Welcome

Welcome to our team. We are really pleased that you have decided to join us and we look forward to getting to know you. We have a strong commitment to providing the right environment for you to develop in, and believe that orientation is the first step in this process.

This orientation book has been designed to help you so please use it to its full advantage. Its overall aim is to prepare you for your role.

By the end of the six week induction programme you will be expected to

- Provide care to an appropriate caseload of patients
- Have formed a knowledge base of Haematology and have attended the department’s induction study day.
- Achieve level appropriate competencies
- Complete mandatory training

There are two spaces for you to add your own objectives for what you want to achieve in your first six weeks. Please discuss and make your mentor aware of these.

At the end of your 6 week period you will be required to present a poster for the education board. This can be any aspect of care you have experienced. Your mentor or PDN are available if you require any help with this.

On your first day on the ward you will meet either the Ward Sister, Junior Sister or PDN, who will give you a tour of the department and go through required paperwork. You will also be assigned a mentor and given a 4 week SN schedule; this may be adapted to suit individual and ward circumstances. Please see appendix 1

Our Service

The clinical haematology ward provides in-patient care. The ward has the capacity to bed 25 patients with 15 side rooms, some of which provide pressurised air. Currently we are increasing our service to include an ambulatory unit for patients that require nursing support as outpatients. The main groups of diseases we treat are Leukaemia, Lymphoma and Myeloma, although we provide care for all haematological disorders. Our service provides a variety of treatment for our patients that range from diagnosis to end of life care. One of the more specialist treatments we provide is Bone marrow transplantation. You will be educated and provided with training on all disease and treatment options throughout your development on the ward.
The haematology ward is part of a wider service for haematology patients. Our patients have complex health needs and require support from a variety of health care professionals. It is important for us to understand the roles so we can better understand the experiences of our patients. As part of your orientation programme you will be visiting some of these areas and spending time with the different professions. If there is a particular area you would like to visit that hasn’t been included in your orientation please speak with your Junior Sister or PDN.

- **Triage**
  assessment unit. Telephone assessments of patients known to haematology, Assessment/treatment area. Pathway to inpatient admission.

- **The Research Unit.** Research nurses who undertake trial studies. They will often have patients on the ward who are involved in trials

- **Dietetics:** A dietician who has specialist knowledge of Cancer patients and their nutritional needs. We also a nutritional assistant.

- **Pharmacy:** Specialist cancer pharmacist who screens chemotherapy and TTO’s. We also have a pharmacy technician who can screen and order ward drugs. Both are available for advice on medications.

- **Line Insertion Service:** A team of nurses who specialise in central line insertion and management

- **Total Parenteral Nutrition Team:** An MDT consisting of specialist nurses, doctors, pharmacist and dietician

- **Palliative Care Team:** A multi-professional team who are available for support, advise and to see patients

- **End of life hospice**

- **Day Treatment Unit** who provide out-patient care for haematology patients.

- **Physiotherapy, Occupational Therapy, SPARC**

- **Intensive Care Outreach Service:** A group of specialist ITU nurses and doctors who are able to review and support us in the care critically ill patients

- **National blood service and the apheresis team:** Provide support for patients requiring stem cell collection and apheresis

- **Maggies centre** provide financial advice for cancer patients.

**The Multi-disciplinary team on the ward**

There are two medical teams that operate on the ward. The Lymphoma team and the Leukemia team, each is run by one of the ward consultants. There is a 3-6 month rotation period in which registrars will be deployed to different areas of the department. We also have four Senior House Officers (FY1-2) who are rotated every four months. There are a number of Clinical Nurse specialists in Myeloma, Lymphoma, Leukaemia and Bone Marrow
Transplant. These nurses are part of the medical team and have expert knowledge in their subject. If you are unsure of which team/medical professional to contact regarding a patient please see the notice board at the nursing station as this holds all current bleep numbers. We also have a ward dietician and assistant who ensure patient nutrition is maintained throughout their stay. Physiotherapy and occupational therapy professionals are often seen on the ward and can provide support and advice for our patients.

We have a specialist cancer pharmacist and technician who visit the ward daily and are available for any medication queries you may have. The Chaplin service is available for any patient wishing to receive religious or spiritual support.

Once a week the multidisciplinary team meet to discuss patient care. This is a good time for the professions to come together and share information; it is also a planning session in which we gain focus for patients over the upcoming week.

**Nursing on the ward**

The Cancer Centre approach to team nursing has evolved through years of development and experience. We believe that patients have the right to be cared for by appropriately skilled nurses. Therefore patient allocation is undertaken on a shift by shift basis balancing the needs of the patient along the knowledge, skills and needs of the staff.

On the ward we have a management team. They are here to manage, support and develop you into experienced haematology nurses, who are capable of caring for the complexities of our patients. They consist of The Ward Sister, Deputy Sister, Junior Sisters and Practice Development Nurse. You will be allocated a Junior Sister but the whole team is approachable so please do not hesitate to inform us if you need help or support.
Nursing Process

Assessment
Patients require assessments throughout their treatment. Assessment provides the basis for planning care. You will perform assessments both on admission of patients and throughout their stay. The assessments that you perform will vary depending on patient’s needs. There are however risk assessments that must be performed on each patient within 24hours of admission.

These are:
- MRSA screening
- Nutritional assessment
- Continence assessment
- Pressure Ulcer assessment
- Falls assessment
- Manual handling assessment

Care Planning
Core care plans are available on the computer (see TSSG website) for many of the common nursing procedures within the department. For any unusual nursing interventions, care plans should be written on an individual basis. Care plans should be reviewed on a shift by shift basis, be individualised and kept at the front of the patient’s folder.

Common professional abbreviations may be used but avoid jargon.
Evaluation
Evaluation of care is documented with all other documentation, in the medical notes. Having all the patient notes in one place provides structure, consistency, continuity and greater awareness for all members of the multidisciplinary team working with the patient. Evaluation should provide a clear account of the patient’s condition, their nursing care with an assessment of the effectiveness of that care. Details of care outlined in the care plan do not need to be recorded in the evaluation; it will be assumed that care has been given according to the care plan. All entries in the medical notes need to be dated, timed, labelled as Nursing and signed with a legible signature including designation i.e. RGN, as per Trust/RCN/NMC Guidelines. Documenting changing care needs on the handover sheet and communicating these with the co-ordinator is also an intrinsic part of your role.

Co-ordination
The ward coordinator is a multi-faceted role and is fundamental to the smooth running of the ward on a shift-by-shift basis. This role only works effectively if all levels of staff work through the coordinator, keeping them informed about any changes in patient condition and discussing problems prior to contacting medical staff. Responsibilities include attending bed meetings twice a day. Daily and weekly MDT meetings, regarding discharges admissions and transfers. Organising admissions and discharges with the support of named nurses. Ordering controlled drugs and chemotherapy. Completing jobs list and general administration including, handover sheets and EPR bed state. Due to the complexities of the role it needs to be performed by an experienced member of staff. Junior members of staff may only undertake this role if they are well supported.

Practicalities

Shift times

Early 07:30-14:30
Late 14:00-20:00
Long day 07:30-20:00
Night 19:30-08:00

Staffing numbers

Early; 6 trained nurses, 2 clinical support workers
Late; 6 trained nurses, 1 clinical support worker.
Night; 5 trained nurses, 1 clinical support worker
1 trained nurse will staff the Ambulatory Unit and may be available to assist the ward, however they will not take patients.

Breaks
2 x 30 minute unpaid breaks for Long days
1 hour unpaid break for night shift
1x 30 minute unpaid break for early and late.
Handover

On the ward we have two main handovers per day. These are performed at 07:30 and 19:30 and will be undertaken by the shift co-ordinator who will give information regarding care for each patient. After main handover and allocation has been performed, individualised handovers are given nurse to nurse. A rough structure to handovers is given below.

- Name/age/resus status
- Diagnosis
- Reason for admission/treatment being provided
- Relevant past medical history
- IV access
- Antibiotics/Drug regime- Any relevant changes
- Chemotherapy regime
- Any abnormal blood results and treatment plan
- Observations
- Fluid balance/weight -any abnormalities and interventions
- Internal/external procedures and transport.
- Any risk assessments and treatment plans.

Discharge

Discharging a patient can be a complicated process, if done correctly it will provide patients with information that will support them when they leave hospital. Below is a short summary of what you should be doing with each patient on discharge. For help with more complex discharges please see the discharge link nurse.

- When the team decide a patient will be sent home ensure the SHO has written the TTO’s and sent the prescription to pharmacy (you can see if this has been completed by looking on case notes under smart forms).
- Ensure the patient has transport arranged
- Liaise with the ward Pharmacist to ensure they are aware of the required TTO.
- Ask the pharmacist when the ward can expect the TTO to be completed. Communicate this with the patient being discharged and the co-ordinator. You can check the process of the TTO on the intranet under prescription tracking.
- When the TTO is ready either ask a CSW to collect, or if you have time collect yourself. The porters will do 2 to 3 rounds a day of pharmacy deliveries but waiting for them may hold up a discharge.
- When you have received the TTO check it against the EIDD on case notes. Be aware that some drugs may not be supplied by pharmacy as the patient may already have them within their POD drugs, or have a supply at home.
- Complete the nursing section on case notes. Publish and print this, giving a copy to the patient.
- Complete a patient medication record and talk the patient/relative through their medications.
- Give patients/relatives the infection risk leaflet and explain how they can minimise their risk of infection and when they should be contacting the ward/triage for support.
- Give and explain the ‘Friends and Family test’.
- If the patient has a cannula in remove and document the VIP score in the medical notes. If the patient has a central venous catheter ensure bungs and dressings are up
to date. Flush with hepsal as per prescription and record VIP score in the medical notes.

- If required ensure a follow-up appointment has been made and the patient is aware of the time and location.
- For patients that do not want to wait for their TTO’s please ensure you clearly document when they will be returning and handover any relevant information.
- If d/c has occurred out of hours ensure they are discharged on EPR

**E-Roster**
The rota is written every 4 weeks. You will be given a username and password and your Team leader can help you to log on if you are having difficulties. For full time posts you can request up to 7 shifts per month. Although the rota writer will try and give you your off duty requests, we ask that you be aware of the difficulties in achieving these as well as maintaining safe and skilled staffing.

Annual leave is requested via E-roster, for more information see the annual leave policy on the intranet.

**E-learning**
E-learning is an electronic system that tests and provides assurance of competency in a variety of nursing issues.

A username and password will be provided and your team leader can help you to log on. As a ward we have chosen to develop this further by having a monthly focus subject. Each month we look further into topics and ensure that training has been completed by all members of the team. You can speak to the ward PDN for more information or if you would like to be involved.

**Link Nurses**
There are a variety of Link nurse roles on the ward. The overall aim of the link nurse is to support patient safety and quality through dissemination of knowledge and best practice. The role includes providing specialist knowledge and understanding of a subject. They are your link between their speciality subject and your practice so use them as a resource to learn. The link nurses will undertake specific tasks as required of them by the management team. If you have an interest in becoming a link nurse please speak with the ward PDN.

**Nursing students**
The ward provides mentoring for 3rd year students from Brookes University and often we have colleagues from other areas that will be gaining experience in aspects of our care. Each visitor will be provided with a mentor but we ask the whole ward to support the education of others and help them during their time on the ward. Once you have developed your skills in haematology nursing you will be required to become a mentor by completing the academic course at Brookes University. Through this we hope to continuously share our knowledge and expertise with colleagues.

**EPR**
As a trust we are moving to electronic patient records as we feel this will provide both an efficient and safe service. You will be given full training in this.

**Infection control**
Due to the nature of our patient group and the treatments we provide many of our patients are severely immune compromised. This means that the ward must operate a strict infection
control policy. It is our duty to maintain infection control standards and prevent cross infection form all staff to patients, from patient to patient and from relatives to patient.

Points to remember in practice regarding infection control.

- As part of the nursing team contribute to achieving and maintaining a 95% audit result.
- To maintain strict hand hygiene pre and post patient contact.
- Ensure you perform aseptic non touch technique when accessing central lines/cannulas.
- Uniforms to be changed on a daily basis and not worn to/from work.
- Change bed linen daily.
- No badges/pens should be worn in a necklace style.
- No wrist watches to be worn.
- Do not allow any staff members/visitor with an infection have any patient contact.
- Support and educate patients on the neutropenic diet and preparation of food.
- No fresh flowers/potted plans

Uniform Policy

- ID tags and name badges must be clearly displayed at all times.
- Uniforms must be clean each day
- No wrist watches
- Wedding bands and one pair of stud earrings are the only jewellery to be worn
- Flat shoes with quiet soles. No open toed shoes/sandals
- Hair is to be above the collar
- Staff should look clean, tidy and professional.

Refer to the OUH Trust uniform Guidelines.

Sickness

Due to the nature of our patients we ask that you be sensible with sickness and not come to work if you have anything contagious that could cause patients harm. If you are unsure if you should be coming to work you can discuss this with the Nurse in charge who will be able to advise you of the best course of action. We ask that you contact the ward at the earliest possible time therefore allowing us to cover your absence. On returning to work you will complete a ‘return to work’ interview with your line manager. For more information on the sickness absence policy please see the intranet.

Rotational Posts

There are two styles of rotational posts within the Cancer Centre:

- A direct swap with one of the oncology wards. These rotations are set up in house, between the managers, to enable staff to development new knowledge and skills.
- A 18 month rotation of The Oncology Ward, The Haematology Ward and The Triage assessment unit. Nurses will spend 6 months in each area.

Please speak to the Ward Sister if you would like to be considered for this.

Basic equipment

We have a number of pieces of equipment we use regularly on the ward. You are required to be familiar with these, and seek assistance when you are unsure. Every year patients suffer harm through nurses not using equipment properly so please make sure you go through the functionality of any equipment you are unsure of. The table below can guide you on this.
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<thead>
<tr>
<th>Name</th>
<th>Function</th>
<th>Practiced Signature</th>
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</thead>
<tbody>
<tr>
<td>Graseby PCA</td>
<td></td>
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<tr>
<td>Graseby MS26 syringe drive</td>
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<td></td>
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<tr>
<td>Graseby syringe pump</td>
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<td></td>
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<tr>
<td>Manual blood pressure cuffs.</td>
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<tr>
<td>Pulse oximeters</td>
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<tr>
<td>Cardiac monitors</td>
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<td>ECG machine</td>
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<tr>
<td>Alaris infusion pump</td>
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<tr>
<td>MR850</td>
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You will receive mandatory training on infusion devices however some of the equipment that we use in haematology is not included in this. You will receive training in the use of the equipment during your induction.

**Pharmacy**

We have a dedicated specialist pharmacist who supports the Ward and the Day Treatment Unit, the pharmacist is available by bleep but also visits the ward daily.

**Stock Drugs**

- Stocked up on Monday and Friday.
- Items required between those times should be ordered from the distribution centre Tel: 30181.

**Non Stock Drugs**

- These should be written in the pharmacy diary. The ward pharmacist or MMT will check this daily and order the drugs. Once the drug has been ordered the pharmacist will write the quantity ordered in green or purple pen and date when this occurred.
- If drugs are required more quickly, the drug chart should be taken to pharmacy (or bleep the pharmacist). A file can be found on the hatch in pharmacy, the request should be recorded in here.

**Patients Own Drugs (POD’s)**

- On admission drug charts and medication bought in from home are screened by the pharmacist. All drugs are then supplied and labelled for that patient.
- On discharge it is important that these drugs are then screened by the pharmacist as part of their TTO’s.
Controlled Drugs

- All staff are required to complete the CD e-learning assessment
- CD’s can be ordered in the CD book. The slip is then either left for the pharmacist or CD pharmacy technician. If the drugs are urgent then take the slip to pharmacy.
- Once the CD’s arrive on the ward they should be checked into the cupboard and recorded in the CD record book by 2 Registered nurses,
- CD stocks are checked daily
- Patients own CD’s should be recorded in the Patient’s Own CD book.

Cytotoxic Drugs

- All cytotoxic drugs are made off the hospital site by Baxters.
- Cytotoxic drugs are delivered to the ward in a yellow or blue bag, by a dedicated driver. They must be stored correctly on arrival. The label on each bag of chemotherapy will inform you if the drug is a fridge item or needs to be stored at room temperature.
- Intrathecal drugs may only be checked by those who have undertaken the N59 equivalent and OUH training package. You will be asked to sign an intrathecal disclaimer form when you start on the ward, this exempts you from being involved in any IT chemotherapy.

Development profile

We believe strongly that a sound orientation is the first step in supporting our staff to build on their current skills and knowledge base. Through continued professional development we hope to build on your knowledge base to develop expertise in the speciality and beyond. We recognise that everyone is different and will chose different pathways and utilise differing learning strategies to reach their objectives. There are various resources that will help you develop as a haematology nurse so please utilise them as much as possible.

Management Team

Your Junior Sister will meet with you every 6 months to perform reviews/appraisals. This is your opportunity to show evidence of your current performance and create a development plan that is individualised to your own needs. Your Junior Sister is also your first point of contact if you need to discuss any issues/concerns you might have. The practice development nurse provides structured support for your development. She is available to help you achieve the objectives set out in your appraisal by providing clinical supervision and educational support. Ward based education programmes are organised by the Practice development nurse and the Clinical nurse specialists and will provide education in haematology nursing.

Clinical Nurse Specialist

There are a variety of Clinical Nurse Specialist who have expert knowledge of the diseases and treatments we provide. These nurses are an excellent resource for learning and should be utilised when possible.
Mentors
As a new starter on the ward you will be assigned a mentor. This will be a senior of member of the nursing team who will guide you through the first 4 weeks of your orientation. The senior nurses on the ward are very knowledgeable not only in the diseases and treatment we provide, but also on the daily running of the ward.

Academic courses
There are a wide range of courses taught at differing levels available to you from various universities. Information on these courses can be obtained through the management team and PDN.

In house training
As well as training in mandatory aspects the ward and wider trust provide in-house training on a variety of topics. Your management team and PDN can advise you on these training sessions but all can be found under the Learning and Development pages on the Trust intranet.

Conferences
We encourage you to attend national and international conferences, both as participants and presenters. There is an expectation that after attending a conference or study day you will bring back any new information, ideas and topics you found interesting and present them to the ward team. Your PDN will help you in this. There are also opportunities to visit other trusts to learn and share ideas about care.

Projects
All of the nursing team are encouraged to bring new ideas and experiences to the fore. These issues can be raised at ward meetings or with the management team. You will be supported to develop your ideas to enhance our practice and to share these ideas with other departments in the trust.

Four Hospitals, One Trust, One Vision

The Haematology ward is part of the Surgery and Oncology directive, meaning that we have
close links to other areas. This is useful in sharing information/ideas and standardising our practice. The Cancer and Haematology Centre, within the Churchill is part of the Oxford University Trust. Along with the Horton, John Radcliffe and The Nuffield Orthopaedic Hospital the Trust provides a host of treatments and services to patients in the Thames Valley and beyond. We are proud to be part of a successful trust and believe that our patients deserve the best possible treatment when they are under our care. This is why we are committed to the Trust’s quality vision which is to be recognised as one of the UK’s highest quality healthcare providers. To continuously work to improve our care and to make patient and staff safety central to what we do.

There are three domains which we believe will contribute to achieving these goals.
Patient Safety

- Eliminate avoidable Grade 2 and above hospital acquired pressure ulcers.
- Ensure PSP is completed on admission and updated weekly. Ensure care plan is implemented and evaluated on patients at risk. Communicate changes in skin condition with team and seek support where required.
- Reduce monthly incidence of medication errors by 10%.
- Complete mandatory and in-house training. Maintain the no disturbance rule in the treatment room. Be aware of contributing factors to errors (see human factor training). Ask for assistance if unsure. Ensure incident forms are completed if required.

Patient Experience

- Increase the number of patients discharged before lunch time by 10%.
- See d/c process. TTO’s have started to be written the day before discharge to speed the process up.
- Ensure ‘family and friend test’ is given to patients on d/c.
- We will ensure patients assessed as having nutritional needs have a care plan to meet their individual needs agreed with them.
- Ensure MUST is complete on admission and weekly. Implement appropriate care plan. Complete Mucositis training and competency. Use Mucositis Care plan if required by patient need. Ensure patients are aware of options available. Use dietician and nutritional assistance as a resource.

Effectiveness and Outcomes

- Ensure treatments are provided in the outpatient setting, where clinically possible.
- Ambulatory care is providing out-patient treatments to haematology patients.
The 6 C’s.
The 6 C’s are core values and behaviours that we believe will encourage us to deliver compassionate care. Compassionate excellence is delivering excellent care in a compassionate way and we feel that our patients will have a better experience because of this.

- Delivering high quality care is what we do. People receiving care expect it to be right for them consistently throughout every stage of their life.
- Compassion is how care is given, through relationships based on empathy, kindness, respect and dignity.
- Competence means we have the knowledge and skills to do the job and have the capability to deliver the highest standards of care based on research and evidence.

Commitment will make our vision for the person receiving care, our professions and our teams happen. We commit to take action to achieve this.

Courage enables us to do the right thing for the people that we care for, be bold when we have good ideas, and speak up when things are wrong.

Good communication involves better listening and shared decision making. ‘no decision about me without me’.

As front line staff it is important that you understand and implement these ideas into your clinical practice. You are the ones delivering the care and therefore vital in achieving our goals. The management team will support you in doing this. If you would like to know more about the trust’s vision for the future or be involved with other quality projects please speak with a member of the management team.
Portfolio

Your portfolio is your evidence that you can perform your role as required and also a showcase for your development. We urge you to spend time in creating and maintaining a comprehensive portfolio. Your PDN is available should you require any support in doing this.

Reflective practice

As a department we proactively support the development of our nurses and believe that reflective practice, associated with clinical supervision, are important aspects of your ongoing development. Reflective practice only works if you take time to really think about what happened. You should never start a reflective cycle knowing the answer. It should be a process that naturally takes you to a point where you understand the issues associated with the event. By doing this you will naturally adapt your practice and become a reflective practitioner.

Appraisal and Review

At the end of the 6 week period you will meet with your Junior Sister to review the orientation period and set a plan of action for the next 3 months. This action plan needs to be followed up at regular intervals. This is both your responsibility and that of your manager. The PDN is available for post appraisal support should you require it.

Your first appraisal will take place at 6 months. This will then give you and your Junior Sister (and/or mentor) an opportunity to review your experience and plan for the next 6-12 months. Whilst appraisal is an annual event, plans should be revised regularly. You can ask for an appraisal review at any time. Below is the appraisal paperwork, please familiarise yourself with it and use it to structure your approach to appraisals.
Please ensure you complete sections 1-4 before your appraisal. This is an opportunity for you to personally review the last year and start planning for the next. Section 5 requires that you have read and made notes on your KSF before your appraisal. A copy is attached for your use.

1. What is it about your present job that you
   a) Like?
   
   b) Find most challenging?

2. How do you work most effectively?

What skills do you have that you feel are not being utilised effectively? How could you use these skills in Clinical Haematology?
3. From your last professional development plan, please evaluate the objectives.

What other things have you achieved?

What did you want to achieve but haven’t and why?

4. What would you like to achieve in the next year?

What new skills will you need in order to achieve this?
The Key Skills framework is a framework by which we measure and develop skills that are required to perform our roles. As you become a more experienced nurse you will proceed up these levels. During your appraisal your Junior Sister will discuss these skills with you, assess what level they think you are performing at and how you could improve. The areas that are important to nursing are communication, assessment of and provision to meet health and wellbeing needs, service improvement, quality, health/safety/security, equality and diversity and personal and people development. If you would like to assess the KSF for your role please see the intranet.

Haematology Nursing

This section is designed to give you some general information about Haematology Nursing, as a foundation for you to build upon.

Haemopoiesis

Haemopoiesis is the process by which blood cells are formed.

Where does haemopoiesis occur?
In the foetus blood formation commences in the yolk sac but the liver and spleen gradually take over the role. Towards birth the bone marrow becomes the primary site for haemopoiesis.
What does bone marrow look like?
Red marrow is found within the bone and consists of a mesh of bony strands containing a thick, red, jelly-like substance. Microscopically the marrow is comprised of fat cells, small blood vessels and islands of immature blood cells.

Mature blood cells and function

Red blood cells/Erythrocytes Delivery of oxygen and removal of carbon dioxide.

Platelets/Thrombocytes Clotting

White blood cells Immune defence.
- Eosinophil
- Neutrophil
- Monocyte/Macrophage
- Basophil
- T-Lymphocyte
- B-Lymphocyte

What happens within the bone marrow?

During childhood the active marrow in the more peripheral bones is replaced with fat and is termed yellow marrow. By adulthood 70% of active (red) marrow exists in the pelvis, vertebrae and sternum.
Within the bone marrow exist pluripotent stem cells. Stem cells have the ability to self-replicate but also differentiate into mature blood cells. A single stem cell produces any type of immature blood cell.

The process of blood cell formation is regulated by growth factors, these substances act upon the bone marrow to speed up the maturation process or stimulate stem cells to mature into specific blood cells. In this way the marrow responds to the needs of the body.

Bone marrow is highly active organ system. The cells proliferate at incredible rates to maintain normal blood counts. Under normal conditions, bone marrow produces 5 million cells every second, this rate can increase dramatically when the body is under pressure. The following estimates have been made for the daily rate of production of blood cells;

- Red cells: 260 billion produced in 24 hours
- Platelets: 130 billion produced in 24 hours
- White cells: 10 billion produced in 24 hours

Normal haemopoiesis requires sufficient supplies of energy, vitamins, minerals and growth factors.

Once the blood cells within the marrow have matured, they are released into the peripheral blood stream to carry out their function.
**What is the lifespan of blood cells?**
Red blood cells remain in the circulation for about 120 days, the cells are then broken down within the liver and spleen. White blood cells and platelets can exist for a matter of hours to several days depending on stresses that are placed on the body eg infection or bleeding.

The diseases that we see in haematology are due to incorrect haematopoiesis, caused by malignant cells that overtake the normal functioning of bone marrow. The cell or cell line that has been affected will result in different abnormalities that require treatment.

**Chemotherapy**
Chemotherapy is the term used to describe the treatment of malignant diseases with cytotoxic drugs.

**How were these drugs developed?**
The use of cytotoxic drugs was first investigated after World War I. It had been observed that soldiers exposed to mustard gas had severely impaired bone marrow function, resulting in very low white cell counts. It was supposed that this might offer a treatment for acute leukaemia. Nitrogen mustard was first used to treat a patient in 1941. Other cytotoxic drugs were then developed, Methotrexate in 1948 and the vinca alkaloids in 1958. Many of these early drugs are still in use.

Cytotoxic drugs are anti-proliferative agents, they are toxic to dividing cells or prevent cell division. Malignant diseases are characterised by the uncontrolled proliferation of tumour cells, the application of cytotoxic drugs inhibits cell replication, destroys the tumour cells and can eradicate the disease.

Cytotoxic drugs will affect normal cells, particularly those with a high rate of cell division. However, because tumour cells are abnormal they will be more vulnerable to the effects of the drugs than healthy tissue.

The dosing of cytotoxic drugs is designed to have the maximum impact on the tumour cells whilst protecting the normal cells from permanent damage.

Cytotoxic drugs can be divided into several classes, which act in different ways. Most chemotherapy regimes will use a combination of drugs from different groups, in this way the tumour cells are affected at different stages of their cell division cycle.

**The cell cycle**
The cell cycle describes the stages in the life of cells. It can be summarised as follows;

<table>
<thead>
<tr>
<th>Phase</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>Resting phase</td>
</tr>
<tr>
<td>S</td>
<td>Synthesis, replication of the chromosomes occurs</td>
</tr>
<tr>
<td>G2</td>
<td>Resting phase</td>
</tr>
<tr>
<td>M</td>
<td>Mitosis, cell division</td>
</tr>
</tbody>
</table>
Classification of cytotoxic drugs

Alkylating agents
These drugs prevent the separation of the DNA. They are not phase specific, they will affect a cell whichever stage of the cell cycle it is in.

Examples  Melphalan  Nitrogen mustard  Chlorambucil
          Cyclophosphamide  Busulphan

Anti-metabolites
These substances mimic the purine and pyrimidine bases in the DNA, preventing chromosome replication. They are effective against cells in the S phase. Methotrexate has a slightly different action, folic acid is required to form the purine bases for DNA replication, Methotrexate prevents the conversion of folic acid into its active form.

Examples  Methotrexate  Cytarabine (ARA-C)
          5FU  6-Mercaptopurine
          Thioguanine

Spindle Poisons
This group is made up of the vinca alkaloids, they prevent the formation of spindle fibres along which the chromosomes separate. These drugs act in S phase.

Examples  Vincristine  Vinblastine  Vindesine

Intercalating Agents
These drugs interfere with DNA function by bonding with the base pairs, they are active in all phases but are most toxic in S phase.

Examples

- Daunorubicin
- Doxorubicin
- Mitoxatrone

Administering cytotoxic drugs

In most cases, cytotoxic drugs are administered intravenously but they can also be given orally, subcutaneously, intrathecally or by intramuscular injection. Cytotoxic drugs are potentially harmful if they come in to contact with healthy tissue. Special training is required to handle, administer or dispose of cytotoxic drugs. All ward nurses should be aware of how to deal with the body fluids of patients during and after chemotherapy and what to do in the case of a spillage. Intrathecal drugs i.e. those given via a lumbar puncture, can only be checked and administered by specially trained staff. This is because of the risk of death related to inadvertent administration of the wrong drugs.

Side effects of cytotoxic drugs

Treatment with cytotoxic drugs can cause a wide range of side effects; some of these side effects are general to most chemotherapy drugs whilst some are very specific. Side effects can be short term or become apparent years after initial treatment.

Bone marrow suppression

Bone marrow cells are highly proliferative and their activity will be inhibited by cytotoxic drugs. The effects on the bone marrow limit the dose of chemotherapy; permanent bone marrow failure will result in the patient’s death. Cycles of chemotherapy are given at intervals to allow the bone marrow to recover.

Bone marrow suppression is associated with anaemia, thrombocytopenia and neutropenia.

Mucositis

Mucous membranes are composed of rapidly dividing cells, which are particularly susceptible to chemotherapy. Patients can experience sore mouths, abdominal discomfort and diarrhoea.

Nausea and vomiting

Caused by many cytotoxic drugs. Loss of appetite and altered taste are also common side effects.

Alopecia

Not all cytotoxic drugs cause hair loss but most regimes used to treat leukaemia result in alopecia. Hair will begin to fall out 2-3 weeks after starting treatment and will begin to grow back about 8 weeks afterwards.
Infertility
Cytotoxic drugs can affect sperm and egg production, this can recover but in some cases fertility will be permanently reduced. In women treatment can result in an early menopause. Following high dose treatment and BMT infertility is usually complete. The risk of genetic abnormality in children born after a parent has had chemotherapy is unknown.

Neuropathy
This is associated with treatment with the vinca alkaloids. This can lead to numbness and tingling in the extremities and constipation. These effects are usually mild and temporary but can lead to permanent disablement.

Major organ damage
Some chemotherapy agents can cause cardiac, renal and liver damage. Pulmonary fibrosis is associated with treatment with busulphan and bleomycin.

Secondary malignancy
Cytotoxic drug can lead to genetic damage within normal cells that can result in future malignant disease. Previous treatment with chemotherapy is a predisposing factor to developing acute myeloid leukaemia.

Tumour lysis syndrome
Cytotoxic drugs are very efficient at destroying tumour cells. In patients with a large tumour load, the initial dose of chemotherapy can cause massive cell death. The affected tumour cells release uric acid into the blood stream. This can lead to acidosis and renal failure. Tumour lysis syndrome is life threatening but can be prevented in most cases by giving Allopurinol, Rasburicase and an intensive IV fluid regime.

Intrathecal Chemotherapy
Some treatment regimes involve the administration of intrathecal chemotherapy. This is when chemotherapy is injected into the cerebral spinal fluid (CSF). There are very few drugs that can be given intrathecally – those used within Clinical Haematology, and administered only by trained Registrars are Methotrexate, Cytarabine and Hydrocortisone.

In February 2001 a teenager died in Nottingham as a result of mistakenly being given an intrathecal injection of Vincristine (Vinka alkaloid). This results in demyelination and at least 13 patients have died or been paralysed since 1985. (NHS Executive 2001). The Department of Health has now issued a report, which lays out clear guidelines on the safe administration of intrathecal chemotherapy (NHS Executive 2001). All trusts have had to implement these guidelines with immediate effect.

The trust policy for the administration and checking of intrathecal chemotherapy is included. It is important that you are aware of this policy, however you will not be involved in checking intrathecal chemotherapy until you have undertaken the training programme.

Neutropenia and immunocompromise

What is neutropenia?
An individual is considered to be neutropenic when their neutrophil count is less than 0.5 x 10⁹/l. However, 1.0 x 10⁹/l with a falling count following treatment is also cause for concern. Newly diagnosed or relapsed leukaemia patients with a high white count/neutrophil count are also considered to be neutropenic because the leukaemia cells are non-functional.
What do we mean by immunocompromise?
The words immunocompromise and immunosuppression are used interchangeably. They describe a condition whereby the patients immune system is not fully functional. This can be due to a number of reasons:

- Disease processes
- Drugs: steroids, chemotherapy, cyclosporin and other anti-rejection drugs
- Infective processes such as shingles
- Graft versus host disease
- Allogeneic/Reduced Intensity Transplant conditioning, 1-2 years post transplant, for immune recovery

What are the causes of neutropenia?
Neutropenia occurs when the bone marrow is unable to produce adequate numbers of neutrophils. This can be due to the underlying disease causing bone marrow failure or be as a result of bone marrow suppression following treatment with cytotoxic drugs.

Haematology patients are particularly at risk of severe infection because they are neutropenic for prolonged periods of time but also due to other factors, such as

- Immunosuppression-this can be due to bone marrow transplantation or treatment with drugs such as cyclosporin or steroids.
- Hickman line - creates a direct pathway for micro-organisms into the blood stream.
- Mucositis - common side effect of chemotherapy
- Reduced inflammatory reaction-due to immunosuppression. Immunosuppressed patients will show fewer signs of an infection. This means that the patient may feel fine but have a life threatening infection.

Infection is a major cause of morbidity and mortality in haematology patients.

Organisms that can cause infections
Infections can be caused by bacteria, fungi or viruses. The most likely cause for infection is the patients own bacterial flora. Some of the common infections will be discussed further.

Bacteria
Most infections are caused by bacteria. In neutropenic patients’ normal commensal organisms can become pathogenic.

Bacteria is broadly divided into two groups, gram-positive bacteria and gram-negative bacteria. Gram-negative infections are often more serious, they can develop very quickly and become life threatening. It should also be noted that gram-negative infection might not produce a pyrexia.
Examples of gram negative organisms - pseudomonas, E.coli, Klebsiella

Most septic episodes are caused by gram +ve bacteria.

Examples of gram-positive organisms - staphlococcus aureus, staphlococcus epidermidis, clostridium difficile

Fungi
Fungal infections are common in neutropenic patients, particularly when they have had broad spectrum antibiotics.
The most common fungal infection is candida, which is naturally present in the mucous membranes. In vulnerable patients candida can invade the lungs, liver or kidneys.

Aspergillus is present in the soil and organic matter. The spores are airborne and can be inhaled, for this reason the lungs are the most common sites of primary infection. Aspergillus can colonise blood vessels and spread to the liver, brain, skin and spleen. Diffuse aspergillus infection has a poor prognosis.

Pneumonia caused by pneumocystis carinii was once a major cause of mortality following bone marrow transplantation. The organism is thought to be fungal in origin but has been effectively controlled with Co-tromoxizole.

Viruses
The reactivation of herpes simplex is common in neutropenic patients; it is rarely problematic and is treated with aciclovir.
Cytomegalovirus (CMV) is a common virus that is carried by about half the population and is not usually pathogenic. Following bone marrow transplantation it can be reactivated or acquired from bone marrow or blood products. CMV chest infection is a serious event and has a very high mortality rate. It can be treated with Gancyclovir or foscarnet. Several interventions are used to reduce the risk of infection

- Prophylactic Acyclovir for CMV negative and HD Acyclovir in CMV positive patients.
- Screening of bone marrow donors and recipients pre transplant.
- Regular screening post transplant.

Shingles is common after bone marrow transplantation due to the reactivation of the latent herpes zoster virus. It is usually successfully treated with acyclovir.

**Preventing infection in neutropenic patients**

It is not possible to eradicate infection in these patients but certain measures can be taken to reduce the risk

- High standards of patient personal hygiene
- Hand washing.
- Care of Hickman lines, see department policy
- Good oral hygiene, see department policy
- Food safety guidelines, see department policy
- Screening of all visitors for infection
- Consider the need for isolation, see department policy
- No flowers or plants on the ward: fresh flowers/plants and the water they sit in, can harbour aspergillus and pseudomonas
- Early detection and prompt treatment of any changes in condition or signs of infection

**How can infection be detected?**

Immunocompromised patients should be assessed for signs of infection every four hours. This is because sepsis can develop very quickly in the immunocompromised patient, leading to acute organ dysfunction and ultimately death. It is the major cause of morbidity in haematology patients (75-85%). Early recognition and prompt treatment will have dramatic effect. An infection can present in a number of ways in this group of patients but you should remember that due to the nature of the disease and the treatment they are undergoing signs of infection may be minimal.

- Temperature is usually the first sign of infection. We initiate the sepsis protocol when a patient has a temperature of 37.5 Celsius. Equally a temperature of 35.5 celsius may be an indication of infection.
- Tachycardia (pulse above 100bpm) and a drop in systolic blood pressure can also be signs of an infection

You should record vital signs on the Track and trigger charts. These will also help to guide you on when to escalate a patient’s condition. The golden rule that we all adhere to is “if in doubt, ask a colleague for advice”. 
Hickman line sites should be checked daily and any erythema reported. Strict ANTT must be adhered to when assessing any line.

Neutropenic patients will not form pus so a slight redness may indicate significant infection. The condition of the oral mucosa should also be observed for ulceration, diarrhoea and vomiting might also be present. In the absence of obvious signs of infection, any patient who appears unwell should be closely observed.

Our patients are also screened for the infection marker CRP. The results of this can be found on casenotes/EPR. Please ensure you are checking this daily in patients with neutropenia.

Infections in neutropenic patients can rapidly progress to septic shock. Therefore, patients should be closely observed and any deterioration escalated immediately and any deterioration escalated immediately

- Hypotension
- Respiratory distress
- Rigor and shivers
- Diarrhoea and or vomiting
- Poor perfusion
- Pain
- Persistent bleeding
- Confusion
- Rash

Other possible indicators:

- Hypotension
- Respiratory distress
- Rigor and shivers
- Diarrhoea and or vomiting
- Poor perfusion
- Pain
- Persistent bleeding
- Confusion.
- Rash

Positive sign of infection

Full set of vital signs including AVPU, urine output, pain and nausea assessment

Inform senior nurse and medical staff

Medical assessment and antibiotic prescribing

Blood cultures both line and peripheral (medical team may also request FBC and biochemistry. Take swabs of obvious infection sites.

Administration of first line antibiotics and other supportive interventions eg IV fluids and fluid balance chart. Be aware that giving antibiotics before blood cultures/swabs will have a negative effect on microbiology results.

Ensure microbiology follow-up is checked and documented on handover sheet

Chest x-ray

Urine and or stool sample

This is a controlled document and therefore must not be changed
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>ALL</td>
<td>Acute Lymphoblastic Leukaemia</td>
</tr>
<tr>
<td>AML</td>
<td>Acute Myeloid Leukaemia</td>
</tr>
<tr>
<td>BM</td>
<td>Bone marrow</td>
</tr>
<tr>
<td>BMT</td>
<td>Bone Marrow Transplant</td>
</tr>
<tr>
<td>Bx</td>
<td>Biopsy</td>
</tr>
<tr>
<td>CML</td>
<td>Chronic Myeloid Leukaemia</td>
</tr>
<tr>
<td>CLL</td>
<td>Chronic Lymphoblastic Leukaemia</td>
</tr>
<tr>
<td>CMV</td>
<td>Cytomegaviruses</td>
</tr>
<tr>
<td>DIC</td>
<td>Disseminated intravascular coagulation</td>
</tr>
<tr>
<td>DMSO</td>
<td>Preservative for stored cells</td>
</tr>
<tr>
<td>DXT</td>
<td>Radiotherapy</td>
</tr>
<tr>
<td>FBC</td>
<td>Full blood count</td>
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<tr>
<td>FFP</td>
<td>Fresh frozen plasma</td>
</tr>
<tr>
<td>G-CSF</td>
<td>Growth colony stimulating factor</td>
</tr>
<tr>
<td>GvHD</td>
<td>Graft-versus-Host Disease</td>
</tr>
<tr>
<td>Hb</td>
<td>Haemaglobin</td>
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<tr>
<td>HLA</td>
<td>Human leukocyte antigen</td>
</tr>
<tr>
<td>IT</td>
<td>Intra-thecal</td>
</tr>
<tr>
<td>LFT's</td>
<td>Liver function tests</td>
</tr>
<tr>
<td>LP</td>
<td>Lumbar puncture</td>
</tr>
<tr>
<td>MDS</td>
<td>Myelodysplasia</td>
</tr>
<tr>
<td>MTX</td>
<td>Methotrexate</td>
</tr>
<tr>
<td>MUD</td>
<td>Matched unrelated donor transplant</td>
</tr>
<tr>
<td>NHL</td>
<td>Non Hodgkin’s Lymphoma</td>
</tr>
<tr>
<td>PBSCH</td>
<td>Peripheral blood stem cell harvest</td>
</tr>
<tr>
<td>PBSCR</td>
<td>Peripheral blood stem cell rescue</td>
</tr>
<tr>
<td>Plts</td>
<td>Platelets</td>
</tr>
<tr>
<td>RIC</td>
<td>Reduced intensity conditioning</td>
</tr>
<tr>
<td>TBI</td>
<td>Total Body irradiation</td>
</tr>
<tr>
<td>TCI</td>
<td>To come in</td>
</tr>
<tr>
<td>TTO’s</td>
<td>Tablets to take out</td>
</tr>
</tbody>
</table>
Resources
There are numerous resources available to you both during your orientation period and throughout your career on Haematology Ward. We hope that you will enjoy exploring these and use them to...
develop your knowledge. The list below is by no means exhaustive, but should give you some idea of where you can find information:

- CHW Policies & Procedures File
- OUH Trust Policies
- CHW Patient Information

Cairns Library, level 3, John Radcliffe Hospital Web-site: [www.medicine.ox.ac.uk/cairns](http://www.medicine.ox.ac.uk/cairns)

Internet access available. Training available on search skills. You can search databases such as Medline and CINHAL.
Common Disorders

This Section is designed to give you an overview of the disorders commonly seen on clinical Haematology. There are a number of ward based resources available to you to further expand your knowledge base, such as colleagues, textbooks, journals and of course your experiences. In order to link your clinical experiences with the theory, we suggest that you use the reflective sheets from section three to explore these conditions as you come across them.

Acute Leukaemia

What is acute leukaemia?

Acute leukaemia is a malignant disease of the haemopoietic cells. The disease develops in early white cell maturation. The normal maturation of these cells is prevented and they proliferate in an unregulated manner, producing large numbers of abnormal leukemic blast cells. These non-functioning cells accumulate in the bone marrow, therefore impairing normal haematopoiesis through overcrowding of the marrow space. This results in bone marrow failure, such as anaemia thrombocytopenia and neutropenia. The non-functioning WBCs spill into the peripheral blood and infiltrate other organs therefore interfering with normal function, 85% of patients will have leukemic blasts in the peripheral blood.

What are the causes of acute leukaemia?

In most cases the cause of acute leukaemia is unknown, making it difficult to consider prevention and early detection. However, some factors are known to increase the risk of developing the disease.

- Radiation
  There is evidence that high exposure to radiation has been linked to the development of leukaemia. However, there are still debates about the risk associated with low levels of radiation exposure.

- Chemical exposure
  Exposure to benzene, a chemical used in the petrochemical industry is a known risk factor and subsequently occupational exposure to benzene in the UK has been regulated.

- Previous chemotherapy and radiotherapy therapy
  Treatment with chemotherapy agents has been known to increase the risk of secondary acute myeloid leukaemia, particularly agents such as Busulphan and cyclophosphamide.

- Genetic Abnormalities
Leukemic cells carry a variety of abnormalities one of which is chromosomal gain, loss and structure. Since the discovery of the Philadelphia chromosome in chronic myeloid leukaemia, chromosomal changes have played a key part in research. It has been found that genetic disorders such as Down syndrome, Bloom’s syndrome, Fanconi’s anaemia and ataxia telangiectasia carry a predisposition towards developing leukaemia.

- **Viruses**
  Although viruses are the main cause of leukaemia in animals, in humans the only link between virus and leukaemia is the human T-cell leukaemia virus (HTLV1) the virus can be found in southwest Japan, the Caribbean and Africa.

Leukaemia is not thought to be due to a single factor but a combination of several.

**Types of acute leukaemia**

Acute leukaemia is a large group of diseases that can be broadly divided into two categories.

- **Acute myeloid leukaemia (AML)**
- **Acute lymphoblastic leukaemia (ALL)**

The specific type of leukaemia is dependent on which type of cell line is affected by the malignancy. In the case of AML it is the myeloid cell line, in ALL malignancy occurs in the lymphoid cell line. In chronic leukaemia more mature cell lines are affected.

**Clinical presentation**

There is often little uniformity in presentation; some patients may be asymptomatic, whereas others are seriously ill. Symptoms associated with bone marrow failure and resulting cytopenia are most common.

- Neutropenia- infections may be recurrent and unresponsive to standard antibiotics.
- Anaemia-pallor, breathlessness, lethargy.
- Thrombocytopenia-petechial, spontaneous bruising, menorrhagia, epistaxis, gingival bleeding.
- Hypermetabolalisum-night sweats, fever, weight loss.
- Lymphadenopathy and splenomegaly, particularly in ALL.

**Diagnosis/classification/staging**

Leukaemia may be suspected from the patients clinical presentation as mentioned above, peripheral blood counts may confirm suspected bone marrow failure. White cell counts may be elevated or usually low. Leukemic blasts may also be seen on a blood film. Examination of the bone marrow; an
Subtypes of AML can be classified using the French-American-British classification system (FAB)

<table>
<thead>
<tr>
<th>FAB no/Type</th>
<th>Name</th>
<th>% of AML patients</th>
<th>Specific clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>minimally differentiated acute myeloblastic leukaemia</td>
<td>5%</td>
<td>Poorer prognosis.</td>
</tr>
<tr>
<td>M1</td>
<td>acute myeloblastic leukaemia, without maturation</td>
<td>15%</td>
<td></td>
</tr>
<tr>
<td>M2</td>
<td>acute myeloblastic leukaemia, with granulocytic maturation</td>
<td>25%</td>
<td>Younger adults favourable prognosis with t(8:21)</td>
</tr>
<tr>
<td>M3</td>
<td>promyelocytic, or acute promyelocytic leukaemia (APML)</td>
<td>10%</td>
<td>Younger adults. Favourable prognosis. Disseminated intravascular coagulation (DIC) MEDICAL EMERGENCY</td>
</tr>
<tr>
<td>M4</td>
<td>acute myelomonocytic leukaemia with and without eosinophilia</td>
<td>20%</td>
<td>Similar to M1 and M2 but with more frequent extra-medullary disease. Good prognosis.</td>
</tr>
<tr>
<td>M5</td>
<td>acute monoblastic leukaemia (M5a) or acute monocytic leukaemia (M5b)</td>
<td>10%</td>
<td>Poorer prognosis—older adults, extra-medullary involvement common.</td>
</tr>
<tr>
<td>M6</td>
<td>acute erythroid leukaemia, including erythroleukaemia (M6a) and very rare pure erythroid leukaemia (M6b)</td>
<td>5%</td>
<td>Poorer prognosis in older adults, may have prolonged onset period</td>
</tr>
<tr>
<td>M7</td>
<td>acute megakaryoblastic leukaemia</td>
<td>5%</td>
<td>Poorer prognosis</td>
</tr>
</tbody>
</table>
The FAB system divides AML into eight subgroups; this is based on the type of cell from which the leukaemia developed its degree of maturity. It also uses cytogenetics to characterise any underlying chromosomal abnormalities. The importance of this is that subtypes have varying prognoses and responses to therapy.

Patients with Acute Promyelocytic Leukaemia (APML) (FAB 3) are considered a medical emergency as granules in the promyelocytes release thromboplastin, which interfere with the coagulation cascade. This causes both bleeding and clotting problems, known as disseminated intravascular coagulation (DIC).

The World Health Organization (WHO) classification of acute myeloid leukemia has been more recently developed. It attempts to be more clinically useful and to produce more meaningful prognostic information including morphology, cytogenetics, molecular genetics and immunologic markers. However the FAB system is still currently more widely used.

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th>ICD-O</th>
</tr>
</thead>
</table>
| AML with characteristic genetic abnormalities | ● AML with translocations between chromosome 8 and 21 [t(8;21)] (ICD-O 9896/3); RUNX1/RUNX1T1  
● AML with inversions in chromosome 16 [inv(16)] (ICD-O 9871/3); CBFβ/MYH11  
● APL with translocations between chromosome 15 and 17 [t(15;17)] (ICD-O 9866/3); RARA;PML | Multiple |
| AML with multilineage dysplasia | This category includes patients who have had a prior myelodysplastic syndrome (MDS) or myeloproliferative disease (MPD) that transforms into AML. This category of AML occurs most often in elderly patients and often has a worse prognosis. | M9895/3 |
| AML and MDS, therapy-related | This category includes patients who have had prior chemotherapy and/or radiation and subsequently develop AML or MDS. These leukaemia’s may be characterized by specific chromosomal abnormalities, and often carry a worse prognosis. | M9920/3 |
| AML not otherwise categorized | Includes subtypes of AML that do not fall into the above categories. | M9861/3 |

Treatment
Without treatment patients with AML are unlikely to survive more than a few months. They will usually succumb to overwhelming infection or experience a major bleed. Before treatment is commenced medical teams will need to assess the patient to ensure they are fit enough to tolerate the toxicity involved. Patients that are not expected to tolerate curative treatment will receive either palliative chemotherapy or supportive care for symptom management.

The treatment for AML is cytotoxic therapy and consists of three stages;
Induction, consolidation and maintenance. The induction phase consists of an intensive course of chemotherapy with the aim to achieve complete remission (CR). After the initial chemotherapy a bone marrow aspirate is performed to assess how effective the treatment has been and whether the patient is in CR.

Complete remission is achieved if there are less than 5% blast cells present in the bone marrow. This does not mean the disease has been cured as only a sample of the bone marrow has been taken, leukaemia cells may still be present and the disease may recur (relapse). The consolidation phase aims to eliminate remaining disease and the maintenance phase consists of low-dose combination given every three to four weeks with the aim to prevent possible relapse. An allogeneic bone marrow transplant may be used as an alternative to consolidation for poor risk patients, particularly if an HLA-matched sibling is available.

Patients that do not achieve complete remission will be given an alternate chemotherapy regime, it should be noted that patients with resistant disease have a poor prognosis.

Bone marrow, peripheral blood stem cell and cord transplantation

Haemopoietic stem cell transplant may be considered as a treatment choice for some patients with poor prognosis/resistant disease and in those that have relapsed. The principle of transplantation is to destroy all myeloid and lymphoid blood cells through high dose chemotherapy (conditioning) and replace it with harvested cells that will colonise and regenerate the patient’s marrow space. Transplantation is not without its risks, life-threatening side effects and toxicities make caring for the transplant patient extremely complex. The risks and benefits must be weighed up very carefully including age, co-morbidities, response to treatment including performance status, disease status and sometimes most importantly the psychosocial status of the patient.

How successful is treatment?

Patients with AML can be divided into risk groups; these are determined by age, initial response to treatment and genetic abnormalities. The survival rate at five years is shown below.

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Number of patient’s</th>
<th>5 year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>30%</td>
<td>70%</td>
</tr>
<tr>
<td>Standard</td>
<td>50%</td>
<td>48%</td>
</tr>
<tr>
<td>Poor</td>
<td>20%</td>
<td>15%</td>
</tr>
</tbody>
</table>

Acute Lymphoblastic Leukaemia (ALL)

As we saw earlier ALL occurs within the lymphoid cell line. The disease is the most common form of cancer in children and particularly affects those between the ages of 2 and 7 years. In adults the likelihood of occurrence is in later years, particularly over the age of 40. The disease is more common in males than females.

Classification

As with AML, classification of Acute Lymphoblastic Leukaemia can be made using the FAB system as shown below.

<table>
<thead>
<tr>
<th>FAB no/type</th>
<th>Morphology of blast cells.</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1</td>
<td>Small ununiformed lymphoblast’s</td>
</tr>
<tr>
<td>L2</td>
<td>Large varied lymphoblast’s</td>
</tr>
<tr>
<td>L3</td>
<td>Large varied lymphoblast’s, vacuoles</td>
</tr>
</tbody>
</table>

Treatment

The treatment for ALL is similar to that of AML. Cytotoxic therapy is used in the same format of induction, consolidation and maintenance in the hopes to achieve complete remission. The type of chemotherapy used differs depending on classification. Prednisolone is used largely in the treatment schedule as is Intrathecal chemotherapy.
Central nervous system involvement
The Central nervous system (CNS) may be a sanctuary for leukemic cells. If the cerebrospinal fluid (CSF) is not treated, up to 40% of adults will develop CNS involvement. Intrathecal methotrexate is the standard preventative therapy.

Factors that indicate a poor prognosis
- High white cell count at diagnosis
- Male gender
- Genetic abnormalities, such as the Philadelphia chromosome
- Failure to achieve CR 14 days after induction chemotherapy
- L3 type as it is more malignant, processes rapidly and responds poorly to chemotherapy.

Aplastic Anaemia

What is aplastic anaemia?
This disease results from a reduction in the number of stem cells in the bone marrow, as a consequence there is a decreased production of all blood cells. Patients with aplastic anaemia will have pancytopenia (low red cell, white cell and platelet counts). The prognosis of the disease is directly related to the severity of bone marrow depression. Severe AA is life threatening and is treated as an emergency.

Severe Aplastic Anaemia is defined as having two out of three of the following.
- Neutrophils <0.5 x 10 to the 9/L
- Platelets <20 x 10 to the 9/L
- Erythrocytes <40 x 10 to the 9/L

How common is aplastic anaemia?
This disease is very rare, affecting 2-5 people per million per year. It is slightly more common in males than females and affects all age groups.

Aplastic Anaemia can be divided into two main groups: ‘inherited’ and ‘acquired’.

Acquired Aplastic Anaemia
AA is seen as an attack on the haemopoietic system, which includes programmed cell death. The primary score for this can include drugs, chemical and viruses.

Drugs
- Antibiotics (chloramphenicol)
- Anti-inflammatory (phenylbutazone)
- Antithyroid (carbimazole)
- Antimalarial (chloroquine)
- Antoconvulsant (phenytoin)

Infective agents
- Viruses (hep A, B and C)
• Bacterial (mycobacteria)
• Epstein-Barr, HIV

Toxins
• Commercial solvents
• Insecticides
Long term exposure can lead to decreased blood cell progenitors and DNA damage.

The severity of the disease depends on the peripheral blood counts at presentation and the reduction in the number of haemopoietic cells in the bone marrow.

What is the treatment for aplastic anaemia?
The management of aplastic anaemia depends on the severity and the underlying cause. Treatment can be categorised as follows

Removal of the cause if the patient is taking any drugs associated with aplastic anaemia

Supportive care to maintain blood counts. However, the use of blood products should be limited as this can exacerbate any auto-immune problems. Antibiotic support for the immune system.

Restoring haemopoiesis this can be achieved by reducing auto-immune effects with steroids, cyclosporin or anti-lymphocyte globulins (ALG and ATG). Alternatively, bone marrow transplantation can repopulate the patient’s bone marrow with healthy stem cells.

How successful is treatment for aplastic anaemia?
In general, 50-60% of patients respond to ALG within 3-6 months, a combination of ALG, steroids and cyclosporin can increase this figure. However, this response cannot always be maintained and treatment with ALG can cause anaphylaxis, serum sickness and severe neutropenia. Patients with aplastic anaemia have an increased risk of developing MDS or acute leukaemia.
In patients with severe aplastic anaemia BMT offers the best chance of long-term cure, with a positive outcome in 70% of patients.

Inherited Aplastic Anaemia
Fanconi’s Anaemia and Dyskeratosis cogenita are associated with Aplastic Anaemia and both are inherited. In FA cells from patients show a high frequency of chromosomal breakage. This is thought to be due to DNA defects, particularly in repairing. A full cytogenetic analysis is required to confirm diagnosis. Haematopoietic defect in FA is evident at the progenitor cell level. DC is a characterised by reticulate skin pigmentation, mucosal leucoplaikia and nail dystrophy. AA occurs in 50% of cases and normally presents in the first 10yrs of life. The precise pathophysiology of bone marrow failure in DC is unknown but it shares many features of AA, including predisposition to malignancy and chromosomal instability.
Treatments for both FA and DC are similar to that of AA, although rates of success are lower due to DNA involvement. BMT remains the most successful treatment option although advancements in gene therapy may provide increased survival rates.

Chronic Myeloid Leukaemia

Chronic myeloid leukaemia (CML) is a stem cell disorder that results in the unregulated production of myeloid white cells. The disease is generally associated with a specific, acquired chromosome
abnormality, the Philadelphia chromosome. Chronic myeloid leukaemia can affect any age group but mainly affects people between the ages of 40 and 60 years. For a small proportion of people, CML will remit spontaneously. More commonly, the disease will become progressively unresponsive to treatment. Eventually it will move from a chronic to an accelerated phase when it transforms into an acute leukaemia. On average, survival is about 3-7 years.

Clinical Features
CML has an insidious onset and is frequently diagnosed by a routine blood test. The usual clinical features include anorexia, weight loss, anaemia and an enlarged liver and spleen. A full blood count will reveal a high white cell count. This can increase blood viscosity and result in such symptoms as headache, blurred vision and breathlessness.

Treatment
The initial treatment involves lowering the white cell count. Apheresis and the use of oral cytotoxic drugs such as Imatinib (Glivec) can help to achieve this. Imatinib is a thrysine kinase (TK) inhibitor and is given life long as it targets the Philadelphia chromosome positive cells in order to prevent abnormal cell proliferation.

Allogeneic stem cell transplantation is the main curative option for those with CML and is best performed during the chronic phase of the disease. The decision to undergo the high risk process of transplantation can be very difficult at this stage, as people may feel relatively well and may still be coming to terms with the implications of their disease. Support from health care professionals, including specialist nurses, can be very important at this time.

Chronic Lymphocytic Leukaemia

Chronic lymphocytic leukaemia (CLL) is a proliferative disorder of the lymphocytes. These cells then accumulate in the blood, bone marrow, lymph nodes and spleen. CLL is the most common form of leukaemia and usually occurs in later life, 95% of cases are seen in people over the age of 50 years.

Clinical Features
In the early stages, the symptoms of CLL are mild and include fatigue, weight loss, and some enlargement of lymph nodes, liver and spleen. However, the disease is marked by a slow but progressive bone marrow failure. The mean survival for patients with CLL is about 10 years. As CLL is essentially a disease of the elderly, patients will often die from complications following treatment.

Treatment
Treatment is generally delayed until symptoms become troublesome, often for a period of years. If symptoms do progress combination chemotherapy FCR (Fludarabine, Cyclophosphamide and Rituximab) is used, oral cytotoxic agents such as chlorambucil can help to control the disease in elderly patients with co-morbidities. Haemopoietic stem cell transplantation may be offered to some relatively young patients in the hope of affecting a cure, but this is not routine at present.

Stages
There are 5 recognised stages of CLL. Treatment will differ according to the stage (progression) of the disease.
Stage 0 CLL
Patients are at low risk and have lymphocytosis, an increase in the number of lymphocytes. A high lymphocyte count is defined as more than 10,000 lymphocytes per cubic millimeter.

Stage 1 CLL
Patients are at intermediate risk and have lymphocytosis, plus enlarged lymph nodes.

Stage II CLL
Patients are at intermediate risk but have lymphocytosis plus an enlarged liver or enlarged spleen, with or without lymphadenopathy.

Stage III CLL
Patients are at high risk and have lymphocytosis plus anemia.

Stage IV CLL
Patients are at high risk but have lymphocytosis plus thrombocytopenia, a low number of blood platelets.
Nursing Care
Many patients with stable and low stage chronic leukaemia receive all of their treatment in busy outpatient clinics. In the past, this meant that many received very little nursing input. In order to rectify this, haematology units are increasingly employing Clinical Nurse Specialists. These nurses can offer support, patient education and advice about symptom management. They can also play a role in co-ordinating patients’ care, educating other professionals, and helping patients to access additional forms of care and support, including community and palliative care support, should this become necessary.

Myelodysplastic Syndrome (MDS)

What is MDS?
The term myelodysplasia describes a group of disorders of the bone marrow. These diseases are characterised by the ineffective production of the myeloid cells. The number of blood cells can be decreased resulting in impaired bone marrow function. In some cases MDS can transform into acute leukaemia.

What are the clinical and laboratory features of MDS?
- Patients tend to be elderly; half of newly diagnosed patients are over 70. However, the disease can occur in young people.
- Anaemia is the most common presentation, present in 85% of patients.
- Neutropenia is seen in 50% of patients
- Thrombocytopenia affects 25% of patients
- Increased cellularity of the bone marrow (hypercellular marrow)
- Chromosomal abnormalities can be present.

What are the causes of MDS?
In most cases the cause of MDS is unknown. In some patients the disease can be attributed to exposure to chemicals such as benzene or previous treatment with cytotoxic drugs or radiation.

<table>
<thead>
<tr>
<th>Type</th>
<th>Relative Cases</th>
<th>Median Survival (yrs)</th>
<th>Progression to AML %</th>
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<tbody>
<tr>
<td>Refractory anaemia</td>
<td>RA 30</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>RA with ring sideroblasts</td>
<td>RARS 25</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>RA with excess blasts</td>
<td>RAEB 20</td>
<td>1</td>
<td>40</td>
</tr>
<tr>
<td>RAEB in transformation</td>
<td>RAEB-t 10</td>
<td>0.5</td>
<td>60</td>
</tr>
<tr>
<td>Chronic myelomonocytic leukaemia</td>
<td>CMM1 15</td>
<td>2</td>
<td>15</td>
</tr>
</tbody>
</table>

How is MDS classified?
This group of disease can vary from a benign anaemia to a disease resembling acute myeloid leukaemia. The categorisation is largely based on the number of blast cells (abnormal, immature cells) present.
MDS that has transformed is then treated as acute leukaemia. However, these diseases are often resistant to chemotherapy.

What is the treatment for MDS?

Supportive care
Maintain blood counts with blood and platelet transfusions.
Prompt antibiotic therapy to treat infections

Growth factors
G-CSF and erythropoeitin may be used to maximise marrow function.

Chemotherapy
Low dose chemotherapy may have some effect in slowing disease progression.

BMT
Allogeneic bone marrow transplantation is the only curative option but is only suitable for younger patients. It should, ideally, take place before transformation. Mini transplants may become a way of offering older patients the chance of cure.

**Multilpe Myeloma**

What is Multiple Myeloma?
Myeloma is a malignant disease of the bone marrow, it results from the uncontrolled proliferation of plasma cells.

What are plasma cells?
These cells exist within the bone marrow and are responsible for the production of immunoglobulins (antibodies).

How common is myeloma?
This disease accounts for 1% of all cancers, its incidence is about 1/100,000 and is thought to be increasing. The mean age of diagnosis is 61 years old but a third of cases occur in people under 60 and about 3% in patients under 40. The onset of the disease is often gradual and the disease may be advanced at the point of diagnosis. Myeloma is currently a treatable but not curable condition.

What are the sign and symptoms of myeloma?
The proliferation of myeloma cells within the bone marrow can lead to bone marrow failure and its consequent complications. Myeloma can also cause bone damage that can be shown on x-ray as punched holes in the bone, these are referred to as lytic lesions. Bone damage can cause severe pain and result in pathological fractures.
The abnormal plasma cells can secrete large quantities of abnormal immunoglobulins (antibodies) into the blood stream. High levels of these immunoglobulins can cause hyperviscosity of the blood and renal failure. Due to low levels of normal immunoglobulins patients with myeloma can be particularly vulnerable to infection.

High levels of calcium (hypercalcaemia) in the blood is also a common feature of myeloma, this can lead to confusion, polyuria, constipation, nausea and lethargy.

How is Myeloma diagnosed?
Some of the following clinical features can be seen in patients with myeloma;
- Anaemia
- Lytic bone lesions
- Renal impairment
- Hypercalcaemia
- Hyperviscosity
- Elevated paraprotein level in the blood
- Presence of Bence-Jones proteins in the urine and free-light chains in the serum
- Increased plasma cells in the bone marrow
- Amyloid, an insoluble protein that is deposited in soft tissues in some cases of myeloma

The diagnosis of myeloma is confirmed if two out of the following are present

- lytic lesions
- > 10% plasma cells in the bone marrow
- High paraprotein level in blood or urine

How is Myeloma treated?
The signs and symptoms of myeloma can be treated as follows;

- Hypercalcaemia: IV hydration, and the use of bisphosphonates such as sodium clodronate (oral) or pamidronate (IV).
- Pain: Local radiotherapy, opiates, vertebroplasty
- Renal failure: may require dialysis
- Infection: usual antibiotic regime
- Anaemia: transfusion
- Hyperviscosity: can be managed with IV hydration but may need plasmapheresis.

Treatment of the underlying disease will depend on the age and well being of the patient. Standard treatment involves intensive chemotherapy regimes such as CDT (cyclophosphamide, dexamethasone and thalidomide) followed by an Autologous stem cell transplant. For elderly patients treatment is given in the form of oral chemotherapy Melphalan and dexamethasone.

With standard treatment the patients can achieve some control of their disease, this is referred to as a plateau phase. Average survival is about 4 years.

What advances have been made in the treatment of Myeloma?
In disease progression further treatment can be given to regain control, the current drugs of choice are Velcade and Lenalidomide. Allogenic transplant is considered only in a select group of patients and may offer only a small chance of cure in a carefully selected patient.

Spinal Cord Compression in Myeloma

Spinal cord compression is an uncommon condition that affects people with certain cancers that have spread to the bones in the spine, or have started in the spine. It is defined as ‘compression of the dural sac and its contents (spinal cord and/or equina) by an extra-dural tumour mass’. This prevents signalling which results in motor dysfunction.

Diagnosis

If the patient is not known to have cancer histology must be obtained as it may affect treatment. Radiological assessment of spine either by MRI, CT, X-ray. (the whole spine must be examined) Neurological and motor assessments The level and severity of SCC can be determined by incorporating mechanical pain, neurological changes and radiology findings.

Treatment

The aim of treatment is to decompress the affected area and restore normal signalling. This should be done as soon as possible to prevent paralysis and provide better overall outcome for the patient. Some patients may require/be suitable for surgery however the majority are treated with symptomatic care.

Non Hodgkin’s Lymphoma (NHL)

What is NHL?

This is the term used to describe a large group of malignant diseases of the lymphoid tissue, distinct from Hodgkin’s disease by the absence of the abnormal giant multinucleated Reed - Sternberg Cells.
NHL is the most common haematological malignancy and its incidence is increasing. NHL can occur at any age but the median age of onset is 50 years. In the UK, NHL is approximately four times more common than HL and is more common in men than women.

What is the cause of NHL?
In most cases the cause of NHL is unknown. However, patients who are immuno-compromised have a higher risk of developing NHL, for example those with

- HIV infection
- Following infection with the Epstein-Barr virus
- Burkitt’s lymphoma is associated with HTLV-1 infection
- Immuno-suppression following organ transplantation
- Prolonged treatment with steroids
- Coeliac disease

What is the clinical presentation of NHL?
Nodal involvement painless lymphadenopathy, cervical region is the most common.

Extranodal involvement NHL can invade any tissue or organ but most commonly it can be seen in the intestine, bone marrow, CNS, testes lungs, liver, breast.

Systemic symptoms night sweats, weight loss, fever, pruritis

How is NHL diagnosed?
Diagnosis is made through biopsy of an affected lymph node. The sub type is determined through histological examination, chromosomal analysis (cytogenetics) and the use of monclonal antibodies (immunophenotyping).

With NHL staging is less significant than for Hodgkin’s disease in predicting outcome. The disease classification and rate of cell division is more important.

What are the poor prognostic factors associated with aggressive NHL?
- Older age group
- Presence of systemic symptoms
- Poor general condition
- Elevated LDH
- Wider nodal involvement.
Extranodal involvement

Bulky disease

How is NHL classified?
There are several schemes for classifying NHL. At present, the Revised European-American Lymphoma system (REAL) is the accepted classification for NHL but the Working Formulation is still widely used;

<table>
<thead>
<tr>
<th>REAL Classification</th>
<th>Incidence</th>
<th>Working Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small lymphocytic lymphoma/leukaemia</td>
<td></td>
<td>Low grade</td>
</tr>
<tr>
<td>Lymphoplasmacytoid lymphoma</td>
<td></td>
<td>Low grade</td>
</tr>
<tr>
<td>Mantle cell lymphoma</td>
<td></td>
<td>Intermediate grade</td>
</tr>
<tr>
<td>Follicle centre lymphoma</td>
<td>35 – 40 %</td>
<td>Low grade</td>
</tr>
<tr>
<td>Burkitt’s lymphoma</td>
<td></td>
<td>High grade</td>
</tr>
<tr>
<td>Diffuse large B cell lymphoma</td>
<td>25 – 30 %</td>
<td>Intermediate/high grade</td>
</tr>
<tr>
<td>Lymphoblastic leukaemia/lymphoma</td>
<td></td>
<td>High grade</td>
</tr>
<tr>
<td>Peripheral T cell lymphomas unspecified</td>
<td></td>
<td>Intermediate/high grade</td>
</tr>
<tr>
<td>Adult T cell leukaemia/lymphoma</td>
<td></td>
<td>High grade</td>
</tr>
<tr>
<td>Angioimmunoblastic T cell lymphoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anaplastic large cell lymphoma</td>
<td></td>
<td>High grade</td>
</tr>
</tbody>
</table>

How is NHL treated?
The treatment for NHL depends on the sub type of the disease and how aggressive it is at presentation.

The less aggressive diseases have a very indolent pattern of progression and are not treated until they become symptomatic. Radiotherapy may be given to treat localised disease; cytotoxic agents such as oral chlorambucil may induce a remission. However, low-grade diseases are rarely cured.

Aggressive lymphomas require treatment with combination chemotherapy regimes such as CHOP. High dose treatment and peripheral stem cell rescue is often the treatment of choice for relapsed disease.

Burkitt’s Lymphoma is treated with a regime that includes intrathecal chemotherapy due to the risk of CNS disease.

The use of monoclonal antibodies e.g Rituximab that specifically target lymphoma cells are now widely used with success, these drugs avoid the general side effects of chemotherapy.

How successful is treatment for lymphoma?
As has been previously the less aggressive diseases are unlikely to be curable and survival averages 6-10 years. For the more aggressive lymphomas, remission can be achieved in 60% of patients treated with CHOP with an overall cure rate of about 30-40%.

Hodgkin’s Lymphoma

What is Hodgkin’s Lymphoma (HL)?
This disease is a malignant disorder of the lymphoid cells. There is a peak incidence between the ages of 20-30 and another peak in the elderly. HD is twice as common in males than females.

What are the causes of HL?
The cause of this disease is unknown but there are suggestions that in some cases it may be related to infection with the Epstein-Barr virus.

What are the clinical features of HL?
- Lymphadenopathy (enlarged lymph nodes), these are usually painless. Cervical nodes are involved in 60-70% of patients, axillary nodes in 10-15% of cases and inguinal nodes in 6-12%. Other nodes may be involved but can only be detected on CT scan.
- Enlarged liver or spleen.
- Systemic symptoms – night sweats, weight loss, pruritis, fever..
- Pleural effusions
- Obstruction of the superior vena cava.
- Bone marrow failure due to infiltration of lymphoma cells.
- Rarely extra nodal disease, HD can infiltrate any organ.

How is HL diagnosed and staged?
Diagnosis is made through a biopsy of an affected lymph node indicating the presence of the Reed-Sternberg cells. The stage of the disease at diagnosis is relevant for treatment and prognostic indications.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Node involvement in a single lymph node area</td>
</tr>
<tr>
<td>II</td>
<td>2 or more areas involved but on the same side of the diaphragm</td>
</tr>
<tr>
<td>III</td>
<td>Nodal involvement above and below the diaphragm</td>
</tr>
<tr>
<td>IV</td>
<td>Extra-nodal disease present</td>
</tr>
<tr>
<td>A or B</td>
<td>If systemic symptoms are present or not</td>
</tr>
</tbody>
</table>

Classification
How is HL treated?

Treatment depends on the stage of the disease at diagnosis.

Stage I or II A  Treated with radiotherapy

Stage I or II B  These patients require treatment with chemotherapy +/-

Stage III & IV  radiotherapy. The most usual regime is ABVD. High dose treatment and autologous stem cell rescue is also an option, particularly for relapsed disease.

How successful is treatment for HL?

Prognosis depends on age and disease stage. However, in general, early stage diseases have an 85% cure rate, whilst more advanced HL has a 70% cure rate.

Patients treated for HL have an increased risk of developing secondary malignancies, particularly AML or NHL. The incidence of secondary malignancies 20 years after treatment is 20%.

**Sickle Cell Disease**

What is Sickle cell Disease?

Sickle cell disease is not a cancer. It is a inherited condition which causes mutation of normal haemoglobin (HbA). Glutamic acid is replaced by valine as the 6th amino acid on the beta-globulin chain. The resulting haemoglobin molecule is referred to as HbS.

Individuals that inherit one normal gene and one for HbS (heterozygous) become carriers of the disease but do not usually display any symptoms, they are said to have sickle cell trait. People who inherit the HbS gene from both parents (homozygous) will have sickle cell anaemia.

There is a second beta-globulin abnormality that produces HbC. Some people will inherit one HbS gene and one HbC gene. This is known as SC disease.
Who is affected by sickle cell disease?
Sickle cell disease is most prevalent in people of African decent but it also occurs in India, Saudi Arabia, Turkey, Greece and southern Italy. The high prevalence of the abnormal gene within the African population is due to the protection the disease offers against malaria. Malaria parasites are not able to exist in red cells containing HbS.

When does the disease become apparent?
Symptoms of sickle cell disease are not normally seen until after the age of 6 months, before this age babies have high levels of foetal haemoglobin (HbF).

What effects does HbS have on red blood cells?
The abnormal haemoglobin molecule forms crystals within the red blood cell when exposed to low oxygen levels. This deforms the shape of the cell to its characteristic sickle shape. These sickle cells are more rigid than normal cells and are not able to pass through small blood vessels.

Sickle cells are haemolysed more rapidly than normal cells and have different oxygen carrying properties.

What are the clinical manifestations of sickle cell disease?
Anaemia
Most people with sickle cell disease will be chronically anaemic, often with haemoglobin levels of around 5g/dl. This is due to high rates of haemolysis. The bone marrow is often highly active and there will be higher numbers of reticulocytes (immature red cells) in the peripheral blood as the body attempts to maximise oxygenation. High rates of haemopoiesis
results in depletion of folate and iron stores. However, in spite of severe anaemia most people remain relatively asymptomatic, this is because the body can adjust to low haemoglobin levels and the fact that HbS releases oxygen more readily than HbA.

Due to rapid haemolysis sickle cell sufferers can, at times, appear jaundiced and have raised LDH and bilirubin levels. They are susceptible to red cell aplasia (absence of red cell production), this usually results from folate depletion or infection with parvo virus. Patients will normally recover spontaneously with folate support.

Sickle cell crisis
Sickle cell disease is characterised by intermittent crises. These crises are triggered by hypoxia leading to sickling of the red cells. High levels of sickling cause veno-occlusion, resulting in tissue infarction.

Sickle cell crises create severe pain in the affected area and can cause strokes, avascular necrosis of the hips and shoulder joints, as well as major organ damage.

Serious infarction in the lungs is referred to as a chest crisis and is life threatening. Other sites that cause major complications are the liver and spleen leading to sequestration of red cells.

What are the causes of a sickle cell crisis?
Often the trigger for a crisis is unknown but there are some factors that are known to precipitate crises:

- stress
- infection
- dehydration
- excessive alcohol consumption
- extreme exercise
- anaesthetics
- child birth

What are the signs and symptoms of a chest crisis?
pleuritic chest pain
shortness of breathe
hypoxia
severe anaemia
changes on chest x-ray

How is a sickle cell crisis treated?
Treatment is mainly supportive. IV fluids are given to reduce blood viscosity at a rate of 3L/m2/day. Adequate pain relief is vital and is normally achieved with diclofenac and an IV morphine infusion, with PCA facility. Antibiotics are given if the patient is febrile. The patient requires close observation of vital signs, oxygen saturations and respiratory rate.

In severe crises or where a chest crisis is suspected an exchange transfusion will be considered. An exchange transfusion is preferred as it will remove cells containing HbS and replace them with normal cells. Care must be taken not to increase blood viscosity. This treatment is reserved for serious cases as repeated transfusion can lead to allo-
immunisation (production of antibodies against transfused blood, this can lead to transfusion reactions and haemolysis) and iron overload.

What other complications are associated with sickle cell disease? Patients can develop lower limb ulcers, retinopathy, growth retardation, cardiac failure, gallstones and priapism.

People with sickle cell disease appear to have immunological abnormalities and are at increased risk of infection. Multiple infarcts in the spleen can inhibit its immune function; this makes patients vulnerable to pneumococcal infection. To lessen this risk they take prophylactic penicillin V.

What alternative treatments are available? It has been found that treatment with hydroxyurea (an oral cytotoxic agent) can reduce the number and severity of crises. However, this drug has a small risk of causing leukaemia.

Routine exchange transfusion can be effective in preventing crises but the disadvantages of iron overload and allo-immunisation have already been discussed.

Bone marrow transplantation has been used as a cure for sickle cell disease but it is normally felt that the risks are too great to justify this action.

Original authors: Liz Rawlings, Sandy Hayes, Mandy Ellis, Rachel Miller.

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<th>Review</th>
<th>Date</th>
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