



Uganda Cancer Institute

REFERRAL GUIDELINES FOR SUSPECTED CANCER

AUGUST 2016

Ugandan Cancer Institute

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SECTION ONE

1.0 INTRODUCTION

1.1 Cancer in Uganda

Cancer is on the rise in Uganda, the cause of this trend is multi-factorial ranging from environmental agents, lifestyle, infection and the HIV epidemic. There are more than 60,000 cases of cancer per year in the country, of which 25,000 are incident cases. Each year about 22, 000 deaths occur in Uganda due to cancer. In addition, the risk of cancer before the age of 65 years is 10%, and in the next five years it is estimated that there will be 80,000 cancer cases in the country at any one time. These alarming trends are also observed at the Uganda Cancer Institute.

Nearly 80 percent of patients presenting to the Uganda Cancer Institute present with advanced disease at diagnosis, hence limited interventions to prolong survival. For all the common cancers, over 50% patients present with distant metastases. This indicates the level of knowledge in the general public and their perception of cancer, its symptoms, where to access treatment and the care given by the general practitioners is lacking.

Late diagnosis of cancer contributes to poor survival among cancer patients 1. This guideline is the first of the type to address referral of suspected cancer in Uganda. It is based on the experience and evidence available at the Uganda Cancer Institute. It takes into consideration the needs of the patient, caretakers and the medical practitioners.

Presently, Uganda is in the process of developing and implementing a National Cancer Control Program. This program refers to an integrated and coordinated approach to reducing cancer incidence, morbidity, and mortality across the cancer control continuum from primary prevention to end-of-life care. A networks-based approach is being advocated in the country by integrating communities and facilities with increasing level of sophistication and personnel to function as an integrated system serviced by a cancer care pathway linking the primary care services to the established regional and National cancer care centres as a conduit through which patient traffic can flow back and forth; this is the essence of this guideline.

1.2 Purpose of the guidelines

Following concerns about poor cancer outcomes linked to late presentation of patients with cancer, the UCI is laying emphasis on the need to develop clinical practice guidelines for smooth referral of suspected cancer patients in Uganda. To support this guideline, the UCI has already changed the admission criteria from histologically confirmed diagnosis of cancer to suspected cancer. This is the first edition of guidelines for referral of suspected cancer in Uganda, with the purpose of facilitating clinicians in clinical decision making and practice when approached by a patient with suspected cancer.

Developing guidelines is an important recommendation for the establishment of better cancer care. The referral process forms an important part of cancer care especially in Uganda where most patients present with advanced stage at cancer diagnosis. This guideline will help the general practitioners to refer suspected cancer patients promptly to Uganda Cancer institute

1.3 Development of the guidelines

The steering committee set-up by the director of the Uganda cancer institute decided to develop guidelines for referral of patients with suspected cancer using three approaches: i) conducting a literature review, ii) reviewing evidence-based clinical practices using results of audits of management of patients presenting with cancer at the Uganda Cancer institute; and iii) consensus among clinicians involved in cancer care at the Uganda cancer institute.

The guidelines have been developed with close reference to the National Health Services (NHS) - National Institute for Health and Clinical Excellence (NICE)2 Referral guidelines for suspected cancer, and the National Comprehensive Cancer Network (NCCN) guidelines.

This guideline entails the best practice advice on referral for suspected cancer in adults and children in Uganda, especially to the Uganda Cancer Institute. The referring clinicians should engage the patient and the caretakers in the referral process, discussing the referral point and expectations.

1.4 Types of Referrals

A. Emergent referral

Refers to an acute admission or referral occurring within a few hours, or even more quickly if necessary

B. Urgent Referral

Refers to an admission or referral where the patient is seen within days to two weeks

C. Non-urgent Referral

This category refers to all other referrals where the patient will be seen within two to six weeks from the time of referral.

1.5 Referral process

a) Making a diagnosis

The diagnosis of any cancer on clinical grounds alone is very difficult. Generally, the medical practitioner attending to any patient should screen for particular symptoms and signs suggestive of particular cancers. These symptoms are at times collectively referred to as "alarm symptoms" or "danger signs". The medical practitioner will conduct a complete clinical examination and thorough history, and refer urgently if cancer is suspected. The primary healthcare provider should be willing to consult a colleague from the UCI to ease the interpretation of particular symptoms and signs when appropriate.

b) **Investigations**

Whenever the symptoms and signs are highly suggestive of cancer, the referral should not be delayed by additional investigations.

However, in patients with less typical symptoms and signs, investigations are necessary prior appropriate referral.

In case specific investigations are not readily available locally, an urgent specialist referral

should be made.

c) Patient support and information

When referring a patient with suspected cancer to UCI, the primary healthcare professional should assess the patient's need for continuing support while in transition. Appropriate information must be given to patients, family and/or carers by the primary healthcare professional. This should cover issues such as:

- Place of referral
- Source of further information and support
- Responsible specialist

1.6 Review of the guidelines

Cancer management is constantly changing as new evidence emerges. For this reason, a guideline working group and expert advisory committee will be charged with updating the guidelines every five years.





SECTION TWO

2.0 Referral guidelines

2.1 Cancer in HIV patients

2.11 Cervical cancer

Cervical cancer is the third most common cancer in women worldwide & the most common cancer in Uganda. For a woman with suspected cancer of the cervix, the first symptom is an alteration in the menstrual cycle, intermenstrual bleeding, postcoital bleeding, postmenopausal bleeding or vaginal discharge. When a patient presents with any of these symptoms, the primary healthcare professional should undertake a full pelvic examination, including speculum examination of the cervix. In patients found on examination of the cervix to have clinical features that raise the suspicion of cervical cancer, an urgent referral should be made.

Risk factors

- Persistent HPV infection: High risk in patients with early age at coitarche, multiple sexual partners, high risk sexual partners, history of STDs (including genital warts);
- High parity;
- Tobacco smoking
- Oral contraceptive use
- Chronic immunosuppression (e.g. HIV);
- Low socioeconomic status

Investigations

The following investigations can be initiated or documented on the referral note.

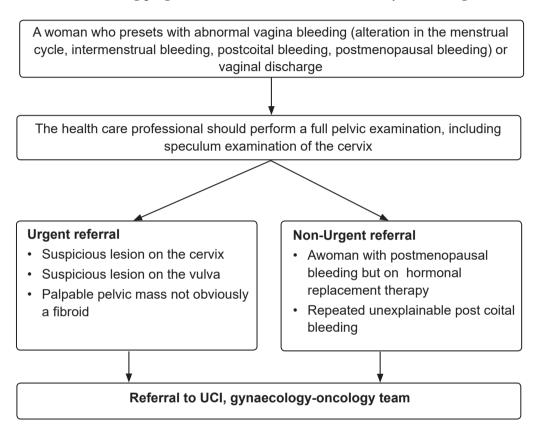
- Cervical PAP smear results
- Pelvic ultrasound scan findings

Table 1: Referral guideline for suspected cancer of the cervix

Cervical cancer urgent referral (appointment within two weeks)	
A woman who presents with persistent intermenstral bleeding	
Any woman with a palpable abdominal or pelvic mass on examination that is not obviously uterine fibroids or not of gastrointestinal or urological origin	
Cervical cancer non-urgent referral	
A woman with post menopausal bleeding but not on hormonal replacement therapy	
Repeated unexplained post-coital bleeding	

Clinical pearls

- A Pap smear test is not required before referral of a woman with suspected cancer of the cervix, and a previous negative result should not delay referral.
- A woman presenting with persistent abnormal vaginal bleeding should be referred to a gynecology-oncology specialist for further evaluation
- A woman presenting with symptoms suggestive of cervical cancer who has not fully participated in a cervical screening programme should be referred immediately for investigation







2.12 Kaposi's sarcoma

Kaposi's sarcoma (KS) is a multifocal angioproliferative disorder of vascular endothelium, primarily affecting mucocutaneous tissues with the potential to involve viscera³. To date, there are four clinical variants of Kaposi's sarcoma; classic, endemic, iatrogenic and epidemic KS⁴; and each has a distinct natural history, site of predilection and prognosis⁵. Currently KS is the second commonest cancer among HIV patients and it is the third commonest cancer seen in either men or women in Uganda.⁶ The oral cavity is the first clinical site of disease in 22% of patients with KS^{5,7-9} and up to 71% of HIV patients may have concurrent cutaneous and visceral involvement^{5,7}.

Risk factors

- HIV infection
- Low social economic status

Investigations

The following investigations can be requested upon referral of patients with suspected Kaposi's sarcoma

- Complete blood count
- Liver-, and renal-function tests
- Fecal occult blood
- Chest x-ray
- Abdomen ultrasound scan
- CD4 T-cell counts

Table 2: Referral guideline for suspected Epidemic Kaposi's sarcoma

Epidemic Kaposi's sarcoma urgent referral (appointment within two weeks)	
Visceral Kaposi's presenting as pulmonary Kaposi's sarcoma or gastrointestinal Kaposi's sarcoma	
Kaposi's sarcoma immune reconstitution inflammatory syndrome (IRIS)	
Severe anemia	
Epidemic Kaposi's sarcoma non-urgent referral	
Epidemic Kaposi's sarcoma not responding to ART	
Lymphedema suspected of Kaposi's sarcoma	

2.13 AIDS associated lymphomas

HIV / AIDS is associated with a greater risk of development of lymphomas as compared to the general population¹⁰. The occurrence of lymphoma in the setting of HIV infection represented advanced stage of immunosuppression referred to as AIDS and hence the term, AIDS associated lymphomas. The AIDS associated Lymphoma has been associated with up to 16% of all deaths due to the pandemic ¹¹.

Patients with ARL present with advanced stage at diagnosis; frequently with extra nodal disease (70-97%), and central nervous system (20 - 40%) involvement as compared to the HIV negative population^{12,13}. The rate of lymphoma complications like tumour Lysis syndrome, bone marrow disease and ENT involvement is very high¹⁴.

Risk factors

- Advanced immunosuppression
- EBV infection
- High HIV1/2 viral load

Investigations

- Complete blood count
- Liver-, and renal-function tests
- Chest x-ray
- Abdomen ultrasound scan
- CD4 T-cell counts

Table 3: Referral guideline for AIDS related Lymphoma

AIDS related lymphoma urgent referral (appointment within two weeks)	
Stridor/ upper airway obstruction	
Central nervous system involvement	
Spinal cord compression	
Severe anemia	
Head and neck involvement	

2.2 Cancer in Children and Young people

2.20 Burkitt's Lymphoma

Burkitts lymphoma is a highly aggressive B-cell NHL characterized by Myc translocation [t (8; 14) (q24; q32) in 85% or variants]. Three distinct clinical forms have been described: Endemic, sporadic, immunodeficiency-associated.

- A. Endemic: Primarily in equatorial Africa (30–50% of childhood cancer), male: female,
- B. 2:1, strongly associated with EBV infection
- C. Sporadic (non-endemic): Occurs in US, Western Europe, affects 30% of pediatric lymphoma (peak age 11), accounts for <1% of adult NHL (peak age 30), with a male: female, 4:1
- D. Immunodeficiency-associated: HIV positive patients, usually CD4 count >200, incidence not impacted by HAART



2.21 Neuroblastomas

The clinical presentation of neuroblastoma may mimic that of acute lymphoblastic leukemia. Most children have symptoms of metastatic disease which may be general in nature (persistent or unexplained bone pain (X-ray also needed) / pallor / fatigue / unexplained irritability / unexplained fever / persistent or recurrent upper respiratory tract infections / generalised lympadenopathy / unexplained bruising).

Table 4: Referral guideline for suspected Neuroblastoma

Neuroblastoma urgent referral	
Proptosis	
Unexplained back pain	
Leg weakness	
Unexplained urinary retention	
Unexplained skin nodules	

Clinical pearls

- A child or young person with any infection that does not resolve as expected should have a complete blood count
- A child presenting with a new squint should be referred urgently to a specialist
- A pre-school child whose caregiver reports a significant reduction in the child's sight should be referred urgently to an ophthalmologist

Investigations

For children with suspected neuroblastoma, the following investigations may be ordered before referral

- Complete blood count (CBC)
- Plain x-ray
- Urine catecholamines
- Alpha feto protein (AFP) germ cell tumours
- Beta human chorionic gonadotropin
- Biopsy of the tumour mass
- Fine needle aspirate (FNA)
- Abdominal examination (± arrange abdomen Ultrasound scan)

2.22 Retinoblastoma

Retinoblastoma affects children mostly under age 2 years, and presents with a white pupillary reflex (leukocoria) noted by the parents, identified in photographs or found on examination.

Table 5: Referral guideline for suspected Retinoblastoma

Retinoblastoma urgent referral	
white pupillary reflex (attend to parental observations)	
new squint or change in visual acuity (and cancer considered)	
Family history of retinoblastoma and visual problems (screening after birth recommended).	
noticing an odd appearance in their child's eye	
A child with a new squint or change in visual acuity	
A family history of retinoblastoma in a child with visual problems	

2.23 Wilm's tumour

Wilm's' tumour most commonly presents with a painless abdominal mass.

Table 6: Referral guideline for suspected Wilm's tumour

Wilm's tumour urgent referral	
A child with persistent or progressive abdominal distention	
Abdominal ultrasound suggestive of a renal mass in a child	
Haematuria in a child or young person	

Clinical pearls

A child or young person with haematuria should have a midstream specimen of urine, renal ultrasound and blood pressure measured

2.24 Leukemia

A child or young person should have a complete blood count and blood film if they have one or more of the following symptoms or signs unexplained convincingly by another illness:

- Persistent or increasing pallor
- Sustained fatigue
- Continuing unexplained irritability
- Fever
- Any infection that does not resolve as expected
- Generalized lympadenopathy
- Persistent or unexplained bone pain
- Unexplained bruising

Clinical pearl

An immediate referral to a specialist should be made if the blood film and complete blood count indicate features of acute leukaemia.



2.25 lymphoma

A child or young person should be referred immediately to a specialist if they have shortness of breath in association with:

- Non-tender, firm or hard lymph nodes
- Lymph nodes greater than 2 cm in size
- Progressively enlarging lymph nodes
- Other features of general ill-health, fever or weight loss
- Axillary node involvement (in the absence of local infection or dermatitis)
- Supraclavicular node involvement

2.3 Breast cancer

Breast cancer, the most common cancer in SSA with nearly 100,000 persons diagnosed in 2012, is characterized by poor survival with less than half of women diagnosed with the disease alive at five years in most countries and remains the second leading cause of cancer death in SSA. 15-17

Breast cancer affects women and men of all ages, therefore all women should be encouraged to undertake regular self breast exam and clinical breast examination at a nearby health unit. Often the first symptom is a lump palpable in the breast; however not all patients referred with a breast lump will end up with a diagnosis of breast cancer. Therefore the clinician attending to a woman with suspected breast cancer should convey hope and give adequate information regarding the diagnostic steps for a breast lump.

Risk factors

- Personal history of breast cancer
- Presence of specific precursor lesions (atypical ductal carcinoma, lobular carcinoma, ductal carcinoma in situ)
- Increased breast density
- Increased age at birth of first child
- Treatment with hormone replacement therapy
- Family history of breast cancer
- Family history of ovarian cancer
- Tobacco smoking
- Alcohol consumption

Investigations

- Mammography (not as a screening test)
- Ultrasound
- Cytology of nipple discharge
- Fine needle aspirate (FNA)
- Cancer antigen 15-3.



Table 7: Referral guideline for suspected Breast cancer

Breast cancer urgent referral (appointment within two weeks)

The following may require urgent referral:

- Female, any age, with a breast lump: discrete, hard lump with fixation, +/- skin tethering
 - Female >30years with
 - a. A breast lump: discrete lump that persists after next period, or presents after menopause
 - b. Asymmetric nodularity
 - Female < 30 years
 - a. a lump that enlarges, is fixed and hard
 - b. in whom there are other reasons for concern such as family history
- Male aged >50 years with a palpable unilateral swelling, firm subareolar mass +/nipple distortion/ skin changes
- Presenting with spontaneous unilateral bloody nipple discharge,
- Previous breast cancer, who present with a further lump or suspicious symptoms
- Unilateral eczematous skin or nipple change that does not respond to topical treatment
 - a. nipple distortion of recent onset
 - b. spontaneous unilateral bloody nipple discharge

Breast cancer non-urgent referral

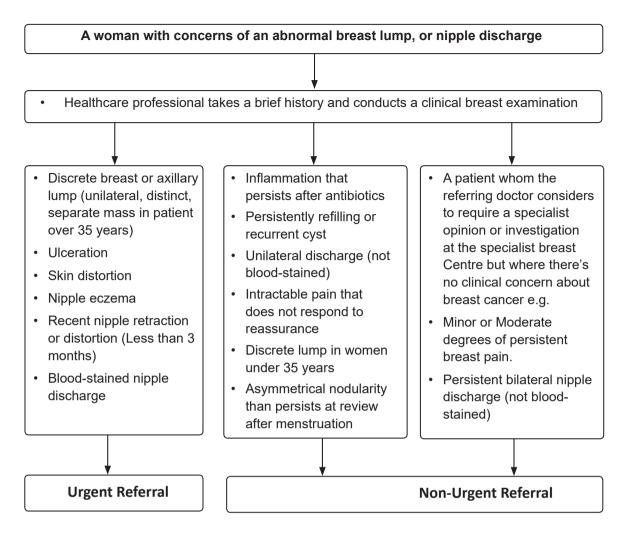
- Women younger than 30 years with a lump
- Patients with breast pain and no palpable abnormality, when initial treatment fails and/or with unexplained persistent symptoms.

Clinical pearls

- An adult man with a unilateral, firm subareaolar mass should be referred to a specialist for further evaluation.
- For a person presenting with symptoms and/or signs suggestive of breast cancer, investigation may be
- instigated by the practitioner, but should not delay referral to a specialist
- A woman under 30 years of age presenting with generalised lumpiness in the breast tissue, where a focal area of concern, unchanged following a menstrual period, is identified, should be referred to a specialist. If a woman has a family history of premature breast cancer an earlier referral for investigation should be considered







2.4 Upper Gastrointestinal cancer

2.41 Oesophageal cancer

Esophageal cancer is fourth commonest cancer in Uganda and the third commonest cancer among men in Uganda. The primary symptom of esophageal cancer is progressive dysphagia leading to anorexia and progressive weight loss. The commonest histology is squamous cell carcinoma in approximately 85% patients and about 15% have adenocarcinoma.

Risk factors

- Tobacco smoking
- Alcohol consumption
- Achalasia
- Esophageal webs
- Obesity
- Barrett esophagus
- Increasing age



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- Male gender
- Long-standing GERD

An urgent referral for endoscopy or to a GI oncologist should be made for patients of any age with dyspepsia who present with any of the following:

- o chronic gastrointestinal bleeding
- dysphagia
- progressive unintentional weight loss
- persistent vomiting
- iron deficiency anaemia
- epigastric mass
- Suspicious barium meal result.

Table 8: Referral guideline for suspected Oesophageal cancer

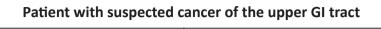
Oesophageal cancer urgent referral	
o Unexplained and persistent recent onset dyspepsia alone, in a patient > 55 years.	
o presenting with dysphagia (interference with the swallowing mechanism that occurs within 5 seconds of having commenced the swallowing process)	
o Unexplained weight loss or iron deficiency anaemia	
Persistent vomiting and weight loss in the absence of dyspepsia	
 Unexplained upper abdominal pain and weight loss, with or without back pain, or an upper abdominal mass without dyspepsia. 	
obstructive jaundice	

Clinical pearl

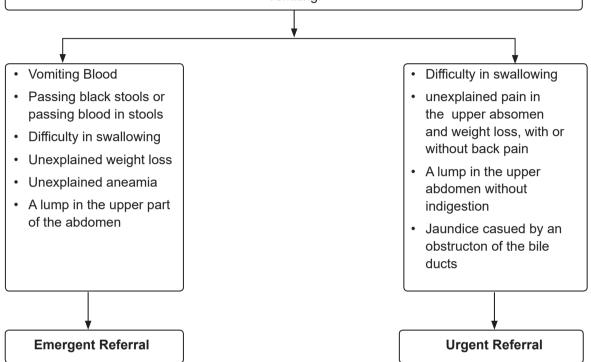
- Endoscopic investigation of dyspepsia is not necessary in the absence of alarm symptoms
- Helicobacter pylori status should not affect the decision to refer for suspected cancer.







Suspect upper GI cancer in a patient with dyspepsia, hematamesis, weight loss, melena, upper abdominal pain, Jaundice, dyspepsia unresponsive to treatment, family history of upper GU cancers, pernicious aneamia, mass on abodominal scan, history of peptic ulcer disease, history of Barrett's oesophagus, history of surgery of peptic ulcers, cervical adenopathy, hepatomegaly, vomiting.



2.42 Gastric cancer

Gastric cancer is the fifth leading cause of cancer among men in Uganda. The most affected site of the stomach is the proximal lesser curvature, followed by the cardia and the oesophageal gastric junction.

Risk factors

- H. pylori
- Tobacco
- Alcohol
- Obesity/Overweight
- Epstein barr virus infection
- Radiation
- Pernicious anemia
- High salt/nitrate diet (synergistic w/H. pylori)
- Precursor lesions: Adenomatous gastric polyps, dysplasia, chronic atrophic gastritis, & intestinal metaplasia

Table 9: Referral for suspected Gastric cancer

Gastric cancer urgent referral	
Dysphagia (at any age)	
Aged 55 years and over with weight loss, and	l
— upper abdominal pain, or	l
— Gastric reflux, or	l
— Dyspepsia	l
Patients with an upper abdominal mass consistent with gastric cancer	
Gastric cancer Non-urgent referral	
Haematemesis (at any age), OR	l
Upper abdominal pain and low hemoglobin, OR	l
Raised platelet count with any of the following	l
- Nausea	l
— Vomiting	l
- Reflux	l
- Weight loss	l
— Dyspepsia	l
— Upper abdominal pain, OR	l
Nausea or vomiting with any of the following;	l
- Weight loss	l
- Reflux	l
— Dyspepsia	l
— Upper abdominal pain	1

2.43 Liver cancer

Liver cancer is the 3rd leading cause of cancer mortality worldwide. In Uganda, the incidence parallels the mortality rates because of limited treatment options for advanced liver cancer.

Risk factors

- HBV & HCV are leading risk factors for HCC
- Excessive alcohol leads to alcoholic cirrhosis which is linked to HCC
- Environmental exposure to aflatoxins from aspergillus fungus
- Tobacco
- Autoimmune hepatitis
- Diabetes mellitus
- Metabolic syndrome
- Non-Alcoholic Steatohepatitis
- Hereditary hemochromatosis



Table 10: Referral for suspected Liver cancer

Liver cancer urgent referral	
Patient with upper abdominal mass consistent with an enlarged liver	

Clinical pearls

• A person with chronic hepatitis B or C should have a blood test for alpha fetoprotein undertaken every six months as a screening test for hepatocellular carcinoma

2.44 Pancreatic cancer

Pancreatic cancer is associated with poor response to treatment and high mortality. In 2012, the 5 year survival rate for pancreatic cancer was less than 0.5%.

Risk factors

- Age (peak incidence 7th & 8th decade)
- Tobacco
- Alcohol consumption
- Obesity
- Chronic pancreatitis
- Occupational exposures
- Diabetes mellitus
- Genetic predisposition
- Peutz–Jeghers syndrome
- Ataxia-telangiectasia
- Hereditary chronic pancreatitis syndrome

Investigations

- Ultrasound
- CBC
- Ferritin
- Liver function tests



Table 11: Referral guideline for suspected pancreatic cancer

Pancreatic cancer urgent referral	
If aged 40 years and over with jaundice	
Aged 60 years and over with weight loss AND any of the following;	
— Diarrhea	
— Back pain	
Abdominal pain	
 Nausea/Vomiting 	
- Constipation	
New-onset diabetes	

Clinical pearl

- Nearly 10% of pancreatic cancers are missed by abdomen ultrasound scans, especially tumours smaller than 3cm.
- A person with an upper abdominal mass should be referred urgently to a specialist

2.45 Gall bladder cancer

Cholangiocarcinoma refers to tumours of the bile duct (BD) epithelium, differentiated by site of origin. Although gall bladder and cholangiocarcinoma have identical histological features, the two entities differ in terms of epidemiology, staging systems and surgical treatment.

Risk factors

- Primary sclerosis cholangitis
- Choledochal cysts
- Chronic calculi of the billiary duct
- HCV and HBV
- Male sex

Table 12: Referral guideline for suspected Gall bladder cancer

Gall bladder cancer urgent referral	
Upper abdominal mass consistent with an enlarged gall bladder	

2.5 Lower Gastrointestinal cancer

2.51 Colorectal cancer

Colorectal cancer (CRC) accounts for 540 new cases annually in Uganda.

Risk factors

- Age, increasing incidence between 40–50 & in each succeeding decade
- Familial syndromes (FAP, HNPCC, MUTYH-associated polyposis, Peutz–Jeghers, Juvenile polyposis)
- Personal or Family history of CRC or adenomatous polyps
- Inflammatory Bowel Disorders: Ulcerative Colitis > Cohn's Disease
- Other associations: Abdominal radiation, long-term immunosuppression, DM, alcohol, obesity & lack of physical activity, cholecystectomy, androgen deprivation therapy (ADT), tobacco, low-fibre diet

Investigations

- In patients with equivocal symptoms, a full blood count may help in identifying the possibility of colorectal cancer by demonstrating iron deficiency anaemia, which should then determine if a referral should be made and its urgency.
- In patients for whom the decision to refer has been made, a full blood count may assist specialist assessment in the outpatient clinic.
- In patients for whom the decision to refer has been made, no examinations or investigations other than those referred to earlier (abdominal and rectal examination, full blood count) are recommended as this may delay referral.

Patients presenting with unexplained symptoms related to the lower gastrointestinal tract, a digital rectal examination should always be carried out, provided this is acceptable to the patient



Table 13: Referral guideline for suspected colorectal cancer

Colorectal cancer urgent referral	
Reporting rectal bleeding with a change of bowel habit towards looser stools and/or increased stool frequency	
Rectal bleeding persisting for 6 weeks or more without a change in bowel habit and without anal symptoms	
Right lower abdominal mass consistent with involvement of the large bowel	
Presenting with a palpable rectal mass (intraluminal and not pelvic)	
Unexplained iron deficiency anaemia and a haemoglobin of 11 g/dL or below	
An unexplained positive Fecal occult Blood test (FOBT)	
Any age with a rectal or abdominal mass	
Colorectal cancer non-urgent referral	
Unexplained rectal bleeding with at least 1 of the following;	
dark rectal bleeding,	
rectal bleeding mixed with stool,	
rectal bleeding in the absence of perianal symptoms,	
rectal bleeding and a change in bowel habits, or	
rectal bleeding and weight loss	
Unexplained Iron Deficiency Anemia (hemoglobin of ≤ 110 g/L for men or ≤ 100 g/L for non-menstruating women and iron level below the normal range)	

Clinical pearls

- A person presenting with a right-sided abdominal mass, should be referred urgently for a surgical opinion
- A person at low risk of colorectal cancer with a significant symptom (rectal bleeding or a change in bowel habit) and a normal rectal examination, no anaemia and no abdominal mass, should be managed by a strategy of treat, watch and review in three months
- In a person presenting with a left-sided abdominal mass, faecal loading should first be excluded as the cause. A referral should then be made for a surgical opinion
- Faecal occult blood and carcinogenic embryonic antigen testing are of little value in a person with symptoms suggestive of colorectal cancer and should not be used
- A person with any unexplained gastrointestinal symptoms and known high risk factors, for example, familial adenomatous polyposis, hereditary non-polyposis colorectal cancer, other familial colorectal syndromes or a past history of lower gastrointestinal cancer should be referred to a specialist





Algorithm for the evaluation of a patient with suspected colorectal cancer

Does the patient have 1 or more of the following signs or symptoms?

- · Rectal bleeding
- · Weight loss
- Rectal mass
- Abdominal mass
- · History of inflammatory bowel disease
- History of colorectal polyps or signs of colorectal cancer on previous investigation
- Tenesmus
- · Family history of colorectal cancer
- General practitioner's opinion that patient has colorectal cancer
- Mucus per rectum
- · Abdominal pain

<u>Urgent</u>

- Palpable rectal mass suspicious for CRC
- Abnormal abdominal imaging result causing suspicion of CRC

Semi-urgent

- Unexplained rectal bleeding with at least 1 of
 - dark rectal bleeding,
 - rectal bleeding mixed with stool,
 - rectal bleeding in the absence of perianal symptoms,
 - rectal bleeding and a change in bowel habits, or
 - rectal bleeding and weight loss
- Unexplained IDA (hemoglobin of ≤ 110 g/L for men or ≤ 100 g/L for nonmenstruating women and iron level below the Normal range)

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2.52 Anal cancer

Anal cancer occurs more frequently among the HIV patients.

Risk factors

- Human Pappiloma Virus infection,
- Receptive anal intercourse
- Immunosuppression (transplant or HIV)
- Hematologic malignancy
- Autoimmune disorders
- **Smoking**

Table 14: Referral guideline for suspected anal cancer

Anal cancer urgent referral (appointment within two weeks)	
An unexplained anal mass	
Unexplained anal ulceration	
Anal bleeding	

2.6 Head and Neck cancer

The head and neck cancers are classified anatomically into five divisions: oral cavity (buccal mucosa, alveolar ridges, floor of mouth, hard palate, tongue (ant 2/3)), oropharnyx (Tongue (base), tonsils, soft palate, post pharyngeal wall to level of hyoid), nasopharynx (Superior to soft palate), hypopharyx (Hyoid bone to cricoid cartilage), and larynx (further divided into supraglottic, glottic; subglottic).

Risk factors

- Epstein barr virus infection
- Human Papilloma Virus infection
- Tobacco smoking
- Family history
- High intake of salt-preserved foods

Investigations

- Fine needle aspirate
- **Biopsy**
- Ultrasound
- Chest x-ray
- CT-scans of the skull base to chest-inlet

Any patient with persistent symptoms or signs related to the oral cavity in which a definitive diagnosis of a benign lesion cannot be made should be referred or followed up until the symptoms and signs disappear. If the symptoms and signs have not disappeared after 6 weeks, an urgent referral should be made.



Table 15: Referral guideline for Head and Neck cancers

Head and neck cancer urgent referral

- unexplained red and white patches (including suspected lichen planus) of the oral mucosa that are: painful, or swollen, or bleeding
- unexplained ulceration of the oral mucosa or mass persisting for more than 3 weeks
- hoarseness persisting for more than 3 weeks, particularly smokers aged 50 years and older and heavy drinkers
- unexplained lump in the neck which has recently appeared or a lump which has not been diagnosed before that has changed over a period of 3 to 6 weeks
- unexplained persistent swelling in the parotid or submandibular gland
- unexplained persistent sore or painful throat
- unilateral unexplained pain in the head and neck area for more than 4 weeks, associated with otalgia (ear ache) but with normal otoscopy
- Localized pigmented lesion.
- Any oral lesion with suspicious features: rapid growth, infiltration, indurations, fixation.
- Non-visible but palpable intraoral lumps.
- Non-explained orofacial pain that persists longer than 4 weeks.
- Unexplained recent neck lump.
- Unexplained dysphagia lasting longer than 3 weeks.
- Unexplained dental mobility lasting longer than 3 weeks that cannot be related to trauma or periodontal disease.
- · Unexplained osseous lesion.
- Decrease of orofacial sensitivity and paralysis of unknown origin

Clinical pearls

- A person presenting with unexplained persistent sore or painful throat or mouth, (particularly unilateral pain) for more than 4 weeks, should be referred urgently to a specialist
- A person presenting with unilateral unexplained pain in the head and neck area for more than 4 weeks, or with paraesthesia or dysaesthesia in an area of nerve distribution should be referred urgently to a specialist
- A person presenting with hoarseness persisting for more than 3 weeks (particularly if a smoker aged 50 years or older, or a heavy drinker) should be referred to an ear, nose and throat specialist, and for a chest x-ray

Suspected head and neck cancer Oral cavity Oropharnyx Nasopharynx Larynx Hypolarynx Ulceration in Dysphagia Nose bleeding Hoarseness Discomfort lasting > in the throat the oral cavity > Unexplained 3weeks 3weeks > 3weeks tooth mobility (especially Oral swelling not associated Stridor in smoker or persisting > 3 with periodontal Head and neck drinker) weeks disease lumps for > 3weeks All red or red and white patches of oral mucosa > 3 weeks

Algorithm for the referral of a patient with suspected head and neck cancer

2.61 Thyroid cancer

Thyroid cancer is the commonest endocrine cancer in Uganda, accounting for over 90% new cases.

Referral to UCI

The median age at diagnosis is early 40s for papillary thyroid cancer, late 40s for follicular cancer, and 60-70 years for anaplastic histology

Risk factors

- Radiation exposure to the thyroid gland
- Age
- Female sex
- Family history
- Multiple endocrine neoplasms -2 syndrome

Investigations

- Thyroid function tests
- Thyroglobulin
- Ultrasound
- Fine needle aspirate
- CT scan
- Biopsy.





Table 16: Referral guideline for suspected thyroid cancer

Thyroid cancer emergent referral	
Patients presenting with symptoms of tracheal compression including stridor due to thyroid swelling	
Thyroid cancer urgent referral	
 Patients presenting with a thyroid swelling associated with any of the following; a solitary nodule increasing in size a history of neck irradiation a family history of an endocrine tumour unexplained hoarseness or voice changes cervical lympadenopathy very young (pre-pubertal) patients Patients aged 65 years and older. 	
Thyroid cancer Non-urgent referral	
Patients with hyper- or hypothyroidism and an associated goitre	

Clinical pearls

For a person presenting with symptoms and/or signs suggestive of thyroid cancer, a referral for an ultrasound investigation may be made, but this should not delay referral to a specialist



Algorithm for the evaluation of a patient with suspected thyroid cancer

Suspected thyroid cancer

Solitary nodule increasing in size, Thyroid swelling in a pre-pubertal patient Unexplained hoarseness, Cervical lympadenopathy, Age > 65yeras Family h/o endocrine tumour, A,

Immediate referral

Presence of symptoms Indicating that the trachea is being obstructed by a swollen thyroid

Gland. These symptoms include stridor (a harsh sound heard when breathing in).

Urgent referral

- A single node (lump) that is growing
 - a history of previous radiotherapy on the neck
 - family history of a hormonal cancer
 - unexplained hoarse voice or voice changes
 - disease of the lymph nodes in the neck
 - the patient has not gone through puberty
 - the patient is 65 years or older.

Non-urgent referral

- · Solitary nodule increasing in size
- · Thyroid swelling in a prepubertal patient
- Unexplained hoarseness
- Cervical lympadenopathy
- Age > 65yeras
- · Family h/o endocrine tumour

Referral to Uganda Cancer Institute



2.7 Gynaecological Cancer

2.71 Ovarian cancer

Ovarian cancer is the second leading cause of death from gynecological cancer in Uganda. The incidence increases with age and the median age at diagnosis is 45 years and over 70% patients present with advanced stage at diagnosis

Ovarian cancer is difficult to diagnose. For a woman who presents with vague unexplained abdominal symptoms carry out: abdominal palpation, consider pelvic examination and CA 125 blood test, refer for urgent abdomen/pelvic ultrasound scan

Investigations

- pelvic ultrasound
- Ca 125.

Table 17: Referral for suspected ovarian cancer

Ovarian Cancer Urgent Referral	
If physical examination identifies any of the following;	
- ascites	
pelvic or abdominal mass (which is not obviously uterine fibroid)	
- persistently elevated CA125 over 50	
persistent abdominal distention (bloating)	
early satiety and/or loss of appetite	
increased urinary urgency and/or frequency	
new onset symptoms suggestive of IBS	
unexplained weight loss	

Woman presents to the healthcare professional Unexplained Physical exam A Woman reports Symptoms are not weight loss identifies any of the following suggestive of ovarian · Ascites and/or symptoms; Fatigue cancer A Pelvic or Persistent Changes in bowel abdominal abdominal mass habits (not obviously distension uterine fibroids) Feeling full and/or loss of appetite · Pelvic or Suspected ca. Ovary abdominal pain Increased urinary urgency and/or frequency No Yes Measure serum CA 125 Normal <35U/mL >35U/mL Re-assess for other causes Abdomen/pelvic of her symptoms USS **Investigate** Follow-up symptoms **Urgent referral**

Figure 4: Algorithm for a woman with suspected cancer of the ovary

2.72 Endometrial cancer

Endometrial cancer is the most common gynecological malignancy in developed countries, and the second most common in developing countries. The most common symptom is abnormal uterine bleeding secondary to unopposed estrogen in peri/postmenopausal women.

Table 18: Referral for suspected endometrial cancer

Endometrial Cancer urgent referral	
Aged 55 years and over with	
 Post-menopausal bleeding (unexplained vaginal bleeding more than 12 months after menstruation has stopped due to menopause) 	
Unexplained symptoms of vaginal discharge occurring for the first time or have thrombocytosis or report hematuria	
Aged 55 and over presenting with visible haematuria and any of the following	
— Low hemoglobin	
- Thrombocytosis	
High blood glucose level	

Clinical pearls

- A premenopausal woman presenting with an alteration in bleeding pattern and taking Tamoxifen should have a transvaginal ultrasound of the endometrial and/or be referred to a specialist
- A woman with an abnormal ultrasound finding should be referred to a specialist

2.73 Vulval cancer

Vulval cancer is the 4th most common gynecologic cancer.

Risk factors

- Tobacco use
- vulval dystrophy
- vulval or CIN
- HPV infection,
- Immunodeficiency syndromes
- prior cervical cancer

Table 19: Referral guideline for Vulval cancer

Vulval Cancer urgent referral	
A woman who presents with any of the following:	
An unexplained vulval lump	
Vulval Ulceration	
Vulval bleeding	

2.8 Lung cancer

Lung cancer is the leading cause of cancer related mortality worldwide and the majority of patients present with advanced stage of illness at diagnosis and hence limited interventions to control the disease. Approximately 85% of patients have Non-small cell lung cancer, while 10-15% of patients have small cell lung cancer. Small cell lung cancer is almost exclusively seen in smokers.

Risk factors

- Cigarette smoking
- Previous radiotherapy to the chest
- Polycyclic aromatic hydrocarbons
- Radon
- Metals
- Asbestos

Earlier identification and referral of patients with lung cancer might ultimately help improve lung cancer morbidity and mortality.

An urgent referral for a chest X-ray should be made when a patient presents with:

- haemoptysis, or any of the following unexplained persistent (that is, lasting more than 3 weeks) symptoms and signs:
 - chest and/or shoulder pain
 - dyspnoea
 - weight loss
 - chest signs
 - hoarseness
 - finger clubbing
 - cervical and/or supraclavicular lympadenopathy
 - Cough with or without any of the above features suggestive of metastasis from a lung cancer (for example, in brain, bone, liver or skin).

Other Investigations

- Complete blood count
- Pleural biopsy
- Pleural fluid cytology
- Spirometry



Table 20: Referral guideline for suspected lung cancer

Lung cancer emergent referral	
signs of superior vena caval obstruction (swelling of the face and/or neck with fixed elevation of jugular venous pressure), and Stridor.	
Lung cancer urgent referral	
persistent haemoptysis in smokers or ex-smokers who are aged 40 years and older a chest X-ray suggestive of lung cancer	
o a nodule or mass,	
o multiple pulmonary nodules,	
o non-resolving pleural effusion,	
o mediastinal or contralateral hilar adenopathy,	
o interstitial infiltrates,	
o slowly resolving or non-resolving pneumonia or	
consolidation,	
o fibroapical disease suggesting possible tuberculosis, or	
o unexplained elevated diaphragm	

Clinical pearls

- A normal chest x-ray does not exclude the diagnosis of lung cancer. According to the 2006 BJGP study of normal and abnormal chest x-rays in lung cancer patients, 23% of lung cancer patients had a negative x-ray.
- The smoking status of all patients should be recorded and regularly updated in the practice notes
- Sputum cytology is not recommended for the investigation of lung cancer

Algorithm for the management of a patient with suspected lung cancer

Does the patient have any of the following signs or symptoms? Persistent hemoptysis A Person who is coughing Unexplained changes swelling affecting up blood persistently and are in existing symptoms in both the face and smokers or ex-smokers aged patients with underlying neck caused by an chronic respiratory 40 years and older; obstruction in the jugular problems with a chest X-ray showing veins (these veins run signs of lung cancer down either side of the with a normal chest X-ray, neck), or stridor (this is but in whom the GP a harsh sound heard strongly suspects lung when breathing in). cancer with a history of asbestos exposure and a chest X-ray showing signs of lung cancer. Chest x-ray film suggestive of or suspicious for lung cancer including; · A nodule or mass · Multiple pulmonary nodules · Non-resolving pleural effusion · Mediastinal or contralateral hilar adenopathy · Interstitial infiltrates • Slowly or non-resolving pneumonia or consolidation · Fibroapical disease suggesting possible Tuberculosis · Unexplained elevated diaphragm **Emergent Referral Urgent Referral Non-Urgent Referral**



2.9 Genitourinary cancer

2.91 Prostate cancer

Prostate cancer is the commonest cancer among men in Uganda, and the leading cause of cancer mortality among men in Uganda. In 2012, there were 2,843 new cases of prostate cancer and approximately 2,288 deaths due to prostate cancer in the same year.

Risk factors

- · Increasing age
- Family history

Patients presenting with symptoms suggesting prostate cancer should have a digital rectal examination (DRE) and prostate-specific antigen (PSA) test after counselling. Symptoms will be related to the lower urinary tract and may be inflammatory or obstructive.

Table 21: Referral guideline for suspected Prostate cancer

Prostate cancer emergent referral	
Prostate cancer associated with spinal cord compression or high risk of spinal cord compression	
o Prostate cancer associated with renal failure.	
Prostate cancer urgent referral	
 o An elderly man presenting with any of the following symptoms e erectile dysfunction haematuria lower back pain bone pain Weight loss, especially in the elderly. o Physical examination findings of a hard, irregular prostate typical of a prostate carcinoma 	
o Patients with a normal prostate, but rising/raised age-specific prostate specific antigen (PSA) (> 20 ng/ml), with or without lower urinary tract symptoms	

Clinical pearls

- An older man presenting with lower urinary tract symptoms (frequency, hesitancy, nocturia) should be recommended to have a digital rectal examination and a PSA test
- A man found to have an enlarged, smooth prostate on digital rectal examination and a normal PSA should only be referred to a specialist if they have macroscopic haematuria
- · A man presenting with macroscopic haematuria should be referred urgently to a specialist

Algorithm for evaluation of a patient with suspected prostate cancer

A Patient aged 50 to 70 years (or from 40 to 70 years if he has a first degree relative with prostate cancer or is of African ethnicity). Asymptomatic men Symptomatic men Male patient presents with: Advise patients on Any of the following features when the advantages and disadvantages of PSA unexplained: testing - Lower urinary tract symptoms e.g. dysuria, urgency, nocturia - Unexplained back pain If prostate assessment Requested perform the **RECOMMENDED INVESTIGATIONS** following: - DRE - Digital Rectal Examination DRE - Digital Rectal - PSA - Prostate Specific Antigen Examination - Creatinine PSA - Prostate Hb, and -Urinalysis Specific Antigen Refer Patient to Rapid Emergency If normal DRE and PSA manage ward if he has symptoms in Primary Care or refer to urology clinic as clinically A second abnormal PSA at 6 indicated. weeks after the first PSA test - Abnormal hard Prostate on DRE Referral to Uganda Cancer Institute





2.92 Renal cancer

Renal cancer represents 5% of male adult malignancies and 3% of female adult malignancies. The peak age is between ages 50–70 years and the M:F ratio is 1.6:1

Risk factors

- · Cigarette smoking
- Obesity
- Other environmental factors

Risk factor

- Chromosome mutations
- Cigarette smoking
- Excess body weight
- Hypertension and/or antihypertensive
- Increased parity
- Occupational exposure e.g., asbestos, petroleum products, dry cleaning solvents

Table 22: Referral guideline for suspected renal cancer

Renal cancer urgent referral	
Aged 45 years and over with either;	
Unexplained visible hematuria without urinary tract infection	
 Visible hematuria that persists or recurs after successful treatment of urinary tract infection 	

Clinical pearls

 A person with persistent microscopic haematuria, with no obvious cause (e.g., menstruation) may have non-cancerous renal pathology and should be assessed for renal disease, including tests for proteinuria, estimated glomerular filtration rate (eGFR) and serum creatinine.

2.93 Bladder cancer

Bladder cancer is the most common malignancy of the urinary system. The most frequent symptom is painless hematuria (typically intermittent and gross), irritative

Table 23: Referral guideline for suspected Bladder cancer

Bladder cancer urgent referral (appointment within two weeks)	
Painless macroscopic hematuria	
Aged 40 years and over with either:	
unexplained visible hematuria without urinary tract infection, OR	
 visible hematuria that persists or recurs after successful treatment of urinary tract infection 	
Aged 50 years and over with unexplained non-visible hematuria and either	
- dysuria, OR	
a raised white cell count on a complete blood count	
Any patient with an abdominal mass identified clinically or on imaging that is thought to be arising from the urinary tract	
Bladder cancer Non-urgent referral	
Patients aged 60 and over with recurrent or persistent urinary tract infection that is unexplained	

2.94 Testicular cancer

Table 24: Referral guideline for Testicular cancer

Testicular cancer urgent referral	
In men with any of the following changes in the testis:	
non-painful enlargement	
 A scrotal mass that does not transilluminate and/or when the body of the testis cannot be distinguished. 	
- change in shape	
change in texture	
unexplained or persistent testicular symptoms	

2.94 Penile cancer

Cancer of the penis is relatively common in Uganda, especially among HIV infected patients. Commonly, the disease presents with a painless lump or an ulcer on the penis.

Risk factors

- HIV infection
- **HPV** infection



The following symptoms may require an urgent referral for suspected penile cancer;

• Progressive ulceration or a mass in the glans or prepuce particularly, but can involve the skin of the penile shaft.

Table 25: Referral guideline for suspected penile cancer

Penile cancer urgent referral	
In men with any of the following;	
 A penile mass An ulcerated lesion (after exclusion of sexually transmitted infections as the cause) Unexplained or persistent symptoms affecting the foreskin or glans 	
Penile cancer Non-urgent referral	
Lumps within the corpora cavernosa not involving the penile skin.	

Clinical pearl

• Lumps within the corpora cavernosa not involving penile skin are usually not cancer but indicate Peyronie's disease, these do not require urgent referral

2.10 Skin cancer

All primary healthcare professionals should be aware of the assessment of pigmented skin lesions especially in the setting of HIV infection. The health care professional who performs skin punch biopsies should ensure the right techniques, and should undertake appropriate continuing professional development.

Patients with persistent or slowly evolving unresponsive skin conditions in which the diagnosis is uncertain and cancer is a possibility should be referred to a dermatologist.

All excised skin specimens should be sent for pathological examination.

On making a referral of a patient in whom an excised lesion has been diagnosed as malignant, a copy of the pathology report should be sent with the referral correspondence, as there may be details (such as tumour thickness, excision margin) that will specifically influence future management.

2.10.1 Melanoma

Melanoma represents only a small percentage of all skin cancer (~4%) but has the highest morbidity & mortality

Risk factors

- Higher number of moles
- atypical nevi
- History of prior melanoma,
- 1st-degree relative with melanoma
- prior non-melanoma skin cancer
- immunosuppression



Change is a key element in diagnosing malignant melanoma. For low suspicion lesions, careful monitoring for change should be undertaken using the 7-point checklist for 8 weeks. Measurement should be made with photographs and a marker scale and/or ruler.

All primary healthcare professionals should use the weighted 7 point checklist in the assessment of pigmented lesions to determine referral:

- Major features of the lesions:
 - o change in size
 - o irregular shape
 - o Irregular colour.
- Minor features of the lesions:
 - largest diameter 7 mm or more
 - inflammation
 - oozing
 - Change in sensation.

Suspicion is greater for lesions scoring 3 points or more (based on major features

Scoring 2 points each and minor features scoring 1 point each). However, if there

Are strong concerns about cancer, any one feature is adequate to prompt urgent referral.

In patients with a lesion suspected to be melanoma, an urgent referral to a dermatologist or other suitable specialist with experience of melanoma diagnosis should be made, and excision in primary care should be avoided.

Table 26: Referral guideline for suspected malignant melanoma

Melanoma skin cancer urgent referral	
Patient who presents with a suspicious pigmented skin lesion that has a weighted 7-point checklist score of 3 or more	
Ceroscopy suggests malignant melanoma of the skin	

Clinical pearls:

ABCDE of Melanoma

Α	Asymmetry
В	Border irregularity
С	Colour variation
D	Diameter greater than 6mm
Е	Evolution and/or elevation

2.10.2 Squamous cell carcinomas

Squamous cell carcinomas present as keratinizing or crusted tumours that may ulcerate. Non-healing lesions larger than 1 cm with significant indurations on palpation, commonly on face, scalp or back of hand with a documented expansion over 8 weeks, may be squamous cell carcinomas and an urgent referral should be made.

Squamous cell carcinomas are common in patients on immunosuppressive treatment, but may be atypical and aggressive. In patients who have had an organ transplant who develop new or growing cutaneous lesions, an urgent referral should be made.

Risk factors

- immunosuppression
- Treatment with psoralens and ultraviolet A light (PUVA)
- Very light skin colour, hazel or blue eyes and blonde or red hair
- Being in an exclusively outdoor occupation
- Severe versus no solar elastosis, freckling and facial telangiectasias
- People with chronically injured or inflamed skin with longstanding ulcers, sinus tracts,

Investigations

• biopsy (punch, shave, excision)

Table 27: Referral guideline for suspected squamous cell carcinoma of the skin

Squamous cell carcinoma of skin urgent referral	
If a patient has a skin lesion that is suspicious of squamous cell carcinoma	

Clinical pearls

 Squamous cell carcinoma are usually raised lesions, a number of typical features have been described: often ulcerated keratinized or crusting lesions and growing typically on the head or back of hand.

2.10.3 Basal cell carcinomas

Basal cell carcinoma, also collectively known as non-melanoma skin cancer, is the most common cancer in US; and it is five times as common as squamous cell carcinoma of the skin. The disease rarely metastasizes however, can be locally aggressive and disfiguring.

Risk factors

- Sunlight
- Fair-skinned individuals at greatest risk
- Radiation exposure at a young age
- Prolonged ultraviolet exposure
- Immunosuppression (organ transplantation)

Basal cell carcinomas are slow growing, usually without significant expansion over 2 months, and usually occur on the face. Where there is a suspicion that the patient has a basal cell

carcinoma, a non-urgent referral should be made.

Investigations

All pigmented lesions that are not viewed as suspicious of melanoma but are excised should have a lateral excision margin of 2 mm of clinically normal skin and cut to include subcutaneous fat in depth.

Table 28: Referral guideline for suspected Basal cell cancer

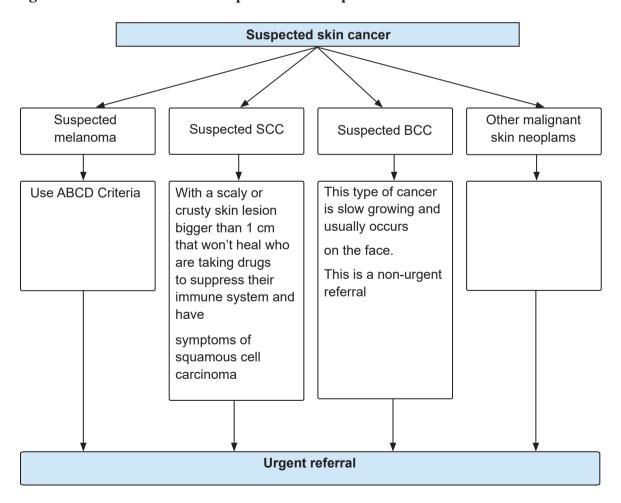
Basal cell carcinoma of the skin urgent referral	
A skin lesion that raises suspicion of a basal cell carcinoma.	

Clinical pearl

Features suggestive of a basal cell carcinoma include;

- An ulcer with raised blood vessels around the lesion,
- Nodules, often waxy or pearly in appearance

Algorithm for the evaluation of a patient with suspected skin cancer



2.11 Haematological cancer

2.11.1 Leukemias

Leukaemia usually presents with a relatively short history of weeks rather than months. The presence of one or more of the following symptoms and signs requires investigation with full blood count and blood film:

- pallor
- fatigue
- unexplained irritability
- unexplained fever
- persistent or recurrent upper respiratory tract infections
- generalised lympadenopathy
- persistent or unexplained bone pain
- Unexplained bruising.

If the blood film or full blood count indicates leukaemia then an urgent referral should be made.

Table 29: Referral for suspected Leukemia

Leukemia emergent referral	
Unexplained signs and symptoms including;	
• Pallor	
Persistent fatigue	
Fever	
Persistent or recurrent infection	
Generalized lympadenopathy	
Bruising	
Bleeding	
Petechiae with either	
Hepatosplenomegaly, or	
Blood counts/film suggestive of acute leukemia	
Leukemia urgent referral	
A child with unexplained petechiea	
Hepatosplenomegaly	
Persistent fatigue	
Fever	
Persistent infections	
Generalized lympadenopathy	
Persistent or unexplained bone pain	
Bruising	
Bleeding	

2.11.2 Lymphomas

Hodgkin's lymphoma presents typically with non-tender cervical and/or supraclavicular lympadenopathy. Lympadenopathy can also present at other sites. The natural history is long (months). Only a minority of patients have systemic symptoms (itching, night sweats, fever).

On the other side, Non-Hodgkin's lymphoma typically shows a more rapid progression of symptoms, and may present with lympadenopathy, breathlessness, superior vena-aval obstruction or abdominal distension.

- Lympadenopathy is more frequently benign in younger children but urgent referral is advised if one or more of the following characteristics are present, particularly if there is no evidence of local infection:
 - o lymph nodes are non-tender, firm or hard
 - o lymph nodes are greater than 2 cm in size
 - o lymph nodes are progressively enlarging other features of general ill-health, fever or weight loss
 - o the axillary nodes are involved (in the absence of local infection or dermatitis)
 - o involvement of supraclavicular nodes.

Table 30: Referral for suspected Lymphoma

rable co. Referral for caopected Lymphoma		
Lymphoma emergent referral		
Patient with fevers, night sweats, shortness of breath, or weight loss who presents with		
Unexplained lympadenopathy, or		
— Hepatosplenomegaly or		
Mediastinal mass, or		
— Hilar mass/adenopathy		
Lymphoma urgent referral		
Adults who present with		
 lymph nodes with the following features: non-tender, firm or hard / > 2 cm / progressively enlarging / maxillary (particularly in absence of local infection/ dermatitis) / supraclavicular node involvement / other features general ill-health, fever/weight loss, persisting for six weeks 		
If shortness of breath and unexplained petechiae or hepatosplenomegaly (particularly if not responding to bronchodilators).		
A child or young person with a mediastinal or hilar mass on chest x ray should be referred immediately.		



2.11.3 Plasma cell dyscrasias

Plasma cell dyscrasias are a spectrum of disorders arising from the plasma cells including Plasmacytoma, Monoclonal gammopathy of undetermined significance (MGUS), Multiple myeloma (MM), plasma cell leukemia, Waldestroms macroglobulinemia, and smoldering myeloma.

The following may require emergent referral for a patient with suspected plasma cell dyscrasia

• Bone pain associated with anemia and a raised ESR or plasma viscosity:

Investigations for haematological cancer

- complete blood count (CBC)
- lymph node biopsy
- Bence-Jones protein
- CT chest/abdomen
- chest x-ray
- serum protein electrophoresis
- Lactate dehydrogenase (LDH).

Table 31: Referral guideline for suspected Multiple myeloma

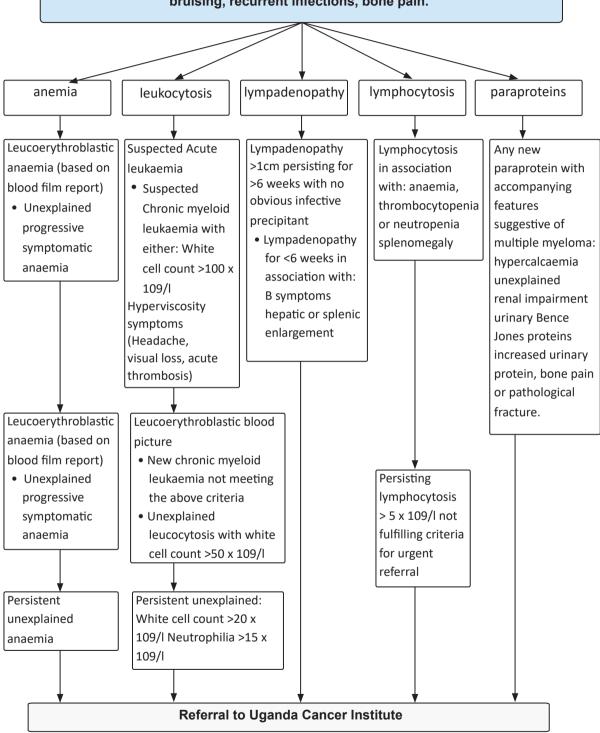
Multiple Myeloma urgent referral	
Aged 60 years and over with;	
Unexplained bone pain, renal dysfunction, unexplained anemia or pancytopenia, recurrent respiratory infections or hypercalcemia	
Unexplained elevated serum calcium, or pathological fractures	
Hypergammaglobulinaemia with paraproteins	

Clinical pearls

- Always evaluate for the CRAB elevated Calcium, Renal failure, Anaemia, and Bone pain.
- For a person presenting with symptoms and/or signs suggestive of myeloma, a Bence-Jones protein and serum protein electrophoresis may be undertaken, but should not delay referral to a specialist

Algorithm for evaluation of a patient with suspected haematological malignancy

Suspect haematological malignancy if a patient has 3 or more of the following symptoms: fatigue, night sweats, weight loss, itching, breathlessness, bruising, recurrent infections, bone pain.







2.12 Bone and soft tissue sarcomas

2.12.1 Bone sarcomas

The most common bone sarcoma is osteosarcoma and Ewing's sarcoma. Other rare bone sarcomas include chondrosarcoma, fibrosarcoma, and giant cell tumour of the bone.

The commonest presentation of bone sarcomas is bone pain or swelling, particularly with activity. Limbs are the most common site for bone tumours, especially around the knee in the case of osteosarcoma.

Frequently, patients present with hematogenous metastases to the lung and bones.

A person with symptoms or signs suggestive of primary or secondary bone cancer should have an x-ray completed and reported within 5 days

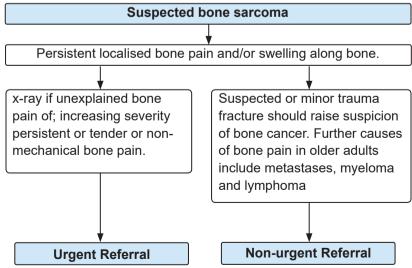
A practitioner should consider primary or secondary bone cancer in a person where a fracture is suspected in the absence of a history of trauma investigations

- x-ray
- CT scan
- fine needle aspirate

Table 32: Referral guideline for suspected Bone sarcomas

Bone sarcoma Emergent referral (appointment within 48 hours)	
A child with unexplained bone swelling or bone pains	
A child with X-rays suggestive of possible bone sarcoma	
Bone sarcoma Urgent referral (appointment within two weeks)	
Rest pain, back pain and unexplained limp that are suggestive of a bone tumour	

Algorithm for the evaluation of a patient with suspect bone sarcoma



2.12.2. Soft tissue sarcomas

These are rare tumours, representing 1% of all cancers, yet over 50 histological types. Soft tissue sarcomas represent a heterogeneous spectrum of malignancies with varied genetic aberrations and clinical features. They are potentially curable if resected early

The following symptoms may require an urgent referral for suspected soft tissue sarcoma:

- A mass that is;
 - o non-tender
 - progressively enlarging
 - associated with a regional lymph node that is enlarging
 - Greater than 2 cm in diameter.
- A soft tissue mass in an unusual location may give rise to misleading local and persistent unexplained symptoms and signs; such as;
 - a. head and neck sarcomas:
 - proptosis
 - persistent unexplained unilateral nasal obstruction with or without discharge and/or bleeding
 - aural polyps/discharge

b. genitourinary tract:

- · urinary retention
- scrotal swelling
- Blood stained vaginal discharge.

Investigations

- Ultrasound
- CT scan
- Fine needle aspirate (FNA)
- X-ray.

Table 33: Referral guideline for suspected Soft-tissue sarcomas

Soft tissue sarcoma emergent referral	
A child with an unexplained lump that is increasing in size	
Soft tissue sarcoma urgent referral	
An adult with an unexplained lump that is increasing in size	
Ultrasound scan findings suggestive of soft-tissue sarcoma	

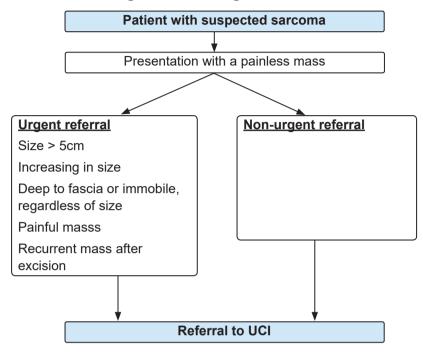
Clinical pearls

A person with an unexplained palpable soft tissue lump (i.e., excluding a sebaceous cyst or lipoma) that is increasing in size, or hard, fixed or tethered should undergo an appropriate imaging investigation of the lump (ultrasound, MRI or CT scan) and should be referred to a specialist before any biopsy or fine needle aspirate



• For a person presenting with symptoms and/or signs suggestive of soft tissue sarcoma, referral for an ultrasound, MRI or CT scan may be made, but this should not delay referral to a specialist

Algorithm for the evaluation of a patient with suspected sarcoma



2.13 Brain and CNS tumours

Persistent headache is a primary symptom for brain tumours; this should prompt a detailed neurological examination by the primary healthcare professional.

Headaches

In patients with headaches of recent onset accompanied by either features suggestive of raised intracranial pressure (for example, vomiting, drowsiness, posture-related headache, headache with pulse-synchronous tinnitus) or other focal or non-focal neurological symptoms (for example, blackout, change in personality or memory), an urgent referral should be made.

Seizures

In patients presenting with a seizure, a physical examination (including cardiac, neurological, mental state) and developmental assessment, where appropriate, should be carried out.

In any patient with suspected recent-onset seizures, an urgent referral to a neurologist should be made.



Table 34: Referral guideline for suspected Brain tumours

Brain cancer emergent referral (appointment within 48 hours)	
A child with newly abnormal central neurological or cerebella function	
Adults with progressive, sub-acute loss of central neurological function	
Headache and vomiting that cause early morning waking or occur on waking are classical signs of raised intracranial pressure;	
new-onset seizures	
cranial nerve abnormalities	
visual disturbances	
gait abnormalities	
motor or sensory signs	
unexplained deteriorating school performance or developmental milestones	
Unexplained behavioral and/or mood changes.	
Reduced levels of consciousness	
Brain cancer urgent referral: (appointment within two weeks)	
abnormal increase in head size	
arrest or regression of motor development	
altered behavior	
abnormal eye movements	
lack of visual following	
Poor feeding/failure to thrive.	

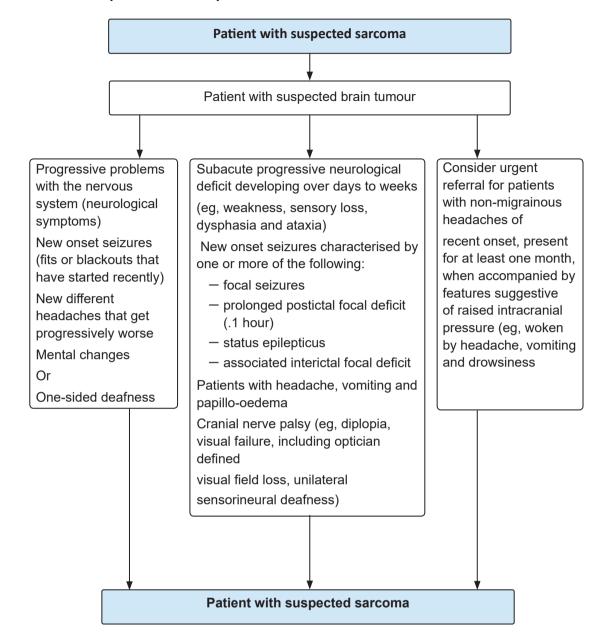
Clinical pearls:

- Headache of recent onset accompanied by features suggestive of raised intracranial pressure, e.g. vomiting, drowsiness, posture-related headache, pulse-synchronous tinnitus, or other focal or non-focal neurological symptoms, such as blackouts or change in personality or memory may require emergent referral to the neurologist
- A person presenting with a single, unexplained seizure, should undergo a physical examination (including cardiac, neurological, mental state), and be referred to a specialist





Evaluation of a patient with suspected brain tumour



SECTION THREE: GUIDELINE IMPLEMENTATION

APPENDICES

Appendix A: Methods

Appendix B: Guideline Development group

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Appendix C: Abbreviations

AFP Alpha feto protein

CBC Complete blood count

CEA Carcinogenic embryonic antigen

CNS Central nervous system

CT Computerized tomography

ESR Erythrocyte sedimentation rate

FNA Fine needle aspirate

GDT Guideline Development Team

MRI Magnetic resonance imaging

PSA Prostate specific antigen

SIGN Scottish Intercollegiate Guideline Network

Appendix D: Glossary

Anemia: Condition where there is less than the normal number of red blood cells

Or less than the normal quantity of hemoglobin in the blood

Anorexia: Symptom of poor appetite, whatever the cause

Barrett's esophagus: An abnormal change in the cells of the lower end of the esophagus

Thought to be caused by damage from chronic acid exposure. Considered to be a pre-malignant condition



Bence-Jones protein: Small proteins (light chains of immunoglobulin) found in the urine.

Testing for these proteins is done to diagnose and monitor multiple myeloma and other similar diseases

Biopsy: Removal of a sample of tissue for examination under a microscope to check for cancer cells

Dyspepsia: For the purposes of this guideline, dyspepsia refers to all sub-classifications (reflux-like, ulcer-like, dysmotility-like, non-specific) and includes epigastric pain or discomfort, heartburn or acid regurgitation, with or without bloating, nausea or vomiting

Dysphagia: Difficulty in swallowing

Dysplasia: Formation of abnormal tissueDyspnoea: Difficulty or pain in breathingDysuria: Difficulty or pain on passing urine

Carcinogen: A cancer-causing substance or agent

Fine needle aspiration: A diagnostic procedure where a thin, hollow needle is inserted into a tumour to extract cells that will be examined under a microscope

Gastric: Referring to the stomach

Haematemesis: A condition in which someone vomits blood, usually because of internal bleeding

Haematuria: Presence of red blood cells in the urine

Microscopic haematuria – red blood cells are only visible under a microscope

Macroscopic haematuria – blood is visible in the urine

Hemoptysis: A condition in which someone coughs up blood from the lungs

Hepatosplenomegaly: Enlargement of both the liver and the spleen

Lymph node: Any of the small, oval or round bodies, located along the lymphatic vessels that supply lymphocytes to the bloodstream and remove bacteria and foreign particles from the lymph

Lympadenopathy: Disease or swelling of the lymph glands

Malignant: Refers to cells or tumours growing in an uncontrolled fashion. Such growths

May spread to and disrupt nearby normal tissue, or reach distant sites via the bloodstream

Metastasis: Spreading of malignant disease from one part of the body to another through the bloodstream or the lymphatic vessels

Nocturia: A need to pass urine frequently at night

Obstructive jaundice: A yellowish discolouration of the skin, the conjunctival membranes over the sclera (whites of the eyes), and other mucous membranes caused by hype bilirubinaemia (increased levels of bilirubin in the blood) as a result of interruption to the drainage of bile in



the biliary system

Referral:

Emergent referral – in this guideline, emergent referral means the patient is seen within a few hours, or more quickly if required

Urgent referral – in this guideline, urgent referral means the patient is seen within 2 weeks Risk factor: An aspect of personal behavior or lifestyle, or environmental exposure,

Or an inherited characteristic that is associated with an increased risk of a person developing a disease





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REFERRAL GUIDELINES FOR SUSPECTED CANCER

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