LUNG CANCER

Contents

0.0 Tissue injury inflammation and regeneration

Homeostasis is preserved though intercellular communication. To maintain homeostasis, every cell in the body must communicate with its neighbours and with cells and tissues in distant portions of the body

1.0 The response to tissue injury involves inflammation and regeneration

Tissue in the body are not isolated they combine to form organs with diverse functions. Any injury affects several tissue types simultaneously, and the repair process depends on the coordinated response of these tissues to restore homeostasis.

Restoring homeostasis after tissue injury involves two related process: inflammation and regeneration.

1.1 Inflammation

First the area is isolated from neighbouring healthy tissues while damaged cells, tissue components and any dangerous microorganisms are cleaned up. This phase which coordinates the activities of several different tissues, is called inflammation or the inflammatory response. It produces several familiar sign and symptoms including swelling heat redness and pain.

Many stimuli – including impact, abrasion chemical irritation, infection (presence of pathogens such as harmful bacteria, viruses of funguses) and extreme temperatures (hot or cold) can produce inflammation. When any of these stimuli either kill cells, damage fibres or injure tissues, they trigger the inflammatory response by stimulating connective tissue cells called mast cells. The mast cells release chemicals (histamine and heparin) that cause local blood vessels to dilate (enlarge in diameter) and become more permeable. The increased blood flow to the injured region makes it red and warm to the touch, and the diffusion of blood plasma causes the injured area to swell. The abnormal tissue conditions and chemicals released by the mast cells also stimulate sensory nerve endings that produce sensation of pain. These local circulatory changes increase the delivery of nutrients, oxygen phagocytic white blood cells, and blood clotting proteins, and they speed up the removal of waste products and toxins. Over a period of hours to days, this coordinated response generally succeeds in eliminating the inflammatory stimulus.

1.2 regeneration

In the second phase following injury, damage tissues are replaced or repaired to restore normal function. This repair process is called regeneration. During regeneration fibroblast produce a dense network of collagen fibres known as scar tissue or fibrous. Over time scar tissue is usually remodelled and gradually assumes a more normal appearance.

Each organ has a different tissue organization, and this affects its ability to regenerate after injury. Epithelia, connective tissues (except cartilage), and smooth muscle tissue usually regenerate well: other muscle tissues and neural tissue regenerate relatively poorly it at all. Your skin, which is made up mostly of epithelia regenerate rapidly.

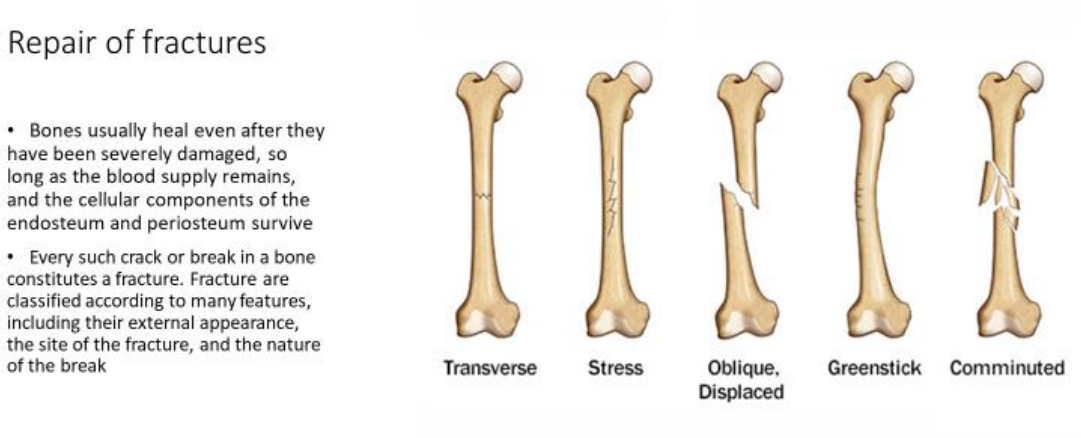
1.3 Fibrosis

In contrast, damage to the heart is more serious because although its connective tissue can be repaired, most of the damage cardiac muscle cells are replaced only by fibrous connective tissue. Such a permanent replacement of normal tissue is called fibrosis. Fibrosis may occur in muscle and other tissues in response to injury, disease or aging.

Inflammation and regeneration are controlled at the tissue level. The two phases overlap: isolation of the area of damaged tissue establishes a framework that guides the cells responsible for reconstruction and repairs are under way well before clean-up operations have ended.

2.0 Repair of fractures

Despite its strength bone will crack or even break if subjected to extreme loads, sudden impacts, or stresses form unusual directions. Every such crack or break in a bone constitutes a fracture. Fracture are classified according to many features, including their external appearance, the site of the fracture, and the nature of the break. Bones usually heal even after they have been severely damaged, so long as the blood supply remains, and the cellular components of the endosteum and periosteum survive.



2.1 Steps in the repair process, which may take from four months to well over a year following a fracture are:

1. In even a small fracture, many blood vessels are broken, and extensive bleeding occurs. A large blood clot, or fracture hematoma (hemato = blood, tumere = to swell), soon forms and closes off the injured blood vessels. Because the resulting lack of blood supply kills osteocytes, dead bone extends in either direction form the break.

2. Cells of the periosteum and endosteum undergo mitosis, and the daughter cells migrate into the fracture zone. There they form localized thickenings – an external callus and an internal callus, respectively. At the canter of the external callus, cells differentiate into chondrocytes and produce hyaline cartilage.

3. Osteoblasts replace the new central cartilage of the external callus with spongy bone. When completed the external and internal calluses from a continuous brace of the spongy bone at the fracture site. The ends of the fracture are now held firmly in place and can withstand normal stresses from muscle contraction.

4. If the fracture required external support in the form of a cast that support can be removed at this stage. When the remodelling is complete, the fragments of dead bone and the spongy bone of the calluses will be gone, and only living compact bone will remain. The repair may be "good as new" with no sign that a fracture occurred, but the bone may be slightly thicker than normal at the fracture site.

The steps in the repair of a fracture:

a. Immediately after the fracture extensive bleeding occurs. Over a period of several hours a large blood clot, or fracture hematoma develops.

b. An internal callus forms as a network of spongy bone unites the inner edges, and an external callus of cartilage and bone stabilizes the outer edges.

c. The cartilage of the external callus has been replaced by bone, and struts of spongy bone now unite the broken ends. Fragments of dead bone and the areas of bone closest to the break have been removed and replaced.

d. A swelling initially marks the location of the fracture. Over time this region will be remodelled, and little evidence of the fracture will remain.

3.0 Chronic inflamation. Osteoarthritis (OA) vs Rheumatoid Arthritis (RA)

Osteoarthritis, rheumatoid arthritis, rheumatism is often used interchangeably in everyday language, in most of the case to describe a pain connected with movement. But in medical language everyone has a different precise meaning.

3.1Arthritis

Arthritis means inflammation of the joints – with pain, stiffness and loss of movement, whilst Rheumatism is a general term usually refers to aches, pain or stiffness arising in the skeletal or muscular system, that can come from muscles tendons, ligaments or joints. There are several major forms of rheumatism. Arthritis includes all the rheumatic diseases that affect synovial joints. Arthritis always involves damage to the articular cartilages, but the specific cause can vary. Arthritis can result from bacterial or viral infection, injury the joint, metabolic problems, or severe physical distress. Arthritis is commonly a secondary condition arising from other diseases.

3.2 Osteoarthritis

Osteoarthritis (degenerative arthritis, or degenerative joint disease) usually affects individuals age 60 or older, but to varying degrees. Most of the population affected can be experience merely as stiff joints. For some the symptoms can include pain, stiffness and swelling and can lead to reduced movement as the condition worsens. It usually develops slowly, although when the condition is more advanced it may include inflammation.

This disease can result from cumulative wear and tear in the hyaline cartilage at the joint surfaces or from genetic factors affecting collagen formation, overweight is also a risk factor. As the cartilage thins with age, cracks appear and penetrate to the bone underneath, and bony growths can also develop. Weight bearing joints such as the hip and the knee are most often affected and the fingers and the spine. In the U.S. population, 25% of woman and 15% of man over age 60 show sign of this disease.

Recommendations for treatment: Massage can be beneficial in providing some pain relief, and gentle mobilisation of the joints may prevent further deterioration, provided more care is taken around any painful joints. Local massage is contraindicated in acute phases. Regular exercise, physical therapy and drugs that reduce inflammation, can slow the progress of osteoarthritis.

3.3 Rheumatoid arthritis

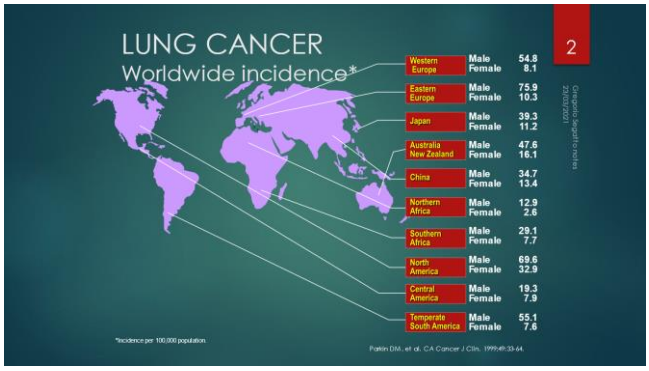
Rheumatoid arthritis is an inflammatory condition, is an auto immune disease in which the immune system mistakenly attacks the body's own tissues in this case the joint tissues. The skin, lungs, eyes and internal organs may all be affected as well as the joints, sometimes also muscles tendons and blood vessels. The onset is usually between 30 – 50 years, can be constant or inconstant, but when inconstant can regularly flare up and then die down.

The joints most affected are usually the hands and feet, often on both sides of the body at once, and sometimes the neck. Inside the joint the synovial membrane becomes inflamed; the fluid builds up and the joints swells. If it progresses, which only happens in a portion of the population affected, the cartilage and then the bone is affected until, over time the joint may be deformed and/or fused together. Surgical procedures can realign or redesign the affected joint. In extreme cases involving the hip the knee elbow or shoulders the defective joint can be replaced by and artificial one. Allergies, bacteria, viruses and genetic factors have all been proposed as contributing to or triggering the destructive inflammation. Affects about 0.5 – 1 % of the population.

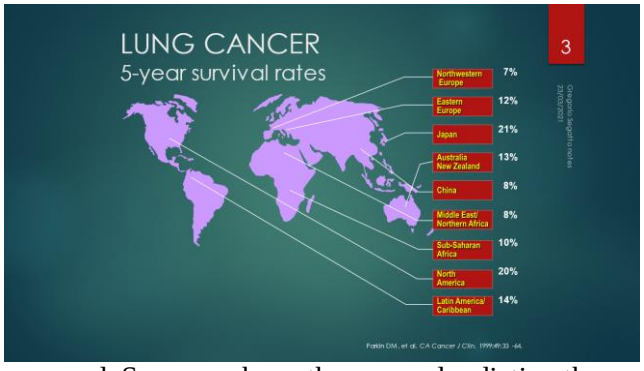
Recommendations for treatment: Massage is contra – indicated in acute stages, at other times, general massage may help reduce stress – a factor in the flaring up of the disease, gentle massage of the tissues around the joints may help relieve pain. Careful movements of the joints can be used to increase mobility. Stretches or manipulations of the spine are contra – indicated, particularly in the cervical region, because this could disturb or break bony fusions that may have developed between the vertebrae.

	Osteo – Arthritis	**Rheumatoid Arthritis**
Degenerative disease	Yes	Can degenerate
Auto immune disease	No	Yes
Onset (years)	Usually over 60	between 30 – 50
Incidence	25% of woman and 15% of man over age 60 (US population)	0.5 – 1 % of the population
Systemic disease	No	Yes, but can affect one single joint or part of the body
Risk factors	Arthritis can result from bacterial or viral infection, injury the joint, metabolic problems, or severe physical distress.	Allergies, bacteria, viruses and genetic factors have all been proposed as contributing to or triggering the destructive inflammation
The most affected joints	the knee, the fingers and the spine	the hands and feet (bilaterally), the neck

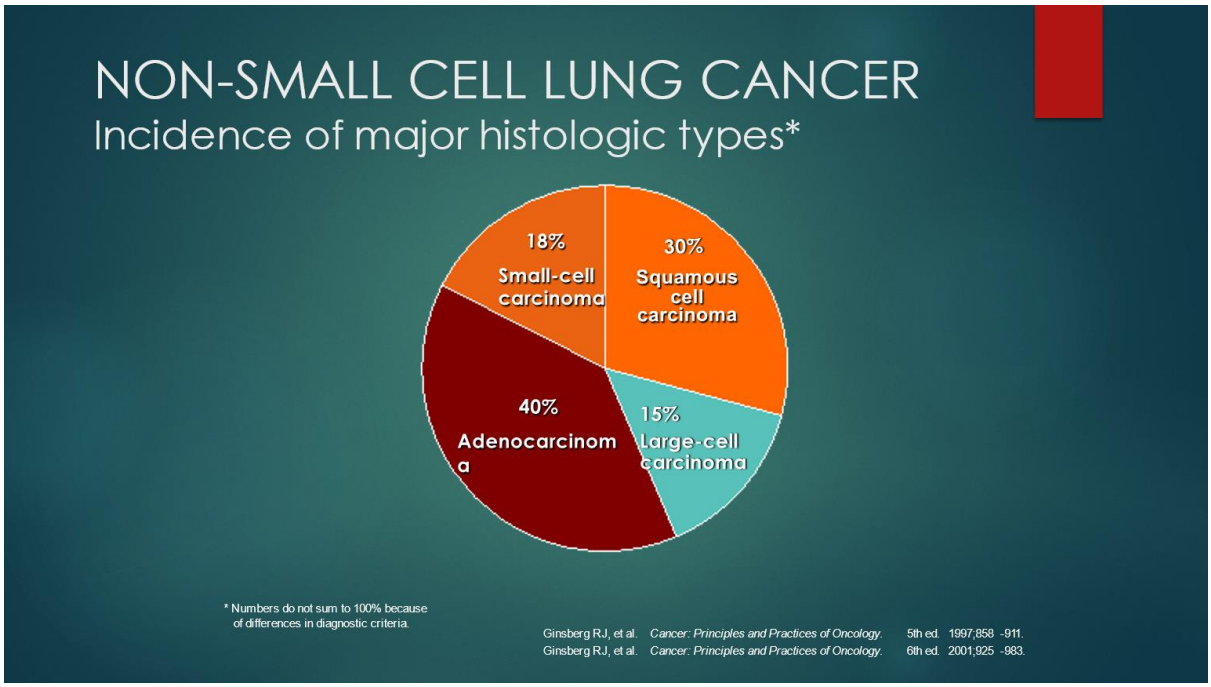
4.0 Lung cancer

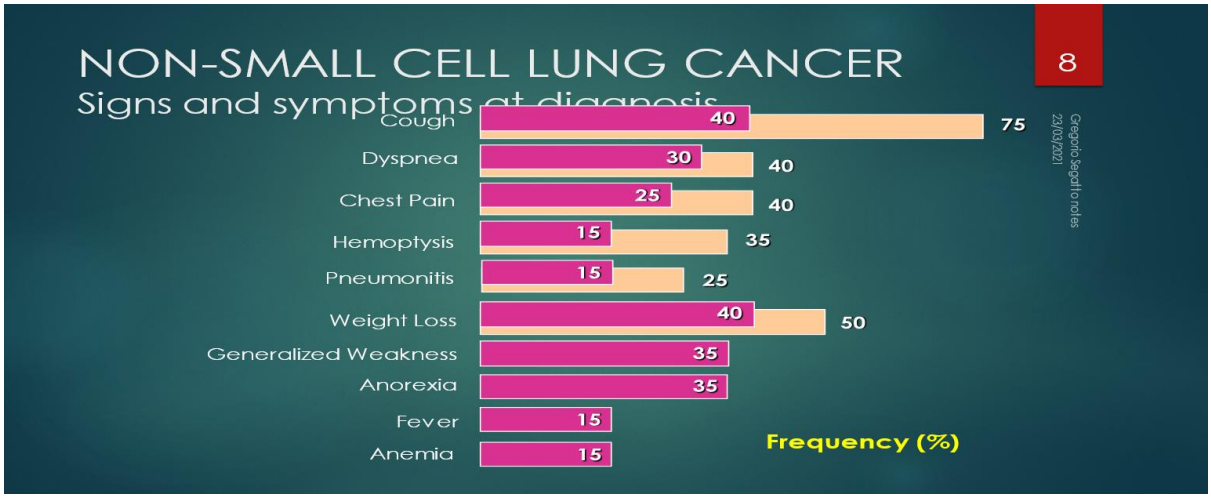


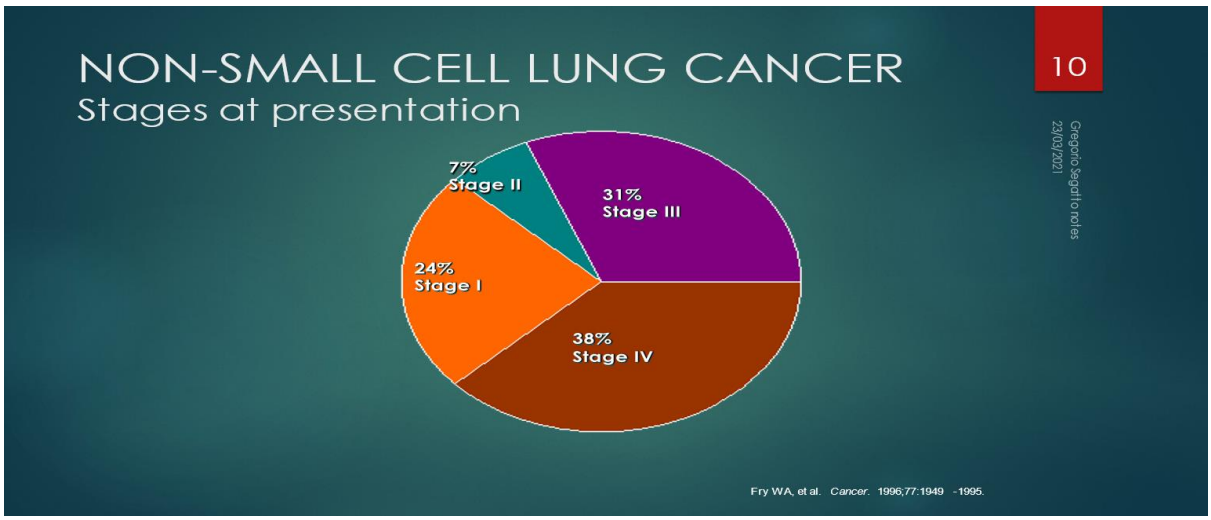
Lung cancer or broncho pulmonary carcinoma is an angressive class of malignancies originating in the bronchial passage – ways or alveoli. These cancers affect the epithelial cells that line conducting passageways, mucous glands or alveoli.

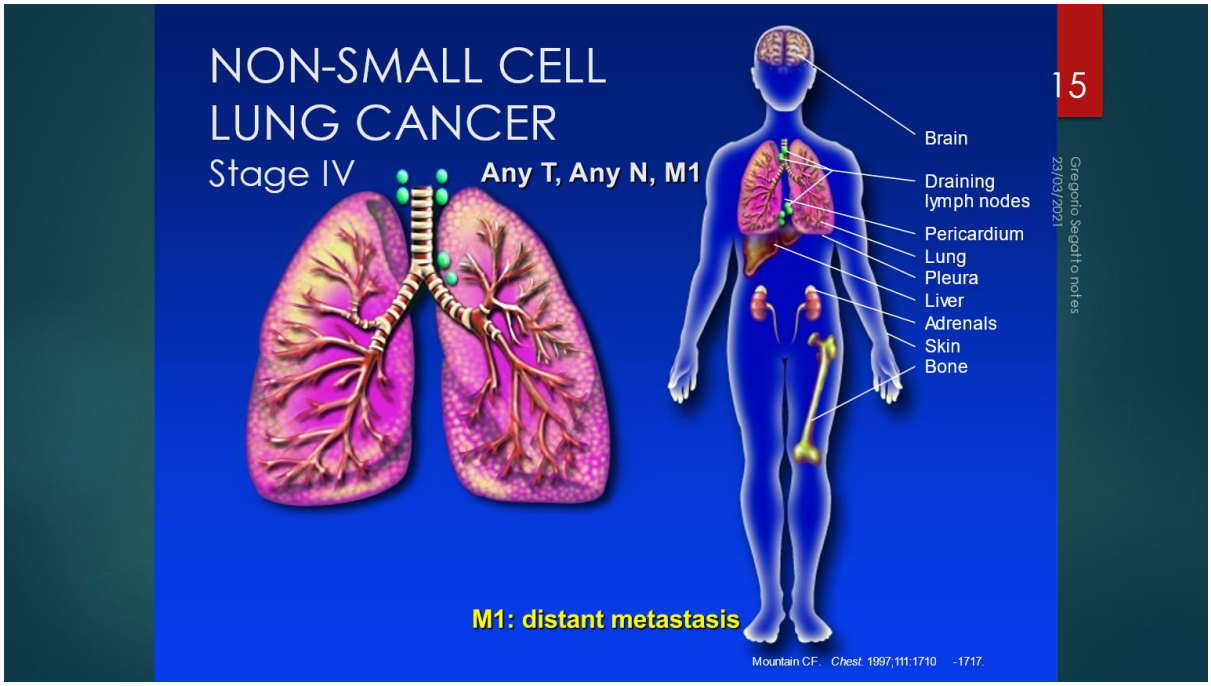


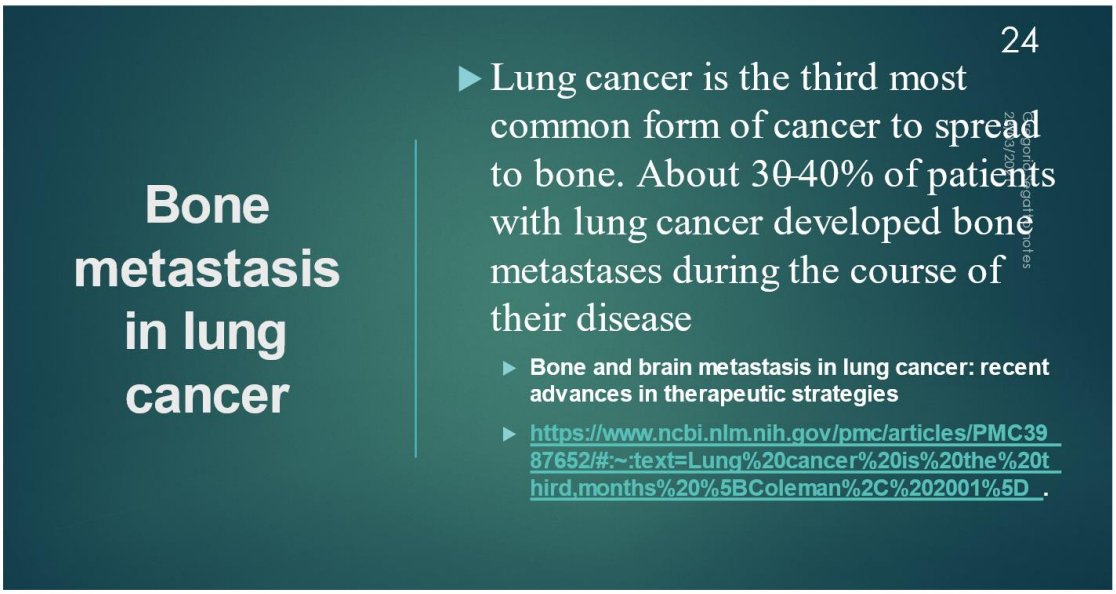
Sign and symptoms generally do not appear until tumors restrict airflow or compress adjacent structures. Chest pain, shortness of breath, a cough or a wheeze, and weight loss commonly occur. Treatment program vary with the cellular organization of the tumor and whether metastasis (cancer cell migration) has occurred. Surgery, chemotherapy and radiation therapu may be involved.




NON-SMALL CELL LUNG CANCER
Signs and symptoms at diagnosis
8
Gregorio Segatto notes 23/03/2021
Cough 40 75
Dyspnea 30 40
Chest Pain 25 40
Hemoptysis 15 35
Pneumonitis 15 25
Weight Loss 40 50
Generalized Weakness 35
Anorexia 35
Fever 15
Anemia 15
Frequency (%)


NON-SMALL CELL LUNG CANCER
Stages at presentation
10
Gregorio Segatto notes 23/03/2021
7% Stage II
31% Stage III
24% Stage I
38% Stage IV
Fry WA, et al. Cancer. 1996;77:1949 -1995.


NON-SMALL CELL LUNG CANCER
Stage IV
Any T, Any N, M1
15
Gregorio Segatto notes 23/03/2021
Brain
Draining lymph nodes
Pericardium
Lung
Pleura
Liver
Adrenals
Skin
Bone
M1: distant metastasis
Mountain CF. Chest. 1997;111:1710 -1717.

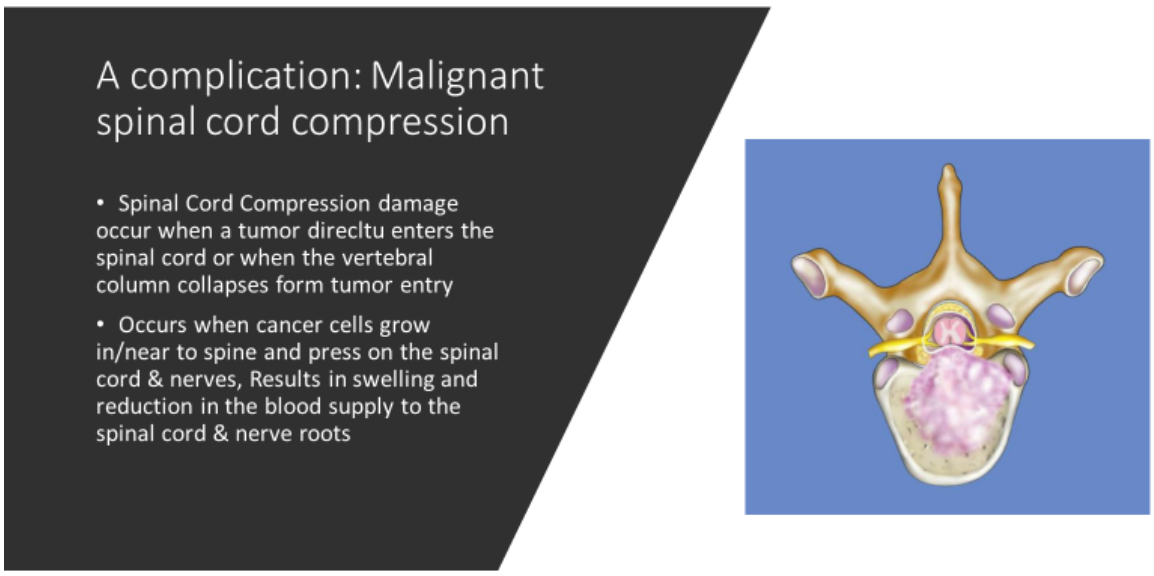


4.1 Malignant spinal cord compression

Definition

Spinal Cord Compression damage occur when a tumor directly enters the spinal cord or when the vertebral column collapses form tumor entry.

Malignant spinal cord compression (MSCC) happens when cancer grows in or near the spine and presses on the spinal cord and nerves. It is a rare condition, but it is potentially serious. Occurs when cancer cells grow in/near to spine and press on the spinal cord & nerves, Results in swelling and reduction in the blood supply to the spinal cord & nerve roots.

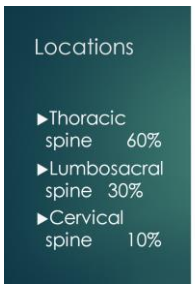


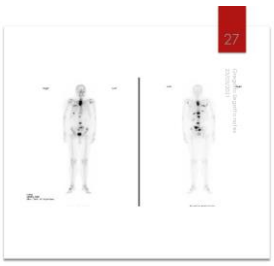
4.2 MSCC types of cancer and location

Any type of cancer can spread to the bones of the spine, but MSCC is more common in people with:

- *Breast*
- *Lung*
- *Prostate*
- *Lymphoma*
- *Myeloma*

3-5% of patients with cancer overall





Locations:

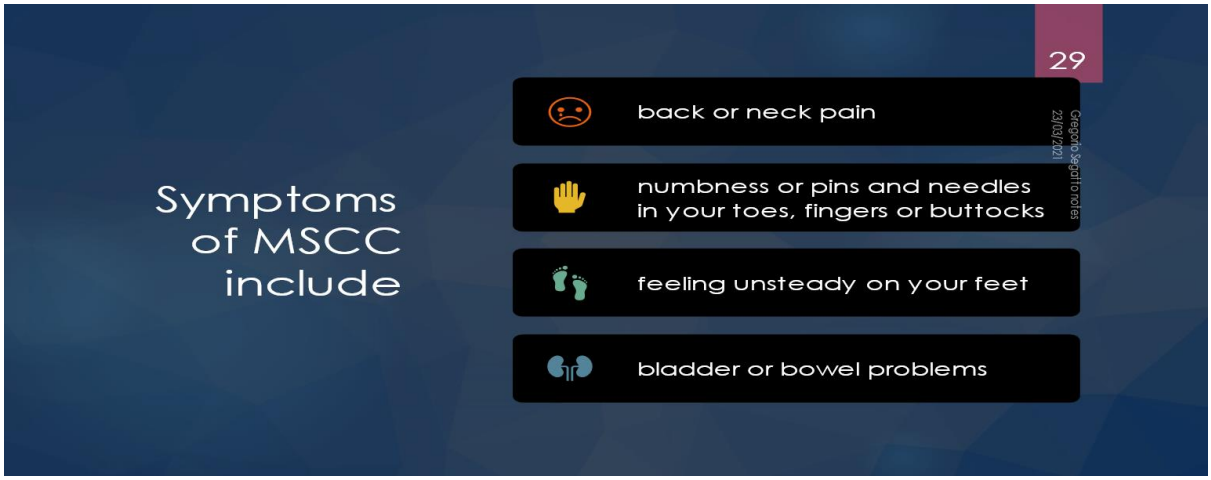
- Thoracic spine 60%
- Lumbosacral spine 30%
- Cervical spine 10%

Method of spread:

- 85%From vertebral body or pedicle
- 10% Through intervertebral foramina (from paravertebral nodes or mass)
- 4% Intramedullary spread
- 1%(Low) Direct spread to epidural space

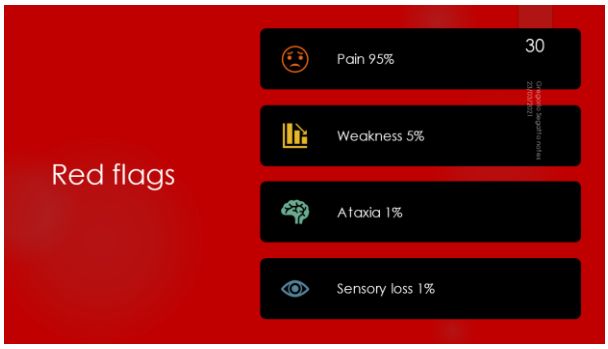
4.3 signs and symptoms – red flags

The symptoms are caused by the increasing pressure (compression) on the spinal cord & nerves



Symptoms of MSCC include:

- *back or neck pain*
- *numbness or pins and needles in your toes, fingers or buttocks*
- *feeling unsteady on your feet*
- *bladder or bowel problems*



First symptoms (Red Flags):

- Pain 95%
- Weakness 5%
- Ataxia 1%
- Sensory loss 1%

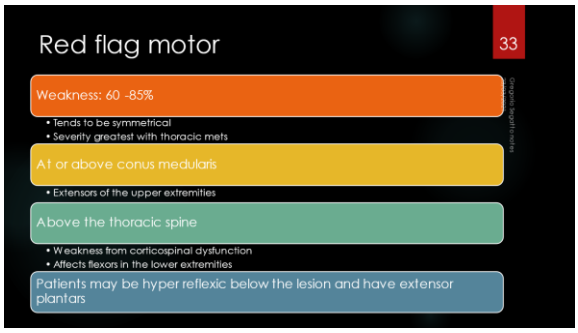
Pain:

- Usually first symptom – 80-90% of the time
- Usually precedes other neurologic symptoms by 7 weeks – Increases in intensity
- Severe local back pain
- Aggravated by lying down – Distension of venous plexus

Back pain

- may be mild at the beginning
- lasts for more than 1 - 2 weeks
- Uremitting pain
- Pain may feel like a belt around the chest or abdomen (radicular)
- Can radiate over the lower back, into the buttocks or legs

Red flag motor:



Weakness: 60-85%

- Tends to be symmetrical
- Severity greatest with thoracic mets
- At or above conus medularis
- Extensors of the upper extremities
- Above the thoracic spine
  - Weakness from corticospinal dysfunction
  - Affects flexors in the lower extremities
- Patients may be hyper reflexic below the lesion and have extensor plantars

Red flag sensory

Less common than motor findings

- Still present in majority of cases
- Ascending numbness and parathesias
- Numbness or 'pins and needles' in toes & fingers or over the buttocks
  - Sensory level
  - Saddle anaesthesia
- Feeling unsteady on feet, having difficulty with walking, or legs giving way

Red flag: Bladder and bowel function

- Loss of bladder and bowel function is late finding
- Problems passing urine
  - Incontinence – may include difficulty controlling bladder function
  - Oliguria – passing very little urine
  - Anuria – passing none at all
- Constipation or problems or controlling bowels
- Autonomic neuropathy presents usually as urinary retention
  - Rarely sole finding

Duration of symptoms before diagnosis: 2 – 5 months median

Requires very prompt diagnosis & treatment to try and prevent catastrophic consequences of paralysisand incontinence. It is an oncological emergency.

4.4 Differential diagnosis:

- Metastatic cancer
- Herniated disc
- Benign bony lesion
- Abscess
- Alcoholic neuropathy
- Primary tumour
- Osteoporosis
- Low potassium

4.5 Investigations, information needed prior and treatment

- MRI scan of the whole spine

    - Can get compression at multiple levels
- Knowledge of cancer type & stage
- Knowledge of patient fitness
- Current neurological function
    - Have they lost power in their legs?
    - Can they walk?
    - Do they need a catheter?
- Do they have pain?

Until spinal stability is confirmed patients should be managed on bed rest, BUT Wherever possible keep the patient moving

4.6 Treatment options include:

1. Steroids & gastric protection
2. Analgesia
3. Surgery – decompression & stabilisation of the spine
4. Radiotherapy
5. Chemotherapy e.g. lymphoma
6. Hormonal manipulation e.g. prostate Ca

Direct decompressive surgery: Relieves compression, Removes tumour and Stabilises spine, but many patients not suitable because Unfit and Tumour factors.

Radiotherapy: Urgent access 24/7, Dose & schedule is depending on neurological deficit, Performans status, previous treatment and cancer features, single fraction vs fractionated treatment

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