 0	Tis	N0	M0
Stage IA1	**T1a(mi)**	**N0**	**M0**
	T1a	**N0**	**M0**
Stage IA2	**T1b**	**N0**	**M0**
Stage IA3	**T1c**	**N0**	**M0**
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
Stage IIB	**T1a to c**	**N1**	**M0**
	T2a	**N1**	**M0**
	T2b	N1	M0
	T3	N0	M0
Stage IIIA	**T1a to c**	**N2**	**M0**

	T2a to b	N2	M0
	T3	N1	M0
	T4	N0	M0
	T4	N1	M0
Stage IIIB	**T1a to c**	**N3**	**M0**
	T2a to b	N3	M0
	T3	**N2**	**M0**
	T4	N2	M0
Stage IIIC	**T3**	**N3**	**M0**
	T4	**N3**	**M0**
Stage IVA	**Any T**	**Any N**	**M1a**
	Any T	**Any N**	**M1b**
Stage IVB	**Any T**	**Any N**	**M1c**

- **Paraneoplastic syndromes**
- are **clinical** syndromes caused by underlying **malignant** disease .
- Systemic manifestations of paraneoplastic syndromes result from the
- **production and release** of physiologically **active substances** by tumor cells

- or by **responses to tumor antigen**

Paraneoplastic effects of tumor are remote بعيدة effects that are not related to the direct invasion, obstruction, or metastasis.

- Associated with many types of lung cancer.
- Can be the first manifestation of disease or disease recurrence.
- About 10% of patients with lung cancer present with a paraneoplastic syndrome.

Endocrine syndromes	Neurological syndromes	Haematologic syndromes	Rarer other syndromes
Hypercalcemia	Myelopathy	**Anemia**	**Hypertrophic pulmonary osteoarthropath**
Cushing syndrome	Stiff-person syndrome	**Thrombocytosis**	**Dermatomyositis and Polymyositis**
SIADH secretion	Subacute sensory neuronopathy	**Eosinophilia**	
	Chronic sensorimotor neuropathy	**Hypercoagulable disorders**	
	Vasculitic neuropathy	**leukocytosis**	
	Autonomic neuropathy		
	Lambert-Eaton myasthenic syndrome Myasthenia gravis		

HYPERCALCEMIA

Elevated calcium in blood is caused by
tumor secretion **of parathyroid hormone-related protein**,
increased **active metabolite of vitamin D** (calcitriol),
and localized **osteolytic hypercalcemia.**

- Occurs in 10–25% of patients with lung cancer.
- Most commonly associated with **squamous cell lung cancer**.
- Median **survival** in patients with lung cancer after diagnosis of hypercalcemia is **about 1 month**.

Presentation

Clinical symptoms of hypercalcemia depend on **calcium level and acuity** of onset:

- For patients with **mild or moderate hypercalcemia**, symptoms include anorexia, polyuria, polydipsia, nausea, vomiting, confusion, abdominal pain, constipation, lethargy and myalgia.
- With **severe hypercalcemia** (serum calcium level > 14.0 mg/dL), symptoms include mental status changes, coma, bradycardia, arrhythmias, and hypotension.
- Hypercalcemia can also cause **severe dehydration**, **acute renal failure** and **nephrocalcinosis.**

Diagnosis

Diagnostic evaluation includes assessment of intact parathyroid hormone, parathyroid hormone-related protein, 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D, calcium, albumin, magnesium, and phosphorus.

Treatment

Patients who are **symptomatic** from hypercalcemia,
or have **significantly elevated** serum calcium levels, **regardless of symptoms**,
require treatment that includes hydration and bisphosphonate

In one study of 1149 consecutive lung cancers, 6 percent had hypercalcemia.

Among those with hypercalcemia,

squamous cell carcinoma 51%

Adenocarcinoma 22%

SCLC 15 %.

Most patients with hypercalcemia have **advanced disease (stage III or IV)**

and **a limited** survival.

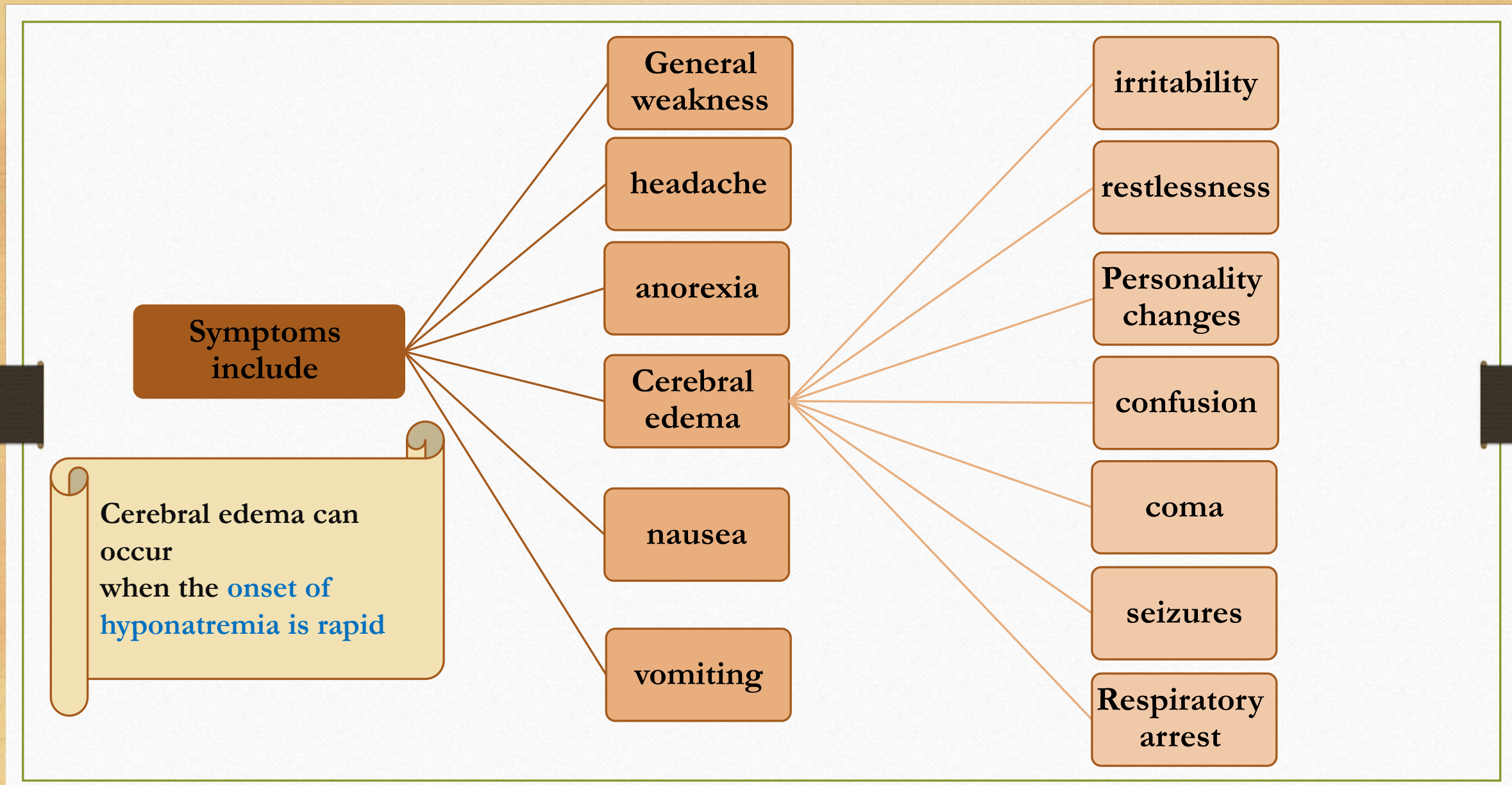
SYNDROME OF INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION (SIADH)

Most commonly associated with **small cell lung cancer** (SCLC).

- ADH is produced by the tumor in an unregulated manner, leading to water retention by reabsorption in renal tubules.
- Manifested as euvolemic hypo-osmolar hyponatremia.
- Approximately **10 percent** of patients who have SCLC exhibit SIADH.
- SCLC accounts for approximately **75** percent of all malignancy-related occurrences of SIADH.

Presentation

Clinical signs and symptoms depend on **degree of hyponatremia and acuity** of hypo-osmolality (the rapidity of the fall in serum sodium).


Symptoms include
General weakness
headache
anorexia
Cerebral edema
nausea
vomiting
irritability
restlessness
Personality changes
confusion
coma
seizures
Respiratory arrest
Cerebral edema can occur when the onset of hyponatremia is rapid

Diagnosis

Lab findings:

- Urine sodium level > 40 mEq/L
- Urine osmolality > 500mOsm/kg
- Serum osmolality < 275mOsm/kg
- Serum uric acid concentration < 4 mg/dL

Treatment

- The treatment of SIADH focuses on **treating the malignancy**.
- In the majority of patients with SCLC, the hyponatremia will resolve **within weeks** of starting chemotherapy.
- **Chronic hyponatremia** or that of unclear duration may be treated with normal saline infusion to euvolemia, fluid restriction and demeclocycline, or a vasopressin-receptor antagonist.
- **Acute and severe hyponatremia** may be carefully treated with hypertonic (3 percent) saline infusion for a correction of 1 to 2 mmol per liter per hour with a correction of not more than 8 to 10 mmol per liter in 24 hours.

CUSHING SYNDROME

Caused by **ectopic** production of **adrenal corticotropin hormone**.

Cushing syndrome **is rare**, but is most commonly seen in patients with **SCLC**, **large** cell neuroendocrine carcinoma, or **carcinoid** tumors of the lung.

Patients with Cushing syndrome and SCLC appear to have **a worse prognosis** than patients with SCLC without Cushing syndrome

Presentation

Clinical manifestations:

Hirsutism	Skin hyperpigmentation	Purple striae	osteoporosis	Peripheral edema
Moon facies	Proximal muscle weakness	Weight gain	Acne	Hypertension
Hypokalemic alkalosis	hyperglycemia			

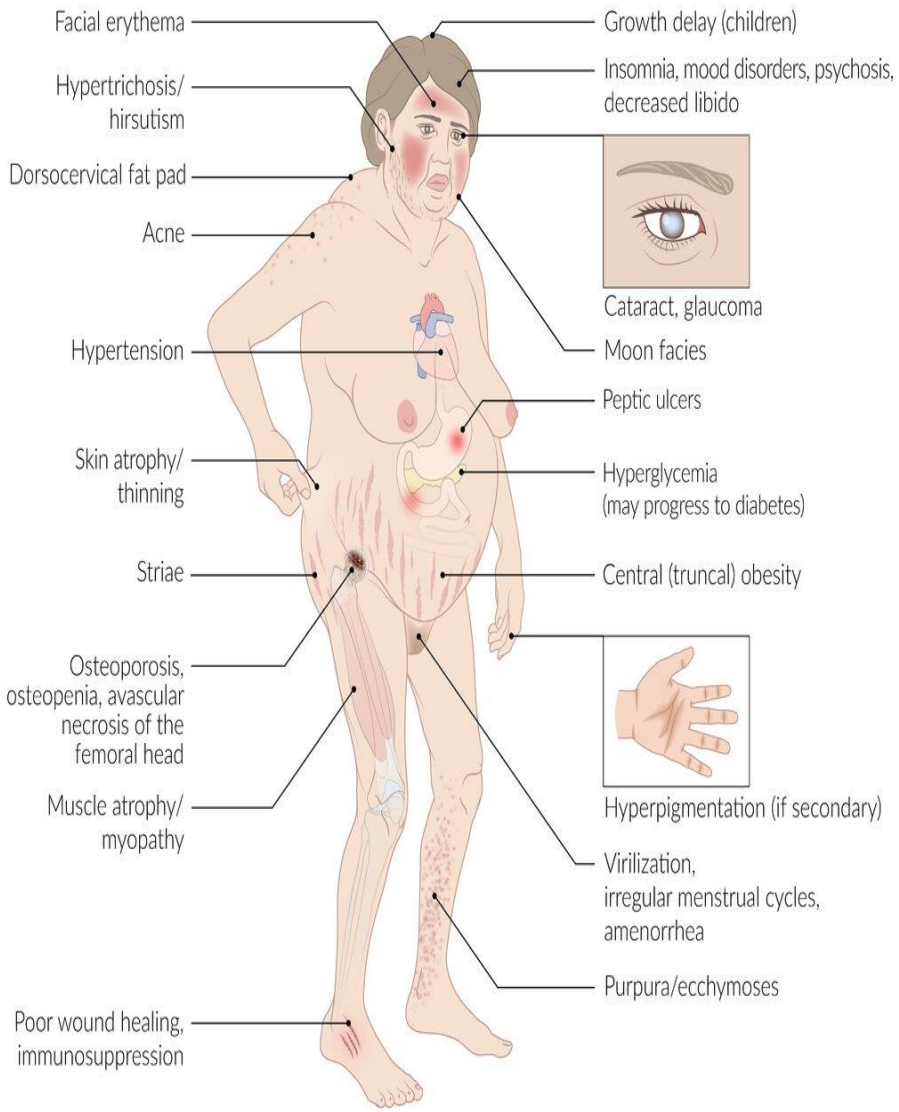
Cushing syndrome (hypercortisolism)

Etiology
- Exogenous (iatrogenic, most common cause of hypercortisolism): prolonged glucocorticoid therapy
- Endogenous

Primary: ACTH-independent (e.g., adrenal adenomas)
Secondary: pituitary ACTH production (e.g., pituitary adenomas) or ectopic ACTH production (e.g., small cell lung cancer)

Diagnosis
Screening test (e.g., 24h urine cortisol)
Determine underlying cause: hormone analysis (e.g., serum ACTH levels), imaging to localize tumor

Treatment
Exogenous Cushing syndrome: reduce glucocorticoid dosage, consider alternatives
Endogenous causes: tumor resection, if inoperable drugs to suppress cortisol synthesis



Diagnosis

Diagnostic laboratory tests:

- **High** plasma adrenocorticotropic hormone (**ACTH)**
- Nonsuppressed **morning cortisol level** after high-dose dexamethasone suppression test
- Elevated 24-hour **urine free cortisol** level

Treatment

Treat underlying disease.

Patients with SCLC and Cushing syndrome have **a worse response to chemotherapy**, shorter survival, and a higher rate of surgical complications.

NEUROLOGIC SYNDROMES

- Paraneoplastic neurologic syndromes are **a heterogeneous group of neurologic** disorders associated with **systemic cancer** and caused by mechanisms other than metastases, metabolic and nutritional deficits, infections, coagulopathy, or side effects of cancer treatment.

- These syndromes may affect **any part** of the nervous system from cerebral cortex to neuromuscular junction and muscle, damaging either one area or multiple areas.

- They can occur **with or without detectable autoantibodies** in serum and cerebrospinal fluid (CSF)

- **lung cancer** is the most common cancer associated with paraneoplastic neurologic syndromes; typically, these are associated with **SCLC.**
- They are caused by **neuronal autoantibodies resulting in Tcell mediated** damage to the central nervous system.
- These diverse neurologic manifestations include:
- Lambert-Eaton myasthenic syndrome (LEMS), cerebellar ataxia, limbic encephalitis, encephalomyelitis, sensory neuropathy, autonomic neuropathy, retinopathy, and opsomyoclonus
- The most common of these is **LEMS**, which may be seen in approximately **3 percent** of patients with SCLC .
- The neurologic symptoms of LEMS **precede the diagnosis** of SCLC in more than **80 percent** of cases, often **by months to years.**

SPINAL CORD SYNDROMES

Myelopathy الاعتلال النخاعي

- Paraneoplastic myelopathy, resulting in **rapidly progressive spastic paresis** with or without bowel and bladder dysfunction,
- usually occurs in association with **involvement of other areas** of the nervous system; examples include encephalitis, sensory neuronopathy, chorea, and optic neuropathy.
- The usual culprit is small cell lung cancer (SCLC).
- Paraneoplastic myelopathy can also occur as an isolated syndrome.
- Most patients **did not improve**, even after oncologic and/or immunosuppressive therapy.

SPINAL CORD SYNDROMES

Stiff-person syndrome

- Stiff-person syndrome is **an uncommon disorder** characterized by progressive muscle stiffness, rigidity, and spasms predominantly involving **the axial muscles of the trunk and proximal muscles of the limbs**.
- usually occurs in patients with **breast cancer or SCLC** .
- The serum of these patients often contains antibodies against amphiphysin

DORSAL ROOT GANGLIA

Subacute sensory neuronopathy

- Selective involvement of the dorsal root ganglia, referred to as sensory neuronopathy, results in a particularly disabling form of sensory loss with prominent sensory ataxia.
- Approximately 80 percent of patients with paraneoplastic subacute sensory neuronopathy have small cell lung cancer (SCLC), usually in association with anti-Hu antibodies

PERIPHERAL NERVE

Chronic sensorimotor neuropathy

- usually associate with small cell lung cancer (SCLC) or thymoma.
- Electrophysiologic studies show a mix of axonal and demyelinating features .
- These neuropathies are very disabling and respond poorly to immunotherapy or treatment of the tumor.

Vasculitic neuropathy

- presents with painful, symmetric or asymmetric sensorimotor deficits resembling a multifocal mononeuropathy and, in some patients, proximal motor weakness
- usually SCLC

PERIPHERAL NERVE

Autonomic neuropathy

- Autonomic dysfunction is associated with a variety of symptoms including, among others, orthostatic hypotension, dry mouth, erectile dysfunction, sphincter incontinence, gastroparesis, intestinal pseudo-obstruction, and cardiac arrhythmias that can lead to sudden death, gastroparesis excessive spontaneous sweating
- The tumor most frequently involved is SCLC; these patients usually have anti-Hu antibodies and, less frequently, anti-CRMP5 antibodies.
- Other tumors include carcinoma of the pancreas,thyroid, and rectum; Hodgkin lymphoma; and carcinoid tumors of the lung

NEUROMUSCULAR JUNCTION

Lambert-Eaton myasthenic syndrome

- The Lambert-Eaton myasthenic syndrome (LEMS) is an autoimmune disorder of the neuromuscular junction caused by antibodies directed against voltage-gated calcium channels (VGCC) interfere with the normal calcium flux and reduce acetylcholine release from the presynaptic nerve terminals.
- Approximately 50 percent of patients with LEMS have cancer, almost always small cell lung cancer (SCLC) and may occur in lymphomas, thymomas, or cancers of the pancreas, rectum, kidney, breast, prostate, or uterus.
- The autoimmunity in LEMS may be nonparaneoplastic, occurring typically in those with underlying immune-mediated conditions or receiving immunosuppression therapies.

- The presence of antibodies against SOX1 in patients with LEMS predicts the presence of an SCLC
- Most cases of LEMS occur among middle-aged adults, but LEMS can affect younger and older adults, and rare cases have been reported in children.
- The age of LEMS onset is earlier in patients with nonparaneoplastic LEMS compared with those with cancer (paraneoplastic LEMS).

Clinical features

Most patients with LEMS present with slowly progressive proximal muscle weakness, particularly involving the legs.
Deep tendon reflexes are typically depressed or absent.
Ocular symptoms, especially ptosis and diplopia, or bulbar muscle weakness may occur with LEMS but are rarely the presenting or dominant feature of the illness.
Most patients do not have significant respiratory muscle weakness, but respiratory failure may occur late in the course.

- Recovery of lost deep tendon reflexes or improvement in muscle strength with vigorous, brief muscle activation is a unique aspect of LEMS.

Diagnosis

- The diagnosis of LEMS is usually made clinically.
- Confirmatory evidence on electrodiagnostic studies includes a reproducible postexercise increase in compound muscle action potential amplitude of at least 60 percent compared with pre-exercise baseline value or a similar increment on high-frequency repetitive nerve stimulation without exercise.
- A high titer P/Q-type VGCC antibody is also strongly suggestive of LEMS in the appropriate clinical setting.
- Antibodies have both a diagnostic and a pathogenic role.

- Immunosuppressive therapy improves muscle strength.
- Treatment of the underlying tumor usually leads to resolution of symptoms.

NEUROMUSCULAR JUNCTION

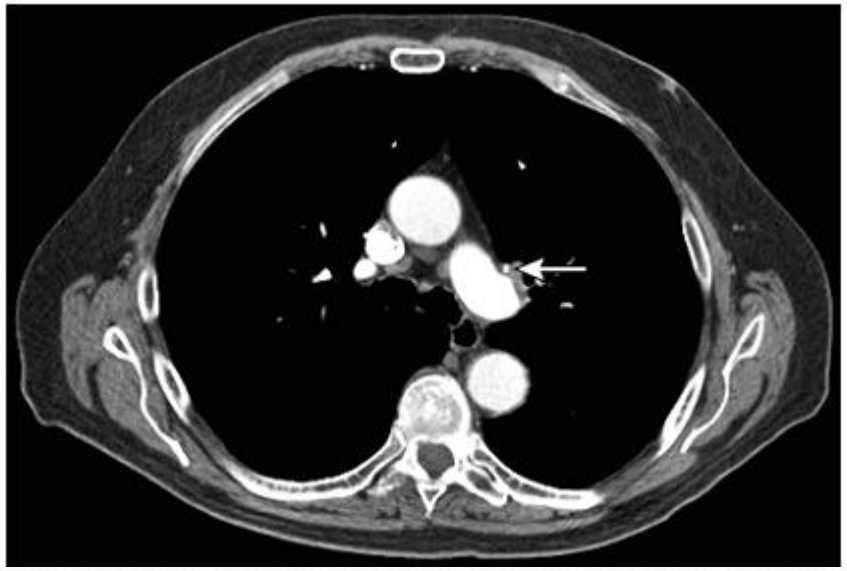
Myasthenia gravis

- most commonly thymoma.
- rarely occurs in patients with other cancers (SCLC, thyroid and breast cancers, and Hodgkin lymphoma).

diagnoses

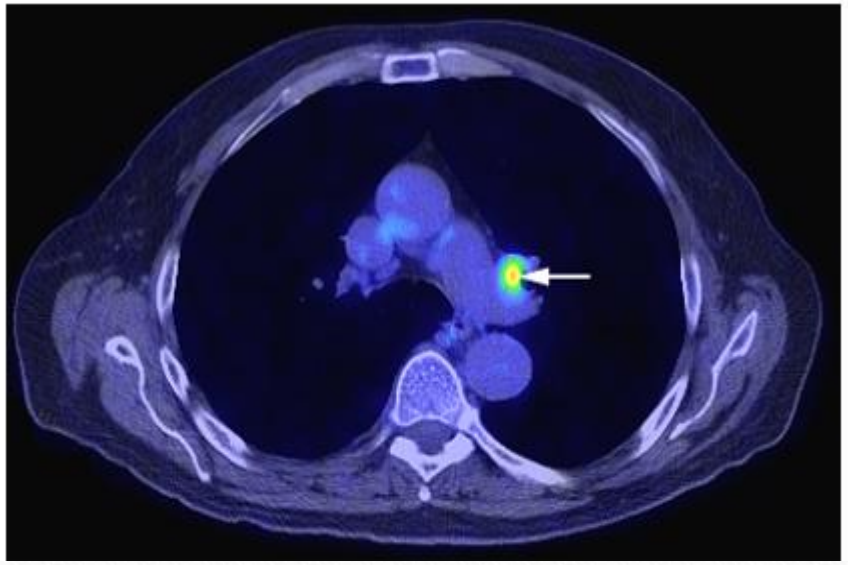
- As many as 70 percent of patients who have SCLC and an associated paraneoplastic neurologic syndrome have limited-stage disease .
- The finding of a paraneoplastic autoantibody in patients presenting with a neurologic syndrome should lead to an evaluation for malignancy.
- A computed tomography (CT) of the chest is indicated in current or former smokers who have a suspected paraneoplastic neurologic syndrome.
- If the CT of the chest is negative, then positron emission tomography (PET) may be useful in identifying the location of a neoplasm.
- Even subtle abnormalities of the lungs or mediastinum require biopsy in this situation

CT negative PET positive paraneoplastic disease



This 71-year-old man presented with a polyneuropathy thought secondary to a paraneoplastic syndrome as he had a high P/Q type calcium channel antibody present in serum. CT showing a normal sized hilar node (arrow).

CT negative PET positive Paraneoplastic disease



This 71-year-old man presented with a polyneuropathy thought secondary to a paraneoplastic syndrome as he had a high P/Q type calcium channel antibody present in serum. PET-CT showing intense metabolic activity (arrow) in a normal sized left hilar node after CT was negative. Ultrasound guided bronchoscopy sampling revealed small cell lung cancer in this hilar node.

Treatment

Paraneoplastic neurologic syndromes generally do not improve with immunosuppressive treatment.
However , symptoms may stabilize with response of the underlying neoplasm to treatment.
Exceptions include Lambert-Eaton myasthenic syndrome and opsoclonus-myoclonus syndrome; most patients may experience resolution or partial remission with immunosuppression and treatment of the cancer .

❑ Anti-Hu Syndrome

ATS

- Most common paraneoplastic neurologic syndrome associated with lung cancer.
- The presence of anti-Hu antibodies has specificity of 99% and sensitivity of 82% for diagnosing a neurogenic paraneoplastic syndrome, but these antibodies are not themselves pathogenic.
- Symptoms include brain stem encephalitis, opsoclonus-myoclonus, cerebellar degeneration, myelopathy, and peripheral nerve palsy.
- Response to therapy for SCLC helps, but does not cure the disease.

ATS

❑ Anti-Yo Syndrome

- Caused by anti-Yo antibodies directed against Purkinje cells in the cerebellum.
- Antibodies have both a diagnostic and a pathogenic role.
- Manifests clinically as cerebellar degeneration.
- Intravenous immunoglobulins may stabilize clinical symptoms if administered early after onset of symptoms.
- Treatment of underlying cancer does not cure the disease.

MUSCLE FUNCTION

DERMATOMYOSITIS AND POLYMYOSITIS

- Dermatomyositis and polymyositis are two distinct forms of inflammatory myopathy, both of which are manifested clinically by muscle weakness.
- These inflammatory myopathies can be the presenting symptom in patients with lung cancer or can develop later in the course of disease.

Approximately 10 to 15 percent of adults with dermatomyositis are diagnosed with a malignancy, usually within the first two to three years after diagnosis

In addition to lung cancer, other frequent primary sites associated with these disorders include the ovary, cervix, pancreas, bladder, and stomach.

Dermatomyositis (DM) and polymyositis (PM)

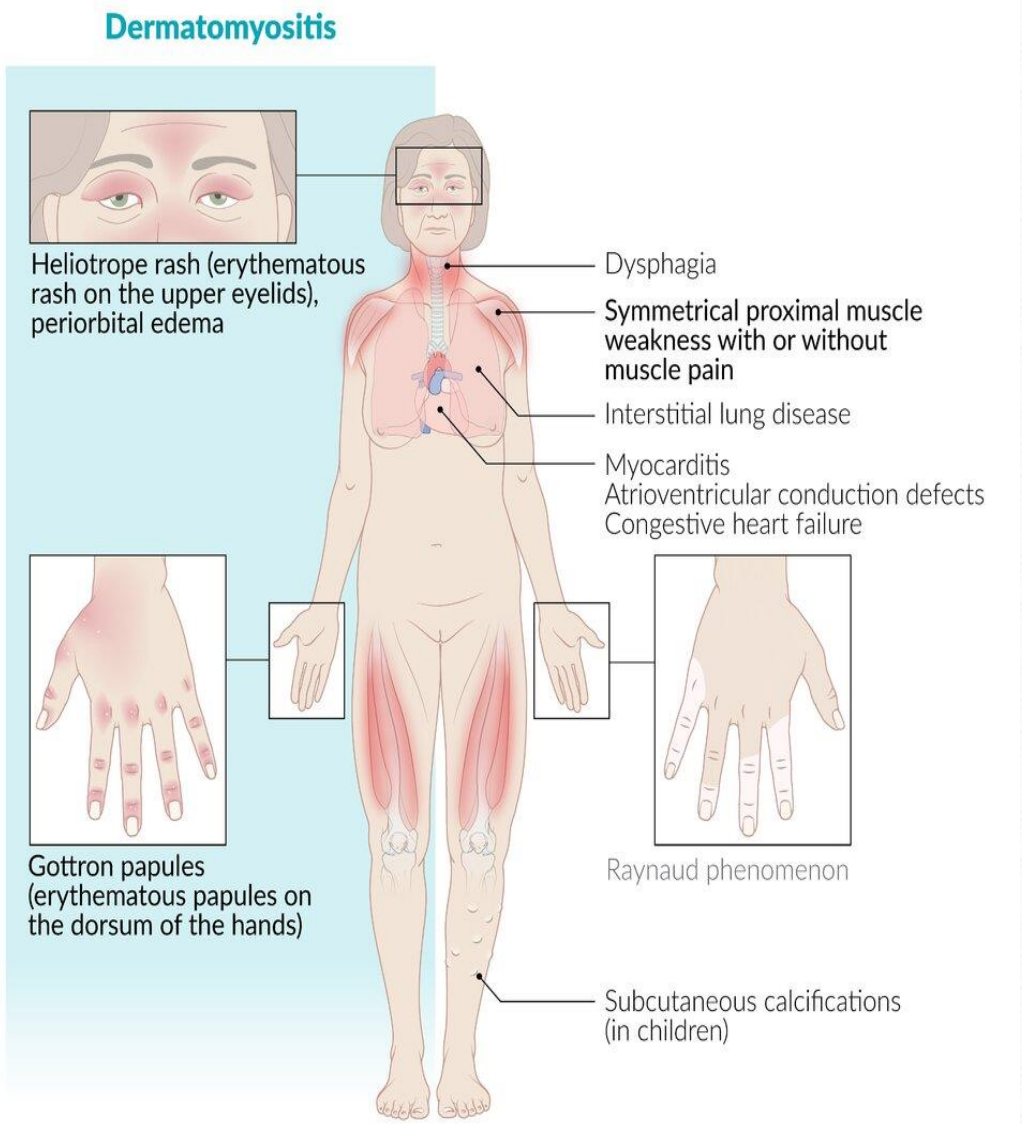
Etiology
Idiopathic; likely antibody-mediated (DM) or cell-mediated (PM) autoimmune cytotoxicity against skeletal muscle antigens
May be assoc. with viral infections (e.g., HIV, HTLV-1, and Coxsackie viruses) or malignancy (i.e., paraneoplastic syndrome)

Epidemiology
♀ > ♂
Peak age: 30–60 years

Serology
ANA (nonspecific)
Anti-Mi-2 antibodies (specific for DM)

Laboratory findings
↑↑ Serum creatine kinase, ↑ Aldolase, ↑ myoglobin, ↑ LDH, ↑ AST, ↑ ALT

Note
Associated with malignancy (esp. in patients with dermatomyositis)
Polymyositis (DM without skin involvement) is a diagnosis of exclusion in the absence of the characteristic findings of the other inflammatory myopathies



MUSCLE FUNCTION

Paraneoplastic neuromyotonia

- Neuromyotonia, also called peripheral nerve hyperexcitability or Isaacs syndrome
- Thymoma, small cell lung cancer (SCLC), and Hodgkin lymphoma are the most commonly associated neoplasms

- **Symptoms** include muscle cramps, muscle twitching (myokymia, fasciculations), stiffness, pseudomyotonia (delayed relaxation), carpopedal spasms, increased sweating, and sometimes motor weakness
- **Treatment** with plasma exchange or intravenous immune globulin (IVIG) is usually of benefit; other potentially effective treatments include phenytoin, carbamazepine, and diazepam

Hematologic manifestations

A number of hematologic abnormalities are seen in patients with lung cancer. These include the following:

❑ Anemia

- Anemia is frequent in patients with lung cancer and can contribute to fatigue and dyspnea.
- 40 percent of untreated patients had a hemoglobin ≤12 g/dL, while the incidence of anemia was 80 percent in those on chemotherapy .
- Anemia may be due to any of a number of causes, including microangiopathic hemolytic anemia and anemia of chronic disease.

❑ Leukocytosis

- tumor-associated leukocytosis was found in 15 % of patients with lung cancer.
- Nearly all had **NSCLC**
- leukocytosis happen due to overproduction of granulocyte-colony stimulating factor .
- Leukocytosis in association with lung cancer is associated with a poor prognosis and has also been associated with hypercalcemia.

❑ Thrombocytosis

- Thrombocytosis is common and may be present in as many as 14 percent of patients with lung cancer at presentation .
- Thrombocytosis at presentation has been identified as an independent predictor of shortened survival

❑ Eosinophilia

- Eosinophilia in tissue or blood is rare but has been reported in patients with **large cell carcinoma**.

❑ Hypercoagulable disorders

Venous thromboembolism occurs within 2 years of diagnosis in 3% of patients with lung cancer.

- Tumor cells directly activate clotting via tissue factor and cancer procoagulant.
- Low-molecular-weight heparin is the preferred treatment.

A variety of hypercoagulable disorders have been associated with lung cancer and other malignancies. These hypercoagulable disorders include:

- Superficial thrombophlebitis (Trousseau syndrome)
- Deep venous thrombosis and thromboembolism
- Disseminated intravascular coagulopathy
- Thrombotic microangiopathy
- Nonbacterial thrombotic endocarditis

HYPERTROPHIC PULMONARY OSTEOARTHROPATHY

Characterized by digital clubbing , painful symmetrical arthropathy (involving the wrists, elbows, ankles, and knees), and periosteal new bone formation in the distal long bones of the limbs.
The metacarpal, metatarsal, and phalangeal bones may also be involved.

- Most commonly associated with **adenocarcinoma** of the lung.
- Histologic features include vascular hyperplasia, edema, and excessive fibroblast and osteoblast proliferation.
- Overexpression of vascular endothelial growth factor may play a role in pathogenesis.

- A radiograph of the long bones (ie, femur , tibia, and fibula) shows characteristic periosteal new bone formation in patients with HPO.
- An isotope bone scan or PET typically demonstrates diffuse uptake by the long bones

Hypertrophic pulmonary osteoarthropathy

Normal bone scan for comparison.

Hypertrophic pulmonary osteoarthropathy

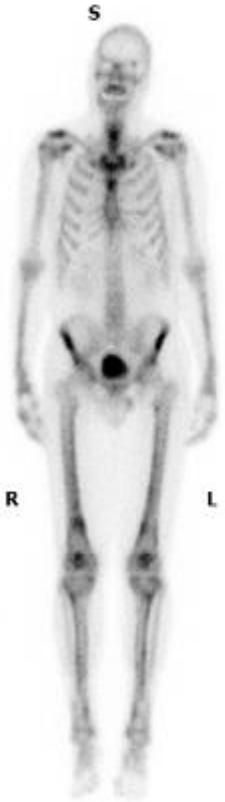
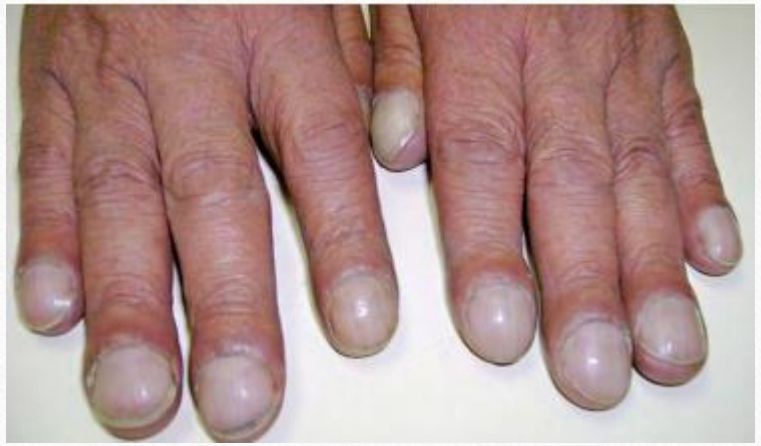


Image from a 69-year-old male with non-small cell lung cancer (NSCLC) and bilateral lower extremity pain. Whole body bone of shows patchy uptake in the periosteal aspects of the long bones typical of hypertrophic pulmonary osteoarthropathy. No clear evidence of skeletal metastases.

The symptoms of HPO may resolve after tumor resection.
For patients who are not operable, the usual treatment is with nonsteroidal anti-inflammatory agents, corticosteroids, or a bisphosphonate.



Digital clubbing is characterized by enlargement of the terminal segments of the fingers

Lung Cancer and Common Paraneoplastic Syndromes

Adenocarcinoma	Small cell lung cancer	Squamous cell lung cancer
Hypertrophic pulmonary osteoarthropathy	• Syndrome of inappropriate antidiuretic hormone secretion. • Cushing syndrome • Carcinoid syndrome • Neurogenic syndromes • Eaton Lambert syndrome	Hypercalcemia

THANK YOU