



LYMPHOMA
CANADA

EXPERT SPEAKERS HOPE
NATIONAL NETWORKING
AID CONFERENCE FORUM
ON LYMPHOMA SUPPORT
CAREGIVERS EDUCATION
SEPTEMBER 29 - 30, 2017
SURVIVORS TORONTO, ON
THERAPIES SIDE EFFECTS

Aggressive Lymphomas - Current

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Conflicts of interest

- I have no conflicts of interest to declare



Outline

- What does aggressive lymphoma mean?
- How do we diagnose it?
- How to we predict how it will behave?
- How do we treat it?
- What can you expect with treatment?



Categories of lymphoma

- Indolent
- Aggressive
- “Other/Special/Unique”



Why does aggressive mean?

- Shorter duration of symptoms
- Generally need treatment at time of diagnosis
 - Immediate, few days, few weeks
- Treatment generally given with the expectation of **remission**, goal of possible **cure**



Aggressive lymphomas

	Incidence (per 100,000)
• Diffuse large B cell	6.9
• Hodgkin	2.7
• T cell lymphomas	2.1
• Mantle cell lymphoma	0.8
• Burkitt lymphoma	0.4
• Gray zone lymphoma	<0.1

SEER Database Incidence 2011-12



Lymphocytes

- **B cells** develop in the bone marrow
 - form antibodies against foreign bodies
 - 90% of all lymphomas
- **T cells** mature in the thymus gland
 - orchestrate the immune response
 - 10% of lymphomas
- **NK (natural killer) cells**
 - destroy viruses and cancers through direct attack
 - Very rare lymphomas



Not only in lymph nodes

Nodal

- Neck
- Supraclavicular
- Axillary
- Groin
- Spleen

Extranodal

- GI tract (stomach)
- Bone marrow
- Liver
- Skin
- Head and neck
- Bone

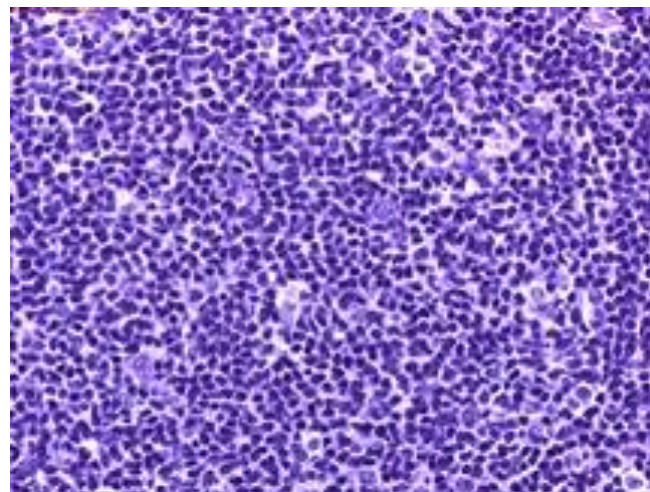
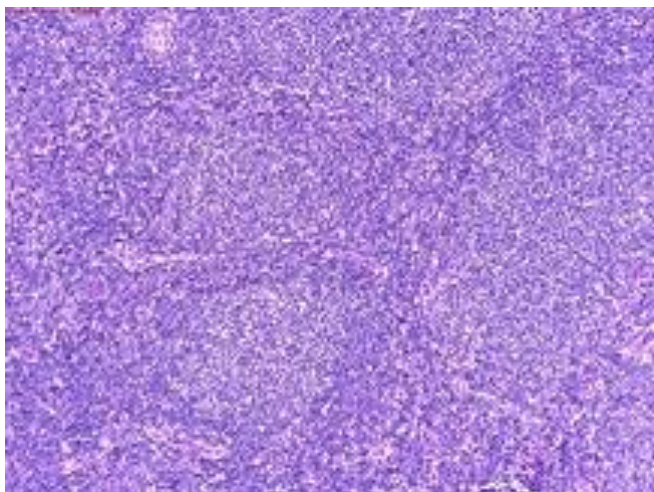


How do we figure out which type you have?

- **Physical Exam**
 - Cardiac, respiratory, abdominal
 - Lymph nodes
- **Biopsy**
 - FNA
 - Incisional biopsy
 - Excisional biopsy
- **Laboratory**
 - CBC and differential
 - LDH (prognostic marker in NHL)
 - ESR (important in HL)
 - Bone marrow aspirate/biopsy
- **Imaging**
 - Chest X-ray
 - Ultrasound
 - CT scan neck/ chest/ abdomen/pelvis
 - Gallium Scan
 - PET
- **Other**
 - LP – if CNS symptoms, or in certain high risk cases of aggressive lymphoma (sinus, testicle, bone marrow)



Biopsies



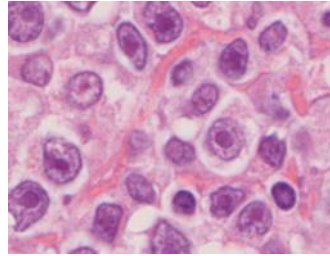
Why is pathology important?

- Need to determine the most appropriate therapy
- Some of the criteria for diagnosis are very specific—and lead to specific treatment choices
 - For example:
 - CD20 “positive” by immunohistochemistry: use of rituximab
 - Burkitt lymphoma: specific chromosome change in lymphoma cells, specific chemotherapy treatment

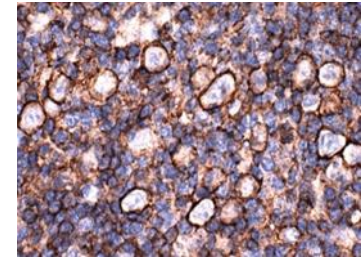


Molecular analysis

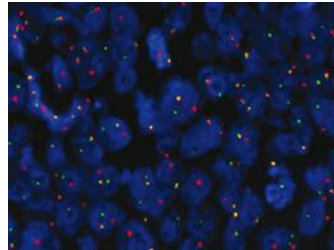
- Morphology



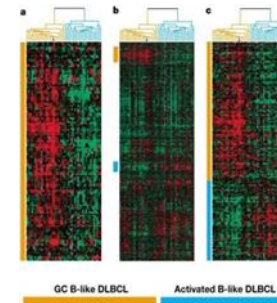
- Immunohistochemistry



- Cytogenetics



- Gene expression profiling



Staging

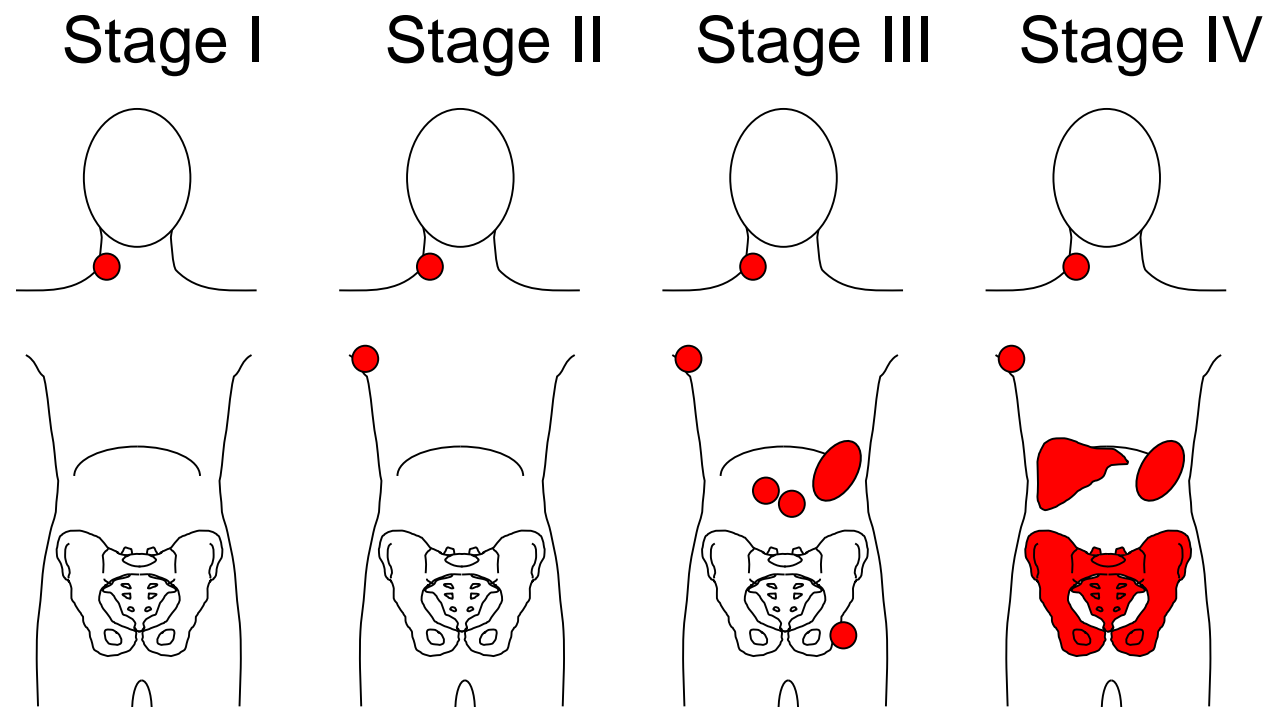
The # of staging investigations is dependent on the type of lymphoma and goals of therapy.

Staging is used to determine:

- Extent of disease
- Bulk of tumour mass
- Potential for complications
- Type of treatment



Ann Arbor Staging System



A – absence of any “B” symptoms

B – Unexplained fever, drenching sweats or weight loss

Bulky > 10 cm mass on imaging



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International Prognostic Index (IPI)

Evaluates 5 variables:

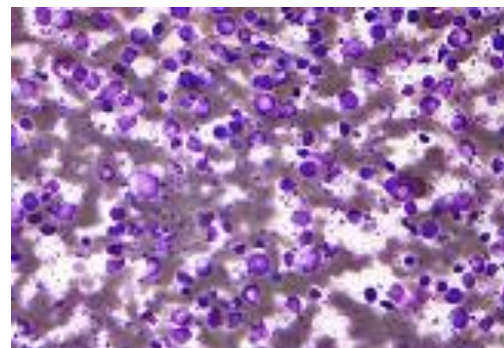
- Age
- Stage
- Performance status: what is the impact of lymphoma (or other medical problems) on daily life – how sick are you?
- Number of extranodal sites
- LDH

https://www.qxmd.com/calculate/calculator_64/diffuse-large-b-cell-lymphoma-prognosis-r-ipi



Diffuse large B cell (DLBCL)

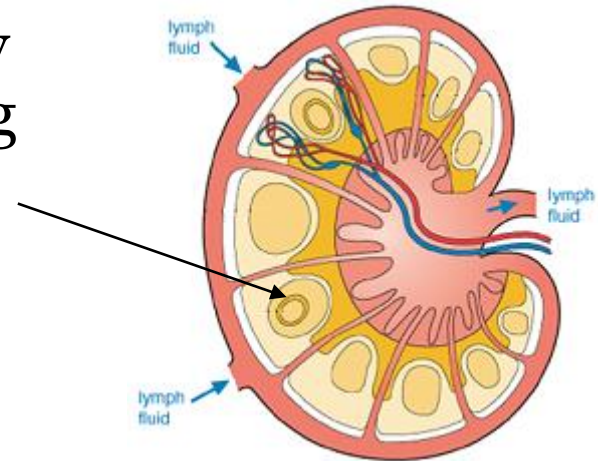
- Most common type of NHL, 30-40% of cases
- Cancer cell appearance led to name – cells are large and spread out
- Can develop in lymph nodes or other areas like the intestines, skin, bone, brain.
- Approx. 50% of patients have organ involvement at diagnosis
- Average age diagnosis 57, but can affect any age group



Diffuse large B cell (DLBCL)

Germinal centre B cell (GCB)

DLBCLs get their name because they develop from lymphoid cells residing in the germinal centre of the lymph node. Patients with GCB-derived disease generally have better outcomes.



Activated B cell (ABC) DLBCLs develop from B cells that are in the process of differentiating from germinal centre B cells to plasma cells. ABC DLBCL is associated with a poorer outcome than GCB DLBC.



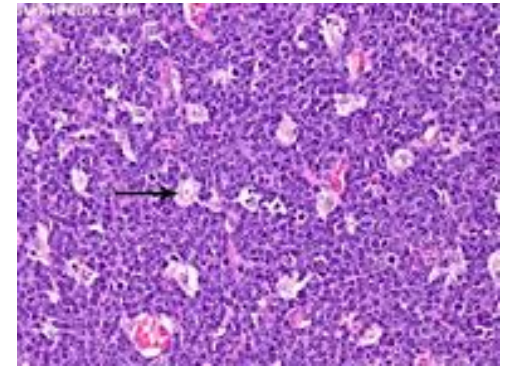
Diffuse large B cell (DLBCL)

- Primary mediastinal B cell lymphoma (PMBL)
- Primary central nervous system (CNS) lymphoma
- EBV-positive DLBCL of the elderly
- T-cell/histiocyte-rich large B cell lymphoma
- Primary effusion lymphoma (PEL)
- Intravascular large B cell lymphoma (ILCL)
- ALK-positive large B cell lymphoma
- Double-expressor lymphomas (DEL)



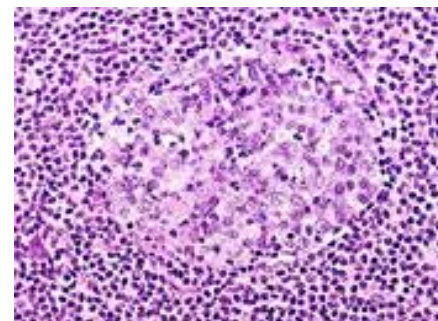
Burkitt lymphoma

- Named after Dr. Denis Burkitt
- Affects children (usually 5-10 yrs) and accounts for 30-40% of childhood lymphomas
- Affects adults (usually 30-50 yrs)
- Can affect other organs like eyes, ovaries, kidneys, CNS or glandular tissues or jaw
- Treatment often involves intrathecal chemotherapy



Mantle cell lymphoma (MCL)

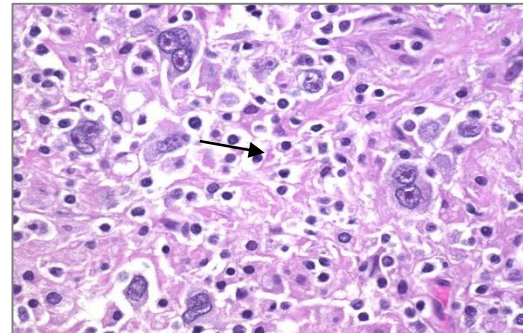
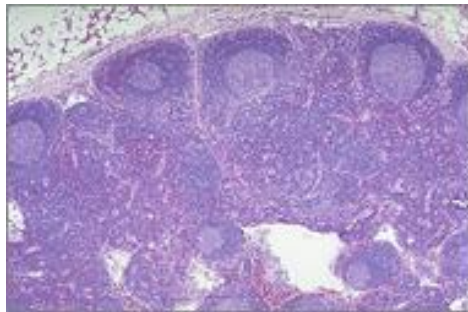
- Develops in the outer edge of a lymph node called the mantle zone
- Rare, 5% of NHLs, usually affecting men over age 50
- Often have many lymph nodes, one or more organ (often GI tract) and bone marrow involved
- Often diagnosed late-stage
- Frequently relapses
- Mantle Cell Lymphoma International Prognostic Index (MIPI): low-, intermediate- and high-risk.



Hodgkin lymphoma

- Named after Dr. Thomas Hodgkin, who described the disease in 1832
- 1000 cases/year in Canada
- Two peaks: young adults and elderly
- Can be difficult to diagnose
 - Cancer cells are in minority in affected nodes
- > 80% curable with chemotherapy +/- radiation

Normal

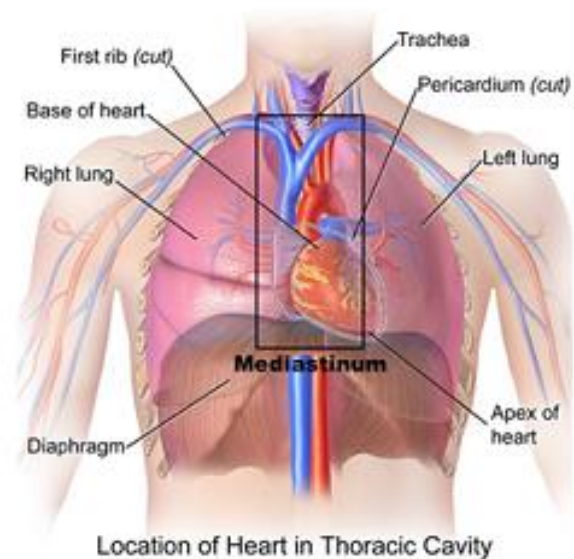


HL
Reed-
Steinberg
cell is the
'malignant
cell'



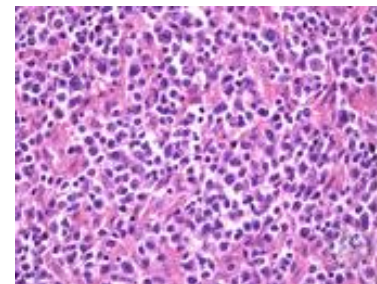
Gray zone lymphoma (GZL)

- Rare, but generally seen in teens & young adults
- Often presents with a large tumour in the chest area (mediastinum)
- Has features of both a large B cell lymphoma and Hodgkin, and is more aggressive
- Can spread to other organs



T Cell lymphoma

- Account for 10% of NHLs
- Peripheral T-cell lymphoma – general term referring to 10+ subtypes
 - Peripheral T-cell lymphoma not otherwise specified (PTCL-NOS)
 - Anaplastic large cell lymphoma (ALCL)
 - Angioimmunoblastic Lymphoma
 - Nasal NK/T-cell Lymphomas
- Lymphoblastic Lymphoma





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Overview of primary treatment options

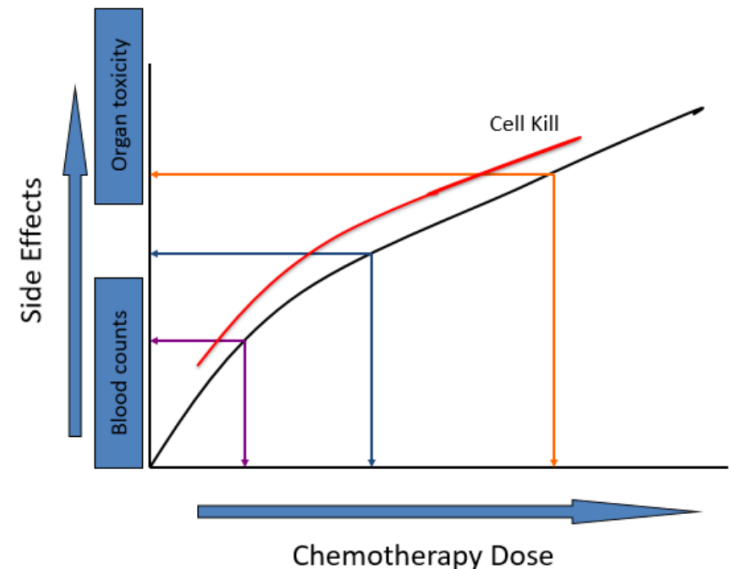
Treatment Option	Description
Chemotherapy	Use of drugs to kill lymphoma cells
Radiation Therapy	Use of high-energy rays to kill lymphoma cells or slow their growth
Immunotherapy	Use of agents designed to target and destroy lymphoma cells
Transplantation	Infusion of healthy stem cells/bone marrow to help the body restore its supply of healthy blood cells

Balance potential toxicity against effectiveness



Chemotherapy

- Backbone of many cancer treatments
- Damages DNA, leading to cell death
- Systemic
- Affects all growing cells
 - Cancer cells
 - Blood cells
 - Lining of GI tract
 - Hair



Common chemotherapy regimens

CHOP - with or without R (Rituxan)

- ✓ Cyclophosphamide
- ✓ Doxorubicin
- ✓ Vincristine
- ✓ Prednisone— pills daily x 5 days



By IV every
3 weeks

4 cycles—if radiation is also part of the plan

6 cycles—most often

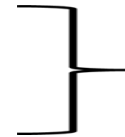
8 cycles—in some circumstances (young people with big masses or other problems)



Common chemotherapy regimens

CVP – with or without R

- Cyclophosphamide
- Vincristine
- Prednisone — pills daily x 5 days



By IV every
3 weeks

For a usual total of 6 to 8 cycles unless disease progression or unacceptable toxicity occurs



Common chemotherapy regimens

CHOEP, with or without R

- Cyclophosphamide
- Doxorubicin
- Vincristine
- Etoposide
- Prednisone — pills daily x 5 days



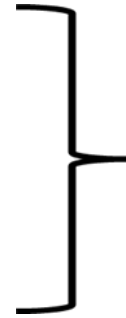
By IV every
3 weeks



Chemotherapy treatments

ABVD, typical HL treatment

- Adriamycin
- Bleomycin
- Vinblastine
- Dacarbazine



1 cycle = 2
treatments and is
given over 4 weeks

ABVD is given every 2 weeks (A and B parts)



Immunotherapy

- Also called biologic therapy
- Drugs designed to boost the body's natural defenses against cancer
- Generally fewer side effects than traditional chemotherapy
- Sometimes used alone, but often combined with chemotherapy

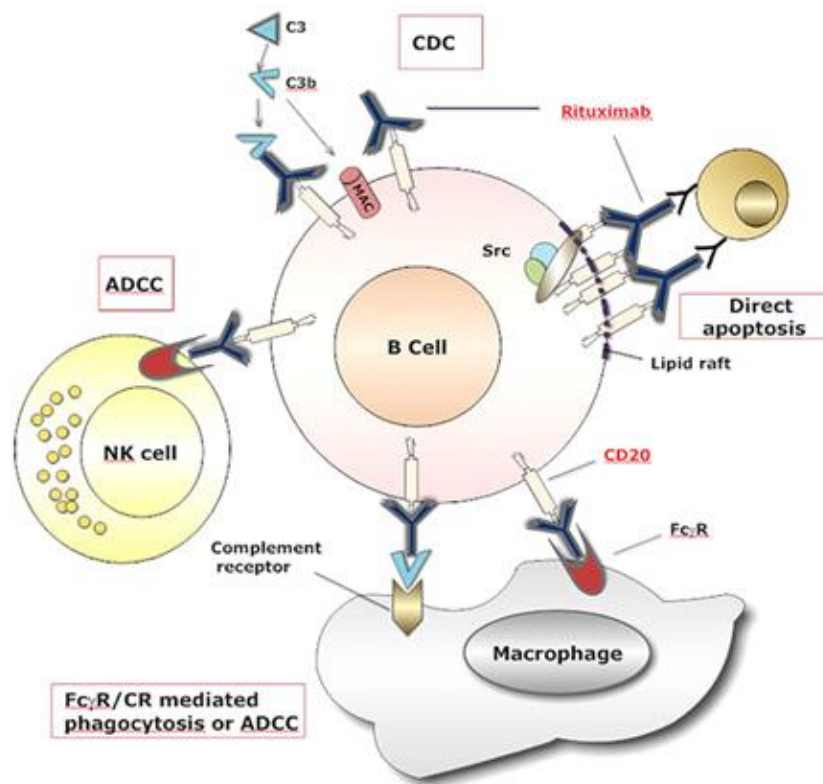


Monoclonal antibodies

Antibodies developed against cancer cells can be administered to patients to destroy the tumour

- Examples:
 - Rituximab
 - Obinutuzumab
 - Brentuximab vedotin

Only work for B cell lymphomas



Samantha M. Jaglowski et al. Blood 2010;116:3705-3714



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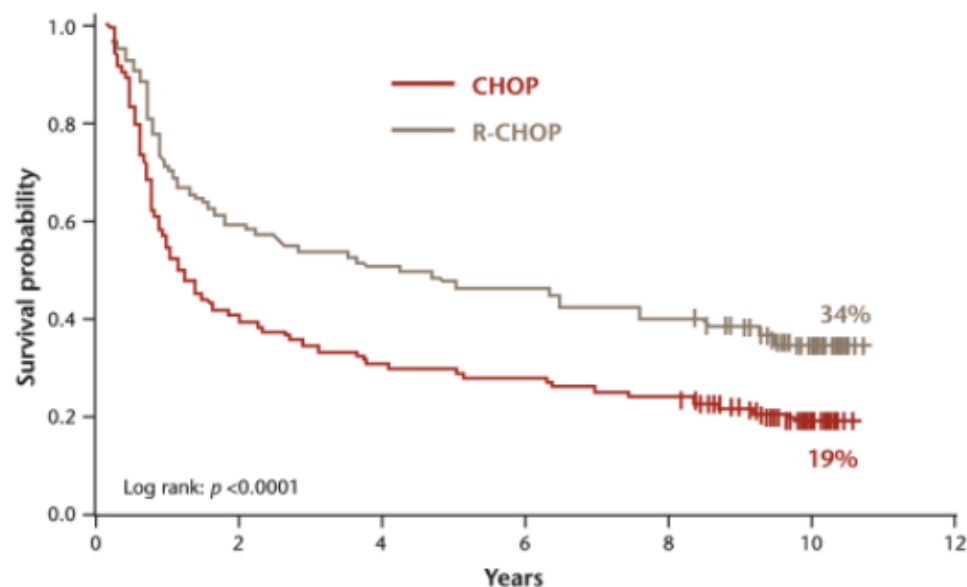


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Why add rituximab?

Addition of anti-CD20 antibody rituximab to chemotherapy: improvement in survival.

Figure 1. Event-free survival in DLBCL patients receiving CHOP or R-CHOP (ten-year median follow-up)



Collier et al, ASH 2009



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Radiation

Medical uses of radiation:

1. **Diagnostic:** low doses of radiation to take images of internal body structure i.e. chest X-ray
2. **Therapeutic:** higher doses of radiation to kill cancer cells

Difference between the two is the amount of energy. Therapeutic radiation can use up to 1,000 times the energy of diagnostic radiation.



Radiation

- X-ray beams interact with atoms, creating a reaction that leads to cell DNA damage
- Damage prevents the cells from dividing and growing
- Lymphocytes are the most sensitive cells in the body to radiation, so can use lower doses of radiation compared to what is used to treat solid tumours.



Radiation

Linear Accelerators

- Machines do not use radioactive sources but instead use electricity to produce X-rays and electrons.
- Versatile as they can produce different energies of radiation, to minimize the normal tissue affected.

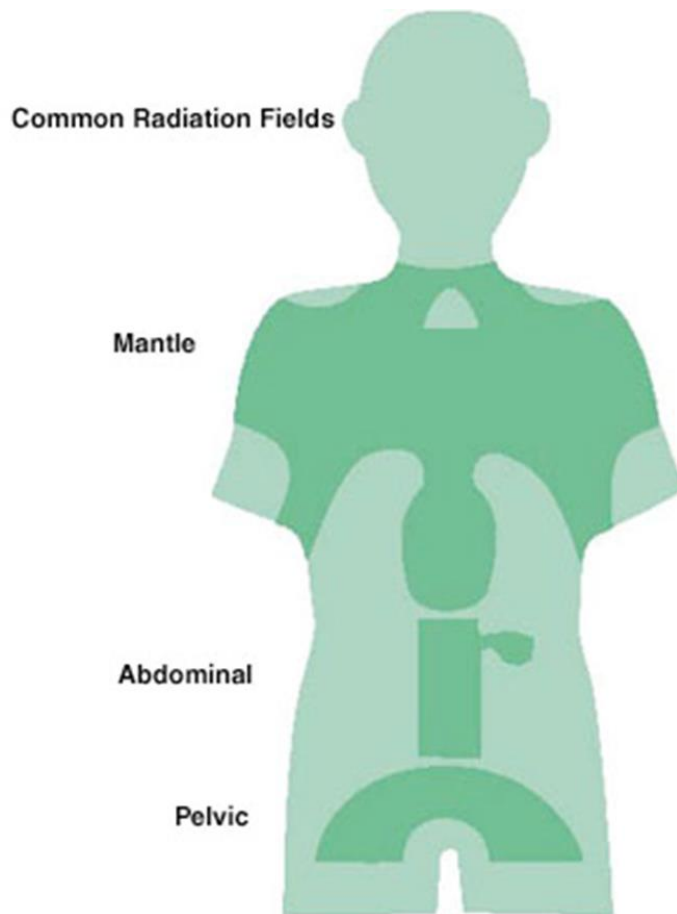


Radiation

- Applies to localized disease
- May not be used in all types of aggressive NHL
- Generally treatment is given daily for 4 weeks (Monday to Friday X 4 weeks = 20 treatments or “fractions”)
- Side effects based on the area that is being radiated (skin and tissue beneath it)

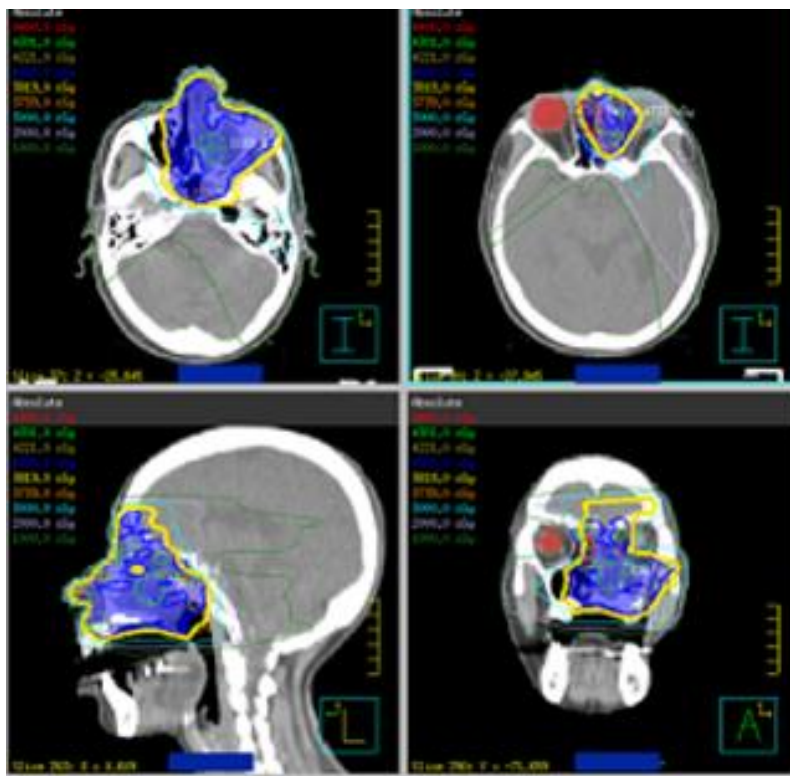


Common radiation fields



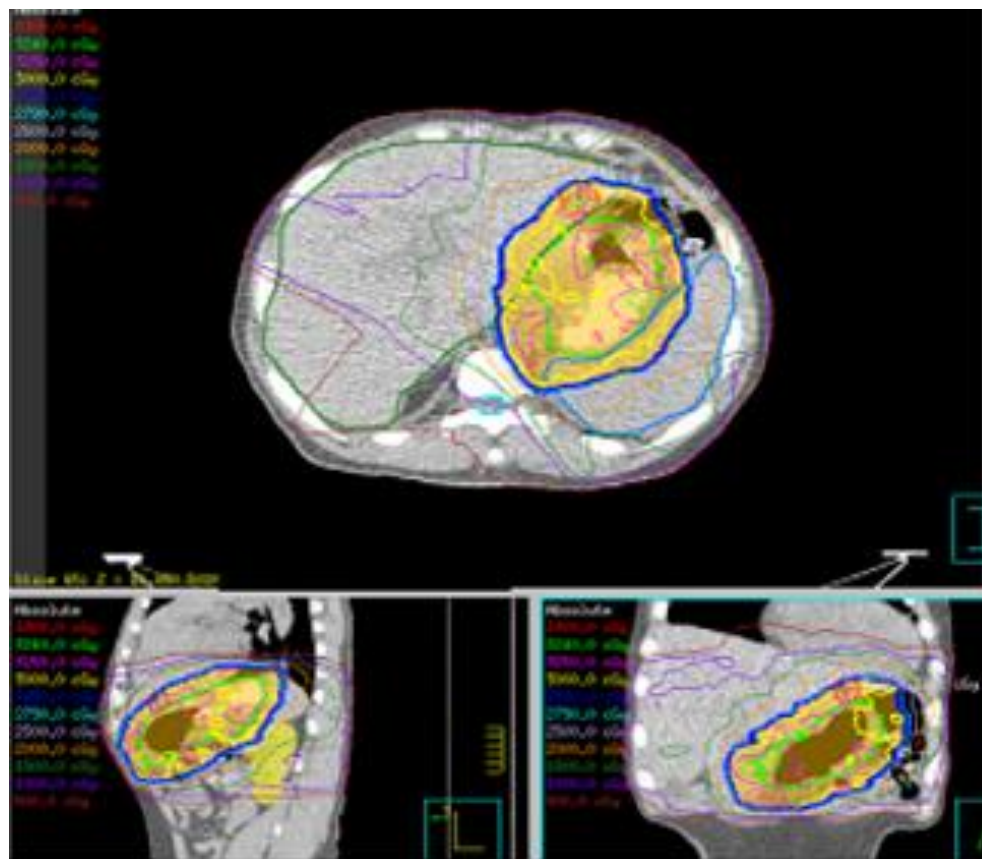
Radiation

Intensity
modulated beams
(IMRT): Sinus
location
lymphoma



Radiation

IMRT:
Gastric
lymphoma



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Combination therapy

- Chemotherapy + radiation
- Radiation (radioactive isotopes) + immunotherapy = radioimmunotherapy
- Chemotherapy + immunotherapy = chemoimmunotherapy



Treatment outcomes

- Variable, depend on many things....
- Greatest chance of cure with initial treatment
- Favourable group (IPI score): 90% relapse-free
- Intermediate prognosis: 60-70%
- Unfavourable: 40-50% relapse-free
- Long-term remission rates lower for elderly, T cell lymphoma, certain subtypes of B cell (defined by chromosomes, for instance)



Relapse/refractory

- Many other treatments available, goals of therapy change
- Single agent chemotherapy drugs
- Combinations (occasionally)
- Radiation to local areas causing symptoms
- Clinical trials of new agents
- Clarification of goals with your oncologist is very important



Relapse/refractory

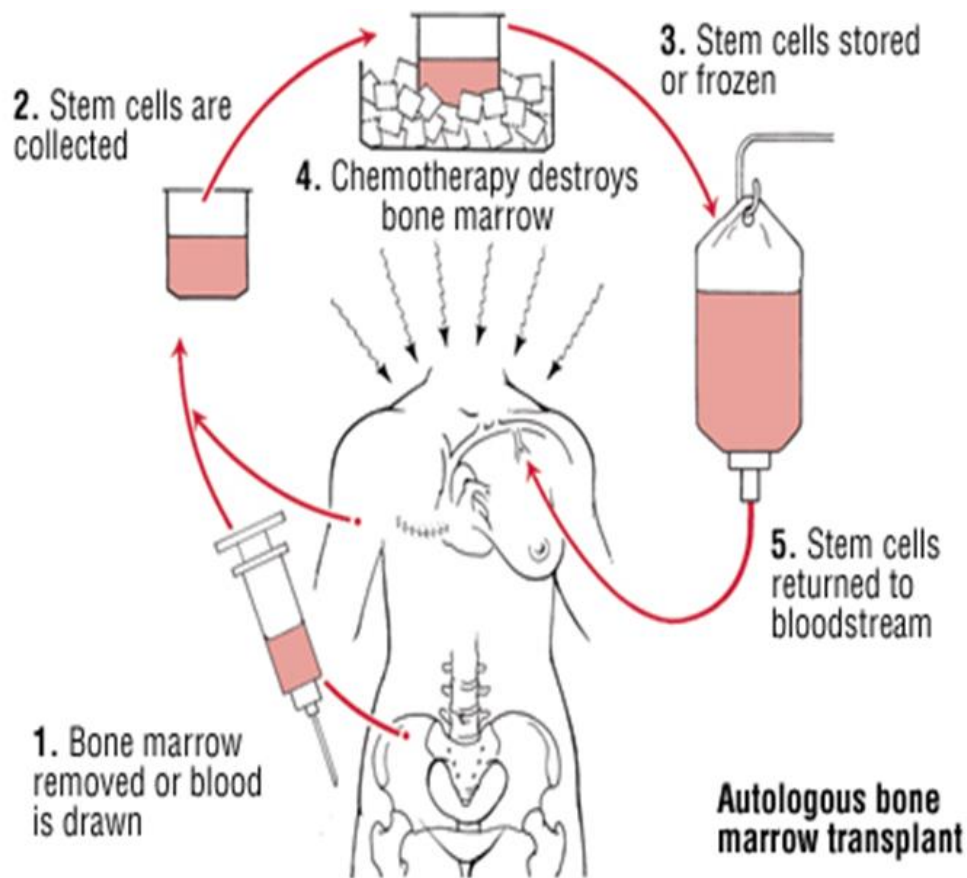
- For young patients: stem cell transplantation considered best option
- Autologous stem cells (patients own)
- Uses very high dose of chemotherapy to try to eliminate resistant lymphoma cells
- Only beneficial if lymphoma responds to a second chemotherapy regimen



Stem cell transplant (SCT)

Autologous

- Use own cells
- Low treatment related mortality
- High rates of remission
- Transplant strategies vary centre-to-centre



Stem cell transplant (SCT)

Allogeneic

- Rare
- HLA matched sibling or matched unrelated donor
- 1 in 4 chance of sibling being a match
- Graft versus lymphoma: good!
- Graft versus host disease: can be very bad, including fatal, and life long
- Higher treatment related mortality



Side effects of treatment

Short term:

- Hair loss
- Nausea, vomiting: controllable with medication
- Fatigue
- Fever: need a thermometer! If >38.3 or 101.5° get a blood test (even Sunday afternoon...)
- Low blood counts



Other possible issues

- Heart function: Small chance of serious damage-may need monitoring
- Peripheral neuropathy (numb hands, feet)
- Difficulty with memory, concentration (multi-tasking)– “chemobrain”
- Fertility



Other possible issues

- Secondary cancers
- Work/school
- Going out in public, infection risks
- Immunization





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