

Le complicanze nei pazienti con carcinoma polmonare

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Oncologic emergencies

- Sign and Symptoms
- Natural history of the primary tumor
- Efficacy of available treatment
- Treatment and goals
 - ✓ Potential cure?
 - ✓ Is prompt palliation require to prevent further debilitation
 - ✓ What is the relative risk vs. the benefit ratio?
 - ✓ Should the treatment withheld if the patient is terminal with limited chance of response to antitumor therapies

Most common oncologic emergencies

- DIC
- Hypercalcemia
- Malignant pleural effusion
- Cardiac Tamponade
- Febrile neutropenia/septic shock
- Spinal cord compression
- Superior vena cava syndrome
- SIADH
- Tumor lysis syndrome

Complicanze più frequenti nel carcinoma polmonare

- Dolore
- Ostruzione/tosse
- Polmonite ostruttiva/ascesso
- Neutropenia Febbrile
- Sindrome della vena cava superiore
- Pericardite/pleurite
- Sindromi paraneoplastiche
- Compressione spinale
- Stato di ipercoagulabilità

Factors related to the development of thrombosis in cancer patients

- *Patient-related factors*
 - Age, race, poor performance status, obesity prior history of thrombosis
- *Cancer-related factors*
 - Origin of cancer, histology of cancer
- *Treatment-related factors*
 - Recent surgery, chemotherapy, antiangiogenic drugs, ESA

Model predicting risk of chemotherapy induced thrombosis in cancer patients

Characteristics	Score
1-Site of cancer Very high risk (stomach, pancreas) High risk (lung, lymphoma, gynecologic, bladder, testicular)	2 1
2-Prechemotherapy platelet count $\geq 350 \times 10^9/L$	1
3-Hemoglobin ≤ 100 g/L or use of red cell growth factors	1
4-Prechemotherapy leukocyte count $\geq 11 \times 10^9/L$	1
5-Body mass index ≥ 35 kg/m ²	1

Risk	Total score *
High	≥ 3
Intermediate	1-2
low	0

* Total score accounts the sum of the scores according to the characteristics described above.

Complicanze più frequenti

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MPE : Common causes

- Implantation on the pleural surface leading to increased permeability
- Obstruction of lymphatic flow by tumor preventing fluid reabsorption
- Tumor obstruction of primary vessels leading to increased capillary hydrostatic pressure
- Necrotic tumor cells shed into the pleural space increasing colloid osmotic pressure
- Thoracic duct perforation

Pleural effusion in lung cancer

- Frequency of MPE in lung cancer
 - NSCLC/SCLC 25% of pts
 - Mesothelioma >90% of pts
- IASLC Staging: cT4 (wet T4) now M1a
 - Lower median survival for wet cT4 vs other cT4
 - 8 m vs 13 m ($p < 0.0001$)
 - Lower 5 YSR
 - 2% vs 15%

MPE : treatment

- Small asymptomatic MPE may be left alone
- Chemotherapy for chemosensitive tumors
- If the tumor is chemo-resistant or refractory to systemic treatment, pleurodesis may be performed
- Thoracentesis provides short-term relief of symptoms
- Thoracostomy tube
- Pleuropericardial shunt
- Pleural stripping

Pleurodesis

- Selection of pts
- pH of pleural fluid > 7.30 ?
 - Poor predictive performance of pH<7.30
- Pleural manometry?
 - No predictive performance proven

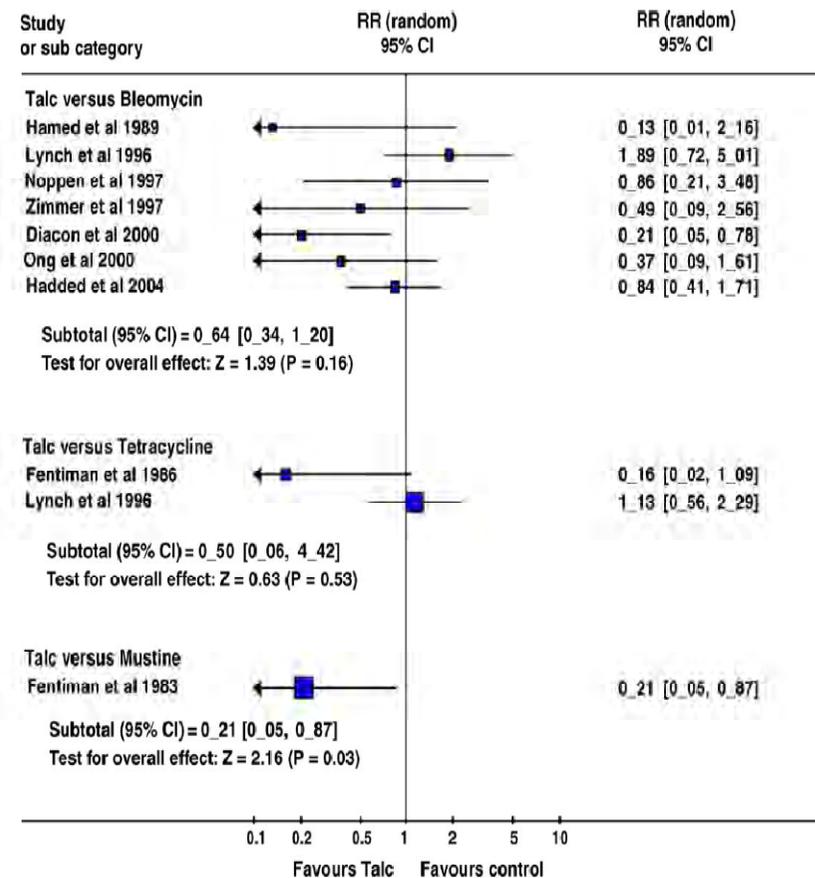
Pleurodesis

- Sclerosants
 - Talc [$\text{Mg}_3(\text{Si}_2\text{O}_5)(\text{OH})_2$] most effective
 - Agent of choice
 - Safety?
 - Different talc preparations
 - Lung infiltrates/hypoxemia(30%)/resp. failure(4-8%)/ARDS
 - Best = with smallest ($<10\mu$) talc particles removed (graded talc)

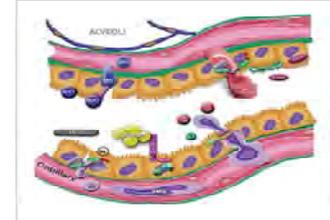
Maskell NA et al. AJRCCM 2004;170:377-82 Janssen JP et al. Lancet 2007;369:1535-39
Antony VB et al. Eur Respir J 2001;18:402-19 Davies HE et al. Thorax 2008;63:572-4
Dressler CM et al. Chest 2005;127:909-15

Pleurodesis

- Sclerosants
 - Other?
 - Tetracyclins
 - Bleomycin
 - Other antineoplastic agents
 - Corynebacterium parvum
 - “...Trends favor talc...”



Future?



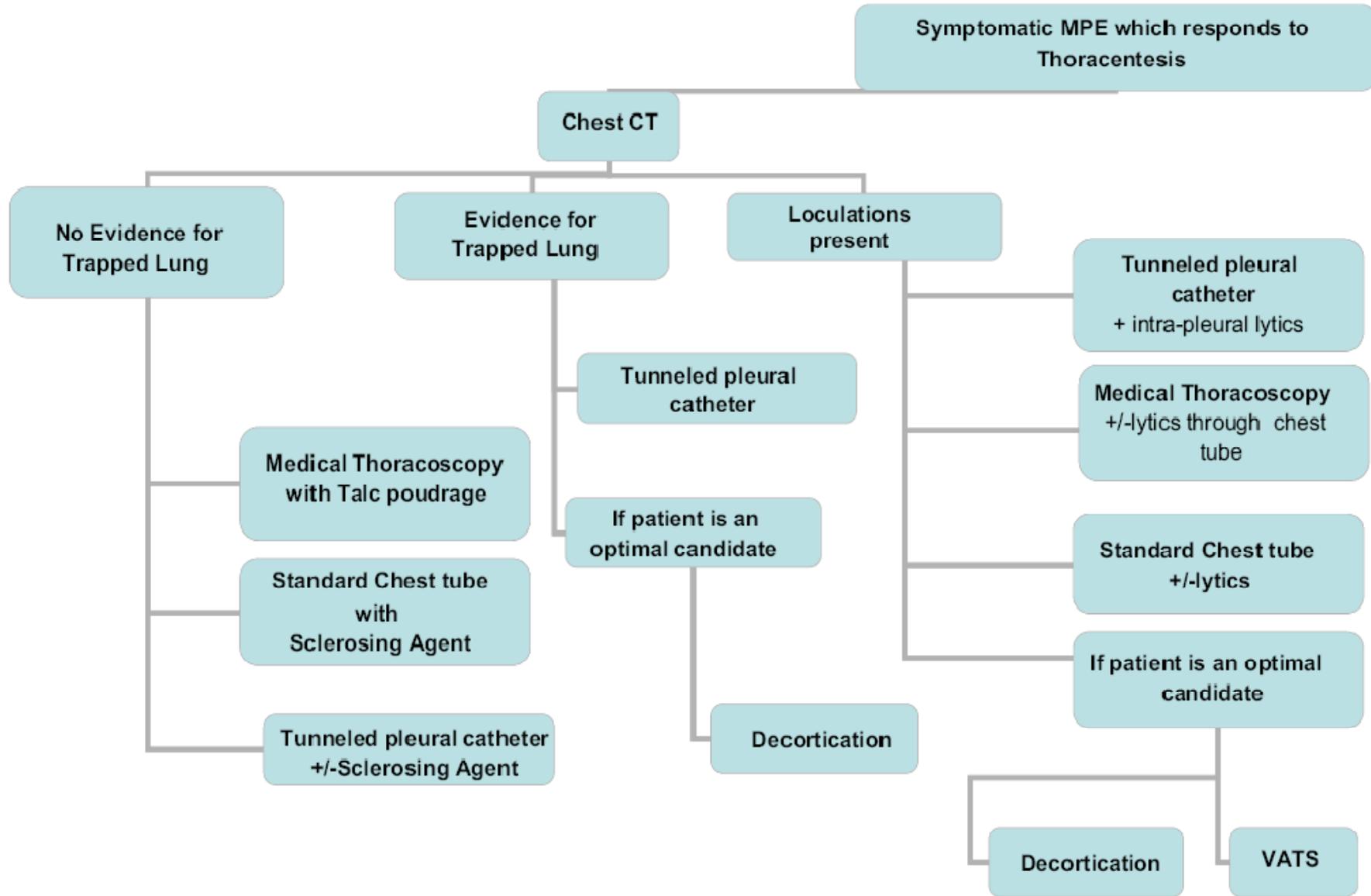
- Multiple cytokines: VEGF, bFGF, TGF β , PDGF...
- Effect of bisphosphonates?
 - Murine MPE model (Lewis LC cells)
 - Zoledronate sc
 - Reduction in pleural vascular permeability
 - Reduction in pleural fluid accumulation

Mutsaers SE et al. Cancer Treat Res 2007;134:1-19

Gary Lee YC. AJRCCM 2008;178:3-5

Stathopoulos GT et al. AJRCCM 2008;178:50-59

Management of pleural effusion (PE)



Cardiac tamponade

- Risk Factors
 1. Malignancy (lung 40%, breast 23%, lymphoma 11%, leukemia 5%)
 2. Constriction of the pericardium from the tumor (hilar masses, left lung lobe masses)
- Sign & symptoms variable on the rate of accumulation & amount of fluid
- Decreased cardiac output, venous congestion, weak heart sounds, chest fullness & discomfort

Cardiac tamponade

- Diagnostic tests
 1. Echocardiography (most sensitive), EKG
 2. CXR, CT, MRI
 3. Serum labs (Hct, ABG may reveal respiratory alkalosis)
- Treatment
 1. Pericardiocentesis with possible sclerosing
 2. Pericardiectomy
 3. Pleuropericardial window
 4. Aggressive fluid therapy (hypovolemia), oxygen, evaluate perfusion, potential for infections

Superior Vena Cava Syndrome

- Invasion or external compression of SVC
- Malignant tumors responsible for 80% cases
 - Infection and thrombosis account for most of the rest
- Symptoms
 - Dyspnea
 - Facial swelling, arm edema, cyanosis
- Signs
 - Venous distension on neck and chest wall
 - Facial edema

SVCS: Primary Pathologic Diagnoses

<i>Histologic Diagnosis</i>	<i>Bell 159 Cases (%)</i>	<i>Schraufnagel 107 Cases (%)</i>	<i>Parish 86 Cases (%)</i>	<i>Total 352 Cases (%)</i>
Lung Cancer	129 (81)	67 (63)	45 (52)	241 (68)
Lymphoma	3 (2)	10 (9)	8 (9)	21 (6)
Other malignancies (primary or metastatic)	4 (3) 2 (1)	14 (13) 16 (15)	14 (16) 19 (22)	32 (9) 39 (11)
Non-neoplastic Undiagnosed	21 (13)			21 (6)

Superior Vena Cava Syndrome

- 60% cases due to malignancy present *without* known diagnosis
- CT preferred diagnostic tool
- Importance of biopsy
 - Short delay not compromise outcome most cases
 - Histology helps determine treatment and prognosis
 - Treatment responsive tumors: SCLC, germ cell tumors, NHL
- Role for intraluminal stents?

Treatment of SVCS

- Symptomatic obstruction is usually a prolonged process
- Most patients are not in immediate danger at presentation
- Most have time for a full diagnostic work up
- Prebiopsy radiation can obscure the diagnosis
- Current strategies aim at accurate diagnosis of underlying etiology before therapy

Intraluminal Stents

- Patients who have recurrent disease in previously irradiated fields
- Tumors refractory chemotherapy
- Patient too ill to tolerate radiation or chemotherapy
- Some data suggests benefit from immediate stent placement in NSCLC at presentation
- Tends to provide more rapid relief of symptoms
- Issue of anticoagulation after is not resolved

Spinal Cord Compression

- Occurs in 5-10% of patients with cancer
- Epidural tumor is the first manifestation of malignancy in about 10% of patients
- Lung cancer is the most common primary (breast and prostate follow)
- Metastatic tumor involves the vertebral column more often than any other part of the bony skeleton

Spinal Cord Compression

- Thoracic spine, lumbosacral, then cervical (70-20-10)
- Breast/prostate produce MULTIPLE lesions
- Lung carcinoma produce SINGLE lesion
- Cord injury occurs when mets to vertebral body or pedicle enlarge and compress the underlying dura, or by direct extension of a paravertebral lesion through the intervertebral foramen (lymphoma, myeloma or pediatric neoplasm)
- Rarely, hematogenous spread to parenchyma of cord occurs

Spinal Cord Compression

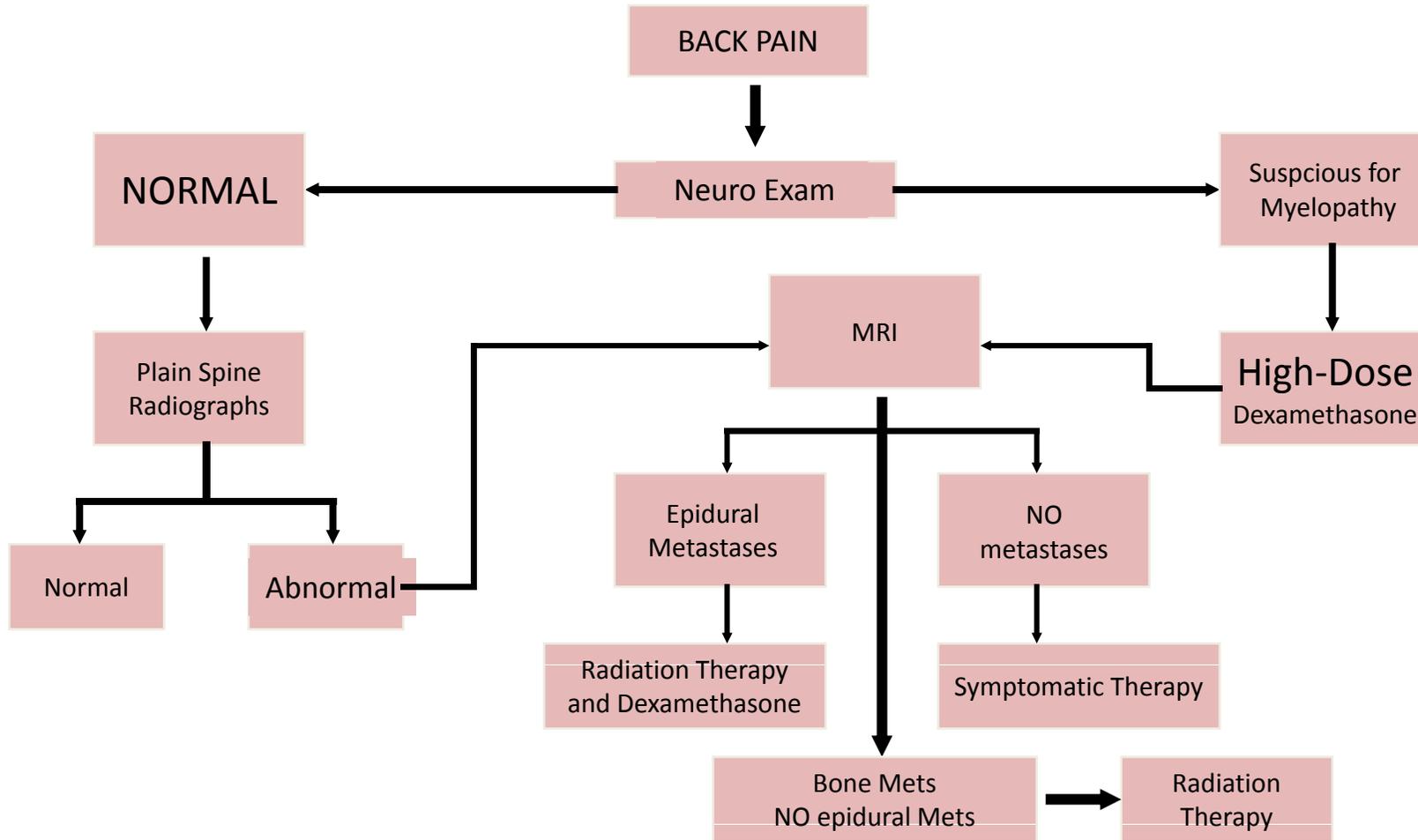
- Localized back pain is most common initially, and tenderness due to involvement of vertebrae by tumor
- Pain usually present for days/months before neurological findings appear. Exacerbated by cough/sneeze
- DIFFERENTIATED from disc disease by the fact that this pain is WORSE WHEN SUPINE (disc is worse when sitting)

Spinal Cord Compression

PHYSICAL EXAM FINDINGS:

- Pain on straight leg raising, neck flexion, vertebral percussion may help to locate level of lesion
- Numbness/paresthesias in extremities or trunk
- Loss of sensation to pinprick, vibration and proprioception can occur
- Weakness, spasticity, abnormal muscle stretching
- Loss of sphincter tone occurs later/distended bladder

Management of cancer patient with back pain



Spinal Cord Compression

DIAGNOSTIC:

- Erosion of pedicles is earliest radiologic finding of vertebral column tumor
- Other Radiographic: Increased intrapedicular distance, vertebral destruction, lytic or sclerotic lesions, scalloped vertebral bodies, and vertebral body collapse
- MRI: Full-length image of cord
 - T1 weighted images demonstrate good contrast between the cord, CSF, and extradural lesions
 - T2 weighted images demonstrate intramedullary bone pathology

Spinal Cord Compression

- Directed toward pain relief/restore neurological function
- Radiation plus glucocorticoids is generally initial TX of choice for compression
- Approx. 75% remain ambulatory when initial TX takes place when ambulatory. Only 10% of others regain ability to ambulate
- Laminectomy ONLY used for tissue diagnosis and for removal of posteriorly localized epidural deposits in ABSENCE of vertebral disease
- Most cases are Anterior/Anterolateral
 - Resection of anterior vertebral body along with tumor, then stabilize spine
 - Good results with low mortality
- Rapid onset and quick progression are POOR prognostic features

Paraneoplastic Syndromes

- 10% of the patients with lung cancer have a clinically obvious paraneoplastic syndrome
- 100% of patients have a paraneoplastic syndrome if we consider cachexia, anemia of chronic disease, fever
- There is not a correlation between paraneoplastic syndromes and the size of primary tumor
- Sometimes they can precede the diagnosis of malignant disease

Paraneoplastic Syndromes Associated with Lung Cancer

Endocrine	Neurologic	Skeletal	Renal	Metabolic
SIADH	Subacute sensory neuropathy	Hypertrophic Osteoarthropathy	Glomerulo Nephritis	Lactic acidosis
Cushing syndrome	Intestinal pseudo-obstruction	Clubbing	Nephrotic syndrome	
Gynecomastia	Lambert-Eaton syndrome			
Hypercalcitonemia	Encephalomyelitis			
Elevated levels of LSH, FSH	Necrotising myelopathy			
Hypoglycaemia	Cancer-associated retinopathy			
Hyperthyroidism				
Carcinoid syndrome				

Hypercalcemia

Pathophysiology:

- Local osteolytic hypercalcemia
- Prostaglandin production
- Cytokine production (IL-6)
- TNF α/β

- Humoral hypercalcemia of malignancy
- PTH- RP (squamous cell carcinoma)

- (Bone metastasis)

Hypercalcemia

- The most common paraneoplastic syndrome, occurring in 10% of patients with advanced cancer
- Most often lung, breast, H&N, kidney, and multiple myeloma
- Increased release of calcium from bone is the main factor
- Prognosis : poor, MST < 1 month
- Associated with > G-CSF secretion by the tumor

Hypercalcemia

- Fatigue, anorexia, abdominal pain, constipation, polydipsia, polyuria, thirst, dehydration, muscle weakness, nausea, and vomiting, confusion and irritability
- Easily attributed to the cancer itself or its treatment so it can be missed
- Evaluate electrolytes, calcium, phosphate, albumin
- 99% of calcium is bound in bones and teeth. Only 1% is in the serum and the majority is ionized
- Use corrected for protein formula to find calcium concentration when ionized calcium is not available
 - Corrected serum calcium = measured total serum calcium (mg/ml) + [4.0-serum albumin value (g/dl)] x 0.8

Hypercalcemia

- Therapy:
 - Fluids (250cc/h until fluid replacement)
 - Furosemide (after fluid replacement)
 - [Phosphate & Sulfate I.V.]
 - [Mithramycin]
 - Gallium nitrate,
 - Biphosphonates (etidronate, pamidronate)
 - Calcitonin for life- threatening hypercalcemia (early onset of action)
 - Antibody against receptor activator of NF κ B

Hypercalcemia

Pathophysiology:

- Bone resorption is increased dramatically via stimulation of proliferation and activity of osteoclasts and bone formation is not stimulated in parallel
- Kidney may resorb more calcium in the distal tubule
- Parathormone-related protein produced by tumors is central mediator of increased calcium in cancer

Ectopic Cushing's Syndrome

- ACTH is the most commonly produced ectopic hormone in lung cancer
- ECS is responsible of 12% of all cases of CS and lung cancer represents 50% of ECS
- Immunoreactive ACTH may be detectable in up to 50% of patients, but only 1 to 5% develop a Cushing syndrome
- Mainly associated to SCLC (but carcinoid also)

Ectopic Cushing's Syndrome

- Presentation differs from classical CS
 - Short-term exposure to excessive CS
 - Aggressive nature of the disease
 - Aberrant processing of POMC (proopiomelanocortin)
- Proximal myopathy (29-61%)
- Moon facies (40-52%)
- Nearly all hypokaliemic and hyperglycemic
- Most have ED and poor response to CT (MST 4 mos)
- Infections such as *P. carinii* pneumonia & invasive pulmonary *Aspergillosis* are common

Ectopic Cushing's Syndrome

- Therapy:
 - Surgical resection of the cancer
 - Chemotherapy
 - Suppression of hormone production:
 - Ketoconazole 1200 mg/die
 - Metyrapone (androgenic side effects may occur and the addition of aminoglutethimide may help to control these symptoms)
 - Mitotane

SIADH

- Excess of production of ADH can be documented in up to 70% of patient with lung cancer, but syndrome of inappropriate ADH is not common
- Mostly associated with SCLC
- The syndrome resolves promptly (< 3 weeks) with the initiation of the therapy, but commonly recurs with tumor progression.
- Prognosis – no different than SCLC without SIADH

Syndrome of Inappropriate Secretion of Antidiuretic Hormone (SIADH)

- Caused by production of arginine vasopressin by tumor cells
 - HYPOnatremia
 - Increase urine osmolarity above plasma
 - Increased sodium excretion in urine without volume depletion
 - Often co-secretion of adrenocorticotrophic hormone (ACTH)
- When conditions the syndrome are shown to be absent (cardiac, renal, adrenal and thyroid disorders) then SIADH is likely the culprit.

Syndrome of Inappropriate Secretion of Antidiuretic Hormone (SIADH)

- Most patients are asymptomatic
- Degree of symptoms and severity are due to:
 - degree of hyponatremia
 - rapidity hyponatremia develops
- Early anorexia, depression, lethargy, irritability, confusion, muscle weakness, marked personality changes
- Plasma sodium falls below 110 mEq/L, extensor plantar responses, areflexia, and pseudobulbar palsy may be noted
- Can lead to coma, convulsions, death

Syndrome of Inappropriate Secretion of Antidiuretic Hormone (SIADH)

- Treat underlying Malignancy
- Restrict water
- Demeclocycline used first. Inhibits effects of vasopressin on distal renal tubule leading to a dose-dependent and reversible decrease in the concentrating abilities of the kidney

Lambert-Eaton Myasthenic Syndrome (LEMS)

- Presynaptic disorder of neuromuscular transmission
- Proximal weakness, areflexia or hyporeflexia, autonomic dysfunction
- 45% to 60% associated with SCLC, reported also with renal cell carcinoma, lymphoma and breast
- Syndrome precedes tumor diagnosis by several months to years

Lambert-Eaton Myasthenic Syndrome (LEMS)

- Onset with proximal lower extremity weakness
- Later proximal upper extremity weakness
- Respiratory and craniobulbar involvement uncommon
- Autonomic dysfunction prominent
 - dry mouth, dry eyes, impotence, orthostatic hypotension, hyperhidrosis
- Facilitation with sustained contraction
- >100% CMAP increase with repetitive stimulation

Lambert-Eaton Myasthenic Syndrome (LEMS)

- >92% with antibodies against P/Q-type voltage-gated calcium channels (presynaptic)
- Impaired influx of calcium into nerve terminal with reduced neuromuscular junction transmission
- A LEMS diagnosis warrants a thorough investigation for underlying carcinoma, SCLC
- Careful observation and serial evaluations until tumor found

Lambert-Eaton Myasthenic Syndrome (LEMS)

- Unlike most paraneoplastic syndromes LEMS usually responds to:
 - plasmapheresis
 - corticosteroids
 - azathioprine
 - intravenous immunoglobulin
- Long-term treatment often needed

Febrile Neutropenia

- **Should be considered an emergency**
 - Early studies have shown high mortality when delay initiation of appropriate antibiotics
 - Before era of empiric antibiotics infection accounted for up to 75% of deaths associated w/ chemotherapy
- **Definitions:**
 - Fever: single temp > 38.3°C (101.3°F) or 38.0°C (100.4°F) sustained greater than 1 hour
 - Neutropenia: usually ANC < 500
 - Absolute neutrophil count (ANC)=total WBC X (%neutrophils + %bands)

Febrile Neutropenia

- Seeding of the bloodstream from endogenous flora in the GI tract most common cause
- Commonly cultured bacterial pathogens
 - Gram neg (Pseudomonas, E Coli, Klebsiella etc..)
 - Gram pos (Coag-neg staph, staph aureus, streptococcus etc...)
- Commonly cultured funga pathogens
 - Candida species, Aspergillus
 - usually arise later as a secondary infection in patients with *prolonged* neutropenia and antibiotic use
- Viral pathogens
 - HSV, VZV

Treatment of Febrile Neutropenia

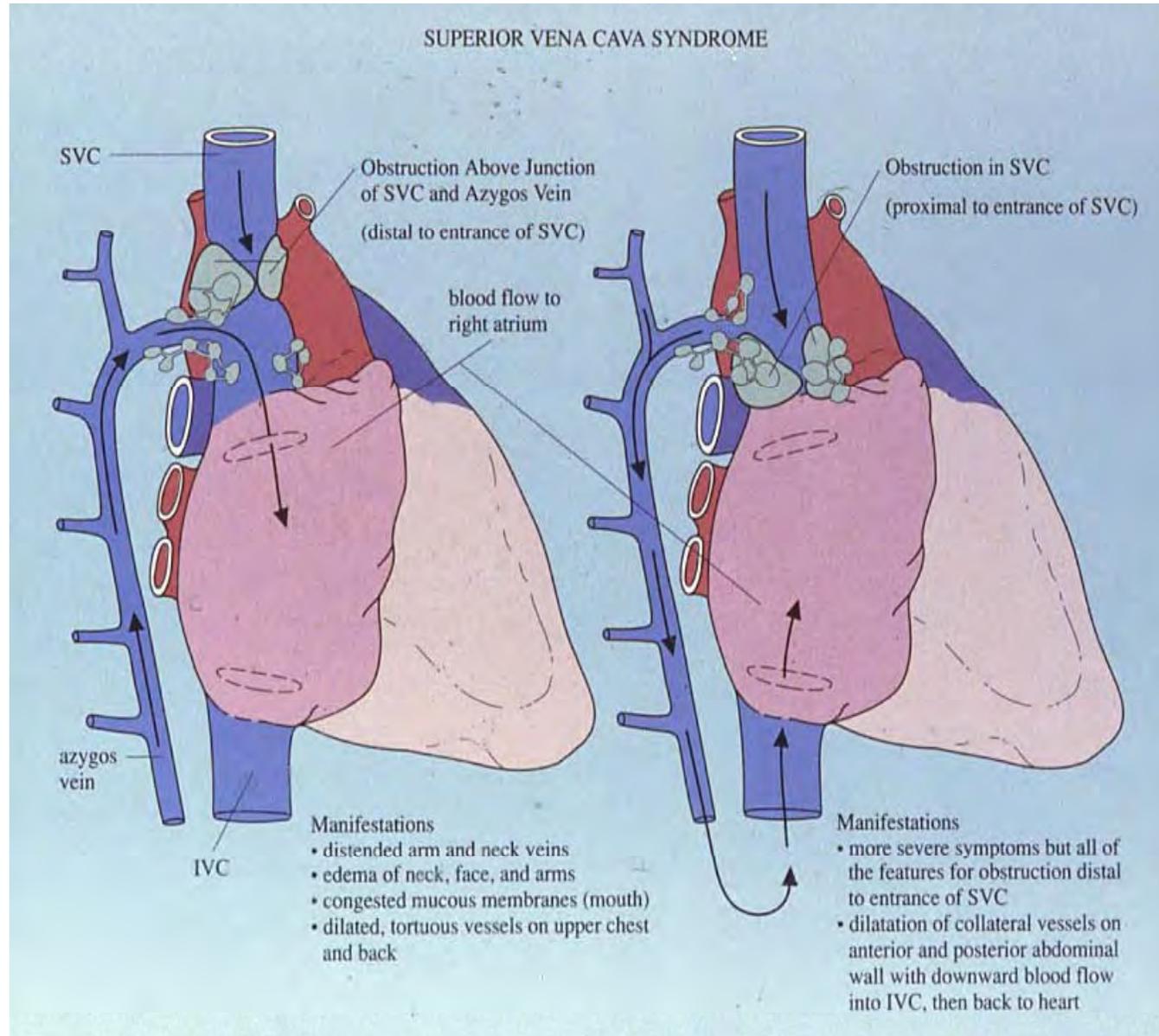
- Empiric Antibiotics
 - Appropriate coverage of known or suspected infection based on history/exam findings/radiographic studies
- Monotherapy:
 - ceftazidime, imipenem, meropenem, or cefepime
- Double coverage:
 - beta-lactam and an aminoglycoside
- Awareness of institutional resistance patterns
- Addition of empiric Vancomycin
 - Skin or **catheter** site infection, hypotensive, hx of MRSA colonization, mucositis, quinolone prophylaxis

Treatment of Febrile Neutropenia

- Empiric anti-fungal coverage with persistent fever on broad-spectrum antibiotics and prolonged neutropenia
 - Amphotericin B (liposomal), caspofungin, voriconazole
- Colony stimulating factors
 - Should not be used routinely
 - Appropriate for critically ill patients

Key concepts when caring for people with cancer

- Identify patients at risk for complications
- Assess with each interaction
- Educate the family about the risk
 - How to assess and report with the onset of complications



Pleural effusion in malignancy

- Malignant effusion (pleuritis)
 - ✓ 22% of all pleural effusions
 - ✓ 50% of pleural effusions in malignancies are ‘benign’
- “Paramalignant” effusions



- » Lymphatic obstruction
- » Airway obstruction
- » Pneumonia/atelectasis
- » Trapped lung
- » Chylothorax
- » Superior vena cava syndrome (SVCS)
- » Decreased oncotic pressure
- » Adverse effects of therapy

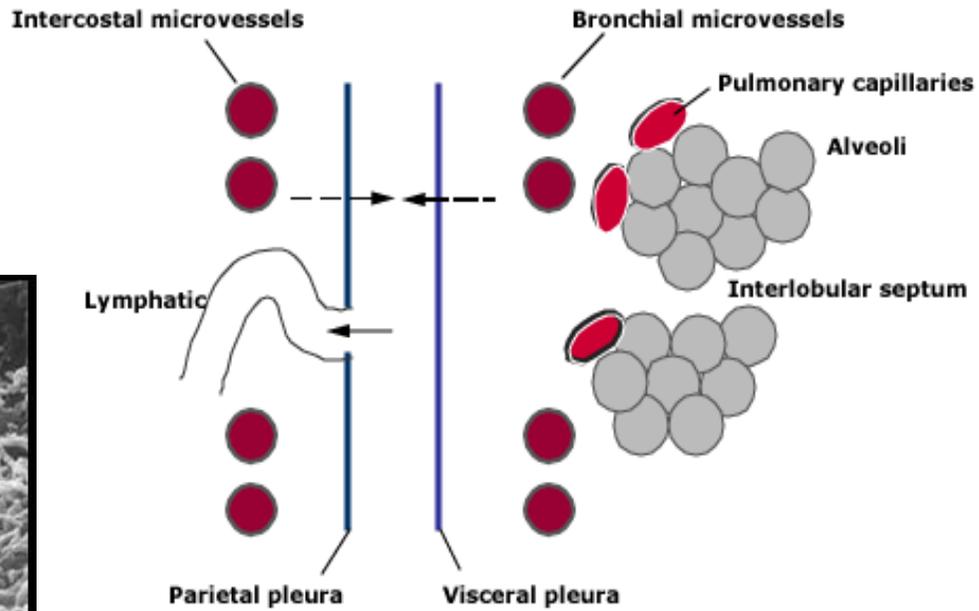
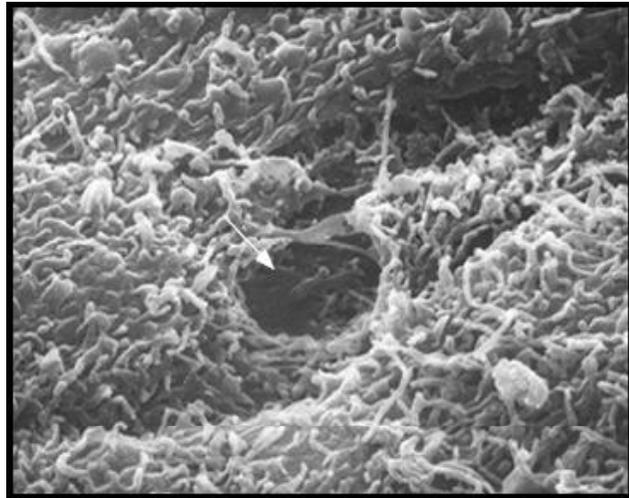
HE Davies et al. Thorax 2008;63:572-4

Khaleeq G, Musani AI. Respiratory Med 2008;102:939-48

Heffner JE, Klein JS. Mayo Clin Proc 2008;83:235-50

Pleural effusion in malignancy

Tumour	n	%
Lung	641	36
Breast	449	25
Lymphoma	187	10
Ovary	88	5
Stomach	42	2
Unknown primary	129	7
Other causes	247	14



Broaddus VC, Sahn SA, Hellingsworth H.
Mechanisms of pleural fluid accumulation in disease
UpToDate® 2009 www.utdol.com

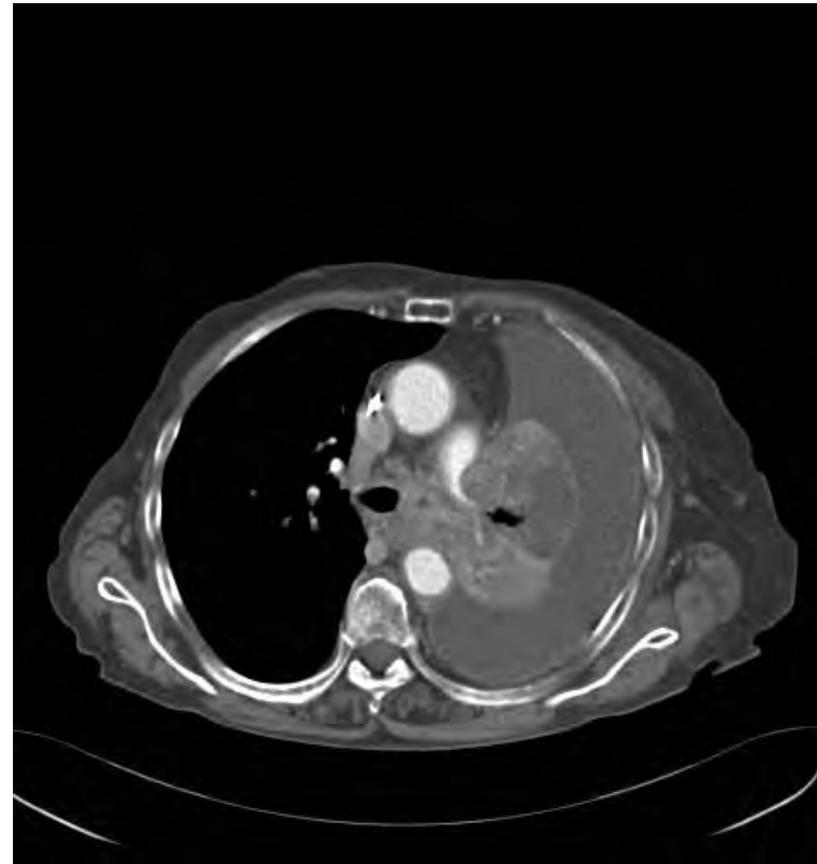
Management of pleural effusion

- **Palliative treatment**
- **Removal of pleural effusion**
- **Pleurodesis**
- **Drainage**
- **Stop pleural effusion formation(?)**

Kvale PA et al.

Palliative Care in lung cancer. ACCP evidence-based clinical practice guidelines
Chest 2007;132:368S-403S

Pleurodesis



“Trapped” lung

Pleurodesis

- Sclerosants

- Other?

- TGF β (animals)

- (Lee YC et al Respirology 2002; Light RW et al AJRCCM 2000)*

- OK-432 (Str.pyogenes)

- (Kishi K et al Eur Respir J 2004; Ishida A et al Respirology 2006; Kasahara K et al Anticancer Res 2006)*

- S. Aureus superantigen

- (Ren S et al Chest 2004)*

Pleurodesis

- Chest tube/catheter + talc slurry
- Thoracoscopy + talc insufflation

- Shaw P et al, Cochrane Database Syst Rev 2004 TI
- Dressler CM et al, Chest 2005 =
- Crnjac A et al, Eur J CT Surg 2004 TI=cath



?



Pleurodesis

Talc poudrage

- N=242
- 78% 30d outcome
- 9 deaths
- 8% respir failure (6†)

Talc slurry (tube)

- N=240
- 71% 30d outcome
- 7 deaths
- 4% respir failure (5†)

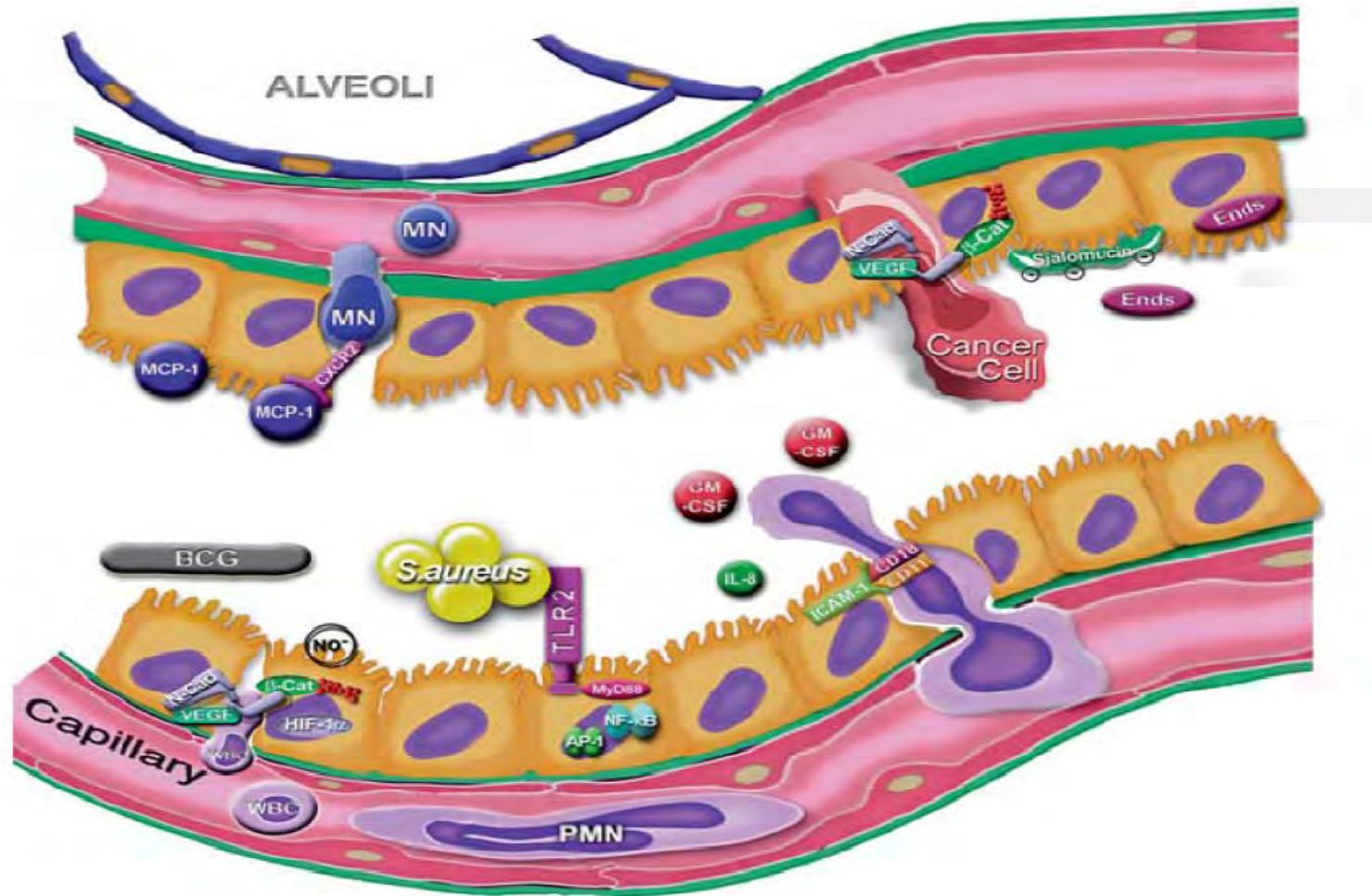
“Both methods of talc delivery are similar in efficacy”

Pleurodesis

- chest tube/thoracoscopy

“In lung cancer pts with symptomatic pleural effusions that recur after thoracocentesis, chest tube drainage and pleurodesis are recommended. Grade of recommendation: 1B”

Future?



Management of pleural effusion (PE)

- **Removal of pleural effusion**
- **Talc pleurodesis**
- **Future?**
 - **Pleural catheters**
 - **New sclerosing agents**
 - **New agents to stop PE formation**

Initial Considerations

- Paraneoplastic syndromes are a group of clinical disorders associated with malignant disease that are not directly related to the physical effects of primary and metastatic tumor
- Pathogenesis - may be due to the production of biologically active substances either by the tumor or in response to the tumor

Digital Clubbing and Hypertrophic Osteoarthropathy

- Adenocarcinoma and mesothelioma are the most common malignancies associated with clubbing.
- Peripheral NSCLC is the most commonly associated malignancy in patients with HOA.
- SCLC is rarely associated with HOA
- Pathogenesis – largely unknown
- Combination of clubbing and HOA is thought to represent a disease continuum

Digital Clubbing and Hypertrophic Osteoarthropathy

- Clubbing may result from alterations in local tissue oxygenation due to either the formation of platelet and megakaryocytic vascular plugs or the abnormal production of vasoactive substances.
- Recent studies support a role for PDGF, in that platelets are thought to release growth factors in the extremities

Digital Clubbing and Hypertrophic Osteoarthropathy

- Signs and Symptoms:
 - Painful symmetrical arthropathy (ankles, wrists and knees)
 - Periosteal new bone formation on the distal long bones
 - Elevated ESR and alkaline phosphatase

Digital Clubbing and Hypertrophic Osteoarthropathy

- Therapy:
 - Treatment of the tumor results in the regression of HOA but not of the clubbing
 - A case report of Hayashi suggested that Gefitinib (EGFR inhibitor) might be a promising option for the treatment of HOA with advanced lung adenocarcinoma

Neurologic Syndromes

- They affect 4-5 % of the patients with lung cancer
- Their diagnosis is a diagnosis of exclusion
- Most of them are autoimmune
- SCLC is the most common type of cancer associated with these syndromes

Lambert Eaton Myasthenic Syndrome

- A defect of neuromuscular transmission with reduced quantal release of Acetyl Choline from the presynaptic nerve terminal
- Pathogenic antibodies directed against voltage gated calcium channels (VGCCS) expressed at the NMJ and autonomic ganglia
- 2/3 patients with LEMS have cancer, most commonly SCLC (express VGCCs)

Lambert Eaton Myasthenic Syndrome

- Clinical features
 - Dry mouth
 - Fatigable weakness of proximal muscles (like MG)
 - Wasting of proximal muscles (X MG)
 - Depressed reflexes (X MG)
 - Ocular and bulbar weakness rare (X MG)

Lambert Eaton Myasthenic Syndrome

Diagnosis

Typical clinical picture

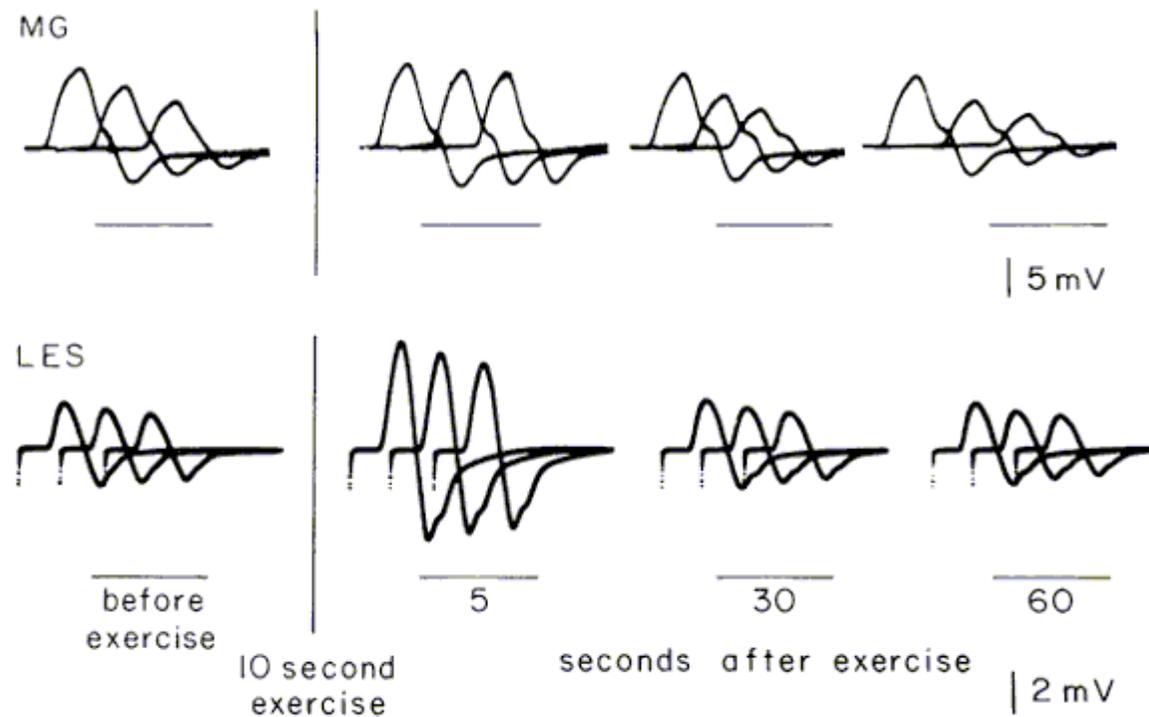
Detection of anti-VGCC antibodies in serum

Positive Tensilon test (like MG)

Repetitive nerve stimulation at low frequency
leads to a decrement in compound muscle
action potential amplitude (like MG)

Repetitive nerve stimulation at high frequency
leads to a increment in compound muscle action
potential amplitude (X MG)

Repetitive Nerve Stimulation (Supramaximal 2Hz)



Lambert Eaton Myasthenic Syndrome

Treatment

- Treating the underlying lung tumour improves LEMS
- Treatment for LEMS per se
 - Symptomatic (mestinon, 3-4 DAP)
 - Immunotherapy (steroids, plasma exchange, IVIG)

Paraneoplastic Cerebellar Degeneration

- PCD sometimes occurs in association with the Lambert-Eaton myasthenic syndrome
- Extensive loss of Purkinje neurons with cerebellar atrophy
- 23% of SCLC with PCD may occur with Hu-antineural antibodies (HuAb); other Ab are Anti-Tr antibodies and Anti-voltage-gated calcium antibodies

Paraneoplastic Cerebellar Degeneration

- Autoantibodies in serum and CSF/cancer
 - anti-Yo ovary, breast
 - anti-Hu SCLC
 - anti-Ri Breast, SCLC,
 - anti-Tr Hodgkin's lymphoma
 - anti-CV2 SCLC
 - anti-Ma proteins Testicular

Paraneoplastic Cerebellar Degeneration

- Pathology
 - CNS may be normal at autopsy
 - usually the cerebellum is atrophic with abnormally widened sulci and small gyri
 - microscopic
 - extensive/complete loss of Purkinje cells of the cerebellar cortex
 - pathologic changes sometimes involving other parts of nervous system

Paraneoplastic Cerebellar Degeneration

■ Symptoms:

- Subacute symptoms: truncal and appendicular ataxia, dysarthria
- After few months: diplopia, horizontal nystagmus, and rotatory or downbeating nystagmus

■ Therapy:

- Intravenous immunoglobulins, steroids or plasmapheresis
- (Therapy of lung cancer)

Sensory Neuronopathy (SN)

- <20% paraneoplastic
- Also occurs in patients with autoimmune disorders, Sjogren's syndrome
- 2/3 of paraneoplastic SN have small-cell lung cancer
- Neurologic syndrome usually precedes diagnosis of cancer
 - dysesthetic pain and numbness of distal extremities
 - severe sensory ataxia
 - all sensory modalities affected, loss of DTRs
 - motor nerve action potentials are normal

Encephalomyelitis

- Cancer patients with clinical signs of damage to more than one area of the nervous system
- Limbic encephalitis
 - rare complication of small-cell lung cancer
 - personality/mood changes develop over days or weeks
 - severe impairment of recent memory
 - sometimes with agitation, confusion, hallucinations, & seizures
 - brain MRI: normal or signal changes in the medial temporal lobe(s)
 - may improve with treatment of underlying tumor

Photoreceptor Degeneration

- Cancer-associated retinopathy (CAR)
- Rare syndrome
- Small-cell lung cancer, melanoma, gynecologic tumors
- Episodic visual obscurations, night blindness, light-induced glare, photosensitivity, impaired color vision progressing to painless vision loss
- Typically precedes diagnosis of cancer
- ? prednisone

Membranous Glomerulonephritis

- Lung cancer is rarely associated with nephrotic syndrome (3% of patient with a initial nephrotic syndrome)
- SCLC is the most common type of cancer associated with this syndrome

Membranous Glomerulonephritis

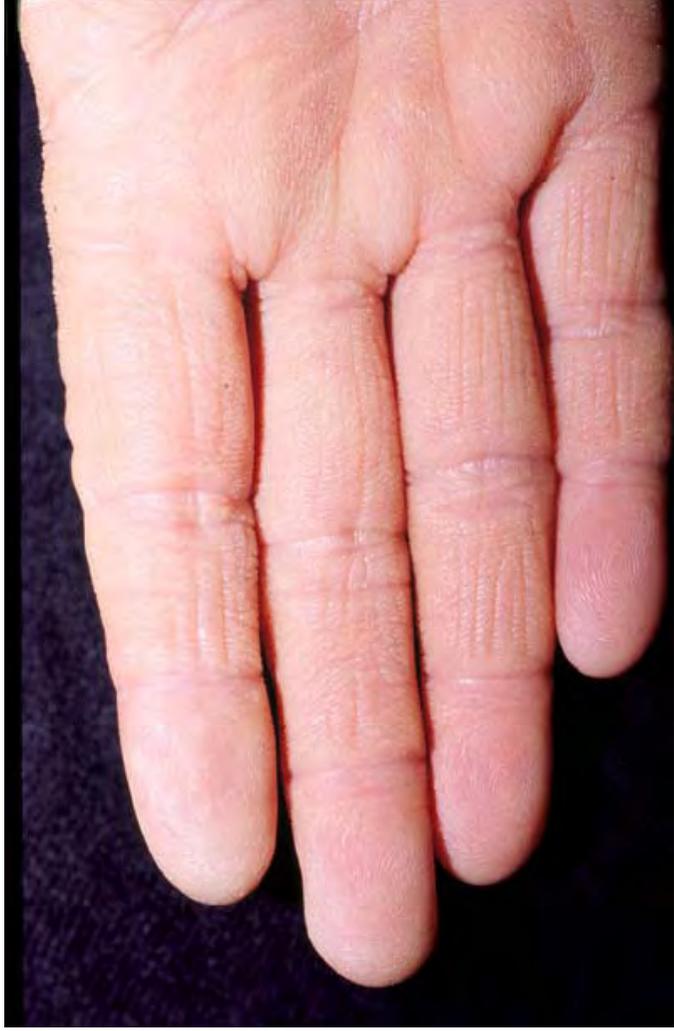
- Pathogenesis:
 - Subepithelial deposition of IgG, complement with tumor antigen (also IgA and CEA were found) that damage the glomerular basement membrane
 - (Renal insufficiency is rare)
- Therapy:
 - Symptomatic treatment
 - Treatment of lung cancer

Dermatologic Paraneoplastic Syndromes

- Early diagnosis
- Age appropriate cancer screens
- Certain dermatologic manifestations are more closely associated with certain types of cancers
- Some genetic syndromes (ie Gardner's, Peutz-Jeghers, NF) associated with derm findings and malignancy.

Tripe Palms

- Rugose, velvety palms; may be associated with AN
- Lung CA most often; gastric CA second in frequency, especially with AN



Bazex's syndrome

- Hyperkeratosis paraneoplastica
- Acral hyperkeratotic papulosquamous lesions, onychodystrophy
- Squamous cell carcinomas of the oropharynx, larynx, bronchi, esophagus



Erythema Gyrratum Repens

- Concentric rings on trunk and proximal extremities; may have pruritus
- Rapidly progressing located on trunk, proximal parts of extremities
- Characteristic swirling
- Lung cancer, most frequent (32%)



Acquired Hypertrichosis Lanuginosa

- Increased hair on face or other areas
- Men: lung first, colorectal second
- Women: colorectal first, lung or breast second

