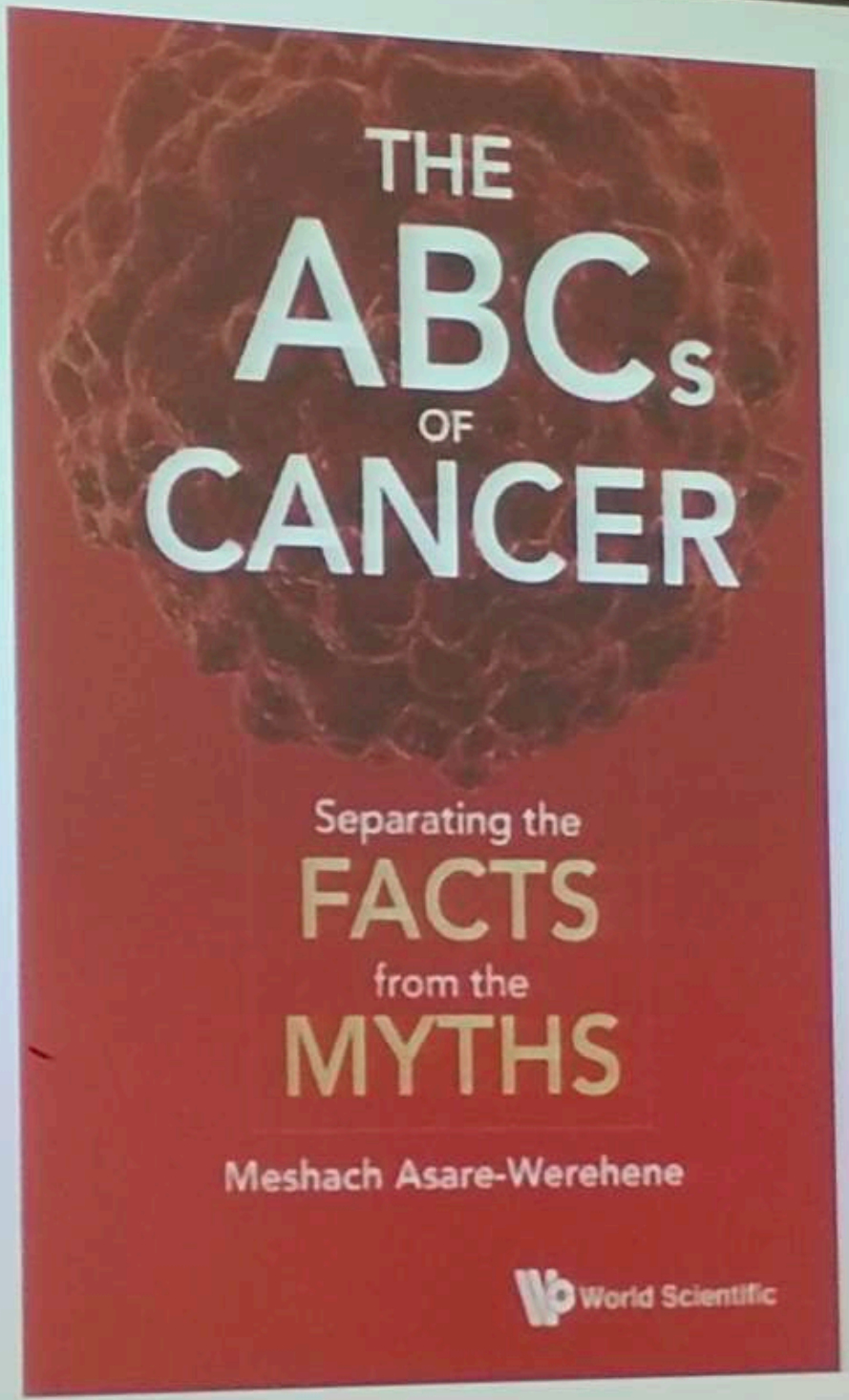
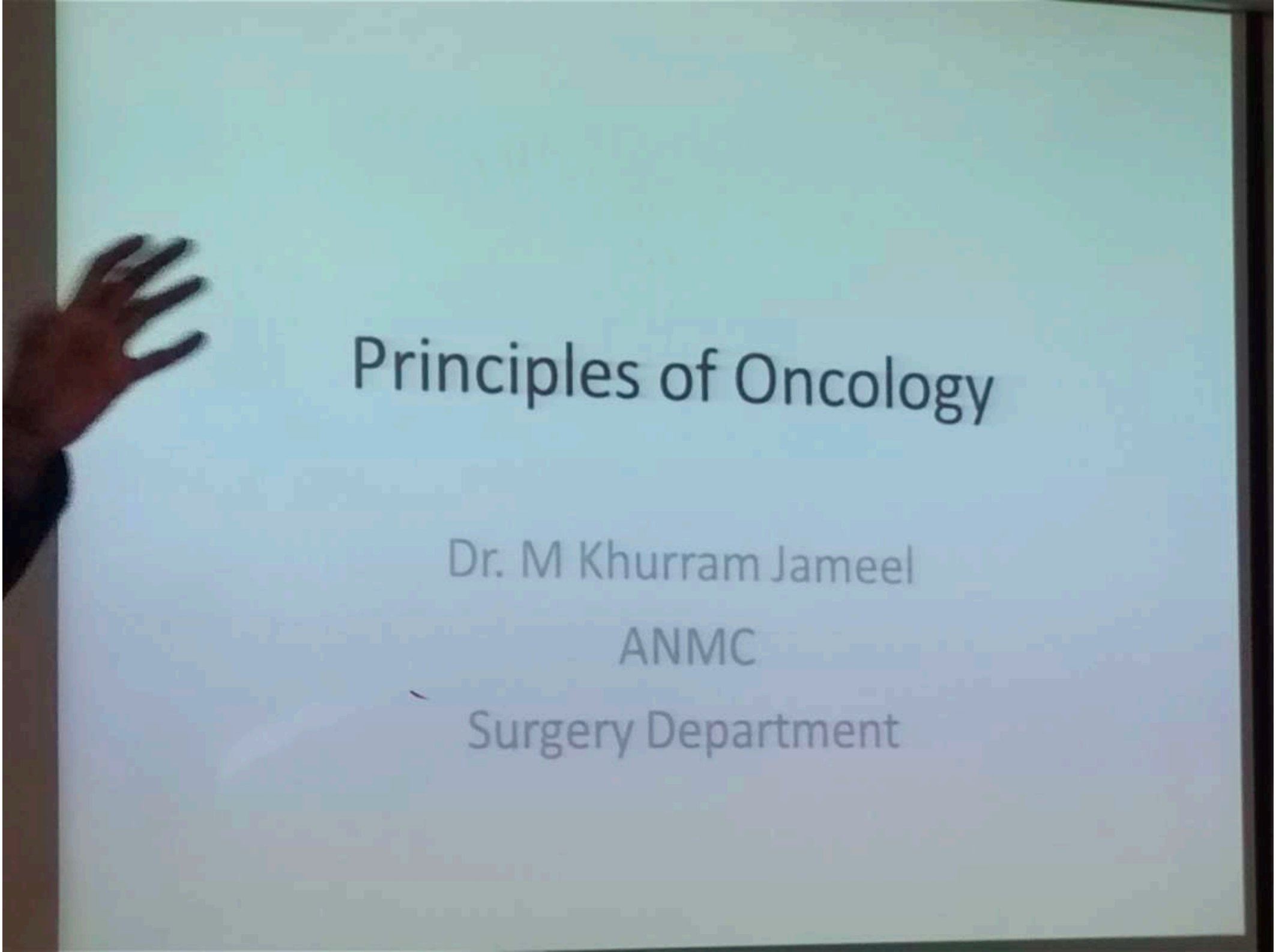

THE
ABCs
OF
CANCER
Separating the
FACTS
from the
MYTHS
Meshach Asare-Werehene
World Scientific


Principles of Oncology
Dr. M Khurram Jameel
ANMC
Surgery Department

- The name cancer from the Greek word for a Crab (καρκινος).

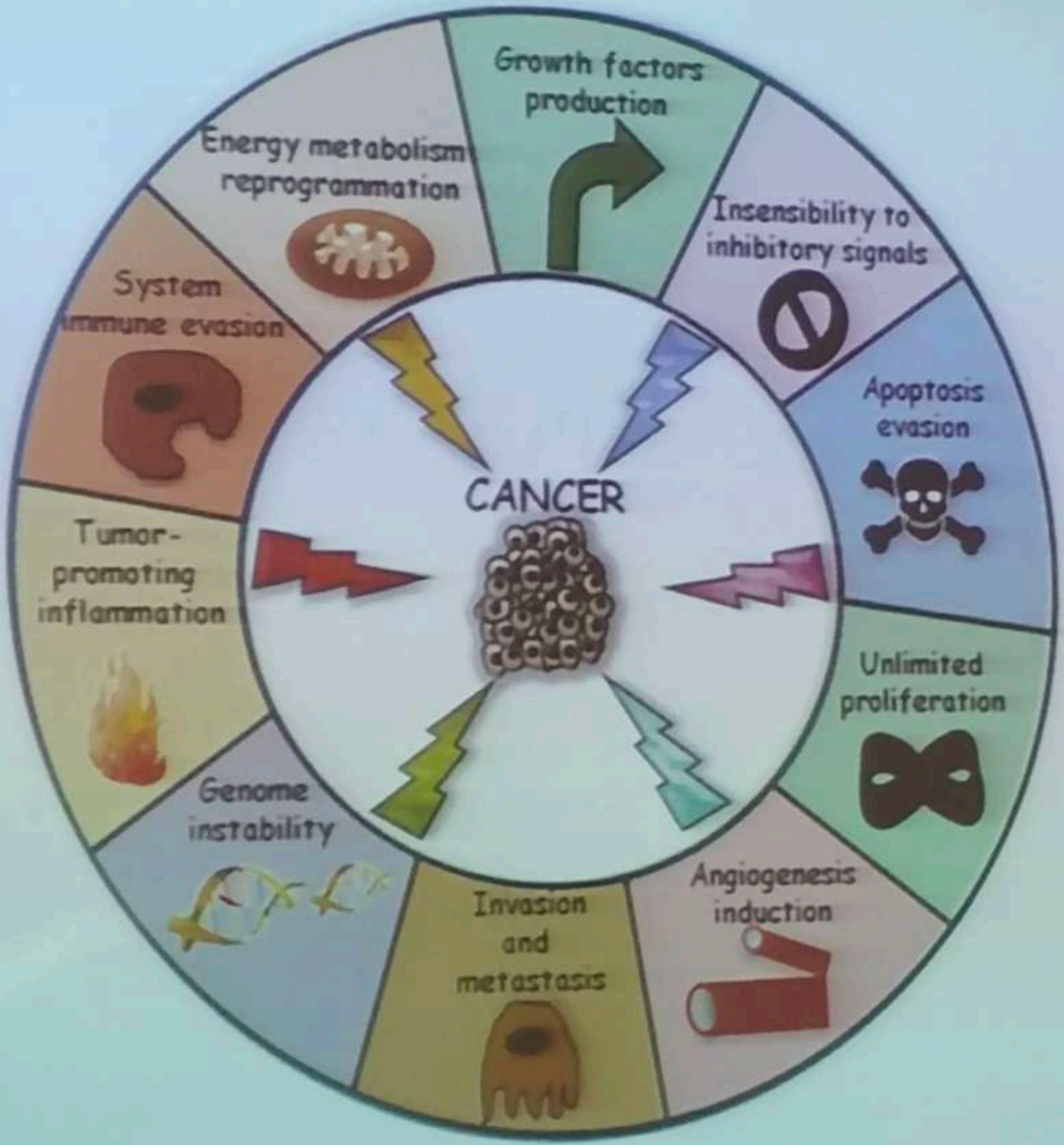
- Rudolf Virchow - cancer is a disease of cells and that the disease progresses as a result of abnormal proliferation
- 'omnes cellula e cellula' (every cell from a cell).

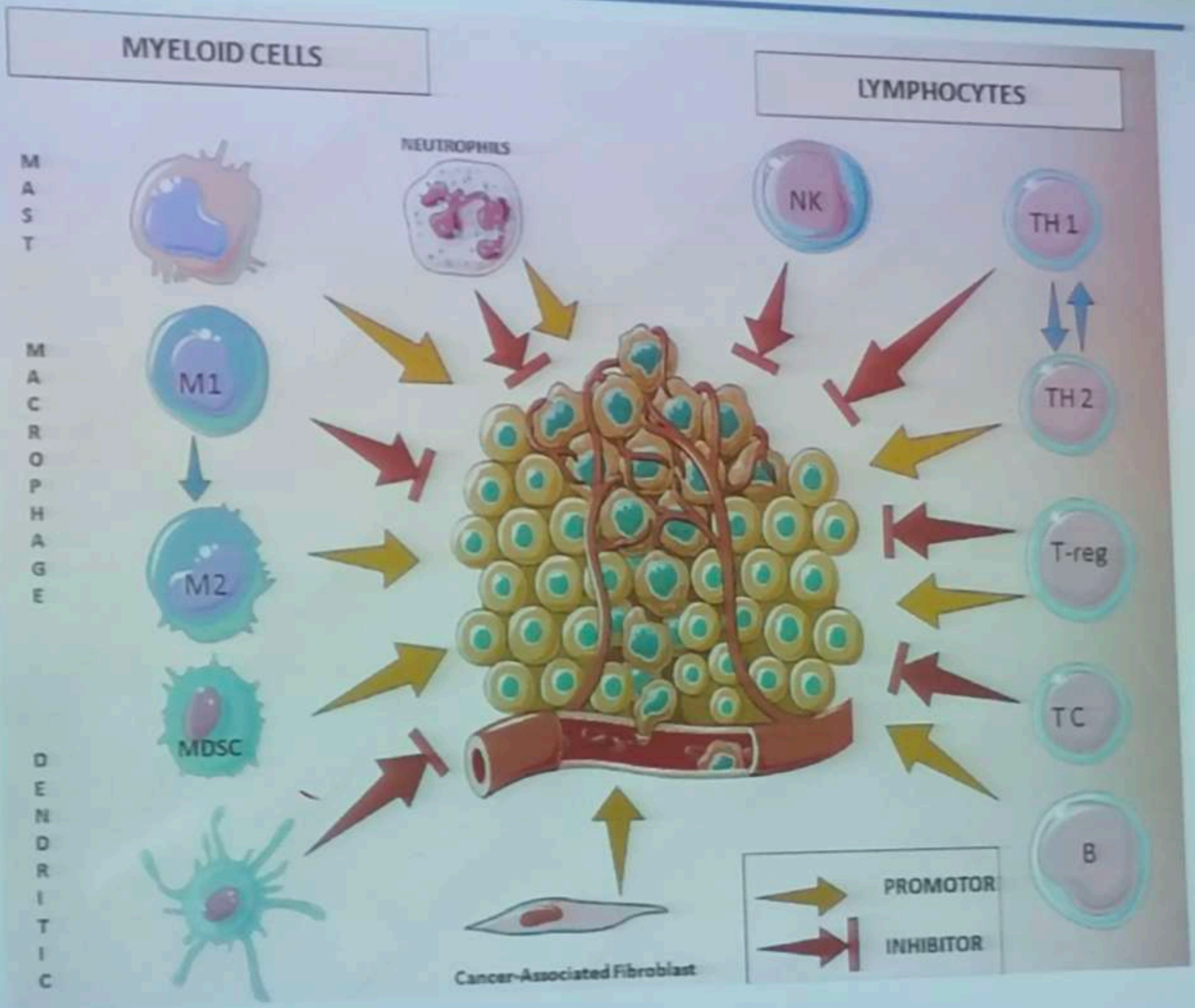
- Cancer cells are psychopaths.

Features of Malignant Transformation

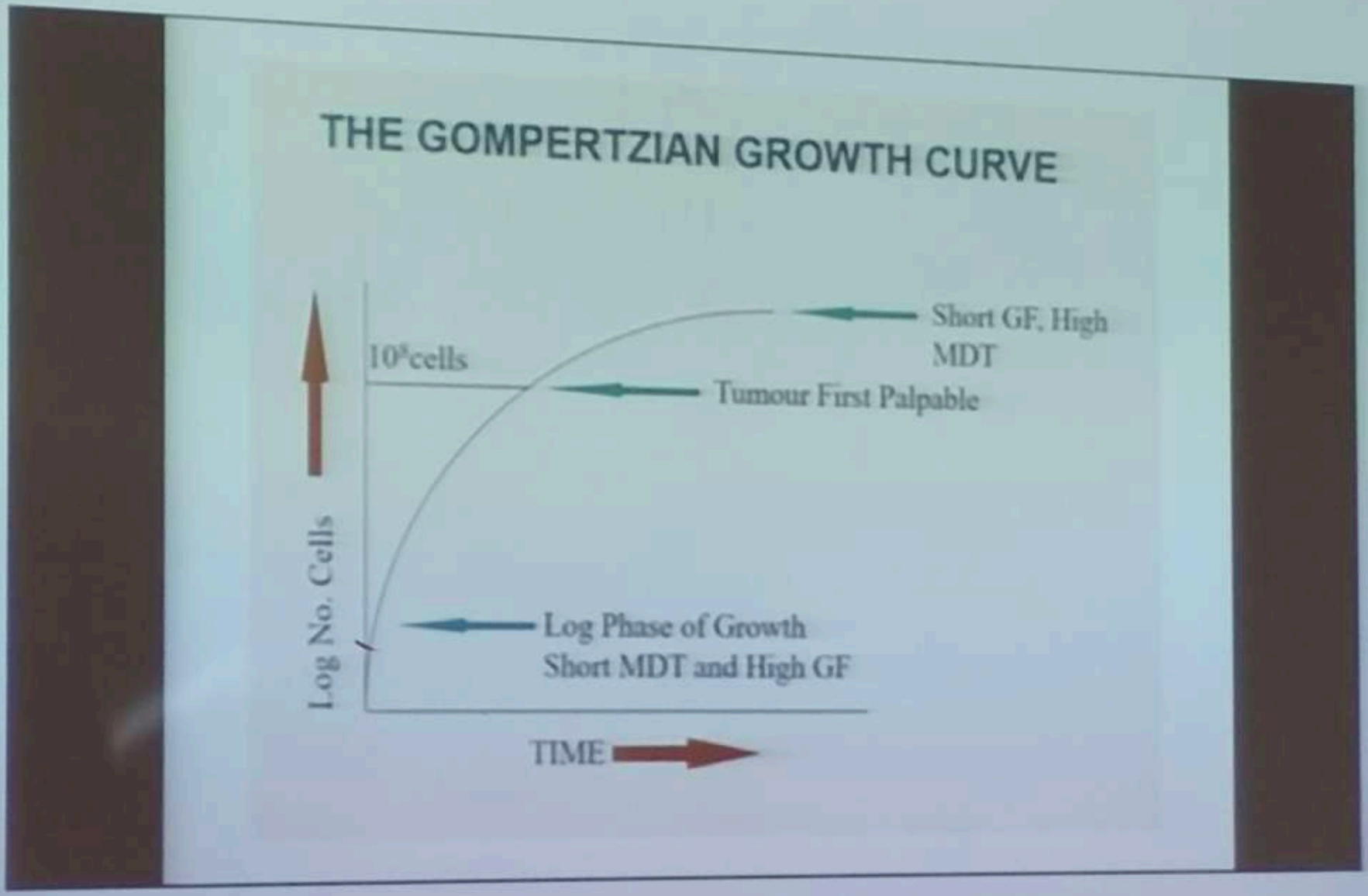
- Establish an autonomous lineage
  - Resist signals that inhibit growth
  - Sustain proliferative signalling

- Obtain replicative immortality
- Evade apoptosis
- Acquire angiogenic competence
- Acquire ability to invade
- Acquire ability to disseminate and implant
- *Evocation of inflammation*
- *Genomic Instability*
- Evade detection/elimination
- Subvert communication to and from the cellular environment
- Develop ability to change energy metabolism


Growth factors production
Insensibility to inhibitory signals
Apoptosis evasion
Unlimited proliferation
Angiogenesis induction
Invasion and metastasis
Genome instability
Tumor-promoting inflammation
System immune evasion
Energy metabolism reprogrammation
CANCER


MYELOID CELLS
LYMPHOCYTES
MAST
NEUTROPHILS
NK
TH 1
MACROPHAGE
M1
TH 2
M2
T-reg
MDSC
TC
DENDRITIC
B
Cancer-Associated Fibroblast
PROMOTOR
INHIBITOR

Tumour Growth Curve



The Implications of Gompertzian growth

- The majority of the growth of a tumour occurs before it is clinically detectable
- By the time they are detected, tumours have passed the period of most rapid growth, that period when they might be most sensitive to antiproliferative drugs
- There has been plenty of time, before diagnosis, for individual cells to detach, invade, implant, and form distant metastases. In many patients cancer may, at the time of presentation, be a systemic disease
- 'Early tumours' are genetically old, yielding many opportunities for mutations to occur, mutations that might confer spontaneous drug resistance (a probability greatly increased by the existence of cell loss)
- The rate of regression of a tumour will depend upon its age (the Norton–Simon hypothesis extends this: chemotherapy results in a rate of regression in tumour volume that is proportional to the rate of growth for an unperturbed tumour of that size.

THE CAUSES OF CANCER

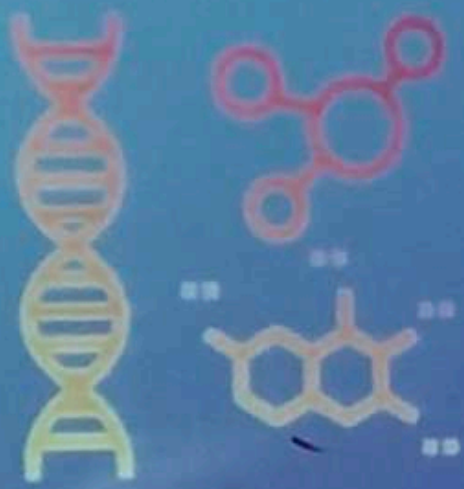
- The interplay between nature and nurture
- Neither influence is totally dominant

Nature

genetics

physical appearance

biological influences



Nurture

environment

upbringing

social influences

Inherited Syndrome with Cancer

Syndrome	Gene	In	Assoc tumor	strategy
FAP	APC	D	Colorectal cancer Papillary carcinoma of the thyroid Cancer of the ampulla of Vater Hepatoblastomas Primary brain tumours (Turcot syndrome),Osteomas of the jaw	Prophylactic panproctocolectomy
HNPCC	DNA Mismatch	D	Colorectal cancer (typically in 40s and 50s) Endometrium, stomach, hepatobiliary (Lynch syndrome 1)	Surveillance colonoscopies / polypectomies NSAID
PETZ JEGURS SYNDROME	STK11	D	Bowel cancer; breast cancer; freckles round the mouth	Surveillance colonoscopy; mammography
COWDEN	PTEN	D	Multiple hamartomas of skin, breast and mucous membranes Breast cancer Neuroendocrine tumours Endometrial cancer Thyroid cancer	Active surveillance

MEN 1	MENIN	D	Parathyroid tumours Islet cell tumours Pituitary tumours	Awareness of associations and paying attention to relevant symptoms
MEN 2		D	Medullary carcinoma of the thyroid Phaeochromocytoma Parathyroid tumours	Regular screening of blood pressure, serum calcitonin and urinary catecholamines Prophylactic thyroidectomy
LI-FRAUMENI	P53	D	Sarcomas , Leukaemia Osteosarcomas Brain tumours Adrenocortical CA	Very difficult, since pattern of tumours is so heterogeneous and varies from patient to patient
Familial Breast Cancer	BRCA 1 , 2	D	Breast cancer Ovarian cancer Papillary serous carcinoma of the peritoneum Prostate cancer	Screening mammography; pelvic ultrasound; PSA (in males) Prophylactic mastectomy; prophylactic oophorectomy

Environmental/ behavioural factor	Associated tumours	Strategy for prevention/early diagnosis
Tobacco	Lung cancer Head and neck cancer	Ban tobacco Ban smoking in public places Punitive taxes on tobacco
Alcohol	Head and neck cancer Oesophageal cancer Hepatoma	Avoid excess alcohol Surveillance of high-risk individuals
UV	Melanoma Non-melanoma skin cancer	Avoid excessive sun exposure, avoid sunbeds
Ionising radiation	Leukaemia Breast cancer Lymphoma Thyroid cancer	Limit medical exposures to absolute minimum; safety precautions at nuclear facilities; monitor radiation workers

imp

Environmental/behavioural factor			Associated tumours	Strategy for prevention/early diagnosis
Viral infections	Human papillomavirus (HPV)		Cervical cancer Penile tumours	Avoid unprotected sex Vaccination
	Human immunodeficiency virus (HIV)		Kaposi's sarcoma Lymphomas Germ cell tumours Anal cancer	Avoid unprotected sex Antiretroviral therapy
	Hepatitis B		Hepatoma	Avoid contaminated injections/ infusions Vaccination
Other infections	Bilharzia		Bladder cancer	Treatment of infection Cystoscopic surveillance
	Helicobacter pylori		Stomach cancer	Eradication therapy
Inhaled particles	Asbestos		Mesothelioma	Protect workers from inhaled dusts and fibres
	Wood dust		Paranasal sinus cancers	
Chemicals	Environmental pollutants/chemicals used in industry		Angiosarcoma (vinyl chloride) Bladder cancer (aniline dyes, vulcanisation of rubber) Lung, nasal cavity (nickel) Skin (arsenic) Lung (beryllium, cadmium, chromium) All sites (dioxins)	Protection of exposed workers; avoid chemical discharge and spillages
	Medical	Alkylating agents used in cytotoxic chemotherapy	Leukaemia Lymphoma Lung cancer	Avoid over-treatment; only combine drugs with ionising radiation when absolutely necessary
		Immunosuppressive treatment	Kaposi's sarcoma	As low a dose as possible, for as short a period as possible
		Stilboestrol	Adenocarcinoma of vagina in daughters of treated mothers	Use of stilboestrol curtailed
		Tamoxifen	Endometrial cancer	Biopsy if patient on tamoxifen develops uterine bleeding
Fungal and plant toxins	Aflatoxins		Hepatoma	Appropriate food storage, screen for fungal contamination of foodstuffs
Obesity/lack of physical exercise			Breast Endometrium Kidney	Maintain ideal body weight, regular exercise

The Management of Cancer

- Management is more important than treatment.

- Prevention
- Screening
- Diagnosis and Classification
- Investigation and staging
- MDT
- Surgery
- Non-Surgery

Criteria for screening

- The disease:
  - Recognisable early stage
  - Treatment at early stage more effective than at later stage
  - Sufficiently common to warrant screening

The test:

Sensitive and specific

Acceptable to the screened population

Safe , Inexpensive

The programme:

- Adequate diagnostic facilities for those with a positive test
- High quality treatment for screen-detected disease to minimise morbidity and mortality
- Screening repeated at intervals if disease of insidious onset

Benefit must outweigh physical and psychological harm

The composition of the multidisciplinary team

- Site-specialist surgeon
- Surgical oncologist
- Plastic and reconstructive surgeon
- Clinical oncologist/radiotherapist
- Medical oncologist
- Diagnostic radiologist
- Palliative care physician
- Pathologist
- Speech therapist
- Physiotherapist
- Prosthetist
- Clinical nurse specialist (rehabilitation, supportive care)
- Macmillan nurse (symptom control, palliative care)
- Social worker/counsellor
- Medical secretary/administrator
- Audit and information coordinator

TABLE 10.6 The advantages and disadvantages of the multidisciplinary team.

Advantages	Disadvantages
Open debate concerning management	An opportunity for rampant egotism and showing-off
Patient has advantage of many simultaneous opinions from many different specialities	Less confident and less articulate members of the team may not be able to express their views, even though their views may be extremely important
Decision-making is open, transparent and explicit	May degenerate into a rubber-stamping exercise in which the class solutions implied by guidelines are unthinkingly applied to disparate individuals
Team members educate each other	Decisions are made in the absence of patients and their carers: the commodification of the person
A useful educational experience for trainees and students	Clinicians are able to avoid having to take responsibility for their decisions and their actions: the fig-leaf of 'corporate responsibility'
Performance can be monitored by managers	Time-consuming and resource-intensive: takes busy clinicians away from clinical practice for hours at a time

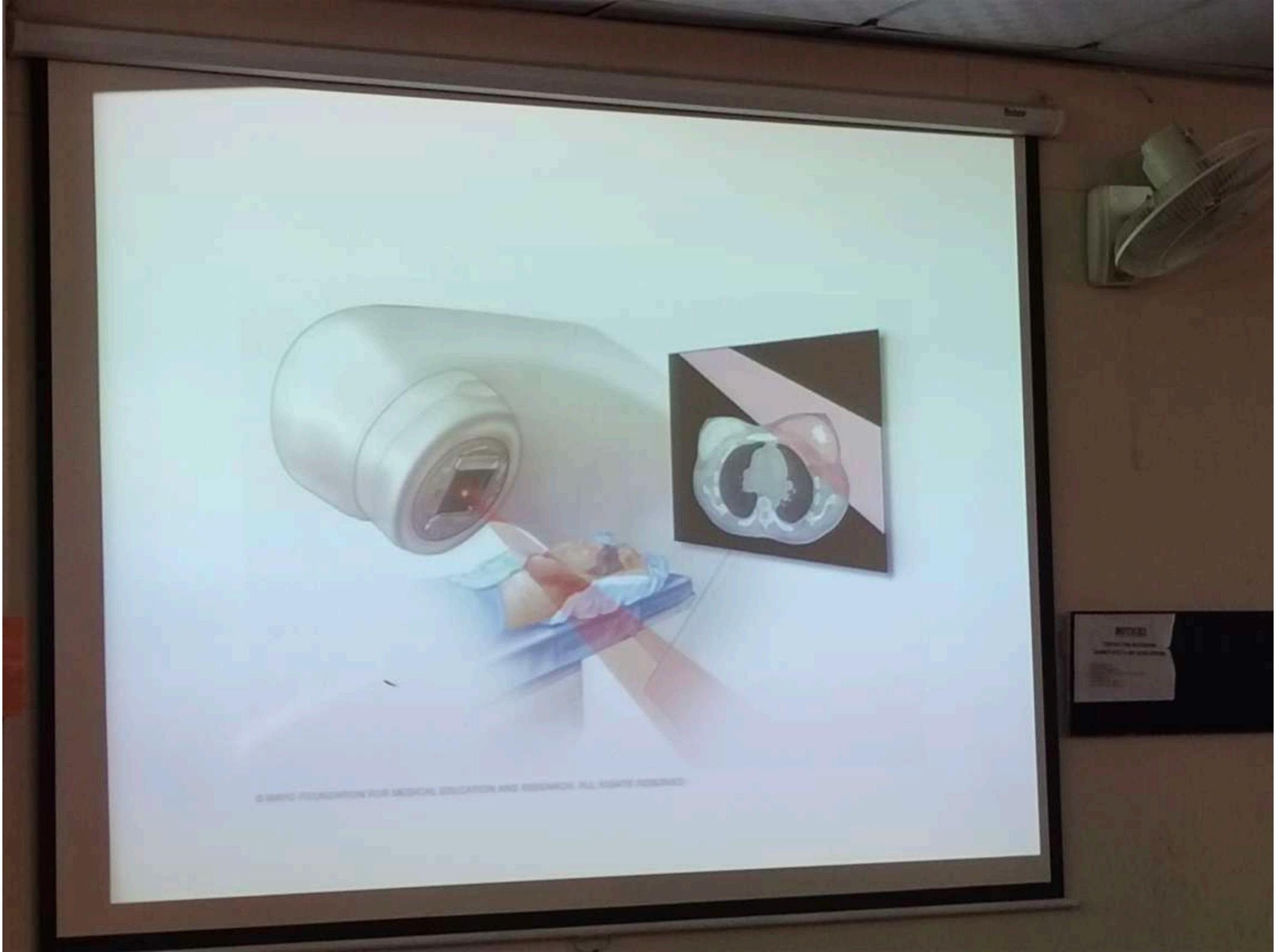

Principle of Cancer Surgery
• Diagnosis and staging
• Removal of primary disease
• Removal of metastatic disease
• Palliation

TABLE 10.4 Staging of colorectal cancer.

TNM	
TX, Primary tumour cannot be assessed	
T0, No evidence of primary tumour	
Tis, Intraepithelial or intramucosal carcinoma	
T1, Tumour invades submucosa	
T2, Tumour invades muscularis propria	
T3, Tumour invades through the muscularis propria into the subserosa or into retroperitoneal (pericolic or perirectal) tissues	a, Minim b, Sligh c, Mod d, Exte
T4, Tumour directly invades beyond bowel	a, Dire b, Per
NX, Regional lymph nodes cannot be assessed	
N0, No metastases in regional nodes	
N1, Metastases in 1–3 regional lymph nodes	
N2, Metastases in ≥4 regional lymph nodes	
MX, Not possible to assess the presence of distant metastases	
M0, No distant metastases	
M1, Distant metastases present	

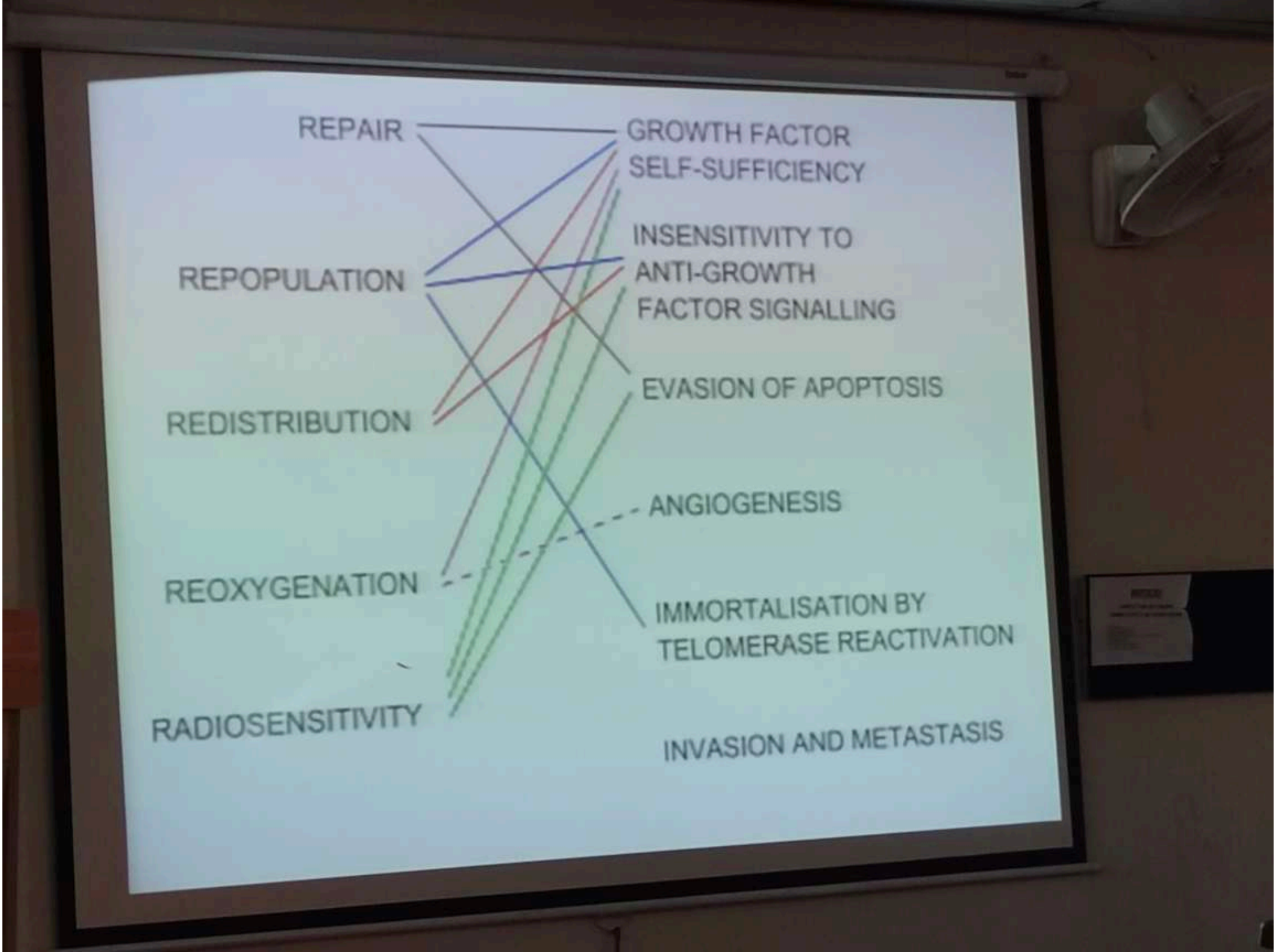
The Non Surgical Management of Cancer

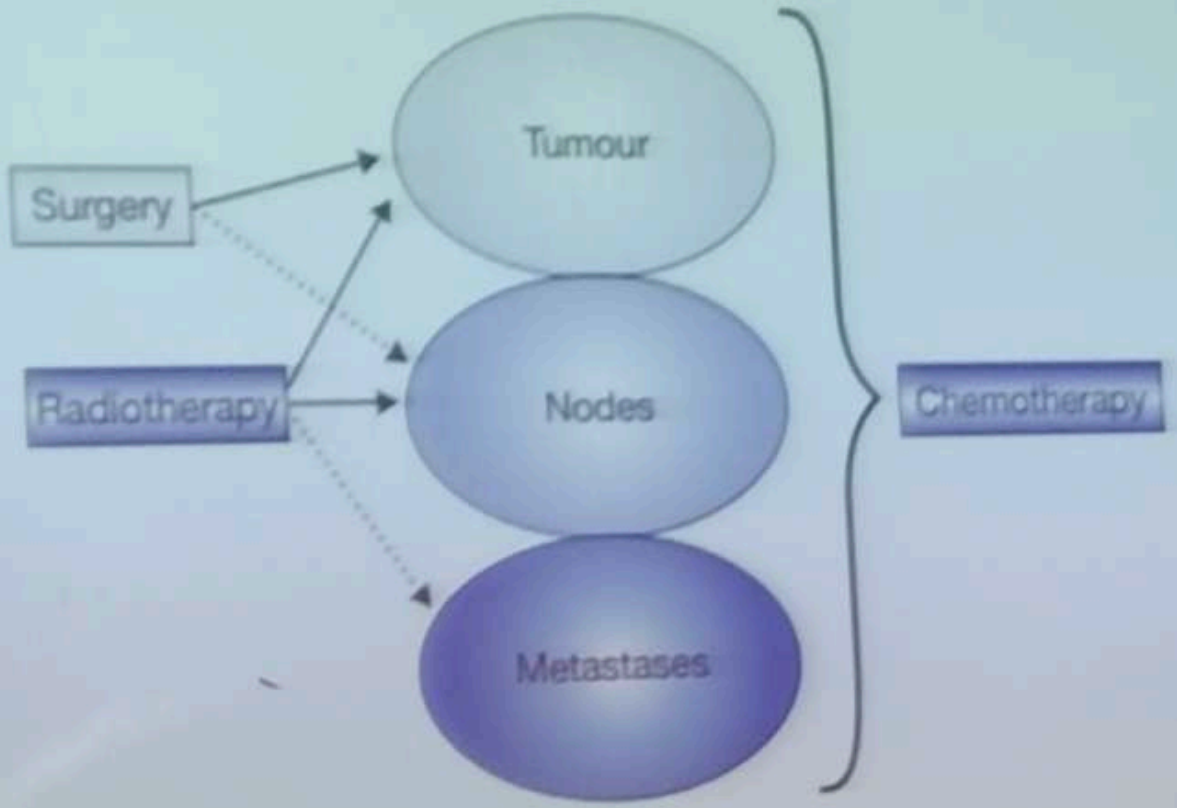
- Chemotherapy
- Radiation
- Combination of Two



The five Rs of radiotherapy

- Repair.
- Reoxygenation.
- Repopulation.
- Redistribution.
- Radio sensitivity.


REPAIR
REPOPULATION
REDISTRIBUTION
REOXYGENATION
RADIOSENSITIVITY
GROWTH FACTOR SELF-SUFFICIENCY
INSENSITIVITY TO ANTI-GROWTH FACTOR SIGNALLING
EVASION OF APOPTOSIS
ANGIOGENESIS
IMMORTALISATION BY TELOMERASE REACTIVATION
INVASION AND METASTASIS


Surgery
Radiotherapy
Tumour
Nodes
Metastases
Chemotherapy

End of Life Care

- Palliative Care : Many years
- End of Life care : Few Months