

Referral guidance for suspected cancer in children and young people

A supporting resource for NICE guideline NG12
Suspected cancer: **recognition and referral**



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A supporting resource for NICE guideline NG12 – Suspected cancer: recognition and referral.

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Overview

This document is a supplement to the NICE guidelines for suspected cancer: recognition and referral (NG12). The NICE guideline covers the identification of symptoms that could be caused by cancer in people of all ages. It outlines appropriate investigations in primary care and selection of people to refer for specialist opinion.

This guidance is specific to children as it is recognised that there are a number of differences in the presentation, referral pathways and care of children with cancer compared with those of adults.

Referral guidance for suspected cancer in children and young people

This booklet accurately reflects recommendations in the NICE guidance on recognition and referral for suspected cancer.

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Rationale and evidence base for a paediatric supplement

Referral guidelines for children with suspected cancer were first published in 2005 and revised in 2015. Whilst the 2015 document provides some evidence to support the guidance offered, this is based on evidence from primary care, which is sparse with respect to presentation of cancer in children. The 2015 guidance also presents most of children's malignancies alongside their adult counterparts. However, there are differences in incidence, presentation and types of malignancies seen in the younger age group. Consequently, key symptoms and signs of children's cancer do not receive due emphasis in the 2015 document.

Following discussions between the Children's Cancer and Leukaemia Group (CCLG, the UK multi-disciplinary professional body for health care professionals caring for children with cancer) and NICE, it was agreed that a practical supplement to the 2015 document should be produced, to address the particular issues around referral of children. This was to draw on expertise from professionals involved in the management of children with cancer, together with input from a wide range of stakeholders, in order to produce a consensus document that would serve as a practical supplement for those working in primary care. Formal evidence was needed to support guidance regarding key symptoms of cancer in children. Therefore, a Delphi process was developed by a CCLG steering committee to gather expert opinions from UK paediatric haematologists and oncologists, complementing the primary care approach employed in the original 2015 document [1].

The CCLG referral guidance steering group formulated 25 draft statements for review. The CCLG emailed its paediatric haematologist/oncologist membership (n=179) and 88 responded (49%). To achieve consensus, statements required $\geq 70\%$ agreement from $\geq 60\%$ of actual respondents, from the denominator (n=88). Fifteen of 25 original statements were accepted at the first round of voting. Three of 25 statements where $>50\%$ did not support were rejected outright. One statement could not be revised without replicating a previously accepted statement. The six remaining statements were revised and a second round of voting undertaken; all six revised statements were accepted. Overall, 21 of 25 statements (84%) met consensus criteria. This expert opinion should help streamline suspected cancer referral in children and help optimise subsequent outcomes [1]. The results of the consensus were used to produce this guideline. The draft guideline was reviewed by a number of stakeholders including paediatricians, paediatric emergency medics and general practitioners. Their feedback on both content and format were used in producing this final document.

Cancer presentation to primary health care

The individual risk of cancer from birth to age 25 years is now 1 in 180, so whilst it may be regarded as an uncommon presentation in primary care, it is important that it is considered in a differential diagnosis in a child presenting with unexplained symptoms.

Referral down a suspected cancer pathway can be highly traumatic for patients and families, and the ability to streamline and standardise this approach is therefore vital. Conversely, whilst it can be difficult to identify those who need further investigation, false reassurance may lead a child down a pathway which is associated with extended diagnostic delay. Early identification of cancer must therefore be a goal for all healthcare practitioners.

The significance of a delayed diagnosis presents a challenge for primary health care professionals, who are required to triage symptoms that may point to a cancer diagnosis from those which are not and make appropriate onward referrals. Many symptoms associated with cancer are non-specific and are seen every day in general practice, whilst a cancer diagnosis is seen infrequently.

Cancer is the most common cause of death in childhood

Death in childhood is a rare event in the developed world. However, cancer remains the most common cause of death in children aged 1-15 years, responsible for over 1 in 5 deaths of children in this age group.[2] Cancer is rarely preventable in childhood, but early identification is likely to reduce morbidity and mortality. Even when treated successfully, cancer is a major cause of long-term morbidity for the affected child, and their family.

There is a problem of time to diagnosis

Delays in the diagnostic pathway may well lead to more advanced disease at presentation, with subsequent greater risk of death, greater morbidity, and inevitably, distrust of the medical system. There is evidence that tumours presenting in childhood in the UK are larger, at a more advanced stage and require more therapy than those presenting in other parts of Europe [3]. Outcomes for childhood cancer, although similar, are worse than some of our European neighbours [4], despite similar or even identical treatment strategies. There is current ongoing collaborative research, aiming to explore and explain the reasons behind these differences.

Early identification of cancer must be a goal for all healthcare practitioners. Clear warnings are needed where possible, but there are many occasions when a pattern of symptoms and signs point strongly to cancer. Individual features alone are too imprecise. Children often cannot express symptoms clearly, and for this reason, the level of suspicion must necessarily be kept high.

Achieving a balance

There is a need for balance when setting criteria for urgent referral - too high a threshold risks continuing to exclude patients who may benefit from earlier diagnosis. Conversely, a threshold that is too low risks causing unnecessary investigations, anxiety and distress to children and their families.

Paediatric tumours are different

There are clear differences between most paediatric and adult tumours, reflecting different biology. Many paediatric tumours are of 'embryonal' origin or other 'high grade' malignancies, whilst carcinomas are uncommon. Paediatric malignancies can progress very rapidly, and delay of even a few days may be associated with substantial clinical deterioration. Conversely, paediatric tumours can sometimes present in a more indolent way, including Hodgkin lymphoma and some low grade intracranial tumours, and malignancy cannot therefore be excluded solely on the basis of a long history.

Cancer predisposition is not commonly seen, but there are specific examples where this must be considered, particularly neurofibromatosis type 1 (NF1). A family history of cancer in young adults (<40 years), particularly breast cancer, sarcoma and leukaemia, should raise suspicion.

Referral pathways are different

Cancer, including leukaemia, in this age group is managed in a highly centralised manner, through one of 21 Principal Treatment Centres in the UK and Ireland.

In most cases, primary care suspected cancer referrals should be made to local acute paediatricians. In patients where there is a very high suspicion of malignancy in primary care, telephone discussion directly with an acute paediatrician, or directly to paediatric oncology/haematology depending on the local service configuration, would be appropriate.

There is good evidence to show that the 'two-week wait' system is not useful for children, with at most 1-3% of referred patients ultimately being diagnosed with cancer [6-8]. It is infrequently used and referrals are predominantly related to enlarged lymph nodes.

Conversely, more than 95% of children with cancer do not reach the oncology service through the two-week wait system [9, 10]. Accordingly, the recommendation is that referral for suspicion of cancer in childhood should not rely on this route. In cases of uncertainty, a telephone discussion with an acute paediatrician (or paediatric haematologist or oncologist) is strongly encouraged and **where a diagnosis of cancer is strongly suspected, referral should be immediate and by telephone.**

Map of Principal Treatment Centres in UK and Ireland.
Reference: CCLG [5]



Assessing children and young people is different

An unwell child may be unable or unwilling to comply with examination, may disguise their impairment, or not admit to difficulties. For example:

- A child with an abdominal mass may be distressed, preventing adequate examination
- A motor weakness may be masked by associated behaviours distracting from the true diagnosis
- A child may not have reached the development stage to be able to describe their symptoms clearly

An appreciation of normal development must underpin the assessment of any child. Developmental regression must always be taken as a significant finding.

Lack of clear evidence of normality may need to be taken as a reason for escalating the suspicion of severe illness.

Repeat presentation with similar symptoms

Repeat presentation to the GP or to secondary care is common in patients who are ultimately found to have cancer [11]. Lack of a common record may obscure the frequency of this.

Each parent should be asked for the number of occasions that they have sought healthcare advice, including NHS111, primary and secondary care.

The diagnostic pathway is likely to be more streamlined if investigations are undertaken following referral, but there are situations in which initial investigations, such as full blood count, radiographs or ultrasounds, might appropriately be arranged from primary care, as detailed in the following sections.

Signs and symptoms of childhood cancer

Leukaemia and lymphoma

Leukaemia

Childhood leukaemia usually presents with a combination of symptoms and signs resulting from bone marrow failure and/or manifestations of extramedullary disease [12]. They include:

- Hepatosplenomegaly
- Pallor
- Unexplained fever
- Spontaneous bruising
- Recurrent/persistent infection
- Persistent and worsening fatigue
- Petechiae
- Unexplained bleeding
- Persistent and unexplained arthralgia (bone pain) and/or limp
- Any of the features of non-Hodgkin lymphoma, listed below

Non-Hodgkin lymphoma (NHL)

NHL is aggressive and rapidly growing. Typical presentation may include:

- Lymphadenopathy, particularly cervical (however, most cervical lymphadenopathy does not have a malignant cause) and/or splenomegaly
- Abdominal distension/swelling
- Breathlessness (suggestive of airway obstruction) - not explained by known respiratory disease history
- Distended veins/venous congestion of upper chest, face, head (secondary to SVC obstruction)
- Night sweats, fever, pruritus and weight loss
- NHL may also present with spinal cord compression or with other symptoms of CNS involvement

Hodgkin lymphoma

- Progressive enlargement of lymph nodes, often over many weeks or even months; typically cervical, axillary and supraclavicular site
- Drenching night sweats
- Unexplained weight loss
- Pruritus
- Fever
- Breathlessness (suggestive of airway obstruction)
- Alcohol induced lymph node pain

Investigations and referral

An unwell child with symptoms consistent with leukaemia or lymphoma needs immediate (same day) referral to hospital by telephone. Well children with a single sign/symptom of leukaemia described above should be offered a very urgent FBC (48hrs).

Mediastinal masses in children and young people

- Mediastinal masses may be the presenting feature of lymphoma, leukaemia and rarely other malignancies such as neuroblastoma, germ cell tumour or sarcoma.
- Clinical presentation includes airway obstruction which may mimic signs of asthma or croup.
- Steroids are essential for treatment of acute lymphoblastic leukaemia and lymphoma. Steroids used to treat presumed asthma or croup will often improve symptoms of lymphoma, but may adversely affect outcome. This is because pre-treatment of lymphoma/leukaemia with steroids could mask the diagnosis, and, lead to tumour lysis syndrome and renal failure, or compromise definitive diagnosis and treatment.
- Chest radiograph to exclude a mediastinal mass should be considered in a child with apparent wheeze where the history is atypical. For example:
 - Increased shortness of breath lying flat,
 - Facial swelling or other concerning features.
 - Lack of atopic history,
 - No previous wheezy episodes,

Where this is the case, a same day chest radiograph should be arranged and reviewed prior to commencement of oral steroids.

Lymphadenopathy in childhood

Enlarged lymph nodes are common and usually the result of infective or inflammatory processes. Concern regarding possible malignancy warrants careful assessment, but indiscriminate referral may lead to unnecessary anxiety.

Lymph nodes <2 cm in diameter and those which are reducing or fluctuating in size are unlikely to be associated with malignancy in the absence of other suspicious features. Tender or painful nodes are usually related to infection.

In children where a single lymph node is greater than 2cm in diameter, any of following additional features may prompt referral to a paediatrician:

- Absence of a clear infectious cause
- Persistence of significantly enlarged nodes (>2cms diameter) for 6 weeks or more with no decrease in size
- Widespread distribution
- Abnormal consistency (firm or hard) or non-mobile
- Absence of pain

Features which should prompt referral regardless of lymph node size would include:

- Supraclavicular site
- Associated splenomegaly, night sweats or weight loss
- Bone pain/limp
- Presence of mediastinal widening on chest radiograph (see 'Mediastinal masses')

Brain and Spinal tumours

Headsmart (www.headsmart.org.uk) is a valuable resource which summarises potential presenting features of primary central nervous system (CNS) tumours. Presentation may vary according to age [13].

Infants (<5 years)

- Persistent or recurrent vomiting
- Balance, coordination or walking problems
- Abnormal eye movements or suspected loss of vision
- Behaviour change or lethargy
- Afebrile seizures
- Head tilt
- Increasing head circumference crossing centiles

Children (5-11years)

- Persistent or recurrent headache
- Balance, coordination or walking problems
- Persistent or recurrent vomiting
- Abnormal eye movements
- Blurred vision or loss of vision
- New onset squint
- Behaviour change
- Seizures
- Head tilt

Teenagers (12-18years)

- Persistent or recurrent vomiting
- Persistent or recurrent headache
- Abnormal eye movements
- Blurred vision or loss of vision
- New onset squint
- Balance, coordination or walking problems
- Behaviour change
- Seizures
- Delayed or arrested puberty

Additional symptoms to consider (any age):

- Reduced consciousness
- Polyuria or polydipsia
- Failure to thrive or abnormal growth
- A new squint which does not correct with correction of refraction, and any paralytic squint, is a strong indicator of a brain tumour and the patient must be referred immediately by telephone

Spinal cord compression

Spinal cord compression (SCC) is a severe, often irreversible complication of intraspinal or paraspinal pathology. It greatly increases the morbidity for any patient, regardless of their underlying illness. It is rare in the paediatric population, but NOT rare in children with cancer. Back pain in a child must be met with a high index of suspicion.

Symptoms which suggest SCC

- Back pain
- Change of sensation
- Bladder or bowel dysfunction
- Weakness

Signs which suggest SCC

- Sensory change in the back, arms or legs
- Sensory loss
- Loss or increase of deep tendon and abdominal reflexes
- Motor loss.
- Scoliosis associated with pain (idiopathic scoliosis is rarely painful)

Look for

- Weakness
- Altered gait
- Altered coordination
- Local tenderness along the spine.
- Scoliosis

Neurological changes may not correspond precisely to dermatomes. Unusual neurological changes must be taken seriously.

A patient presenting with symptoms and/or signs of SCC must be investigated and treated without delay.

The urgency for investigation is increased if any neurological deficit is identified: irreversible paraplegia may develop rapidly unless decompression is achieved.

Neuroblastoma

Neuroblastoma presentation depends on age and dissemination of tumour. Symptoms and signs may include the following:

- Palpable abdominal mass
- Unexplained neurological symptoms, suggestive of spinal cord compression [see separate section]
- Hypertension
- Periorbital bruising
- Horner's syndrome
- Skin lesions in infants ('blueberry muffin' appearance)
- Unexplained systemic symptoms, including
 - bone pain
 - pallor
 - bruising
 - fever
 - fatigue
 - irritability
 - lymphadenopathy

Renal tumours

Renal tumours typically present with abdominal distension in a well child. Careful clinical examination of the abdomen is critical to help differentiate from constipation.

Consider in the presence of:

- Palpable abdominal mass \pm pain
- Frank haematuria
- Hypertension
- Persistent microscopic haematuria
- Associated fever

Wilms' tumour may be associated with underlying genetic conditions, particularly overgrowth syndromes and hemihypertrophy.

Soft tissue sarcoma (STS)

These are most commonly rhabdomyosarcoma in children and present as a mass, leading to symptoms according to affected site. Children with an unexplained enlarging mass, or a soft tissue mass should be urgently referred to paediatrics (2 weeks). However, in the interim, a very urgent direct access ultrasound scan to be performed within 48 hours could be considered. However, this should not delay referral to paediatrics.

Commonly affected sites include:

- Limbs
- Thorax
- Intra-abdominal (retroperitoneal, bladder/prostate)
- Para-testicular
- Naso-oro-facial

Symptoms and signs may therefore include:

- Persistent soft tissue mass anywhere on the body - usually firm/hard, tethered, deep to the fascia, non-tender, increasing in size
- Proptosis
- Persistent/recurrent bloody/purulent discharge or obstruction from ear/nose
- Urinary retention
- Scrotal swelling
- Enlargement of draining lymph nodes
- Blood-stained vaginal discharge
- Back pain, lower limb pain or weakness (see spinal cord compression)
- Weight loss associated with any of the above symptoms

Bone tumours

Bone tumours are commonly associated with substantial delays in diagnosis. Many patients will remember a minor trauma, after which the swelling developed: this may provide false reassurance of the cause. Bone tumours can also be associated with systemic symptoms, such as malaise and fever. Refer children or young people with:

- Rest pain
- Back pain
- Unexplained limp
- Persistent localised bone pain and/or swelling

Children with persistent localised bone pain and/or swelling should be referred very urgently (48hrs). A parallel very urgent direct access X-ray could also be considered (48hrs) but this should not delay referral. Radiograph findings suggestive of cancer should be immediately referred to an acute paediatric consultant or paediatric oncologist.

Liver tumours

Many children diagnosed with a liver tumour have few symptoms at diagnosis other than a mass. However, presenting features include:

- Hepatomegaly
- Abdominal pain
- Systemic symptoms, such as fever, fatigue and loss of appetite
- Rarely, jaundice

Germ cell tumours

Germ cell tumours present at a variety of different sites, mainly gonadal and midline, including:

- Testis (with or without pain)
- Ovary (abdominal mass with or without pain)
- Midline retroperitoneal
- Mediastinum (see also lymphoma)
- Central nervous system
- Sacrococcygeal region (infants and young children)

In addition, may present with:

- Gynaecomastia
- Virilisation
- Precocious puberty

The histiocytoses: LCH and HLH

Langerhans cell histiocytosis (LCH)

This is a rare condition which may present at single or multiple sites and involve single or multiple organ systems.

Presenting features vary according to site of disease. This may involve bone and soft tissues, skin, lungs, lymph nodes (see section on lymphadenopathy), liver and spleen, gastrointestinal tract and CNS. Non-specific symptoms such as fever and weight loss are sometimes seen.

Particular symptoms of note which are more specific for LCH and might not otherwise necessarily trigger urgent tertiary referral, include bone, skin and CNS (posterior pituitary) manifestations:

Bone

- Pain and local swelling
- Lesions may be single or multiple
- Lytic lesion on plain X-ray

Skin

- Unusual rash (unexplained and persistent/fluctuant)
- 'Eczema' unresponsive to treatment
- Cradle cap (severe/persistent)
- Otorrhoea (persistent/recurrent otitis externa)
- Anal excoriation

Posterior pituitary

- Polydipsia/polyuria

Haemophagocytic lymphohistiocytosis (HLH)

This is a rare systemic disorder. Typically, the child is unwell at presentation and requires an immediate referral by telephone to arrange same day assessment.

Typical clinical features include:

- Fever
- Splenomegaly
- Pallor
- Fatigue
- Bruising/bleeding

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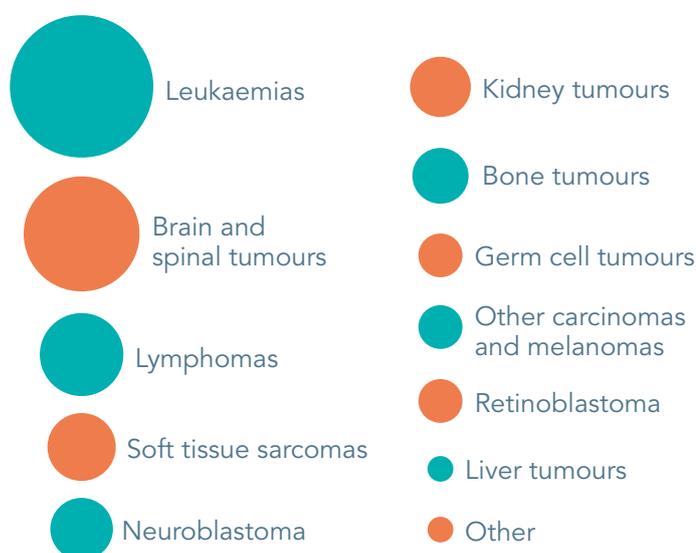
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Childhood cancer facts

Children's cancers in the UK

Proportion of all children's cancer cases by cancer group

● ● Larger circles indicate more UK cancer cases



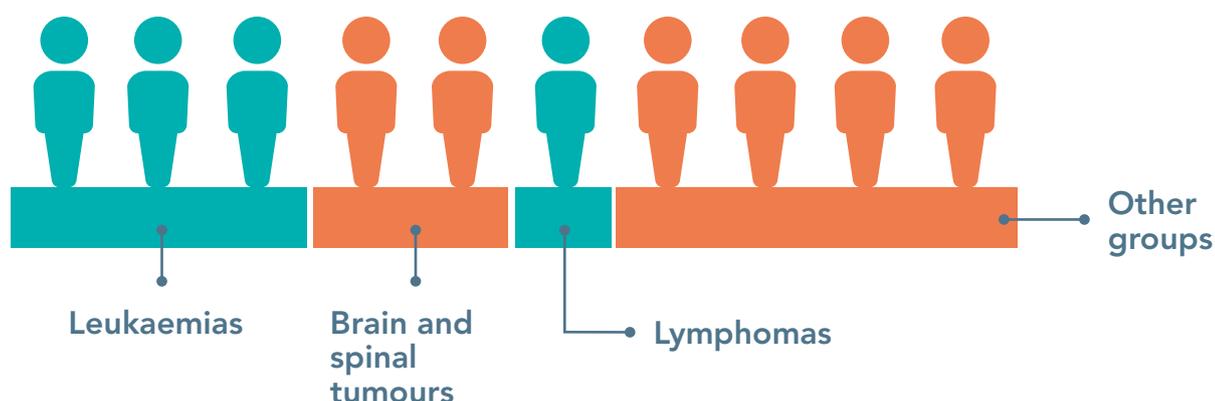
Around
1,900
cases of cancer
in children
every year

Peak incidence
rate is

0-4
years old

Most common children's cancers

The 76 types of children's cancer can be put into 12 groups, and some groups are more common than others. The most common groups in the UK are:



Figures jointly produced with CRUK.

Appendix

Table of findings that may be associated with a cancer diagnosis in childhood.

Symptoms and signs which require referral have been suggested in the table below. However, there are many occasions when it is instead a pattern of symptoms and signs that point towards a diagnosis of cancer. Individual features alone are too imprecise. Additionally, children often cannot express symptoms clearly, and for this reason, the level of suspicion must necessarily be kept high. Telephone discussion with a paediatrician in cases where the need or timescale for referral is unclear is highly recommended.

GREEN: Reassuring features - consider watchful wait.

AMBER: Concerning features - consider referral or discussion with paediatrician.

RED: High-risk features - requires referral:

- Urgent referral (2 week wait)
- Very urgent referral (48 hours) e.g. paediatric rapid access clinic or acute paediatric service according to local service arrangements
- Immediate referral (telephone referral within a few hours) to acute paediatric service

	CONSIDER WATCHFUL WAIT	CONSIDER REFERRAL	REQUIRES REFERRAL	
Ear, Nose and Throat		<ul style="list-style-type: none"> • Otorrhoea (persistent/recurrent otitis externa) • Persistent/recurrent bloody/purulent discharge from ear/nose • Obstruction of ear/nose 	<ul style="list-style-type: none"> • Swallowing difficulties (in absence of local cause) 	Very urgent referral (48hrs)
			<ul style="list-style-type: none"> • Abnormal mass within the nasopharyngeal space 	Immediate referral
Endocrine		<ul style="list-style-type: none"> • Polyuria/polydipsia • Delayed/arrested puberty • Abnormal growth 	<ul style="list-style-type: none"> • Precocious puberty • Galactorrhoea 	Urgent referral
Gastrointestinal		<ul style="list-style-type: none"> • Constipation not responsive to simple laxatives in appropriate dosage • Abdominal distension 	<ul style="list-style-type: none"> • Persistent vomiting on awakening 	Needs referral: urgency depends on length of history and associated symptoms/signs
			<ul style="list-style-type: none"> • Unexplained palpable abdominal mass 	Needs an urgent referral, and in many cases immediate referral if symptoms such as pain, hypertension, reduced urine output, rapid increase in size
			<ul style="list-style-type: none"> • Unexplained hepatomegaly 	Immediate referral
Haematology		<ul style="list-style-type: none"> • Localised petechiae/bruising (unexplained) • Bleeding (unexplained) • Pallor • Fatigue (persistent) • Infection (recurrent, persistent or unexplained) • Generalised lymphadenopathy • Generalised bone pain (All should be offered a very urgent FBC and referral to paediatrics considered. Some children with these symptoms will need immediate referral) 	<ul style="list-style-type: none"> • Splenomegaly - either in isolation or in association with night sweats, weight loss, pruritus or fever 	Very urgent referral
			<ul style="list-style-type: none"> • Widespread petechiae/bruising 	Immediate referral

	CONSIDER WATCHFUL WAIT	CONSIDER REFERRAL	REQUIRES REFERRAL	
Lymphadenopathy	<ul style="list-style-type: none"> • Clear infectious cause • <2cm • Responsive to antibiotics 	<ul style="list-style-type: none"> • Widespread distribution (offer very urgent FBC) • Abnormal consistency (firm or hard) • Non-mobile • Absence of pain 	<ul style="list-style-type: none"> • Persistent enlarged nodes >2cms for >6 weeks with no decrease in size • Supraclavicular site 	Urgent referral
			<ul style="list-style-type: none"> • Associated splenomegaly, night sweats, weight loss or pruritus 	Very urgent referral (48hrs)
			<ul style="list-style-type: none"> • Symptoms/signs of mediastinal mass • Associated bone pain 	Immediate referral
Musculoskeletal	<ul style="list-style-type: none"> • Night pain • Back pain • Pain limiting activities • Pain at rest • Unexplained or persistent generalised bone pain (offer very urgent FBC) 	<ul style="list-style-type: none"> • Unexplained enlarging mass • Soft tissue mass with local lymphadenopathy • Localised unexplained bone pain (consider very urgent x-ray alongside referral) • Ultrasound scan of a mass suggests soft tissue sarcoma or is uncertain and clinical concern persists • X-ray suggests the possibility of bone sarcoma 	<ul style="list-style-type: none"> • Limp with fever • Painful scoliosis 	Urgent referral
			<ul style="list-style-type: none"> • Immediate referral 	Immediate referral
Neurology	<ul style="list-style-type: none"> • Headache with vomiting • Behaviour or personality change • Reducing school performance 	<ul style="list-style-type: none"> • Afebrile seizures • Increasing head circumference across centiles • Headache worse in the morning or waking from sleep • Persistent headache in a child <4years • Abnormal gait • Abnormal coordination • Confusion or disorientation occurring with headache • New bladder or bowel dysfunction • Development regression • Focal motor or sensory abnormalities • Abnormal head position, such as wry neck, head tilt, or stiff neck 	<ul style="list-style-type: none"> • Urgent referral 	Urgent referral
			<ul style="list-style-type: none"> • Very urgent referral (48hrs) 	Very urgent referral (48hrs)
			<ul style="list-style-type: none"> • Immediate referral 	Immediate referral
Ophthalmology		<ul style="list-style-type: none"> • Absent red reflex • Proptosis • Abnormal eye movements • Blurred/double vision • Papilloedema • New onset paralytic (non-concomitant) squint 	<ul style="list-style-type: none"> • Urgent referral, but in infants very urgent referral (48hrs) appropriate 	Urgent referral, but in infants very urgent referral (48hrs) appropriate
			<ul style="list-style-type: none"> • Very urgent referral (48hrs) to ophthalmology and/or paediatrics 	Very urgent referral (48hrs) to ophthalmology and/or paediatrics
			<ul style="list-style-type: none"> • Immediate referral 	Immediate referral
Renal		<ul style="list-style-type: none"> • Persistent unexplained microscopic haematuria • Hypertension (>95th centile, or for children aged 13 and over, >130/80). Severe hypertension needs immediate referral – see below. • Frank haematuria • Severe hypertension (>95th centile +12mmHg or >140/90 – whichever is lower) 	<ul style="list-style-type: none"> • Urgent referral 	Urgent referral
			<ul style="list-style-type: none"> • Very urgent referral, but consider immediate referral if in association with abdominal mass, hypertension, abnormal renal function or other clinical concerns 	Very urgent referral, but consider immediate referral if in association with abdominal mass, hypertension, abnormal renal function or other clinical concerns
Respiratory	<ul style="list-style-type: none"> • New/changed wheeze/stridor in absence of typical history for asthma/viral induced wheeze 	<ul style="list-style-type: none"> • New wheeze/stridor with orthopnoea • Difficulty breathing with facial swelling • Mediastinal widening on chest radiograph 	<ul style="list-style-type: none"> • Immediate referral 	Immediate referral
Miscellaneous	<ul style="list-style-type: none"> • Genetic cancer predisposition syndromes • Strong family history of malignancy • Repeated presentation to health professionals • Severe or persistent cradle cap • Unexplained weight loss • Abnormal growth • Blood-stained vaginal discharge • Persistent parental/patient concern or anxiety about symptoms, even if the symptoms are most likely to have a benign cause 	<ul style="list-style-type: none"> • Testicular mass 	<ul style="list-style-type: none"> • Very urgent referral (48hrs) 	Very urgent referral (48hrs)



Children's Cancer and Leukaemia Group (CCLG) is a leading national charity and expert voice for all childhood cancers.

Each week in the UK and Ireland, more than 30 children are diagnosed with cancer. Our network of dedicated professional members work together in treatment, care and research to help shape a future where all children with cancer survive and live happy, healthy and independent lives.

We fund and support innovative world-class research and collaborate, both nationally and internationally, to drive forward improvements in childhood cancer. Our award-winning information resources help lessen the anxiety, stress and loneliness commonly felt by families, giving support throughout the cancer journey.

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