

# ΚΑΡΚΙΝΟΣ ΠΝΕΥΜΟΝΑ

Αριστοτέλης Μπάμιας  
Καθηγητής Θεραπευτικής-Παθολογίας-Ογκολογίας ΕΚΠΑ  
Δ/ντης Β' Προπαιδευτικής Παθολογικής Κλινικής  
Ιατρική Σχολή ΕΚΠΑ  
ΠΓΝΑ ΑΤΤΙΚΟΝ

# Κατάταξη

- Μικροκυτταρικός 20%
- Μη μικροκυτταρικός 70-75%
  - Αδενοκαρκίνωμα
  - Πλακώδες
  - Μεγαλοκυτταρικό
- Βρογχοκυψελιδικό
- Καρκινοειδές
- Άλλα

# Επιδημιολογία-Παράγοντες κινδύνου

- Ο συχνότερος καρκίνος στους άνδρες
  - 21% όλων των καρκίνων
  - 29% των θανάτων από καρκίνο
- Παράγοντες κινδύνου
  - ΚΑΠΝΙΣΜΑ
  - Ατμοσφαιρική ρύπανση
  - Έκθεση σε αμίαντο
  - Επαγγελματική έκθεση
    - Αρσενικό, νικέλιο, πυρίτιο, πίσσες, ορυκτέλαια, ραδόνιο

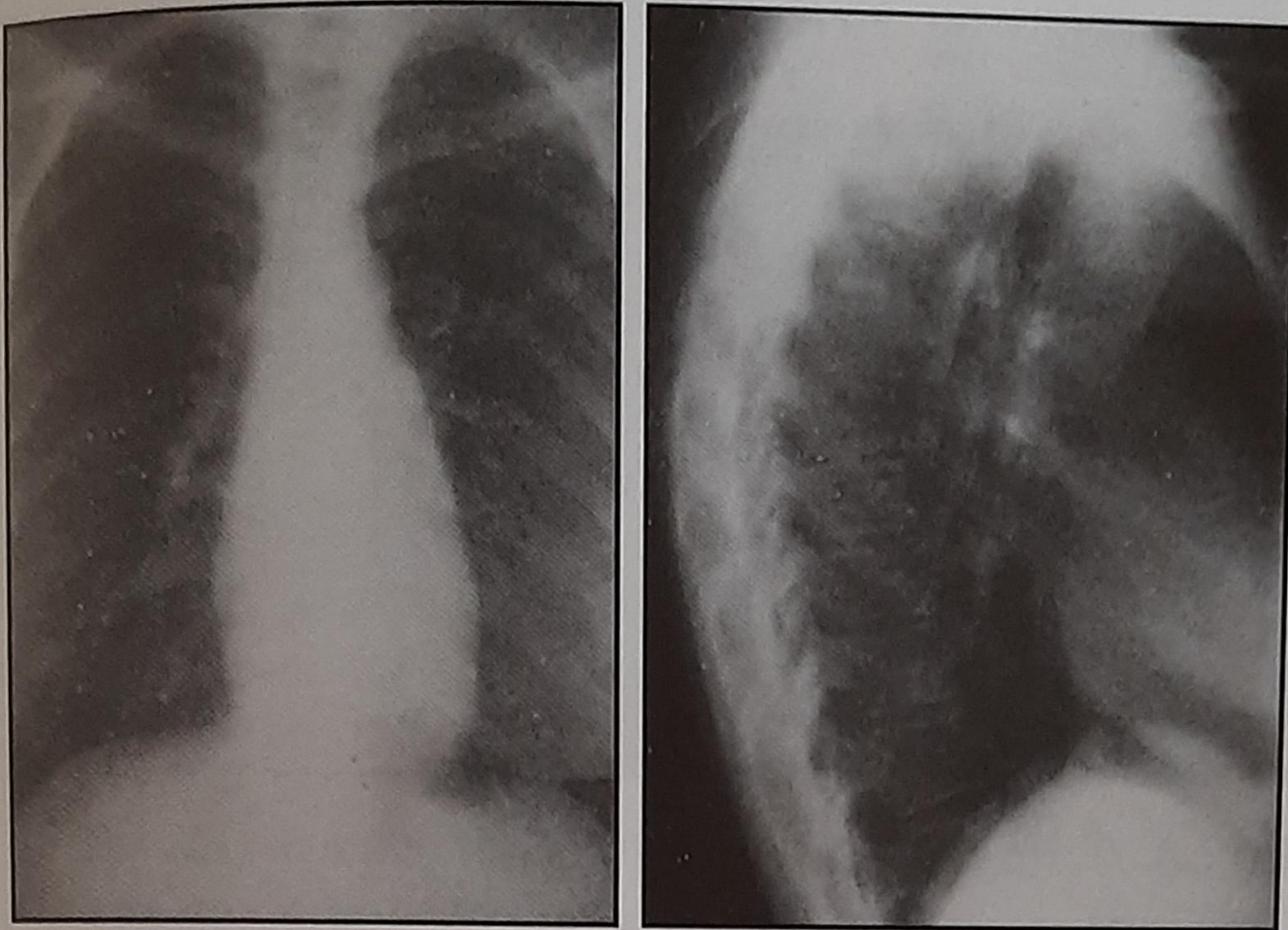
# Κλινική εικόνα

- Τυχαίος έλεγχος (μικρό ποσοστό)
  - Προσυμπτωματική διάγνωση (screening) σε καπνιστές;
- Γενικά συμπτώματα
  - Ανορεξία, Απώλεια ΣΒ, Πυρετός, Καταβολή
- Τοπική ανάπτυξη του όγκου
  - Βήχας, Απόχρεμψη, Αιμόπτυση, Θωρακικό άλγος, Δύσπνοια, Μη υποχωρούσα η υποτροπιάζουσα πνευμονία
- Μεταστάσεις
  - Άλγος, Κεφαλαγία, Ζάλη, Ληθαργικότητα, Επιληπτικές κρίσεις, Νευρολογική συνδρομή
- Παρανεοπλασματικά σύνδρομα
  - Νευρολογικά (Eaton-Lambert), Δερματικά, Μεταβολικά, Θρομβώσεις

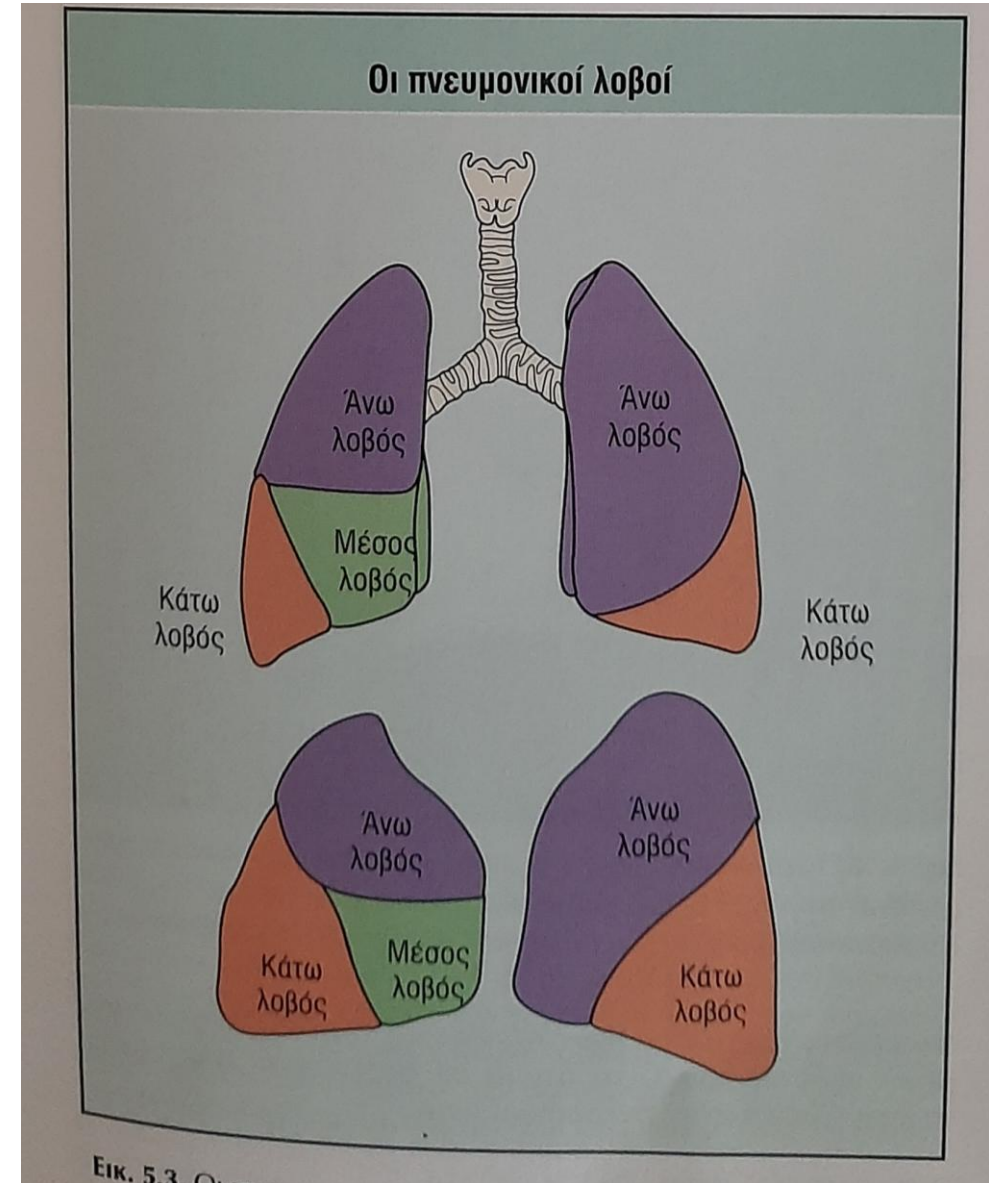
# Κλινική εικόνα (τοπική ανάπτυξη του όγκου)

- Κεντρική εντόπιση του όγκου
  - Βήχας, Απόχρεμψη, Αιμόπτυση, Δύσπνοια, Μη υποχωρούσα η υποτροπιάζουσα πνευμονία
- Περιφερική εντόπιση του όγκου
  - Δύσπνοια, Πλευριτικό άλγος, Σ. Horner (προσβολή βραχιονίου πλέγματος)
- Ενδοθωρακική ανάπτυξη
  - Βράχος φωνής (προσβολή λαρυγγικού νεύρου)
  - Παράδοξη αναπνοή (προσβολή φρενικού νεύρου-πάρεση ημιδιαφράγματος)
  - Σύνδρομο άνω κοίλης φλέβας (θρόμβωση, πίεση εκ των έξω)
  - Δυσφαγία (προσβολή οισοφάγου)
  - Δύσπνοια (περικαρδιακή συλλογή)

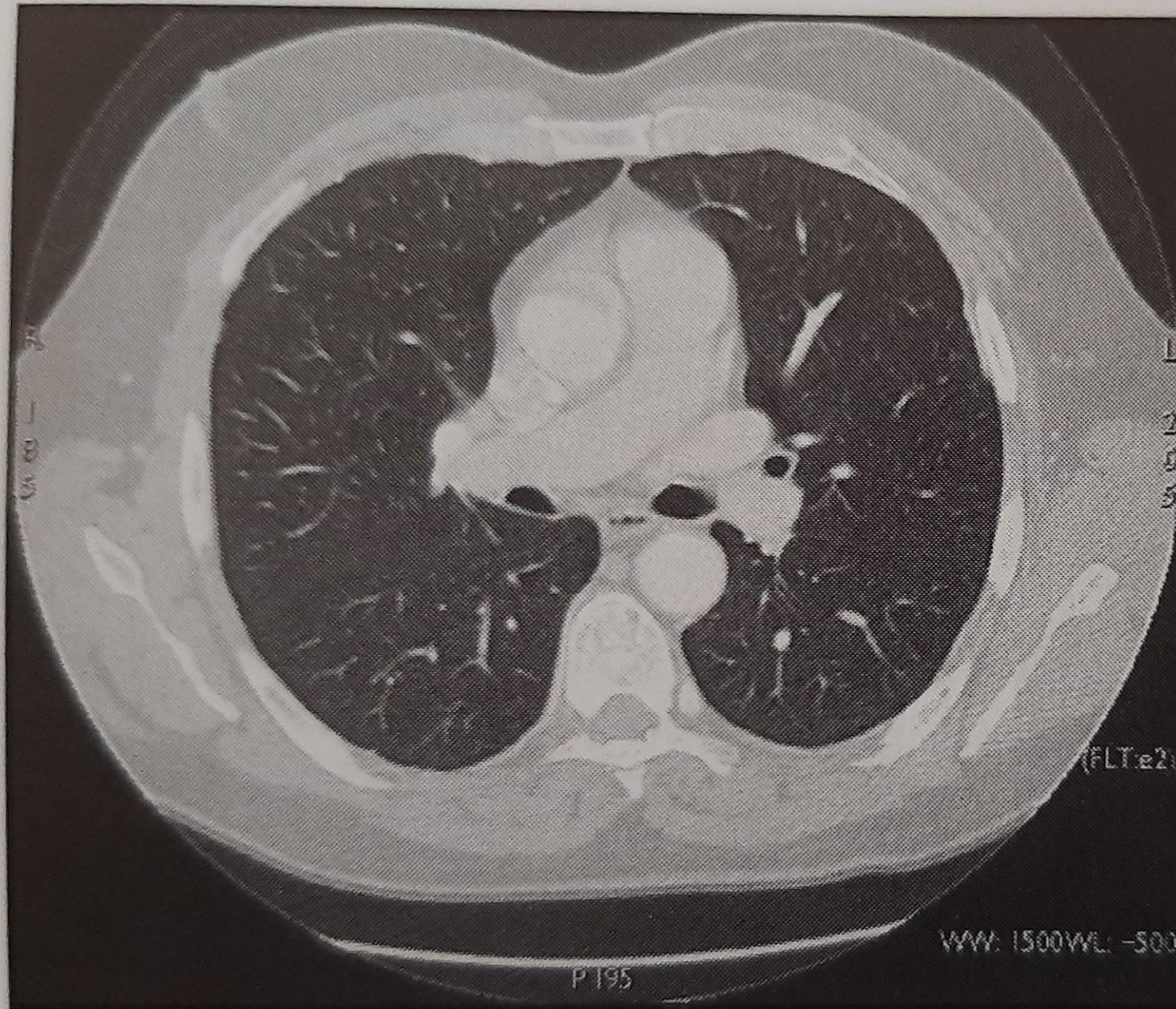
# Εντόπιση



Εικ. 5.2. Φυσιολογική ακτινογραφία: οπισθοπρόσθια προβολή (αριστερά) και πλάγια προβολή (δεξιά).

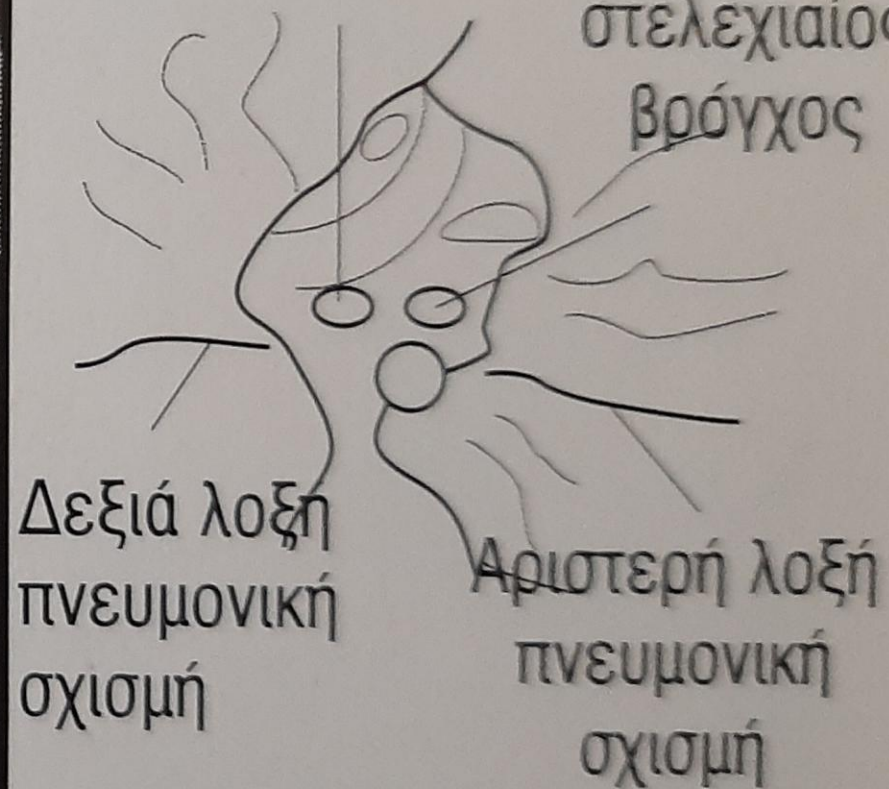


Εικ. 5.3. Οι πνευμονικοί λοβοί



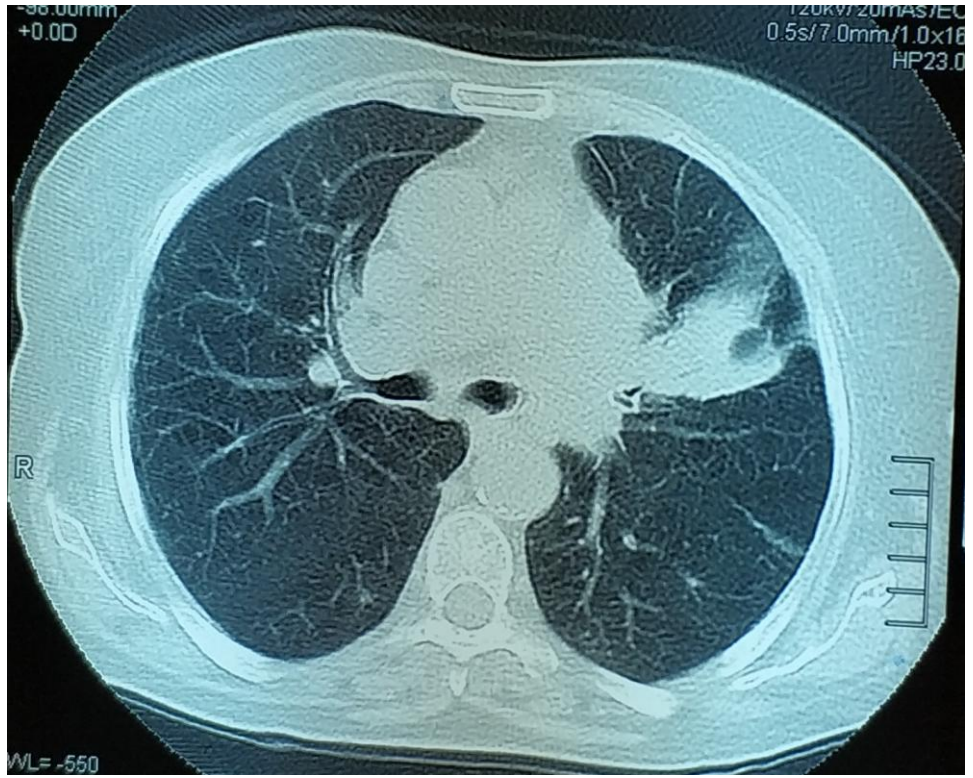
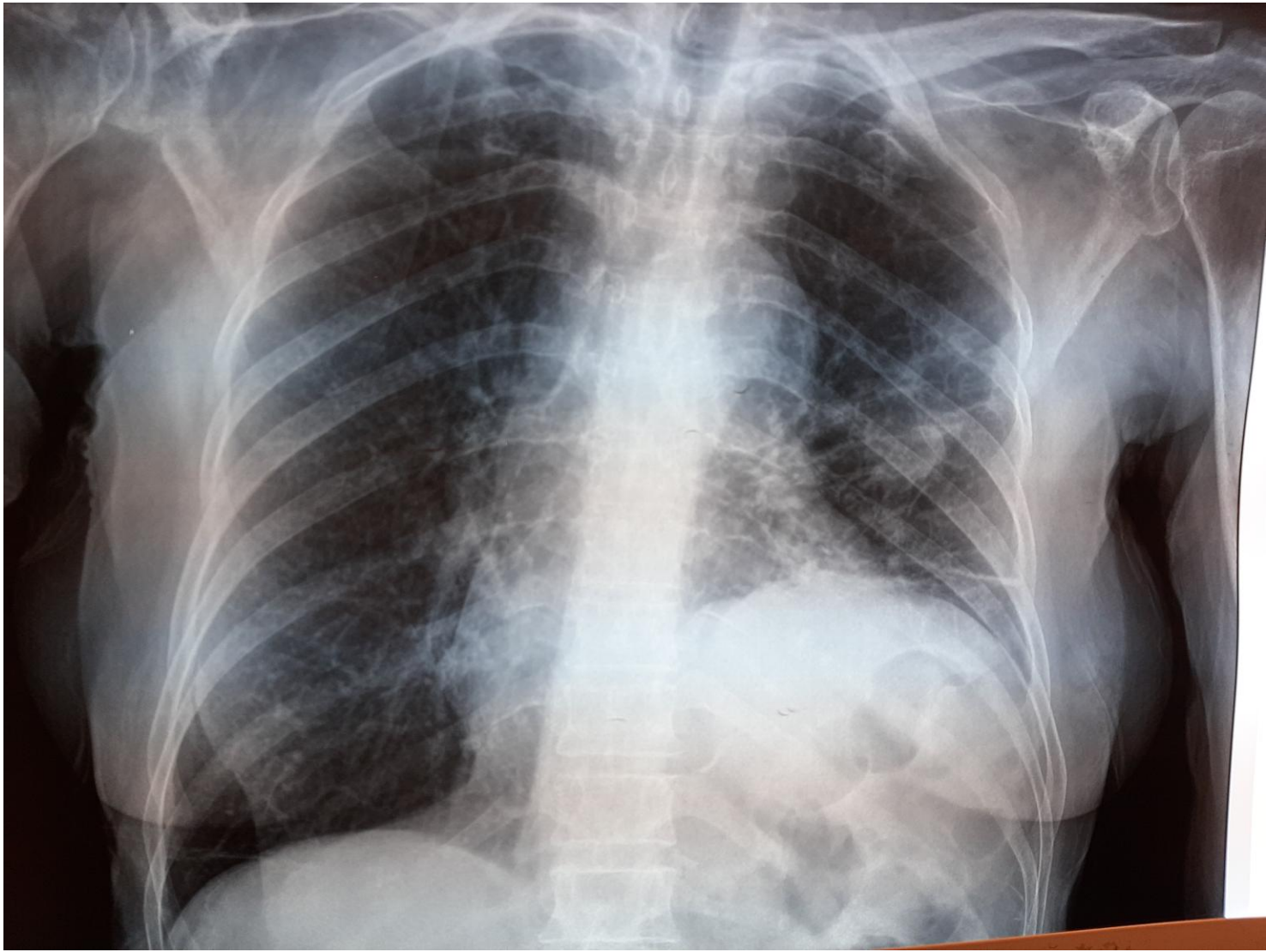
Δεξιός  
στελεχιαίος  
βρόγχος

Αριστερός  
στελεχιαίος  
βρόγχος



Δεξιά λοξή  
πνευμονική  
σχισμή

Αριστερή λοξή  
πνευμονική  
σχισμή

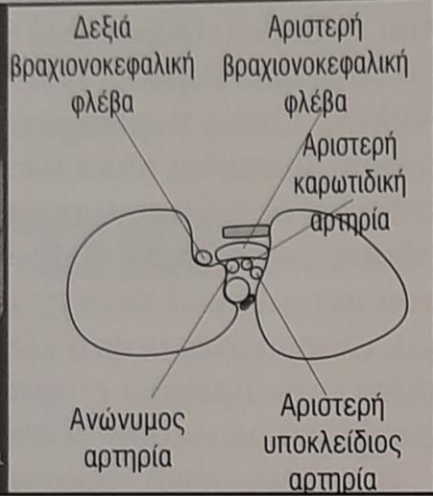
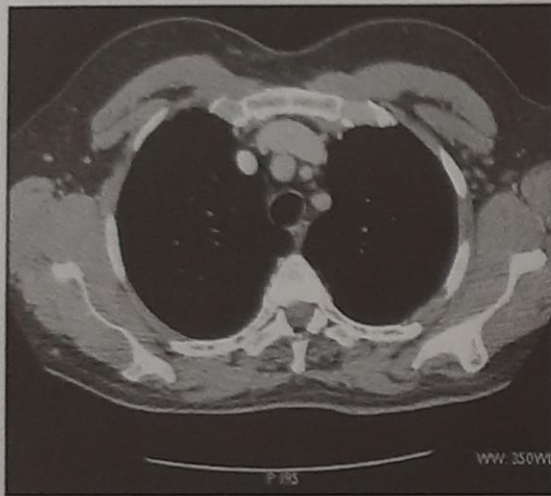




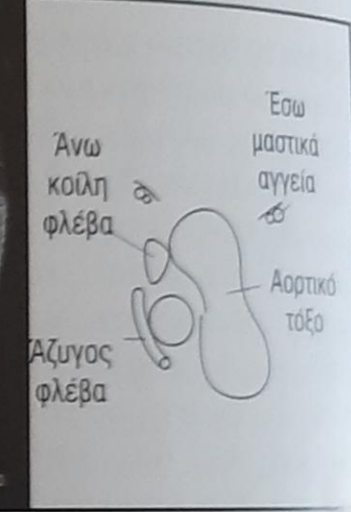


# Σύνδρομο άνω κοίλης φλέβας

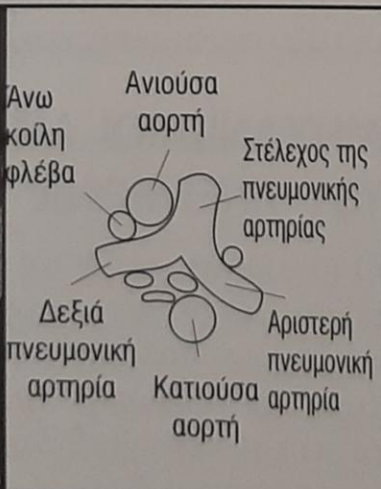
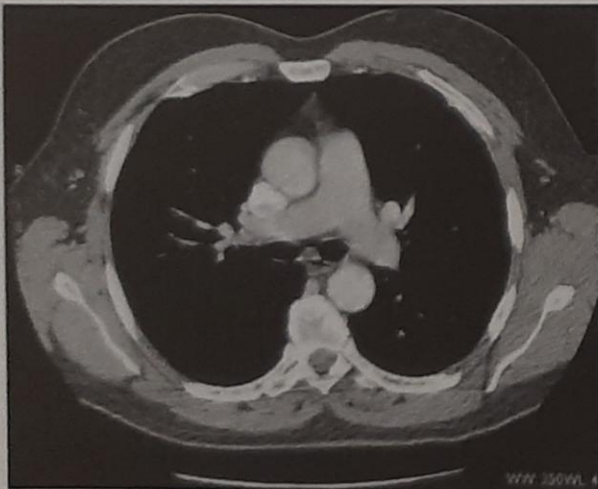




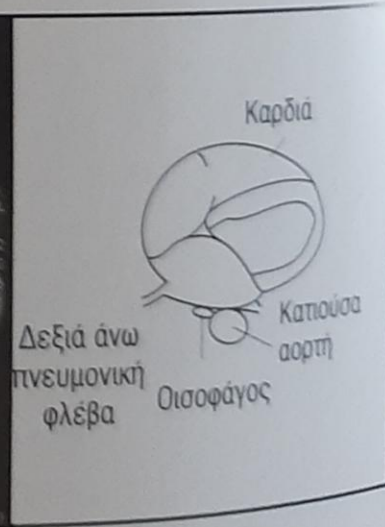
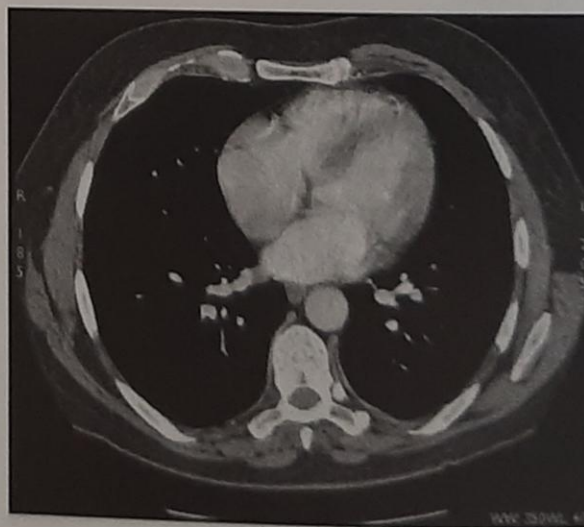
**Εικ. 5.5.** ΥΤ στο επίπεδο της θωρακικής εισόδου (λίγο πάνω από την τρόπιδα)



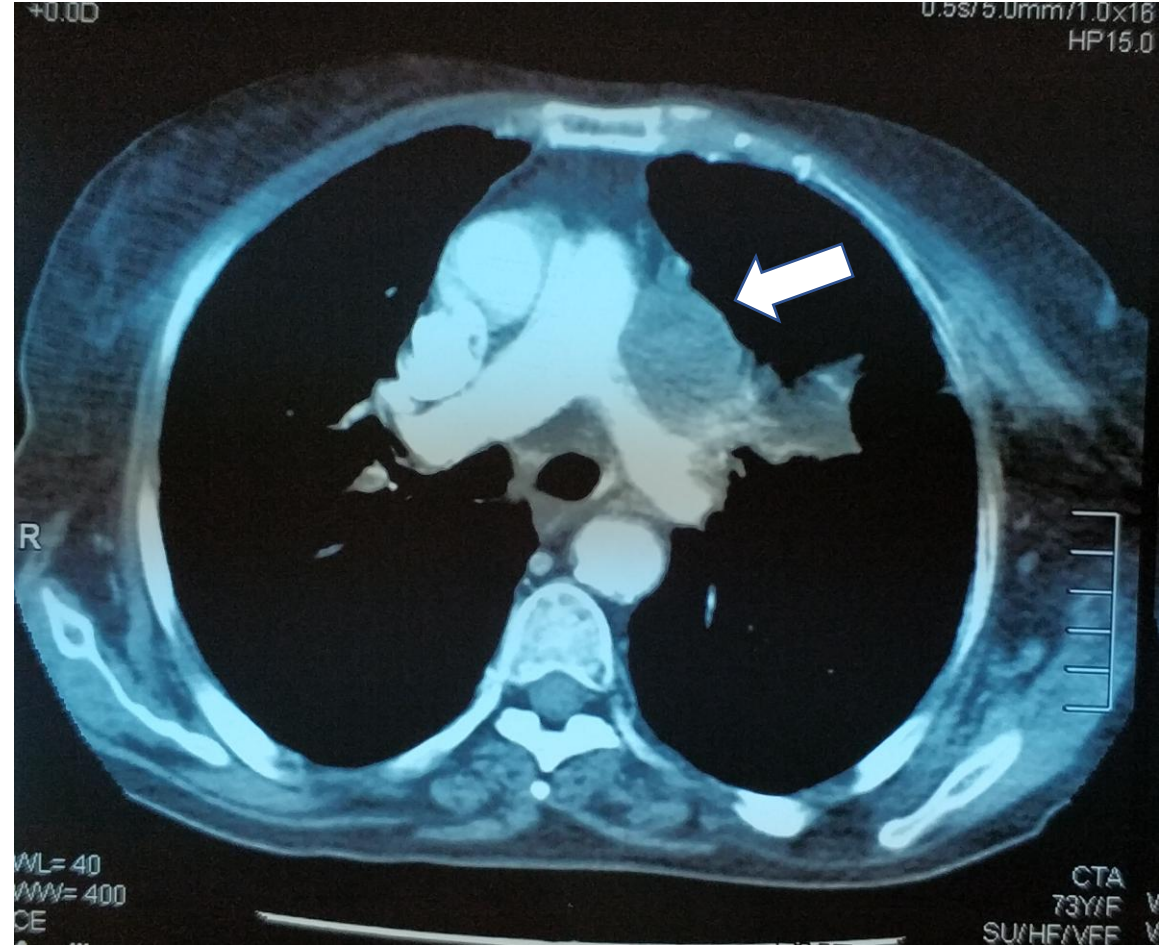
**Εικ. 5.6.** ΥΤ στο επίπεδο του αορτικού τόξου.



**Εικ. 5.7.** ΥΤ στο επίπεδο της τρόπιδας.



**Εικ. 5.8.** ΥΤ στο επίπεδο της μεσότητας του αριστερού κόλπου.



# Σύνδρομο Horner

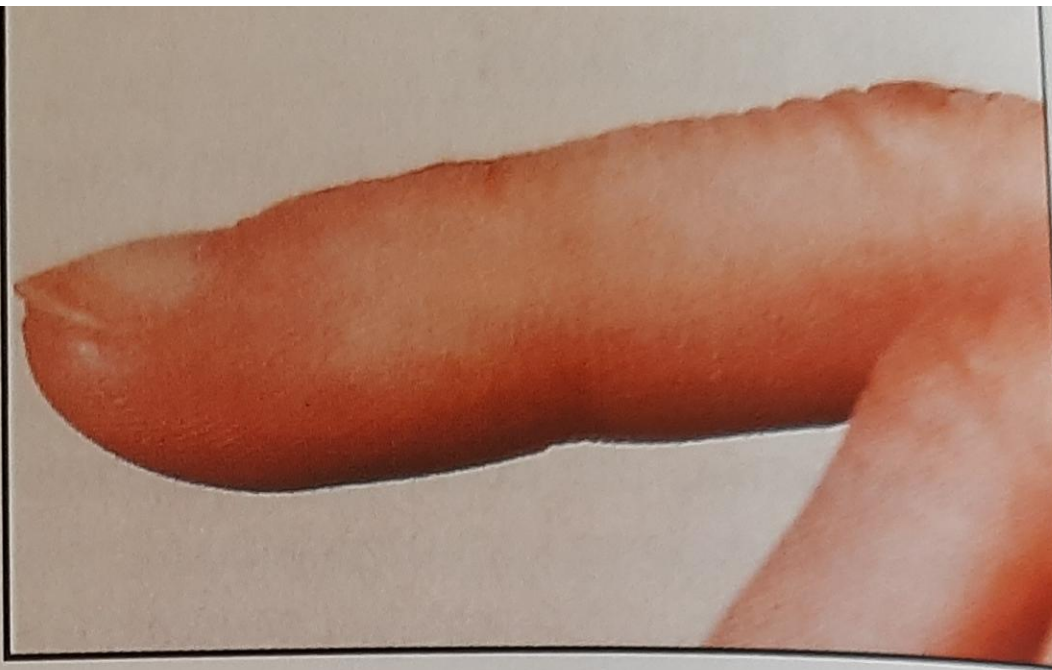
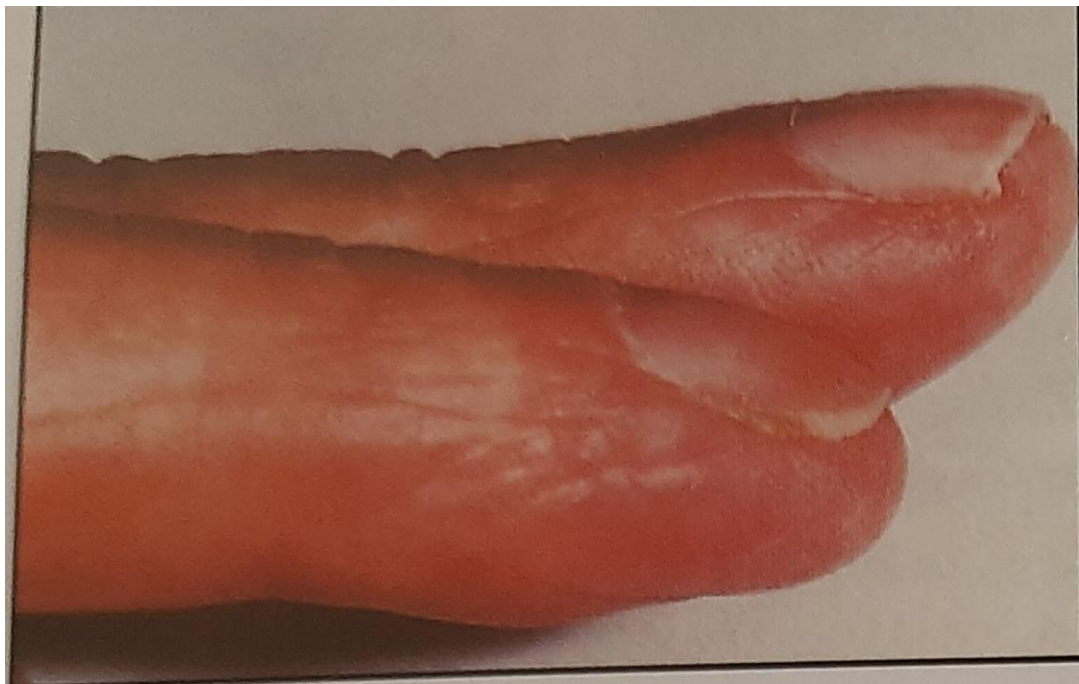


# Σύνδρομο Horner



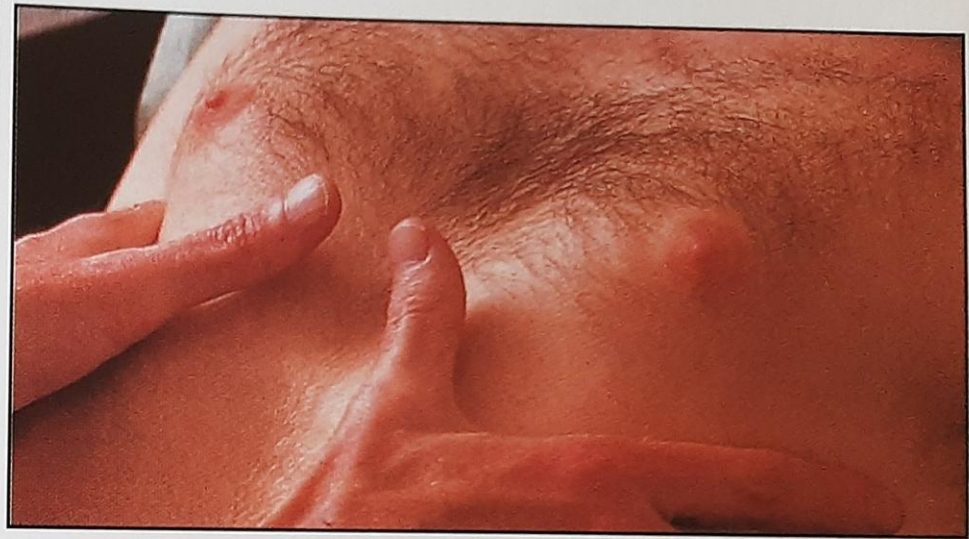
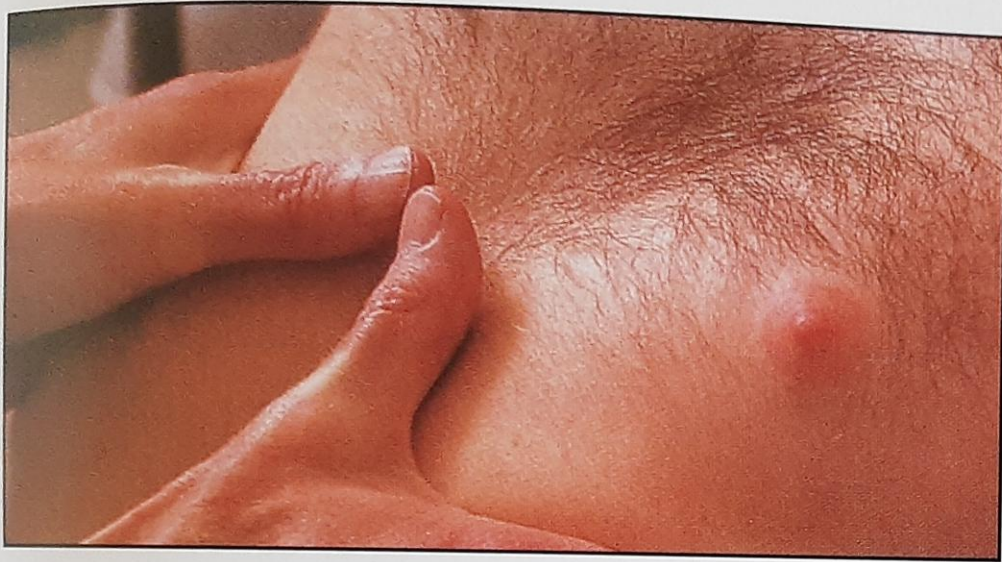
Tumor de Pancoast





Πληκτροδακτυλία





**Εικ. 5.44.** Εκτίμηση της έκπτυξης του θώρακα κατά την εκπνοή (αριστερά) και κατά την εισπνοή (δεξιά).



**Εικ. 5.45.** Επίκρουση στην πρόσθια επιφάνεια του θώρακα.



**Εικ. 5.46.** Άμεση επίκρουση στο μέσον της κλειδας για τον έλεγχο της κορυφής του πνεύμονα.



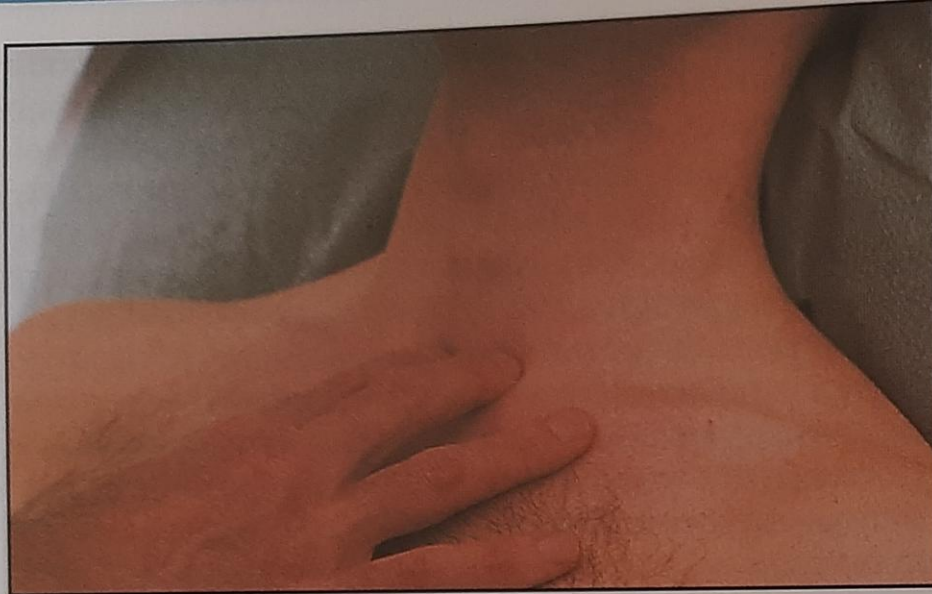


FIGURE 1. Chest examination with a stethoscope.

# Αντικειμενικά ευρήματα

- Επισκόπηση
  - Σύνδρομο άνω κοίλης, Σύνδρομο Horner
- Ψηλάφηση
  - Μετατόπιση τραχείας
  - Μειωμένη έκπτυξη
- Επίκρουση
  - Αμβλύτητα (Υγρό, Μάζα, Ατελεκτασία)
- Ακρόαση
  - Μείωση αναπνευστικού ψιθυρίσματος (Υγρό, Μάζα, Ατελεκτασία)
  - Σωληνώδες φύσημα (Υγρό, Πύκνωση)
- Φωνητικές δονήσεις+Φωνητική αντήχηση
  - Μειωμένες (Υγρό)
  - Αυξημένες (Πύκνωση)

# Υγρό vs ατελεκτασία



Εικ. 5.42. Ψηλάφηση της τραχείας.



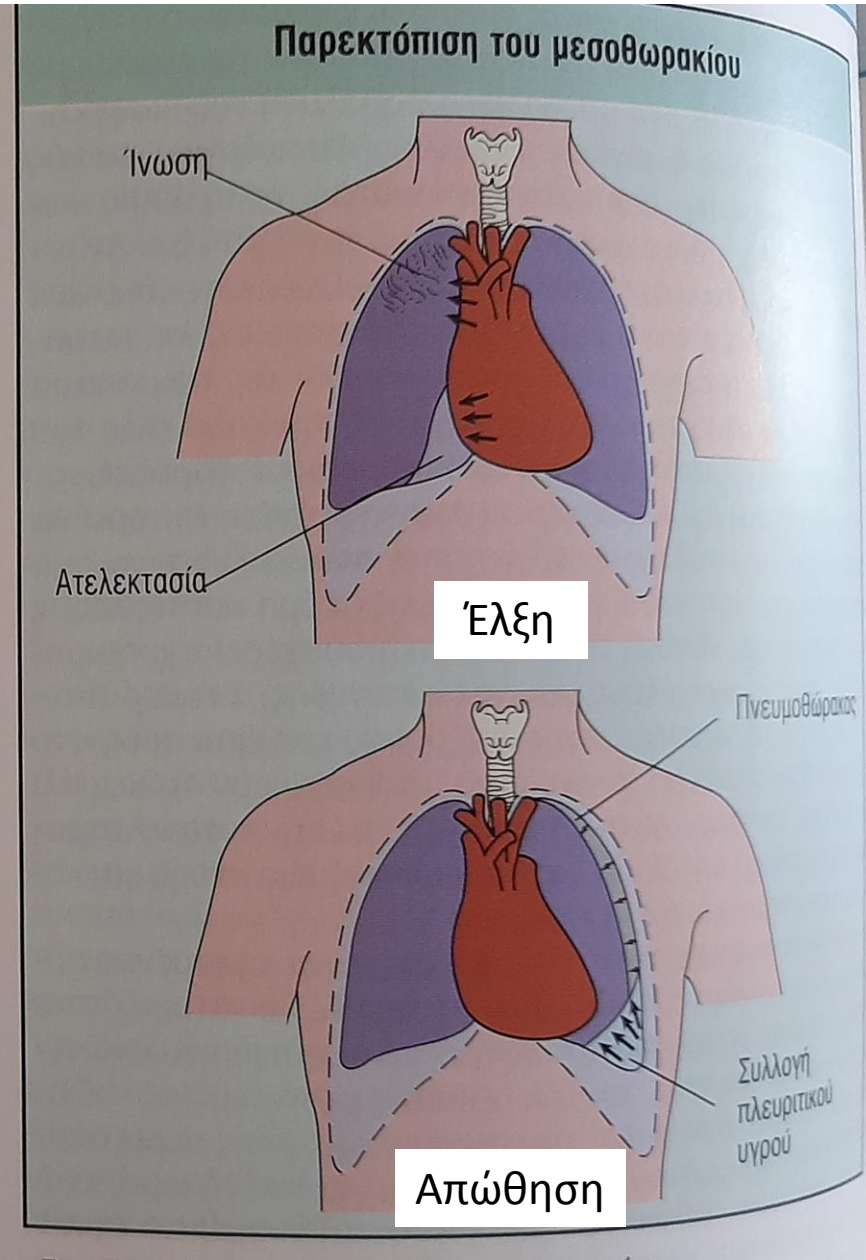
Διαφορική διάγνωση  
**Παρεκτόπιση μεσοθωρακίου**

**Απώθηση από την βλάβη**

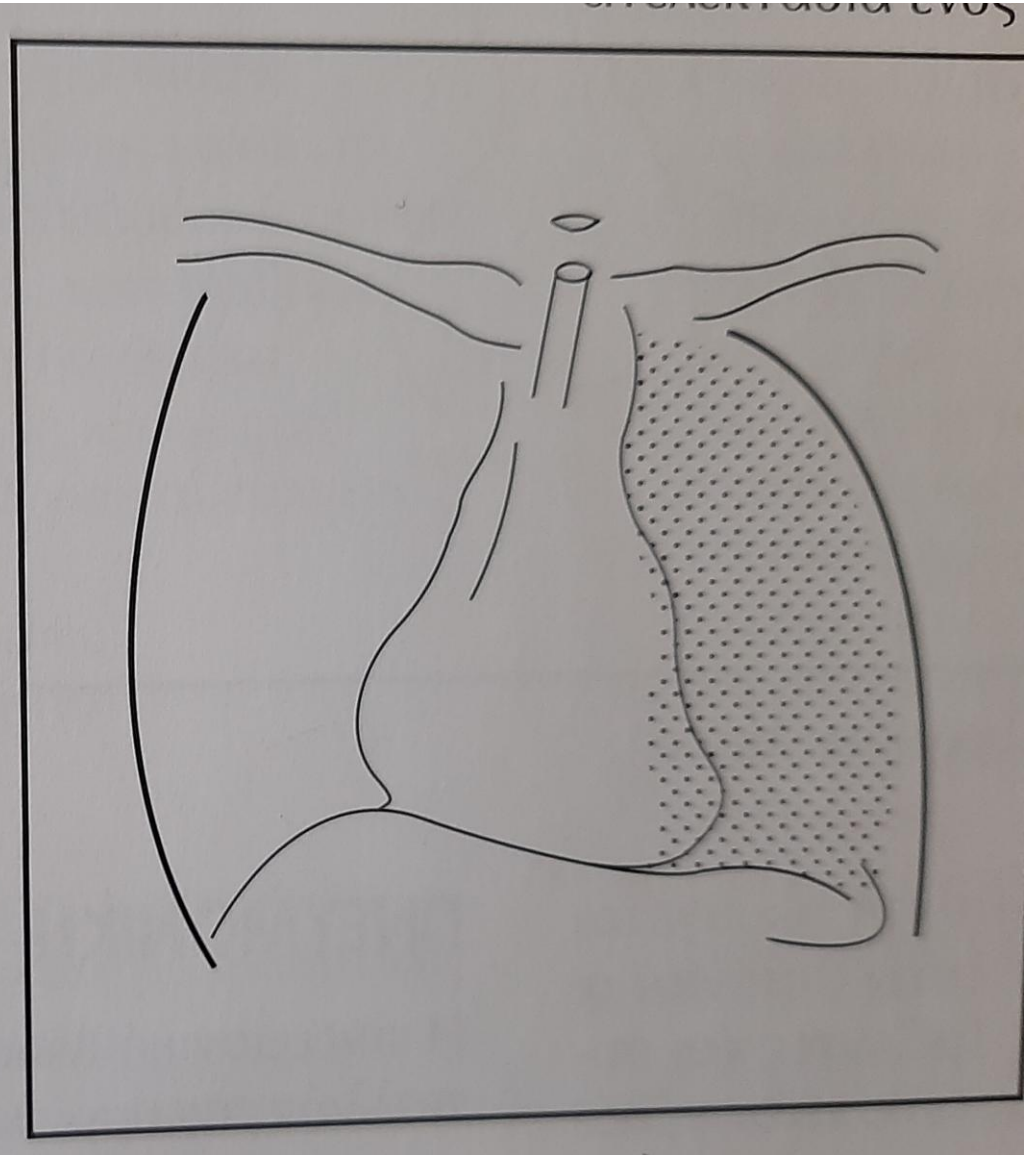
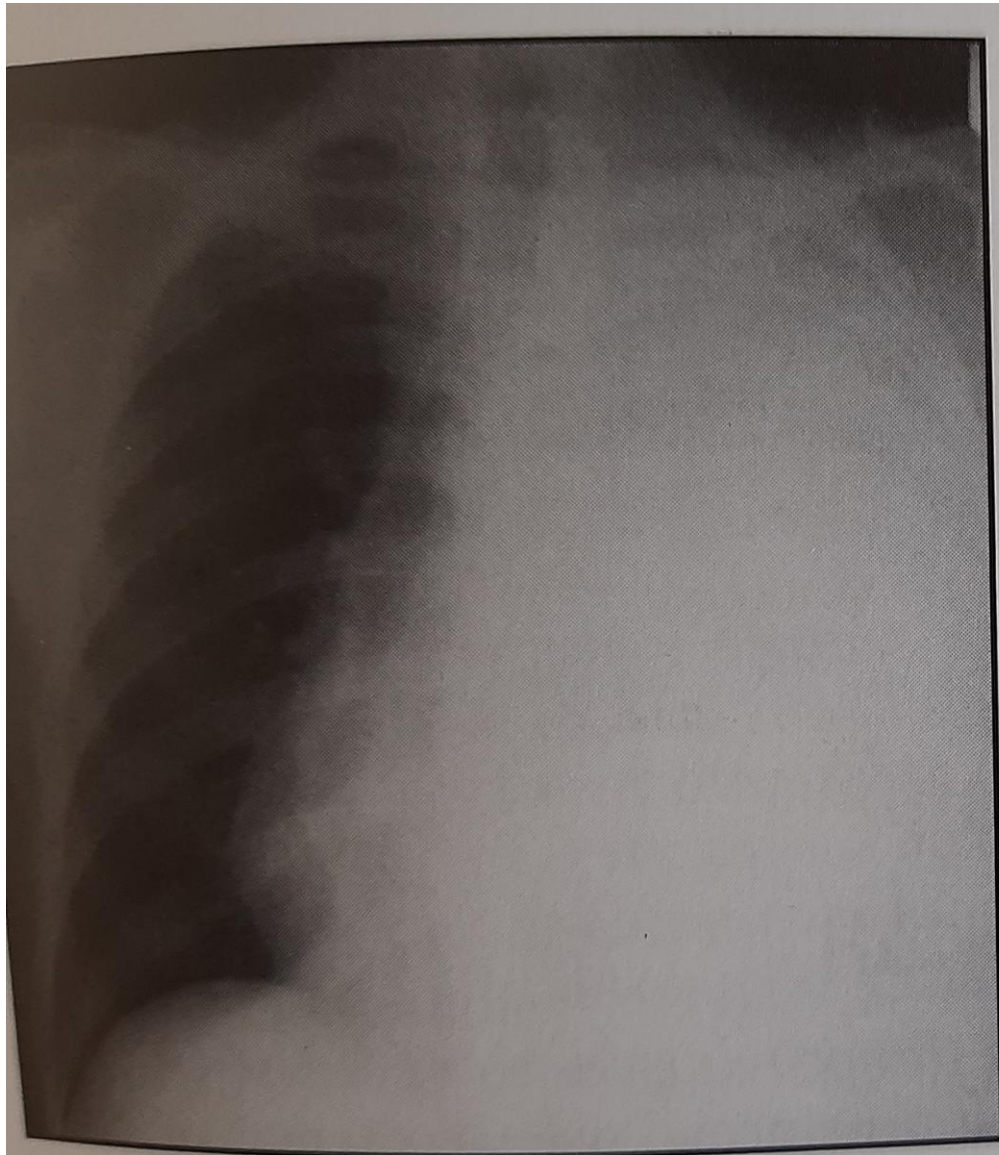
- Πνευμοθώρακας
- Υπεζωκοτική συλλογή (μεγάλη)

**Έλξη προς την βλάβη**

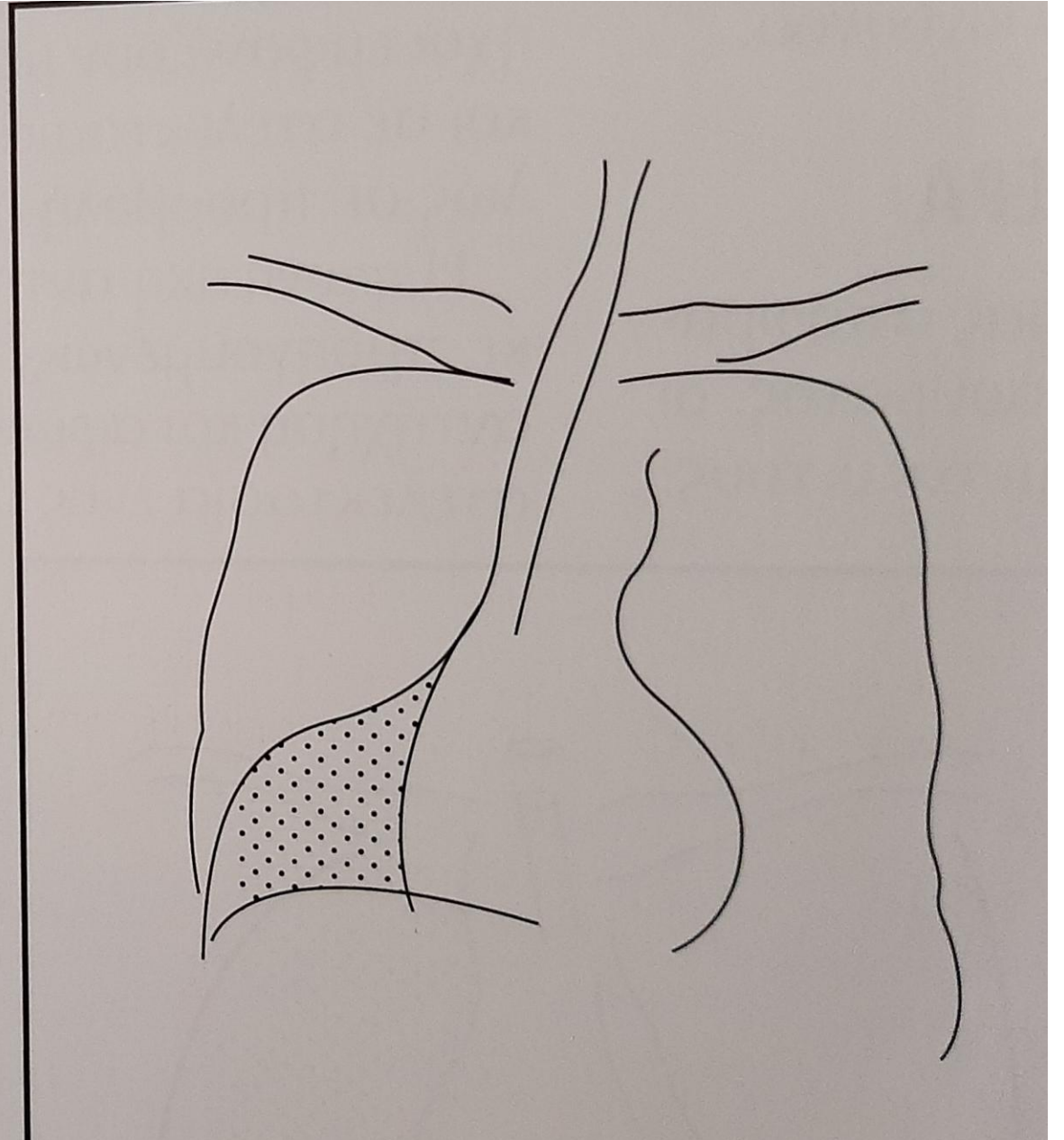
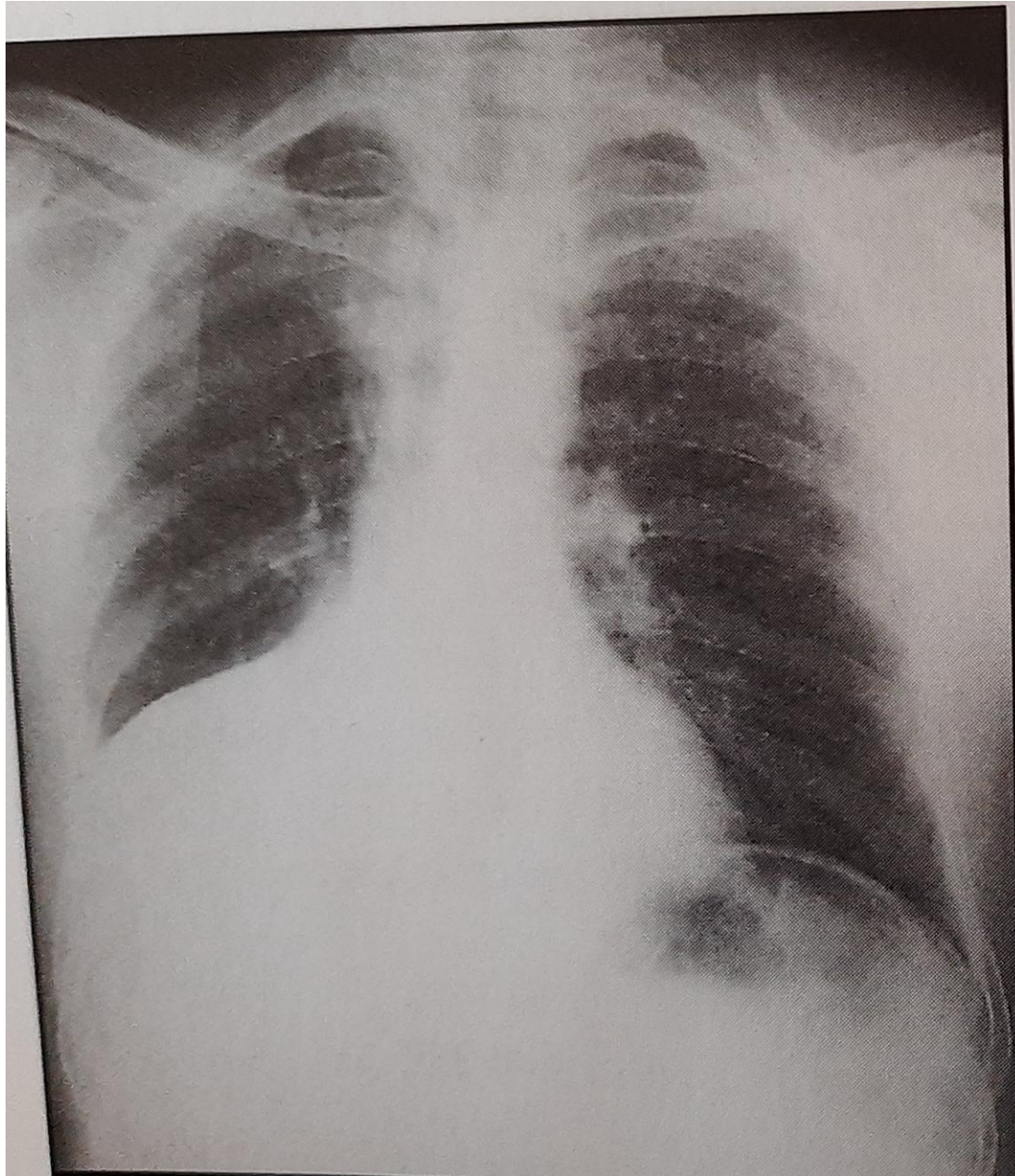
- Ατελεκτασία πνευμόνων λόγω απόφραξης των ανώτερων αεραγωγών
- Εντοπισμένη ίνωση




# Πλευριτική συλλογή



# Ατελεκτασία




**TABLE 1. Paraneoplastic Endocrine Syndromes<sup>a,b</sup>**

Syndrome	Clinical presentation	Laboratory findings	Associated cancers
SIADH			

**TABLE 1. Paraneoplastic Endocrine Syndromes<sup>a,b</sup>**

Syndrome	Clinical presentation	Laboratory findings	Associated cancers
SIADH	Gait disturbances, falls, headache, nausea, fatigue, muscle cramps, anorexia, confusion, lethargy, seizures, respiratory depression, coma		

**TABLE 1. Paraneoplastic Endocrine Syndromes<sup>a,b</sup>**

Syndrome	Clinical presentation	Laboratory findings	Associated cancers
SIADH	Gait disturbances, falls, headache, nausea, fatigue, muscle cramps, anorexia, confusion, lethargy, seizures, respiratory depression, coma	Hyponatremia: mild, sodium 130-134 mEq/L; moderate, sodium, 125-129 mEq/L; severe, sodium <125 mEq/L Increased urine osmolality (>100 mOsm/kg in the context of euvolemic hyponatremia)	



**TABLE 1. Paraneoplastic Endocrine Syndromes<sup>a,b</sup>**

Syndrome	Clinical presentation	Laboratory findings	Associated cancers
SIADH	Gait disturbances, falls, headache, nausea, fatigue, muscle cramps, anorexia, confusion, lethargy, seizures, respiratory depression, coma	Hyponatremia: mild, sodium 130-134 mEq/L; moderate, sodium, 125-129 mEq/L; severe, sodium <125 mEq/L Increased urine osmolality (>100 mOsm/kg in the context of euolemic hyponatremia)	Small cell lung cancer, mesothelioma, bladder, ureteral, endometrial, prostate, oropharyngeal, thymoma, lymphoma, Ewing sarcoma, brain, GI, breast, adrenal

Hyper-  
calcemia



Hyper-  
calcemia

Altered mental status,  
weakness, ataxia, lethargy,  
hypertonia, renal failure,  
nausea/vomiting,  
hypertension, bradycardia



Hyper-  
calcemia

Altered mental status,  
weakness, ataxia, lethargy,  
hypertonia, renal failure,  
nausea/vomiting,  
hypertension, bradycardia

Hypercalcemia: mild, calcium  
10.5-11.9 mg/dL; moderate,  
calcium 12.0-13.9 mg/dL;  
severe, calcium  $\geq$ 14.0 mg/dL  
Low to normal (<20 pg/mL)  
PTH level  
Elevated PTHrP level



Hyper-  
calcemia

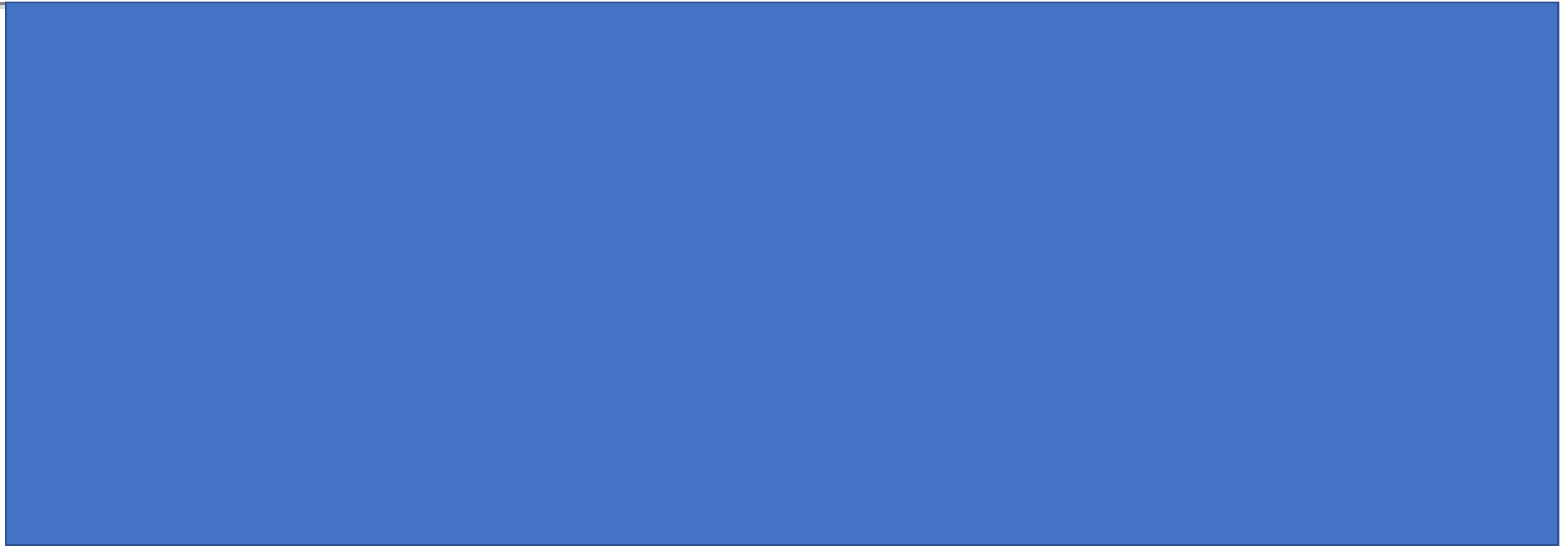
Altered mental status,  
weakness, ataxia, lethargy,  
hypertonia, renal failure,  
nausea/vomiting,  
hypertension, bradycardia

Hypercalcemia: mild, calcium  
10.5-11.9 mg/dL; moderate,  
calcium 12.0-13.9 mg/dL;  
severe, calcium  $\geq$ 14.0 mg/dL  
Low to normal (<20 pg/mL)  
PTH level  
Elevated PTHrP level

Breast, multiple myeloma,  
renal cell, squamous cell  
cancers (especially lung),  
lymphoma (including  
HTLV-associated  
lymphoma), ovarian,  
endometrial

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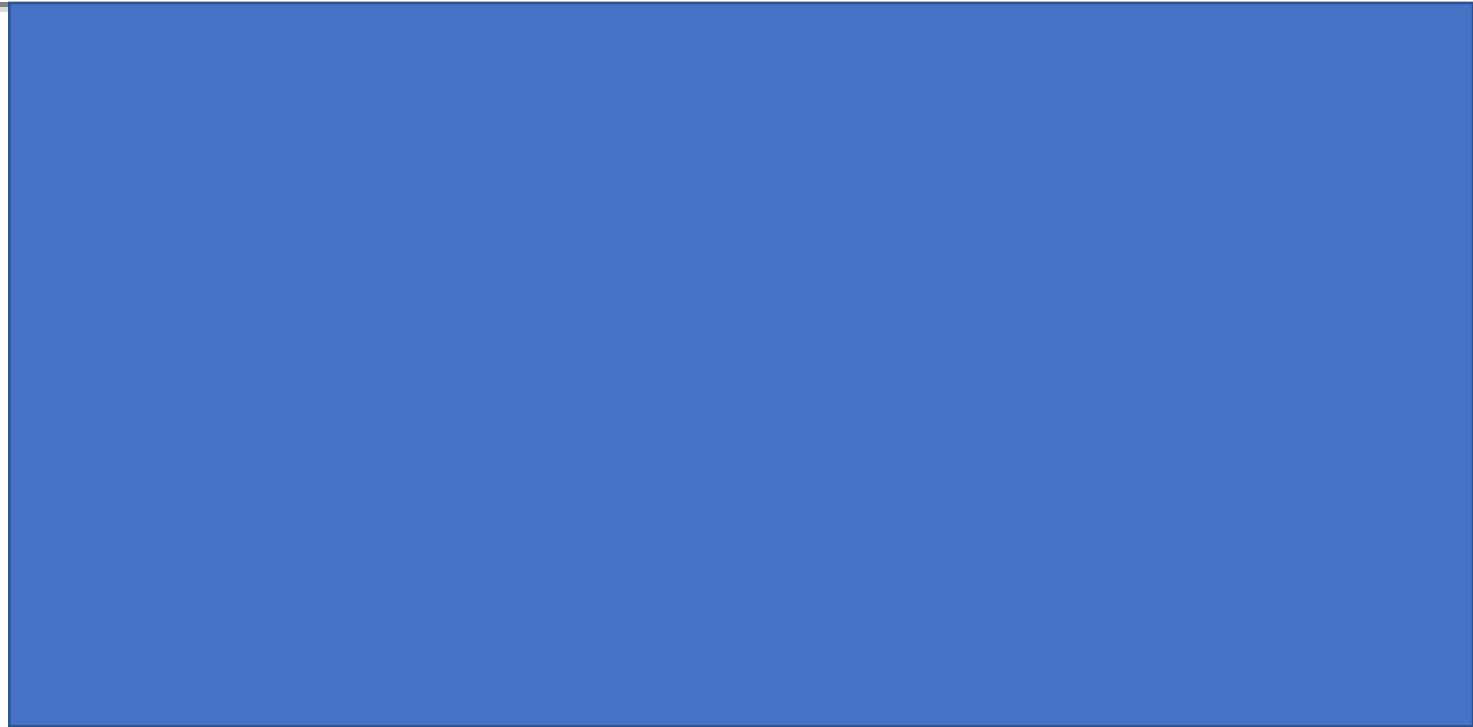
Cushing  
syndrome



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Cushing  
syndrome

Muscle weakness,  
peripheral edema,  
hypertension, weight gain,  
centripetal fat distribution

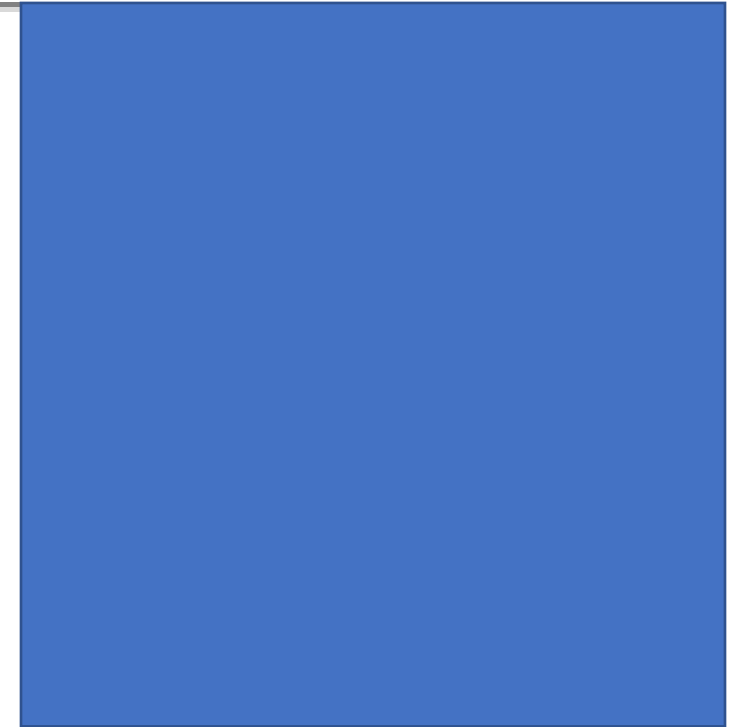


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Cushing  
syndrome

Muscle weakness,  
peripheral edema,  
hypertension, weight gain,  
centripetal fat distribution

Hypokalemia (usually  
<3.0 mmol/L), elevated  
baseline serum cortisol  
(>29.0 µg/dL), normal to  
elevated midnight serum  
ACTH (>100 ng/L)  
not suppressed with  
dexamethasone





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Cushing  
syndrome

Muscle weakness,  
peripheral edema,  
hypertension, weight gain,  
centripetal fat distribution

Hypokalemia (usually  
<3.0 mmol/L), elevated  
baseline serum cortisol  
(>29.0 µg/dL), normal to  
elevated midnight serum  
ACTH (>100 ng/L)  
not suppressed with  
dexamethasone

Small cell lung cancer,  
bronchial carcinoid  
(neuroendocrine lung  
tumors account for  
~50%-60% of cases of  
paraneoplastic Cushing  
syndrome), thymoma,  
medullary thyroid cancer,  
GI, pancreatic, adrenal,  
ovarian

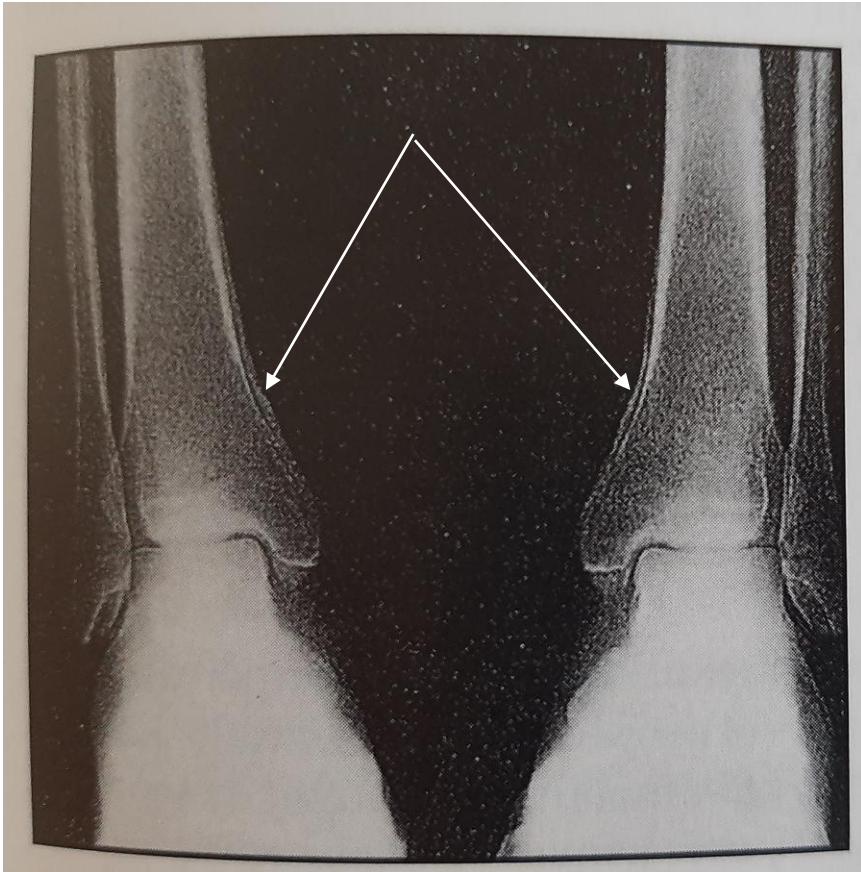


**Dermatomyositis (DM)**

Heliotrope rash (violaceous, edematous rash on upper eyelids); Gottron papules (scaly papules on bony surfaces); erythematous rash on face, neck, chest, back, or shoulders (the last of which is known as *shawl sign*); rash may be photosensitive; proximal muscle weakness; swallowing difficulty; respiratory difficulty; muscle pain

Laboratory findings: elevated serum CK, AST, ALT, LDH, and aldolase; EMG: increased spontaneous activity with fibrillations, complex repetitive discharges, and positive sharp waves; Muscle biopsy: perivascular or interfascicular septal inflammation and perifascicular atrophy

Ovarian, breast, prostate, lung, colorectal, non-Hodgkin lymphoma, nasopharyngeal



**Hypertrophic osteoarthropathy**

Subperiosteal new bone formation on phalangeal shafts ("clubbing"), synovial effusions (mainly large joints), pain, swelling along affected bones and joints

Plain radiography: periosteal reaction along long bones  
Nuclear bone scan: intense and symmetric uptake in long bones

Intrathoracic tumors, metastases to lung, metastases to bone, nasopharyngeal carcinoma, rhabdomyosarcoma

Οζώδες  
ερύθημα



# Οφθαλμός (1)

Paraneoplastic syndrome	Underlying neoplasm	Circulating antibodies in peripheral blood	Clinical findings	Histopathological findings	Genetic findings	Source
CAR	small-cell carcinoma of the lung, other neoplasm of the lung, breast cancer, cancers of the cervix, ovary, uterus and thymus, osteosarcoma, Warthin tumor of parotid gland, prostate, pancreatic neuroendocrine, small bowel, bladder and laryngeal neoplasms, lymphomas (systemic follicular cell lymphoma) and colon adenomas	Recoverin (23-kDa), retinal enolase (46-kDa), TULP1, hsc-70 and 60, AIPL1, IRBP, PNR, GAPDH (36-kDa), aldolase C (40-kDa), transducin-α  possibly: GCAPs, HSP27 and Rab6A, CA II (30-kDa), CRMP5 and anti-Hu, antiretinal autoantibodies against 48-kDa (arrestin) and 64-kDa and 94-kDa	cone dysfunction: photosensitivity, prolonged glare, decreased BCVA, color discrimination and central scotomas; rod dysfunction: night blindness, prolonged adaptation to darkness and peripheral or ring scotomas  arteriolar narrowing, retinal pigment epithelial thinning and mottling, vitritis, cells in anterior chamber, sheathing of retinal arterioles, periphlebitis and pallor of the optic disc	relatively small cells with little cytoplasm  intensively positive for recoverin as well as positive for NSE, Ki-67 and <i>tp53</i>	no additional data available apart from data that confirms the circulating antigens involvement	Weixler, Oertli and Nebiker 2016; Dalin et al. 2016; S. Yang et al. 2016; Adamus, Yang and Weleber 2016; Bhavsar et al. 2015; Adamus 2015; M. Morita et al. 2014; Turaka et al. 2014; Machida et al. 2014; Adamus, Choi, et al. 2013; M. Saito et al. 2014; Adamus, Bonnah, et al. 2013; Makiyama et al. 2013; W. Saito et al. 2013
CACD	small-cell endometrial cancer, primary cervical intraepithelial neoplasia, occult small cell lung carcinoma and laryngeal carcinoma	recoverin and protein whose molecular weight is 50 and 40 kDa	mild to moderate best-corrected visual acuity loss, sudden photosensitivity, total or subtotal loss of color perception, visual acuity improvement while wearing sunglasses	no data	no data	Finger, Thirkill and Borruat 2012; Javaid et al. 2015; Parc et al. 2006; Hargitai et al. 2004
MAR and MAR-like retinopathies	cutaneous melanoma	TRPM1, α-enolase, recoverin or hsc-70, CA II, IRBP, Bestrophin, myelin basic protein, mitoflin, titin, and rod outer segment proteins	sudden shimmering, flickering, difficulty with night vision and photopsias (pulsating continuous or intermittent) with occasional hyperphotosensitivity and floaters	local retinal thinning with the damaged inner nuclear layer and outer plexiform layer  positive melanoma-associated autoantibodies directly against transient receptor potential M1 channels that target the ON-bipolar cell structures in the inner nuclear and outer plexiform layers in PVtR	no additional data available apart from data that confirms the circulating antigens involvement	Lincoff et al. 2016; Wang et al. 2012; Dalal et al. 2013; Xiong et al. 2013; Y. Morita et al. 2014; Dhingra et al. 2011; Aro now et al 2012

# Οφθαλμός (2)

Paraneoplastic syndrome	Underlying neoplasm	Circulating antibodies in peripheral blood	Clinical findings	Histopathological findings	Genetic findings	Source
BDUMP	ovarian, cervix, uterus, colon and rectum cancer, gallbladder cancer, neoplasm of the retroperitoneal space, and a variety of lung cancers	CMEP factor, AAbs against 35-kDa, 46-kDa, 30-kDa, 50-kDa, and 70-kDa proteins	classical findings: slow, painless, bilateral (usually asymmetric), progressive loss of vision for several months, subretinal infiltration and exudative retinal detachment that result as outer retinal damage  development of cataract, iridocyclitis or glaucoma  additional clinical findings: iris nodules, pigmented keratic precipitates, anterior chamber and vitreous cells, peripheral retinal arterial areas of non-perfusion, loss of RPE in a pattern described as nummular or dermal, conjunctival melanocytic proliferation	infiltration consisted of more benign-appearing melanocytes – stained positively with melan-A	deletions in chromosome 19, gain in chromosomes 5, 6, 8q and X  lack of mutations in <i>GNAQ</i> , <i>GNA11</i> and <i>BRAF<sup>V600F</sup></i>	Mittal et al. 2015; Mudhar et al. 2012; Rahimy, Coffee and McCannel 2015; Lin and Mruthyunjaya 2012; Navajas et al. 2011; Yonekawa, Shildkrot and Elliott 2013; Pulido et al. 2013; Jansen et al. 2015; Adamus et al. 2013; Miles et al. 2012
PON	adenocarcinoma and small cell carcinoma of the lung, prostate carcinoma, stomach carcinoid tumor, colon adenocarcinoma, cutaneous melanoma, occult pancreatic non-secretory neuroendocrine tumor, thymoma	CRMP5, aquaporin 4, MBP, ANNA-1, recoverin, enolase	neuroretinitis and positive autoantigens against neuronal part of retina and the optic nerve	no histological data available in recent papers due to tissue sampling consequences concerning visual function	no additional data available apart from data that confirms the circulating antigens involvement	Verschuur, Kooi and Troost 2015; M. Saito et al. 2014; Adamus et al. 2011; Finger, Thirkill and Borruat 2012; Carboni et al. 2012; Al-Harbi et al. 2014; Chao et al. 2013; Slamovits et al. 2013; Schoenberger, Kim and Lavin 2012; H. K. Yang et al. 2014; Iyer et al. 2014

CAR – cancer-associated retinopathy; CACD – cancer-associated cone dysfunction; MAR – melanoma-associated retinopathy; BDUMP – bilateral diffuse uveal melanocytic proliferation; BCVA – best-corrected visual acuity; RPE – retinal pigment epithelium; PON – paraneoplastic optic neuritis; PVtr – paraneoplastic vitelliform retinopathy; *TULP1* – Tubby-like protein 1; *hsc-70* – heat shock cognate protein 70; *TRPM1* – transient receptor potential cation channel; subfamily M member 1 (that is labeled on ON-bipolar cells); CA II – carbonic anhydrase II; IRBP – interphotoreceptor retinoid binding protein; CMEP factor – cultured melanocyte elongation and proliferation factor; CRMP5 – collapsin response mediator protein 5; MBP – myelin binding protein; ANNA-1 – type 1 antineuronal nuclear antibody; *GCAPs* – guanylyl cyclase-activating proteins; HSP27 – heat shock protein 27; *Rab6A* – Rab6A GTPase; PNR – photoreceptor cell-specific nuclear receptor; *GAPDH* – glyceraldehyde 3-phosphate dehydrogenase; *AiPL1* – aryl hydrocarbon receptor interacting protein-like 1.