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# Stages of lung cancer



## **Objective of lecture**

**1- Grading and Staging of cancer**

**2-Staging of lung cancer and prognosis of lung cancer**

**3-Paraneoplastic syndrome**

## CASE-1

A 58y old men has developed cough with blood –streaked sputum and Wight loss . A CXR reveals a 5 cm consolidated area near the RT hilum(central) with L.N enlargement . Multiple hepatic nodules by sonar examination .

A sputum cytology reveals the presence of clusters of small cells having large hyper- chromatic pleomorphic nuclei with scanty cytoplasm but are larger than lymphocytes .

## **Grading Tumors**

**How much the tumor cells resembles original normal-tissue cells**

**Based on microscopic features (Differentiation and mitotic-rate)**

**.Grades I-III/IV (higher grades are more anaplastic)-**

**Malignant tumors only and Dysplasia of the cervix are-  
”“graded**

**Tumor grade is important in treatment plan and prognosis-**

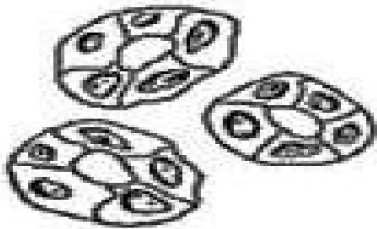
## Grading Of Cancer

**Grade I (low grade) ,well differentiated -The cells are slightly differed • from the normal cells , with Good prognosis**

**Grade II (moderate grade) , moderate differentiated -The cells are • moderate abnormal ,with Moderate prognosis**

**Grade III (high grade ) poor differentiated -The cells are very differed • and abnormal with Poor prognosis**

**Grade IV (high grade) very poor differentiated -The cells are • immediate and primitive and undifferentiated with very Poor prognosis**



**G1**



**G2**



**G3**



**G4**

Example for glandular structure

## **Staging of tumors**

**For malignant tumors only-**

**How far has the tumor spread-**

**Based on Tumor size (T), lymph node (N) involvement, -  
distant metastases (M)**

**Staging often involves: the Pathologist, radiology or-  
other imaging, lab tests (tumor markers) and  
interoperation examination**

**CIS(carcinoma in situ is referred to as Stage Zero-**

**Tumor stage American Joint Committee on Cancer (AJCC)  
.TNM system**

**Depends on pathological and clinical information  
.CT scan , US, bone marrow examination....etc**

**TNM staging system**

**T= Primary tumor size**

**N= Regional lymph node involvement**

**M= Metastasis**

**TNM, Help to-decide treatment  
and prognosis**

# Lung cancer stages

The most frequently used system for staging lung cancer is the **American Joint Committee on cancer (AJCC)** is depend on World health organization(WHO) classification of tumor **TNM** ,Which is based on :-

**T**=size of the tumor

**N**=Lymph node involvement

**M**= metastasis to other organ



# Lung Cancer Staging

**WHO Classification  
Depend on TNM**

**Non-Small Cell**

**Small Cell**

**Stage O**

**Stage I**

**Stage II**

**Stage III**

**Stage IV**

**Limited**

**Extensive**

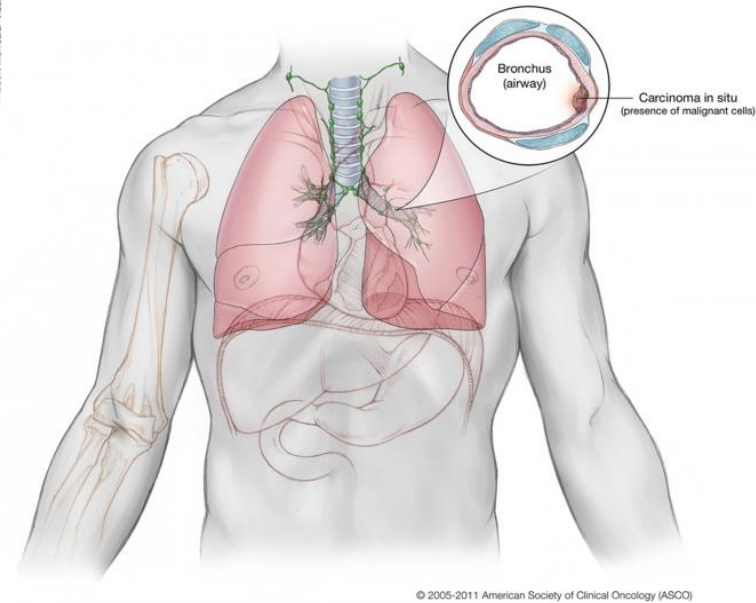
# Stages of NSCLC

## Stage 0 ( carcinoma in situ)

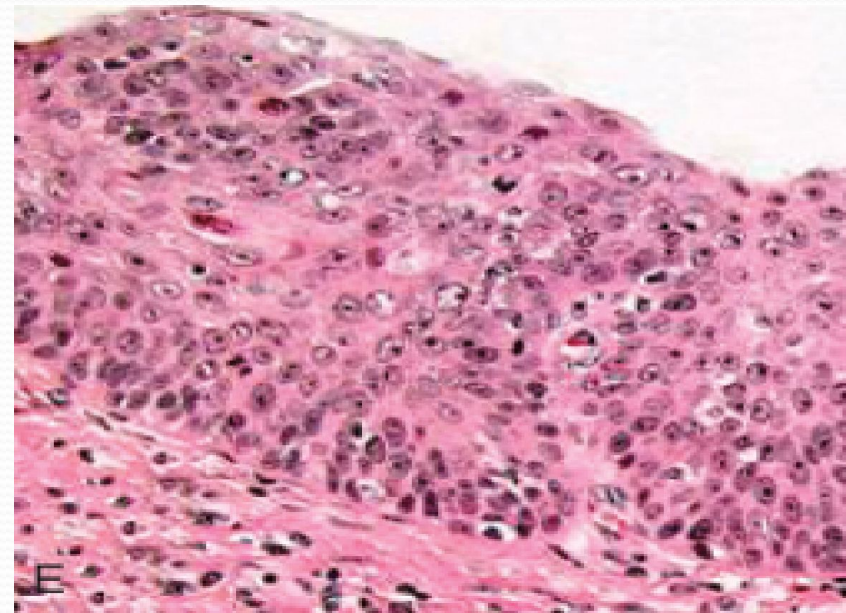
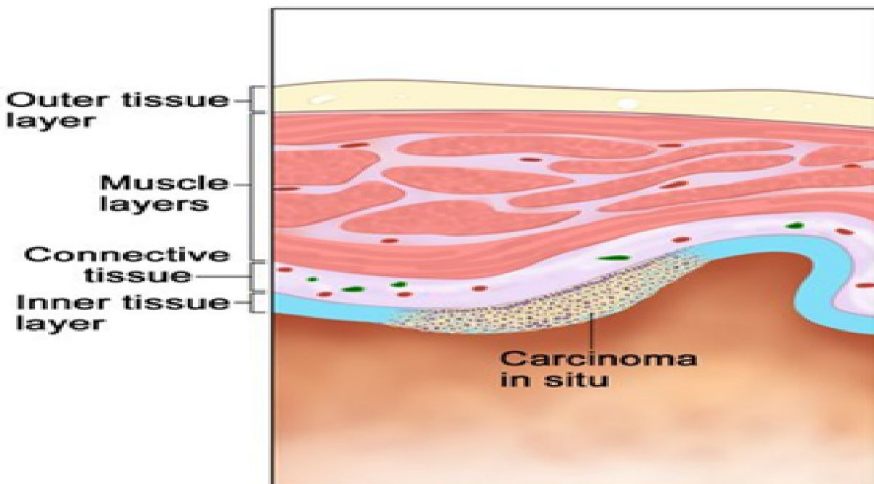
Cancer cells within epithelium with intact basement membrane  
no tumor size , no L.N involvement(N0) and no metastasis (M0) . Treatment by surgery , excellent prognosis

Robert Marmel/ Visual Explanations, LLC

Stage 0

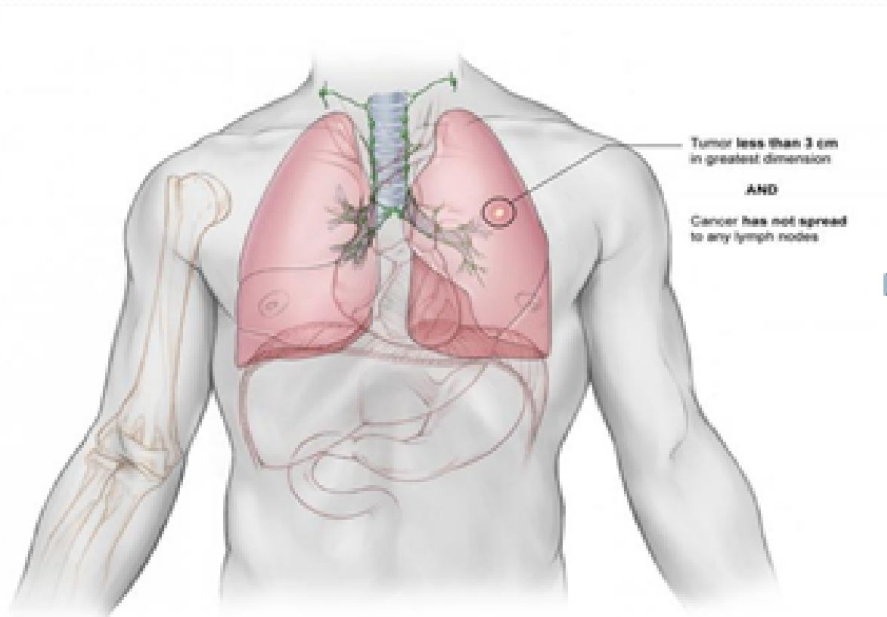


Carcinoma in situ



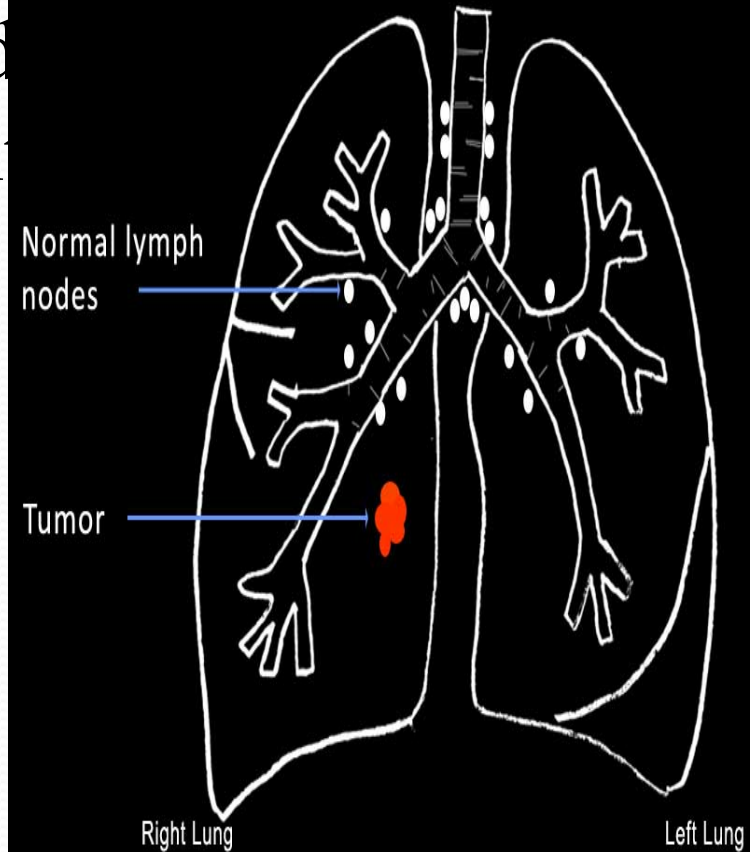
# Stage I

Invasive tumor of any size is found only in lung and no L.N involvement (N0) and no metastasis (M0) Treatment by surgery , good prognosis



## Lung Cancer Stage 1

Dr Ogwudu- Minimally Invasive Thoracic Surgeon



Treatment: Minimally invasive lung surgery to remove the section of lung containing the tumor

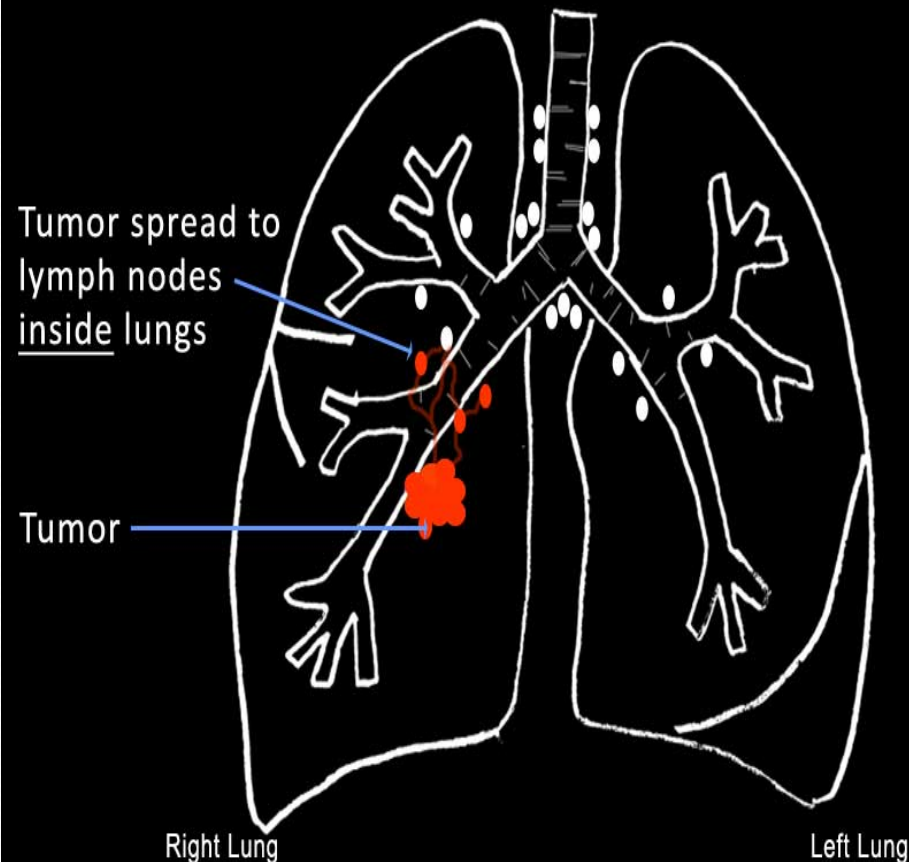
## Stage II

Invasive tumor has spread to lymph nodes around bronchiole inside lungs and the same side of the lung and no metastasis (M0) .

Treatment by surgery , good prognosis

## Lung Cancer Stage 2

Dr Ogwudu- Minimally Invasive Thoracic Surgeon



Because the tumor is still localized, minimally invasive lung surgery to remove the section of lung containing the tumor is recommended

**Stage IIIA:-Invasive** tumor has spread to L.Ns in the tracheal area ,including chest wall and diaphragm on the same side of the lung tumor. Treated by surgery with chemotherapy or chemotherapy + radiation .

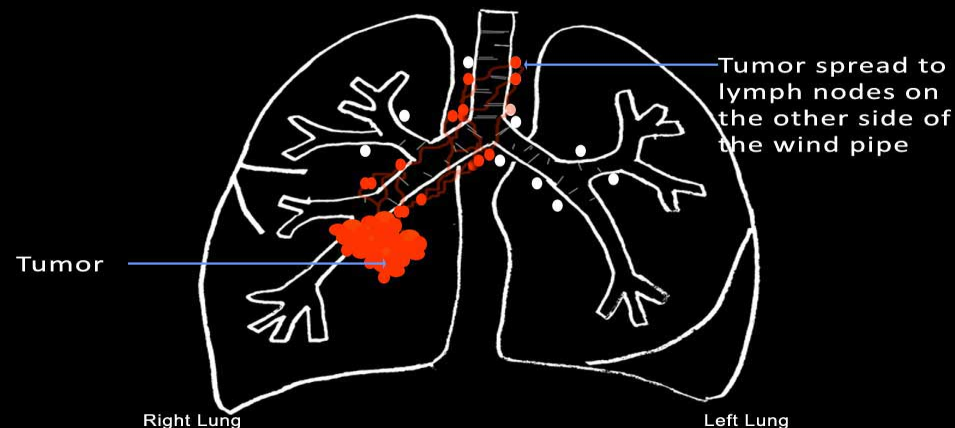
Moderate-poor prognosis

**Stage III B:- Invasive** tumor has spread to L.Ns to other side of trachea and lung or in neck . Treated by chemotherapy and radiation . Poor prognosis

**Stage IV :-**Tumor has spread beyond the chest. Treated by chemotherapy and radiation . very poor prognosis

### Lung Cancer Stage **3B**

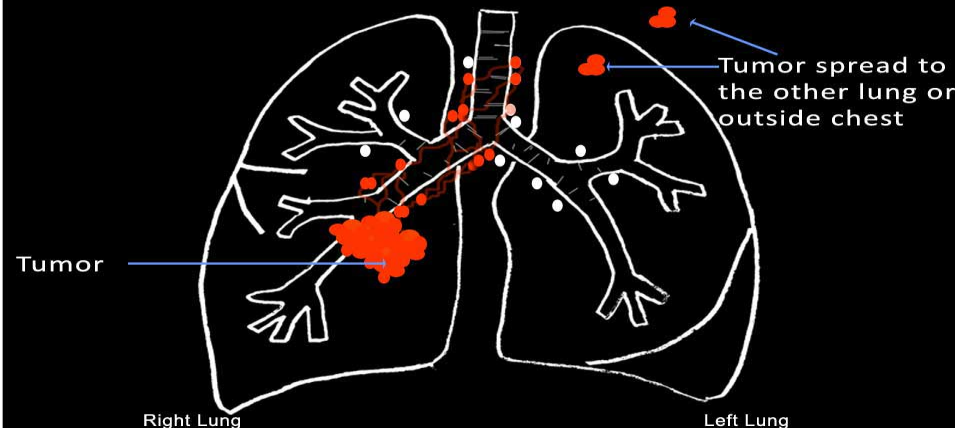
Dr Ogwudu- Minimally Invasive Thoracic Surgeon



Because of the extent of the lymph nodes involved, surgery is not recommended. Chemotherapy with Radiation therapy is the treatment for stage 3B

### Lung Cancer Stage **4**

Dr Ogwudu- Minimally Invasive Thoracic Surgeon



Because the cancer is widespread, surgery is not recommended. Chemotherapy with radiation therapy is the treatment for stage 4

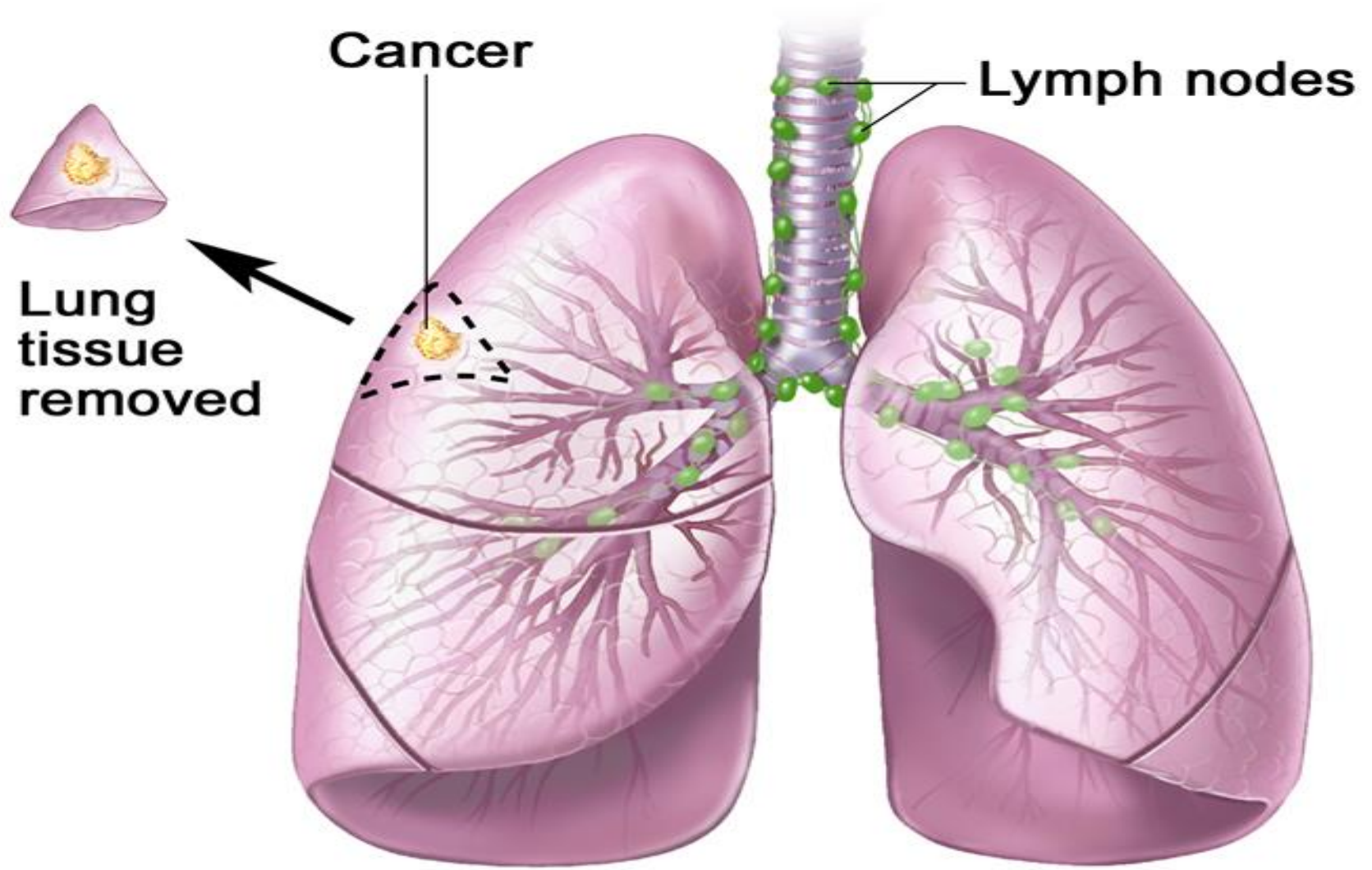
# Prognosis of lung cancer

The prognosis of lung cancer depends on **stage** at presentation .

The overall 5-year survival rate is 15% although surgical resection of solitary tumors has a better survival rate 48%

Despite treatment ,the **prognosis is poor** .

# Wedge Resection of the Lung



# Para-neoplastic syndromes

**-Endocrine /Metabolic syndromes are mediated by humeral factors like**

**1-ectopic hormones or (hormone-like factors elaborated) excreted by tumor cells .**

**2- cytokines or antibodies which mediated by an immune response against the tumor.**

**-Most of PNS are mediated by immune responses triggered by neuronal proteins (onco-neural antigens) expressed by tumors both humeral (antibodies) and cell mediated immunity (CD4,CD8) are activated .**

**-These immune responses have complex mechanism hence these PNS are resistance to therapy**



**-PNS can occur before ,or during or after cancer diagnosis.**

**-Up to 10% of all patients with lung cancer develop clinically overt paraneoplastic syndromes.**

**-Small cell carcinoma is most commonly produce paraneoplastic syndromes.**

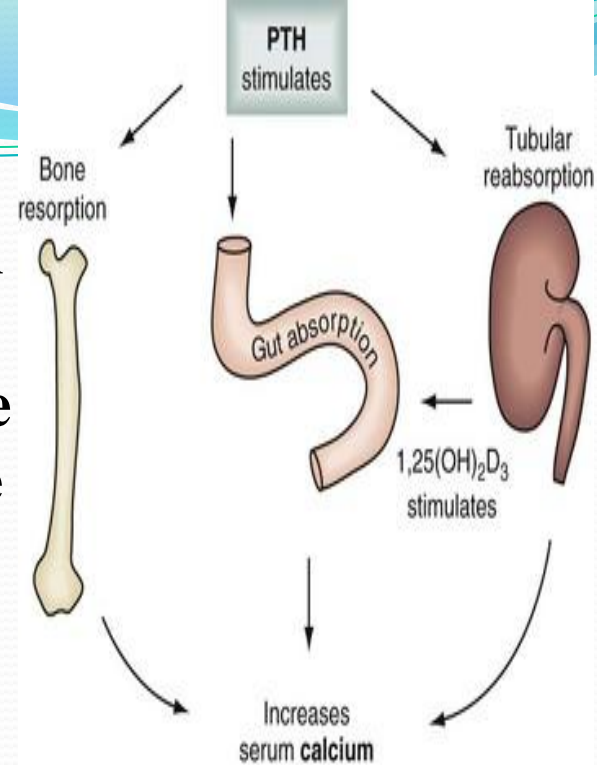
# The hormones or hormone-like factors elaborated include:

**1-Hypercalcemia** secondary to ectopic secretion of a parathyroid hormone-related peptide, excreted by tumor cells of bronchogenic ca. (the most important mechanism). Another possible mechanism for hypercalcemia is widespread osteolytic metastatic disease of bone.

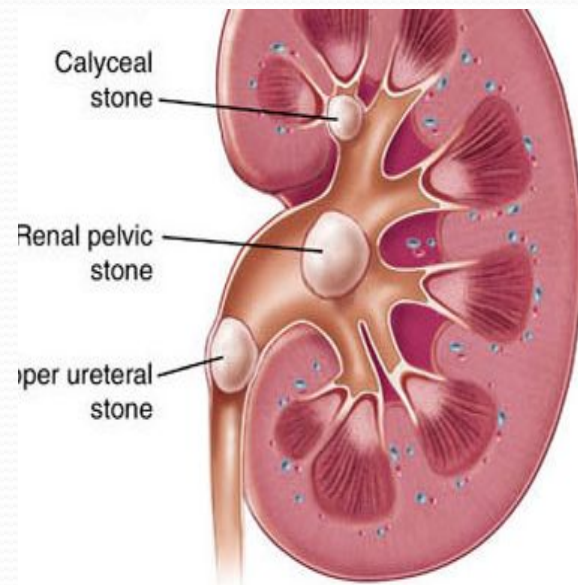
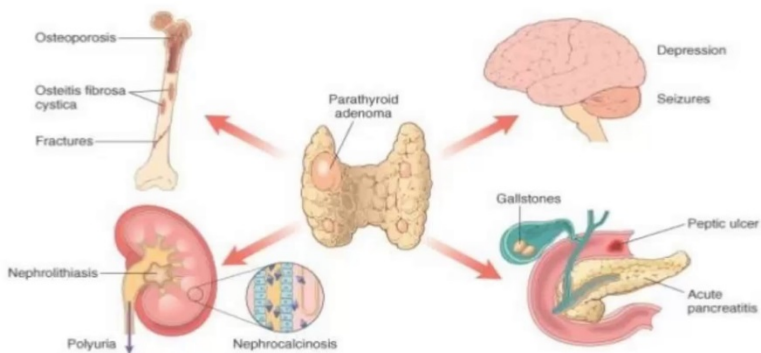
## Sign and symptom of hypercalcemia

Painful bone pain and osteoporosis

Renal colic and Renal stone or gall bladder stone



## Hypercalcemia



## 2- Cushing syndrome secondary to production of ectopic adrenocorticotrophic hormone (ACTH).

### Sign and symptom

Moon face and buffalo neck

Hyperglycemia

Thin skin and striae

Amenorrhea and hirsutism

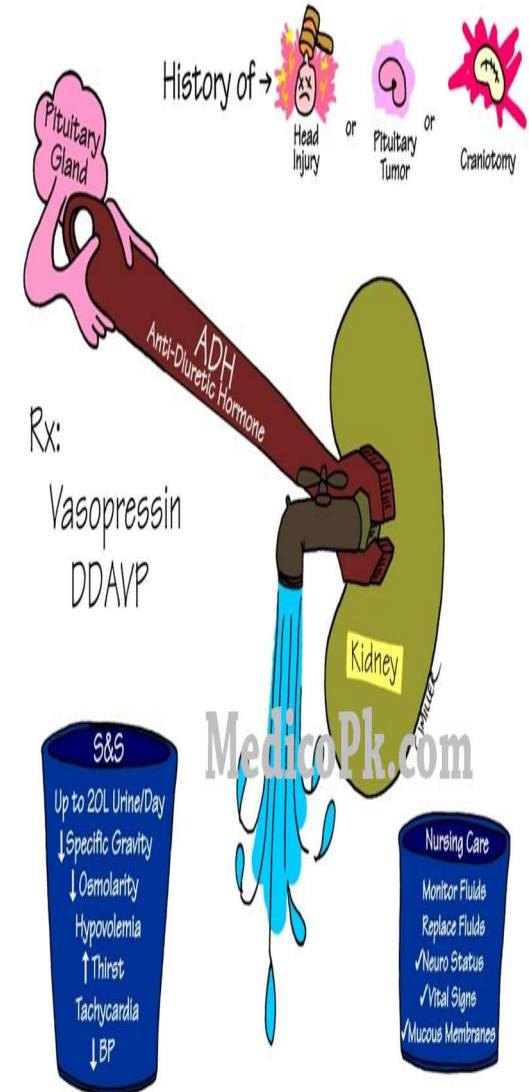
Gynecomastia in male



# 3-Syndrome of inappropriate (i.e. excess) secretion of ectopic antidiuretic hormone (SIADH) lead to:-

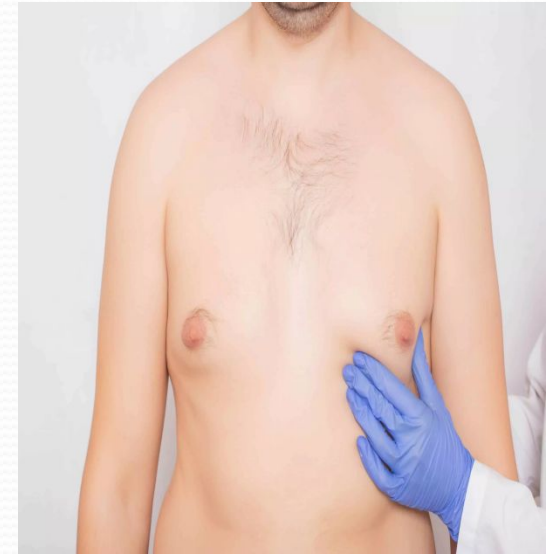
- Water retention
- Hyponatremia .
- Increased BP .
- Increased osmolality (concentration) of urine
- Decreased osmolality of plasma .

## DIABETES INSIPIDUS



**4-Hypocalcemia** due to ectopic secretion of calcitonin .

**5- Gynecomastia** is an increase in the amount of breast gland tissue in boys or men, caused by an imbalance of the hormones estrogen and testosterone.  
due to ectopic secretion of gonadotropins.



**6-Hypoglycemia** due to ectopic secretion of insulin or insulin-like substance from malignant cells .

## 7-Acanthosis nigricans :-

hyperpigmentation of the skin ,found in the body folds ,Brown to black ,poorly defined , due to **ectopic secretion of insulin** or **insulin-like substance** from malignant cells .

Increased insulin lead to activates insulin-like growth factor receptors (**ILGFR**) which may lead to keratinocyte and dermal fibroblast proliferation .



## 8-Carcinoid syndrome

Due to ectopic secretion of serotonin and histamine .

Clinical features :-

### Clinical Features of carcinoid syndrome

- Cutaneous flushing
- Venous telangiectasia
- diarrhoea
- bronchospasm
- cardiac valvular lesions



-Facial Flushing occurs as a result of dilatation of the blood vessels, which are present under the surface of the skin.

-Watery diarrhea and bronchospasm.

-Telangiectasia :-dilatation of small blood vessels and capillaries , which are present under the surface of the skin. (hypoxia lead to increased stimulation of VEGF which in turn lead to endothelial proliferation and telangiectasia



## Other paraneoplastic syndromes include

**1- Hypertrophic pulmonary osteoarthropathy is characterized by periosteal new bone formation , clubbing of the fingers and arthritis .This due to hypoxia which stimulate VEGF for proliferation of end plate of bone which lead to bone pain .**

**periosteal new bone formation**

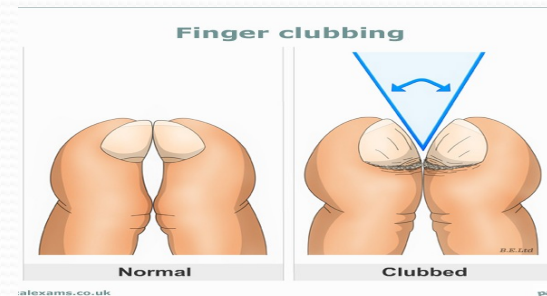




**Clubbing of the fingers** which mean increased depth and bulk of distal portion of fingers . (2- theories )

-Hypoxia stimulate VEGF induces vascular hyperplasia ,edema ,fibroblast or osteoblast proliferation of end plate of fingers .

-Hypoxia leading to vasodilatation and proliferation of subcutaneous tissue of nail bed and there is an increased in the capillary permeability leading to interstitial edema

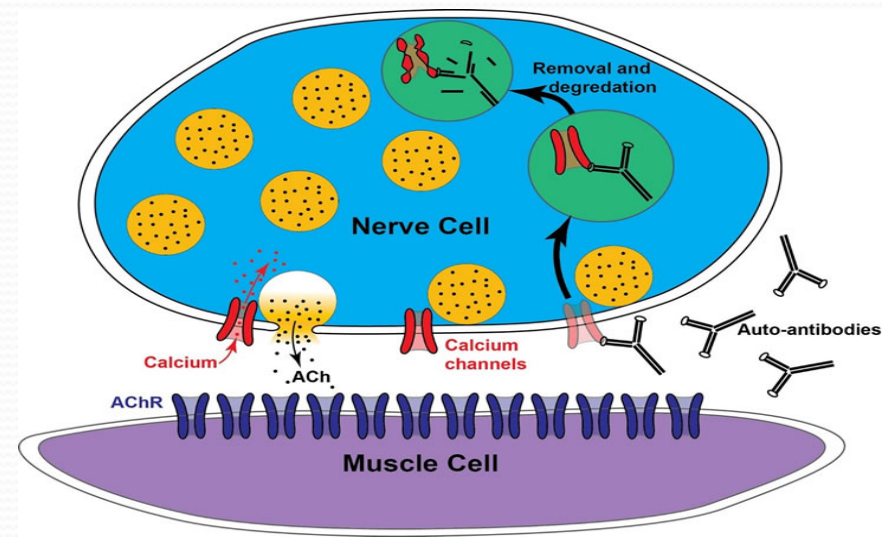


## 2- Lambert –Eaton Myasthenic syndrome (LEMS) :-

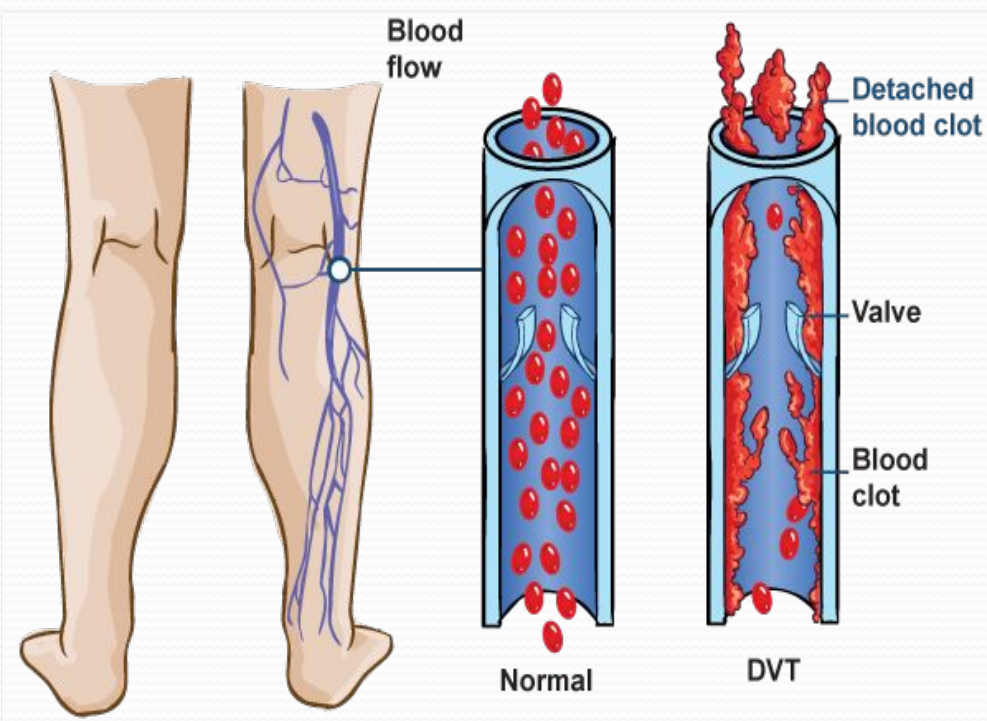
- Means presynaptic disorder of the neuromuscular junction
- LEMS** :- malignant cells produce auto-antibodies against the presynaptic calcium channels of the neuromuscular junction which lead to decreased acetylcholine release and impaired in neuronal transmission

### **LEMS include the following :-**

- Proximal muscle weakness , It starts in the proximal muscles of the legs or arms. , fatigue and pain .
- Muscle weakness of the eyes .
- Swallowing problems, dry mouth
- Speech impairment .

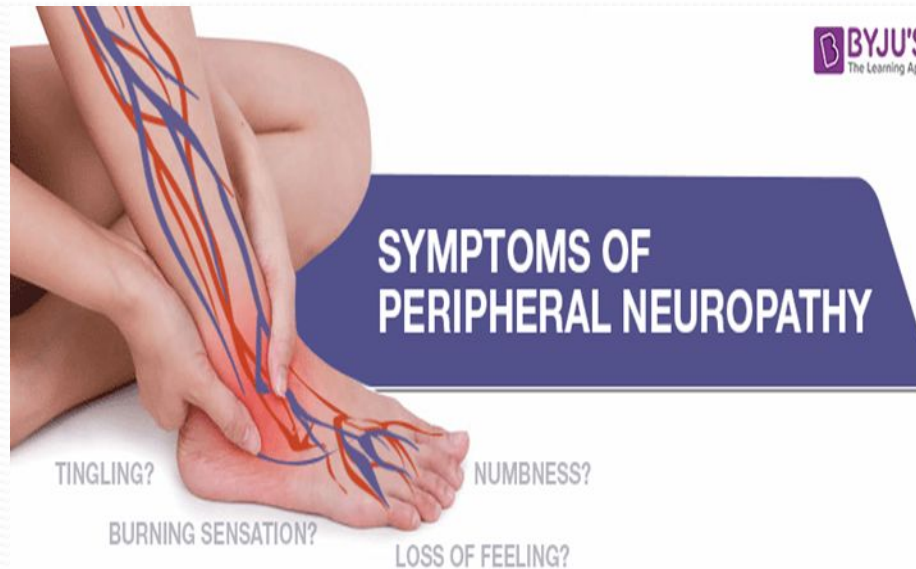


**3- Hematological manifestations** :- manifest as hypercoagulability, including migratory thrombophlebitis (repeated attacks of multiple venous thrombosis at different sites due to the pro-coagulant factors formed by cancer cells) , and disseminated intravascular coagulation(DIC) .



## 4-Peripheral neuropathy, and polymyositis due to autoantibodies production .

numbness ,burning sensation , tingling ,loss of feeling



**\*Hypercalcemia is most often encountered with squamous cell carcinoma & adenocarcinomas.**

**\*The remaining syndromes are much more common with small-cell neoplasms.**

# **Metastatic carcinoma to the lung(secondary carcinoma)**

**-The common primary sites are the breast, stomach, pancreas, and colon.**

**Metastatic carcinoma of the lung.**

**CXR show :- Multiple 'cannon ball' nodules**



**lung shows numerous nodules of metastatic carcinoma**



all my love  
for you →



you →



Thanks