Presentation of malignancy

The Formation & Growth of Cancer (REVIEW)

I. Random genetic mutations. BRCA1 (breast ca gene 1) human tumor suppressor gene (also known as a caretaker gene).

II. Resisting cell death:

1. *Apoptosis(programmed).reduced in ca. Regulated by the TP53.*
2. *Autophagy* a catabolic process during which cellular constituents are degraded by lysosoms within the cell.
3. *Necrosis* is the premature death of cells.done by inflaammatory response(stimulatory signals for proliferation.
4. Sustaining proliferative signaling
   - Cancer cells can sustain proliferation beyond what would be expected for normal cells; this is typically due to disturbances in intracellular growth factors.

- The most important regulator of apoptosis is the TP53 tumour suppressor gene.
- often described as the ‘guardian of the genome’, as it is able to induce apoptosis in response to sufficient levels of genomic damage.

III. Activating invasion and metastasis:

- Cadherin-1 (CDH1) is a calcium-dependent cell–cell adhesion glycoprotein that facilitates assembly of organized cell sheets in tissues.
- Increased expression is recognized as an antagonist of invasion and metastasis.

RISK

- **Tobacco**: **30%** of cancers (Lung, Nasopharyngeal, Urinary bladder)

Diet and alcohol:

- 30% of cancers (Oesophagus, Stomach, Liver, Colon, Breast).
- low fiber -high fat-preservatives –toxins.

Dietary factors	Low-roughage/high-fat content diet	Colonic cancer
	High nitrosamine intake	Gastric cancer
	Aflatoxin from contamination of *Aspergillus flavus*	Hepatocellular cancer

- Infections: 15% of cancers (Cervix, Stomach, Liver,NP UB).

Viral infection	Epstein–Barr virus Human papillomavirus Hepatitis B and C viruses	Burkitt's lymphoma and nasopharyngeal cancer Cervical cancer Hepatocellular carcinoma
Bacterial infection	*Helicobacter pylori*	Gastric MALT lymphomas, gastric cancer
Parasitic infection	Liver fluke (*Opisthorchis sinensis*) *Schistosoma haematobium*	Cholangiocarcinoma Squamous cell bladder cancer

Environmental aetiology	Processes	Diseases
Occupational exposure (see also ultraviolet and radiation)	Dye and rubber manufacturing (aromatic amines)	Bladder cancer
	Asbestos mining, construction work, shipbuilding (asbestos)	Lung cancer and mesothelioma
	Vinyl chloride (PVC) manufacturing	Liver angiosarcoma
	Petroleum industry (benzene)	Acute leukaemia
Chemicals	Chemotherapy (e.g. melphalan, cyclophosphamide)	Acute myeloid leukaemia
Cigarette smoking	Exposure to carcinogens from inhaled smoke	Lung and bladder cancer
Viral infection	Epstein–Barr virus	Burkitt's lymphoma and nasopharyngeal cancer
	Human papillomavirus	Cervical cancer
	Hepatitis B and C viruses	Hepatocellular carcinoma
Bacterial infection	*Helicobacter pylori*	Gastric mucosa-associated lymphoid tissue (MALT) lymphomas, gastric cancer
Parasitic infection	Liver fluke *(Opisthorchis sinensis)*	Cholangiocarcinoma
	Schistosoma haematobium	Squamous cell bladder cancer
Dietary factors	Low-roughage/high-fat content diet	Colonic cancer
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	Aflatoxin from contamination of *Aspergillus flavus*	Hepatocellular cancer
Radiation	Ultraviolet (UV) exposure	Basal cell carcinoma
		Melanoma
		Non-melanocytic skin cancer
	Nuclear fallout following explosion (e.g. Hiroshima)	Leukaemia
		Solid tumours, e.g. thyroid
	Diagnostic exposure (e.g. computed tomography (CT))	Cholangiocarcinoma following thorotrast usage
	Occupational exposure (e.g. beryllium and strontium mining)	Lung cancer
	Therapeutic radiotherapy	Medullary thyroid cancer
		Sarcoma
Inflammatory diseases	Ulcerative colitis	Colon cancer
Hormonal	Use of diethylstilbestrol	Vaginal cancer
	Oestrogens	Endometrial cancer
		Breast cancer

Prevention:

- The prevention of disease by altering susceptibility or reducing exposure for susceptible individuals.

Screening:

- The application of tests to detect cancer in asymptomatic people.

Early Detection:

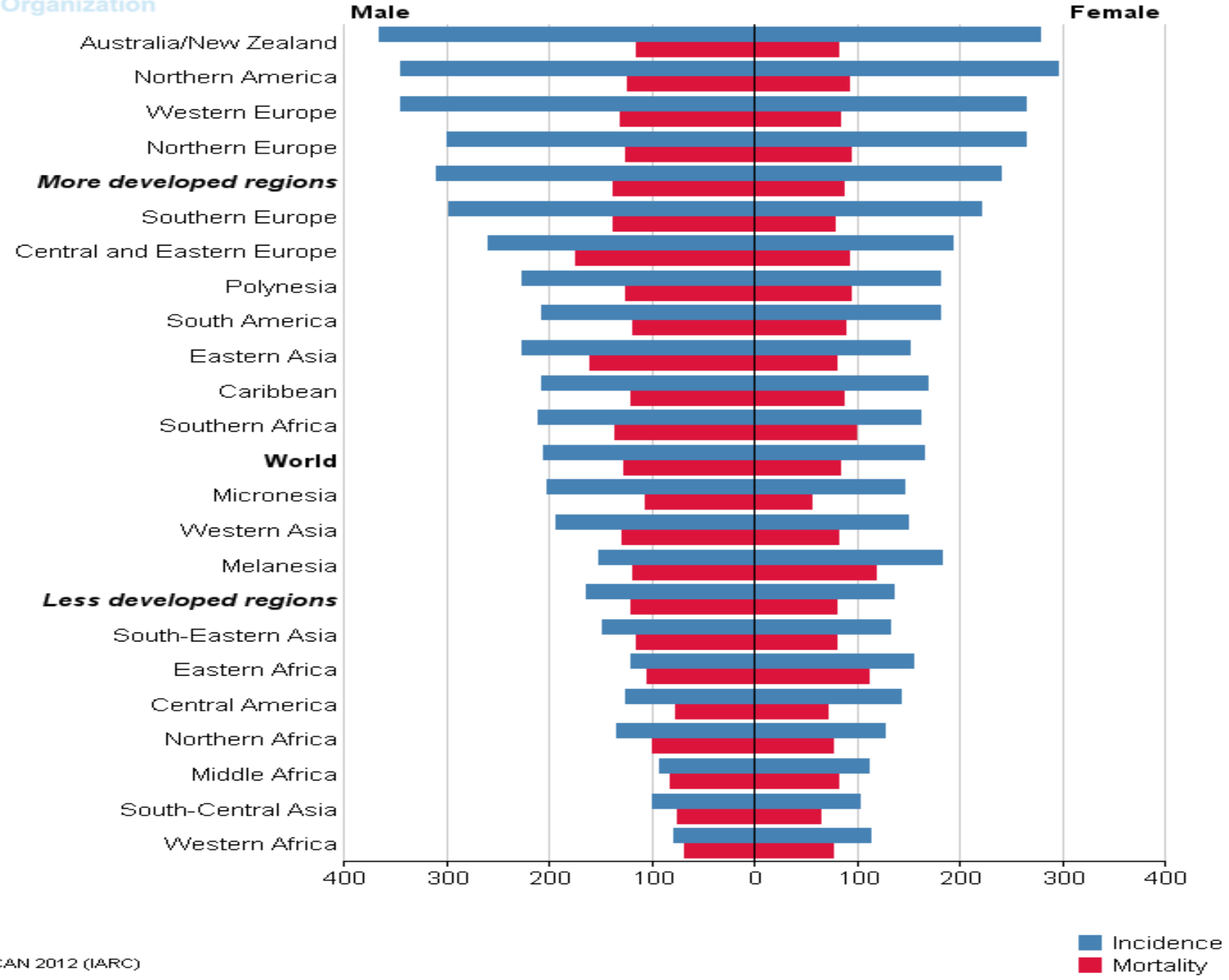
- Physician evaluation of a person who may or may not have symptoms.

Risk reduction:

- Smocking, high fat diet, increase fruits ..

Most Common Cancers

Men		Women	
Incidence	Mortality	Incidence	Mortality
1. Prostate	1. Lung	1. Breast	1 Lung
2. Lung	2. Prostate	2. Lung	2. Breast
Colorectal		Colorectal	



GLOBOCAN 2012 (IARC)

Approach..

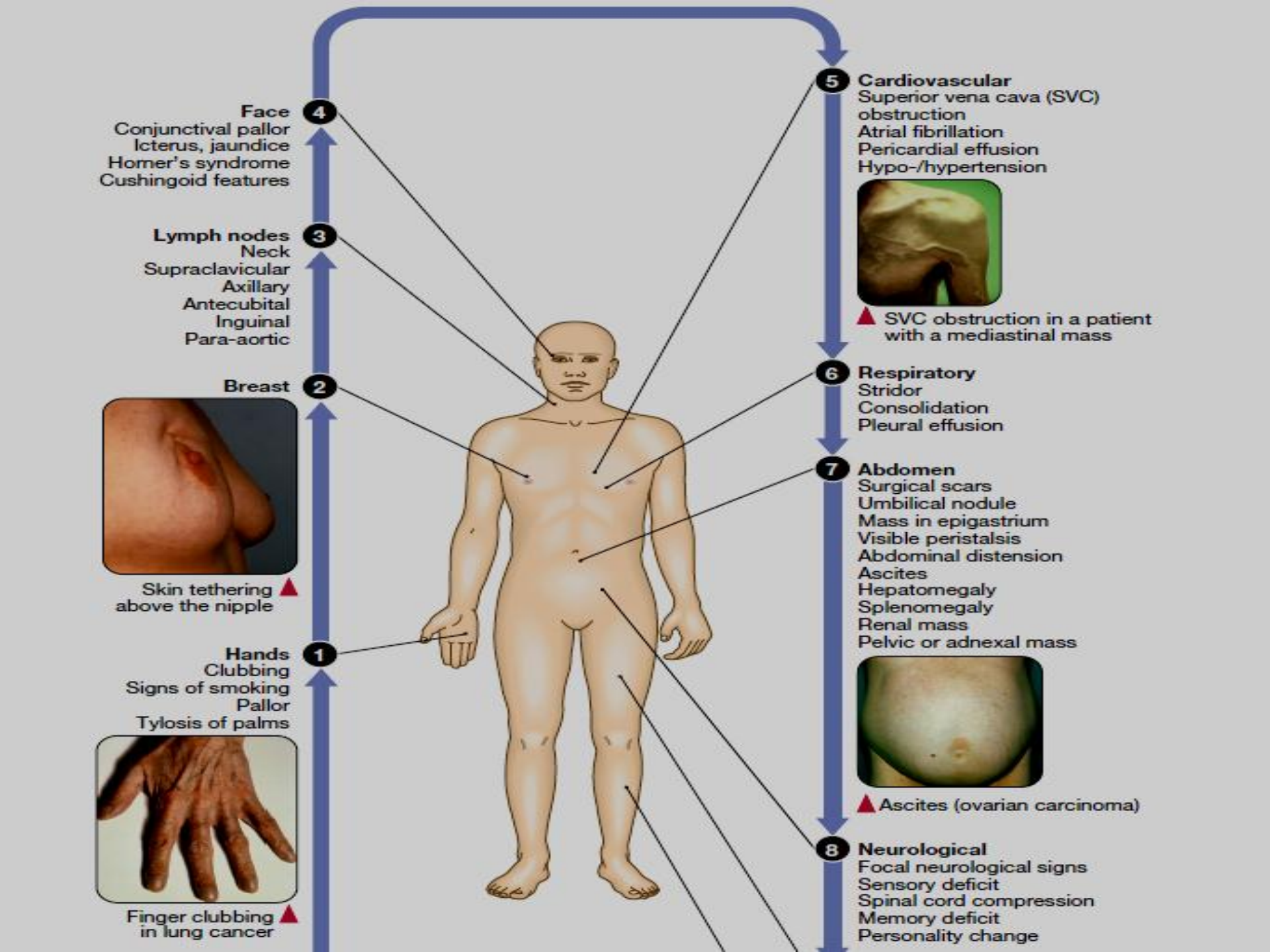
Taking history:

- Full history including risk factors.
- Family or personal history of cancer.
- Tobacco use & Alcohol consumption.
- Eating behaviours.
- Sexual practice.
- Occupation.
- Medications >> hormones.

Examination & Tests

- Thorough clinical examination.
- Information needed on:

A. Type of tumour.
B. Extent of disease (staging)
C. The patient's general condition and any co morbidity.


1 Hands
Clubbing
Signs of smoking
Pallor
Tylosis of palms
Finger clubbing in lung cancer
2 Breast
Skin tethering above the nipple
3 Lymph nodes
Neck
Supraclavicular
Axillary
Antecubital
Inguinal
Para-aortic
4 Face
Conjunctival pallor
Icterus, jaundice
Horner's syndrome
Cushingoid features
5 Cardiovascular
Superior vena cava (SVC) obstruction
Atrial fibrillation
Pericardial effusion
Hypo-/hypertension
SVC obstruction in a patient with a mediastinal mass
6 Respiratory
Stridor
Consolidation
Pleural effusion
7 Abdomen
Surgical scars
Umbilical nodule
Mass in epigastrium
Visible peristalsis
Abdominal distension
Ascites
Hepatomegaly
Splenomegaly
Renal mass
Pelvic or adnexal mass
Ascites (ovarian carcinoma)
8 Neurological
Focal neurological signs
Sensory deficit
Spinal cord compression
Memory deficit
Personality change

Cushing's syndrome in a patient with ectopic adrenocorticotrophic hormone (ACTH) production

Observation

- Skin changes
- Ascites
- Cushingoid appearance
- Cachexia
- Dehydration

9 Skeletal survey

Focal bone tenderness (pelvis, spine, long bones)

Wrist tenderness (hypertrophic pulmonary osteoarthropathy)

10 Periphery

Calf tenderness, venous thrombosis

Clubbing (if present in hands)

11.6 Local features of malignant disease

Symptom	Typical site or possible tumour
Haemorrhage	Stomach, colon, bronchus, endometrium, bladder, kidney
Lump	Breast, lymph node (any site), testicle
Bone pain or fracture	Bone (primary sarcoma, secondary metastasis from breast, prostate, bronchus, thyroid, kidney)
Skin abnormality	Melanoma, basal cell carcinoma (rodent ulcer)
Ulcer	Oesophagus, stomach, anus, skin
Dysphagia	Oesophagus, bronchus, gastric
Increasing constipation, abdominal discomfort or pain	Colon, rectum, ovary
Airway obstruction, stridor, cough, recurrent infection	Bronchus, thyroid
Odynophagia, early satiety, vomiting	Bronchus, stomach, oesophagus, colon, rectum
Abdominal swelling (ascites)	Ovary, stomach, pancreas

HISTOPATHOLOGY

- Biopsy.
- Light microscopy -e/m
- Immuno-Histo-chemical staining.
- Cytogenetic studies.

RADIOLOGY

- X-ray
- Uss
- CT
- MRI
- Bone scans etc

Tumor markers

- Many tumours produce tumour markers (TM).
- Not sufficiently sensitive or specific to be used in isolation.
- **AFP**: HCC, ovarian germ cell tumours (non-seminomatous, testicular teratoma).
- **CEA**: colon, rectum, breast, stomach, ovary.
- **CA-19-9**: pancreas, colon, stomach, ovary.
- **PSA**: prostate (95%).

11.5 Commonly used serum tumour markers

Name	Natural occurrence	Tumours
Alpha-fetoprotein (AFP)	Glycoprotein found in yolk sac and fetal liver tissue. Transient elevation in liver diseases. Has a role in screening during pregnancy for the detection of neural tube defects and Down's syndrome	Ovarian non-seminomatous germ cell tumours (80%), testicular teratoma (80%), hepatocellular cancer (50%)
Calcitonin	32 amino acid peptide from C cells of thyroid. Used to screen for MEN-2	Medullary cell carcinoma of thyroid
Cancer antigen 125 (CA-125)	Differentiation antigen of coelomic epithelium (Muller's duct). Raised in any cause of ascites, pleural effusion or heart failure. Can be raised in inflammatory conditions	Ovarian epithelial cancer (75%), gastrointestinal cancer (10%), lung cancer (5%) and breast cancer (5%)
CA-19.9	A mucin found in epithelium of fetal stomach, intestine and pancreas. It is eliminated exclusively via bile and so any degree of cholestasis can cause levels to rise	Pancreatic cancer (80%), mucinous tumour of the ovary (65%), gastric cancer (30%), colon cancer (30%)
Carcinoembryonic antigen (CEA)	Glycoprotein found in intestinal mucosa during embryonic and fetal life. Elevated in smokers, cirrhosis, chronic hepatitis, ulcerative colitis, pneumonia	Colorectal cancer, particularly with liver metastasis, gastric cancer, breast cancer, lung cancer, mucinous cancer of the ovary
Human chorionic gonadotrophin (hCG)	Glycoprotein hormone, 14KD α subunit and 24KD β subunit from placental syncytiotrophoblasts. Used for disease monitoring in hydatidiform mole and as the basis of a pregnancy test	Choriocarcinoma (100%), hydatidiform moles (97%), ovarian non-seminomatous germ cell tumours (50–80%), seminoma (15%)
Placental alkaline phosphatase (PLAP)	Isoenzyme of alkaline phosphatase	Seminoma (40%), ovarian dysgerminoma (50%)
Prostate-specific antigen (PSA)	Glycoprotein member of human kallikrein gene family. PSA is a serine protease that liquefies semen in excretory ducts of prostate. Can be elevated in benign prostatic hypertrophy and prostatitis	Prostate cancer (95%)
Thyroglobulin	Matrix protein for thyroid hormone synthesis in normal thyroid follicles	Papillary and follicular thyroid cancer
β-2-microglobulin	A human leucocyte antigen (HLA) common fragment present on surface of lymphocytes, macrophages and some epithelial cells. Can be elevated in autoimmune disease and renal glomerular disease	Non-Hodgkin's lymphoma, myeloma

PRESENTING PROBLEMS IN ONCOLOGY

- Bleeding.
- Mass /lump.
- Bone pain or fracture.
- Skin abnormality.
- Increase size of moles.
- Ulcer.
- Dysphagia, abdominal swelling (ascites).
- Loss of weight
- Change in elimination, increasing constipation, abdominal pain.

NON METASTATIC MANIFESTATIONS OF CANCER

- Fever: lymphoma, leukaemia, HepCCa, RenCCa.
- Weight loss and anorexia: lung, GIT cancers.
- Hypercalcaemia: myeloma, breast, kidney.
- Lambert- Eaton myasthenia like synd.: SCLungCa.
- Acanthosis nigricans: stomach, oesophagus.
- Dermatomyositis/polymyositis: stomach, lung.
- Ectopic ACTH: SCLC.
- SIADH: SCLC.

11.9 Ectopic hormone production by tumours

Hormone	Consequence	Tumours
ADH	Hyponatraemia	SCLC
ACTH	Cushing's syndrome	SCLC
FGF-23	Hypophosphataemic osteomalacia	Mesenchymal tumours
Insulin	Hypoglycaemia	Insulinoma
Erythropoietin	Polycythaemia	Kidney, hepatoma, cerebellar haemangioblastoma, uterine fibroids
PTHrP	Hypercalcaemia	NSCLC (squamous cell), breast, kidney

(ACTH = adrenocorticotrophic hormone; ADH = antidiuretic hormone; FGF = fibroblast growth factor; NSCLC = non-small cell lung cancer; PTHrP = parathyroid hormone-related protein; SCLC = small cell lung cancer)

NEUROLOGICAL PNS
Lambert-Eaton syndrome

- 60%: underlying cancer.
- Proximal muscle weakness that improves on exercise.
- Abs to pre-synaptic calcium channels.
- Diagnosis: EMG.

METASTATIC DISEASE

- Major cause of death in cancer patients.
- The principal cause of morbidity.
- Treatment:
  - Solitary may be curative.
  - Palliative.

SHARED DECISION-MAKING MEETS GUIDELINE-BASED MEDICINE.

Cancer	Preferred Method	Population	Age group	Frequency	Reduction in cancer related death
Breast	Mammography	**Avg Risk**	40-75	Annual	30%
Cervix	PAP smear	**Avg Risk**	21-65	Once every 3 years	70%
Colon	Fecal Occult Blood/ Colonoscopy	**Avg Risk**	>50	Annual/ Once every 10 years	25%
Oral	Clinical Examination	**High Risk**	-	Annual	-
Lung	LDCT scan	**High Risk**	50-74	Annual	20%
Prostate	DRE+PSA	**Avg Risk**	50-70	Once every 2 years	44%