A CLINICAL APPROACH TO PATIENTS WITH A SUSPECTED MALIGNANCY

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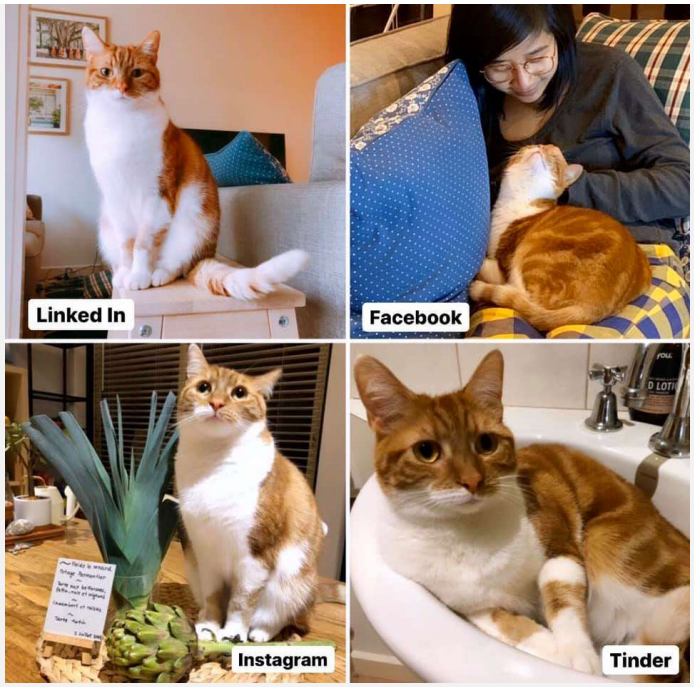
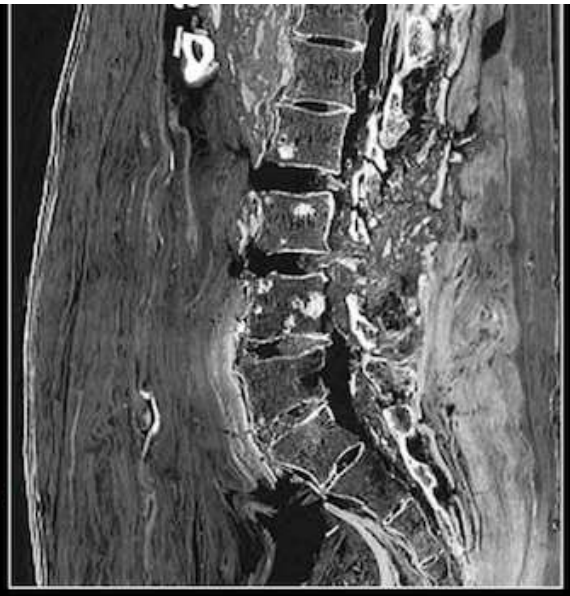


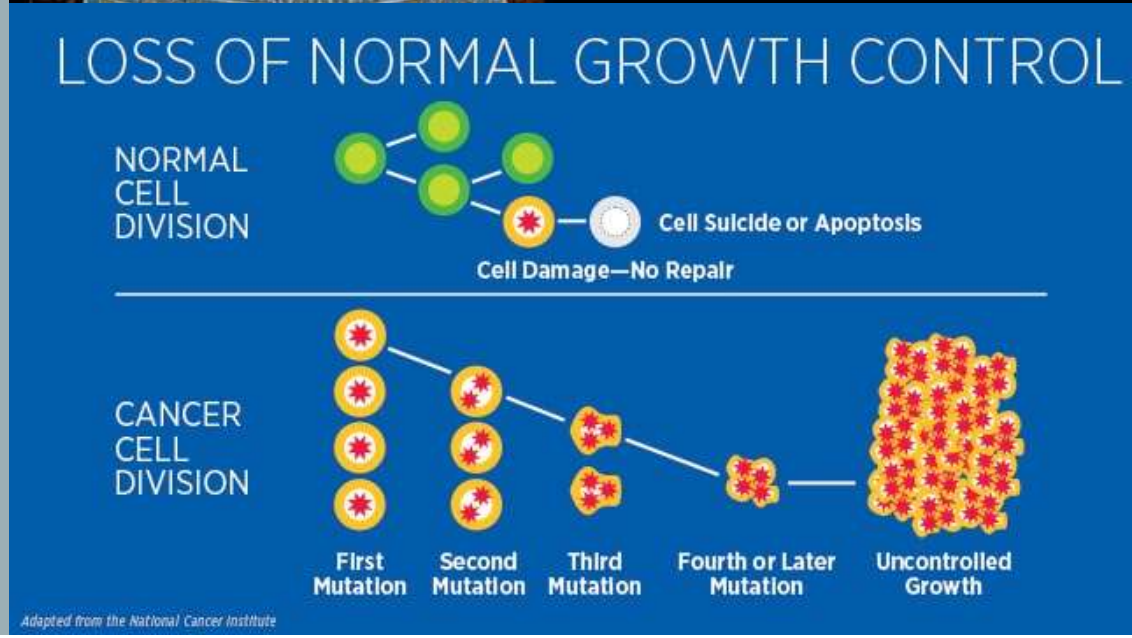
A BIT ABOUT ME…

- Graduated UniMelb **2011**
- Internship → Basic Physician Training (HMO2-5).
  - HMO3-5: Medical Registrar + BIG Exams
- Applied for centralised medical oncology admission
- 3 years of Medical Oncology
  - 2 core medical oncology reg years
  - 1 non-core year (Oncology Fellow – trials/clinics/research)
- FRACP letters end of **2019**
- Now I work 4 part time jobs…
  - 2 days – Medical Oncologist at Ballarat Health
  - 2.5 days – Registry based Research Fellow at WEHI
  - 0.5 day – UniMelb medical school teaching
  - 1 in 2 weekends – Locum Oncologist for Private

WHAT IS CANCER?

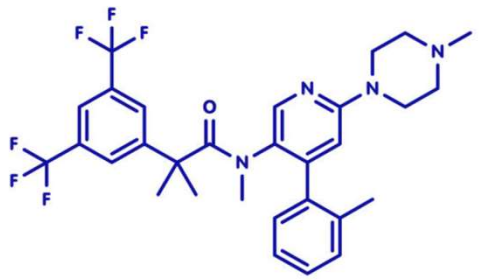


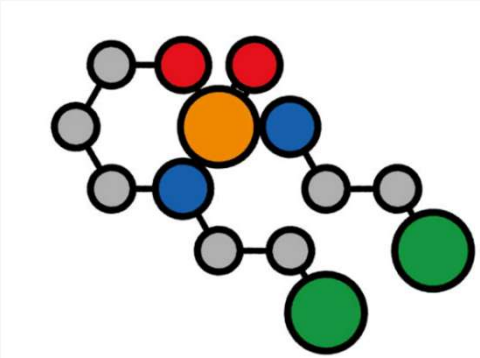
LOSS OF NORMAL GROWTH CONTROL



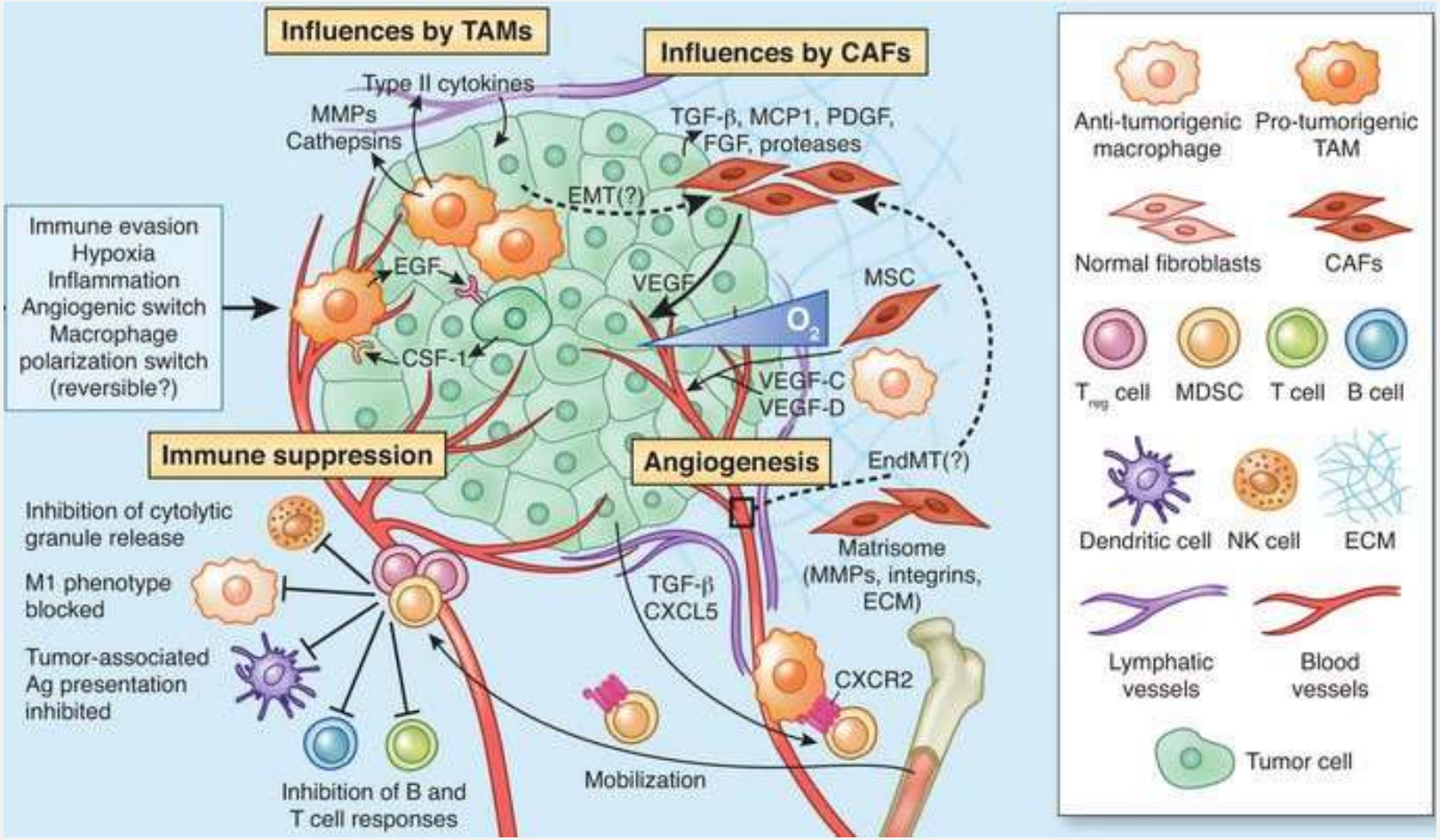
Adapted from the National Cancer Institute

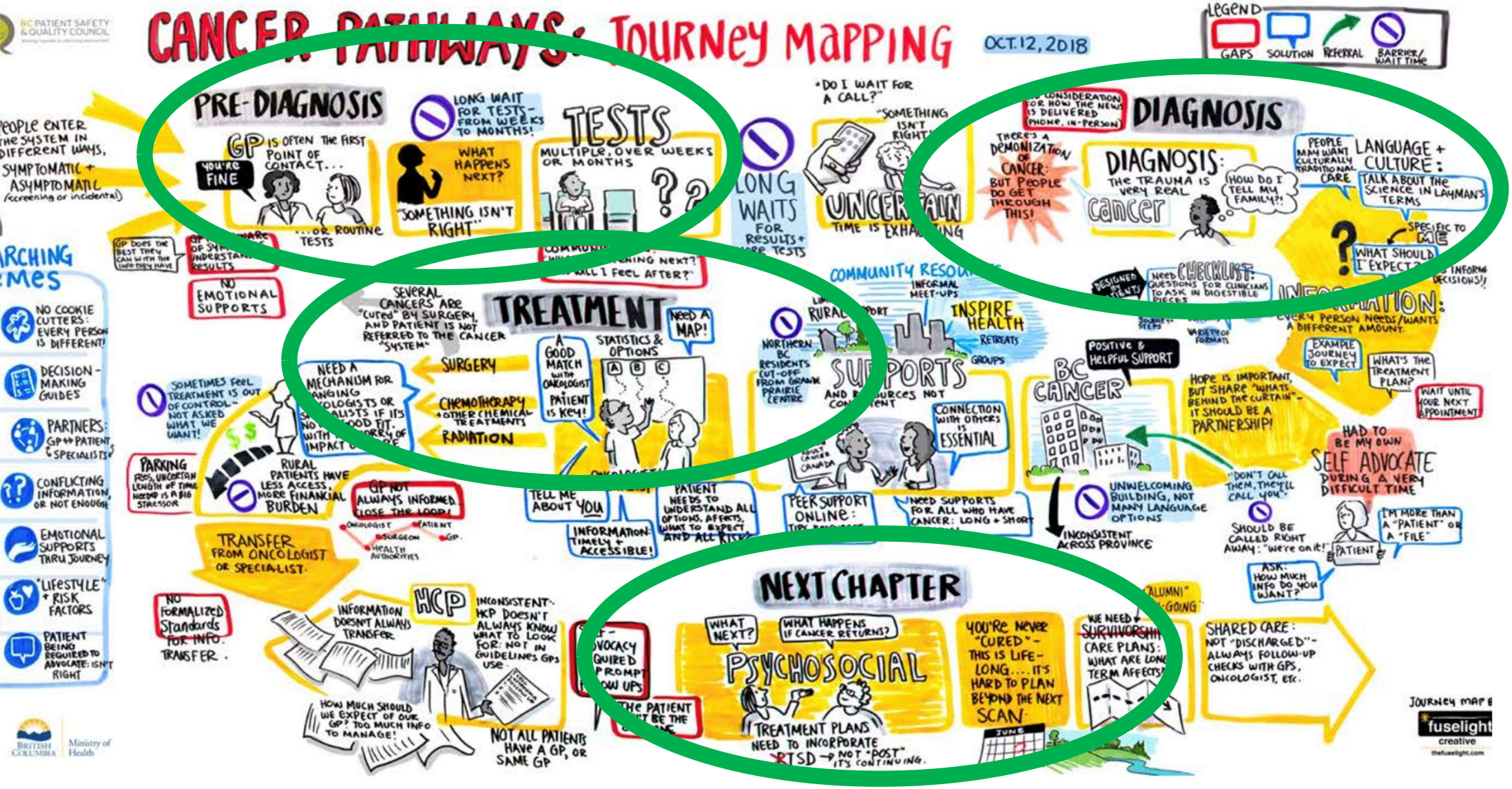
THIS IS NOT A TALK ABOUT MOLECULES, PATHWAYS, BASIC SCIENCE





ifosfamide




BC PATIENT SAFETY & QUALITY COUNCIL
CANCER PATHWAYS: JOURNEY MAPPING
OCT. 12, 2018
LEGEND
GAPS
SOLUTION
REFERRAL
BARRIER/ WAIT TIME
PRE-DIAGNOSIS
GP IS OFTEN THE FIRST POINT OF CONTACT...
YOU'RE FINE
...OR ROUTINE TESTS
LONG WAIT FOR TESTS - FROM WEEKS TO MONTHS!
WHAT HAPPENS NEXT?
"SOMETHING ISN'T RIGHT"
TESTS
MULTIPLE, OVER WEEKS OR MONTHS
LONG WAITS FOR RESULTS + MORE TESTS
"DO I WAIT FOR A CALL?"
"SOMETHING ISN'T RIGHT"
UNCERTAIN
TIME IS EXHAUSTING
DIAGNOSIS
THERE'S A DEMONIZATION OF CANCER: BUT PEOPLE DO GET THROUGH THIS!
DIAGNOSIS: THE TRAUMA IS VERY REAL
cancer
HOW DO I TELL MY FAMILY?!
PEOPLE MAY WANT CULTURALLY TRADITIONAL CARE
LANGUAGE + CULTURE:
TALK ABOUT THE SCIENCE IN LAYMAN'S TERMS
SPECIFIC TO ME
WHAT SHOULD I EXPECT?
INFORMATION:
EVERY PERSON NEEDS/WANTS A DIFFERENT AMOUNT
EXAMPLE JOURNEY TO EXPECT
WHAT'S THE TREATMENT PLAN?
WAIT UNTIL YOUR NEXT APPOINTMENT
CHECKLIST: QUESTIONS FOR CLINICIANS TO ASK IN DIGESTIBLE PIECES
TREATMENT
SEVERAL CANCERS ARE "CURED" BY SURGERY, AND PATIENT IS NOT REFERRED TO THE CANCER "SYSTEM"
NEED A MAP!
A GOOD MATCH WITH ONCOLOGIST PATIENT IS KEY!
STATISTICS & OPTIONS
SURGERY
CHEMOTHERAPY + OTHER CHEMICAL TREATMENTS
RADIATION
NEED A MECHANISM FOR ANGING ONCOLOGISTS OR ALISTS IF IT'S OOD FIT.
SOMETIMES FEEL TREATMENT IS OUT OF CONTROL - NOT ASKED WHAT WE WANT!
PARKING FEES, UNCERTAIN LENGTH OF TIME NEEDED IS A BIG STRESSOR
RURAL PATIENTS HAVE LESS ACCESS, MORE FINANCIAL BURDEN
GP NOT ALWAYS INFORMED. CLOSE THE LOOP!
ONCOLOGIST
PATIENT
SURGEON
GP
HEALTH AUTHORITIES
TELL ME ABOUT YOU
INFORMATION: TIMELY + ACCESSIBLE!
PATIENT NEEDS TO UNDERSTAND ALL OPTIONS, AFFECTS, WHAT TO EXPECT AND ALL RISKS
TRANSFER FROM ONCOLOGIST OR SPECIALIST
NO FORMALIZED Standards FOR INFO. TRANSFER.
INFORMATION DOESN'T ALWAYS TRANSFER
HCP
INCONSISTENT - HCP DOESN'T ALWAYS KNOW WHAT TO LOOK FOR: NOT IN GUIDELINES GPs USE
HOW MUCH SHOULD WE EXPECT OF OUR GP? TOO MUCH INFO TO MANAGE!
NOT ALL PATIENTS HAVE A GP, OR SAME GP
COMMUNITY RESOURCES
INFORMAL MEET-UPS
INSPIRE HEALTH
RETREATS
GROUPS
NORTHERN BC RESIDENTS CUT-OFF FROM GRANDE PRAIRIE CENTRE
SUPPORTS
CONNECTION WITH OTHERS IS ESSENTIAL
PEER SUPPORT ONLINE:
NEED SUPPORTS FOR ALL WHO HAVE CANCER: LONG + SHORT
BC CANCER
POSITIVE & HELPFUL SUPPORT
HOPE IS IMPORTANT, BUT SHARE "WHATS BEHIND THE CURTAIN" - IT SHOULD BE A PARTNERSHIP!
UNWELCOMING BUILDING, NOT MANY LANGUAGE OPTIONS
INCONSISTENT ACROSS PROVINCE
"DON'T CALL THEM, THEY'LL CALL YOU"
SHOULD BE CALLED RIGHT AWAY: "We're on it!"
ASK: HOW MUCH INFO DO YOU WANT?
HAD TO BE MY OWN SELF ADVOCATE DURING A VERY DIFFICULT TIME
PATIENT
I'M MORE THAN A "PATIENT" OR A "FILE"
NEXT CHAPTER
WHAT NEXT?
WHAT HAPPENS IF CANCER RETURNS?
PSYCHOSOCIAL
TREATMENT PLANS NEED TO INCORPORATE RTSD - NOT "POST" IT'S CONTINUING.
YOU'RE NEVER "CURED" - THIS IS LIFE-LONG.... IT'S HARD TO PLAN BEYOND THE NEXT SCAN
WE NEED SURVIVORSHIP CARE PLANS: WHAT ARE LONG TERM AFFECTS?
"ALUMNI" GOING
SHARED CARE: NOT "DISCHARGED" - ALWAYS FOLLOW-UP CHECKS WITH GPs, ONCOLOGIST, ETC.
PEOPLE ENTER THE SYSTEM IN DIFFERENT WAYS, SYMPTOMATIC + ASYMPTOMATIC (screening or incidental)
ARCHING mes
NO COOKIE CUTTERS: EVERY PERSON IS DIFFERENT!
DECISION-MAKING GUIDES
PARTNERS: GP ↔ PATIENT & SPECIALISTS
CONFLICTING INFORMATION, OR NOT ENOUGH
EMOTIONAL SUPPORTS THRU JOURNEY
"LIFESTYLE" + RISK FACTORS
PATIENT BEING REQUIRED TO ADVOCATE: ISN'T RIGHT
NO EMOTIONAL SUPPORTS
GP DOES THE BEST THEY CAN WITH THE INFO THEY HAVE
BRITISH COLUMBIA
Ministry of Health
JOURNEY MAP
fuselight creative
thefuselight.com

TOPICS

- Clinical diagnosis – history and examination
- Investigations – radiology, tumour markers, biopsies and histopathology
- Oncology emergencies
- Learning the oncology glossary

ZARA, BREAST LUMP

- 48 yo woman presents with a right breast mass to her GP
- Otherwise systemically well
- Medical Hx – Gastro-oesophageal reflux on her proton-pump inhibitor
- NKA
- Family history
  - Mother - breast cancer at age 60, older sister - breast cancer at age 45
  - Maternal aunt - ovarian cancer at age 55, maternal uncle - prostate cancer at age 60
- Social history
  - Current smoker – 10/day
  - 2 healthy children – both breastfed

What questions about clinical risk factors do we still need to ask?

RISK FACTORS FOR BREAST CANCER

- Established high risk factors
  - Risk increases with older age
    - Age 50-59 – 1 in 42 women, Age 70+ - 1 in 9 women
  - BMI > 30 in post menopausal women
  - Earlier menarche (<13yo) or later menopause
  - Dense breast tissue (ratio of parenchyma:adipose tissue)
  - Long term use of HRT
  - Nulliparous women
  - Smoking

Personal history of breast cancer or DCIS

Family history of breast cancer
- 1 affected first-degree relative = 2x increase
- 2 affected first-degree relatives = 3x increase
- If first degree relative was diagnosed before age 30
  - 3x increased risk
- If first degree relative was diagnosed after age 60
  - 1.5x increased risk

Inherited genetic mutations
- BRCA1 and BRCA2
- P53, STK11, CDH1, PALB2, PTEN

PROTECTIVE FACTORS TO REDUCE BREAST CANCER

- Breastfeeding
  - Every 12 months of breast feeding, 4% reduction in relative risk of breast cancer
  - Thought is that this helps remove cells with potential DNA damage
- Regular physical activity

PHYSICAL EXAM

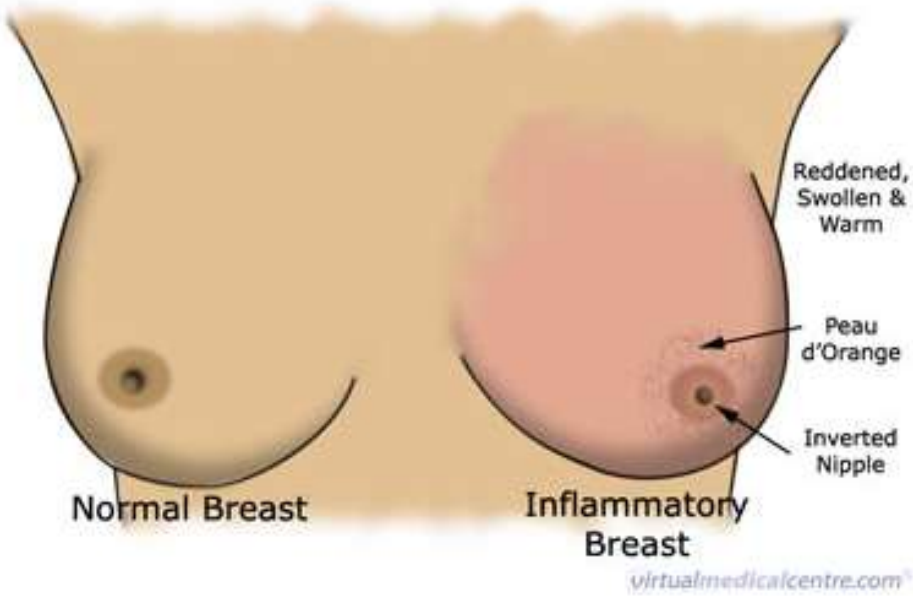
Breast exam
- Amount of breast tissue
- Distortion, dimpling, skin changes, cording
- Nipple – fixed or tethered, discharge, inverted
- Describe the mass – hard, calcified, painful
- Location from nipple and use a clock face

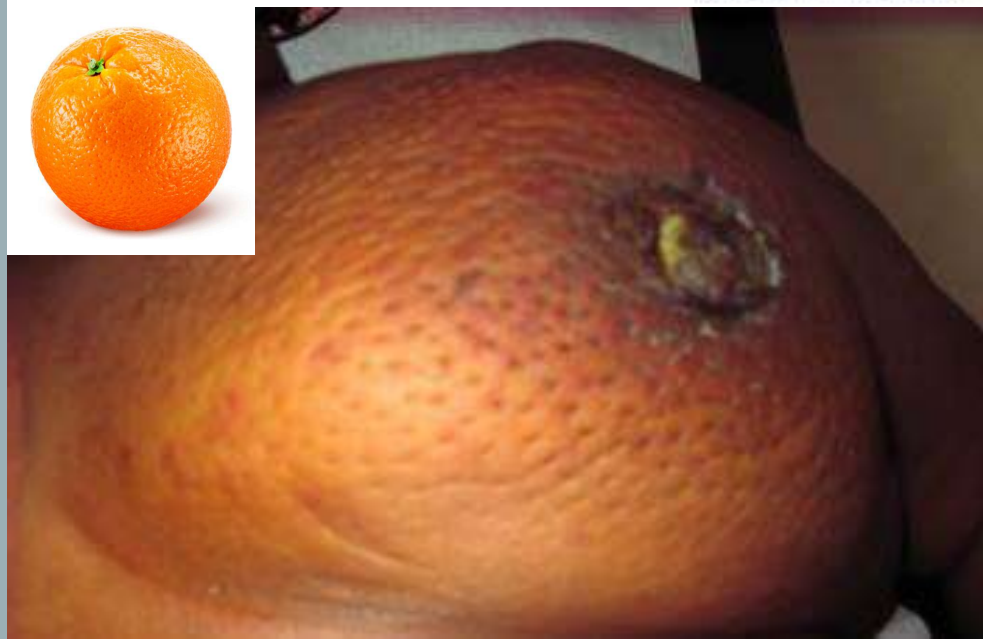
Axillary lymph nodes

Supraclavicular and cervical lymph nodes

General physical exam

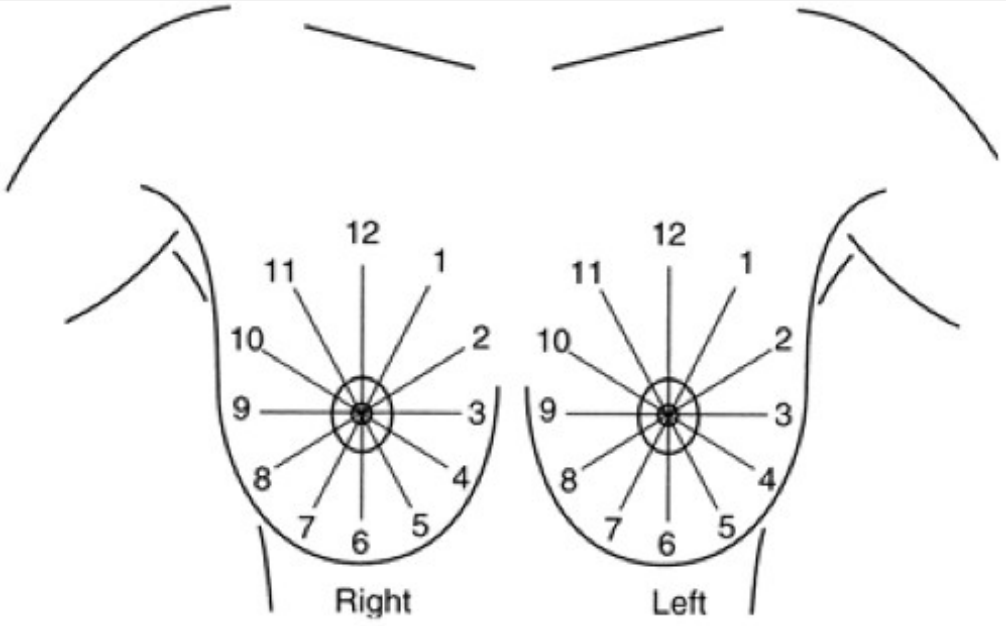
What is inflammatory breast cancer?





DIFFERENTIAL DIAGNOSIS FOR BREAST LUMP

- Breast cancer
- Carcinoma in situ
- Benign causes include:
  - Fibroadenoma ("the breast mouse") – firm, very mobile
  - Cyst (in relation to menstrual cycle)
  - Fibrocystic changes
  - Galactocoele
  - Fat necrosis (trauma, implants)
  - Breast abscess (mastitis)

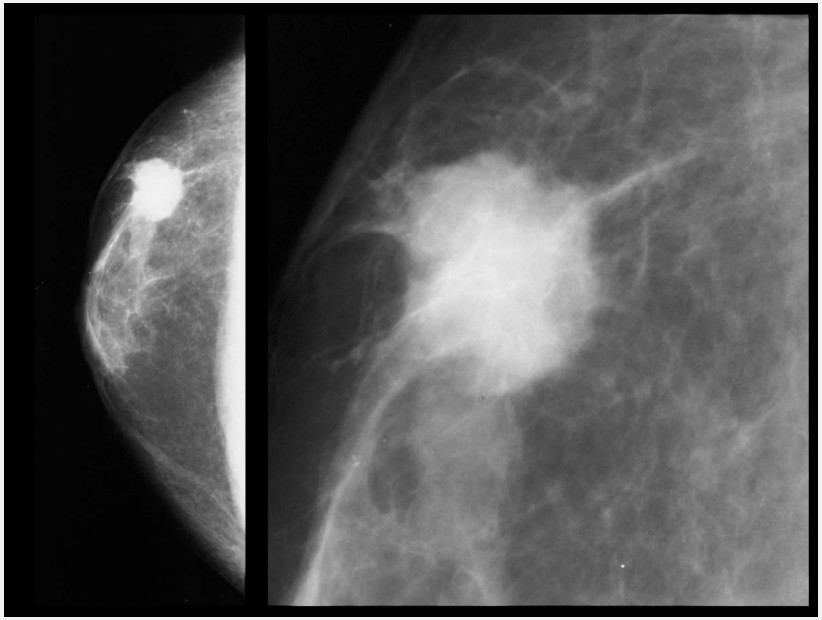


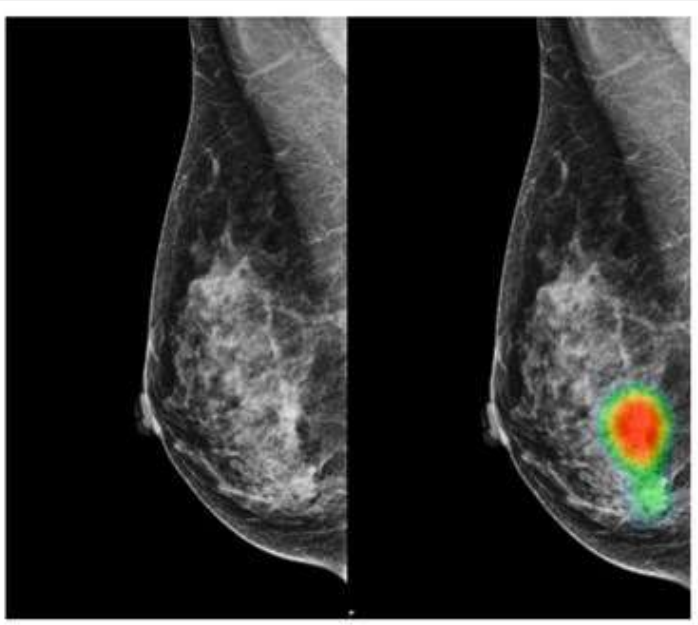
INVESTIGATIONS

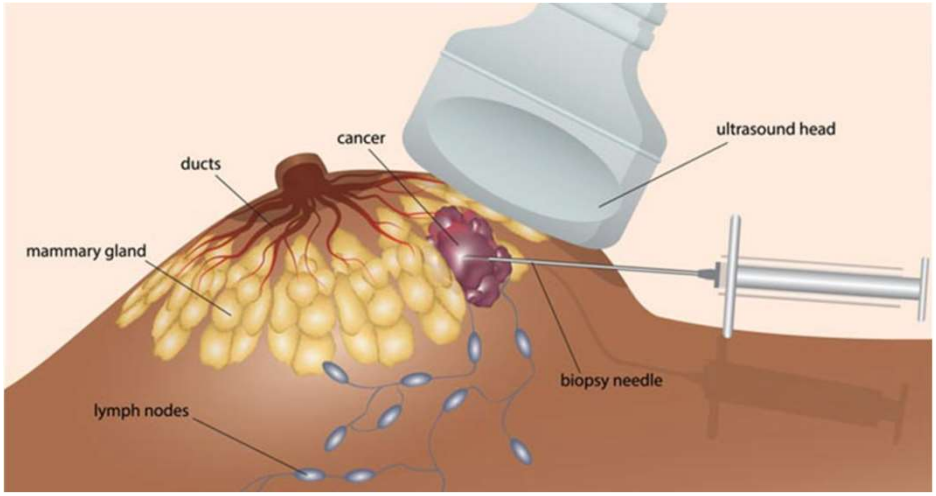
MMG
- Limited by breast density

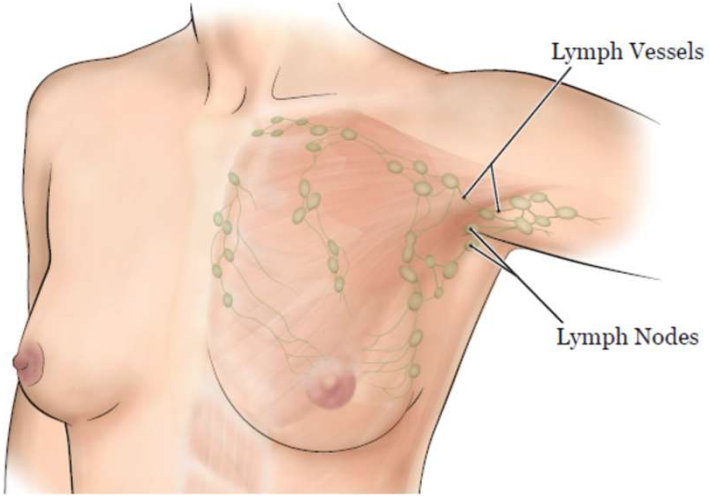
Findings suggestive of cancer:
Spiculated soft tissue mass
Microcalcifications

MRI used more in younger pt
but becoming more mainstream



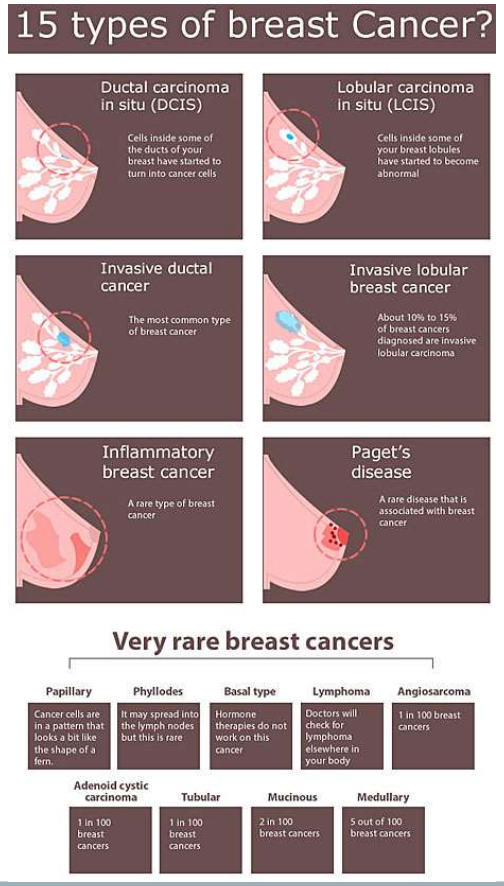


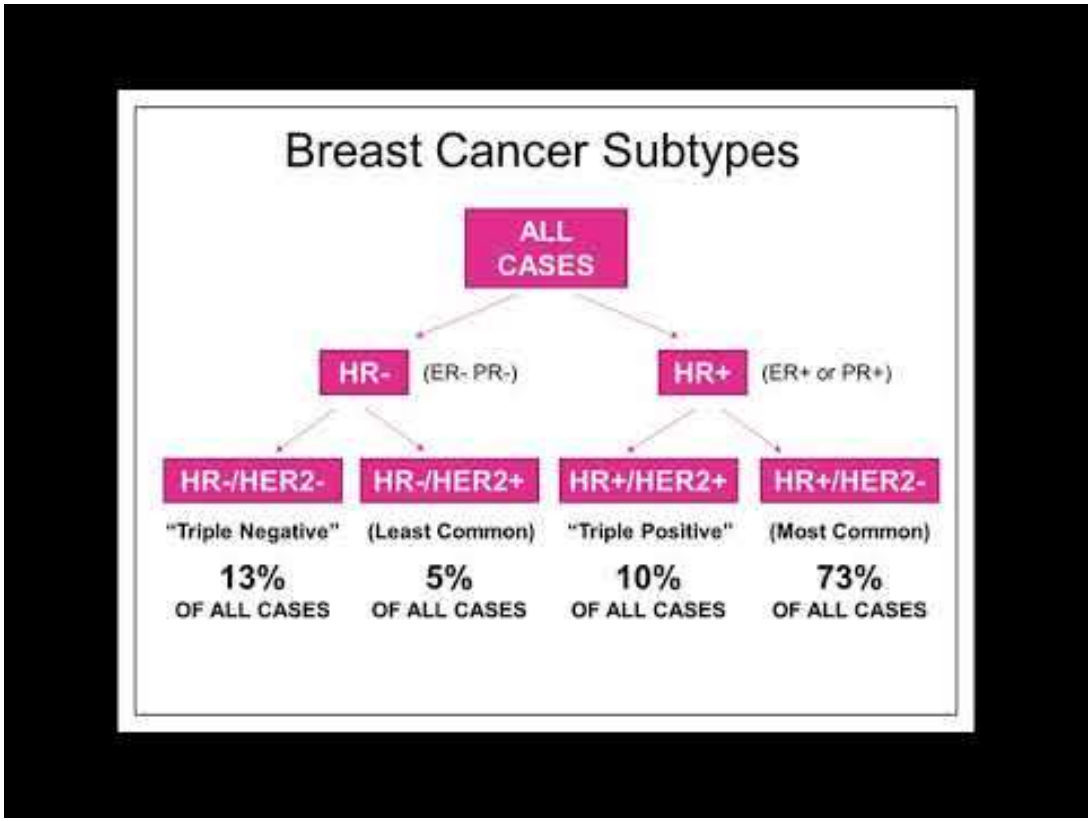




BREAST US +/- BIOPSY

AXILLARY US +/- BIOPSY





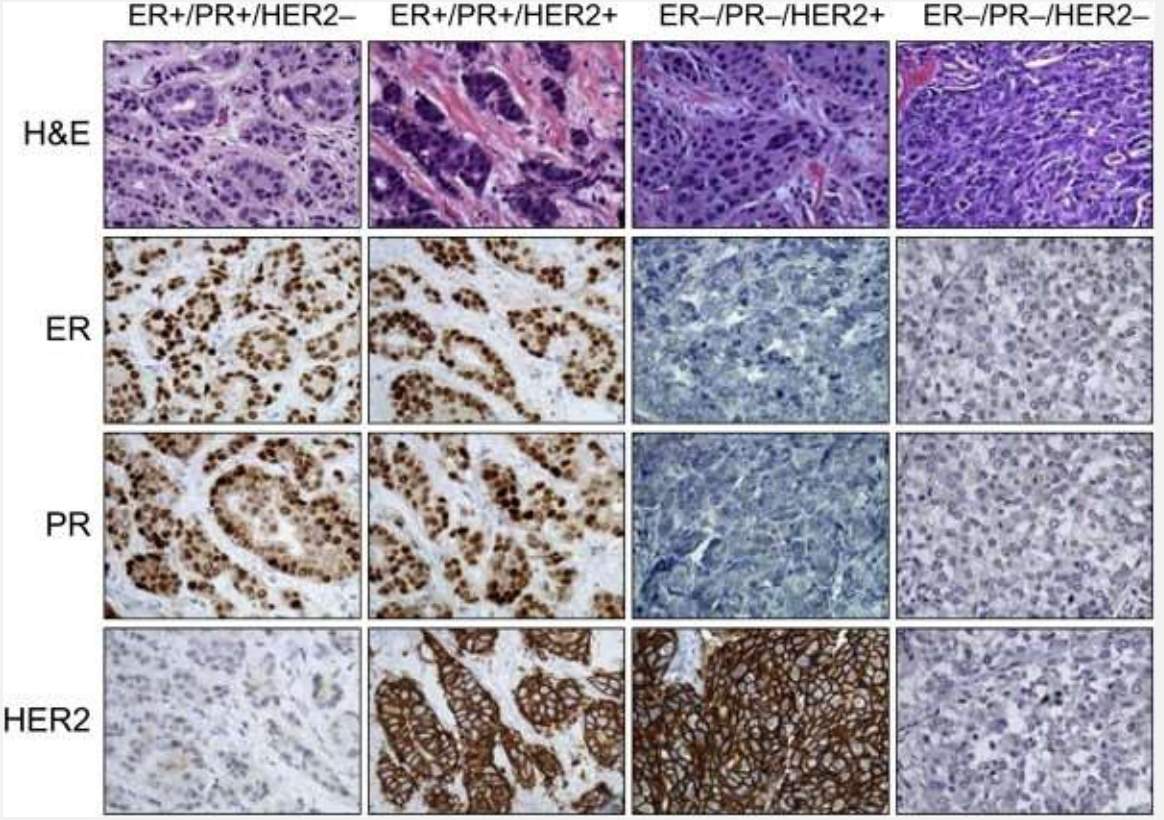
BUT WHY DO WE NEED A BIOPSY IF WE ALREADY KNOW ITS BREAST CANCER?

HISTOPATHOLOGY

"no tissue, no issue"

Morphology
Tumour size*
Tumour grade
Type of cells tumour arises from (glandular, lobular)
Tumour differentiation
Ki67 ("proliferation index")

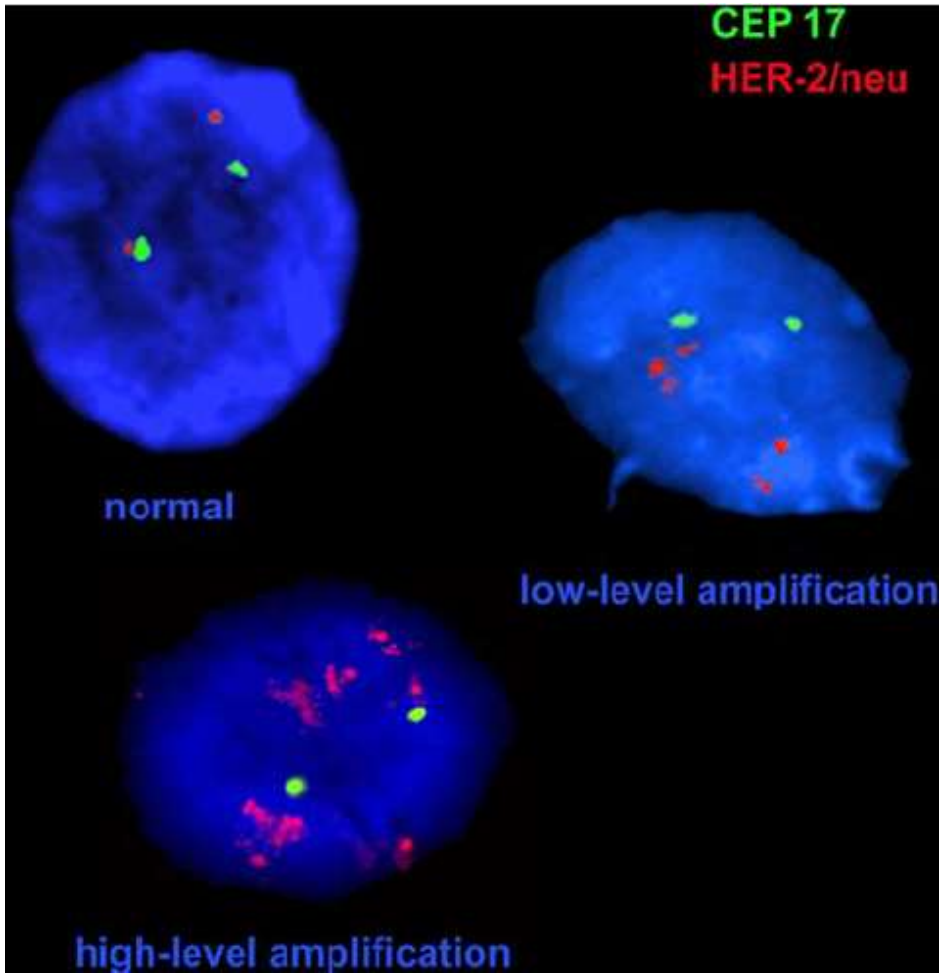
Immunohistochemistry (IHC)
Oestrogen receptor + or -, %
Progesterone receptor + or -, %
HER2 + or –



FLUORESECENT IN SITU HYBRIDISATION (FISH)

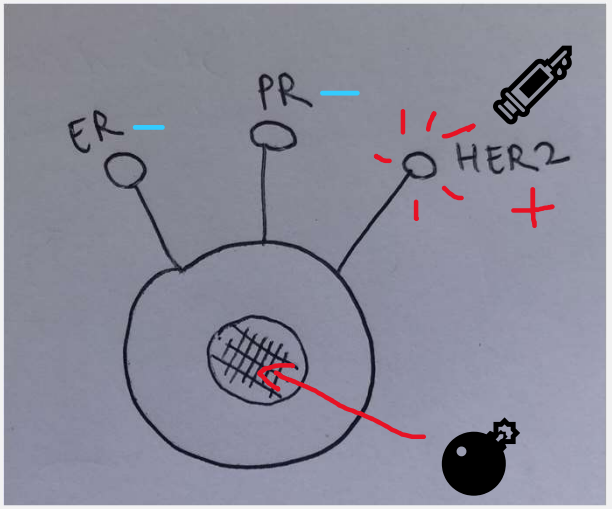
Labeled probe (RNA or DNA)
Localises gene expression in a cell

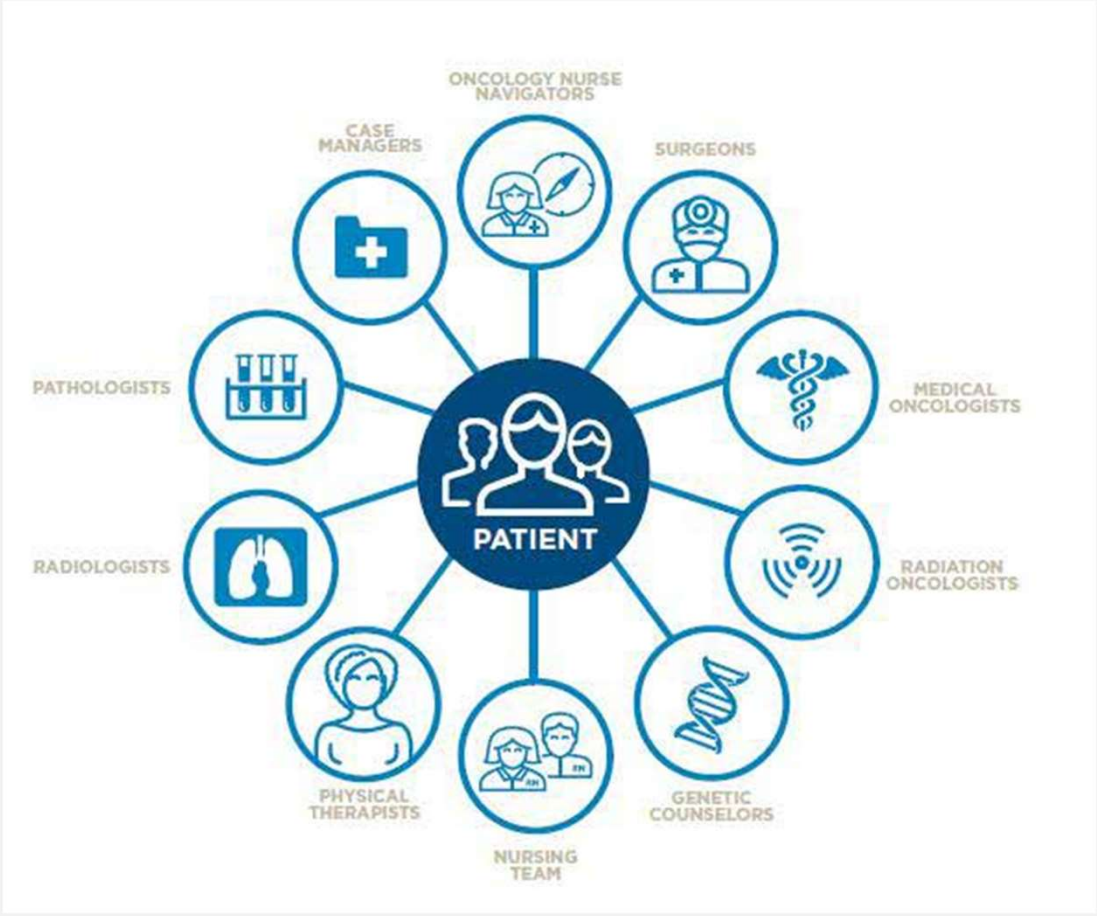
This special label attaches to HER2 proteins
Labels have chemicals and colours to glow



ZARA, BREAST LUMP

- Clinically – inflammatory breast cancer
- MMG and US – large 5cm mass with enlarged axillary lymph nodes
- Biopsy of both breast mass and lymph nodes
  - Grade 3, poorly differentiated, ductal carcinoma, Ki67 high
  - ER negative, PR negative, HER2 + and HER2 ISH positive
- Case is presented at Multi-Disciplinary Meeting (MDM)
  - For ***neoadjuvant intent*** chemotherapy + HER2 directed treatment, followed up by mastectomy and axillary lymph node dissection, radiotherapy to SCF, surveillance
  - ? Referral to Familial Cancer Centre




ONCOLOGY NURSE NAVIGATORS
CASE MANAGERS
SURGEONS
PATHOLOGISTS
MEDICAL ONCOLOGISTS
PATIENT
RADIOLOGISTS
RADIATION ONCOLOGISTS
PHYSICAL THERAPISTS
GENETIC COUNSELORS
NURSING TEAM

WHAT DOES INTENT OF TREATMENT MEAN?

CURATIVE

- Neoadjuvant
  - Before the curative local intent treatment
  - Aim is to downstage, look for pathological response, get systemic treatment in early before the delay of surgery and post-op recovery

- Curative local intent treatment
  - Surgery – aim for clear resection margins and lymph node dissection
  - Radiotherapy – cover cancer area

- Adjuvant
  - After the curative local intent treatment
  - Aim is to decrease rate of recurrence

PALLIATIVE

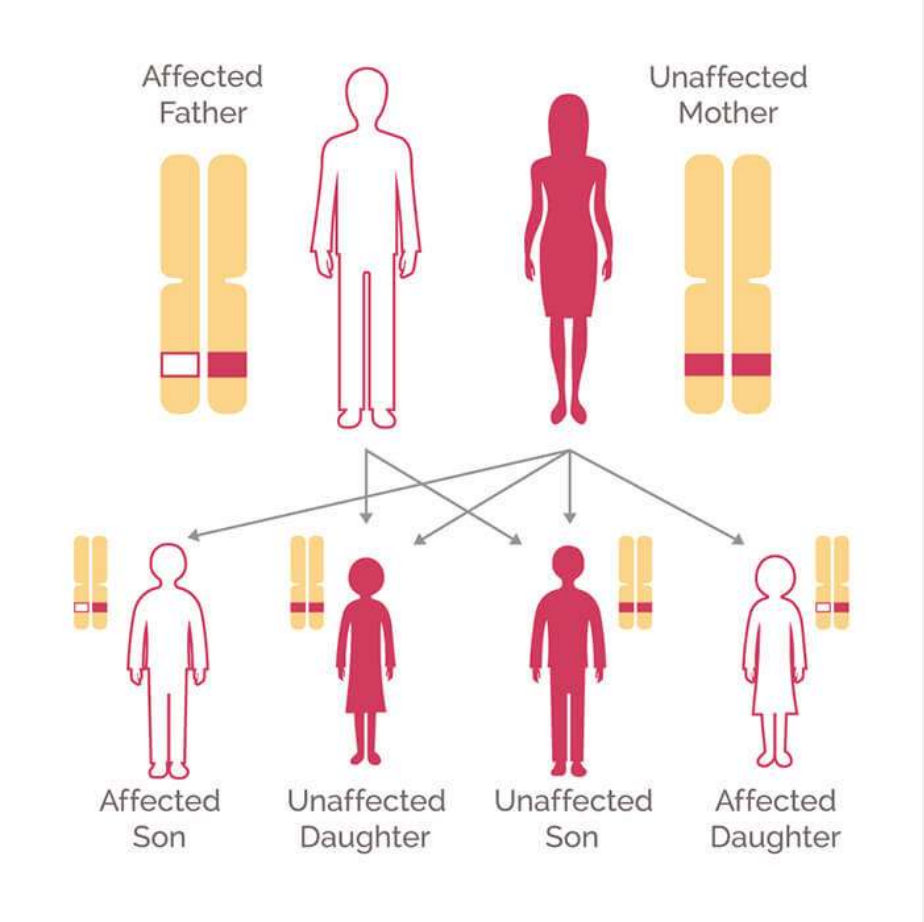
- Palliative treatment
  - In the metastatic setting (cancer is usually incurable)
  - Increase survival and manage symptoms
- "Best Supportive Care"

WHY WOULD WE REFER HER TO FAMILIAL CANCER CENTRE?

Discuss BRCA1 and BRCA2 mutation testing
***tumour suppressor genes**

When to test:

1. Individuals with a combined BRCA1 and BRCA2 pathogenic variant probability > 10% ("Manchester Score")
2. Individuals affected with breast cancer
   - Triple negative < 50 years
   - Triple negative breast cancer at any age + close relative with breast or ovarian cancer
   - Diagnosed with any breast cancer < 40 years
3. Individuals with high grade ovarian cancer at any age
4. Males affected with prostate cancer who meet specific cancer testing criteria
5. Familial BRCA1 or BRCA2 variant has been found
6. Personal/family history of breast, ovarian, prostate or pancreatic cancer where a common founder variant exists
7. Ashkenazi Jewish ancestry



BRCA and Cancer

Although the risk of cancer is greater for women than men with BRCA 1/2 gene mutations, both sexes face elevated lifetime chances of several types of cancer. *Risk of cancer as a percentage, by gender.*

Cancer type	U.S. white	BRCA1 mutation carriers	BRCA2 mutation carriers
MEN			
Breast	0.1%	1-5%	7%
Prostate	16	*	25
Melanoma	2	N.S.	5
Pancreas	1	Up to 3	3-5
WOMEN			
Breast	13%	60-80%	50-70%
Ovary	1-2	20-45	10-20
Melanoma	2	N.S.	Up to 5
Pancreas	1	Up to 3	3-5

N.S. = Not significant; *Some evidence of an increased risk for men younger than 65

ZARA, THREE YEARS LATER

Presents to her GP with 6 weeks of mid to lower back pain

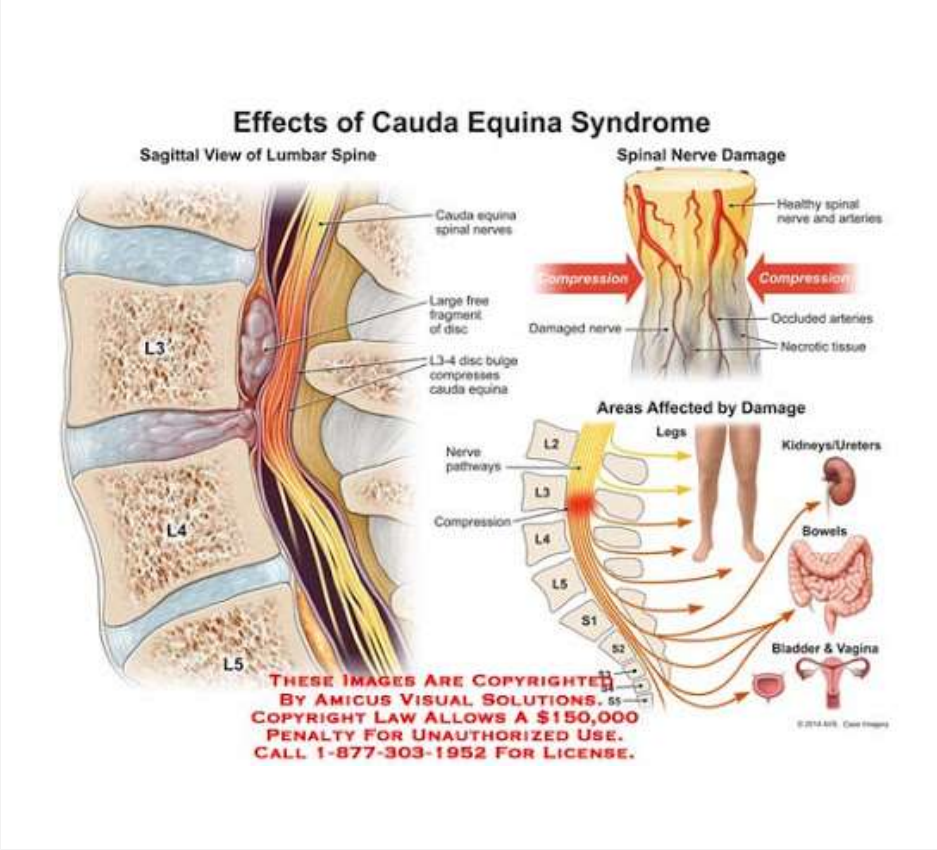
Progressive, night pain, radiating around from her back

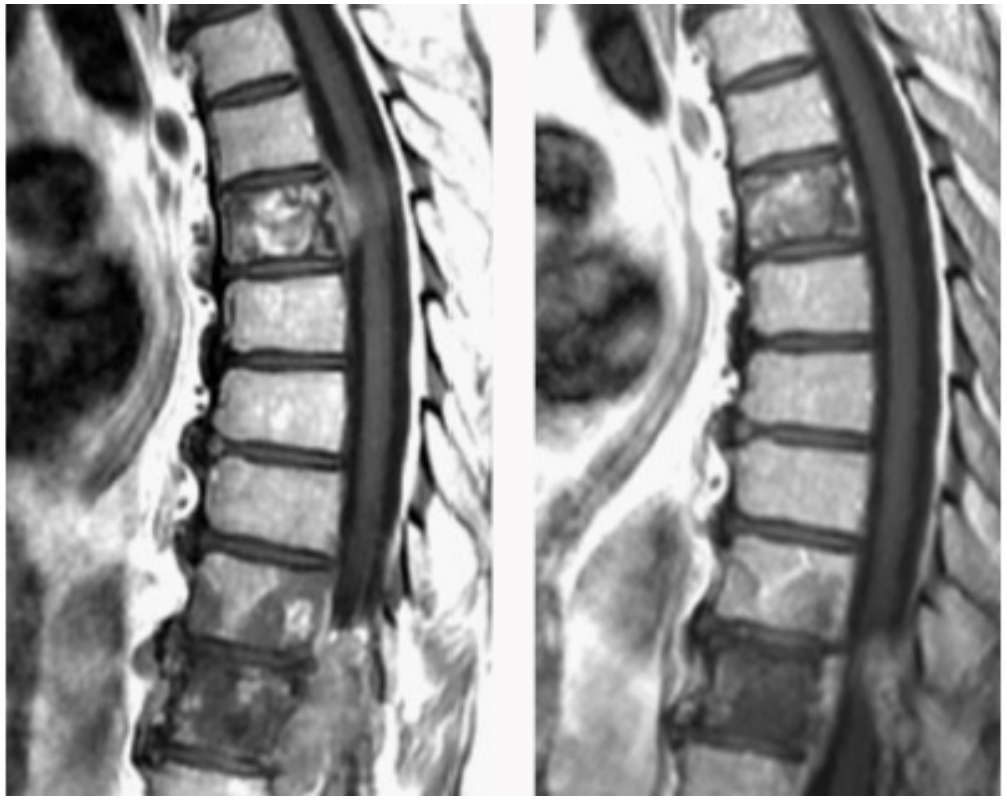
No trauma, no fevers/infection

Unsure if she has lost weight, appetite is okay

Decided to present to GP now as:

- Embarassing episode of faecal incontinence
- Followed by a near fall in the supermarket





INVESTIGATIONS

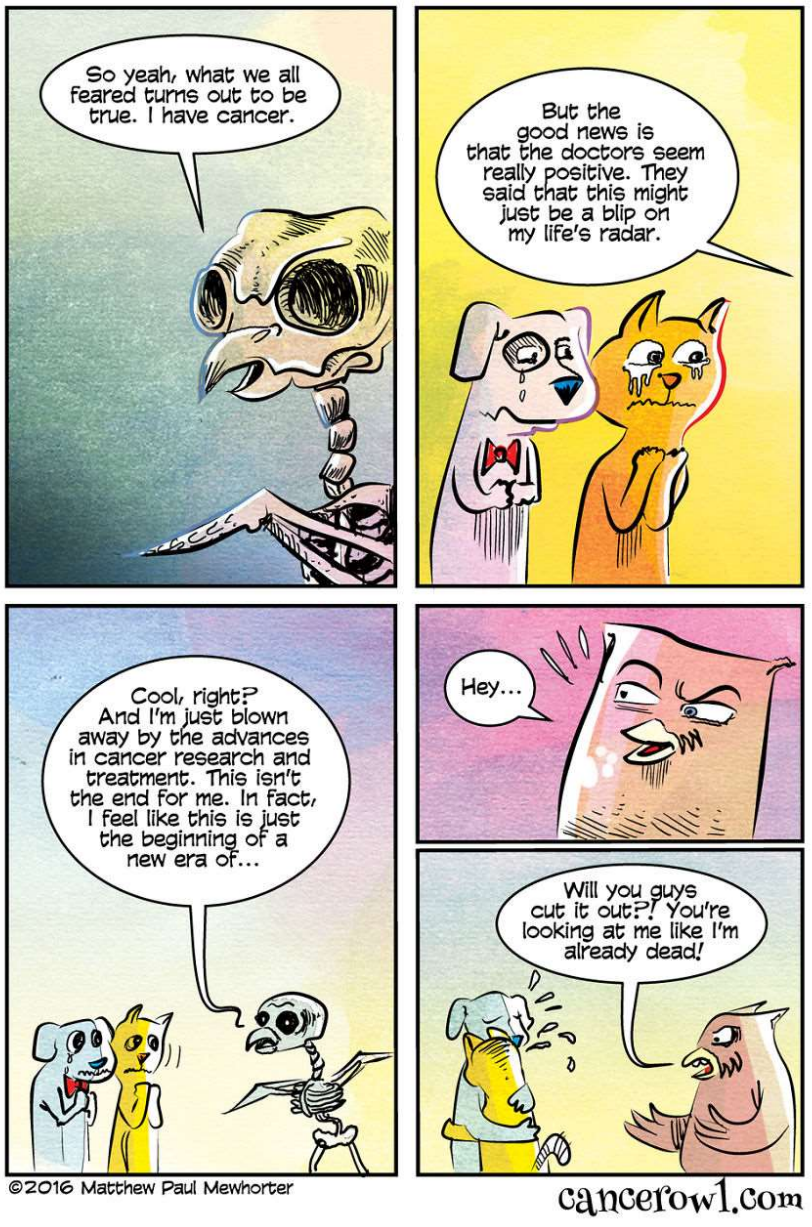
Need to do a neuro exam
(CN, UL, LL, Cerebellar)
Imaging – ideally MRI whole spine
Staging – CT stage patient to see if any other metastatic spread

Management
- IV dexamethasone 8mg BD
- Call neurosurgery and radiation oncology
- Analgesia
- Treat underlying cancer

WOULD YOU REPEAT A BIOPSY?

- Cannot assume the bone 'secondary' originates from breast cancer
- 1 in 7 breast cancers change their subtypes

A PAUSE FOR QUESTIONS



MRS CHEY, COUGH AND DYSPNOEA

- 70 yo woman, originally from Cambodia, presents with cough and dyspnea
- Occasional haemoptysis
- SOBOE and progressive, now can only walk 20m
- Loss of weight – 15kg (now 55kg) over 6 months
- Loss of appetite
- Fatigued, described as ECOG 2, by doctor handing over to you
- Betel-chewing, active heavy smoker 30/day
- PMHx: COPD on ipratropium
- No FamHx of cancer

WHAT IS THIS ECOG?

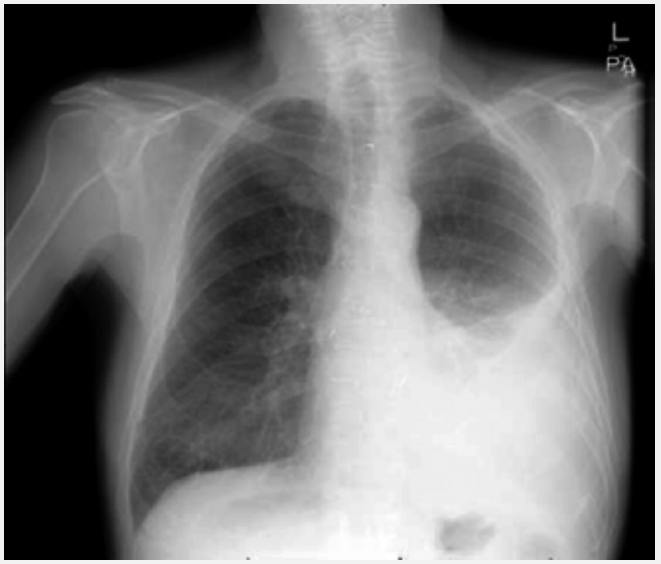
Eastern Cooperative Oncology Group score

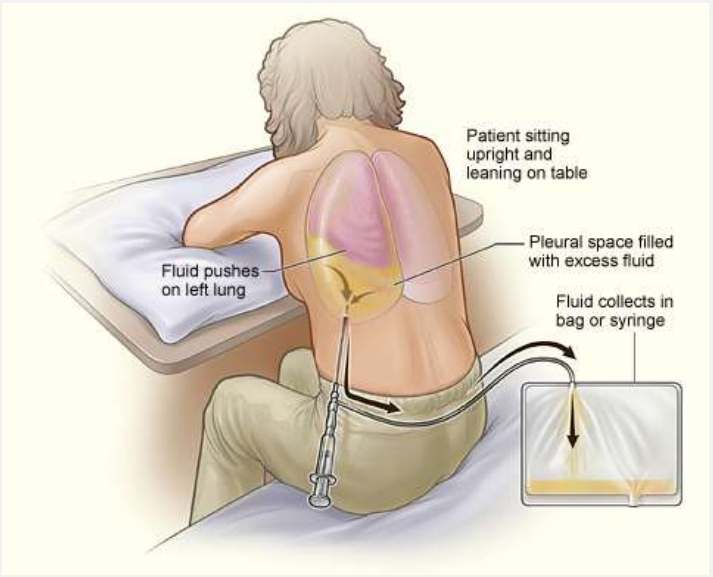
Grade	ECOG
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

A way of describing functional status for oncologists

EXAM AND INVESTIGATIONS

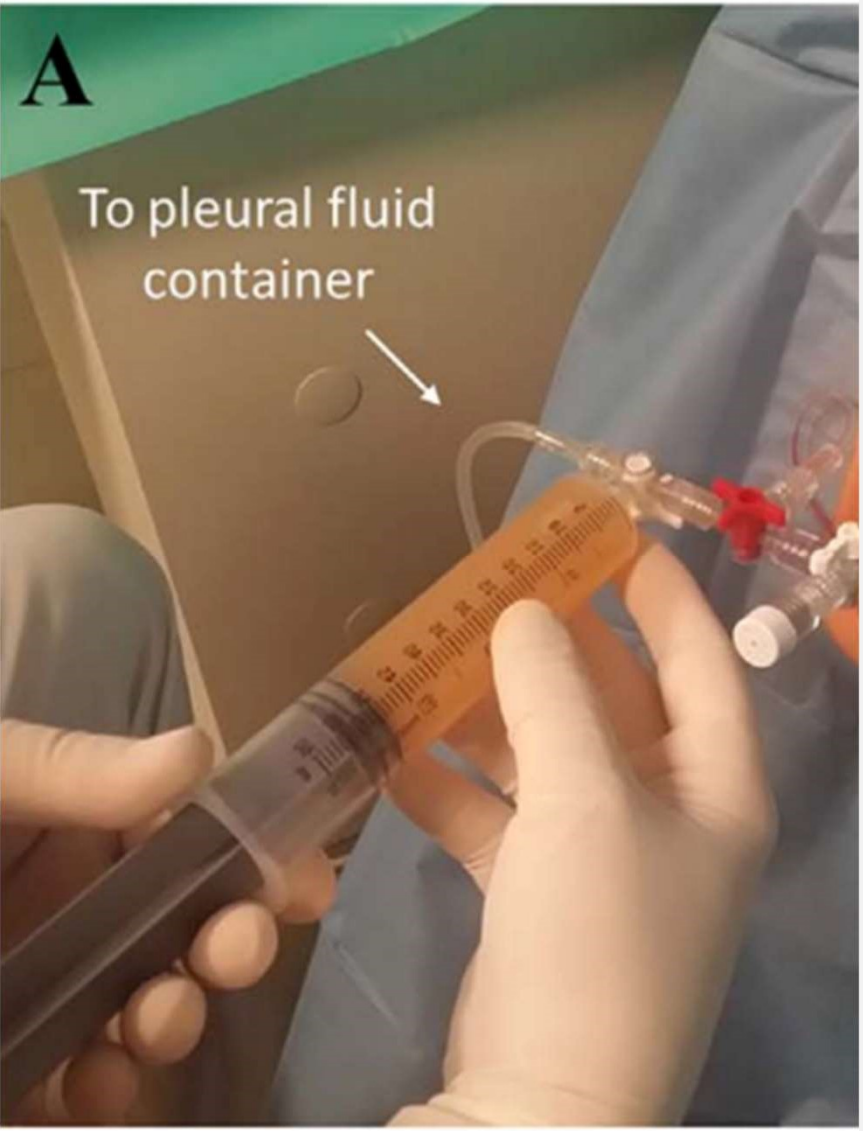
- Respiratory exam
  - Decreased AE on left lower lung with bronchial breath sounds on left midzone
  - Dullness to percussion on LLZ, decreased vocal resonance
  - Sats are 89% RA
  - Cannot lie flat for CT scan





PLEURAL FLUID ANALYSIS

	Light's Criteria	
	Transudate	Exudate
Pleural:Serum Protein	< 0.5	≥ 0.5
Pleural:Serum LDH	< 0.6	≥ 0.6
Pleural fluid LDH	< 2/3 upper limit of normal	> 2/3 upper limit of normal
Main Causes	• CHF • Cirrhosis • Nephrotic syndrome • Pulmonary embolism	• Malignancy • Bacterial/Viral pneumonia • Tuberculosis • Pulmonary embolism • Pancreatitis • Esophageal rupture • Collagen vascular disease • Chylothorax/Hemothorax



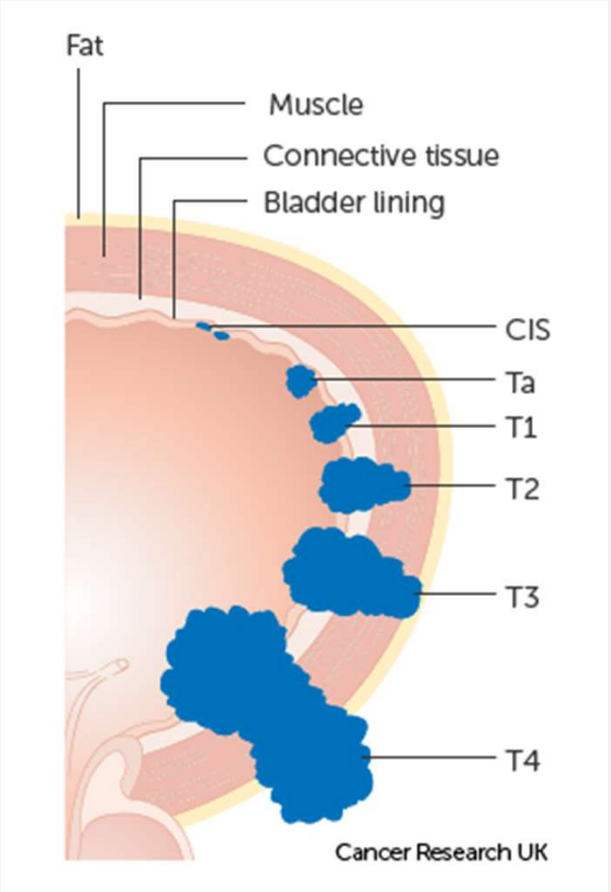
MRS GT'S RESULTS

- From the pleural fluid – cytology – cell block
- No acid-fast bacilli
- No other bacteria seen
- Lung adenocarcinoma
- Stains positive for PDL1 80%
- Sent for Next Generation molecular screening
    - Negative for ALK and EGFR mutation

- **Given pleural involvement – already Stage 4 disease**
- **What does Stage 4 mean?**

STAGING

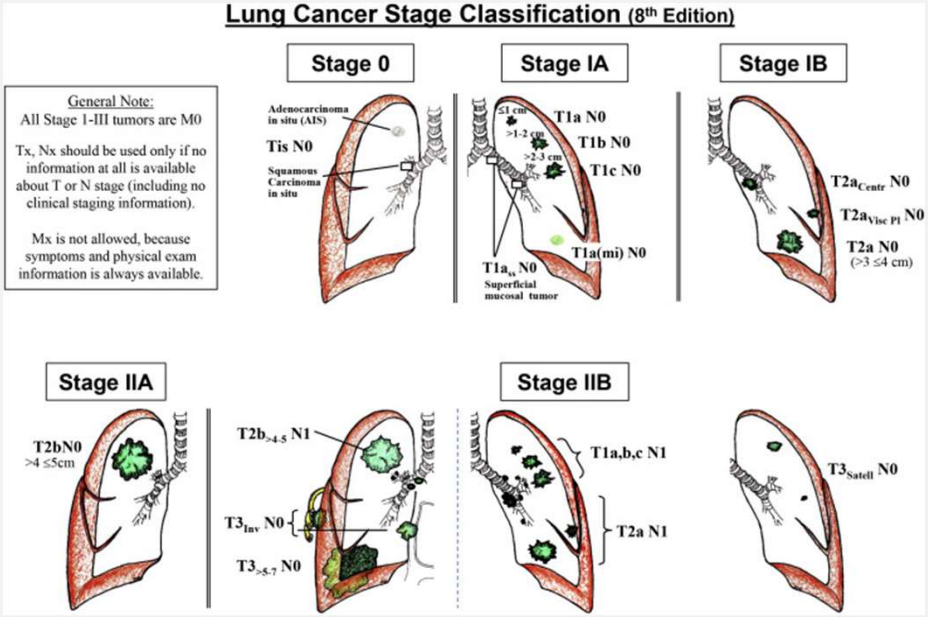
- Most detailed way of staging is TNM (via AJCC guidelines)
  - T (Tumour), T1-4
    - Accounting for size, extent and invasion of cancer
  - N (Nodes), N0-3
    - Regional lymph node involvement, number and extent of spread
  - M (Metastases), M0-1
    - Presence of distant metastasis
- Prefixes include c (clinical), p (pathological), y (following initial neoadjuvant treatment)
- Each cancer has its own definitions of TNM to Staging



TNM 8th - Primary tumor characteristics

T_x	Tumor in sputum/bronchial washings but not be assessed in imaging or bronchoscopy
T_0	No evidence of tumor
T_{is}	Carcinoma in situ
T_1	≤ 3 cm surrounded by lung/visceral pleura, not involving main bronchus
$T_{1a(mi)}$	Minimally invasive carcinoma
T_{1a}	≤ 1 cm
T_{1b}	> 1 to ≤ 2 cm
T_{1c}	> 2 to ≤ 3 cm
T_2	> 3 to ≤ 5 cm *or* involvement of main bronchus without carina, regardless of distance from carina or invasion visceral pleural *or* atelectasis or post obstructive pneumonitis extending to hilum
T_{2a}	>3 to ≤4cm
T_{2b}	>4 to ≤5cm
T_3	>5 to ≤7cm in greatest dimension *or* tumor of any size that involves chest wall, pericardium, phrenic nerve *or* satellite nodules in the same lobe
T_4	> 7cm in greatest dimension *or* any tumor with invasion of mediastinum, diaphragm, heart, great vessels, recurrent laryngeal nerve, carina, trachea, oesophagus, spine *or* separate tumor in different lobe of ipsilateral lung
N_1	Ipsilateral peribronchial and/or hilar nodes and intrapulmonary nodes
2	Ipsilateral mediastinal and/or subcarinal nodes
3	Contralateral mediastinal or hilar; ipsilateral/contralateral scalene/ supraclavicular
M_1	Distant metastasis
M_{1a}	Tumor in contralateral lung or pleural/pericardial nodule/malignant effusion
M_{1b}	Single extrathoracic metastasis, including single non-regional lymphnode
M_{1c}	Multiple extrathoracic metastases in one or more organs

	N0	N1	N2	N3
T1	IA	IIB	IIIA	IIIB
T2a	IB	IIB	IIIA	IIIB
T2b	IIA	IIB	IIIA	IIIB
T3	IIB	IIIA	IIIB	IIIC
T4	IIIA	IIIA	IIIB	IIIC
M1a	IVA	IVA	IVA	IVA
M1b	IVA	IVA	IVA	IVA
M1c	IVB	IVB	IVB	IVB

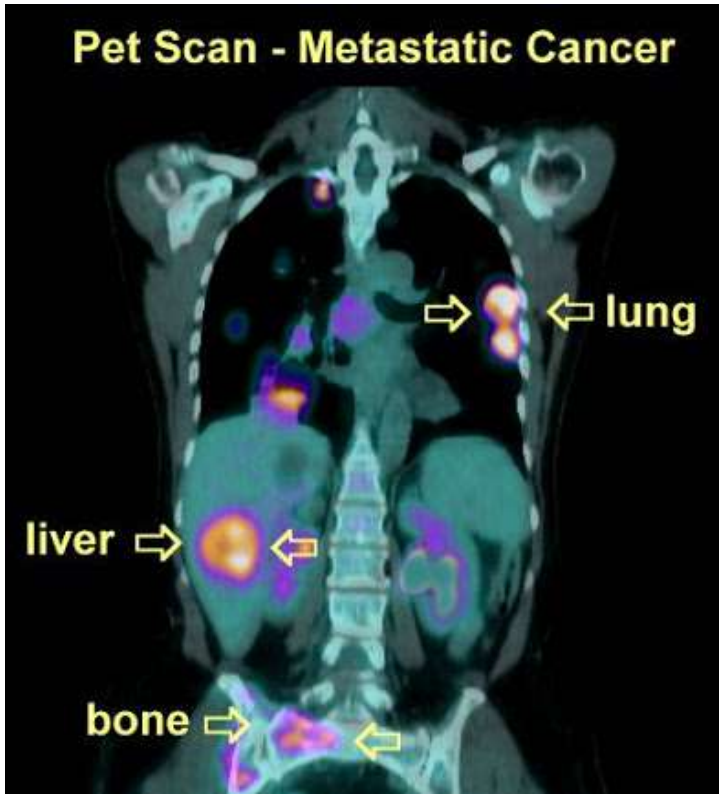


… MORE SIMPLISTICALLY

Curative intent*
- Stage 1 – Small and local
- Stage 2 – Bigger and local
- Stage 3 – Involving lymph nodes

Palliative intent*
- Stage 4 – Metastatic

Accurate staging at diagnosis with use of radiology (CT, MRI, PET, bone scans) is important as it guides treatment decisions



Metastatic synonymous with 'Stage 4', 'advanced', 'end-stage', 'secondaries in…'

CAVEATS TO THIS

EARLY STAGE CANCER
MAY NOT BE CURATIVE INTENT AS

- Invasive cancer (T4) into other structures and unable to curatively surgically resect or use RT in a field for cure

- Patient factors
  - Not fit for treatment because of poor ECOG, medical comorbidities, older age
  - Declining treatment
  - Treatment not available

METASTATIC CANCER
MAY NOT BE PALLIATIVE INTENT AS

- Type of cancer
  - Testicular cancer
  - Germ cell cancers
  - Lymphoma

- 'Oligometastatic disease'
  - Breast
  - Colorectal

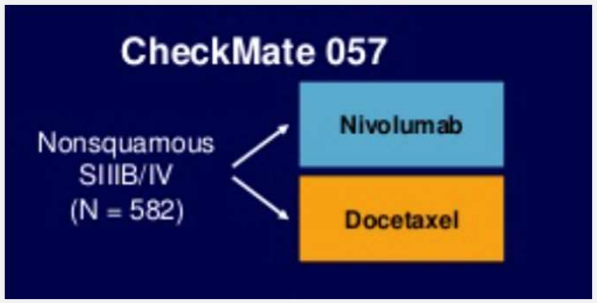
MRS GT AND THE RESULTS

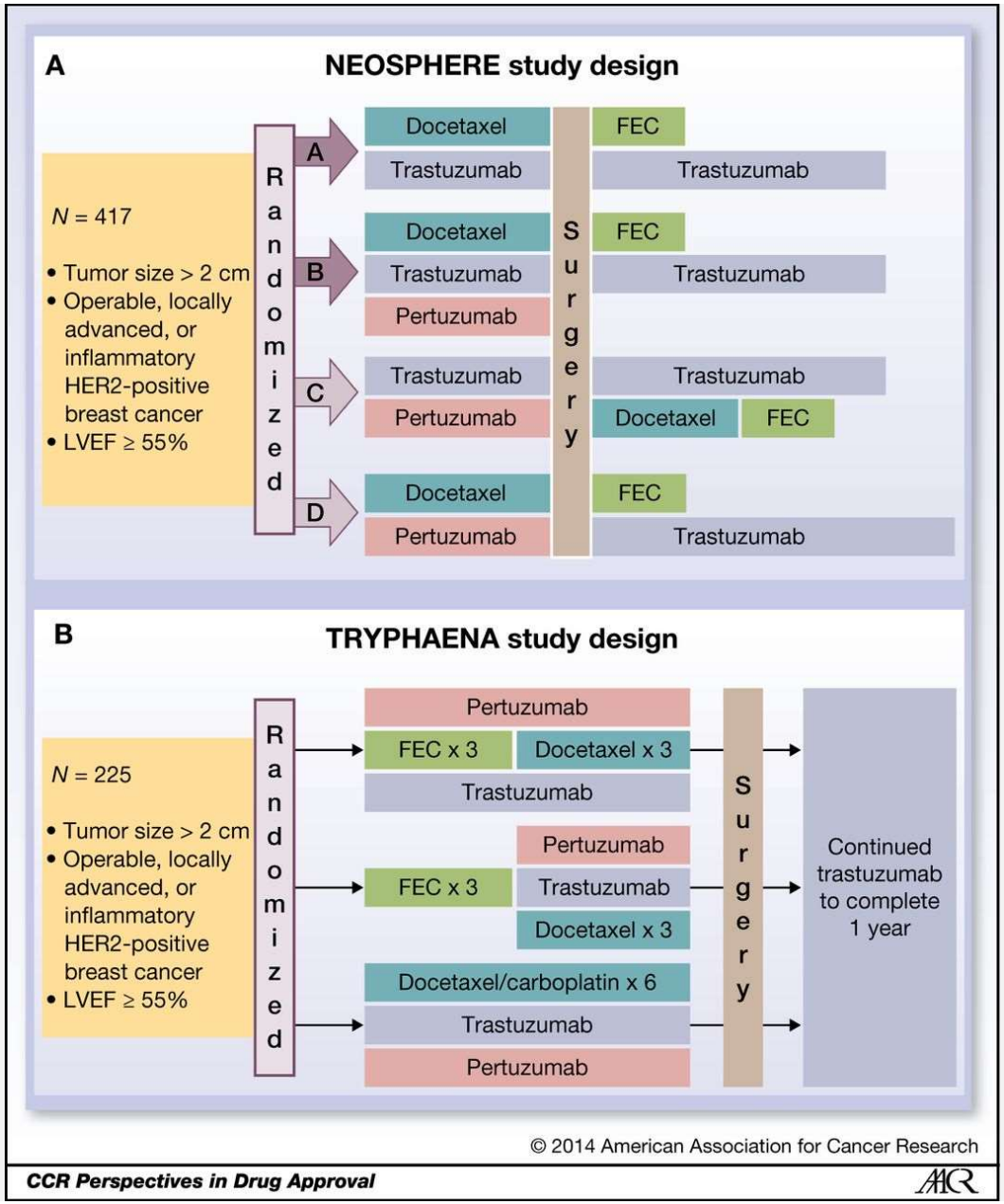
- Have to break bad news to Mrs Chey and family, using interpreter
- Stage 4 (of 4), metastatic, incurable cancer
  - Nodal, liver and bone metastases (secondaries)
- Median prognosis is 6-10 months, with treatment 12-18 months
- Mrs Chey feels a bit better after fluid has been drained, now ECOG 1
- No immediate local mass effect from primary cancer or metastases
- Mrs Chey and family want to know if there are any treatment options?
  - ‘Do I just go home and wait to die?’

TYPES OF CANCER TREATMENT

- **Chemotherapy** = 'atomic bomb', 'poison'
- **Immunotherapy** = 'takes the brakes off your own immune system', 'priming your own soldiers to do the work'
- **Targeted therapy** = 'sniper attack'
- **Surgery** = 'knife'
- **Radiation** = 'fire', 'laser'

Clinical Trial Phases





2002

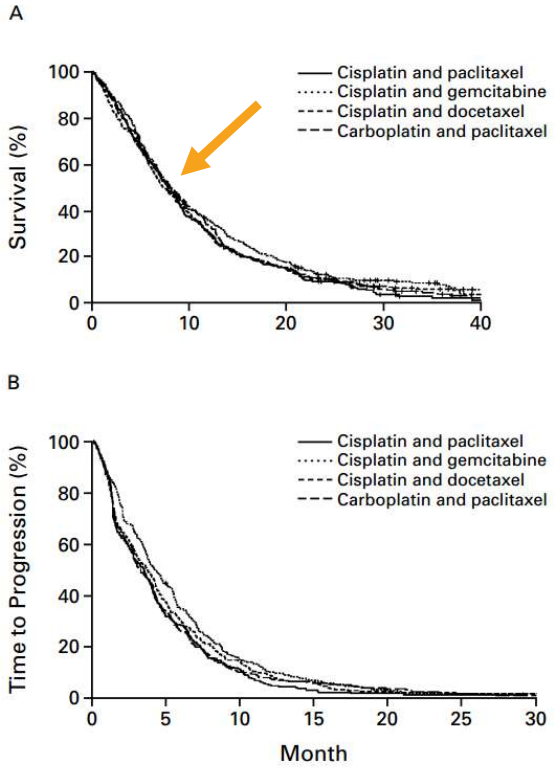


Figure 2. Kaplan–Meier Estimates of Overall Survival (Panel A) and the Time to Progression of Disease (Panel B) in the Study Patients, According to the Assigned Treatment.

The New England Journal of Medicine

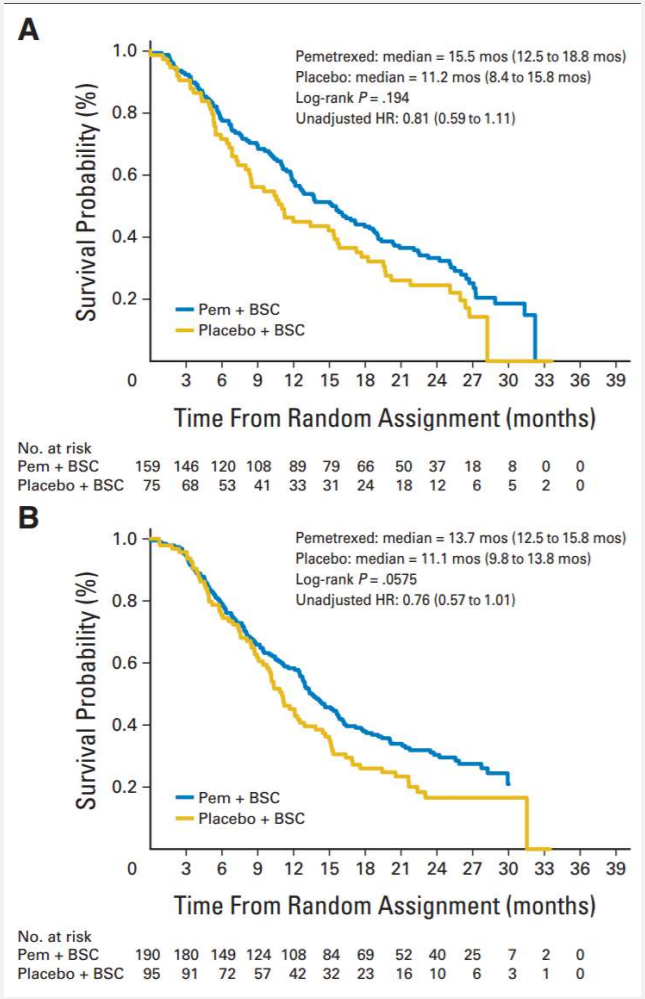
COMPARISON OF FOUR CHEMOTHERAPY REGIMENS FOR ADVANCED NON–SMALL-CELL LUNG CANCER

JOAN H. SCHILLER, M.D., DAVID HARRINGTON, PH.D., CHANDRA P. BELANI, M.D., COREY LANGER, M.D., ALAN SANDLER, M.D., JAMES KROOK, M.D., JUNMING ZHU, PH.D., AND DAVID H. JOHNSON, M.D., FOR THE EASTERN COOPERATIVE ONCOLOGY GROUP

Kaplan Meier survival curves
x axis – survival months
y axis – population of patients still alive at that survival

Can see it's about 10 months median OS

2013



2015

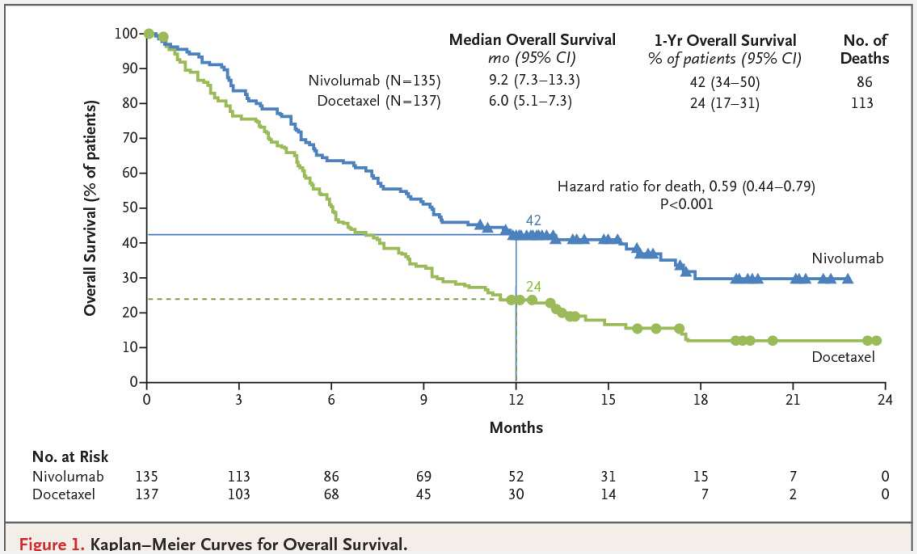
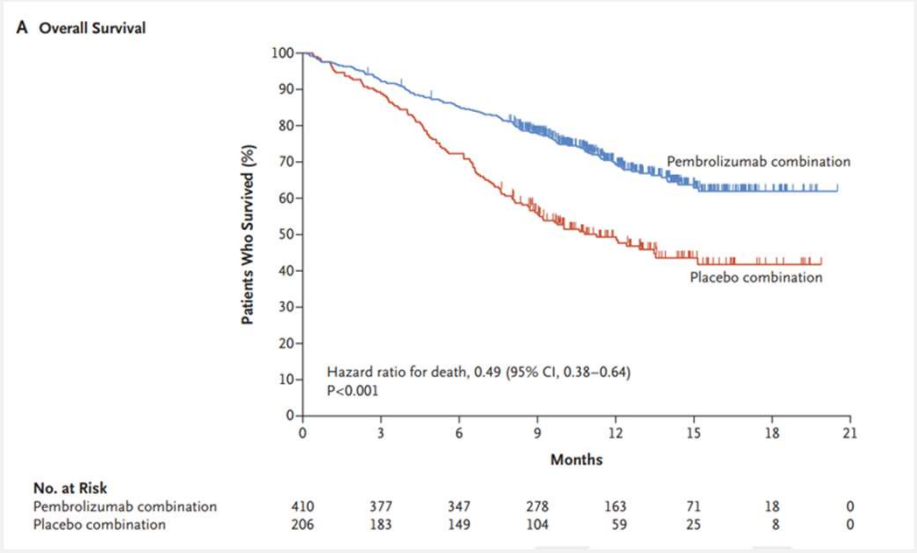


Figure 1. Kaplan–Meier Curves for Overall Survival.

2018



EARLY REFERRAL TO PALLIATIVE CARE

- Attention to physical and psychosocial symptoms
- Establishing goals of care
- Assisting with decision making
- Coordinating care between allied health

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early Palliative Care for Patients with Metastatic Non–Small-Cell Lung Cancer

Jennifer S. Temel, M.D., Joseph A. Greer, Ph.D., Alona Muzikansky, M.A., Emily R. Gallagher, R.N., Sonal Admane, M.B., B.S., M.P.H., Vicki A. Jackson, M.D., M.P.H., Constance M. Dahlin, A.P.N., Craig D. Blinderman, M.D., Juliet Jacobsen, M.D., William F. Pirl, M.D., M.P.H., J. Andrew Billings, M.D., and Thomas J. Lynch, M.D.

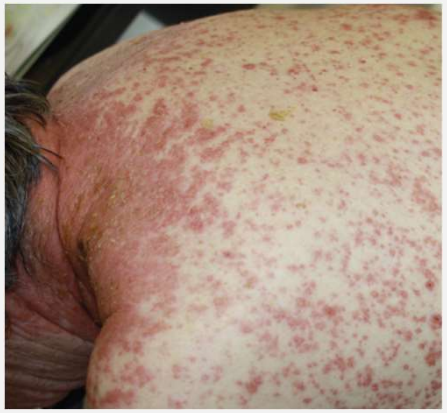
ABSTRACT

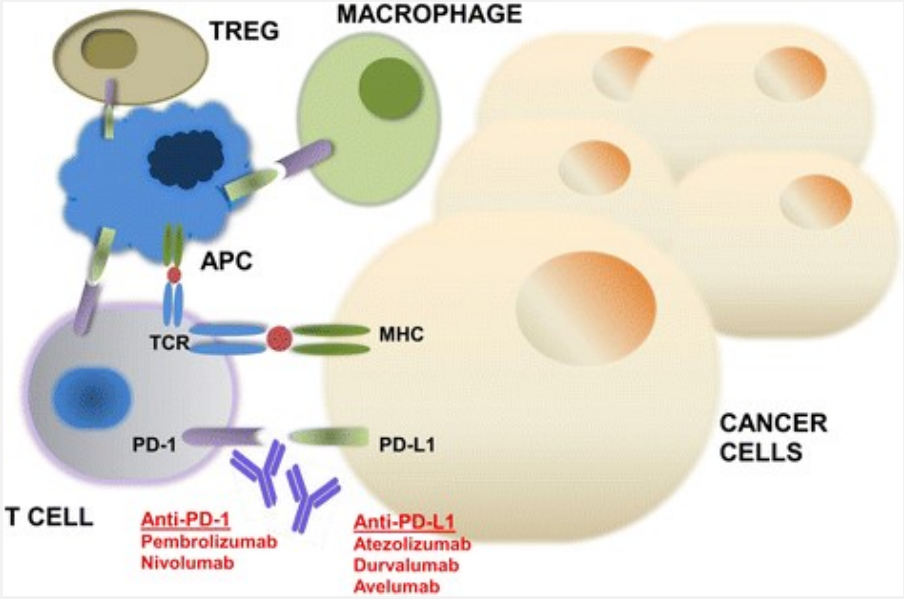
Better quality of life, less depressive symptoms, less aggressive end of life care, longer survival


Cure sometimes, treat often, comfort always.
Hippocrates

MRS CHEY, 2 MONTHS LATER

- Mrs Chey is started on first line immunotherapy, pembrolizumab, anti PD1 agent
- A fortnight ago, CT staging shows cancer is responding (partial response)
- Has had a few immunotherapy related side effects
  - Dermatitis
  - Thyroiditis– leading to hypothyroidism



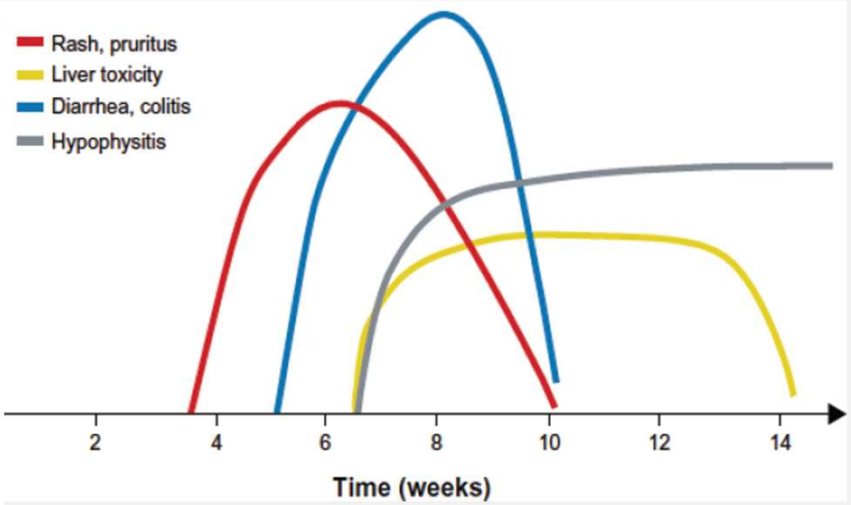


PD1 is a protein found on T immune cells
Cell surface receptor that "down-regulates the immune system"
Suppressing T cell inflammatory activity (stopping T cells from killing other cells)

IMMUNOTHERAPY SIDE EFFECTS

- "Anything that ends with –itis"

System	Immune Related Adverse Events
Gastrointestinal	Colitis (diarrhea, perforation)
Renal	Acute interstitial nephritis (increased serum creatinine)
Pulmonary	Pneumonitis (dyspnea, cough)
Dermatologic	Dermatitis (lichenoid/spongiotic dermatitis, rash), vitaligo
Hepatic	Hepatitis (elevated LFTs)
Neurologic	Central and peripheral (aseptic meningitis, Guillan-Barre Syndrome, myasthenia gravis)
Endocrine	Hypophysitis, thyroiditis, adrenal insufficiency
Ocular	Uveitis, iritis



Doublet immunotherapy (anti CTLA-4 and anti PDL1) = 50% risk of iRAE
Single immunotherapy (anti PDL1) = 10% risk of iRAE

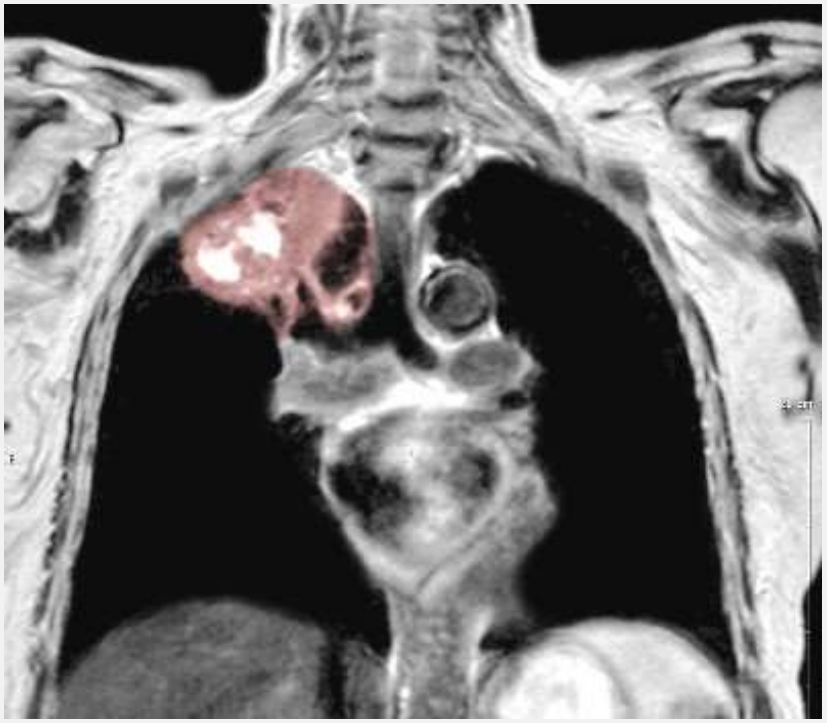
MRS CHEY, 1 MONTH LATER

- Sudden onset shortness of breath
- Rushed to ED, O2 sats 79% and drowsy
- What are some of the differential ddx?
  - Mass related (all about anatomy)
  - Treatment related (all related to what the drugs do)
  - General malignancy related (how does cancer change our physiology)

DYSPNOEA DDX IN MALIGNANCY

Cancer-mass related

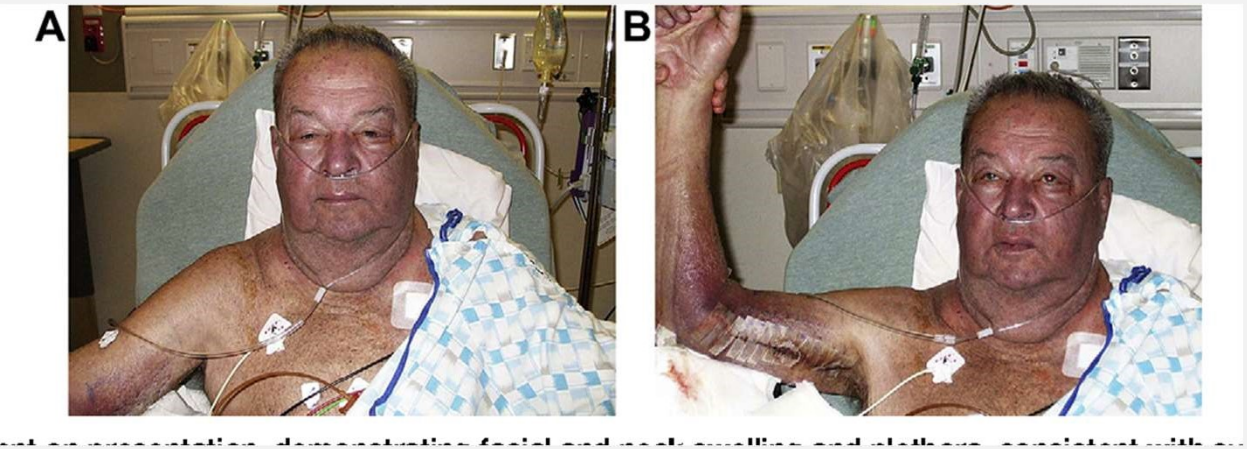
- Progressively growing cancer
- Pleural effusion
- Lung collapse
- Superior vena-caval obstruction (SVCO)

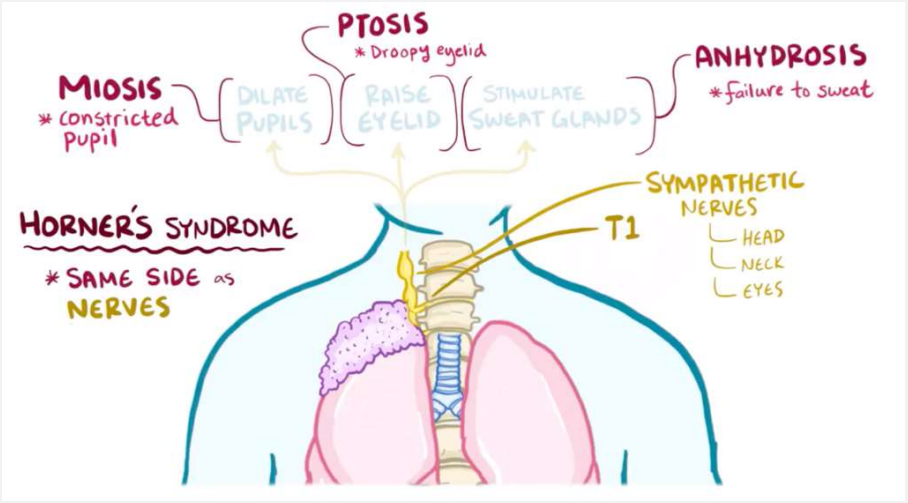


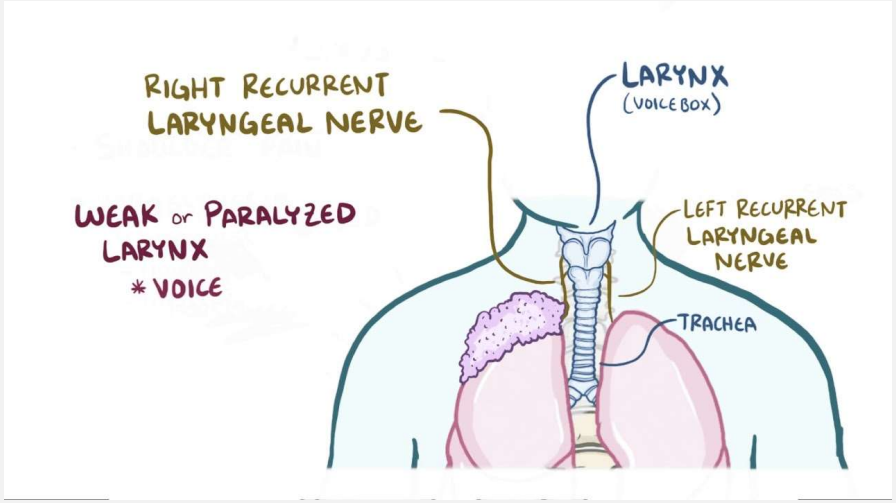
Pancoast tumour - SVCO
Obstructed brachiocephalic vein
Obstructed SVC
Disruption of the recurrent laryngeal nerve
Disruption of the sympathetic chain

What SVCO clinical symptoms might you see with this?

SVCO







Facial and upper extremity oedema
Shortness of breath
Headache, chest pain
Facial plethora, distended neck and chest veins
Pemberton's sign positive

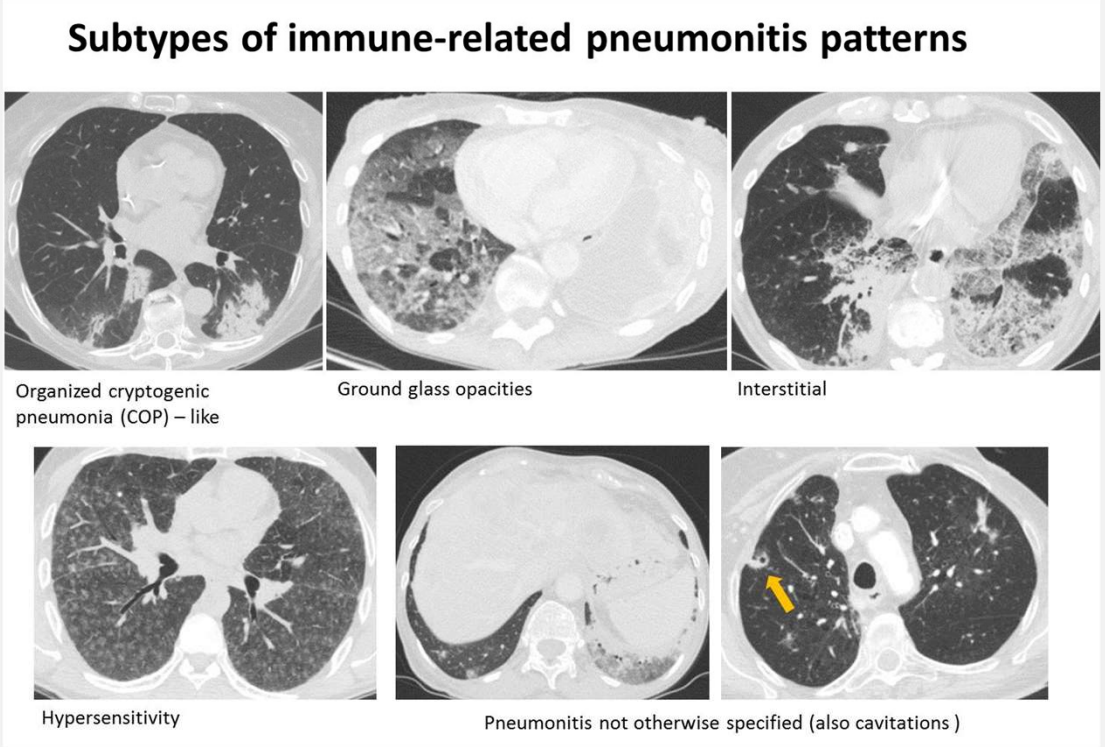
Horner's syndrome
Hoarse voice

DYSPNOEA DDX IN MALIGNANCY

Treatment related
Pneumonia (immunosuppression from chemo)

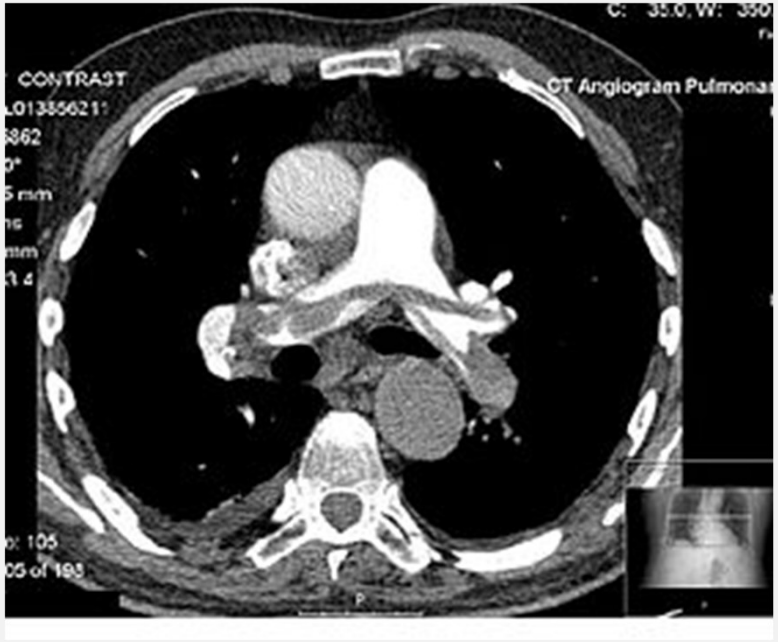
Pneumonitis (immune related pneumonitis, radiation induced pneumonitis)

Anaemia (BM suppression)



WHAT ABOUT A PULMONARY EMBOLUS?

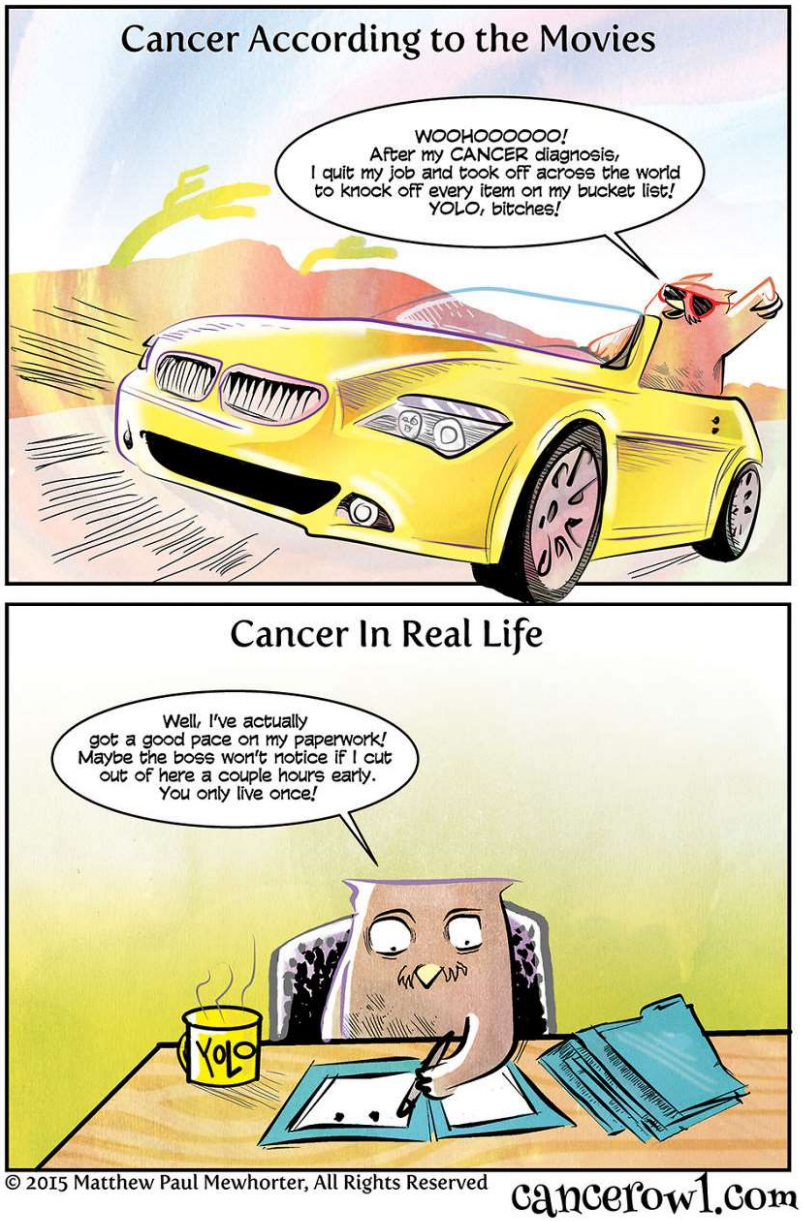
- General malignancy related
  - Cancer is an immunosuppressive state – infections, anaemia
  - Cancer is an inflammatory state – risk of CV disease
  - Worsens underlying diseases – exac COPD, exac CCF
  - Cancer is a pro coagulant risk – venous thrombosis (DVT), pulmonary embolus
    - 25% cancer patients will have VTE at some stage, 3-fold increase in recurrent VTE



Management

Supportive care – O2
Anti-coagulation:
If symptomatic – clexane
If asymptomatic – NOACs
Lifelong anti coagulation

A PAUSE FOR QUESTIONS



FRED, PR BLEEDING

- 55 yo bright red PR bleeding for 3 weeks
- Thought it was haemorrhoids at first, but has not ceased
- Now strange sensation, of after emptying bowels, feels urge to go again
- Yet to do Bowel Cancer Screening test
- PMHx/SHx – non-smoker, non-ETOH, no other issues
- Adopted, so unclear of family history
- Digital rectal exam – external haemorrhoids seen, hard mass in rectum, no melaena on glove

What are some ddx of PR bleeding?
What are cancer screening guidelines?
Why could family history be important?

CANCER SCREENING IN AUSTRALIA

3 PROGRAMS

National bowel screening program

- Faecal occult blood test (FOBT) – age 50-74 yo every 2 years

Breastscreen Australia

- Mammograms – age 50-74yo every 2 years for women

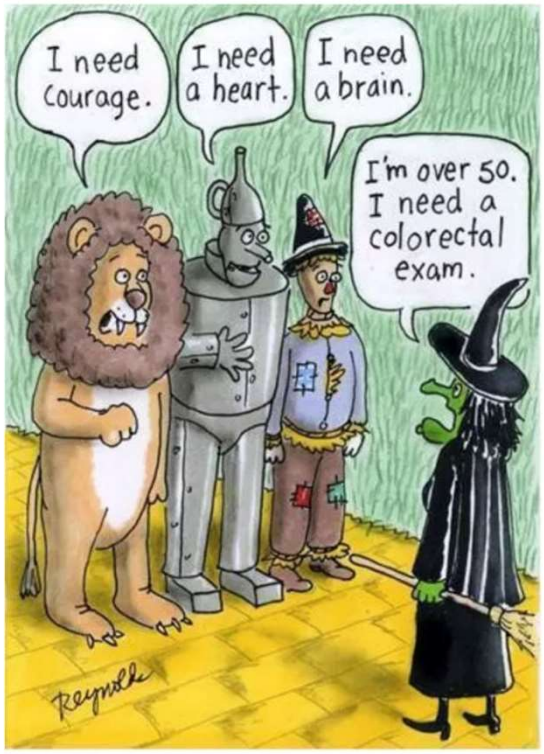
National cervical screening program

- Cervical screening test (HPV and abnormal cells)

Age 25 to 74yo, every 5 years for women

In addition, your GP may suggest:

1. Regular skin exams
2. What about Prostate Specific Antigen?
    1. Screening of asymptomatic (low-risk) men is not advised
    2. Need to discuss benefits and harms (overdiagnosis, overtreatment)



CAN'T WE JUST DO A BLOOD TEST FOR TUMOUR MARKERS TO SCREEN EVERYONE FOR CANCER?

- Traditionally, proteins are made by cancer cells **and** normal cells but expressed in higher quantities by cancer cells
- **NOT** to be used for diagnosis or screening alone
- Best used in surveillance (?recurrence), or when having treatment to assess for early response
- Now upcoming research on circulating tumour cells (melanoma) or circulating tumour DNA (colorectal)
  *The new more effective tumour markers

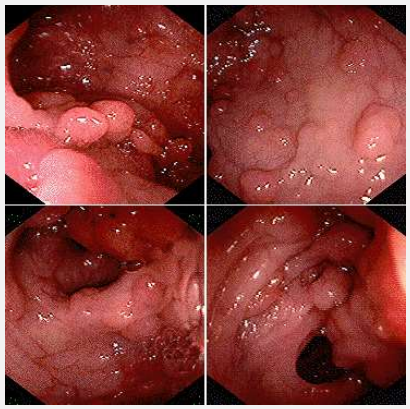
Cancer	Marker(s)
Colorectal	CEA
Hepatocellular	AFP
Pancreatic	CA 19-9
Ovarian	CA 125
Breast	CA 15-3
Prostate	PSA
Germ cell	AFP, HCG
Lung (non-small cell)	CYFRA 21-1, SCC
Lung (small cell)	NSE, proGRP
Melanoma	S100
Trophoblastic	HCG
Thyroid (differentiated)	thyroglobulin

SCC = Squamous cell carcinoma; NSE = neuron-specific enolase.

HEREDITARY COLORECTAL CANCER SYNDROMES

Familial adenomatous polyposis (FAP)

- Presence of 100-1000s colonic adenomatous polyps
- Variant in the APC, tumour suppressor gene
- Autosomal dominant
- Colorectal cancer will occur in 100% patients if FAP is left untreated, around age 40yo
- Colectomy is recommended for patients



Lynch syndrome
(hereditary non polyposis colorectal cancer)

- Autosomal dominant
- Germline mutation in one of the DNA mismatch repair genes (MMR) – MLH1, MSH2, MSH6, PMS2
- Predominately right sided in location, more mucinous, more signet ring
- Includes – endometrial, small bowel, ureter, renal pelvis

- Amsterdam criteria to suspect:
  - 3 relatives with suspected Lynch syndrome with 1 being first-degree relative of other 2
  - 2 successive generations
  - 1 < age 50

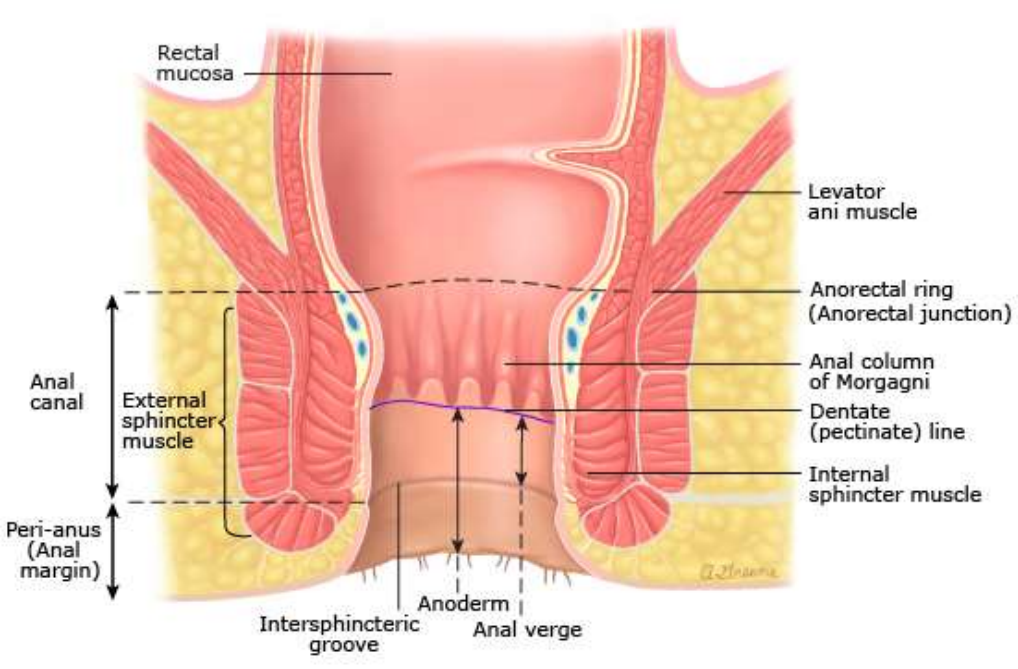
FRED, 55YO, PR BLEEDING

Differentials for PR bleeding

- Haemorrhoids
- Anal fissure
- Colonic AVM
- Diverticulosis
- Infection – shigella, campylobacter, salmonella
- Inflammatory bowel disease – Ulcerative colitis > Crohn's at this age
- Colonic polyps
- Colon cancer
- Rectal cancer

FRED, 55YO, PR BLEEDING

- Colonoscopy and biopsy
  - Rectal cancer 7cm from anal verge
  - Histopathology – T3N2 rectal adenocarcinoma
- MRI rectum
  - Confirms histopathological diagnosis
  - Invading the mesorectal fascia – thus a decreased likelihood of achieving a tumour free circumferential resection margin (CRM) with upfront surgery
- CT staging – chest/abdomen/pelvis
  - No metastatic disease (likely locations would be liver, lung, peritoneal space)
- MDM discussion – for upfront neoadjuvant chemo-radiation, followed by surgery (?sphincter-sparing)



WHAT IS RADIOTHERAPY?

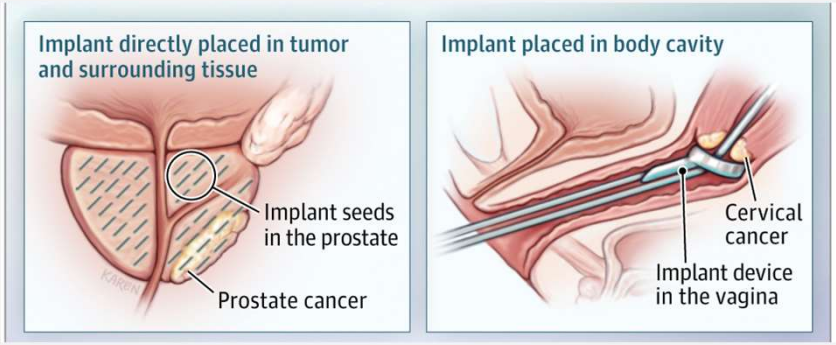
- Radiotherapy uses radiation, such as x-rays, gamma rays, electron beams or protons, to kill or damage cancer cells so they cannot grow or multiply.
- It is a localised treatment, which means it generally only affects the part of the body where the radiation is targeted.
- Cancer cells are more susceptible to radiation than healthy, non-cancerous cells
  - Less organized than non-cancerous cells, thus damage done cannot be undone as quickly

TWO MAIN TYPES OF RADIOTHERAPY:

External beam radiotherapy

- Radiation delivered by a linear accelerator from multiple angles
- Number of fractions (sessions) can vary from a single fraction to treatments every weekday for consecutive weeks. Treatment usually takes less than 10min.
- Dose is measured in Gray (Gy)

Brachytherapy (Internal Radiation Therapy)



- Radioactive implants that are placed very near or within a tumour and delivers high doses of radiation with less damage to other organs than external radiation.
- Can be temporary or permanent.

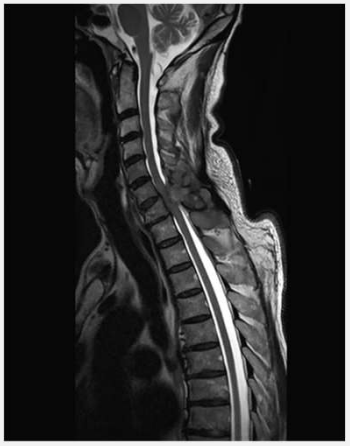
WHAT IS RADIOTHERAPY USED FOR?

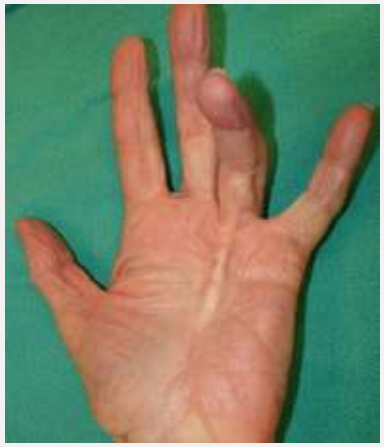
Cancer

- Curative intent
  - Neoadjuvant (prior to surgery)
    - i.e. rectal cancer
  - Definitive treatment
    - I.e. prostate cancer, H&N cancer, cervical cancer
  - Adjuvant (after surgery to prevent recurrence)
    - i.e. breast cancer
- Palliative intent
  - For Example:
    - Spinal cord compression
    - Bone metastases
    - SVC Obstruction

Benign conditions

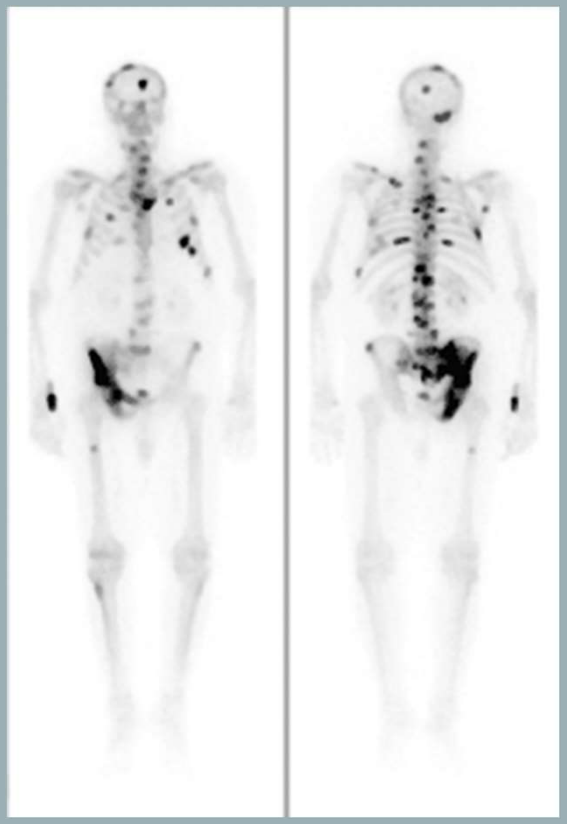
- For Example:
  - Keloid scar
  - Heterotrophic ossification
  - Dupuytren's Contracture





A PAUSE FOR QUESTIONS

IMRAN, 70YO METASTATIC PROSTATE CANCER



- Diagnosed 2 months ago with metastatic prostate cancer with iliac chain lymph node metastases and bone metastases in the axial and appendicular skeleton, PSA 120
- Initially started on 3-monthly Androgen Deprivation Therapy – GnRH agonist with initial Anti-androgen cover
- PSA improved to 60 after 1st month

What kind of treatment is ADT?
What is targeted treatment?
What is hormonal treatment?

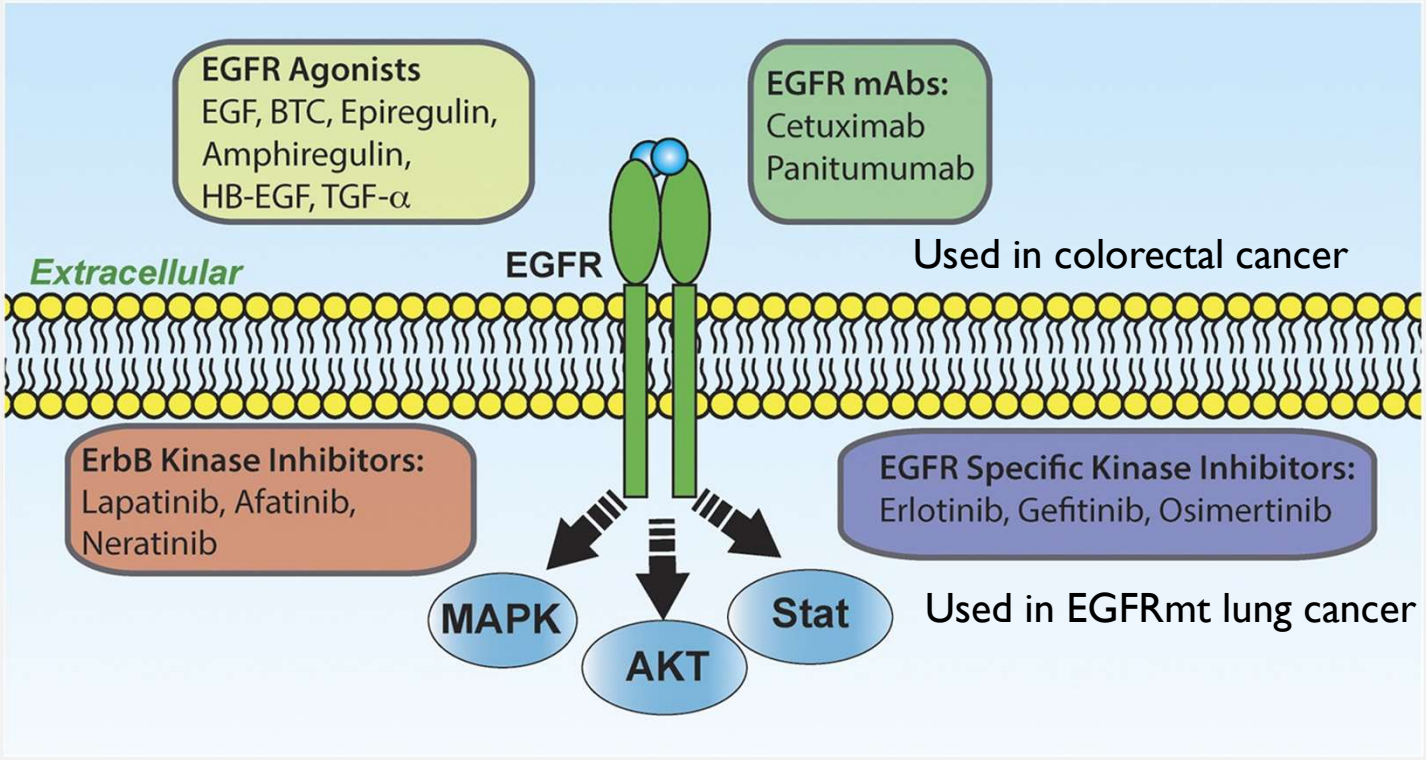
TARGETED TREATMENT

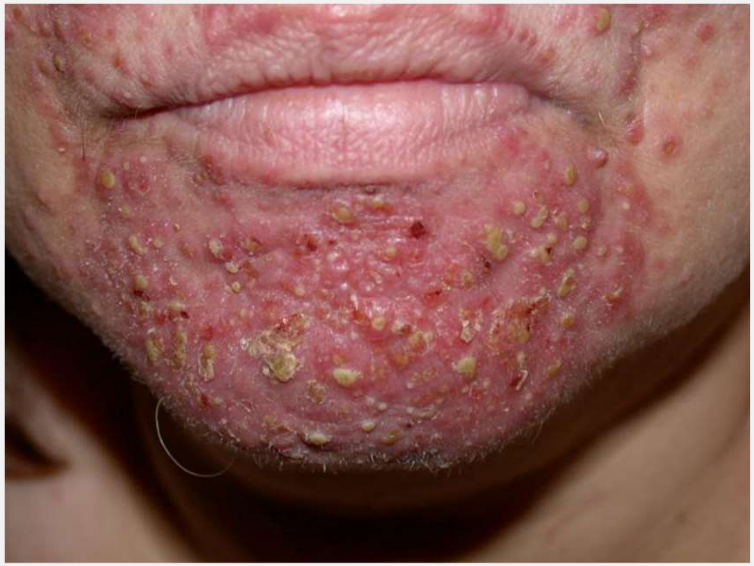
Target

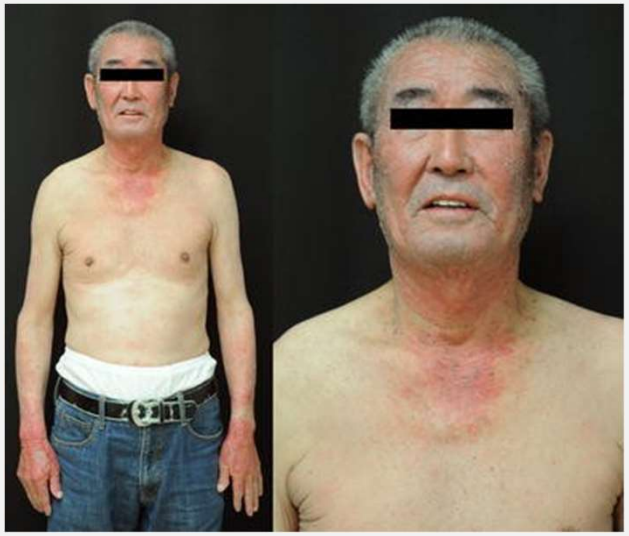
- Epidermal growth factors
- Angiogenesis
- Protein signaling pathways

Arrow

- Hormonal agents
- Monoclonal antibodies “the -abs”
- Small molecular drugs – tyrosine kinase inhibitors “the -ibs”
- One target vs many targets

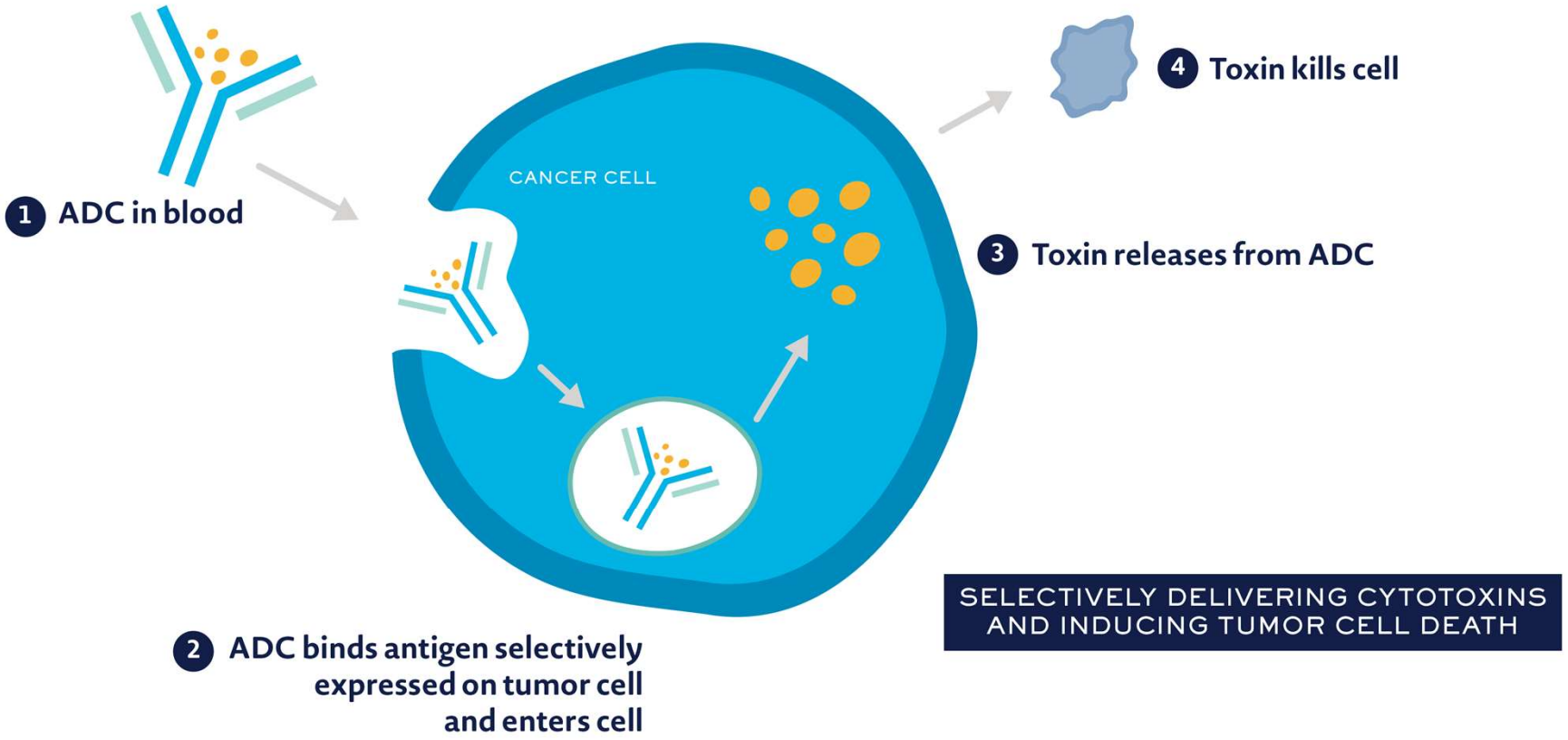




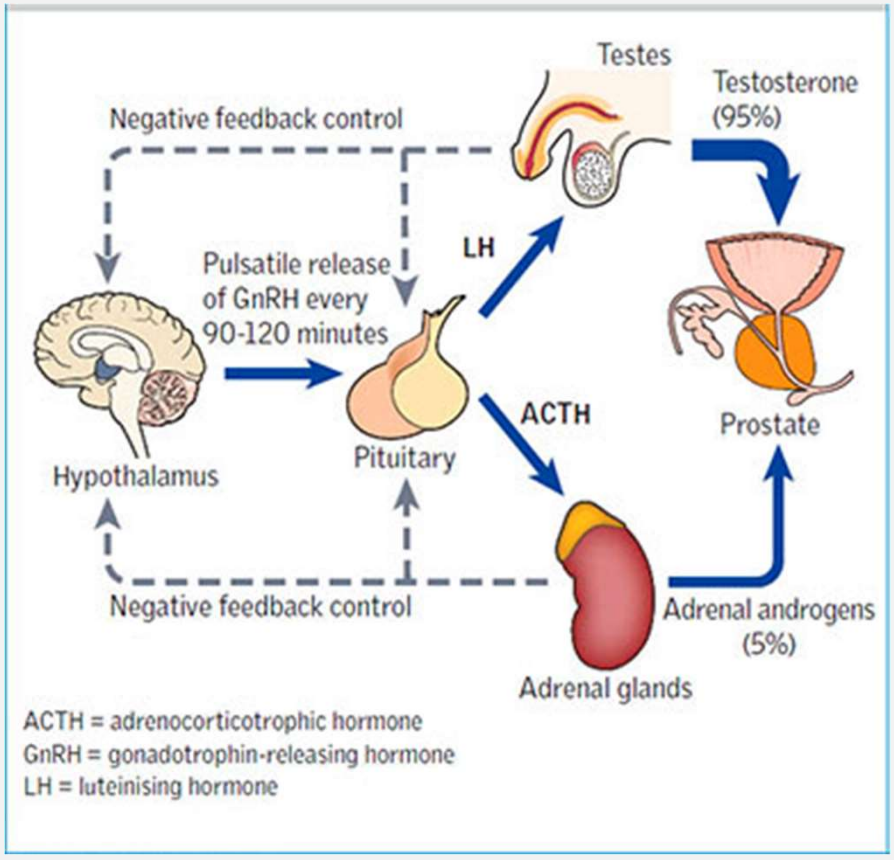


Lapatinib and neratinib used in breast cancer
Afatinib used in ALKmt lung cancer

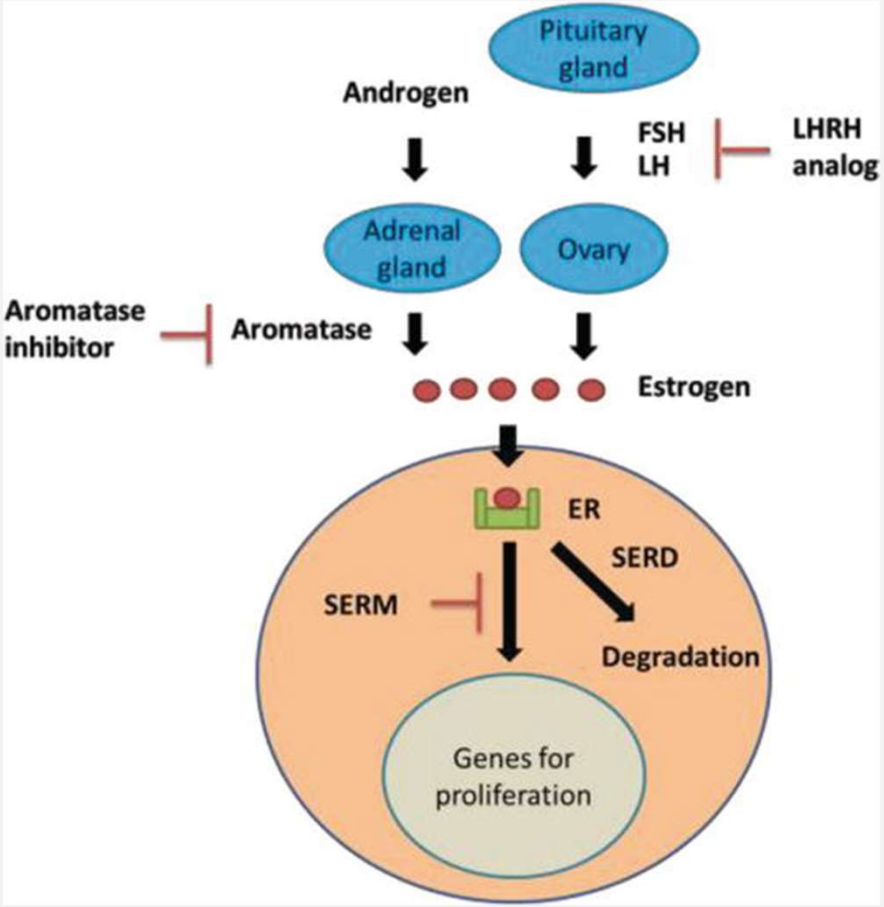
ANTIBODY-DRUG CONJUGATES



PROSTATE CANCER – GNRH AGONISTS, ANTI ANDROGENS



- **Breast cancer – tamoxifen (SERM) aromatase inhibitors**



COMMON HORMONAL AGENT SE

"Menopausal" symptoms

Hot flushes

Vaginal dryness

Erectile dysfunction

Decreased libido

Mood changes

Increased adiposity, decrease muscle mass

Decreased bone mineral density → osteoporosis

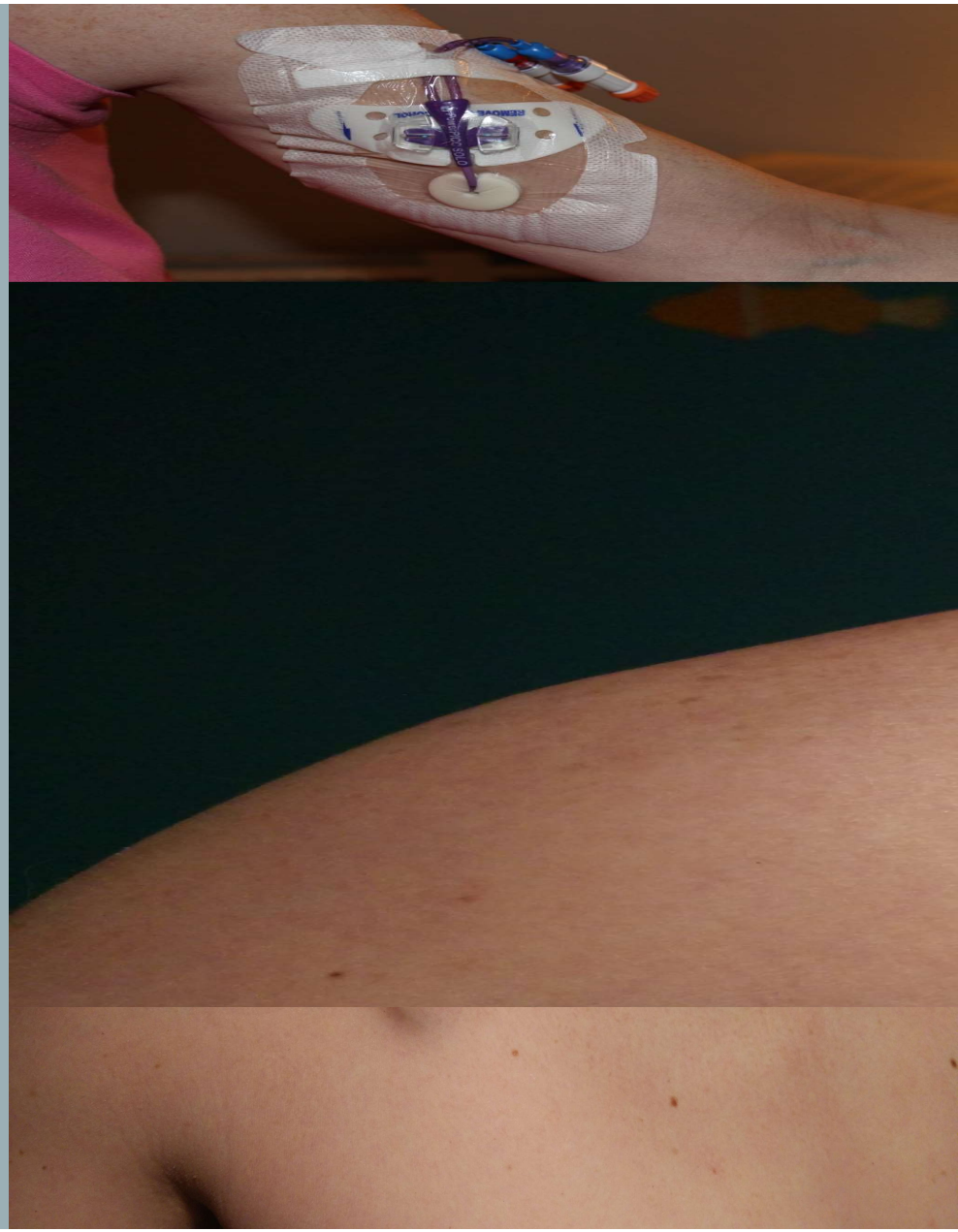
Increased risk of CV risk factors

MR SA, 70YO METASTATIC PROSTATE CANCER

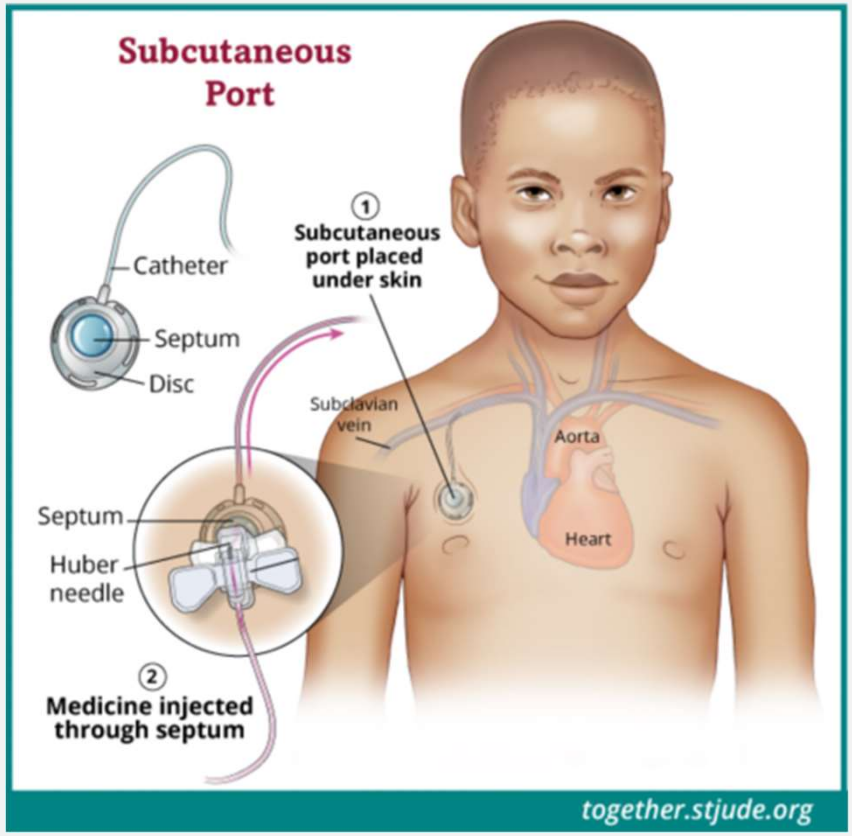
Central venous access– PORT inserted

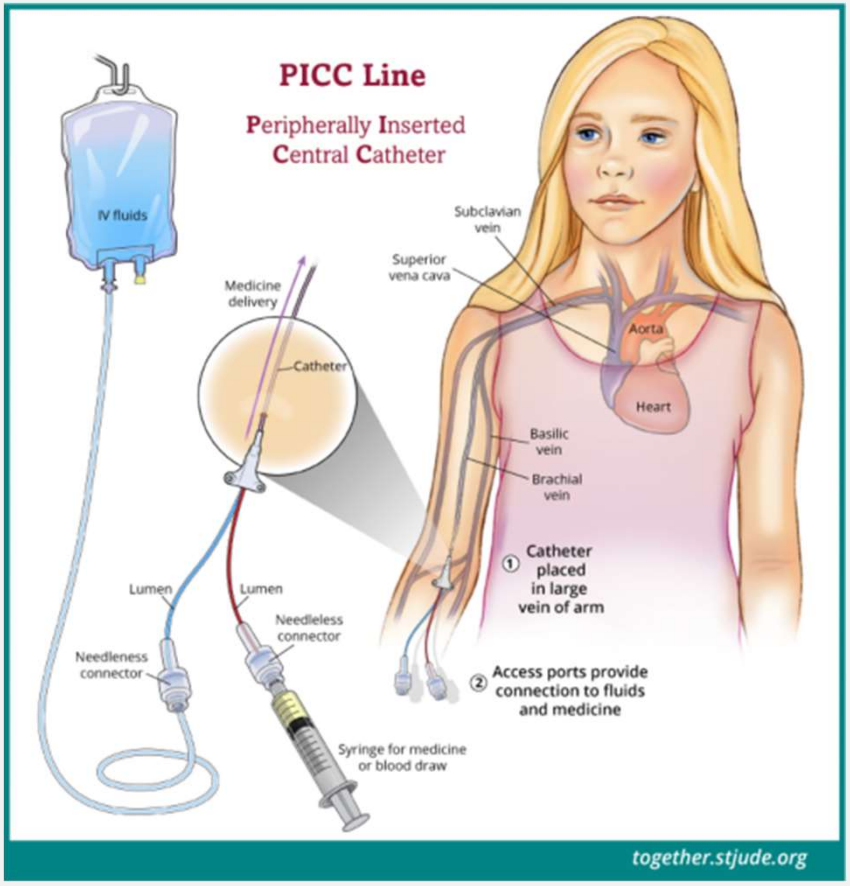
Started on q3 weekly docetaxel chemotherapy

He asks about side effects as he has heard that your hands can get 'affected by the chemo' and he likes to do woodwork in his garage

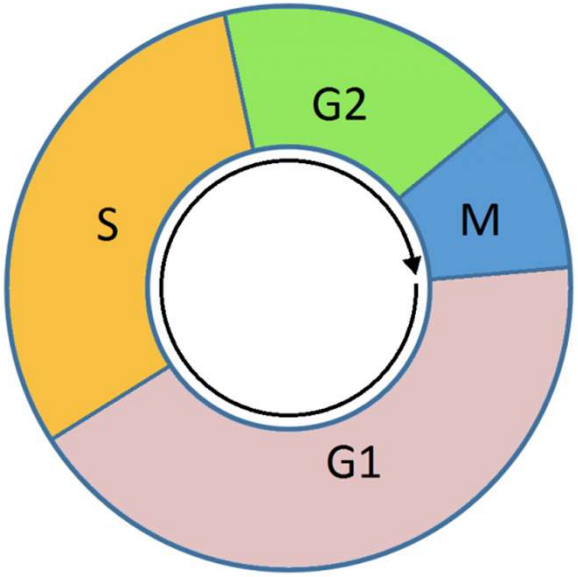


WHAT IS CENTRAL VENOUS ACCESS





WHAT IS CHEMOTHERAPY?

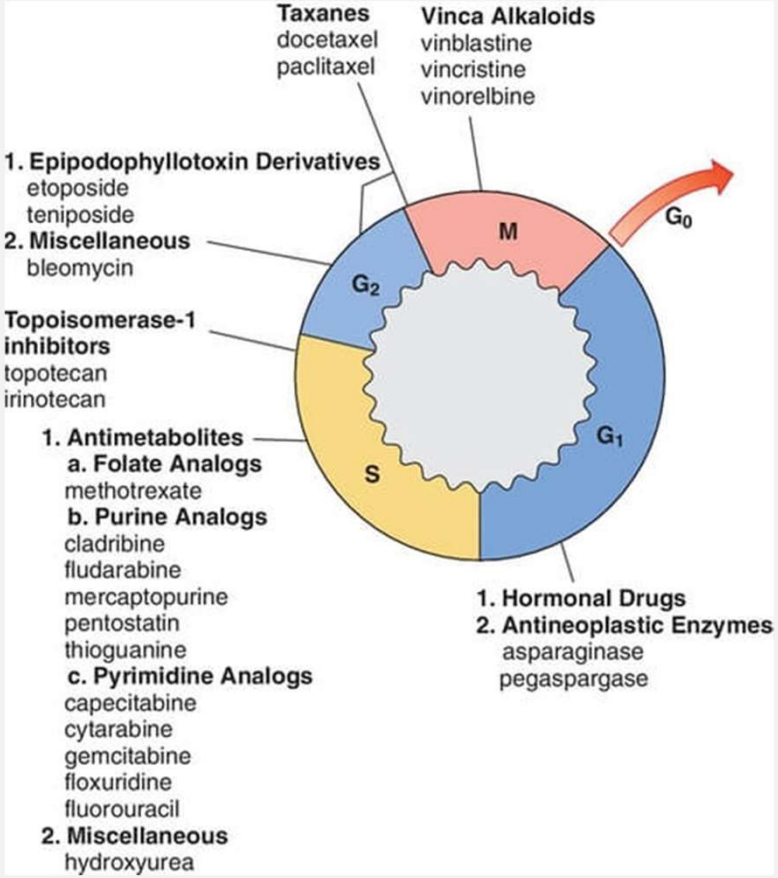


G1 - Growth

S - DNA synthesis

G2 - Growth and preparation for mitosis

M - Mitosis (cell division)

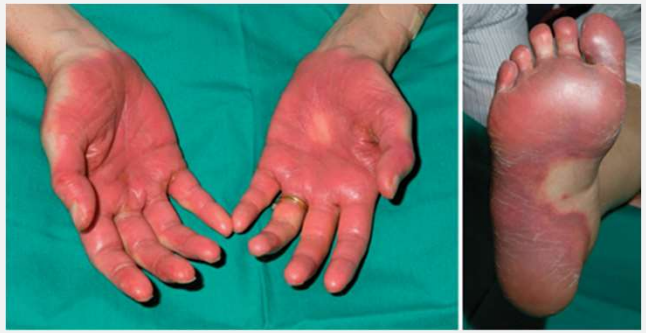


Cycle of chemotherapy (how many days, eg 28 days)
Day of treatments (receive chemo D1, D8, D15)
… this is how we keep track – pt is on C3D8

COMMON CHEMOTHERAPY SIDE EFFECTS

- All chemotherapy, in varying degrees, cause
  - FATIGUE
  - Myelosuppression
  - Risk of febrile neutropenia
  - Mouth ulcers
  - GI toxicities (nausea, vomiting, diarrhea)
  - Smell and taste changes
  - Loss of appetite
  - Hair thinning
  - Skin and nail changes

Management
- Dose reduction
- Dose delay
- Omitting agents
- Supportive medications
- Haematological support
- Involve other specialities



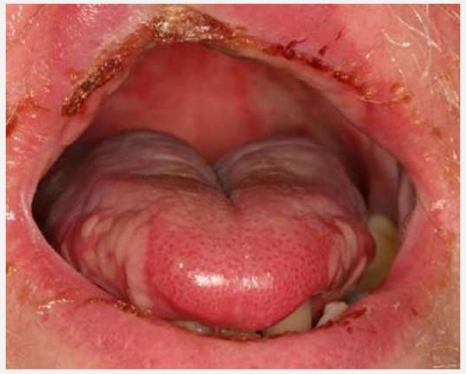
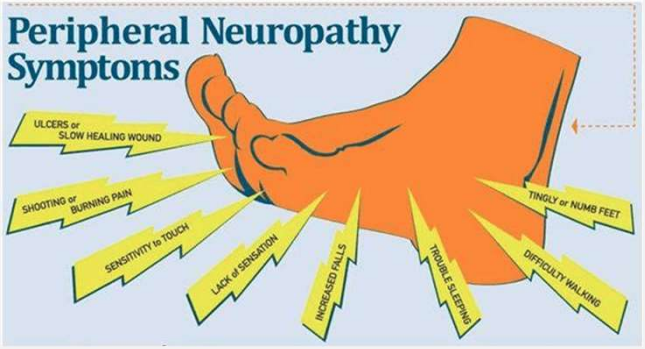
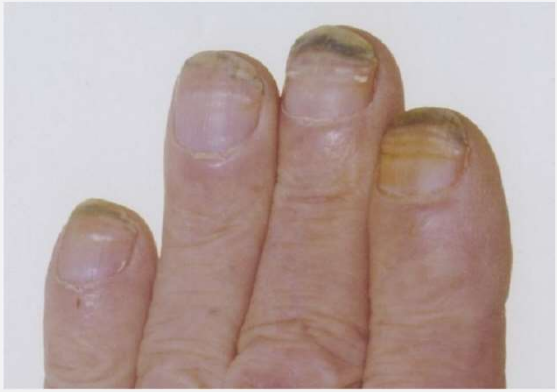


Table 2 Chemotherapy toxicities

Classes	Examples	Side effects
Antimetabolites	5-fluorouracil	GI, BM, mucositis, diarrhea, angina, palmar-plantar dysesthesias
	Capecitabine	
	Gemcitabine	GI, BM, pulmonary, HUS
Antifolates	Methotrexate	BM, mucositis, GI, rash
	Pemetrexed	
Taxanes	Paclitaxel	Interactions (P450), BM, GI, stomatitis, hypersensitivity, bradycardia
	Docetaxel	
Vinca alkaloids	Vincristine	Neurotoxicity, BM
	Vinorelbine	
	Vinblastine	
Topoisomerase inhibitors	Irinotecan	BM, GI (diarrhea)
	Anthracyclines	BM, alopecia, mucositis, cardiotoxic
	Etoposide	BM, hypersensitivity, liver, mucositis
Alkylating agents	Cyclophosphamide	BM, pulmonary, renal/bladder, infertility
Platinum analogs	Cisplatin	GI, renal, ototoxic, BM, neuropathy, rash
	Carboplatin	
	Oxaliplatin	
Thalidomide analogs	Revlimid	BM, constipation, rash, neuropathy, DVT
Molecular targeted drugs	Monoclonal antibodies	BM, GI, skin rash, cardiac (heart failure, hypertension, thromboembolism), fatigue, pulmonary, mucositis, hypersensitivity reactions
	Kinase inhibitors	

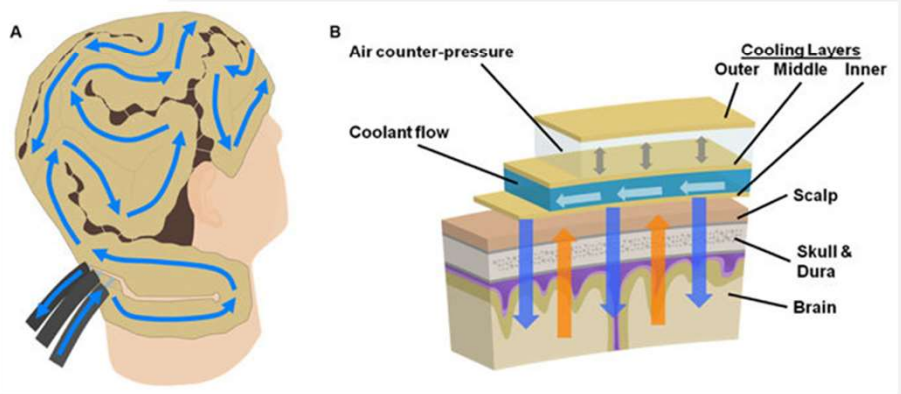




Drugs that May Cause Chemotherapy-Induced Alopecia

Drug Class	Drug and Incidence of Hair Loss		
Antimicrotubules	• Cabazitaxel (10%) • Docetaxel (56%-76%)	• Eribulin (45%) • Ixabepilone (48%)	• Paclitaxel (87%)
Anthracyclines	• Doxorubicin (not defined) • Epirubicin (70%-96%)	• Idarubicin (25%-30%) • Daunorubicin (>10%)	
Alkylating Agents	• Cisplatin <1% • Bendamustine <1% • Busulfan (17%) • Carboplatin (2%-3%)	• Ifosfamide (83%-90%) • Melphalan (not defined) • Oxaliplatin (3%) • Temozolomide (55%)	Frequency not defined: • Cyclophosphamide • Lomustine • Procarbazine • Methchlorethamine • Dacarbazine
Antimetabolites	• Fluorouracil (dependent on rate/duration of therapy)	• Gemcitabine (15%-16%) • Floxuridine (1%-10%)	• Capecitabine (6%)

Source: Lacy, et al. Drug Information



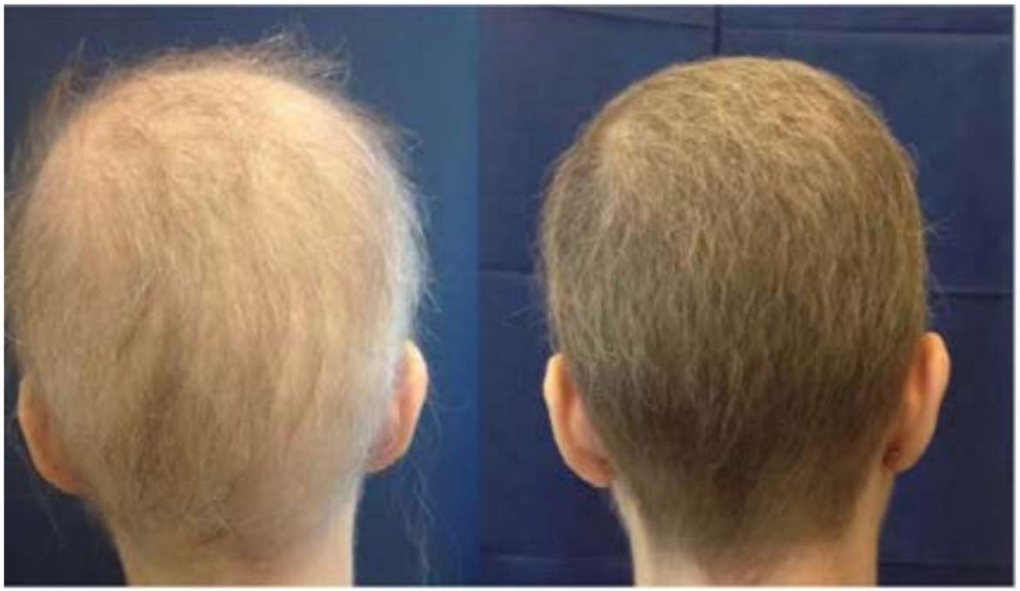


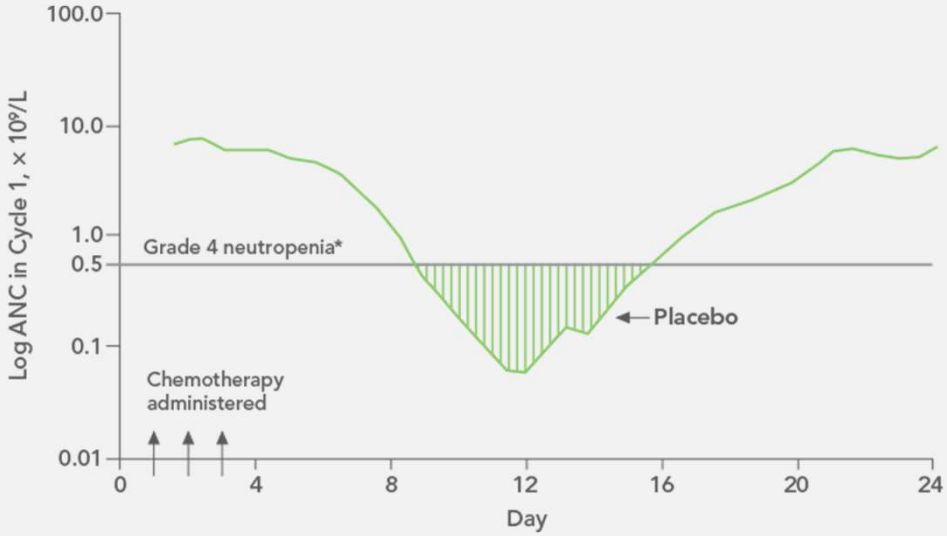
Figure 1 On the left, grade 2 alopecia after four cycles of docetaxel, carboplatin, and trastuzumab, before starting scalp cooling. On the right, hair regrowth after 5th cycle with scalp cooling and topical minoxidil 5%.

MY ONCOLOGIST DOES MY HAIR

A PAUSE FOR QUESTIONS

IMRAN STARTS CHEMOTHERAPY

- Presents with fever 38.8C, rigors, on C2D10
- HR 110, O2 96% RA, BP 120/80
- Otherwise no other specific findings on exam



Could this just be viral and can he just take some paracetamol and go home?
Does he need to be admitted to hospital?
What is the significance of day 10 of treatment?

FEBRILE NEUTROPENIA

- Fever over 38C
- Neutrophils < 1.0 or Neutrophils < 1.5 and predicted to fall
- Suspect with chemotherapy in the last 4 weeks

MANAGEMENT

1. 2 x set of blood cultures (peripheral and central)
2. Broad spectrum 4th generation antibiotics (Tazocin, Ceftazadine) +/- Vancomycin if suspicious of MRSA
3. Supportive care (fluids, pain management etc)
4. Look for source of infection (including hidden locations – dental/ear/joints/skin)
    1. 50% of time – do not find an infection – likely from GU/GI source

18 MONTHS LATER, IMRAN PRESENTS WITH CONFUSION, CONSTIPATION AND DEHYDRATION

- No signs of infection
- CTB – no brain mets
- Blood tests
  - Hypercalcaemia – Ca 3.3 (calcium normal is < 2.5)

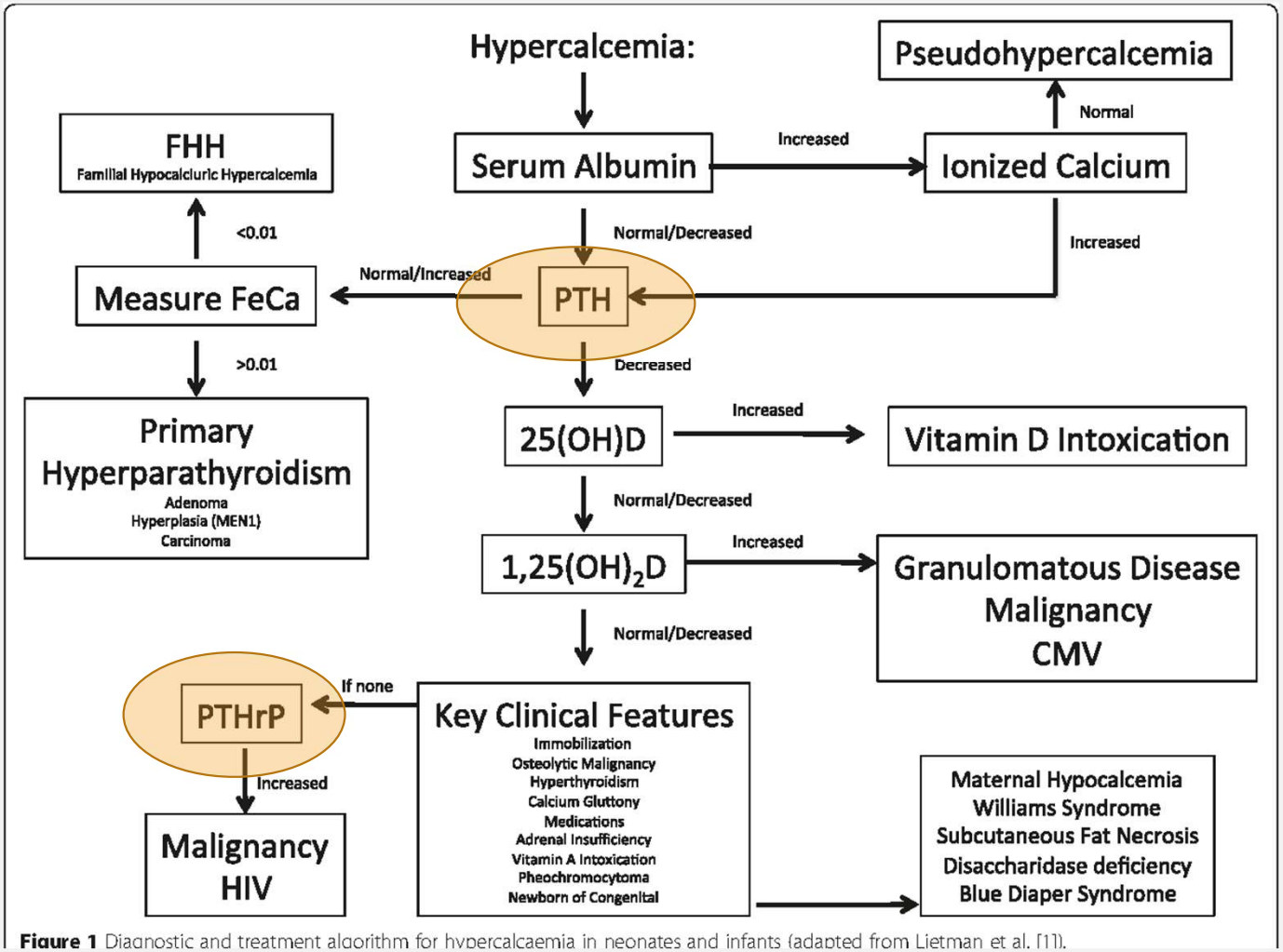
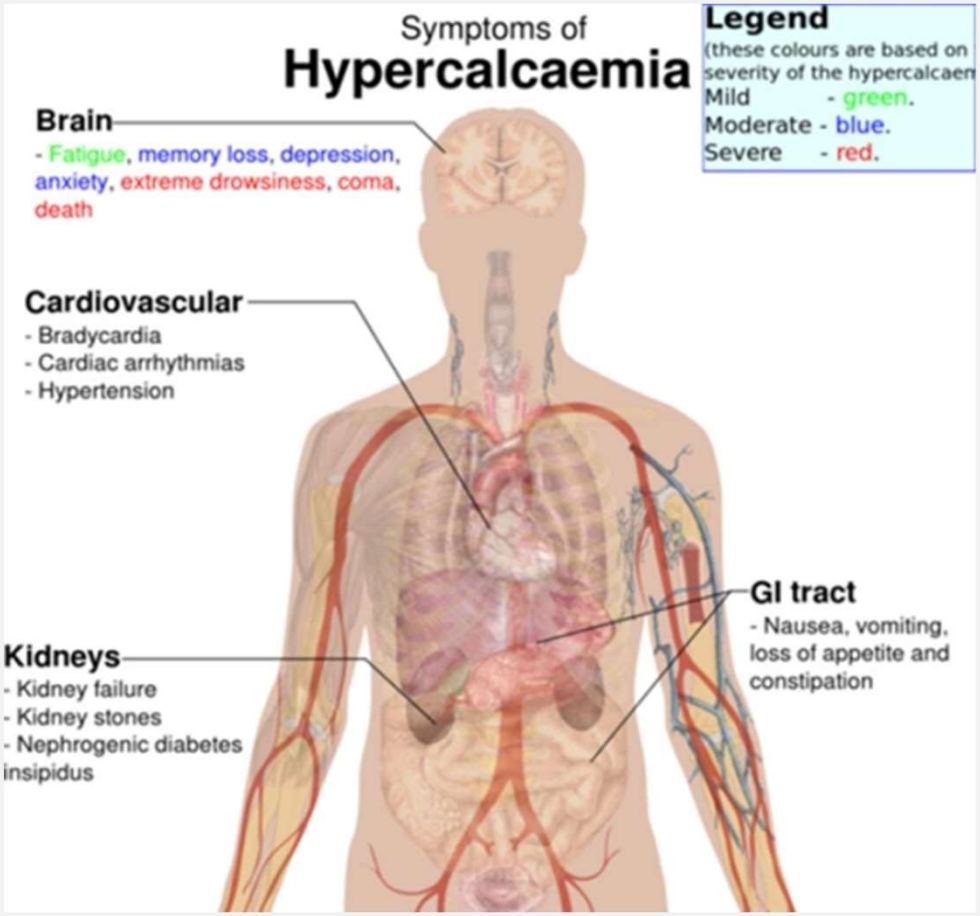


Figure 1 Diagnostic and treatment algorithm for hypercalcaemia in neonates and infants (adapted from Lietman et al. [11]).

HYPERCALCAEMIA OF MALIGNANCY



"Stones, bones, abdominal groans, psychic moans"

Other symptoms include

- Abdominal pain
- Vomiting
- Polyuria
- Polydipsia
- Anorexia
- Weakness
- Renal failure

MANAGEMENT

Fluids (normal saline)
Bisphosphonates
Calcitonin
Glucocorticoids
Haemofiltration
Involve Endocrinology

END OF THE SCIENCE BIT OF THE TALK

WHAT DOES A WORK DAY LOOK LIKE FOR ME?

DEPENDS WHICH DAY OF THE WEEK

Monday and Tuesday

Ballarat

Morning MDM – 730am

Outpatient clinic
- New patients
- Patients on treatment review
- Patients requiring surveillance
- Patients on symptom management

Phone calls from Chemo Day Unit, Inpatients, Palliative Care, other specialities about my patients

Lunch MDM

Outpatient clinic

Admin – trials, dictating letters, referrals

Home – 530pm

Wednesday to Friday

WEHI and UniMelb
Work from home life

Zoom meetings about research grants, pharma / special interest group sponsors, designing clinical trials, registry data output

Reading, analysing, writing – protocols, grants, abstracts, manuscripts

Zoom teaching for Unimelb

Play with cat, cook ridiculously long recipes, annoy husband

Weekend cover (1 in 2)

Different private hospitals

Handover from patients' usual oncologists – Friday 5pm

Ward round to see inpatients, chemo day unit, referrals

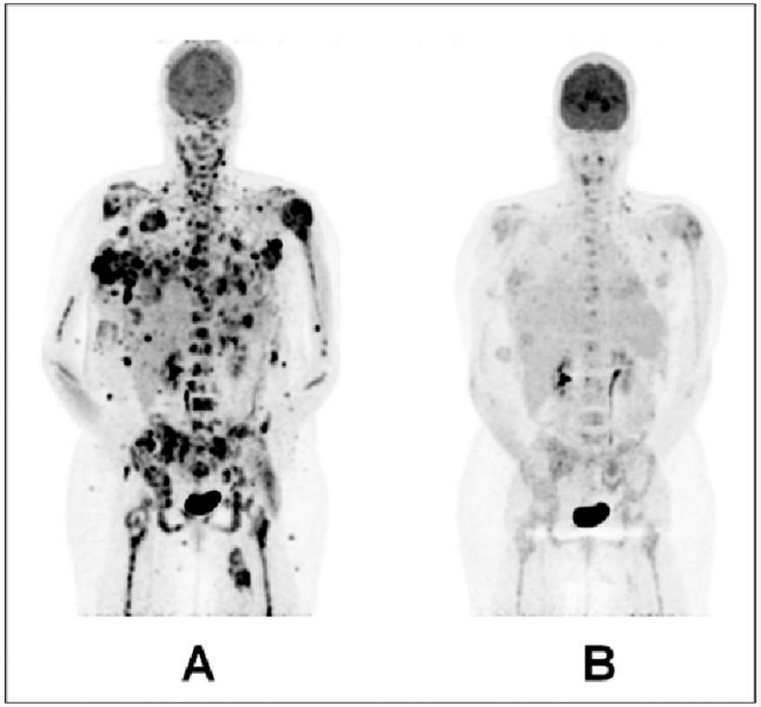
On-call for the hospital 24/7

Handover – Monday 8am

+ CONFERENCES
+ WORKSHOPS
+ TALKS

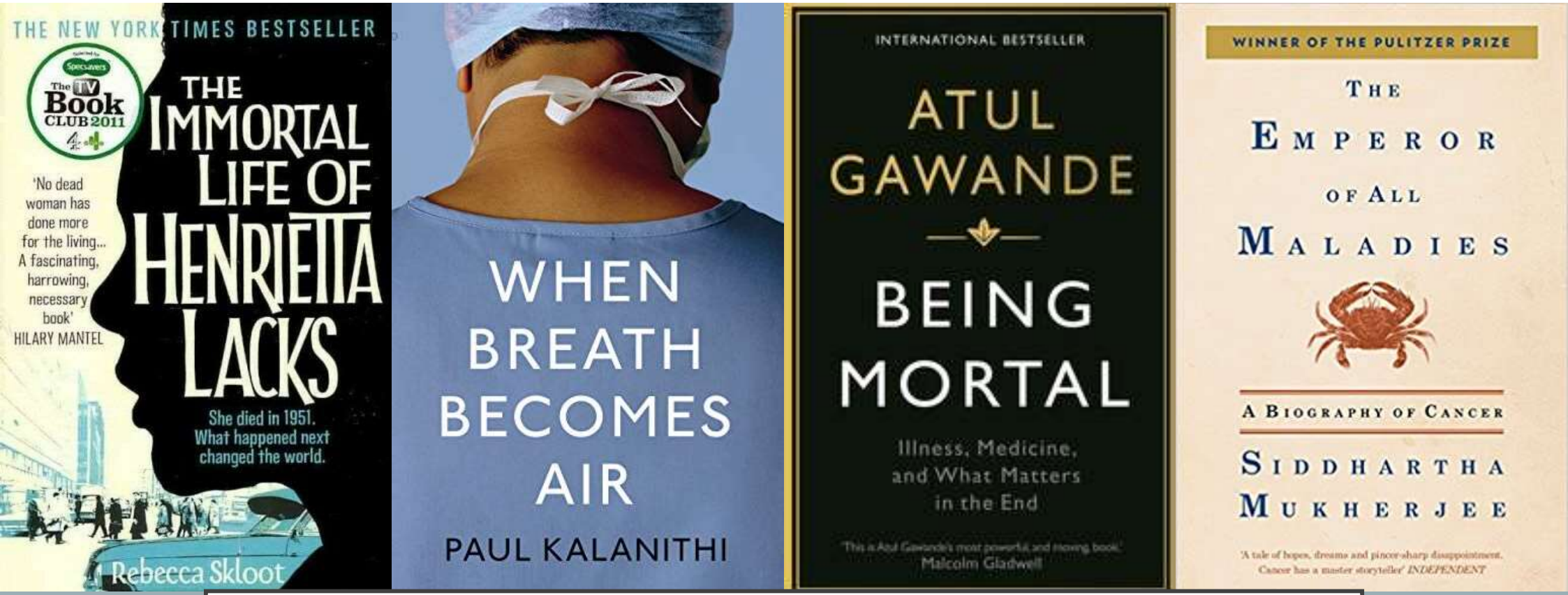
WHY DO ONCOLOGISTS CHOOSE TO DO ONCOLOGY?

- Biologically fascinating
- Incorporates all systems of the body (I am not an 'organ' specialist)
- Cutting edge research and trials
- Treat cancer in the context of their other medical issues
- Pathology that you can 'see' (radiologically)
- **The patients, the patients, the patients**



BUT… ISN'T IT A VERY DEPRESSING SPECIALITY?

- Yes, it can be…
- Stigma
- Art of breaking bad news
- Meet a lot of very fascinating patients
- Intimately enjoy their philosophical musings on their BC and AC life
- Cancer often brings families together
- Get to explain difficult concepts to patients
- There is also a lot of hope



BOOKS THAT ONCOLOGISTS READ

LAST CHANCE FOR QUESTIONS

HAPPY FOR YOU TO EMAIL ME
WONG.V@WEHI.EDU.AU