



PHILIPPINE CANCER SOCIETY

TERTIARY PREVENTION OF CANCER: CLINICAL TREATMENT GUIDELINES

The Philippine Cancer Society Guidelines are constructed using the Clinical Algorithm Standards of the Society of Medical Decision Making [1]. These charts are made of conditional logic (if/then) statements that have been mapped out. In navigating through these maps, 4 kinds of symbols are used:

1. Clinical State Boxes (rounded rectangles) – These boxes define the clinical state or problem. They have only one exit path, and may or may not have an entry path. Clinical state boxes always appear at the beginning of an algorithm.
2. Decision Boxes (hexagons) – These boxes contain a question (?) that is answerable by yes or no. Two alternative paths always branch out from these boxes – the “yes” (Y) path usually exists to the right, while the “no” (N) path usually exits downwards. Decision boxes always have an entry path.
3. Action Boxes (angles rectangles) – These boxes contain an action, commonly either therapeutic or diagnostic in nature. They may not have an exit, but they always have an entry path.
4. Link Boxes (small ovals) – These boxes are used to link algorithms that cannot fit in a single page, to maintain path continuity.

Annotations ((A), (B), (C)...) are given as needed for a particular algorithm. The algorithms are so designed so that *a large majority of patients presenting with a particular oncology problem can be handled with a minimum of tests, interventions or referrals, particularly in consideration of the Philippine setting.* They serve as guidelines to the management of common oncology problems (with typical presentations), aiding the thinking process of the physician. It must be added, however, that some patients have clinical cancer presentations that are atypical, hence the need for other diagnostic procedures that may not be mentioned in the algorithms.

The major resource and reference of the cancer treatment guidelines is the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (NCCN). For further information go to <http://www.nccn.org/>

The Philippine Cancer Society Inc has the following Clinical Cancer Treatment algorithms for:

1. Primary Cancer Sites
 - a. Breast
 - b. Lung
 - c. Lymph Node, Primary
 - d. H & N, un-resectable
 - e. Nasopharynx
 - f. Esophagus
 - g. Stomach
 - h. Colon
 - i. Rectum
 - j. Liver
 - k. Pancreas
 - l. Ovary
 - m. Uterine Fundus
 - n. Uterine Cervix
 - o. Prostate
 - p. Testis
 - q. Renal
 - r. Urinary Bladder
 - s. Soft Tissue
 - t. Bone
 - u. Brain
 - v. Unknown Primary
2. Palliative Management – Advanced Cancer
3. Oncologic Emergencies
 - w. Superior Vena Cava Syndrome
 - x. Spinal Cord Compression
 - y. Malignant Pleural Effusion
4. Supportive Care
 - z. Cancer Pain
 - aa. Chemotherapy-induced Anemia
 - bb. Chemotherapy-induced Neutropenia
 - cc. Chemotherapy-induce Emesis

BREAST CANCER

The management of breast cancer must be multi-disciplinary interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

- (A) Most breast cancer (hard, painless, movable, then becomes fixed to the chest wall/skin, with/without nipple retraction) are found by palpation by the patient, her partner or her physician. As tumor size increases, the likelihood that distant metastasis has taken place rises. It is better to detect and treat early (asymptomatic <1cm diameter tumor size). Mammography can detect very early <1 cm tumor mass and hence effective in screening.
- (B) If total mastectomy is anticipated, it is best to confirm the diagnosis with open biopsy. For preliminary screens, FNAB cytology is done. A (-) FNAB should not dissuade the surgeon from excision biopsy if a discrete lump is present, particularly if there is high clinical suspicion of cancer.

Mammography can be done to localize areas with high probability of cancer aiding direction of FNAB.

Review of slides is done to verify presence and type of cancer for those patients already with biopsy slides.

- (C) Majority of breast cancer are invasive ductal carcinoma. Three major cancer types are: noninvasive (intraductal and lobular), invasive, and Paget's disease of the nipple. Poor prognosis types are atypical medullary and not otherwise specified. Other histopathologic findings that correlate with poor prognosis are low nuclear grade and presence of tubule formation.

For treatment purposes, breast cancer may be divided into:

- a. Pure noninvasive carcinoma (Stage 0)
 - i. ductal carcinoma in situ (DCIS; Stage 0)
 - ii. lobular carcinoma in situ (LCIS)
- b. Operable locoregional invasive carcinoma (Stage I, II and some stage IIIA)
- c. Inoperable locoregional invasive carcinoma (Stage IIIB, IIIC and some stage IIIA tumors)
- d. Metastatic or recurrent carcinoma (Stage IV)

- (D) Staging considerations:

History and physical exam (PE), and at a minimum alkaline phosphatase, chest x-ray, abdominal ultrasound are done for baseline. Bone scan is indicated if the patient has symptoms related to bone or if there is elevated alkaline phosphatase level. CT scan of whole abdomen is indicated if abdominal ultrasound is inconclusive but there are symptoms referable to the abdominal organs.

At a minimum baseline CBC, creatinine, and ECG are done in preparation for treatment.

PET scan can be an option to determine presence of metastatic sites highly suspected but not shown by CT scan/ bone scan. For brain metastasis suspect, MRI may be the better option compared to CT scan.

- (E) The goal of treatment of in-situ carcinoma is either preventing the occurrence of invasive disease or diagnosing the invasive component when still localized to the breast.

Observation alone is the preferred option for women diagnosed with lobular carcinoma-in-situ (LCIS) because their risk of developing invasive carcinoma is low. Bilateral mastectomy may be considered in special circumstances.

Tamoxifen treatment may be considered in women with estrogen receptor-positive [ER(+)] ductal carcinoma-in-situ (DCIS) treated with breast conserving therapy or with mastectomy.

- (F) Fresh surgical breast mass specimen must be routinely taken at FIRST surgery for estrogen receptor/ progesterone receptor (ER/PR) assay and level of HER-2/neu expression, needed to plan drug treatment of patient. For Stage IV or for those cases not previously performed, it is best to determine from the excision biopsy specimen the ER/PR and HER-2 status.

Hormonal therapy (Tx) has been shown to reduce overall tumor recurrence and mortality in ER(+) women. Tamoxifen or an aromatase inhibitor agent is the usual hormone therapy drug. The best responder would be an ER(+)/PR(+) patient; for those premenopausal, tamoxifen can be given; for those post-menopausal, tamoxifen or aromatase inhibitor can be given. For those ER(+)/PR(-), the PR(-) status may be a marker for epidermal growth factor overexpression (Her-2 overexpression) and this subgroup of post-menopausal patients may be best started on aromatase inhibitors.

HER-2-neu overexpression denotes an aggressive cancer, resistance to CMF but responsiveness to anti-Her-2-neu immunotherapy (trastuzumab). A combination of HER-2-neu \geq ++/ PR(-) connotes resistance to CMF-based regimen and tamoxifen.

- (G) The purpose of surgery is to remove the local and regional disease. A number of randomized trials document that in the majority of women with Stage I and II invasive breast CA, mastectomy with axillary dissection versus breast conserving therapy with lumpectomy, axillary dissection and breast irradiation (breast conserving

therapy) are medically equivalent primary therapeutic options. MRM still remains the better option for clinical settings with low patient follow-up rates or low resource settings.

Surgical management is the responsibility of the surgical oncologist.

- (H) For high risk patients with ≥ 4 (+)LN and (-)ER or for those premenopausal and (-)LN or with HER-2-neu over expression, anthracycline-containing adjuvant chemotherapy is given. Otherwise, CMF can be given, particularly for elderly and or patients with heart disease; taxanes can also be given particularly for young, ALN(+) 0-3, aggressive and ER/PR(-) tumors.
- (I) If adjuvant chemotherapy is indicated, RT should be given after chemotherapy is completed. Radiotherapy is the responsibility of the radiation oncologist.

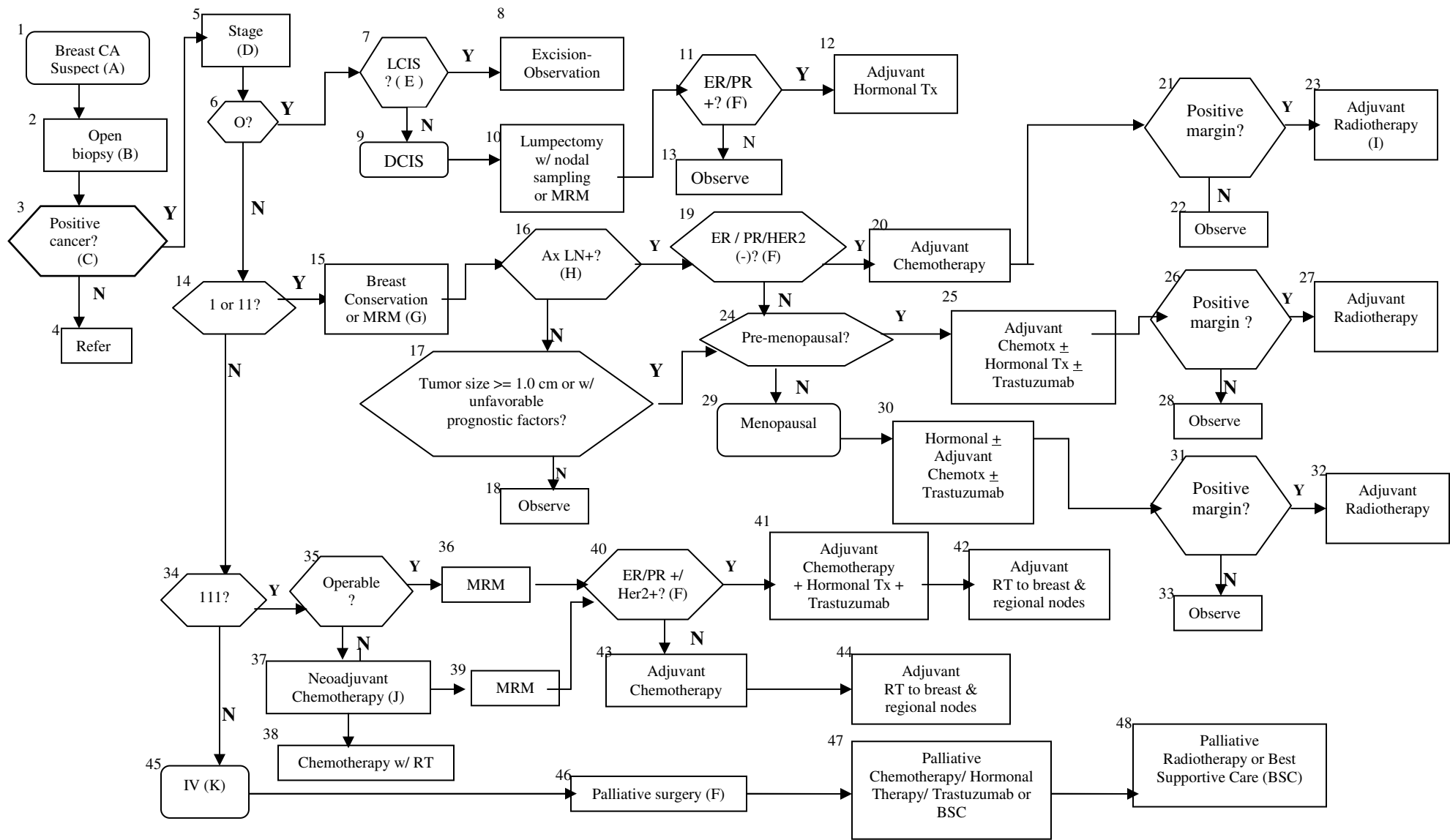
It was hoped that post-op RT could prevent locoregional recurrence and improve disease-free and overall survival. It is now evident, however that this has not occurred to the degree hoped for, probably because remaining tumor burden is too great. Hence, adjuvant systemic chemotherapy is given.

More common chemotherapeutic drugs used currently in breast cancer management (neoadjuvant, adjuvant, or palliative setting) are doxorubicin and the other anthracyclines, cyclophosphamide, fluorouracil, taxanes, navelbine, capecitabine, gemcitabine, methotrexate, vincristine, mitomycin-c, carboplatin, trastuzumab.

Drug management (from hormonotherapy to gene therapy in the adjuvant to palliative setting) is the responsibility of the medical oncologist who does the planning, the administration, and the monitoring of drug therapeutic and safety effects.

- (J) Preoperative chemotherapy for large clinical Stage IIA and IIB tumors and T3N1Mo tumors should be considered for women who meet the criteria for breast conserving therapy.
- (K) Metastatic sites for breast cancer are usually the regional LNs, skin, lung, liver, bone, brain, etc. Stage IV breast cancer can be those with:
 1. 'operable-like' breast mass but with distant metastasis wherein simple mastectomy followed by radiotherapy of target breast & regional LNs sites and symptomatic metastatic sites plus chemotherapy/ hormonotherapy, OR wherein radiotherapy to target breast lesion/ other symptomatic metastatic sites plus chemotherapy/ hormonotherapy can be done,
 2. 'inoperable-like' breast mass (adherent, ulcerated, etc) with distant metastasis, wherein toilette mastectomy can be done with chemotherapy/ hormonotherapy or radiotherapy or best supportive care.

Surgery, chemotherapy, radiotherapy procedures in Stage IV disease are all palliative in goal, although several patients can respond very well to chemotherapy \pm radiotherapy and have significantly long time to disease progression interval. Best supportive care mainly includes management of nutrition, pain, infection, psychological well-being, nursing and rehabilitative care, and other pertinent quality of life patient care.



LUNG CANCER

The management of lung cancer must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

- (A) A change in pulmonary habits is the most significant sign of lung cancer. Coughs, chest pain, rust colored-streaked sputum, hemoptysis, hoarseness, weight loss, and dyspnea are common symptoms of lung cancer.
- (B) Postero-anterior and lateral chest films are the most valuable first tools to establish the diagnosis when there is clinical suspicion of lung cancer.
- (C) The CT scan can detect asymptomatic smaller tumors. For lung cancer suspect, do CT scan of chest, upper abdomen and adrenal glands. CT scan is also the most useful of all modalities for determining the characteristics of T and N in the thorax and M in the brain and liver.
- (D) Bronchoscopy yields (+) histology only if the lung cancer is centrally located or has invaded centrally. Cytological studies include sputum and bronchial washing exams by Papanicolaou technique.
- (E) Percutaneous needle biopsy guided by fluoroscopy or CT scan gives accurate cytologic diagnosis from peripheral lung lesions and also from liver/bone metastatic lesions.
- (F) Pleural fluid can undergo cytologic exam when pleural effusion is the presenting symptomatology.
- (G) There are 2 major histological types, whose management differ accordingly: 1) small cell anaplastic carcinoma (SCLC)- tends to be disseminated at diagnosis; rapidly growing, 2) Non-small cell carcinoma (NSCLC)- slow growing; with three cell types: a) epidermoid carcinoma – most common centrally located, b) adenocarcinoma – tends to be peripherally located, c) large cell anaplastic carcinoma – similar to adenocarcinoma in metastatic pattern.

For both SCLC and NSCLC, staging work-up includes CT scan of chest, upper abdomen and adrenal glands (if not yet done in diagnostic work-up), ultrasound of the liver (if upper abdomen CT scan was not done), brain and bone scans (if symptomatic).

- (H) SCLC Stage:
 - 1) Limited disease – confined to lung and regional lymph nodes.
 - 2) Extensive disease – denotes metastasis outside lung and regional lymph nodes.
- (I) NSCLC stage by TNM classification
 - A. TNM**
 - a. **T_{is}** carcinoma *in situ*
 - b. **T₁** <3 cm tumor size not involving the visceral pleura
 - c. **T₂** >3 cm tumor size, >2cm from the carina, (+) visceral
 - i. pleural involvement, partial atelectasis
 - d. **T₃** tumor involves the chest wall, diaphragm, mediastinum
 - i. pleura or parietal pericardium, <2 cm from the carina, complete atelectasis of either lung
 - e. **T₄** tumor involves the mediastinum, heart, trachea,
 - i. carina, vertebral body; presence of malignant pleural/pericardial effusion; presence of satellite nodule/tumor
 - f. **N₀** No spread to lymph nodes (LN)
 - g. **N₁** Spread to LN within the lungs, ipsilateral hilar LNs
 - h. **N₂** Spread to subcarinal or ipsilateral mediastinal LNs
 - i. **N₃** Spread to cervical LNs or contralateral hilar and
 - i. mediastinal LNs
 - j. **M₀** No distant spread
 - k. **M₁** Spread to distant organs, to other lobes of the
 - i. lungs or to LNs further than those mentioned in N stage
 - B. STAGE**
 - a. 0 - T_{is}N₀M₀
 - b. IA - T₁N₀M₀
 - c. IB - T₂N₀M₀
 - d. IIA - T₁N₁M₀
 - e. IIB - T₂N₁M₀, T₃N₀M₀
 - f. IIIA - T₁-T₃N₂M₀, T₃N₁M₀
 - g. IIIB - AnyT₃N₃M₀, T₄AnyN₀M₀
 - h. IVB - AnyT AnyN M₁
- (J) In SCLC T₁-N₀M₀ and NSCLC Stage I and II, surgery is done to achieve complete tumor resection. Avoid an exploratory thoracotomy or an incomplete surgical resection. The choice of surgical procedure – lobectomy, pneumonectomy, segmental or sleeve resection – depends on disease extent and patient's functional status.

Here, surgery may not be done if with medical contraindications. The presence of distant metastases or extrahepatic metastasis is indicative of inoperability and a surgical procedure is an absolute contraindication.

Surgical management is the responsibility of the surgical thoracic oncologist.

- (K) Irradiation is used to achieve:
- 1) Definitive irradiation of localized lung cancer
 - 2) As part of a combined treatment approach
 - 3) Palliation of symptoms

Radiotherapy can be given in combination with chemotherapy if a patient is assessed (age, ECOG performance status, co-morbidities, preference) to be able to receive combination modality of treatment.

Radiotherapy is the responsibility of the Radiation Oncologist.

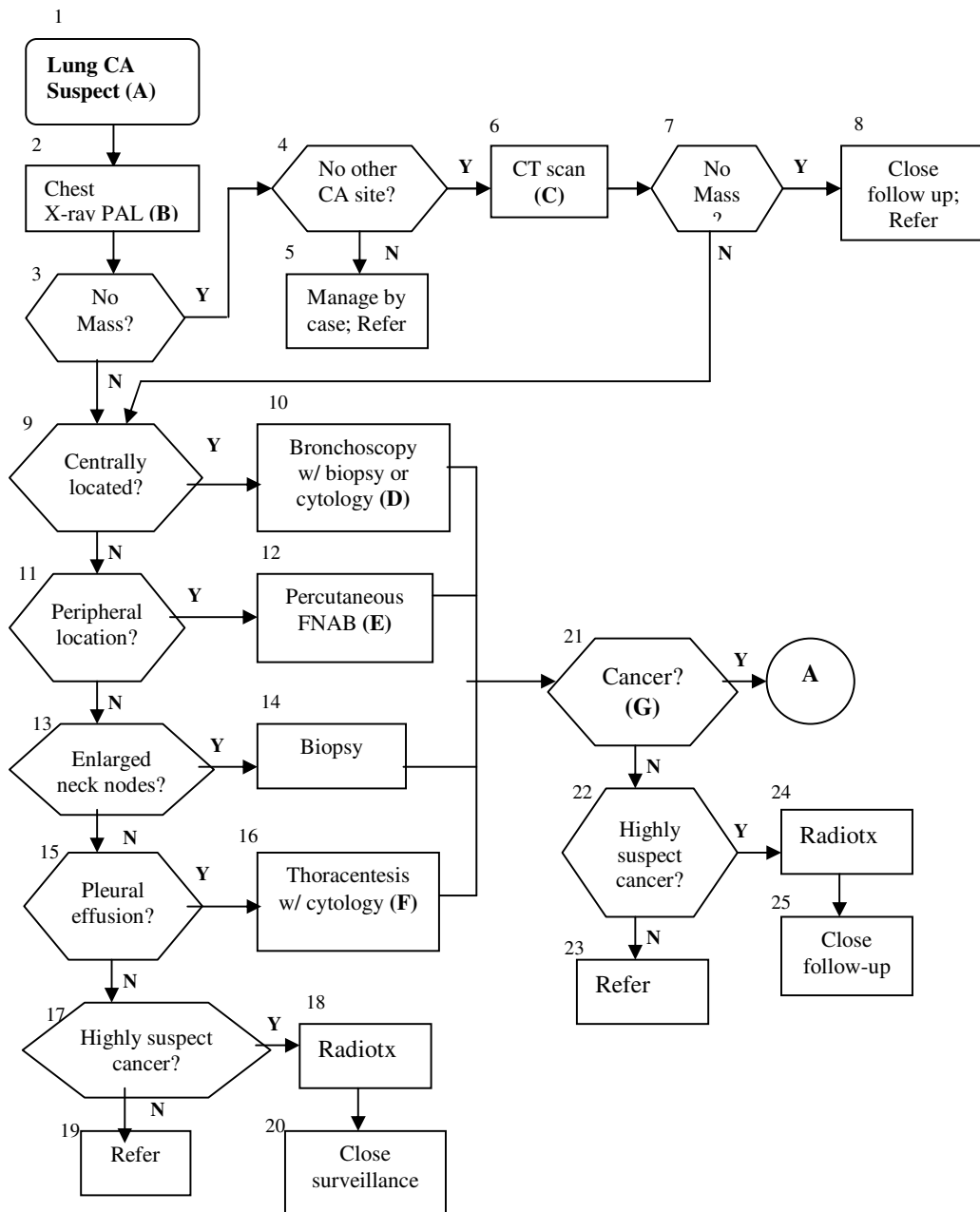
- (L) In SCLC, combination chemotherapy is the treatment of choice for all stages. Drugs used are cisplatin, carboplatin, paclitaxel, docetaxel, adriamycin, vincristine, cyclophosphamide, etoposide, ifosfamide, irinotecan.

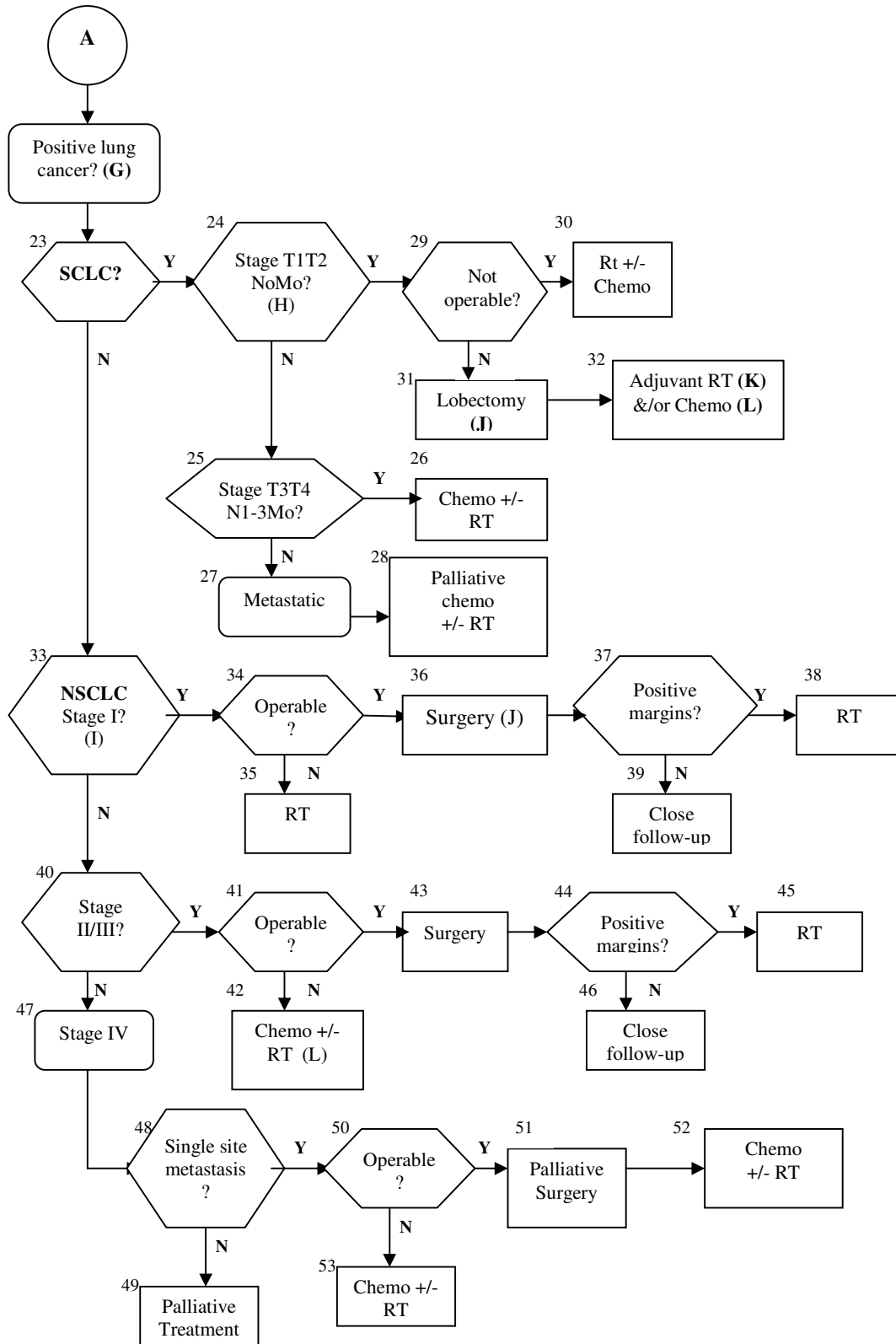
In NSCLC, chemotherapy is used for recurrent or metastatic disease and for palliation of inoperable symptomatic patients whose disease is beyond radiotherapy control. Recent data also suggested benefits for Stage III disease after surgery or radiotherapy. In NSCLC, common chemotherapeutic agents used are cisplatin, carboplatin, paclitaxel, docetaxel, gemcitabine, vinorelbine, ifosfamide, etoposide, erlotinib, and gefitinib (gefitinib for Asian, female, adenocarcinoma).

Neoadjuvant chemotherapy is reported to be promising due to better staging procedures and use of cisplatin/taxane containing regimens. Drugs used are cisplatin, carboplatin, paclitaxel, docetaxel, etoposide.

Drug therapy for cancer is the responsibility of the Medical Oncologist.

Initial work up prior to chemotherapy includes baseline CBC, creatinine, serum electrolytes, LDH, ECG.





MALIGNANT LYMPHOMA

The management of malignant lymphoma must be multi-disciplinary interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient. The main responsible is the medical oncologist.

- (A) The typical presentation of lymphoma is painless node enlargement. Symptoms and signs of non-Hodgkin's Lymphoma (NHL) are similar to those in Hodgkin's Lymphoma (HD), except for the following generalizations: 1) unlike HD, noncontiguous spread is the rule in NHL, and the mediastinum is often spared. Unsuspected bone marrow involvement occurs much more frequently. Early involvement of oropharyngeal lymphoid tissue, skin, the GI tract, and bone is frequent; 2) leukemic transformation with a high peripheral lymphocyte count occurs in about 13% of patients with lymphocytic lymphoma; 3) autoimmune anemia with positive antiglobulin (Coombs) tests occurs in a minority of NHL patients. Complete PE is done with CBC, LDG, Calcium, Urinalysis, Kidney and Liver function test, Chest X-ray, CT-Scan of the abdomen and pelvis
- (B) Surgical biopsy establishes the diagnosis. The most suspicious node should be selected for excision biopsy. The largest most central node in an enlarged group is most likely to be diagnostic. The biopsy of cervical node is preferred because chronic inflammatory changes are more commonly present in inguinal and axillary nodes. Frozen sections and needle biopsies are discouraged. Aspiration of bone marrow or effusions may provide the diagnostics and obviate the need for a LN biopsy. Special tests of blood, LN, or bone marrow establish the exact type of lymphoma e.g. cell surface markers and genetic studies (if needed). Cell surface markers are proteins in the surface of lymphoma cells that identify the kind of lymphoma. In chronic lymphocytic lymphoma (CLL), CD5, CD19, CD23 and CD20 are present. For leukemia the presence of CD38 helps determine prognosis. For mucosa-associated lymphoid tissue (MALT) lymphoma, cell tumor markers include (+) CD20, (-) CD10, (-) CD5.

Surgery is often used to get a tissue sample to diagnose and classify lymphoma but it is very rarely used as a treatment option because lymphoma is a cancer of the lymphatic system that circulates lymph fluid throughout the body. It is a systemic disease. However, surgery is sometimes used to treat lymphoma that start in certain extra nodal organs, such as thyroid, stomach, that have not spread beyond these organs.

Surgery is the responsibility of the surgical oncologists.

- (C) The presence of Reed Sternberg (RS) cells (in HD) differentiates Hodgkin's from Non-Hodgkin's lymphoma. NHL types are 1) Slow-growing/Indolent 2) Aggressive 3) Highly aggressive. NHL is of T-cell or B-cell origin. Included in the slow growing group are: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma, Follicular Lymphoma, and MALT Lymphoma. Diffuse Large B Cell Lymphoma is classified under the Aggressive type of NHL Lymphoma. Burkitt's Lymphoma, Lymphoblastic Lymphoma and AIDS-related Lymphoma is considered Highly Aggressive NHL. The many specific types are sometimes grouped together into slow-growing (indolent), aggressive, or very aggressive categories. Aggressive and highly aggressive lymphomas grow more rapidly and spread throughout the body quickly. Without treatment most patients live only a short time. Fortunately, aggressive and highly aggressive lymphoma responds well to chemotherapy, and many can be cured.
- (D) For NHL, the stage of disease is less predictive of outcome compared with HD. The histological type of NHL is the most important prognostic determinant. Staging system is the same for HD and NHL (Ann Arbor).

Stage I	The lymphoma is in lymph node or nodes in only one region, such as the neck, groin or underarm.
Stage II	The lymphoma is in two groups of lymph nodes, and these are on the same side of the diaphragm.
Stage III	The lymphoma is only in lymph nodes but on both sides of the diaphragm.
Stage IV	The lymphoma is widespread in an organ or organs or skin including bone marrow.
*All stages:	A – without weight loss/fever/sweats B – with weight loss/fever/sweats

- (E) Treatment should be considered in patients:
- who have large tumor masses,
 - with a steady tumor growth in the past 6 months,
 - with immune system that is destroying the blood cells,
 - with occurrence of frequent serious infections,
 - with vital organ damage,
 - with low blood counts,
 - with lymphocyte count doubling within a year,

- h. eligible for a clinical trial and
- i. who wants treatment.

Chemotherapy (CTx/ chemotx) is the mainstay of treatment when lymphoma is not a localized disease; it is the treatment of choice for majority of NHL. The general approach is to treat patients until they achieve CR and then administer 2 additional cycles.

In stage I/II, tumor lesion < 4 inches, subsequent 3-4 cycles of chemotherapy are given before RT, more cycles may be given if lactic dehydrogenase (LDH) or Beta-2 microglobulin level is high or if lymphoma is in the chest. If lymphoma is > 4 inches, 6-8 cycles may be given. Each cycle is given every 3 weeks. Rituximab may be given for CD20 positive patients.

Stage III/IV disease, is treated mainly with CHOP therapy. If International Prognostic Index (IPI) is low, 6-8 cycles are given with or without Rituximab. If the IPI is high, a clinical trial with peripheral stem cell transplantation may be done. If lymphoma never shrunk by 50% or not completely given by end of treatment or lymphoma is recurrent, new treatment is needed. Favorable IPI for all patients are age <60 years, Stage I-II, number of extranodal sites <1, ECOG 0-1, and LDH normal; in patients <60 years, favorable IPI are Stage I-II, ECOG 0-1, LDH normal.

Chemotherapy can be used alone or in combination with radiotherapy. Drugs can be used singly (e.g., rituximab particularly for CD-20(+) lymphoma) or usually in combination (CHOP, CHOP-Rituximab, DHAP, ICE, MIME).

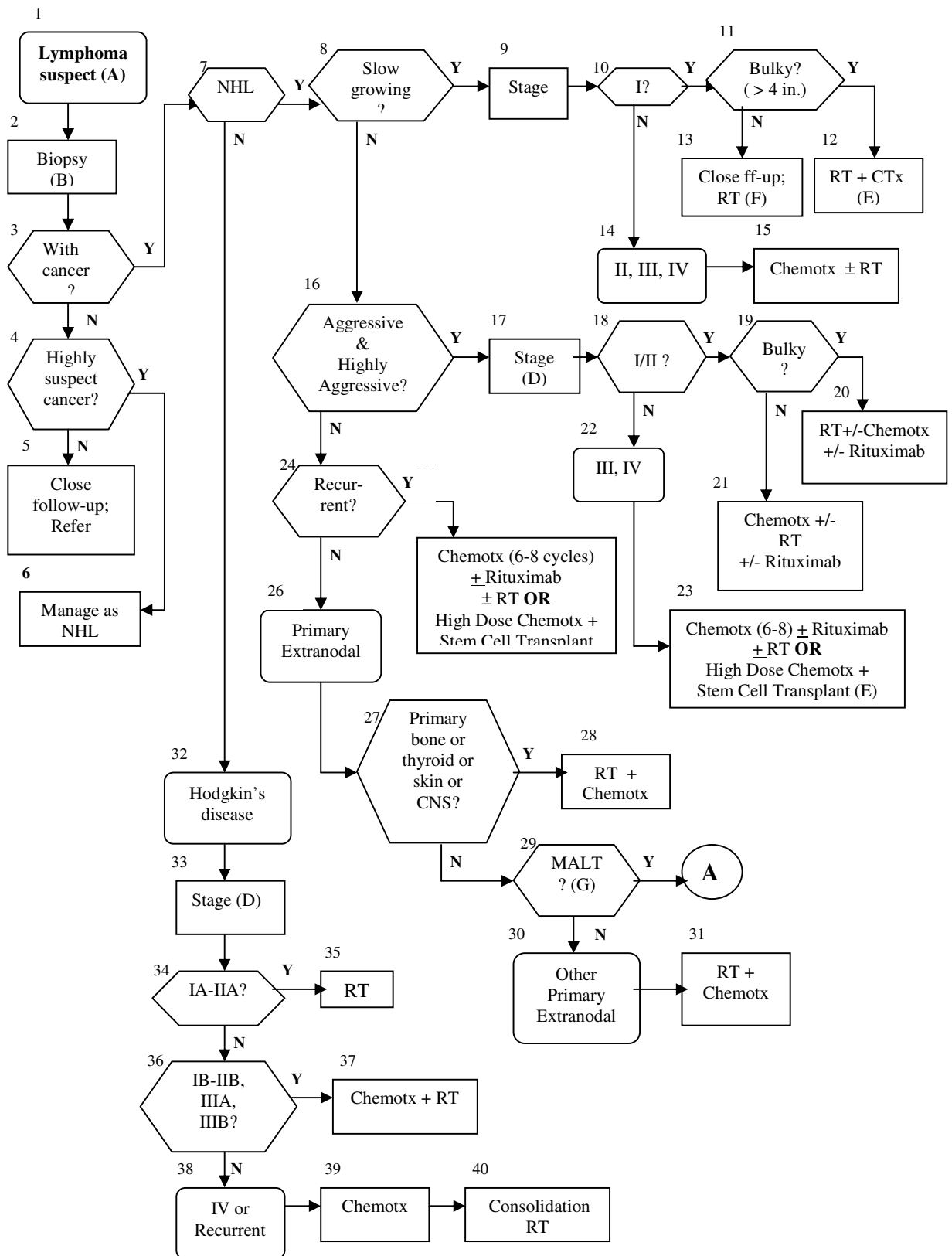
In recurrent or aggressive NHL, high dose chemotherapy plus autologous stem cell transplant is an option.

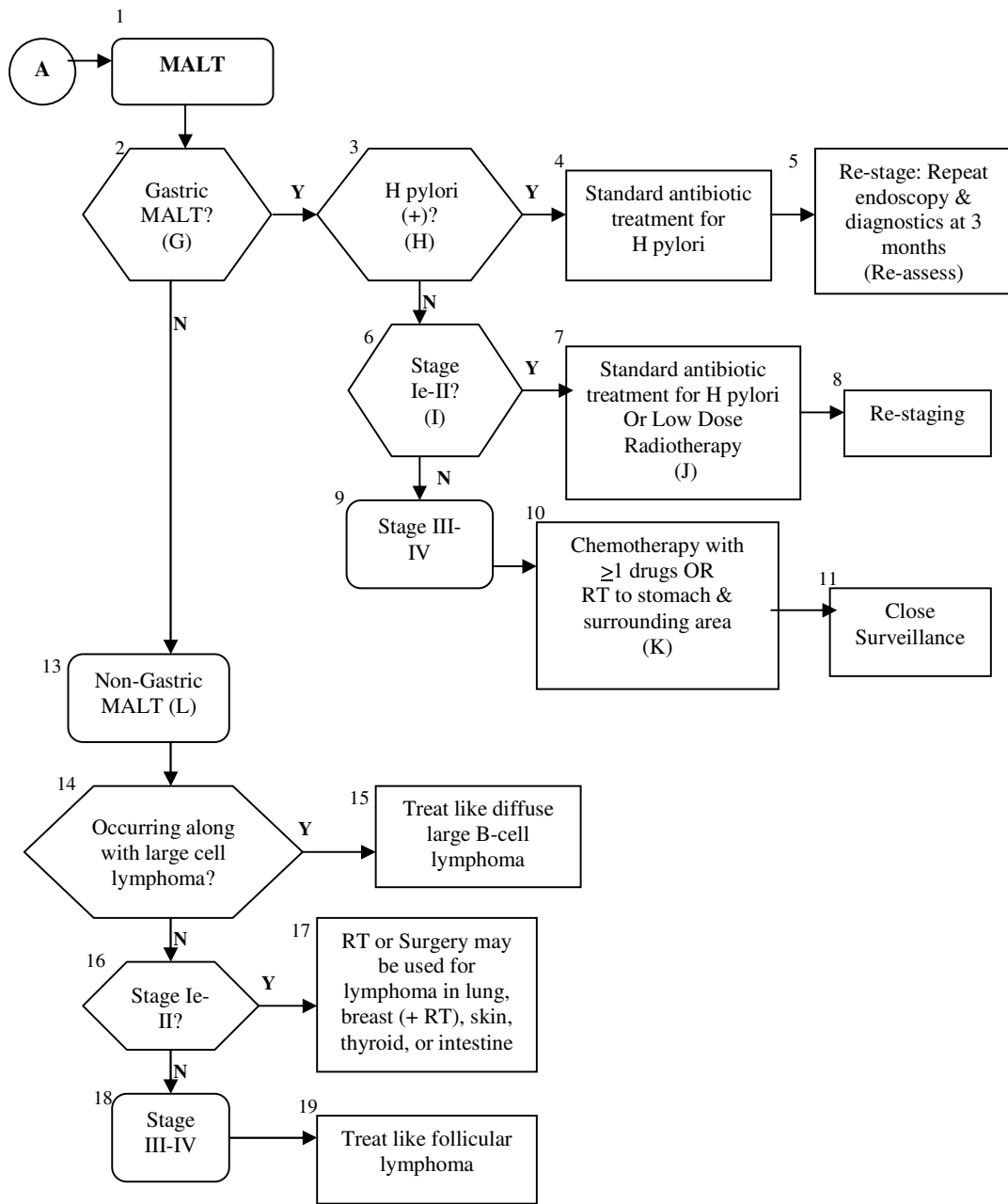
Chemotherapy is the responsibility of the medical oncologists.

- (F) Radiotherapy (RT) is the primary treatment modality for majority of patients with early stages of HD (Stage I/II). The role of radiotherapy for NHL has progressively decreased as chemotherapy regimens have become more effective; it can be the primary or adjuvant treatment in selected patients. It is also used in the palliative setting for lesions in the brain, and in spinal cord compression or in nerve compression causing pain.

Radiotherapy is the responsibility of radio-oncologists.

- (G) For Gastric MALT, re-staging and re-evaluation with follow-up endoscopy with biopsy is done every 3 months. If neither lymphoma nor H pylori is found no further treatment is needed. If H pylori is gone but lymphoma persists, then 3 more months of observation is suggested or radiation therapy can be given to the stomach, particularly if there are symptoms. If lymphoma is gone but H pylori persist, then another course of different antibiotics should be given. If both lymphoma and H pylori persist, a second course of different antibiotics can be given if lymphoma is not growing. If it is growing, RT to the stomach and surrounding area is suggested. If lymphoma has returned after RT, it should be treated like follicular lymphoma. If lymphoma has returned after antibiotic therapy, RT is given. If it has spread away from the stomach, treat as follicular lymphoma.
- (H) H. pylori can cause acute and chronic gastritis, duodenitis, gastric peptic ulcer and duodenal ulcer and non-ulcer dyspepsia. H. pylori has been identified as a risk factor for gastric carcinoma and MALT Lymphoma. Nearly 90% of patients with duodenal ulcer and > 70% of those with gastric ulcer and > 80% of patient with gastric cancer have H. pylori infection. Several effective treatments include use of antibiotic such as, clarithromycin, metronidazole and omeprazole.
- (I) Stage Ie-II - localized to one area of the body.
Stage III-IV - low grade
- (J) Treatment with only antibiotic is suggested if the lymphoma is confined to the stomach and infection with H. pylori is found. If the lymphoma is a little more advanced and affects surrounding lymph nodes, radiation therapy maybe added.
- (K) For more advanced stages, widespread lymph node or organ involvement, chemotherapy maybe given if there are reasons for treatment. Reasons for treatment are presence of bleeding from stomach, vital organ damage, very large tumor, steady growth of lymphoma, symptoms, or patient wants treatment. For these stages, the lymphoma may be treated as if it were a slow growing or follicular lymphoma.
- (L) Usual sites of non-gastric MALT lymphomas are salivary glands, skin, breast, small or large intestines, thyroid, tissue around the eyes, and lung.





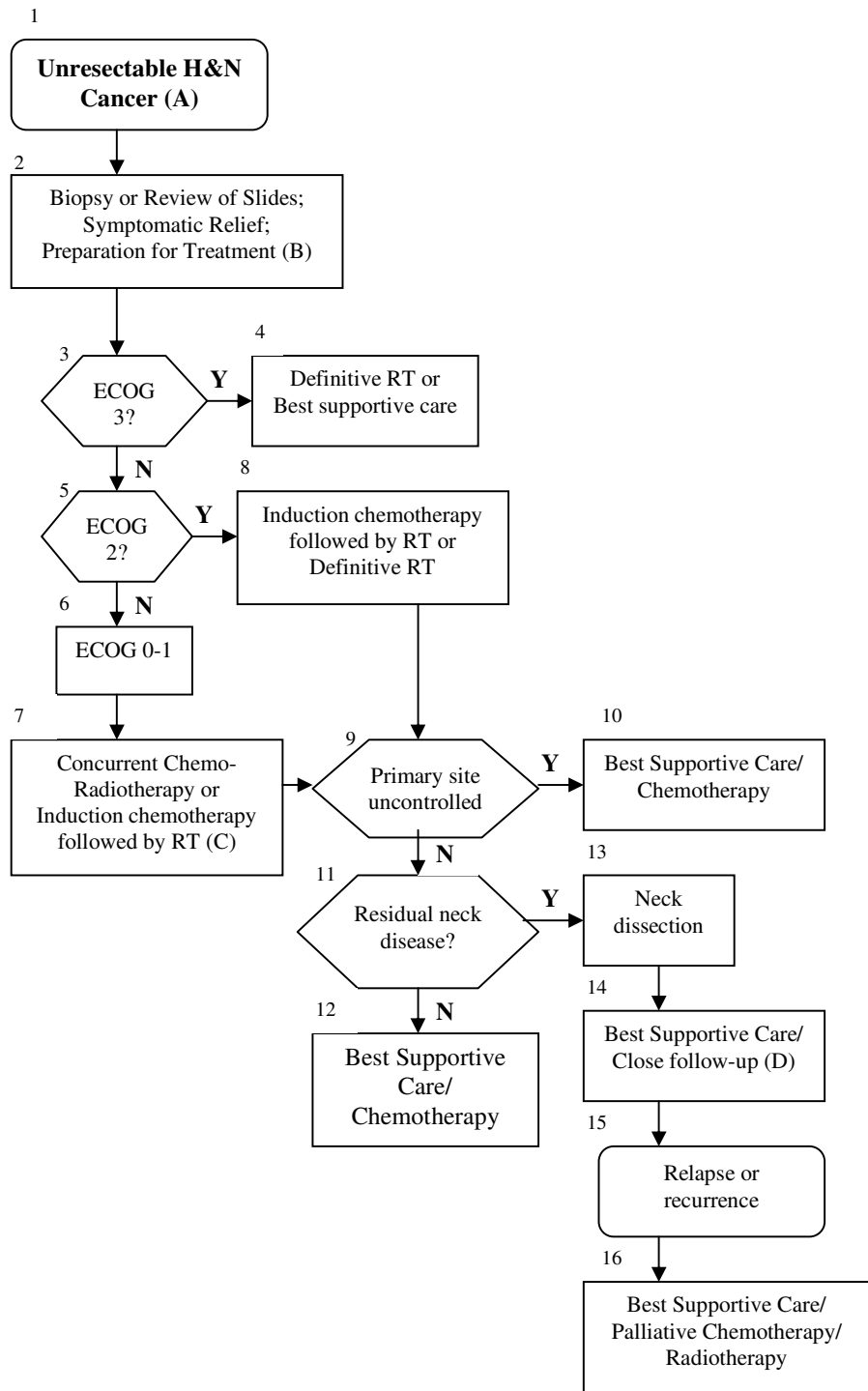
UNRESECTABLE HEAD AND NECK CANCER

The management of unresectable H&N cancer must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient. Here, members of the team are surgeon, supportive care internist, radio-oncologist, and medical oncologist.

- (A) Unresectable head and neck (H&N) cancer refers to newly diagnosed T4b (tumor regionally), any N, or unresectable N+, M0 disease, or disease wherein surgeon doubts the ability to remove all gross tumor on anatomic grounds or unable to remove without imposing unacceptable morbidity.
- (B) Histological diagnosis of cancer is ascertained by review of slides. Symptomatic relief (pain, nutrition, infection, support group) is done while preparing the patient for definitive treatment. M0 stage is ascertained – do chest x-ray (chest CT is considered for patients at high risk for thoracic metastasis), ultrasound of liver, bone scan/ brain scan (if symptomatic). Do dental clearance. Do speech and swallowing evaluation as indicated.
- (C) Treatment is usually concurrent chemoradiation with ≥ 70 Gy for primary and gross adenopathy and 44-50 Gy to low risk neck nodes. Higher doses of definitive RT without chemotherapy can be given for medically unfit or those who refuse chemotherapy.

The choice of chemotherapy should be individualized based on patient characteristics (performance status, goals of therapy). Chemotherapy drugs active in H&N cancers are cisplatin, 5-FU, hydroxyurea, paclitaxel, carboplatin, docetaxel, capecitabine, methotrexate, ifosfamide, bleomycin, gemcitabine, cetuximab, fluorouracil. Uncontrolled disease can be given 2nd line chemotherapy +/- radiotherapy.

- (D) For those patients post neck dissection or in complete response (CR) or major response, follow-up can be done as follows:
 - Physical exam:
 - Year 1, every 1-3 months
 - Year 2, every 2-4 months
 - Year 3-5, every 4-6 months
 - Thyroid stimulating hormone (TSH) every 6-12 months, if neck irradiated
 - Speech and swallowing evaluation and rehabilitation as indicated



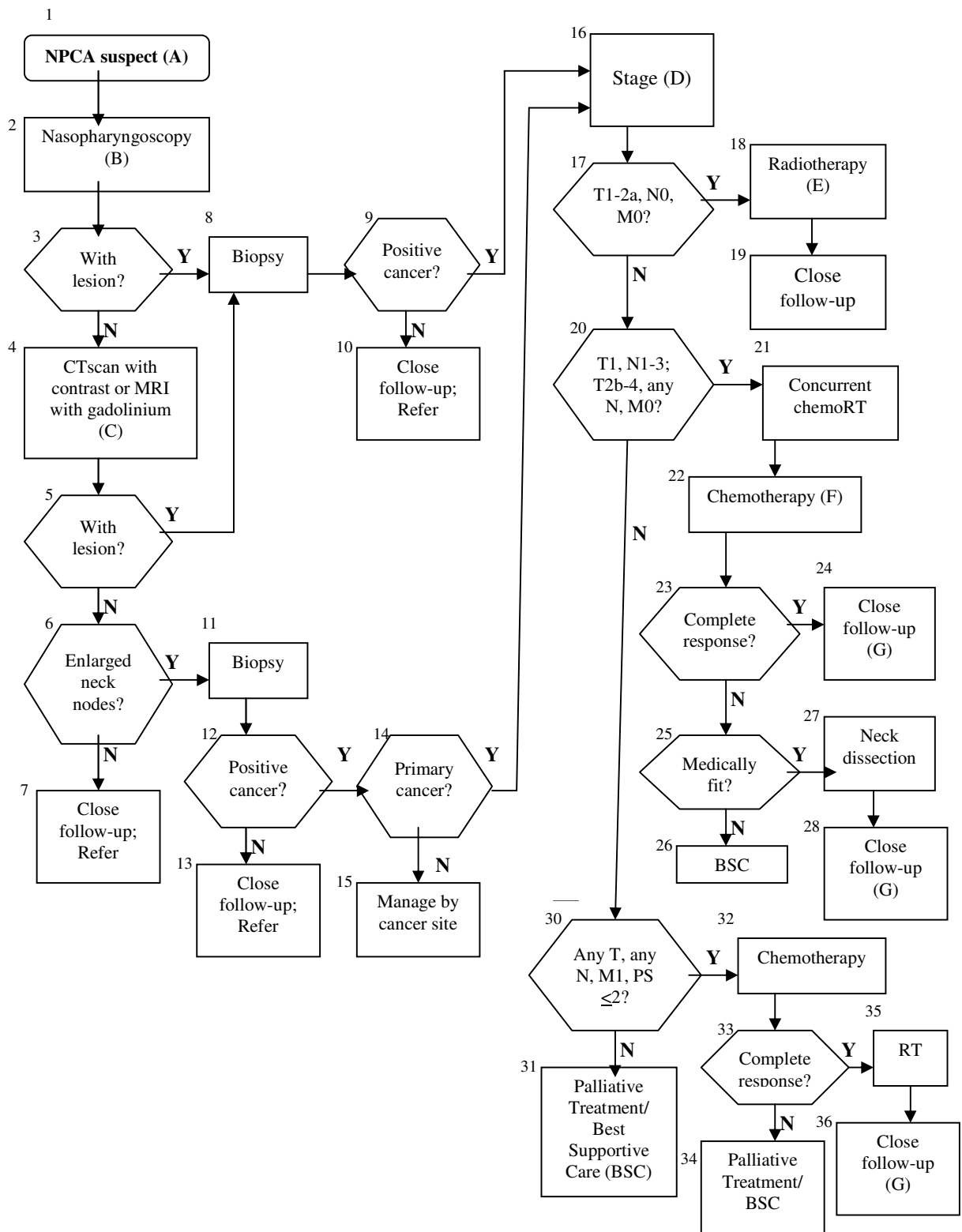
NASOPHARYNGEAL CARCINOMA (NPCA)

The management of NPCA must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient. Here, members of the team are surgeon, supportive care internist, radio-oncologist, and medical oncologist.

- (A) Common presentations are lymph adenopathies (cervical LNs), otologic (obstruction to Eustachian tube), and nasal. Atypical pain is due to trigeminal nerve involvement. Cranial nerve involvement occurs in 15% of cases and commonly involves CN V and/or VI.
- (B) Nasopharyngoscopy with a nasopharyngeal mirror or via fiber optic nasopharyngoscope is mandatory.
- (C) Do complete history & PE. Do chest x-ray or chest CT (considered for patients at high risk for thoracic metastasis), CT with contrast or MRI with gadolinium of nasopharynx and base of skull to clavicles. CTscan allows excellent visualization of the nasopharynx (and its extent) and can detect lesions not seen on nasopharyngoscope.
Do dental evaluation and clearance. Do speech and swallowing evaluation as indicated.
- (D) Imaging for distant metastases (chest, liver, bone) for N2-3 disease includes CT. PET scan can be done, as indicated. Staging is according to AJCC 2006:

Stage 0	Tis Carcinoma-in-situ N0M0
Stage I	T1 Confined to nasopharynx N0M0
Stage IIA	T2a Extends to oropharynx and/or nasal cavity w/out parapharyngeal extension N0M0
Stage IIB	T1N1 Unilateral LN metastasis, <=6cm in greatest dimension, above supraclavicular fossa T2 Extends to soft tissues N1M0 T2aN1M0 T2b Any tumor with parapharyngeal extension N0M0 T2bN1M0
Stage III	T1N2 Bilateral metastasis in LNs, <=6 cm in greatest dimension, above supraclavicular fossa T2aN2M0 T2bN2M0 T3 Invades bony structures and/or paranasal sinuses N0M0 T3N1M0 T3N2M0
Stage IVAT4	Intracranial extension and/or involvement of cranial nerves, infratemporal fossa, hypopharynx, orbit, or masticator space N0M0 T4N1M0 T4N2M0
Stage IVBAny	T N3 Metastasis in a LN/s >6cm and/or to supraclavicular fossa M0
Stage IVCAny	T Any NM1

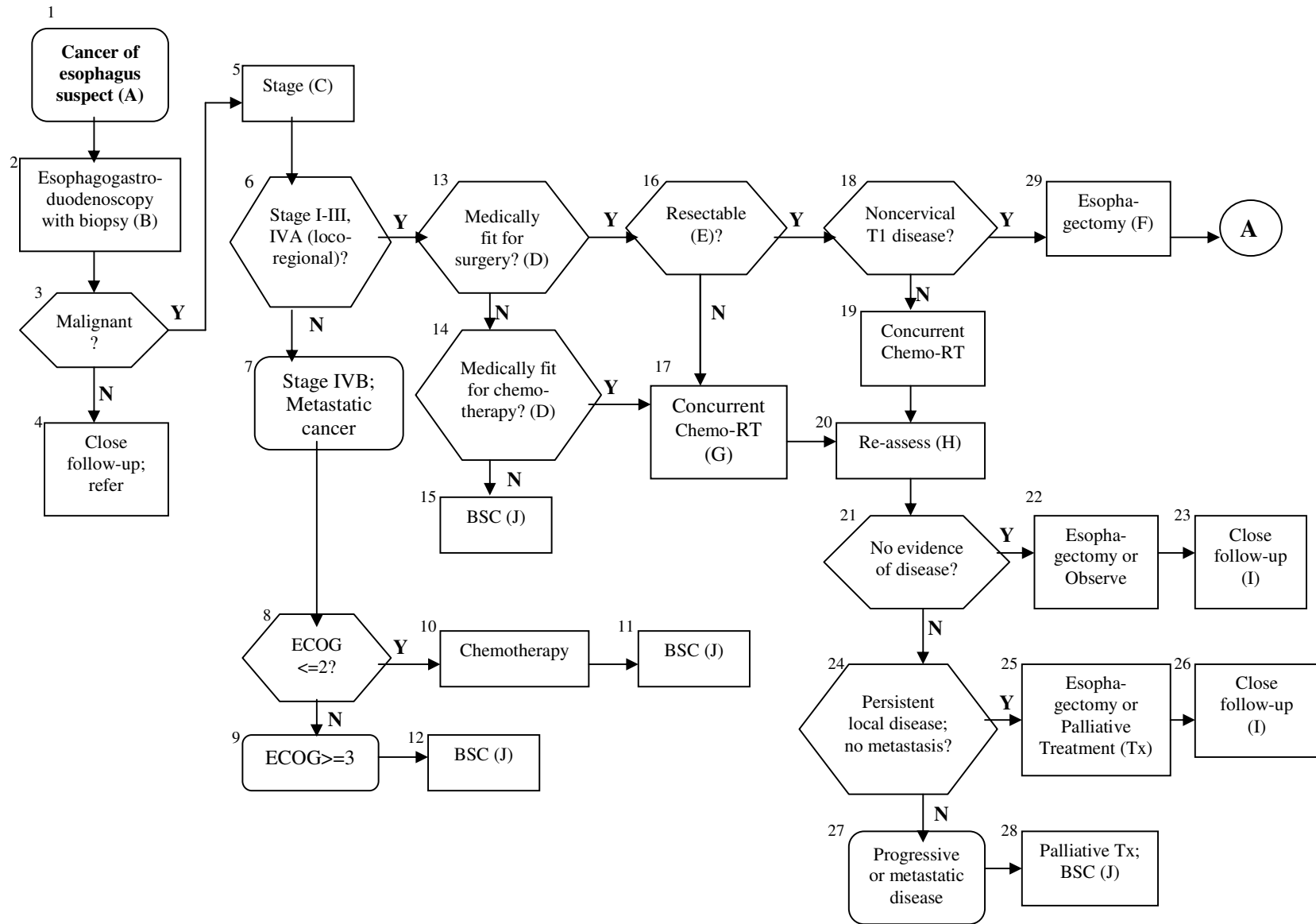
- (E) The inaccessibility of the nasopharynx, the proximity of tumors to skull base and to cranial nerves and the widespread lymphatic involvement, dictate radiotherapy rather than surgery as the procedure of choice. Occasionally, neck dissection may be indicated for persistent lymph adenopathy if primary is controlled and distant metastasis is absent. Definitive radiotherapy (RT) includes ≥ 70 Gy for primary and gross adenopathy, and ≥ 50 Gy for low-risk nodal stations.
- (F) Concurrent chemotherapy-RT (chemoRT) followed by chemotherapy (chemotx) alone is preferred for T1, N1-3; T2b-T4, any N disease:
Commonly cisplatin+RT followed by cisplatin-FU. Other drugs include gemcitabine, methotrexate, bleomycin, capecitabine, carboplatin, paclitaxel, docetaxel.
- (G) Follow-up schedule includes PE every 1-3 months for year 1, every 2-4 months for year 2, every 4-6 months for year 3-5, and every 6-12 months thereafter after 5 years. TSH is taken every 6-12 months, if neck is irradiated. Speech and swallowing rehabilitation is done as indicated.

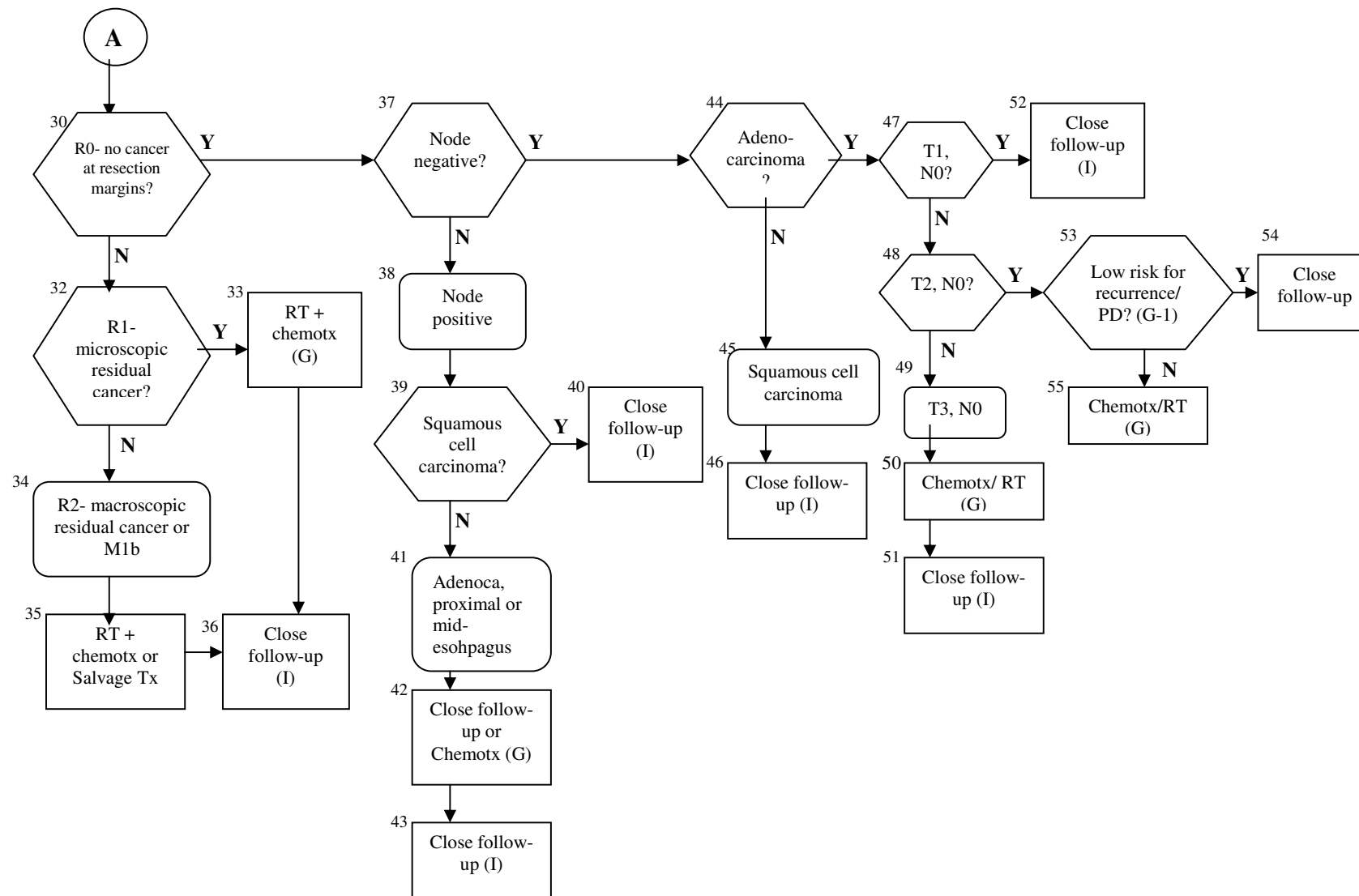


CANCER OF THE ESOPHAGUS

The management of esophageal cancer must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

- (E) Dysphagia and weight loss are the most common symptom at presentation in about 90% of patients. Hematemesis is an uncommon occurrence and can herald a rapid fatal outcome due to aortic wall penetration by the cancer. Early symptomatology includes chest pain or odynophagia but usually not severe enough to stimulate medical attention. Signs of invasion of adjacent organs are late and include hoarseness, SVC syndrome, cough due to tracheo- or bronchio-esophageal fistula, Horner's syndrome, paralyzed diaphragm, malignant pleural effusion or massive hematemesis.
- (F) Esophagogastroduodenoscopy to visualize entire upper GI tract, if possible, with biopsy. Do complete history & physical exam (H&P). Esophagogram is useful alternative to detect and define primary lesions. Irregular filling defects or ulcerative strictures, deviation or angulations of the barium column are signs of malignancy. Double contrast with air and barium is useful for smaller lesions. Barium swallow determines the length of the lesion, extent and circumferential involvement and degree of obstruction but the combination of endoscopy with cytology brushing and perimeter biopsies of a mass will have the diagnosis of cancer with 90% accuracy. SMA-12 can be done as a tumor marker.
- (G) Do chest x-ray or chest CT scan. Abdominal CT scan can evaluate the presence of nodal involvement, invasion to adjacent structures and metastatic areas. AJCC staging (2002) is as follows:
- | | |
|-----------|--|
| Stage I | T1N0M0, tumor invades lamina propria or submucosa |
| Stage IIA | T2-3N0M0, tumor invades muscularis propria-adventitia |
| Stage IIB | T1-2N1M0, regional LN involvement |
| Stage III | T3N1M0/ T4anyNM0, tumor invades adventitia-adjacent structures |
| Stage IV | anyTanyNM1 |
| Stage IVA | anyTanyNM1a, |
| Stage IVB | anyTanyNM1b |
-
- | | | |
|----|---|---|
| M1 | Distant metastasis | |
| | Tumors of the lower thoracic esophagus: | M1a – metastasis in celiac LNs
M1b – other distant metastasis |
| | Tumors of the mid-thoracic esophagus: | M1a – not applicable
M1b – nonregional LNs &/or other distant metastasis |
| | Tumors of the upper thoracic esophagus: | M1a – metastasis in cervical nodes
M1b – other distant metastasis |
- (H) Medically fit to tolerate major abdominal and/or thoracic surgery. A cardiopulmonary clearance is required.
- (I) Resectable T4 – involvement of pleura, pericardium or diaphragm; unresectable T4 – invasion of aorta, trachea, heart, great vessels
- (J) Transhiatal or trans-thoracic, or minimally invasive; gastric reconstruction preferred. Feeding jejunostomy for postoperative nutritional support, generally preferred
- (K) Chemoradiotherapy is the preferred modality for cervical esophageal carcinoma. 5FU/cisplatin in conjunction with RT (50-50.4 Gy) is usual therapy. Esophageal squamous cell carcinoma (more common histopathological diagnosis) is radiosensitive and local tumor eradication for T1 disease is frequently attainable. Other chemotherapy drugs include taxane-based, irinotecan-based; investigational drugs include capecitabine, gemcitabine, oxaliplatin. Pre-op and/ or post-op chemotherapy can be given. For metastatic cancer, chemotherapy may be tried for 2 sequential regimens; if failed, do BSC.
- G-1: In T2N0M0 adenocarcinoma, just surgery may be done, except for higher risk patients such as poorly differentiated histology, lymphovascular invasion, neurovascular invasion or young patients. Limit to esophageal or GE junction patients.
- (L) Assessment >=4 weeks, endoscopy with biopsy and brushings
- (M) Close surveillance in asymptomatic patients includes – H&P with nutritional counseling every 4 months for 1 year, every 6 months for 2 years, then annually. As indicated tests are – chemistry profile/ CBC, chest x-ray, radiology and endoscopy (eg, persistent or recurrent dysphagia), dilatation for anastomotic stenosis. For recurrent disease – surgery can be done if recurrence limited to anastomosis, otherwise radiotherapy (RT)-chemotherapy (chemotx) and/or endoscopic therapy is done as salvage therapy.
- (N) Best supportive care (BSC) includes: a) obstruction – stent, laser, photodynamic therapy, RT, b) nutrition – enteral feeding, c) bleeding – RT or surgery and/ or endoscopic therapy, d) esophageal dilatation





GASTRIC (STOMACH) CARCINOMA

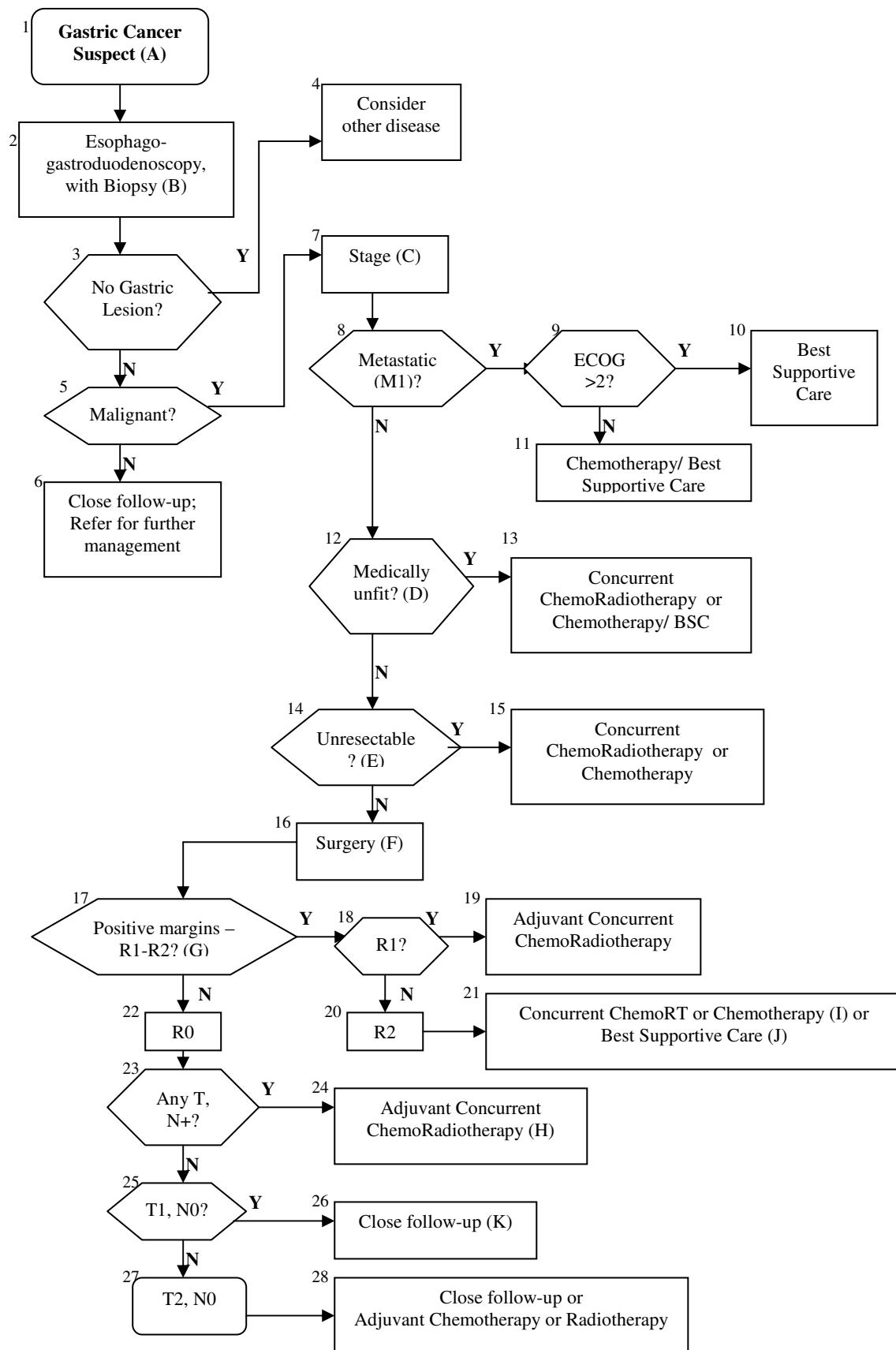
The management of gastric carcinoma must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

- (A) Vague epigastric discomfort is the most frequent symptom associated with gastric cancer and 90% of patients experience epigastric pain. Weight loss occurs in 80% of patients, early satiety in 65%, anorexia in 60%, and 50% of patients experience dysphagia and vomiting. Only 1% of patients are asymptomatic. The physical signs of gastric cancer are invariably related to metastatic or unresectable disease. 1/3 of patients will have signs of metastatic disease, i.e., palpable epigastric mass, ascitis, jaundice, supraclavicular adenopathy, left axillary adenopathy, hepatomegaly, rectal shelf, generalized cachexia, on their initial presentation. A complete history and PE is done.
- (B) Flexible esophagogastroduodenoscopy or gastroscopy is a very accurate modality for detecting and defining primary lesions, and allows biopsies of most gastric lesions. Generous biopsies of all gastric ulcers should be performed. Infiltrative lesions are the type least likely to undergo biopsy accurately. The gross appearance of gastric adenocarcinoma is characterized by 4 different types of presentation which are important for their varied prognosis:
- Ulcerative carcinoma – most common
 - Polypoid cancers or fungating
 - Scirrhus carcinoma – worst prognosis, with lesions infiltrating the gastric wall producing a thickened, nodular, shortened stomach (called linitis plastica)
 - Superficial gastric cancer is an uncommon variety, characterized by sheet-like collections of cancer cells replacing the normal mucosa
- (C) Abdomino-pelvis CT scan is the most valuable of all modalities for determining local invasion and distant metastasis. Do chest x-ray PA-L, LFT, CEA, CA 19-9. In preparation for therapy, get CBC, creatinine. AJCC TNM Staging (2002) is used:
- T1 - Tumor invades lamina propria or submucosa
 - T2 - Tumor invades muscularis propria or subserosa
 - T2a - Tumor invades muscularis propria
 - T2b - Tumor invades subserosa
 - T3 - Tumor penetrates serosa (visceral peritoneum) without invasion of adjacent structures
 - T4 - Tumor invades adjacent structures
 - N0 - No regional LN metastasis
 - N+ - N1 (1-6 LNs), N2 (7-15 LNs), N3 (>15 LNs)
 - M0 - No distant metastasis
 - M1 - Distant metastasis
- (D) Medically able to tolerate major abdominal surgery – usually ECOG \leq 2 without co-morbidities
- (E) Criteria for unresectability for cure are:
- Peritoneal seeding or distant metastasis
 - Inability to perform a complete resection
 - Invasion or encasement of major vascular structure
- (F) Surgery is the standard modality of treatment. The surgery procedures are:
- Distal (body + antrum) – prefer subtotal gastrectomy
 - Proximal (cardia) – total or proximal gastrectomy
- Subtotal gastrectomy entails removal of a large part of the stomach en bloc with greater and lesser omenta, and distal pancreatectomy, with regional lymph node dissection (include greater curvature, lesser curvature, splenic, celiac, and hepatic LNs). Splenectomy is avoided. Consider placing a feeding jejunostomy tube. A >5cm proximal and distal margins from gross tumor is preferred. A minimum of 15 LNs should be evaluated. Give Vitamin B12 supplement for gastrectomized patients.
- (G) R classification refers to amount of residual cancer remaining after tumor resection:
- R0 - No macroscopic/ microscopic residual disease (i.e., negative lines of resection or margins)
 - R1 - Positive microscopic residual disease (i.e., positive lines of resection)
 - R2 - Positive macroscopic residual disease; no distant metastasis
- (H) Concurrent chemo-radiotherapy can be given as follows - Chemotherapy is used as a cytotoxic and/ or preferably a radiosensitization agent.
- Pre-operative – recommended in localized unresectable cases
 - 5-FU+leucovorin
 - Capecitabine-based
 - Cisplatin-based
 - Taxane-based
 - Irinotecan-based
 - Post-operative –
 - 5-FU+leucovorin

- Capecitabine-based
- 5-FU+ cisplatin
- Taxane-based

Radiotherapy in combination with chemotherapy is given at 45-50.4 Gy. For R0 T2-N0 patients, adjunctive treatment can be observe or chemotherapy (5-FU-based) +/- RT (with RT if with high risk features such as poorly differentiated or higher grade cancer, lymphovascular invasion, neural invasion, or <50 years of age).

- (I) Chemotherapy alone can be given as single or combination (e.g., ECF, DCF, FOLFIRI, XELIRI) with the following drugs - 5-FU+leucovorin, capecitabine, irinotecan, oxaliplatin, cisplatin, taxane (e.g., docetaxel), anthracycline (e.g., epirubicin), mitomycin-C, nitrosureas.
- (J) Supportive care modalities include stent/ laser/ photodynamic therapy/ RT/ surgery (for obstruction), enteral feeding/ nutritional counselling (for nutrition), RT/ analgesics (for pain control), RT/ surgery/ endoscopic therapy (for bleeding)
- (K) For R0, T1-N0 patients and other patients in complete response (CR) or major response after post-operative adjunctive treatment, close surveillance is done every 4-6 months for 3 years and then annually, with radiologic imaging (CXR, ultrasound or abdomino-pelvic CT), or endoscopy as clinically indicated. PET scan can be used to find suspected metastasis upon surveillance.



COLON RECTUM CANCER

The management of colon rectum cancer must be multi-disciplinary interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

- (A) A change in bowel habit, whether constipation or diarrhea, in a patient >40 years old directs suspicion of colon cancer.
- COLON: A tumor in the ascending colon may present with microcytic anemia, occult blood in the stool, or a palpable mass in the right lower quadrant. A tumor in the descending colon presents with hematochezia, obstructive symptoms and small caliber stools.
- RECTUM: Lesions in the rectum present with local bleeding, pain, change in bowel habits and stool caliber, and then tenesmus.
- (B) COLON: Colonoscopy is a very accurate diagnostic tool for detecting and defining primary colon lesions. Double contrast barium enema can also be a useful tool in detecting and defining primary colon lesions, particularly in absence of colonoscopy equipment.
- RECTUM: Most cancers can be detected by simple digital exam (65-80%). Once discovered, proctosigmoidoscopy with biopsy follows to establish diagnosis.
- (C) First-degree relatives of patients with diagnosed adenomas or invasive carcinoma are at increased risk for colorectal cancer. Colon cancer patients, especially those 50 years or younger and those with suspected hereditary non-polyposis colon cancer (HNPCC), familial adenomatous polyposis (FAP) and attenuated FAP should be counseled regarding family history.
- (D) Carcinoembryonic antigen (CEA) is a tumor marker for colorectal cancer. It is not recommended for use as a screening tool for colorectal cancer because of high false positive rates. Elevated levels upon serial determination, however, may raise the suspicion of an occult malignancy. Consider doing tumors markers for a highly suspected cancer case who is negative for biopsy (CEA, CA-19-9, CA-125, AFP).
- (E) More than 90% of colorectal cancers are adenocarcinomas.
- (F) The TNM staging according to the AJCC (6th ed.) depends on the depth of wall invasion and presence or absence of nodal metastases. Minimum staging workup aside from the pathological evidence includes chest x-ray PA-L and CT scan of whole abdomen. Colon rectum cancer usually metastasizes to the adjacent structures (e.g., mesentery, LNs), liver, lung, and bone. CT scan is the most valuable of all modalities for detecting local invasion and distant metastasis.

Rectal cancer should be fully staged. Endoscopic biopsy specimens of the lesions should undergo careful pathology review for evidence of invasion into the muscularis mucosa. Endorectal UTZ and MRI are recommended to assess the depth of invasion and lymph node status. T1-2 N0 should be based on assessment of endorectal UTZ or MRI

Primary Tumor (T)

Tx	Primary tumor can not be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ: intraepithelial or invasion of lamina propria
T1	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades through the muscularis propria into the subserosa, or into non-peritoneum pericolic or perirectal tissues
T4	Tumor directly invades other organs or structures, and/or perforates visceral peritoneum

Regional Lymph Node (N)

Nx	Regional lymph nodes can not be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1 to 3 regional lymph nodes
N2	Metastasis in 4 or more regional lymph nodes

Distant Metastasis (M)

Mx	Distant metastasis can not be assessed
M0	No distant metastasis
M1	Distant metastasis

Stage Grouping

Stage	T	N	M	Dukes
0	Tis	N0	M0	-
I	T1	N0	M0	A
	T2	N0	M0	A
IIA	T3	N0	M0	B
IIB	T4	N0	M0	B
IIIA	T1-T2	N1	M0	C
IIIB	T3-T4	N1	M0	C
IIIC	Any T	N2	M0	C
IV	Any T	Any N	M1	D

- (G) Surgery is the primary mode of treatment for colorectal cancer. The principles of surgical treatment are: 1) laparotomy for staging, 2) wide en bloc resection of the tumor, 3) lymphadenectomy for staging as well as possible therapeutic benefit. By-pass surgery (e.g., colostomy) can be done for palliation.

RECTUM: For abdomino-perineal resection or low anterior resection or colo-anal anastomosis using total meso-rectal excision, a minimum of 4 lymph nodes is to be examined.

CRITERIA FOR RESECTABILITY OF METASTASES:

Liver: Complete resection must be feasible. There should be no unresectable extrahepatic sites of disease. Re-evaluation for resection can be considered in otherwise unresectable patients after neoadjuvant therapy.

Lung: Complete resection based on anatomic location and extent of disease with maintenance of adequate function is required. Resectable extrapulmonary metastases do not preclude resection. The primary tumor must be controlled. Re-resection can be considered in selected patients.

- (H) Chemotherapy is the primary mode of treatment after surgery. Medical oncology specialists plan for, administer and monitor effects of the chemotherapy, after the surgical oncology physicians have done the definitive surgery. Chemotherapy can either be: 1) neo-adjuvant before definitive surgery mainly to decrease tumor to 'operable' size, 2) adjuvant after definitive surgery to eradicate micro metastasis and to prolong window prior tumor recurrence/ metastasis, and 3) palliative to reduce pain, obstruction, mainly promoting cancer disease symptom control. Chemotherapy can be given as 1st line or 2nd line or 3rd line, such that colon cancer can be responsive to another drug regimen if it recurred or progressed after a previous drug regimen. Currently more frequently used chemotherapy drugs in colon adenocarcinomas are 5-FU, capecitabine, CPT-11 or irinotecan, oxaliplatin, bevacizumab. Usual chemotherapy combination regimens are FUFA, FOLFOX, FOLFIRI, XELOX, or XELIRI ± bevacizumab. 2nd line combination chemotherapy + cetuximab can be used in K-ras wild type colon cancers.

- (I) Colon cancer patients who are high risk for systemic recurrence after colon resection are those with histological grade 3-4, lymphatic/vascular invasion and bowel obstruction.

Probability for rectum cancer to recur is relatively low if: 1) < 30 % circumference of bowel, 2) < 3 cm in size, 3) margin clear (3 > mm), 4) mobile, non fixed, 5) within 8 cm of anal verge, 6) T1 or T2, 7) fragmented polyp, 8) no lymphovascular or perineural invasion, 9) well to moderately differentiated, and or 10) no evidence of lymphadenopathy on pretreatment imaging.

Minimum surveillance work-up aside from complete physical exam (plus colostomy site), symptom & weight monitoring, are chest x-ray PA-L and CT scan of whole abdomen every 4-6 months during the 1st 2 years and every year or as symptoms dictate thereafter.

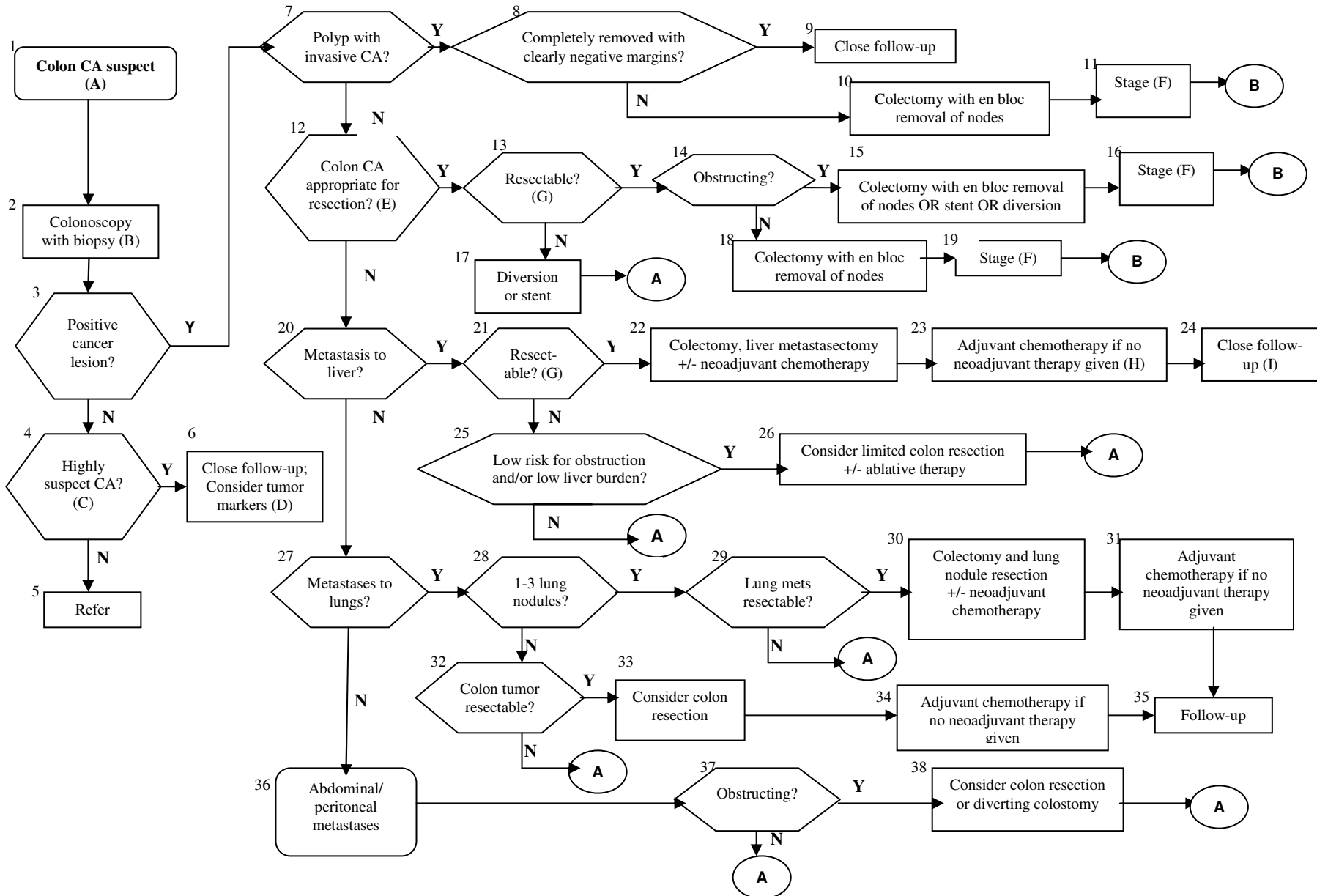
- (J) Best Supportive Care mainly includes management of nutrition, pain, infection, psychosocial well-being, nursing and rehabilitative care, and other pertinent quality of life patient care.
- (K) Radiotherapy under the responsibility of the radiation oncologists is usually an adjunct to surgery/ chemotherapy and for symptom relief particularly in bone pain (metastatic bone lesions).

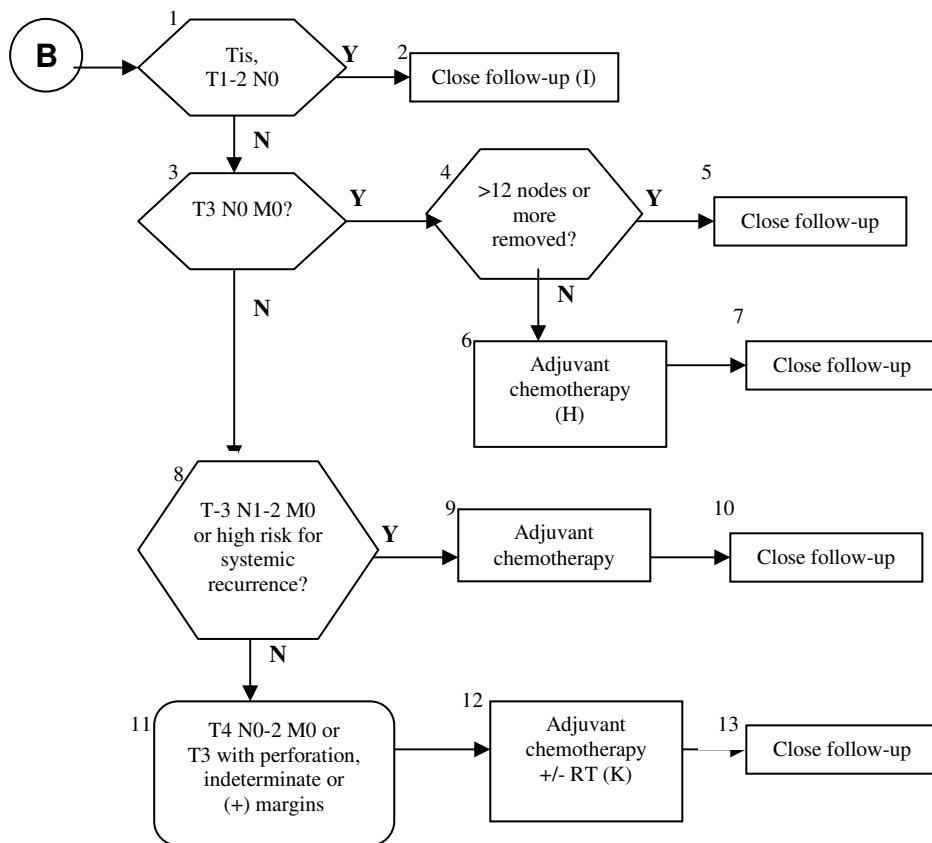
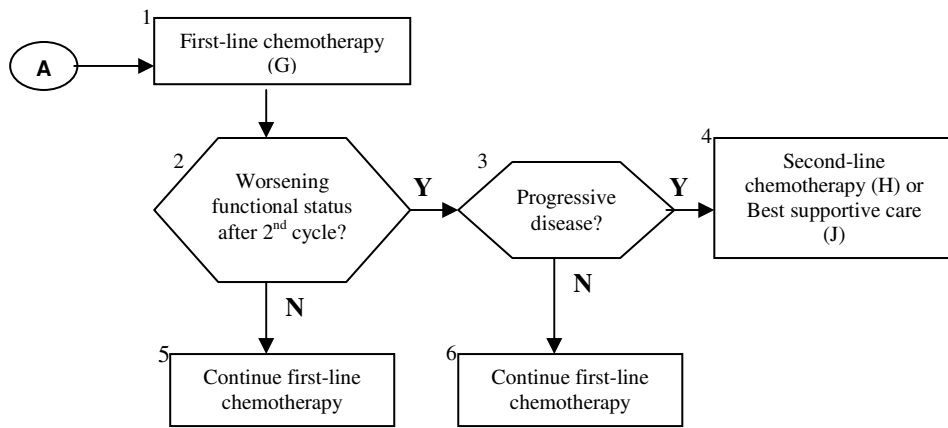
COLON: There is no well-defined role of radiotherapy for primary therapy or adjuvant therapy of colon cancers; it can be used for palliation.

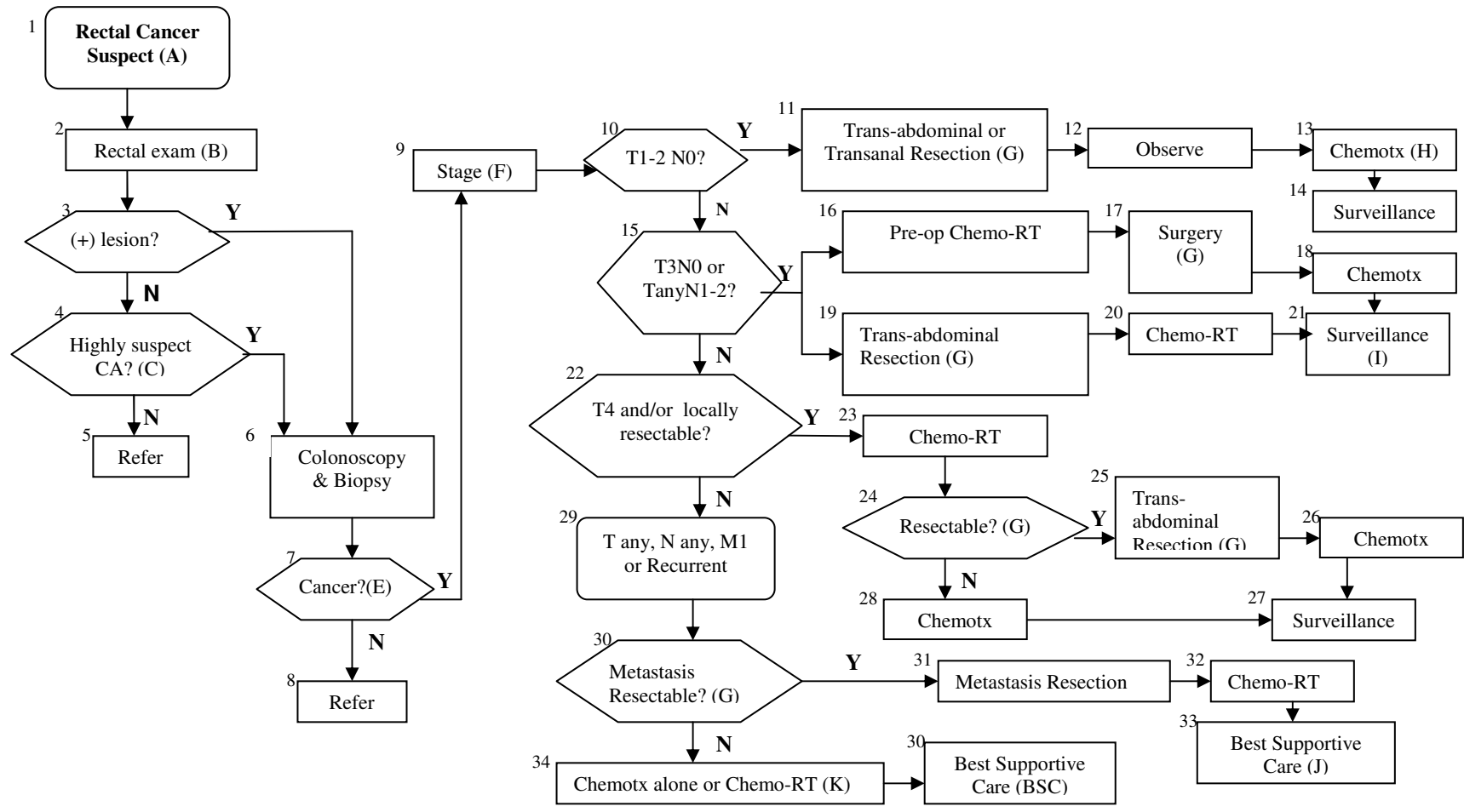
RECTUM: The roles of radiotherapy in rectum cancer are:

- 1) primary treatment if patient is considered medically inoperable
- 2) palliative treatment for pain/ bleeding
- 3) treatment for recurrent disease
- 4) adjuvant treatment after disease resection of Duke's B and C

Radiation treatment fields should include tumor with a 2-5 cm margin, the pre-sacral nodes and internal iliac nodes







PRIMARY HEPATOCELLULAR CARCINOMA (HCC)

The management of HCC must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

- (A) When seen, most Filipino patients (Domingo EO, 1982) will manifest right upper quadrant pain, hepatomegaly, weight loss, and anorexia. Jaundice can occur. On physical exam (PE), there is usually hepatomegaly, ascitis, portal hypertension associated with esophageal varices and splenomegaly. Hepatocellular carcinoma has been associated with cirrhosis (50% or more; mostly macronodular), hepatitis B (70-90% with hepatitis B antigen) and aflatoxin. Do complete history and PE, Hepatitis profile (HepB surface antigen, Hep C antibodies), LFT, creatinine, CBC, AFP, Chest x-ray, prothrombin time (PT).
- (B) Imaging studies with ultrasound are highly sensitive for detecting the disease and directing percutaneous fine needle aspirate biopsies. Using AFP and ultrasound is a sensitive screening system for high-risk population. If there is a history of rising AFP, and ultrasound is negative, do CTscan of the whole abdomen; if no mass is seen, screen every 3 months with AFP, liver ultrasound
- (C) Biopsy can be achieved percutaneously (ultrasound or CTScan-guided) or visually (laparoscopy). 70-90% of primary liver cancer is hepatocellular carcinoma.
- (D) Using radioimmunoassay technique, 70-85% of patients (in high incidence areas, i.e., Asia) with primary liver cancer have elevated AFP (>400 ng/mL). If there is a history of rising AFP, and ultrasound is negative, do CTscan of the whole abdomen; if no mass is seen, screen every 3 months with AFP, liver ultrasound. If AFP is >4000 ng/mL, HepBsAg(+) or AFP is >400 ng/mL, HepBsAg(-), biopsy is not required. In highly suspected metastatic HCC, where AFP<400 ng/mL, HepBsAg(-) or AFP <4000 ng/mL, Hep BsAg(+), in the absence of no biopsy, consider biopsy.
- (E) Once diagnosis is made, further diagnostic workup is necessary to determine disease stage and thus respectability – CXR/CTscan; CTscan of the whole abdomen; if with elevated alkaline phosphatase, do bone scan. CTscan defines extent and number of primary lesions, vascular anatomy, involvement with tumor, and extrahepatic disease; helical CT includes arterial phase enhancement.
TNM classification for carcinoma of liver (HCC; intrahepatic bile duct carcinoma) can be used:
- T1 - solitary, <=2 cm, without vascular invasion
 - T2 - solitary, <=2 cm, with vascular invasion, or multiple, one lobe, <=2 cm, without vascular invasion or solitary, >2 cm, without vascular invasion
 - T3 - solitary, >2 cm, with vascular invasion, or multiple, one lobe, <=2 cm, with vascular invasion, or multiple, one lobe, >2 cm, with or without vascular invasion, or multiple, >1 lobe
 - T4 - tumor beyond the confines of the liver
 - N - N0 or N(+)
 - M - M0 or M(+)
- (F) Two stages of HCC are defined, which dictate choice of subsequent management:
- T1-3, N0 = resectable
 - T4, Nany; M(+) = unresectable

Operability in respectable tumors depends on the performance status or comorbidity of the patient. The Child-Pugh Score, reflecting liver reserve and comorbidity, can be used to determine operative risk of patient (Pugh R et al. Br J Surg 973):

Chemical and Biochemical Parameters	Scores (Points) for increasing abnormality		
	1	2	3
Encephalopathy	None	1-2	3-4
Ascitis	None	Slight	Moderate
Albumin (g/dL)	>3.5	2.8-3.5	<2.8
Prolonged PT	1-4	4-6	>6
Bilirubin (mg/dL)	1-2	2-3	>3
Primary Cirrhosis	1-4	4-10	>10

Class A: 5-6 points, good operative risk

Class B: 7-9 points, moderate operative risk

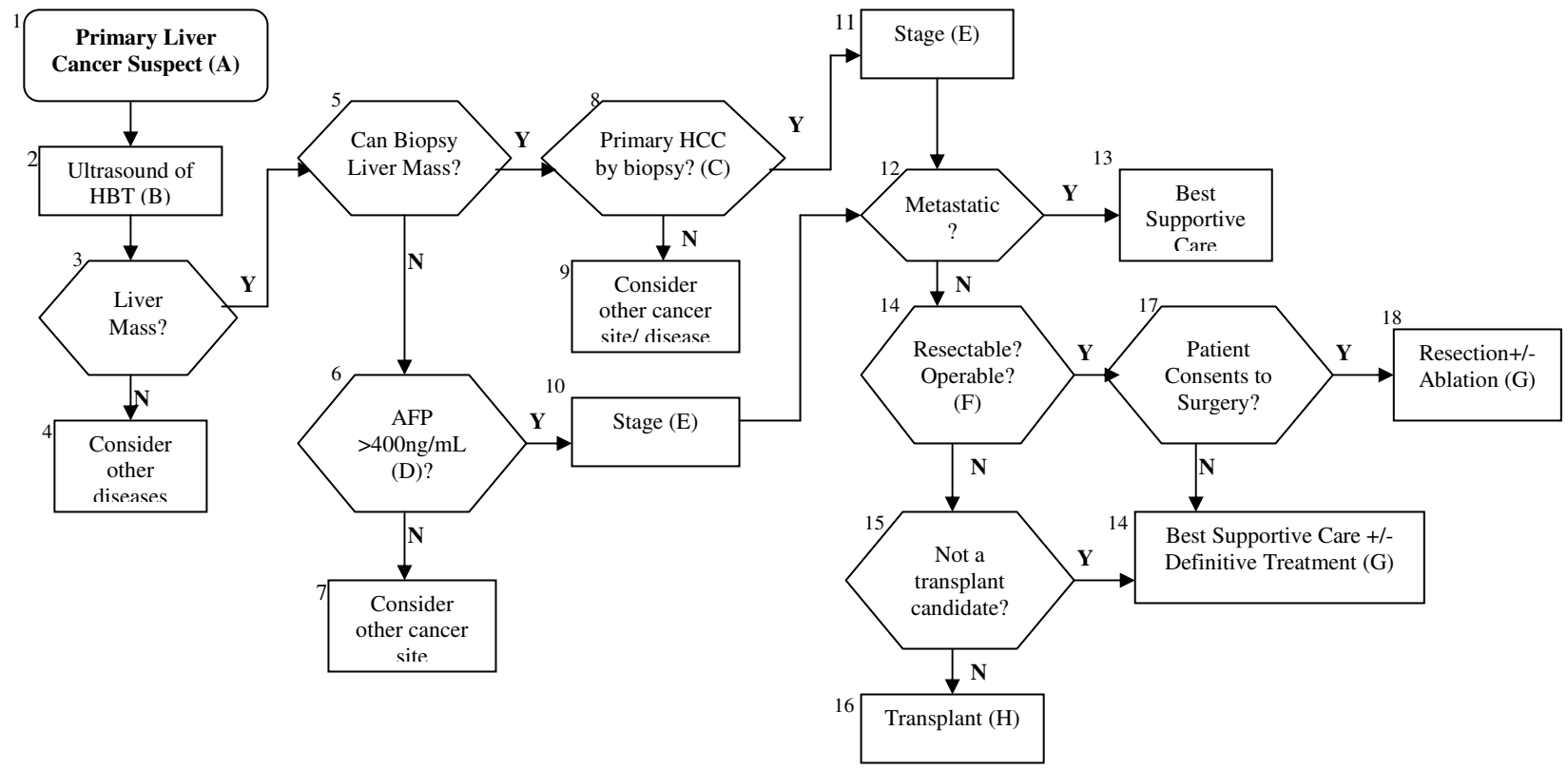
Class C: 10-15 points, poor operative risk

- (G) For T1-3, N0, total hepatic lobectomy can be performed. Tumor resection is the only curative therapy. Concomitant cirrhosis generally precludes surgery because of associated high operative mortality. The non-cirrhotic patient must be free of jaundice and ascitis and the lesion must be solitary or localized to a single lobe of the liver; there must be no nodal or distant spread. Discuss surgical treatment with patient and determine whether patient is amenable to surgery. Ablation options are – radiofrequency, alcohol, cryotherapy or microwave. Surveillance after resection includes imaging every 3-6 months for 2 years, and then annually, plus AFP (if initially elevated) is done every 3 months for 12 years, then every 6 months
- (H) Criteria for cadaveric transplant (UNOS criteria) are (Mazzaferro V et al. NEJM 1996):

- Patient is not a liver resection candidate
- Patient has a tumor ≤ 5 cm in diameter or 2-3 tumors ≤ 3 cm each
- No macrovascular involvement
- No extrahepatic spread of tumor to surrounding lymph nodes, lungs, abdominal organs, or bone

Surveillance after transplant includes imaging every 3-6 months for 2 years and then annually, plus AFP (if initially elevated) is done every 3 months for 12 years, then every 6 months

- (I) There have been efforts to treat unresectable HCC with systemic, intrahepatic artery chemotherapy, or chemoembolization, or radiotherapy (conformal or stereotactic or microspheres). Chemoembolization is contraindicated in cases of main portal thrombosis or Child's C. Doxorubicin, etoposide, 5-FU, capecitabine have been used. In a small percentage of cases, there is shrinkage of the tumor but the effect is temporary and of no advantage to patient survival compared with the untreated patients. Best supportive care is always part of the management. Biological drugs like erlotinib, bevacizumab, cetuximab, sorafenib, sunitinib, have been tested in clinical trials to benefit HCC.



PANCREATIC ADENOCARCINOMA

The management of pancreatic cancer must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

- (A) Very early evidence of this cancer is dilated duct (stricture), even if without a mass in pancreas on imaging. Unfortunately this cancer is invariably diagnosed when it is advanced because of lack of specific symptoms or signs. Most Filipino cases were seen at advanced stage (Pantangco, 1958; Solano, 1983; Limson, 1987), with abdominal or back pain, weight loss and jaundice top be the common manifestations. Other symptoms are anorexia, early satiety, dyspepsia, weakness, fatigue, bloating, nausea and vomiting. If the cancer is located in the head of the pancreas, signs of obstructive jaundice will predominate. Lesions in the tail of the gland often go undiagnosed until there are advanced extensions or distant metastasis.

Physical exam (PE) may include weight loss, jaundice, abdominal mass, epigastric tenderness, palpable gallbladder, and hepatomegaly; at least half of the patients have no physical findings. Metastatic sign include supraclavicular adenopathy.

- (B) The current test of choice for pancreatic carcinoma and the initial test for suspected carcinoma of the head and tail of the pancreas, is the CT scan, preferably dynamic-phase spiral CT. It is more reliable (85%-95% accuracy) than ultrasound in detecting a mass in the gland and in determining the level of obstruction, and is also helpful in determining direct extension to duodenum, stomach, retroperitoneum, portal vein, lymph nodes (LNs) and liver.

CA 19-9 can be done as a tumor marker; in presence of jaundice, get CA 19-9 if biliary decompression is complete and bilirubin is within normal range.

Do also chest x-ray and LFT as routine metastatic and medical tests.

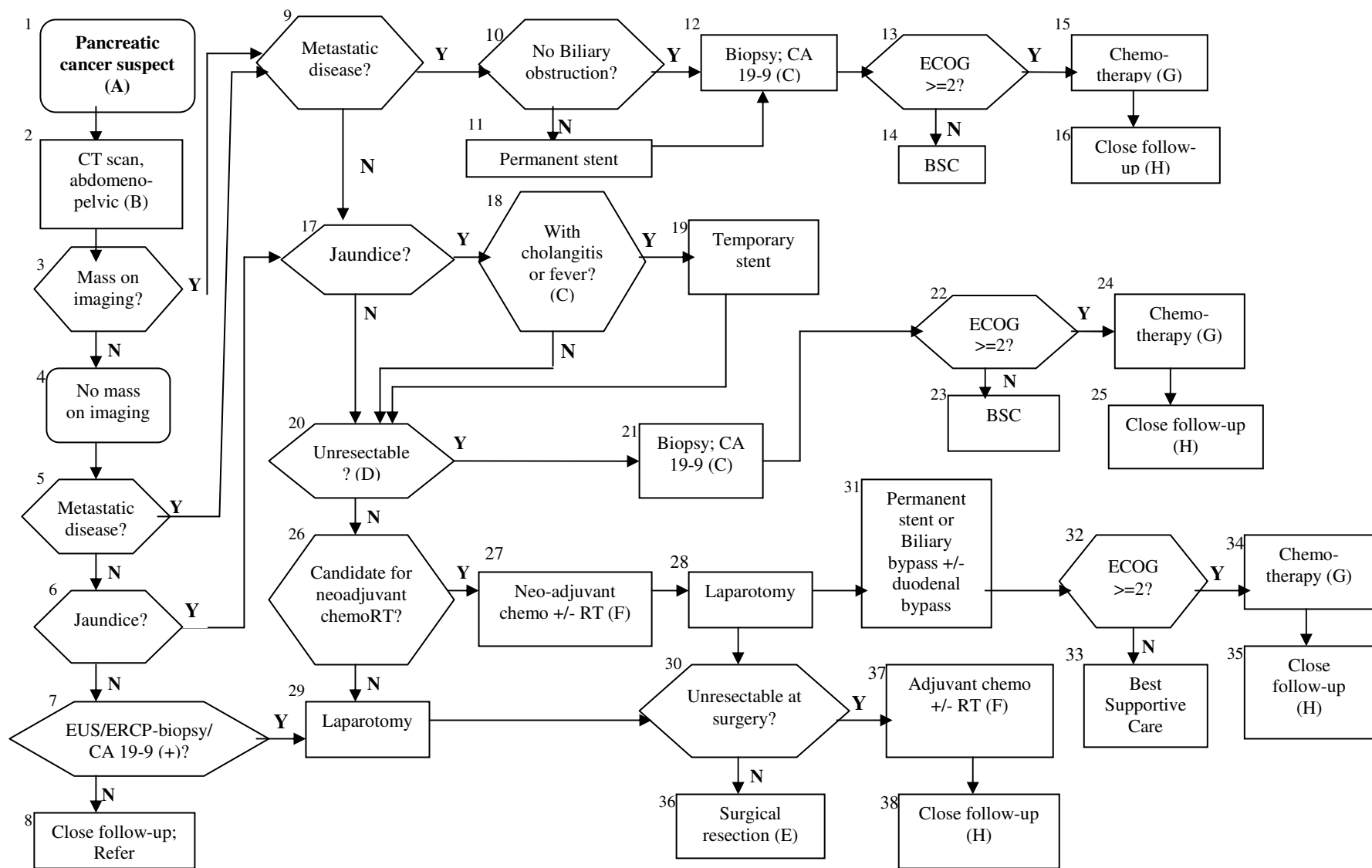
- (C) 1-57% of cases in some series do not have histological proof of cancer. Surgeons have been reluctant to perform operative pancreatic wedge or needle biopsies directly because of high biopsy complications. CT scan-guided transduodenal biopsies for lesions of the head of the pancreas are popular and fine needle biopsies are usually done. Endoscopic ultrasonography (EUS) and/ or endoscopic retrograde cholangiopancreatography (ERCP) with biopsy may be done as clinically indicated. EUS may be complimentary to CT. EUS-directed FNA biopsy may be preferable to a CT-guided FNA in patients with respectable disease because of the lower risk of peritoneal seeding with EUS FNA when compared with the percutaneous approach. A negative biopsy should be confirmed by at least 1 repeat EUS biopsy. ERCP is helpful, if patient is jaundiced and the site of obstruction is not defined; it allows visualization (and biopsy) of the duodenum and Vater's ampulla, and visualization (and cytology) of both the pancreatic and bile duct, which could be important for resection.

Frequently, however, the diagnosis is made indirectly by a biopsy of a metastatic site that reveals a histology compatible with pancreatic origin, and other findings that include – a) appropriate presentation for pancreatic carcinoma, b) a mass in the pancreas detected by imaging, b) absence of another primary. 80% of pancreatic cancer is of adenocarcinoma histopathology.

- (D) Criteria for resectability:

- Resectable
 - Head/Body/Tail
 - No distant metastasis
 - Clear flat plane around celiac and superior mesenteric arteries (SMA)
 - Patent superior mesenteric vein (SMV)/ portal vein
- Borderline Resectable – for any of these tumors where an incomplete resection is anticipated, prefer chemoradiation prior surgery
 - Head/Body
 - Severe unilateral SMV/ portal impairment
 - Tumor abutment on SMA
 - Gastroduodenal artery (GDA) encasement up to origin at hepatic artery
 - Tumors briefly involving the IVC
 - SMV occlusion, if of a short segment, with open vein both proximally and distally (if proximal SMV were occluded up to the portal vein branches then it would be unresectable)
 - Tail
 - Adrenal, colon or mesocolon, or kidney invasion
 - Preoperative evidence of biopsy-positive peripancreatic LN
- Unresectable
 - Head
 - Distant metastases (includes celiac and/ or para-aortic LNs)
 - SMA, celiac encasement
 - SMV/ portal occlusion
 - Aortic, inferior vena cava (IVC) invasion or encasement
 - Invasion of SMV below transverse mesocolon
 - Body
 - Distant metastases (includes celiac and/ or para-aortic LNs; body and tail lesions that have positive celiac and/or paraaortic nodes in close vicinity to the primary may also be borderline rather than unresectable)
 - SMA, celiac, hepatic encasement
 - SMV/ portal occlusion
 - Aortic encasement
 - Tail

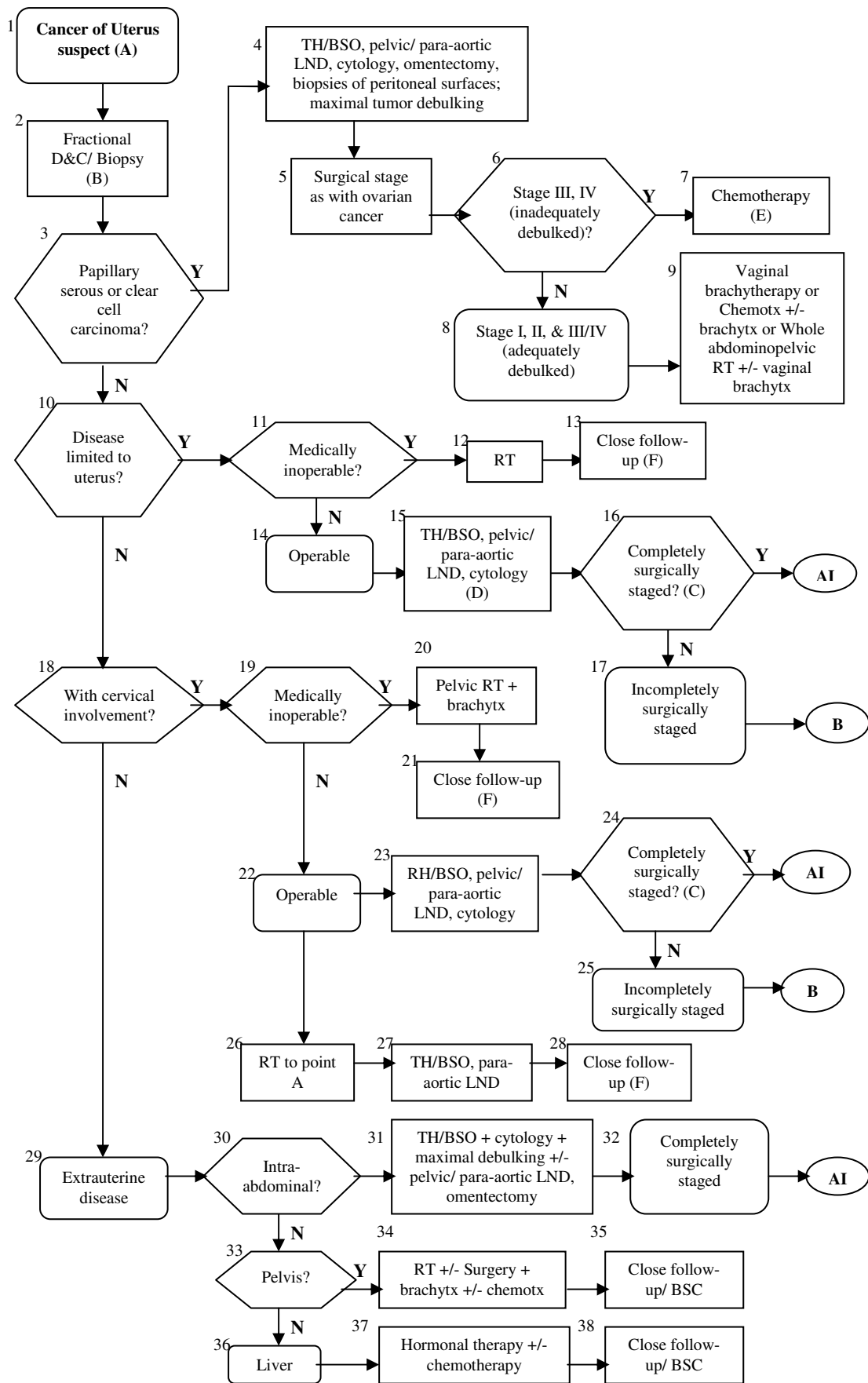
- Distant metastases (includes celiac and/ or para-aortic LNs; body/ tail lesions that have positive celiac and/ or paraaortic nodes in close vicinity to the primary may also be borderline rather than unresectable)
 - SMA, celiac encasement
 - Rib, vertebral invasion
- (E) The standard operation for lesions in the tail of the pancreas is partial pancreatectomy. For lesions in the head, a pancreaticoduodenostomy or Whipple's procedure is standard. This operation consists of en bloc removal of the duodenum, head of pancreas, distal portion of the common duct, and distal stomach with the pylorus. Palliation procedures include biliary-enteric bypass to relieve the jaundice, gastroenteric bypass if duodenal obstruction exists or is highly likely, and celiac axis alcohol or phenol block for pain relief.
- (F) Radiation therapy is indicated as:
- Adjuvant – when there is no residual disease but highly likely to recur or when microscopic or macroscopic disease has been left behind. Standard of care is 5 FU-based chemoradiotherapy. Capecitabine is an alternative drug.
 - Definitive – particularly when the disease is considered locally unresectable, and there is no evidence of distant metastasis. 5-FU, capecitabine, gemcitabine plus radiotherapy can be given.
- (G) Chemotherapy is used in the adjuvant and in the management of locally advanced unresectable and metastatic disease. Gemcitabine is considered standard front-line therapy for patients with metastatic disease. Gemcitabine or gemcitabine-based combination therapy without RT may be considered as an alternative to 5-FU-based chemoradiation for patients with locally advanced, unresectable disease or as adjuvant therapy. Gemcitabine can be combined with cisplatin, oxaliplatin, erlotinib, capecitabine, cetuximab, bevacizumab.
Second-line therapy after gemcitabine includes capecitabine or 5-FU + oxaliplatin
- (H) Close surveillance every 3-6 months for 2 years, then annually with clinical history and physical exam (H&P), CT scan, CA 19-9.

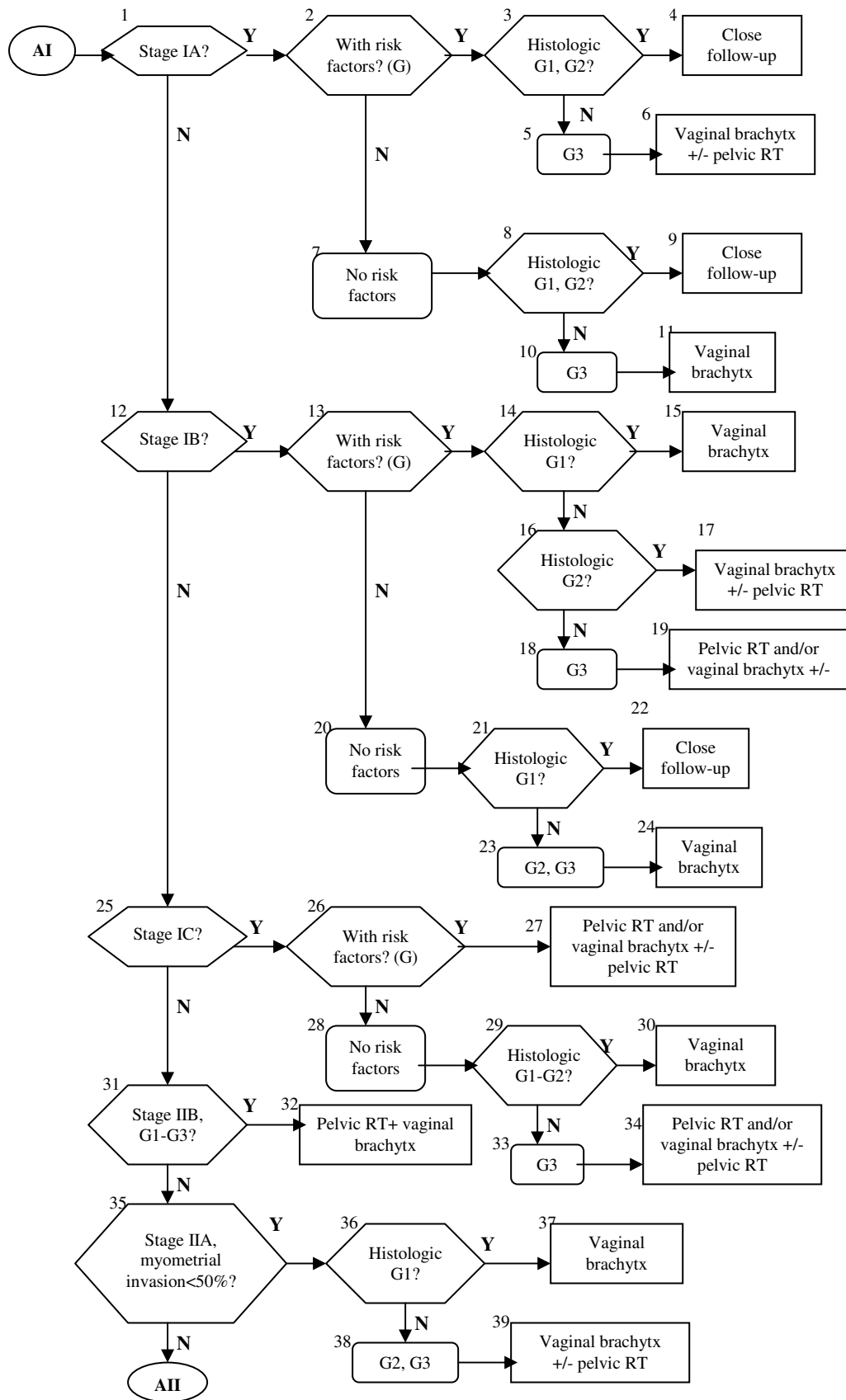


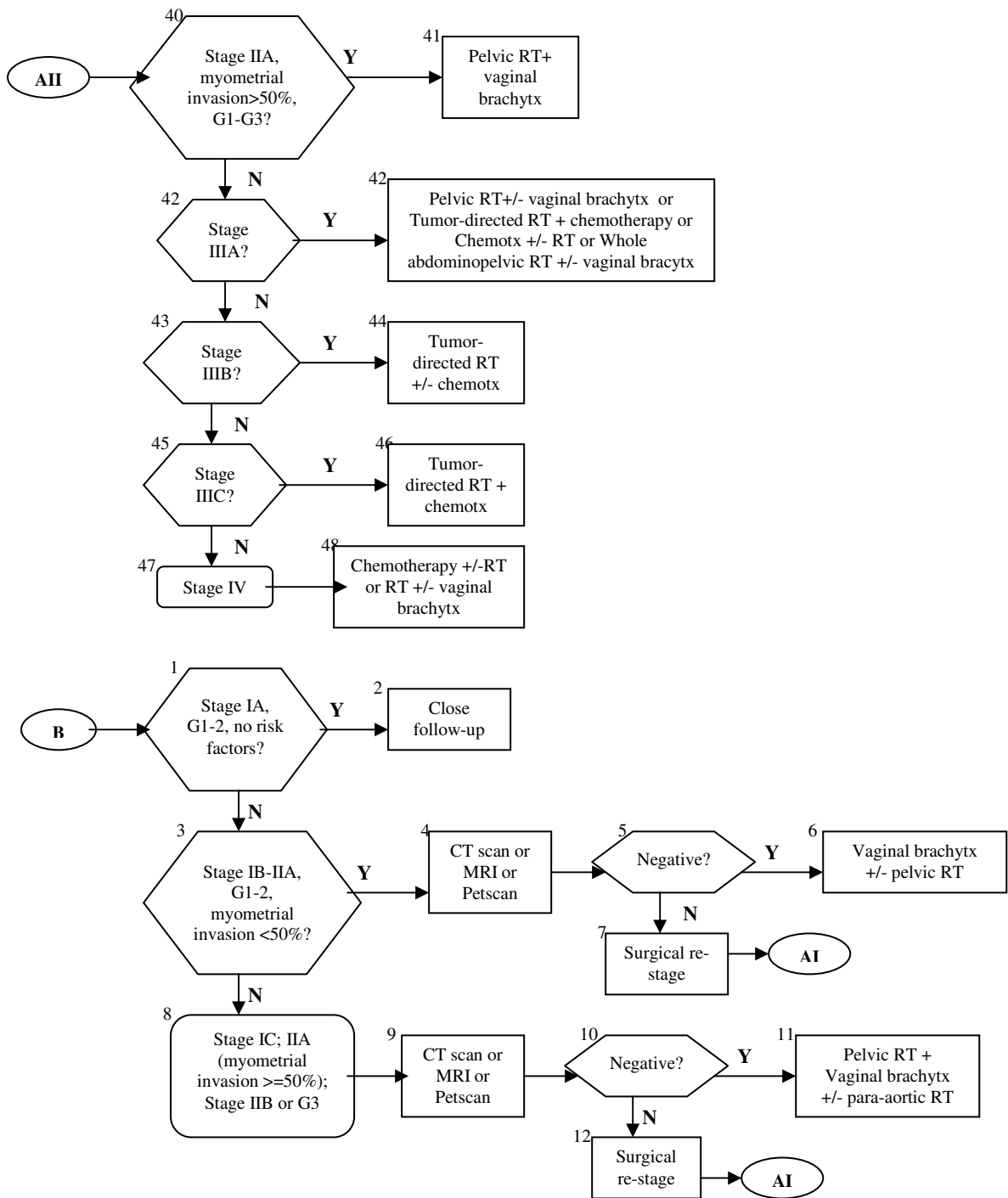
CANCER OF THE UTERINE FUNDUS

The management of uterine cancer must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

- (A) The most common symptom is abnormal uterine bleeding which occurs in >90%. Post-menopausal bleeding is always abnormal and uterine tissue sampling is mandatory.
- (B) Fractional dilatation & curettage (D&C) of uterus has been the standard diagnostic method for endometrial carcinoma.
For suspected or gross cervical involvement, do cervical biopsy.
Pathology results may reveal endometrioid histologies (carcinoma), papillary serous or clear cell carcinoma or sarcoma.
Endometrioid histologies can be classified to: 1) disease limited to uterus, 2) gross cervical involvement, and 3) extrauterine disease (intra-abdominal – ascites, omentum, nodal, ovarian, peritoneal; pelvis – vaginal, bladder, bowel/ rectum, parametrial; liver).
Pathologic assessment should include: 1) ratio of depth of myometrial invasion to myometrial thickness, 2) tumor size, 3) tumor location (fundus vs lower uterine segment/ cervix), 4) histologic subtype with grade, 5) lymphovascular space invasion, and 6) frozen section as indicated.
- (C) Routine tests include complete history & PE, chest x-ray, CBC, evaluation of hepatic and renal function. If pelvic mass is present, CT scan or MRI and CA-125 are often performed. Staging is by FIGO, 2000:
- | | |
|------------|--|
| Stage 0 | Carcinoma-in-situ |
| Stage I | Confined to corpus uteri |
| Stage IA | Limited to endometrium |
| Stage IB | Invades \leq 1/2 of myometrium |
| Stage IC | Invades $>$ 1/2 of myometrium |
| Stage II | Invades cervix but does not extend beyond uterus |
| Stage IIA | Endocervical glandular involvement only |
| Stage IIB | Cervical stromal invasion |
| Stage III | Local and/ or regional spread as specified in IIIA, B, C |
| Stage IIIA | Involves serosa and/ or adnexa (direct extension or metastasis) and/ or cancer cells in ascites or peritoneal washings |
| Stage IIIB | Vaginal involvement (direct extension or metastasis) |
| Stage IIIC | Metastasis to pelvic and/ or para-aortic LNs |
| Stage IVA | Invades bladder mucosa and/ or bowel mucosa (the presence of bullous edema is not sufficient to classify tumor as T4) |
| Stage IVB | Distant metastasis (excluding metastasis to vagina, pelvic serosa, or adnexa; including metastasis to intra-abdominal LNs other than para-aortic and/ or inguinal LNs) |
- (D) Surgery for operable lesions is THBSO (total hysterectomy and bilateral salpingoophorectomy) with lymph node dissection (pelvic lymphadenectomy and para-aortic lymphadenectomy); sometimes radical hysterectomy (RH) + BSO.
- (E) Therapy for metastatic disease includes Hormonal therapy (progestational agents, tamoxifen, or aromatase inhibitors). Tumors with high levels of estrogen and progesterone receptors are more likely to respond to progestin therapy; receptor (+) tumor is more likely to be well differentiated. Tamoxifen may be of benefit for patients progressing on progestin therapy or on an alternating schedule with a progestin.
Cytotoxic chemotherapy can be given to patients with an unresectable recurrence within a previously irradiated field, or to patients with systemic disease in either a recurrent or primary setting. Drugs include cisplatin, carboplatin, paclitaxel, and doxorubicin.
- (F) Surveillance includes PE every 3-6 months for 2 years, then 6 months or annually, with CA-125, annual chest x-ray, every 6 monthly vaginal cytology for 2 years then annually
- (G) Risk factors include: >60 years age, positive lymphovascular invasion, large tumor size, lower uterine involvement







OVARIAN CANCER

The management of ovarian cancer must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

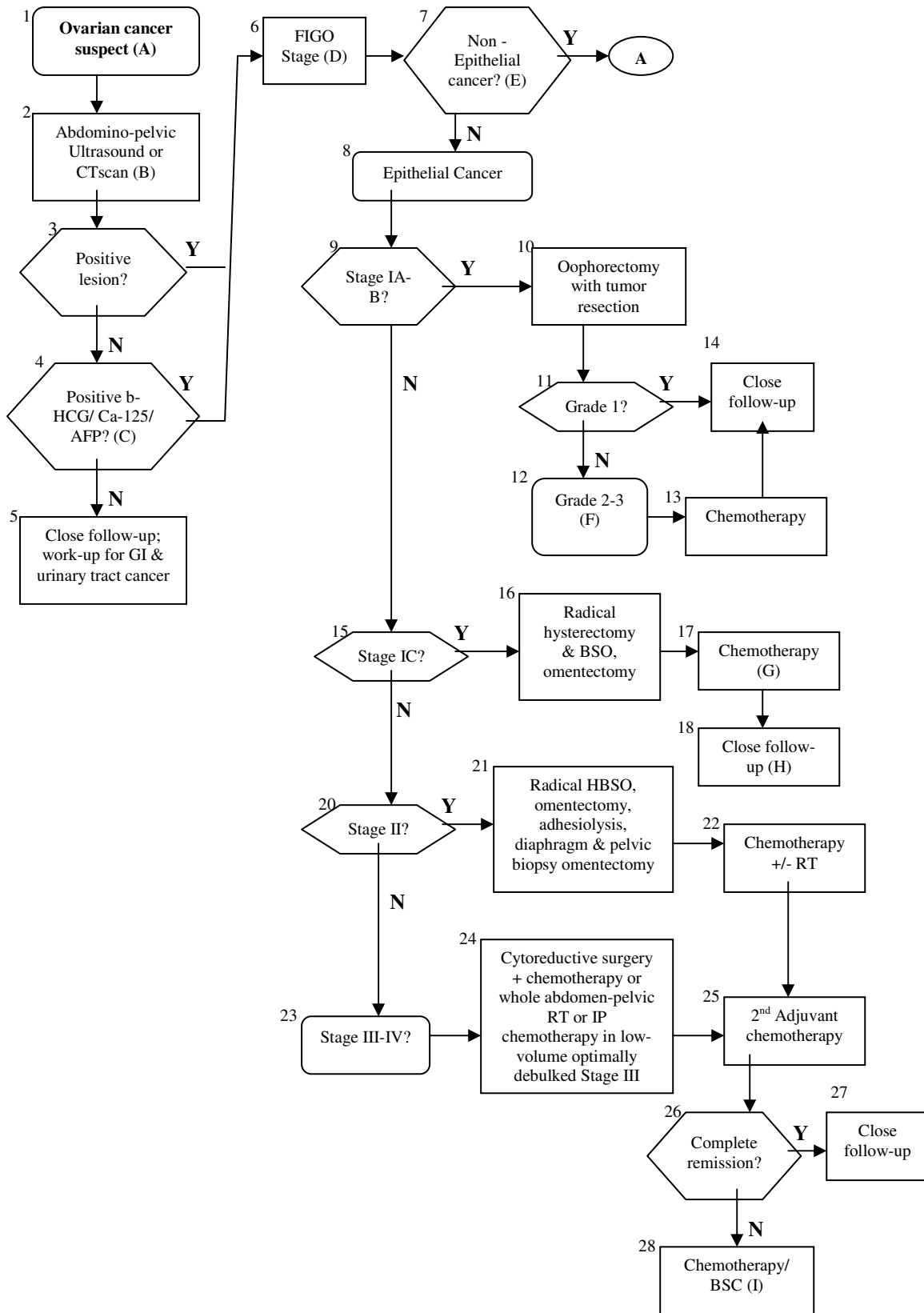
- (A) Presentation ranges from completely asymptomatic to vague complaints – abdominal pain, dyspneic, bowel pain, abnormal vaginal bleeding, dyspareunia, constipation, dyspnea, pleuritic pain, cachexia and fatigue. Physical exam (PE) shows ascitis, cul-de-sac nodularity, pleural effusion among others. A palpable ovary in a postmenopausal patient is highly suspected for ovarian neoplasm
- (B) Ultrasound or better CTscan provide information regarding pelvic mass as possible cancer – complex adnexal mass, ascitis, cul-de-sac nodules, omental disease, pelvic or paraortic nodes, pleural effusion and/or large adnexal masses.
- (C) A number of tumor antigens may be elevated: 1) CA-125 may detect persistent disease prior surgery, 2) AFP and BHCG are also extremely useful in the follow-up response to treatment and in detecting persistent diseases in germ-cell tumors that are antigen positive (such as endodermal sinus tumor, embryonal carcinoma, and choriocarcinoma)
- (D) Diagnosis depends on obtaining an adequate histologic specimen which usually entails exploratory laparotomy with ovarian resection. If an ovarian cancer is confirmed, disease extent is determined and surgical removal of all possible tumor done. Anatomical staging is according to FIGO (2002):

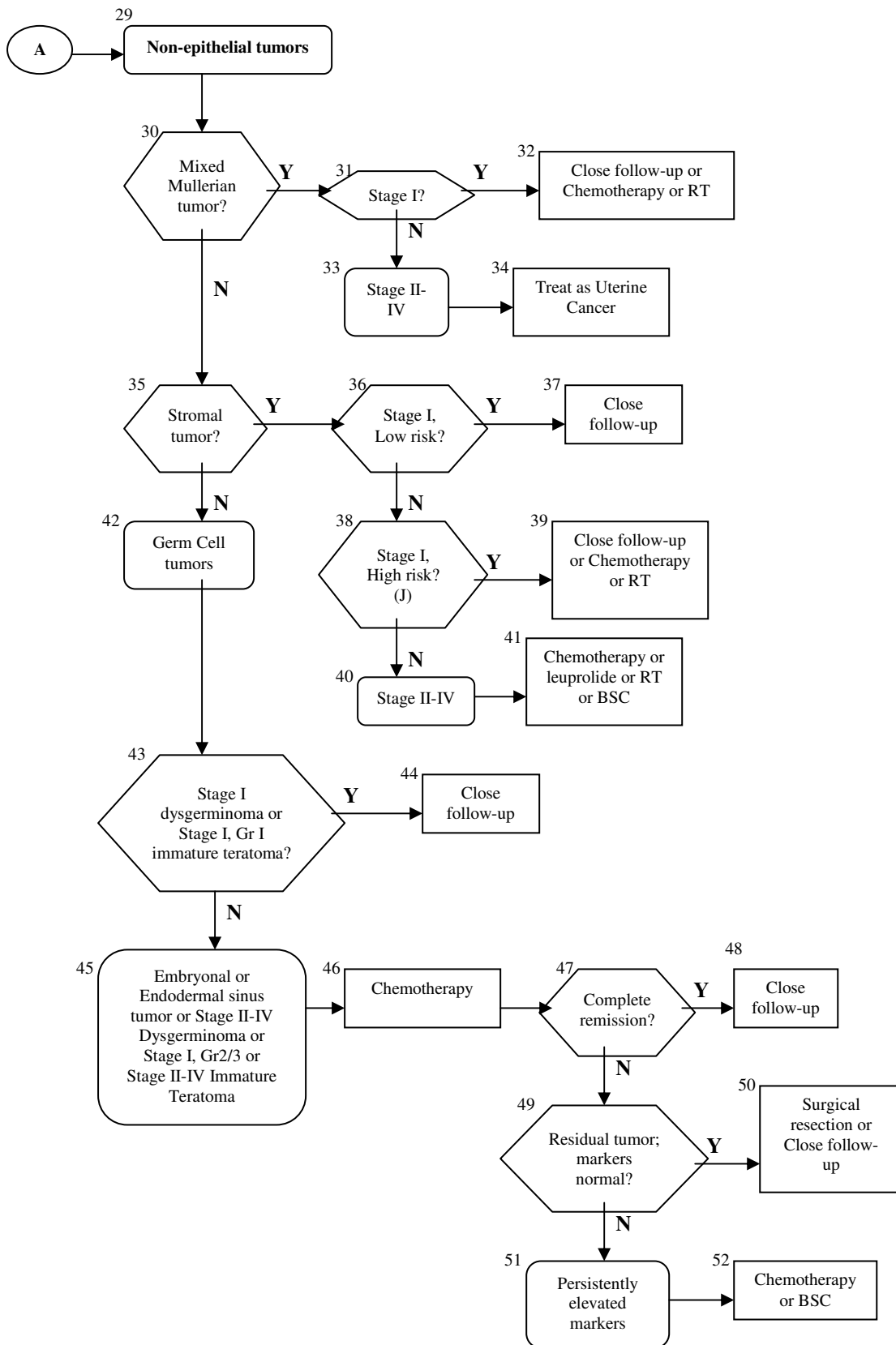
Stage	IA	T1aN0M0 Limited to one ovary, capsule intact, no tumor on surface
	IB	T1bN0M0 Limited to both ovaries, capsule intact, no tumor on surface
	IC	T1cN0M0 Capsule ruptured, tumor on surface, +ca in ascitic/ peritoneal fluid
	IIA	T2aN0M0 Pelvic extension – uterus, tube/s
	IIB	T2bN0M0 Other pelvic masses; (-) ca in ascitic/peritoneal fluid
	IIC	T2cN0M0 (+) cancer in ascitic/peritoneal fluid
	III	Peritoneal metastasis beyond pelvis and/or regional lymph node metastasis
	IV	Distant metastasis (excludes peritoneal metastasis)

Complete PE and history is done. Chest x-ray, GI evaluation, creatinine, LFT, CBC are done for epithelial carcinomas. For non-epithelial tumors, include magnesium, LDH. Family history evaluation is done. Consider fertility sparing particularly in Stage I tumors.

- (E) Less common ovarian histology types (aside from more common epithelial carcinoma) are Germ Cell tumors (dysgerminoma, immature teratoma, embryonal tumor, endodermal sinus tumor), Stromal tumors, and Mixed Mullerian tumors (carcinosarcoma).
- (F) Chemotherapy is currently the predominant approach to treating ovarian carcinoma. Preferred 1st line adjuvant for epithelial carcinoma is paclitaxel/ docetaxel + carboplatin. Acceptable recurrence chemotherapy drugs in epithelial carcinomas are bevacizumab, anastrozole, carboplatin, cisplatin, cyclophosphamide, docetaxel, gemcitabine, ifosfamide, irinotecan, letrozole, liposomal doxorubicin, melphalan, etoposide, oxaliplatin, paclitaxel, tamoxifen, vinorelbine. Patients receiving primary chemotherapy will be monitored as follows:
- Pelvic exams at least every 2 cycles
 - Interim CBC with platelets as indicated
 - Chemistry profiles if indicated
 - CA-125 levels prior to each cycle of chemotherapy, if informative
 - Radiographic imaging if indicated
- For germ cell tumors, etoposide-carboplatin, or BEP (belomycin-etoposide-cisplatin) or TIP (paclitaxel-ifosfamide-cisplatin) is used. For stromal tumors, cisplatin or carboplatin/ paclitaxel are preferred. For non-epithelial tumors, acceptable recurrence modalities are cisplatin, etoposide, TIP, docetaxel/ carboplatin, VIP, VeIP (vinblastin, ifosfamide, cisplatin), VAC (vincristine, dactinomycin, cyclophosphamide), paclitaxel, docetaxel, leuprolide.
- (G) Clear-cell pathology is Grade 3.
- (H) Monitoring follow-up includes:
- Visits every 2-4 months for 2 years, then every 6 months for 3 years, then annually
 - CBC every 12 month
 - CA-125 every visit if initially elevated
 - Chemistry profile as indicated
 - PE with pelvic exam
 - Chest/ abdominal/ pelvic CT or PET as clinically indicated
 - Chest x-ray as indicated
- (I) Patients who progress on 2 consecutive single-agent regimens without evidence of clinical benefit are unlikely to benefit from additional chemotherapy regimens and may be offered best supportive care or clinical trial. Ancillary palliative surgical procedures include – paracentesis, thoracentesis/ pleurodesis, ureteral stents/ nephrostomy, surgical relief of intestinal obstruction, enteral feeding tube, gastrostomy tube, vascular access device, indwelling peritoneal or pleural catheter, intestinal stents, video-assisted thoracoscopy.

(J) High risk – e.g., ruptured Stage IC or poorly differentiated Stage I





CANCER OF THE UTERINE CERVIX

The management of cervix cancer must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient. The gynecologist oncologist takes the primary role.

- (A) Early stage clinical presentation includes vaginal bleeding, usually contact bleeding, vaginal discharge, irregularities of menstruation.
Advanced stage clinical presentation includes pelvic discomfort or flank pain in the suprapubic or sacral region, urinary frequency, change of bowel habits, dysuria, hematuria, pain radiating to thighs, unilateral leg edema, white patches (leukoplakia), extensive red patches (erythroplasia).
History may reveal risk factors such as early age at first sexual intercourse, multiparity, multiple sexual partners or partner with multiple sexual partners, exposure to human papilloma virus types 16, 18, 31, 45, 56, and herpes simplex
- (B) Clinical examination includes internal examination with speculum and Pap smear, followed by a gynecological rectal examination, which may show a palpable pelvic mass. On internal exam a frank cervix lesion may be seen, and biopsy can be done.
- (C) Pap test can show pre-cancerous lesions: cervical intraepithelial neoplasia (CIN) I, II, III and invasive carcinoma. CIN III (or carcinoma-in-situ (CIS)) has a very high probability of becoming invasive carcinoma.
- (D) Colposcopy with colpo-guided biopsy to get better biopsy specimen can follow an abnormal Pap smear. In the absence of a colposcope, Schiller's test is done (painting of cervix and vaginal mucosa with Lugol's solution); samples for biopsy are taken from the unstained areas.
Endocervical curettage (ECC) is done if the lesion seen colposcopically disappears into the endocervical canal so that the upper limit of the lesion is not visualized. If this turns out to be positive, a cone biopsy is done to rule out stromal invasion.
- (E) The invasive carcinomas are commonly of squamous cell type (squamous cell carcinoma, verrucous carcinoma, condylomatous carcinoma, papillary squamous cell carcinoma, lymphoepithelioma-like carcinoma) followed by glandular type (adenocarcinoma-in-situ, mucinous adenocarcinoma, clear cell adenocarcinoma, serous adenocarcinoma, mesonephric carcinoma, villoglandular adenocarcinoma, minimal deviation adenocarcinoma). Other non-common pathology types are adenosquamous carcinoma, glassy cell carcinoma, adenoid cystic carcinoma, adenoid basal carcinoma, carcinoid tumor, small cell carcinoma, undifferentiated carcinoma.
- (F) Conization is a cone-shaped biopsy encompassing the lining of the endocervical canal below the internal os and the squamous-columnar junction, the lateral margin to include the lesions visualized colposcopically or delineated by Schiller's test. An alternative procedure is the loop electrosurgical excision procedure (LEEP) or large loop excision of the transformation zone (LLETZ) which makes use of thin wire loop electrodes and electrosurgical generators to excise the lesions.
- (G) Pap smear every 6 months for the first 2 years, then yearly thereafter, with complete physical exam and careful recto vaginal exam.
- (H) Cervical cancer generally spreads by direct extension to neighbouring tissues. Procedures for clinical staging includes chest x-ray, CTScan of lower abdomen to pelvis, and optional - bone scan, proctosigmoidoscopy, cystoscopy, KUB-IVB. FIGO staging is as follows:
- | | |
|------|--|
| Tis | Carcinoma-in-situ; CIN III |
| T1 | Confined to cervix only |
| T1a | Microinvasive carcinoma |
| T1a1 | Stromal invasion of not more than 3.0mm in depth and extension of not more than 7.0mm |
| T1a2 | Stromal invasion of more than 3.0 mm and not more than 5.0mm with an extension of not more than 7.0mm |
| T1b | Clinical visible lesions limited to cervix or subclinical cancers greater than Stage IA |
| T1b1 | Clinical visible lesions not larger than 4.0cm |
| T1b2 | Clinically visible lesions larger than 4.0cm |
| T2 | Carcinoma extends beyond cervix but has not extended to pelvic wall; involves vagina but not lower third |
| T2a | No obvious parametrial involvement |
| T2b | Obvious parametrial involvement |
| T3 | Carcinoma extended to pelvic wall and lower third of vagina, including all cases with cancer-related hydronephrosis or nonfunctioning kidney |
| T3a | No extension to pelvic wall |
| T3b | Extension to pelvic wall and/ or hydronephrosis or non-functioning kidney |
| T4 | Carcinoma extended beyond true pelvis or has clinically involved mucosa of the bladder or rectum |
| T4a | Spread to adjacent organs |
| M1 | Spread to distant organs |
- (I) If the patient is already pregnant;
- During 1st half of pregnancy,
 - for Stage I-IIA
 - good surgical risk do radical hysterectomy and bilateral lymph node dissection (RHBLND) with or without bilateral salpingo-oophorectomy (BSO);

- 2. poor surgical risk, do complete radiotherapy;
 - ii. for Stage IIB-IV, do chemoradiation
- b. During 2nd half of pregnancy
 - i. for Stage I-IIA
 - 1. good surgical risk, do cesarian section (at earliest time for fetal survival) and RHBLND with or without BSO;
 - 2. poor surgical risk – do cesarian section then complete radiotherapy;
 - ii. for Stage IIB-IV, do cesarian section followed by chemoradiation.

(J) Chemoradiation is the standard treatment for Stage IB2 and above or for unfavourable histologic types (small cell, clear cell, gassy cell, adenosquamous cell). Usual chemoradiation regimen is cisplatin weekly or every 21 days concomitant with radiotherapy (external and internal). Other drugs include capecitabine, gemcitabine, fluorouracil.

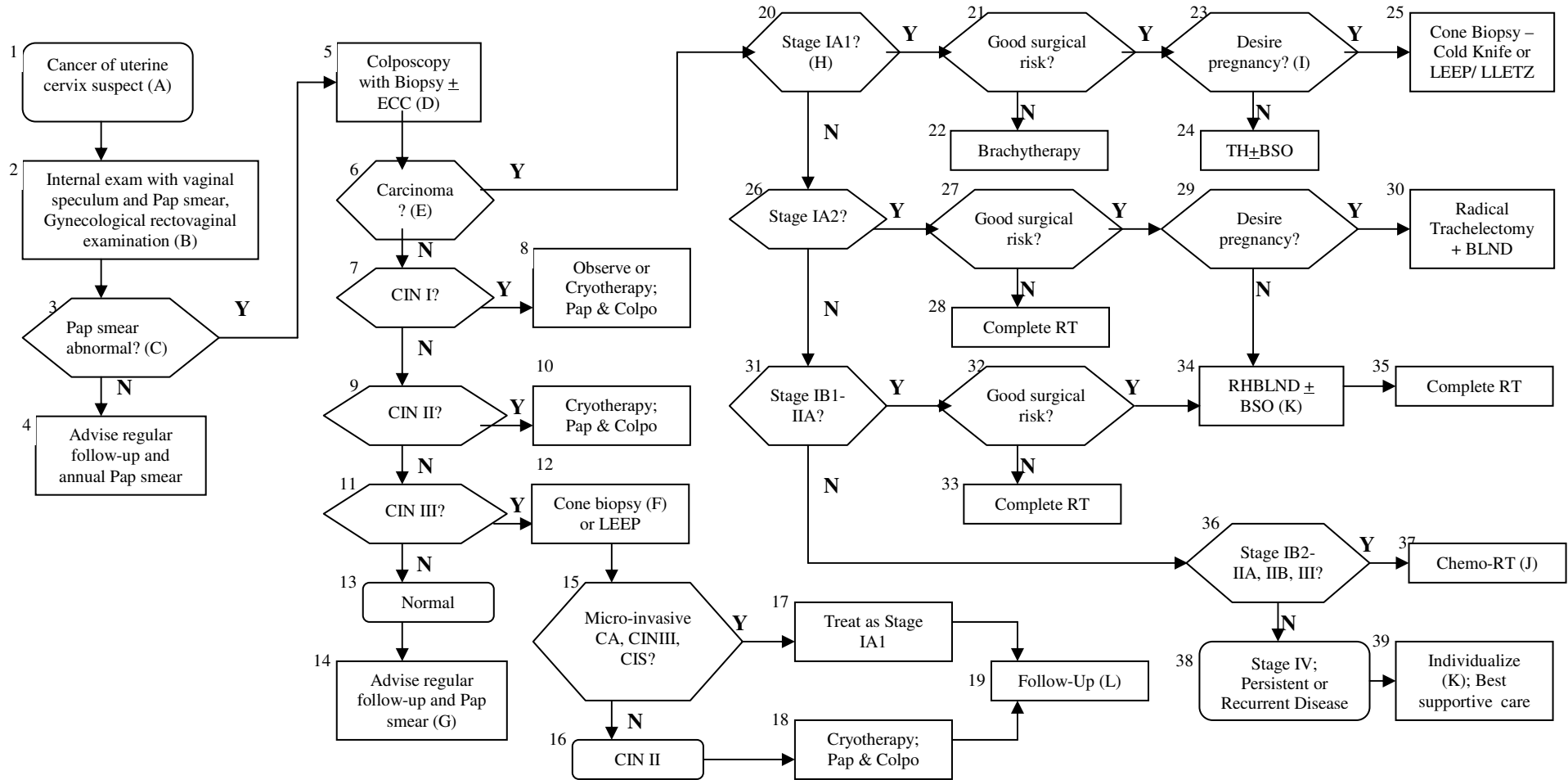
For bulky Stage IB and IIA diseases – neoadjuvant chemotherapy or radiotherapy or chemoradiation is followed by radical surgery. There is also a potential for adjuvant chemotherapy to delay/ prevent distant metastasis. Poor prognostic factors are tumor size >2cm, positive LN metastasis, >50% stromal invasion, positive lines of resection.

(K) Individualization also applies to special clinical situations:

- a. Unfavorable cell types
 - i. Stage IA/IB/IIA – give neoadjuvant chemotherapy followed by RHBSO-BLND then adjuvant chemotherapy
 - ii. Stage IB2/IIA – give chemoradiation OR neoadjuvant chemoradiation followed by RHBSO-BLND, then adjuvant chemotherapy
 - iii. Stage IIB, III - chemoradiation
- b. Pelvic inflammatory disease and/ or adnexal masses – do BSO before chemoradiation or laparoscopic BSO
- c. Barrel-shaped tumors – do total or radical hysterectomy, BSO with or without BLND after chemoradiation; interstitial brachytherapy
- d. Primary cases with urinary obstruction – urinary diversion, followed by complete RT with or without chemotherapy
- e. Primary cases with GUT obstruction – medical decompression (or surgical decompression) followed by complete RT with or without chemotherapy

(L) Follow-up

- a. After completion of treatment, complete PE with careful rectovaginal examination
- b. Pap smear every 6 months for the 1st 2 years, then yearly thereafter
- c. Chest x-ray every 6 months (more often if symptomatic).
- d. Annual CTScan of pelvis for the 1st 3 years post-treatment



CANCER OF THE PROSTATE

The management of prostate cancer must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

- (A) Usual symptomatology includes – hematuria, UTI, azotemia, and edema, but usually it is detected on routine rectal exam, or after signs of obstruction, after TUR, and when symptomatology of metastatic bone lesions appears.
A digital rectal exam (DRE) should always be performed, which may reveal an enlarged prostate and local extent.
- (B) Trans-rectal sonography has 90% sensitivity and 95% specificity for prostatic mass detection. For extracapsular penetration, overall accuracy is 90% but detection of seminal vesicle invasion is only 77%.
- (C) Prostatic specific antigen (PSA) is elevated (>10ng/mL): Stage I – 38-57%, Stage II – 95%, Stage III-IV – 100%. However, with cutoff level of 10ng/mL, the specificity versus benign diseases of the prostate is 90%. PSA levels may be temporarily elevated after DRE, urinary retention, lasering, ergometry, prostatic surgery, cystoscopy, catheterization or needle biopsy, hence do the PSA test prior these procedures or a week after.
The 2 main applications of PSA assay are firstly for monitoring the course and therapeutic response of prostatic cancer, and secondly for monitoring patients with BPH so as to detect the presence of prostatic carcinoma as early as possible.

- (D) Chest x-ray, bone scan, CT scan of pelvis and abdomen are done for staging. AJCC (2002) gives the following staging
- | | |
|-----|---|
| T1 | Clinically inapparent tumor neither palpable nor visible by imaging |
| T1a | tumor incidental histologic finding in ≤5% of tissue resected |
| T1b | >5% of tissue |
| T1c | tumor identified by needle biopsy (e.g., because of high PSA) |
| T2 | Tumor confined within the prostate |
| T2a | tumor involves ½ of ≤1 lobe |
| T2b | >1/2 of one lobe but not both lobes |
| T2c | both lobes |
| T3 | Tumor extends through the prostatic capsule |
| T3a | extracapsular extension (unilateral or bilateral) |
| T3b | tumor invades seminal vessel/s |
| T4 | Tumor is fixed or invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles, and/ or pelvic wall |
| N0 | No positive regional node |
| N1 | Metastases in regional node/s |
| M0 | No distant metastases |
| M1 | Distant metastases |
| M1a | Non-regional LNs |
| M1b | Bone/s |
| M1c | other site/s with or without bone disease |

Histopathology Grade by Gleason Score is the optimal method of grading:

- | | |
|------|---|
| GX | grade cannot be assessed |
| G1 | well differentiated (slight anaplasia) – Gleason 2-4 |
| G2 | moderately differentiated (moderate anaplasia) – Gleason 5-6 |
| G3-4 | poorly differentiated or undifferentiated (marked anaplasia) – Gleason 7-10 |

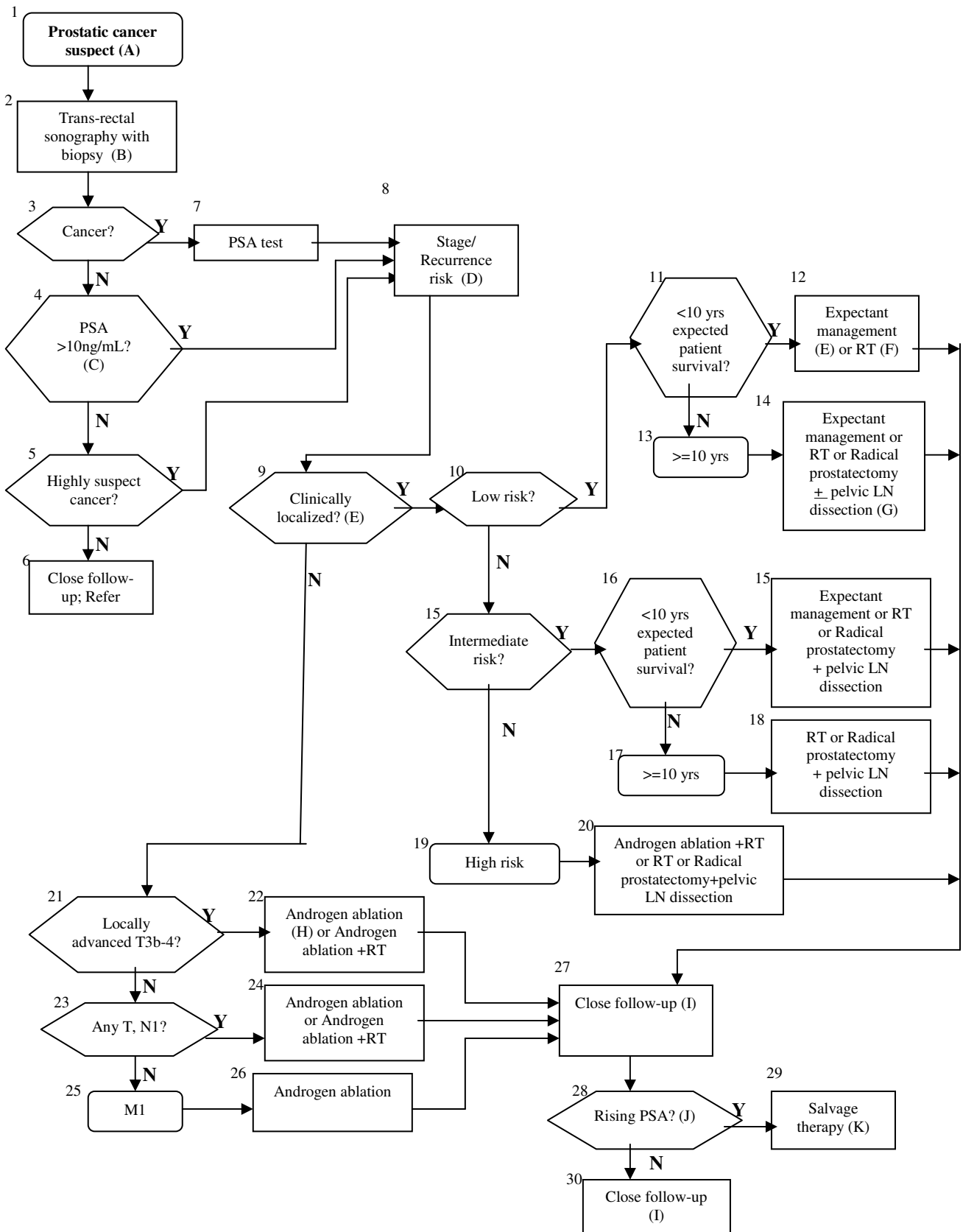
PSA, Tumor burden (T), and/ or Gleason score together predicts risk for clinical recurrence and life expectancy:

- Clinically localized:
 - Low risk: T1-2a and Gleason score 2-6 and PSA <10ng/mL
 - Intermediate risk: T2b-T2c or Gleason score 7 or PSA 10-20 ng/mL (patients with multiple adverse factors may be shifted to next higher risk group)
 - High risk: T3a or Gleason score 8-10 or PSA >20ng/mL
 - Locally advanced: Very high – T3b-T4
 - Metastatic: anyT, anyN, M1
- (E) Expectant management involves actively monitoring the course of disease with the expectation to intervene if the cancer progresses or if symptoms become imminent. Patients should have regular follow-up with: a) DRE and PSA every 6 months, b) needle biopsy repeated within 6 months of diagnosis if initial biopsy was <10 cores or assessment discordant or repeated within 18 months if >10 cores obtained initially, then periodically, c) repeat biopsy is indicated for any sign of disease progression by exam or markers
- (F) Radiotherapy includes external beam RT – preferably 3D conformal or IMRT at doses 70-75 Gy in 35-41 fractions to prostate (+/- seminal vesicles) in low risk cases. For intermediate or high risk cases, 74-80 Gy. Those at high-risk are candidates for pelvic LN RT and addition of neoadjuvant +/- adjuvant ablation therapy.
Radiotherapy can also be done using brachytherapy – as monotherapy in low risk cases and combined with neoadjuvant androgen ablation in intermediate risk patients. Patients with large prostate (>60 gm), symptoms of bladder outlet obstruction (IPSS score >15), or a previous TURP are not ideal candidates

because of increased risk of urinary morbidity. Neoadjuvant androgen ablation may shrink prostate to acceptable size.

Adjuvant RT can be given in positive margins (NO) after radical prostatectomy in clinically localized disease patients.

- (G) Radical prostatectomy (retropubic or perineal approach – RRP or RPP) is done for any patient with clinically localized prostate cancer that can be completely excised surgically, who have a life expectancy of 10 years or more and no serious co-morbid conditions that would contraindicate an elective operation. Radical prostatectomy (RP) and pelvic LN dissection (PLND) may be done in selected patients with T3 or N+ cancer. Adverse events are blood loss, urinary incontinence, loss of erection, anastomotic strictures.
- (H) Medical (LHRH agonist alone +/- antiandrogen for 2-4 weeks for flare or LHRH agonist + antiandrogen or high dose antiandrogen) or surgical (orchiectomy) castration seems to be more effective than antiandrogen monotherapy. Intermittent androgen ablation can reduce side effects in long term treatment. LHRH agonist and bilateral orchiectomy are equally effective. In inadequate serum testosterone suppression (<50 ng/mL) with medical or surgical castration, additional hormonal therapy with estrogen, antiandrogens or steroids can be given. In failure of initial androgen ablation (AAT), may give antiandrogens such as ketoconazole or estrogens. Patients being treated with medical or surgical castration are at risk for having or developing osteoporosis. Supplemental calcium (500 mg daily) and vit D (400 IU) is given. For treatment of osteoporosis, give bisphosphonate therapy (e.g., ibandronic acid 150 mg tab monthly). In clinically localized disease patients, androgen ablation is given for 2-3 years. Adjuvant androgen ablation can be given in presence of LN metastasis after radical prostatectomy in clinically localized disease patients.
- (I) After initial-definitive therapy, follow-up includes: PSA every 6 months for 6 years, then every year, and DRE every year. For N1 or M1, follow-up includes PE + DRE +PSA every 3-6 months.
- (J) A rising PSA value consists of 3 consecutive rising PSA values at least 3 months apart. For post-radical prostatectomy, 2 consecutive rising PSA levels. If PSA doubling time is >10 months or PSA <2 ng/mL, there is a lower risk of metastasis. If PSA doubling time is <3 months or positive seminal vesicles or LNs, there is higher risk of metastasis. Bone scan +/- abd/pelvic CT is done upon rising PSA (>0.3 ng/mL and rising on >=2 determinations) and or DRE, particularly for those patients who are candidates for local therapy: (a) original clinical stager T1-T2, NX or M0, b) life expectancy >10 years, c) PSA now <10ng/mL).
- (K) Salvage radical prostatectomy is an option for highly selected patients with local recurrence after EBRT, brachytherapy, or cryotherapy in the absence of metastases, but the morbidity (incontinence, loss of erection, anastomotic stricture) is high. Primary salvage therapy when PSA does not fall to undetectable levels with persistent local tumor is preferably RT +/- androgen ablation or androgen ablation alone. For those without evidence of persistent local tumor burden but low risk for metastasis, primary salvage therapy is preferably RT or androgen ablation or observation; for those at high risk of metastasis, androgen ablation (AAT) or observation. If patient has metastatic disease, androgen ablation is preferred or observation. Assure castrate levels of testosterone. Secondary salvage therapy after AAT failure includes bisphosphonate treatment (such as ibandronate, zoledronate, clodronate, icandronate) for metastatic bone disease and any of - chemotherapy (docetaxel-based preferred with prednisone or estramustine) or supportive care or systemic RT (samarium or strontium). Other drugs include ketoconazole/ doxorubicin, etoposide/estramustine, mitoxantrone/ prednisone, estramustine/ paclitaxel. For visceral or soft tissue masses of neuroendocrine type give cisplatin/ etoposide or carboplatin/ etoposide.



TESTICULAR CANCER

The management of testicular cancer must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

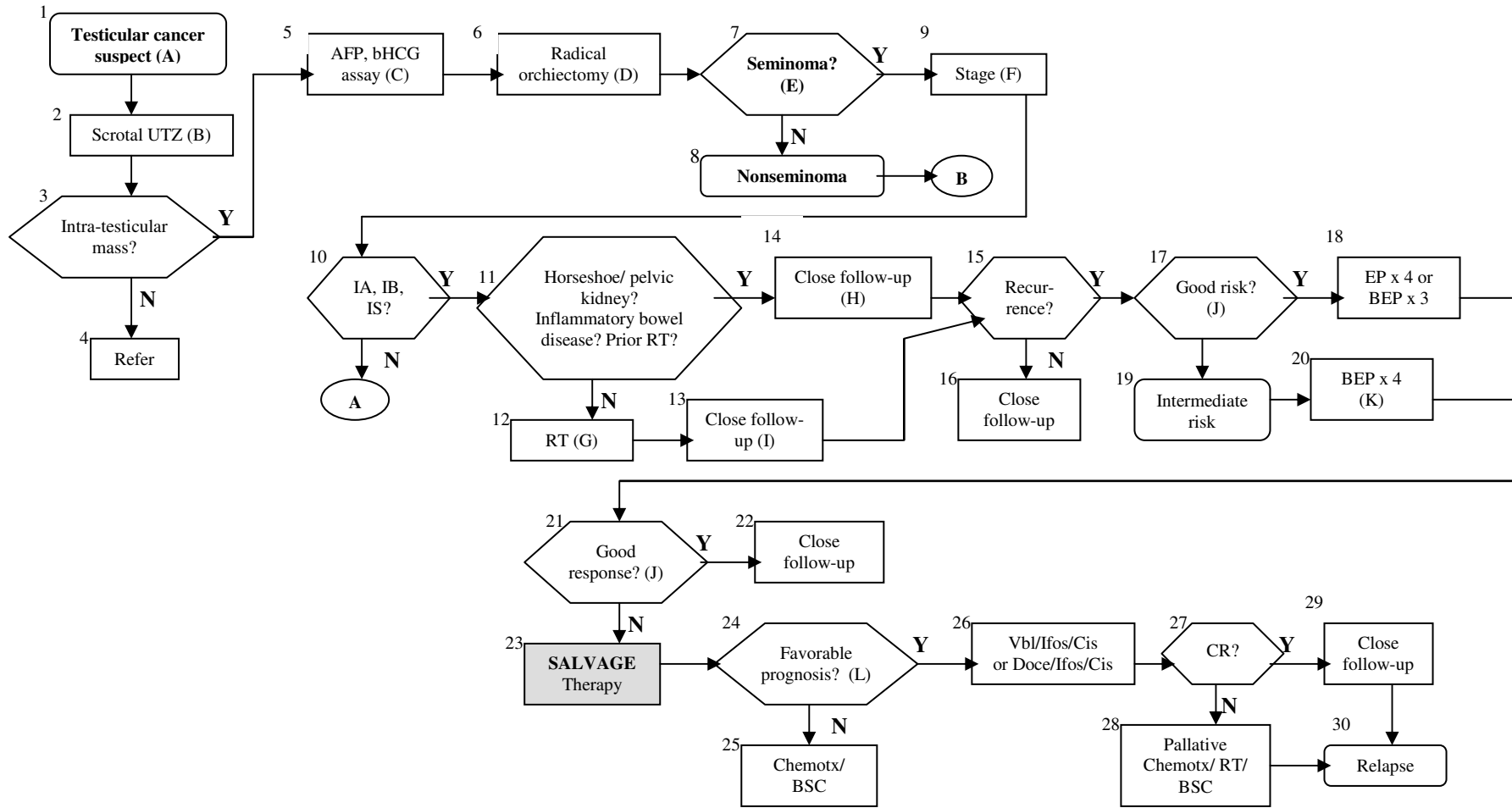
- (A) Testicular cancer gradually presents as a painless mass. Minor trauma to the testes often draws attention to the mass. Symptoms related to metastases includes abdominal fullness, palpable mass, pain, lower extremity edema, left supraclavicular mass, and systemic symptoms, such as fatigue. Cryptorchidism is a risk factor, and abdominal testes have 4x the risk of inguinal testicular cancer. Do complete clinical history & physical exam (H&P).
- (B) Scrotal ultrasound is the test of choice to distinguish between intratesticular and extratesticular location of the mass. Extratesticular masses are generally benign (i.e., varicocele, hydrocoele, hematocele, orchitis, and hernia) and subsequent management may be just conservative or surgical. Intratesticular masses are malignant unless proven otherwise.
- (C) 85% of cases will have elevation of at least one of the 2 markers – alpha-feto protein (AFP) and beta-human chorionic gonadotrophin (b-HCG). 10% of patients with early-stage seminomas can have elevated b-HCG whereas AFP is never elevated in pure seminomas. Patients with elevated AFP, regardless of the histology should be treated as non-seminomatous germ cell tumors. Pure seminomas, dysgerminomas, and differentiated teratomas are always AFP(-), pure yolk-sac tumors are always AFP(+), while embryonic carcinomas and combined tumors can – depending on the mass of endodermal structures – be more or less strongly AFP-(+) or (-). AFP is the 2nd most important marker for germ cell tumors aside from b-HCG.
- (D) Radical orchiectomy (performed by inguinal approach) establishes accurate histopathologic diagnoses and provides other information needed for anatomic staging. 96% of testicular tumors are germ cell tumors (the other 4% are benign stromal tumors).
- (E) Seminomas are the most common (40% of all germ cell tumors). Nonseminomas include embryonal carcinoma, teratocarcinoma, and yolk sac tumors. Treatment of pure seminomas and nonseminomas differ.
- (F) CT is the method of choice for staging and follow-up. Pelvic, abdominal, and chest CTscans are used to uncover nodal or pulmonary metastasis. If CTscan is not available or affordable, chest tomography and pelvic/abdominal ultrasound are used, although with less sensitivity and specificity. Do also chemistry profile, including LDH.

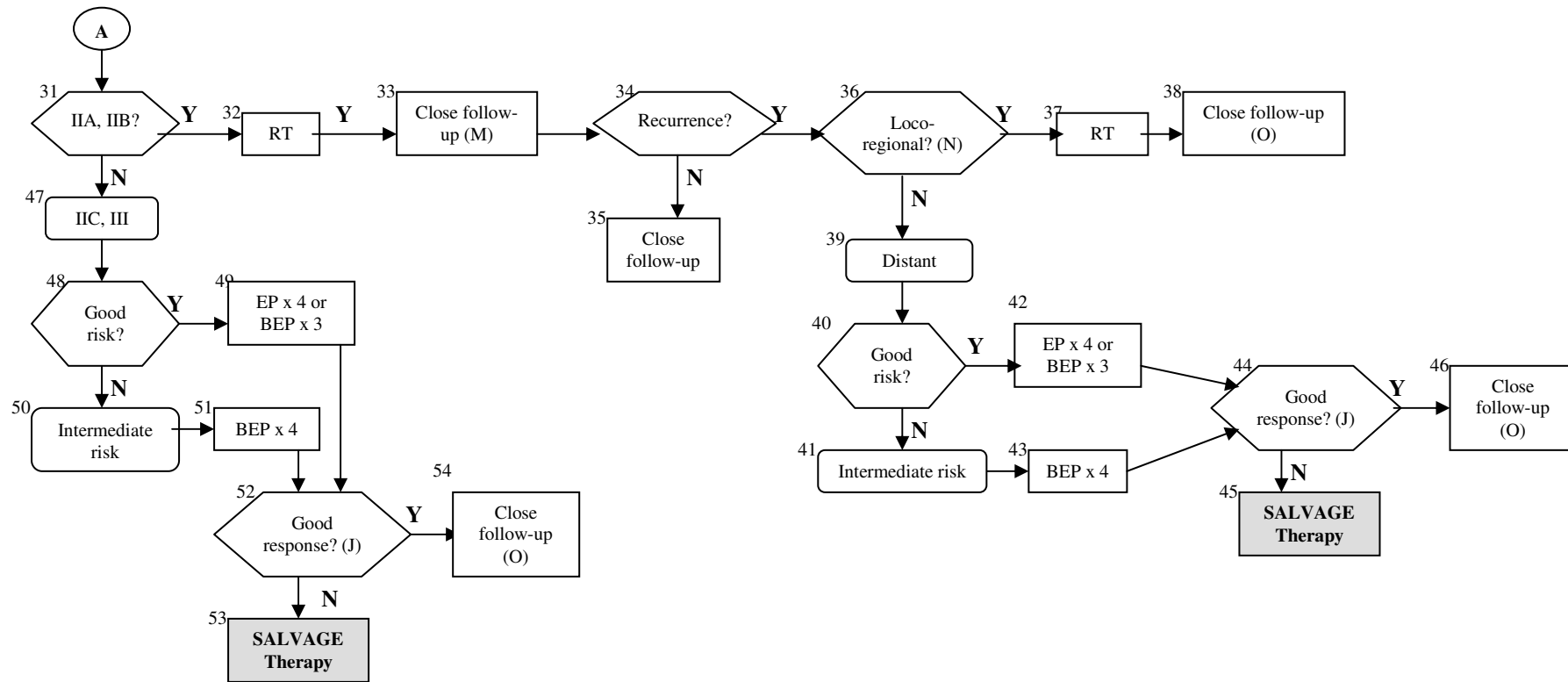
The AJCC (2002) staging indicates:

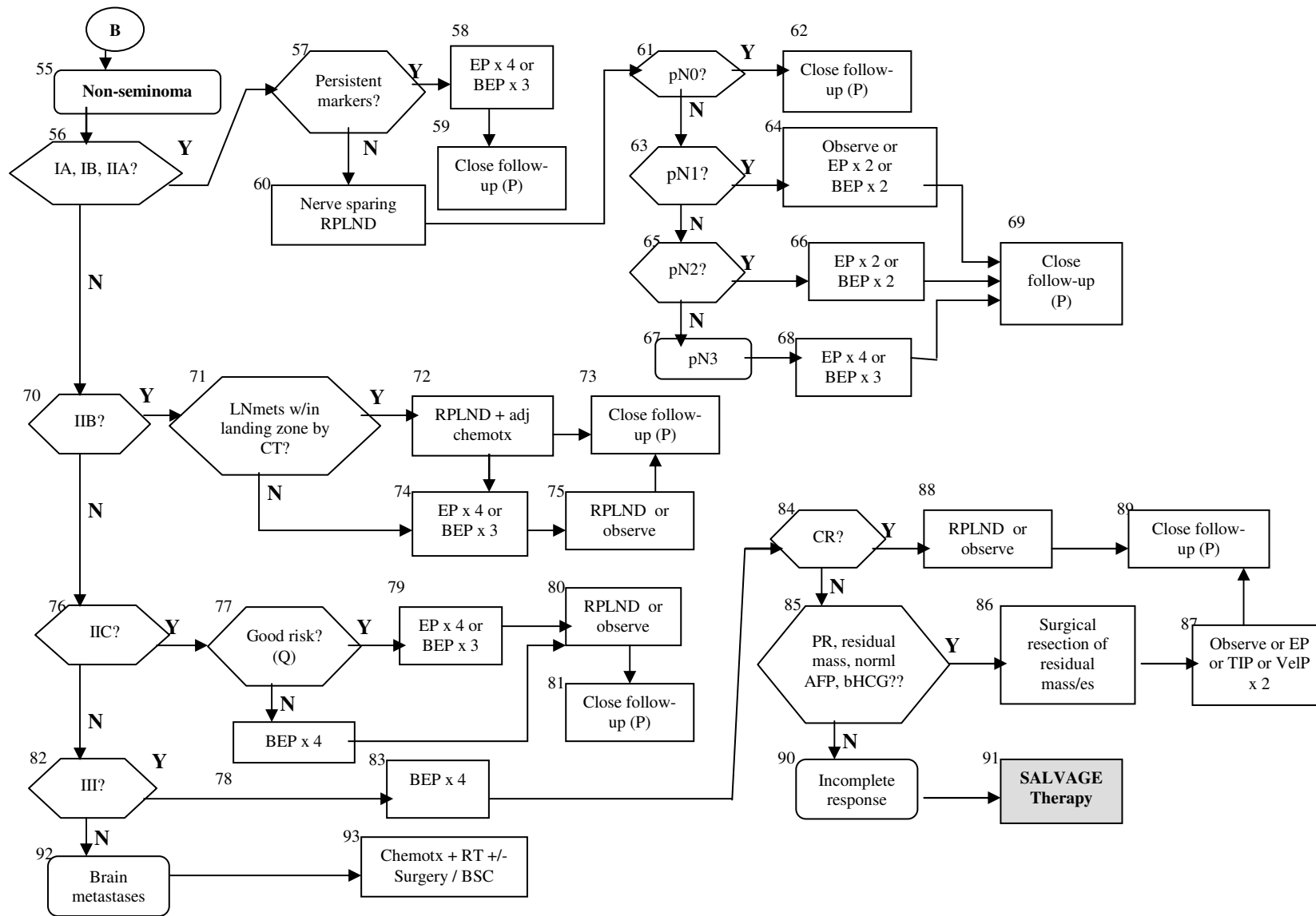
Stage I	pT1-4N0M0S0 S0 – marker study levels within normal limits
Stage IIA	anyTN1M0S0-1 S1 – LDH<1.5N, HCG<5000mlu/mL, AFP<1000 ng/mL N1 – mets with LN mass <=2cm or multiple LNs, none >2cm in greatest dimension
Stage IIB	anyTN2M0S0-1 N2 – mets with LN mass >2, <5 cm or multiple LNs any one mass >2cm but not >5 cm in greatest dimension
Stage IIC	anyTN3M0S0-1 N3 – mets with LN mass >5cm in greatest dimension
Stage IIIA	anyTanyNM1aS2 S2 – LDH=1.5-10xN or HCG=5000-50000 or AFP= 1000-10000 M1a – Non-regional nodal or pulmonary metastasis
Stage IIIB	anyTN1-3M0S2 or anyTanyNM0S3 S3 – LDH>10xN or HCG>50000 or AFP>10000
Stage IIIC	anyTN1-3M0S3 or anyTanyNM1aS3 or anyTanyNM1banyS M1b – distant metastasis other than to non-regional LNs and lungs

- (G) For Stage IA, IB, IS seminoma, primary treatment is RT to infradiaphragmatic or paraaortic LN; consider also to ipsilateral ileoinguinal nodes.
- (H) Follow-up for Stage IA, IB, IS post radical orchiectomy, post-RT includes H&P, chest x-ray, AFP, bHCG, LDH every 3-4 months for year 1, every 6 month for year 2, then annually; pelvic CT annually for 3 years for s/p aortic RT
- (I) For Stage IA, IB, IS post radical orchiectomy followed by observation, follow-up includes H&P, AFP, bHCG, LDH every 3-4 months for years 1-3, every 6 months for years 4-7, then annually; abdominal/ pelvic CT is done at each visit with chest x-ray at alternative visits up to year 10

- (J) Seminoma risk classification: 1) Good risk = any primary site, absence of nonpulmonary visceral metastases, normal AFP, any bHCG, any LHD; 2) Intermediate risk = any primary site, presence of nonpulmonary metastases and normal AFP, any HCG, any LDH
- (K) Chemotherapy regimen: a) EP = etoposide/ cisplatin, b) BEP = bleomycin/etoposide/cisplatin
- (L) For seminomas, favourable prognosis for salvage therapy is predicted by - low markers, low volume, CR on 1st line therapy, and testis primary; unfavourable prognosticators are incomplete response, high markers, high volume, extratesticular primary, late relapse
- (M) For seminomas Stage IIA, IIB post-RT primary treatment, follow-up includes H&P, chest x-ray, AFP, b-HCG, LDH every 3-4 months for years 1-3, every 6 months for year 4, then annually; abdominal CT at month 4 of year 1
- (N) Seminoma can develop locoregional recurrence of small volume (<5 cm) or abdominal/ retroperitoneal recurrence meeting criteria for clinical N2 or less. Distant recurrence is appearance of bulky nodal disease (>5 cm).
- (O) For seminoma, follow-up after treatment of 1st relapse includes H&P, chest x-ray, AFP bHCG, LDH every 2 months for year 1, every 3 months for year 2, every 4 months for year 3, every 6 months for year 4, then annually. Abdominal/ pelvic CT at month 4 of year 1 s/p surgery, otherwise abdominal/pelvic CT every 3 months until stable. May do PET scan.
- (P) Follow-up for non-seminoma: Stage IA, IB - markers & chest x-ray every 1-2 months year 1, every 2 months year 2, every 3 months year 3, every 4 months year 4, every 5 months year 6, annually thereafter; abdominal/ pelvic CT every 2-3 months year 1, every 3-4 months year 2, every 4 months year 3, every 6 months year 4, then annually thereafter. For follow-up after CR to chemotherapy and/ or RPLND, follow-up includes markers, chest x-ray every 2-3 months years 1-2, every 4 months years 3-4, every 6 months year 5, then annually thereafter; abdomino/pelvic CT every 6 months year 1, every 12 months years thereafter
- (Q) Nonseminoma risk classification: 1) Good risk = testicular or retroperitoneal primary tumor, no pulmonary visceral metastases, all of markers - AFP<1000 ng/mL, bHCG<5000 iu/L, LDH<1.5 x ULN; 2) Intermediate risk = testicular or retroperitoneal primary tumor, no pulmonary visceral metastases, any of markers - AFP 1000-10000 ng/mL, bHCG 5000-50000 iu/L, LDH 1.5-10 x ULN; 3) Poor risk = mediastinal primary tumor or nonpulmonary visceral metastases or any of markers AFP> 10000 ng/mL, bHCG> 50000 iu/L, LDH> 10xUNL
- (R) Chemotherapy regimen: TIP = paclitaxel/ ifosfamide/ cisplatin; VeIP = vinblastine/ ifosfamide/ cisplatin



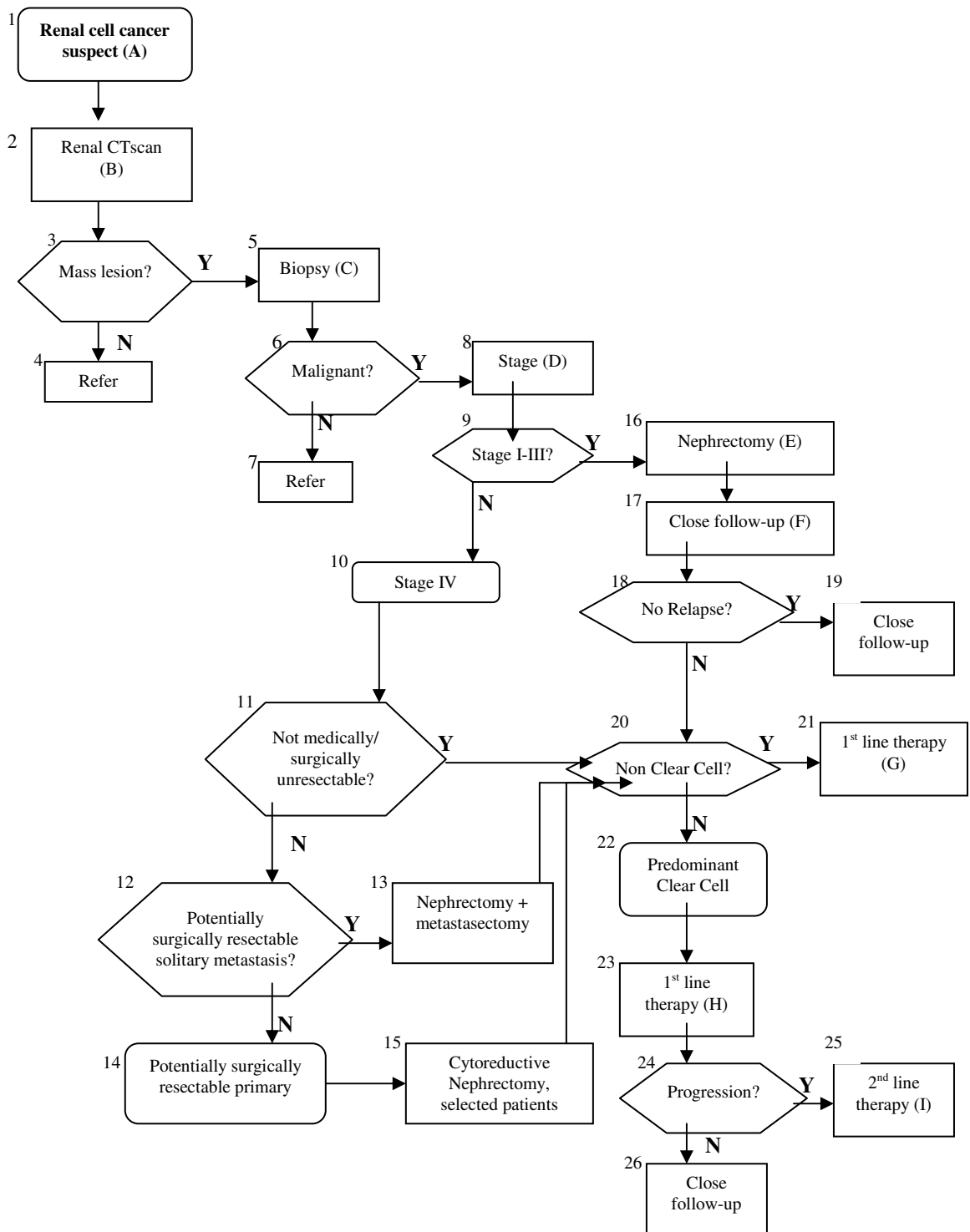




RENAL CELL CARCINOMA (RCC)

The management of RCC must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

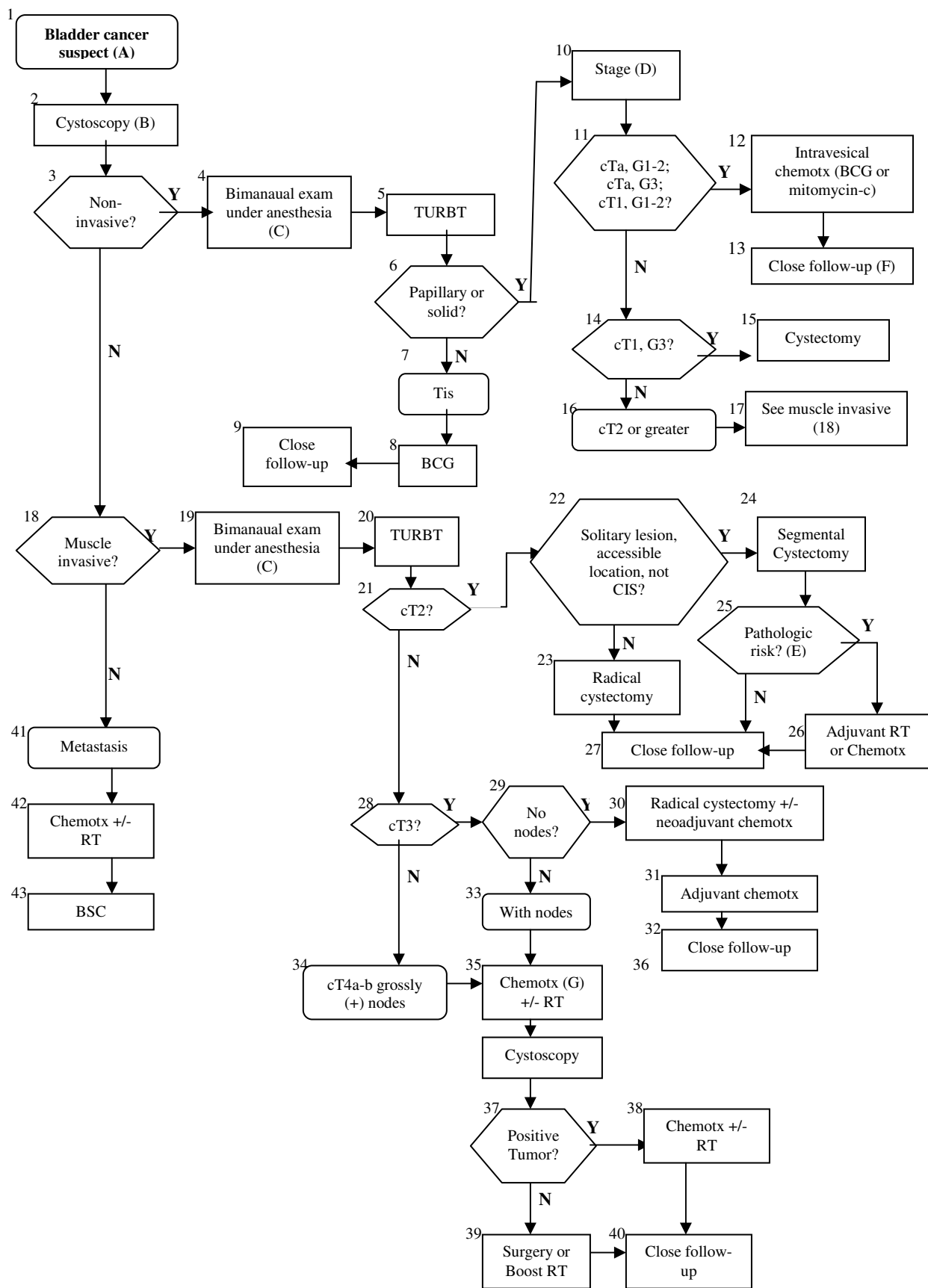
- (A) The most frequent traditional presentations are hematuria (56%), pain (38%), palpable mass (36%), weight loss and fatigue (27%), fever (11%), varicocele (2%), and incidental (6%). When asymptomatic, it is found incidentally by ultrasound, CT scan, or MRI scan for other regions. Other presentations are related to metastasis (lung, bone, skin, liver, brain) and paraneoplastic signs (30%), like anemia, gynecomastia, etc.
A complete history & PE is done. Do CBC, LDH, urinalysis, metabolic panel.
- (B) CT scan is currently the more sensitive and specific affordable test (90% accuracy). MRI is competitive with CT and gives similar if not more information with similar accuracy (96%). The latter has the advantage of demonstrating vascular invasion and renal hilar nodes better. Patients allergic to contrast media are ideal for MRI. Disadvantage of MRI is higher cost.
Ultrasound is helpful in differentiating a cystic lesion from a solid tumor. It is less sensitive and less specific than CT for tumor extent.
- (C) Biopsy can be fluoroscopic, ultrasound or CT-guided. Histologic diagnosis is 80-90% adenocarcinoma. The terms renal cell carcinoma, renal adenocarcinoma, clear cell carcinoma, hypernephroma, and Grawitz tumor are synonymous.
- (D) Staging is based on AJCC (2002), and guided by CT scan prior operation:
- | | | | |
|-----------|------------|----|--|
| Stage I | T1N0M0 | T1 | Tumor ≤2.5cm/ limited to kidney |
| Stage II | T2N0M0 | T2 | Tumor >2.5cm/ Limited to kidney |
| Stage III | T1N1M0 | T3 | a) perinephric invasion |
| | T2N1M0 | | b) major veins |
| | T3aN0-1M0 | T4 | Invades beyond Gerota's capsule |
| Stage IV | T3bN0-1M0 | | |
| | T4NanyM0 | N1 | Single, ≤2cm |
| | TanyN2-3M0 | N2 | Single, >2cm and ≤5cm; N3 Multiple, ≤5cm or >5cm |
| | TanyNanyM1 | M1 | With distant metastasis |
- Do Chest CT if abnormal chest x-ray and or advanced lesions, bone scan or brain MRI if clinically indicated.
- (E) Cornerstone of renal cancer therapy is radical nephrectomy. Early ligation of renal vein pedicle to preclude tumor embolization is a principle of the operation.
Nephron-sparing surgery may be indicated in selected patients – multiple primaries, uninephric state, renal insufficiency, small (<4 cm) unilateral tumors. Lymph node dissection is optional.
- (F) For post-nephrectomy Stage I-III cases, follow-up every 4-6 months for 2 years, then every 6 months for 3-5 years, then annually, looking at complete history & PE, chest x-ray, metabolic panel, LDH. At 4-6 months, then annually or as indicated do abdominal CT.
- (G) 1st line therapy in non-clear cell RCC includes sorafenib, sunitinib, bevacizumab; for sarcomatoid histologies, gemcitabine, capecitabine, 5-FU, doxorubicin. Palliative RT or metastatectomy and BSC can be done. Radiotherapy may be effective for the relief of pain, bone and CNS metastasis. Adjuvant RT for Stage I-III cases is optional. Under Best Supportive Care (BSC), bisphosphonates can be given for Metastatic Bone Disease (MBD).
- (H) 1st line therapy in predominantly clear cell RCC includes high dose IL-2 for selected patients, sorafenib, sunitinib, bevacizumab, IFN or low dose IL-2+/-IFN. Palliative RT or metastatectomy and BSC can be done.
- (I) 2nd line therapy (use cross-over regimen) includes sorafenib, sunitinib, IFN, IL-2, bevacizumab. Palliative RT or metastatectomy and BSC can be done.



URETHELIAL CANCER OF THE URINARY BLADDER

The management of urinary bladder cancer must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

- (A) The most common symptom is hematuria (70-95%); there can also be dysuria, UTI, and symptoms related to distant metastasis. Do complete history & PE.
- (B) Cystoscopic with biopsy appearance may reveal non-invasive disease, muscle invasion, and metastatic disease.
- (C) Primary tumor assessment includes bimanual examination under anesthesia before and after endoscopic surgery (biopsy or transurethral resection) and histologic verification of the presence or absence of tumor when indicated – Clinical Staging ("c"). The finding of bladder wall thickening, a mobile mass or a fixed mass suggests the presence of T3a, T3b, and T4b disease, respectively.
- Appropriate imaging techniques for lymph node evaluation is used. Evaluate for distant metastases. Imaging may include IVP, CI urography, renal ultrasound with retrograde pyelogram, or MRI urogram. Do CBC, alkaline phosphatase, chest x-ray, bone scan if alkaline phosphatase elevated or with symptoms, ECG, creatinine clearance.
- (D) Pathologic Staging – microscopic examination and confirmation of extent are required. Total cystectomy and LN dissection generally required for this staging. The histopathologic types are – Urothelial (transitional cell) carcinoma in situ (papillary, flat, with squamous metaplasia, with glandular metaplasia, with squamous and glandular metaplasia), squamous cell carcinoma, adenocarcinoma, undifferentiated carcinoma. Histopathologic Grade (G):
- | | |
|------|---|
| GX | not assessed |
| G1 | well differentiated |
| G2 | moderately differentiated |
| G3-4 | poorly differentiated or undifferentiated |
- AJCC 2002 Stage Grouping is as follows:
- | | |
|------------|--|
| Stage 0a | Ta- non-invasive papillary carcinoma N0 M0 |
| Stage 0is | Tis – carcinoma-in-situ, 'flat tumor' N0 M0 |
| Stage I | T1 – invades subepithelial connective tissue N0 M0 |
| Stage IIA | T2a – invades superficial muscle (inner half) N0 M0 |
| Stage IIB | T2b – invades deep muscle (outer half) N0 M0 |
| Stage IIIA | T3a – invades perivesical tissue microscopically N0 M0 |
| Stage IIIB | T3b – invades perivesical tissue macroscopically N0 M0 |
| Stage IIIC | T4a – invades prostate, uterus, vagina N0 M0 |
| Stage IV | T4b – invades pelvic wall, abdominal wall N0 M0 |
| | Any T N1M0 |
| | Any T N2M0 |
| | Any T N3M0 |
| | Any T Any NM1 |
- (E) Pathologic risk – positive nodes, positive margin, high-grade, pT3^c. Uncertain complete resection is based on – size/ location, no muscle in specimen, inadequate staging, lymphovascular invasion
- (F) Close follow-up includes urinalysis and cystoscopy initially at 3 months and increasing interval as appropriate (3monthly for 2 years, then every 6 months for 2 years, then annually); biopsy/ cytology as needed; imaging of upper collecting system every 1-2 years (IVP, CT urography, retrograde pyelogram, or MRI urogram); vitamin B12
- (G) Chemotherapy includes MVAC, gemcitabine/ paclitaxel and cisplatin/ carboplatin for transitional cell carcinoma; for adenocarcinoma – 5FU-based chemotherapy



SOFT TISSUE SARCOMA (STS)

The management of STS must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

- (A) A high index of suspicion is invaluable – these can be unexplained soft tissues masses. These tumors grow insidiously, are often in inaccessible sites, and have poor encapsulation. Most sarcomas are not painful at presentation. Fixation of a mass to subcutaneous tissue or skin, or underlying fascia or muscle and presence of warmth or a distended local venous pattern are all clinical indications of a malignant lesion. A complete history & PE is done. Do imaging of primary site with CT or MRI with contrast, as clinically indicated. Do Chest imaging.
- (B) Any soft tissue mass should undergo biopsy at once. Because the mode of therapy is determined in large part by the histology of the tumor, ample tissue must be delivered to the pathologist. CT-guided core biopsy is preferred, particularly for patients receiving pre-op RT or chemotherapy. Pre-resection biopsy may not be done for respectable retroperitoneal sarcoma. Incisional biopsy should be done for low-grade or intermediate lesions, lesions with extensive necrosis, and/ or insufficient tissue for definitive diagnosis.
- (C) The STS discussed in this guideline are desmoid tumors, sarcomas of the extremity, retroperitoneum, and intraabdomen (except GIST) – alveolar soft-part sarcoma, desmoplastic small round cell tumor, epithelioid sarcoma, clear cell sarcoma, chondrosarcoma, extraskeletal, osteosarcoma extraskeletal, primitive neuroectodermal tumor, fibrosarcoma, leiomyosarcoma, liposarcoma, malignant fibrous histiocytoma, malignant hemangiopericytoma, malignant peripheral nerve sheath tumor, rhabdomyosarcoma, synovial sarcoma, sarcoma, NOS.
- (D) For desmoids, microscopic positive margins may be acceptable if achieving negative margins would produce excessive morbidity
- (E) Physical exam with appropriate imaging every 3-6 months for 2-3 years, then annually
- (F) Combination chemotherapy regimens include – AIM (doxorubicin, ifosfamide, mesna), MAID (mesna, doxorubicin, ifosfamide, dacarbazine), AD (doxorubicin, dacarbazine), gemcitabine/docetaxel. For desmoid tumors – tamoxiphen, methotrexate, vinblastine, low-dose interferon, doxorubicin-based regimens can be used. For rhabdomyosarcoma, second-line therapy can be irinotecan, cyclophosphamide/topotecan. For angiosarcoma – taxanes, interferon, vinorelbine.
- (G) The most important prognostic factor for STS patients is the histologic grade (AJCC 2002):

GX	Grade cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated
G4	Poorly differentiated or undifferentiated (4-tiered systems only)

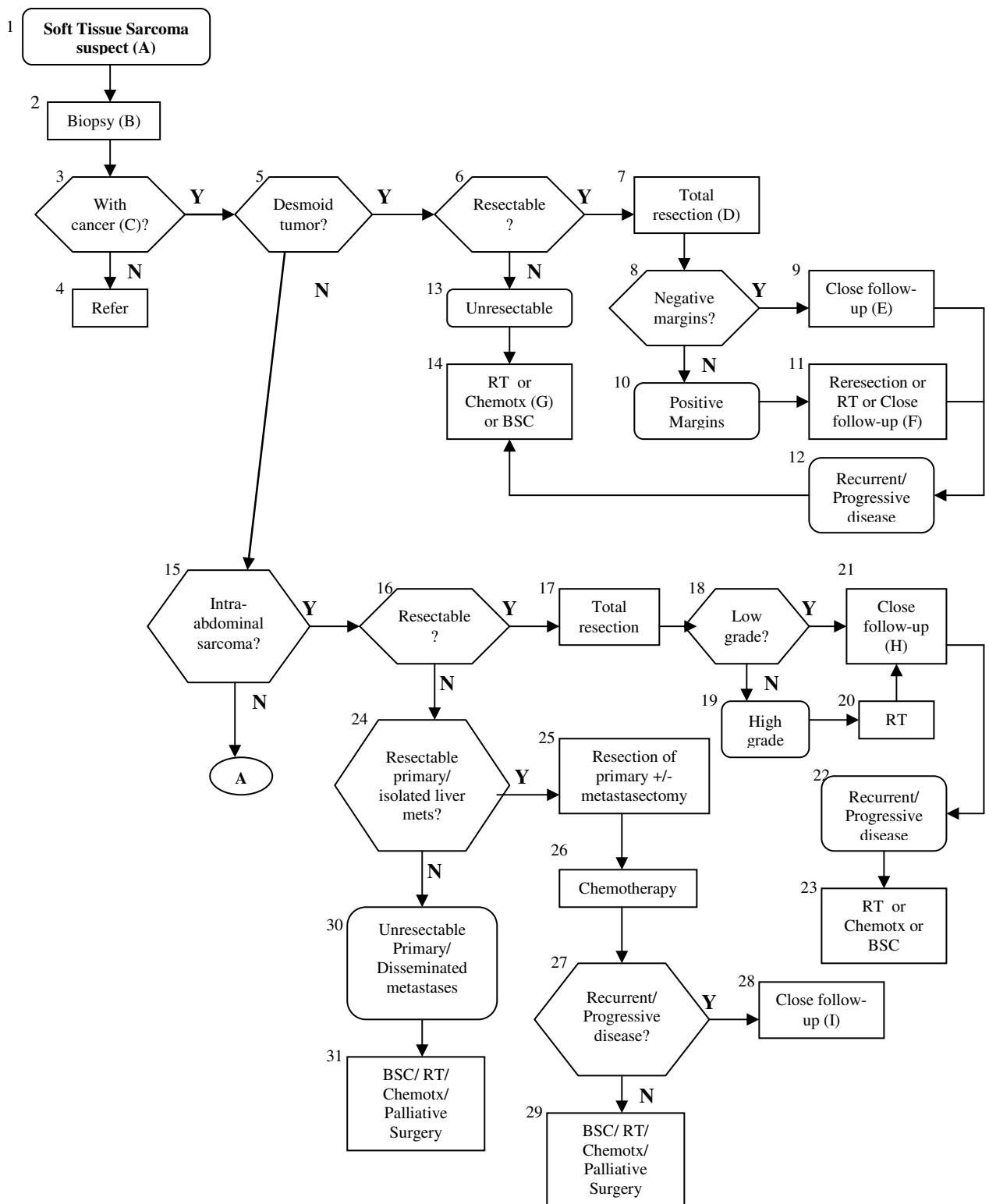
The grade of the sarcoma dominates the stage determination not the anatomic extent of the tumor (AJCC 2002):

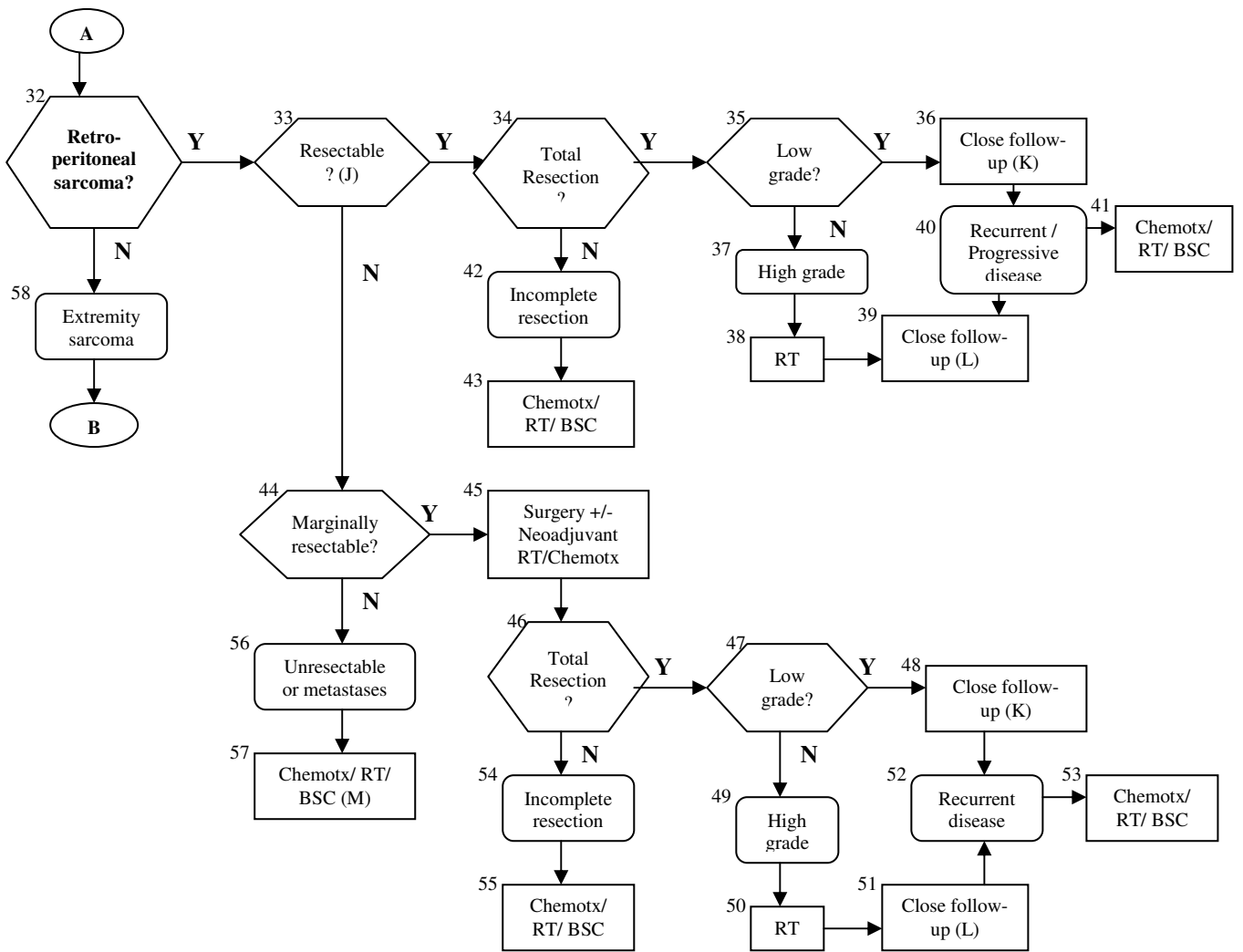
Stage I	T1a-2bN0M0	G1-2	G1	Low
Stage II	T1a-2aN0M0	G3-4	G2-3	High
Stage III	T2bN0M0	G3-4	G2-3	High
Stage IV	anyTN1M0	any G	any G	High or Low
	anyTN0M1	any G	any G	High or Low

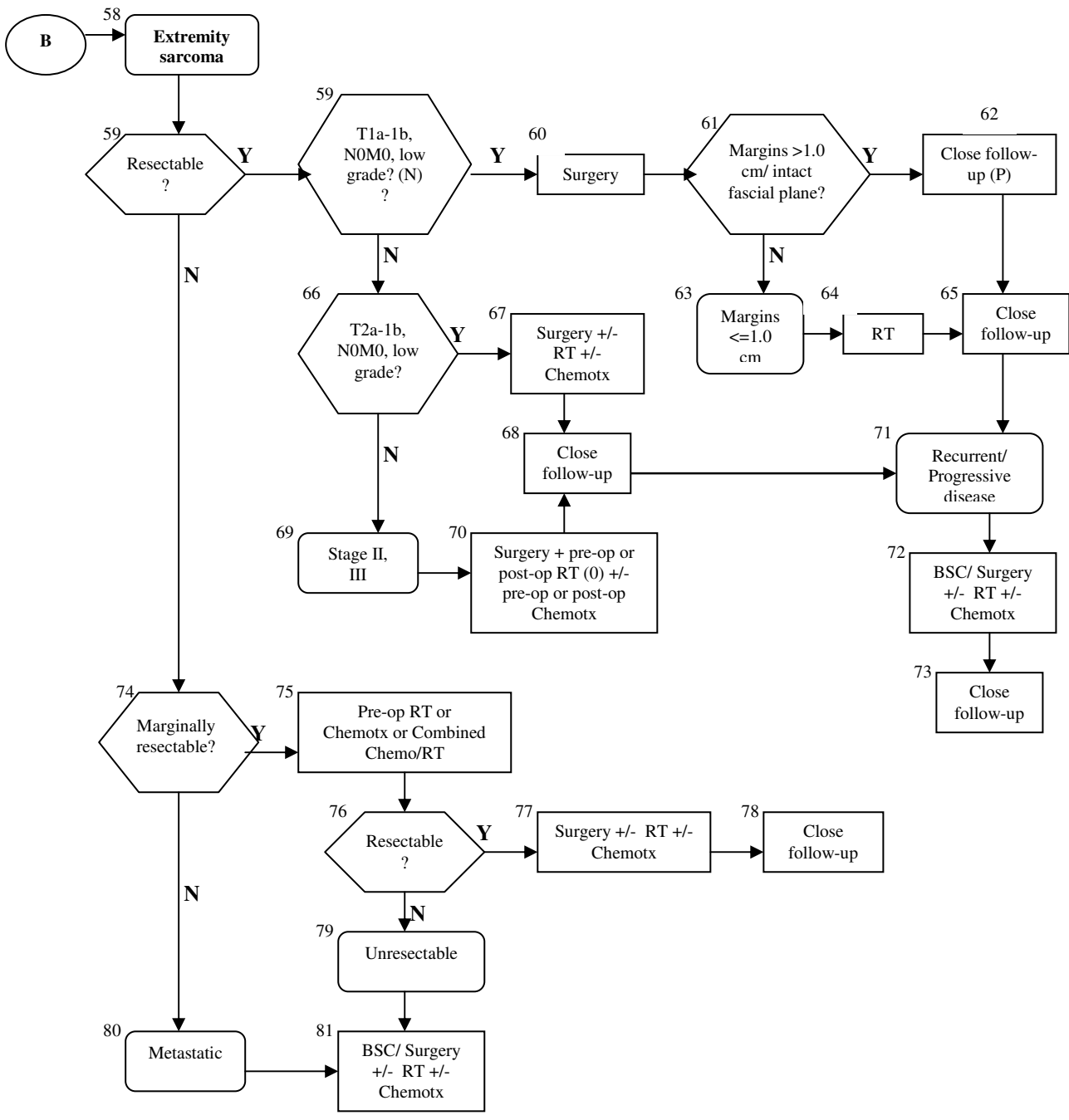
CT or MRI is useful to stage tumor locally for medullary and soft tumor extension (CT) as well as presence of matrix or cortical disruption (MRI) – an information essential in planning limb conservation surgery and radiation portal shaping. Chest roentgenograms are essential for all tumor types. CTscan of lungs is done if CXR is negative for lesions and if treatment decisions hinge upon presence or absence of lung metastasis. Bone scan can be done to evaluate presence of multiple bone lesions, particularly if metastatic bone disease is being considered.

- (H) Physical exam (PE) with imaging (chest/abdominal/pelvic CT) every 3-6 months for 2-3 years, then annually for respectable low grade intra-abdominal sarcomas. For resectable high grade, PE with imaging (chest/abdominal/pelvic CT) every 3-4 months for 3 years, then every 6 months for the next 2 years, then annually. For others (unresectable, with limited liver metastasis, disseminated disease), clinical history & physical exam (H&P) every 3-6 month for 5 years, then annually; abdominal/ pelvic CT every 3-6 months for 3-5 years then annually.
- (I) Resectability is defined as follows: a) respectable – not close to adjacent viscera or critical neurovascular structure and <5cm, b) marginally respectable – high probability of positive margins, abutment of neurovascular structures, requiring resection of adjacent viscera, and c) unresectable or metastasis.
- (J) For low grade retroperitoneal STS, follow-up includes physical exam (PE) with imaging (abdominal/ pelvic CT) every 3-6 months for 2-3 years, then annually; for high grade, PE with imaging (abdominal/ pelvic CT) every 3-6 months for 2-3 years, then every 6 months for next 2 years, then annually. Consider Chest imaging.
- (K) For unresectable or metastatic retroperitoneal STS, balance the risks of the treatment options, with the likelihood of rendering patient respectable, performance status of patient, and potential clinical benefits. Best supportive care (BSC) may also be the best option.

- (L) T1 – tumor 5cm or less in greatest dimension: T1a – superficial tumor (above superficial fascia without invasion of fascia); T1b – deep tumor located either exclusively beneath the superficial fascia, superficial to the fascia with invasion of or through the fascia, or both superficial yet beneath the fascia – retroperitoneal, mediastinal, pelvic sarcomas are classified as deep tumors.
- T2 – Tumor more than 5 cm in greatest dimension: T2a – superficial tumor; T2b – deep tumor
- (M) Surgery for STS has the following guides: a) optimal margins and oncologic control. Re-resection may be required to achieve optimal margins, b) maximal function with minimal morbidity, c) limb sparing generally preferable, d) consider preoperative chemotherapy (chemotx)/ radiotherapy (RT), e) pathology expertise in sarcomas important.
- (N) Pre-operative RT is EBRT followed by surgery with clips, followed by post-op brachytherapy.
- (O) Follow-up after treatment of Stage I extremity STS includes history and physical exam (H&P) every 3-6 months for 2-3 years, then annually with periodic imaging of surgical site; chest x-ray every 6-12 months; for stage II-III, H&P and chest imaging (CXR or CT) every 3-6 months for 2-3 years, then every 6 months for the next 2 years, then annually, with periodic imaging of primary site.







PRIMARY BONE SARCOMA

The management of primary bone sarcoma must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient. The core group includes an orthopedic oncologist, bone pathologist, medical/ pediatric oncologist, radiation oncologist, and musculoskeletal radiologist.

- (A) Pain in area of lesion, which is not activity-related and commonly worsens at night, is the usual signal for a bone tumor. In more advanced cases, a mass or swelling (with significant periosteal reaction or erosion through bony cortex) or pathologic fracture, or with stiffness of joint.
- (B) Roentgenograms are the single most important diagnostic tool which also indicate prognosis. They can detect lesions which are >2cm. Lesions may be –
- Lytic – destroying bone or
 - Blastic – forming bone or inducing reactive bone formation:
 - Circumscribed area of bone destruction – slow growing (e.g., lower grade tumor – giant cell tumor or chondrosarcoma)
 - Moth-eaten – aggressive with cortical destruction, multiple – intermediate growth
 - Permeative pattern – extremely rapid with diffuse lytic destruction associated with cortical disruption and extraosseous tissue mass
- (C) Work-up for potential bone metastasis includes complete history and PE, bone scan, chest x-ray, ALP, CBC, LDH, chest/abdominal/ pelvic CT, PSA, mammogram. Definitive treatment is according to primary site. **Metastatic bone disease (MBD)** is usually from carcinomas. Consider use of bisphosphonates particularly for multiple and or painful metastatic bone disease from carcinoma:
- May use:
 - Ibandronic acid 6 mg IV every 21 days or 50 mg/ tab daily
 - Zoledronic acid 4 mg IV every 3-4 weeks
 - Pamidronic acid 90 mg IV every 3-4 weeks
 - Clodronate 1600 mg/ day or 1040 mg/ day po or 300 mg/day IV for 5-7 days
 - Incadronate 10 mg IV single dose or 2 mg IV every 2 weeks
 - In absence of hypercalcemia, give Vit D 400 IU cap po daily and calcium 500 mg tab po dialy as supplement
- (D) Bone scan is essential to determine if bone lesion is monostotic or polyostotic and can detect tumor foci not visualized on standard radiographs
- (E) CTscan or MRI is useful to stage tumor locally for medullary and soft tissue extension as well as presence of matrix or cortical disruption, particularly for monostotic primary bone tumor
- (F) Biopsy (preferable incisional) should be performed after CT and bone scan evaluations of local extent of lesion is completed and accurate localization of lesion is done. Take the periphery of the lesion, where less interface differentiation of cancer cell occurs between normal and tumor tissues can be assessed, and so as not to predispose to pathologic fracture. Biopsy is optimally performed at hospital which will do definitive management, following same principle for open/needle biopsy. Fresh tissue is needed for molecular studies.
- (G) 4 types of Bone Sarcoma are included in this algorithm:
- Osteosarcoma – work-up includes Chest x-ray, Chest CT, MRI+/- CT of lesion, bone scan, LDH, CBC, alkaline phosphatase. 20% of surface tumors will be high-grade surface osteosarcomas
 - Ewing's sarcoma – work-up includes MRI+/- CT, Chest CT, bone scan, optional bone marrow biopsy, cytogenetics/ molecular studies (90% of Ewing's family tumors will have 1 of 4 specific cytogenic translocations- t(11;22) translocation), LDH
 - Chondrosarcoma
 - Giant cell sarcoma
- (H) Stage is according to Musculoskeletal Tumor Society (MTS):

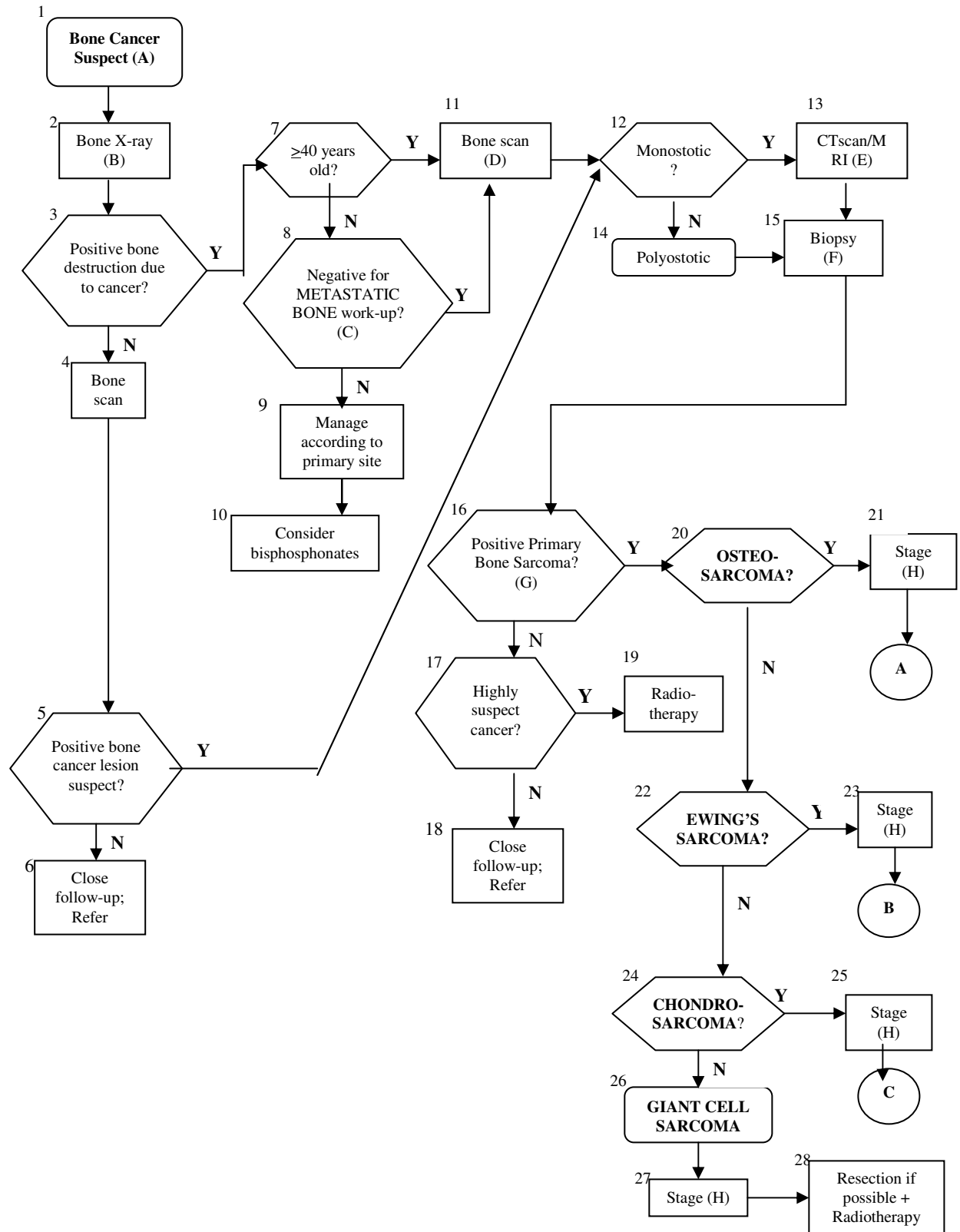
STAGE	GRADE	SITE	METASTASIS
IA	G1	T1	M0
IB	G1	T2	M0
IIA	G2	T1	M0
IIB	G2	T2	M0
III	Any G	Any T	Regional or distant metastasis

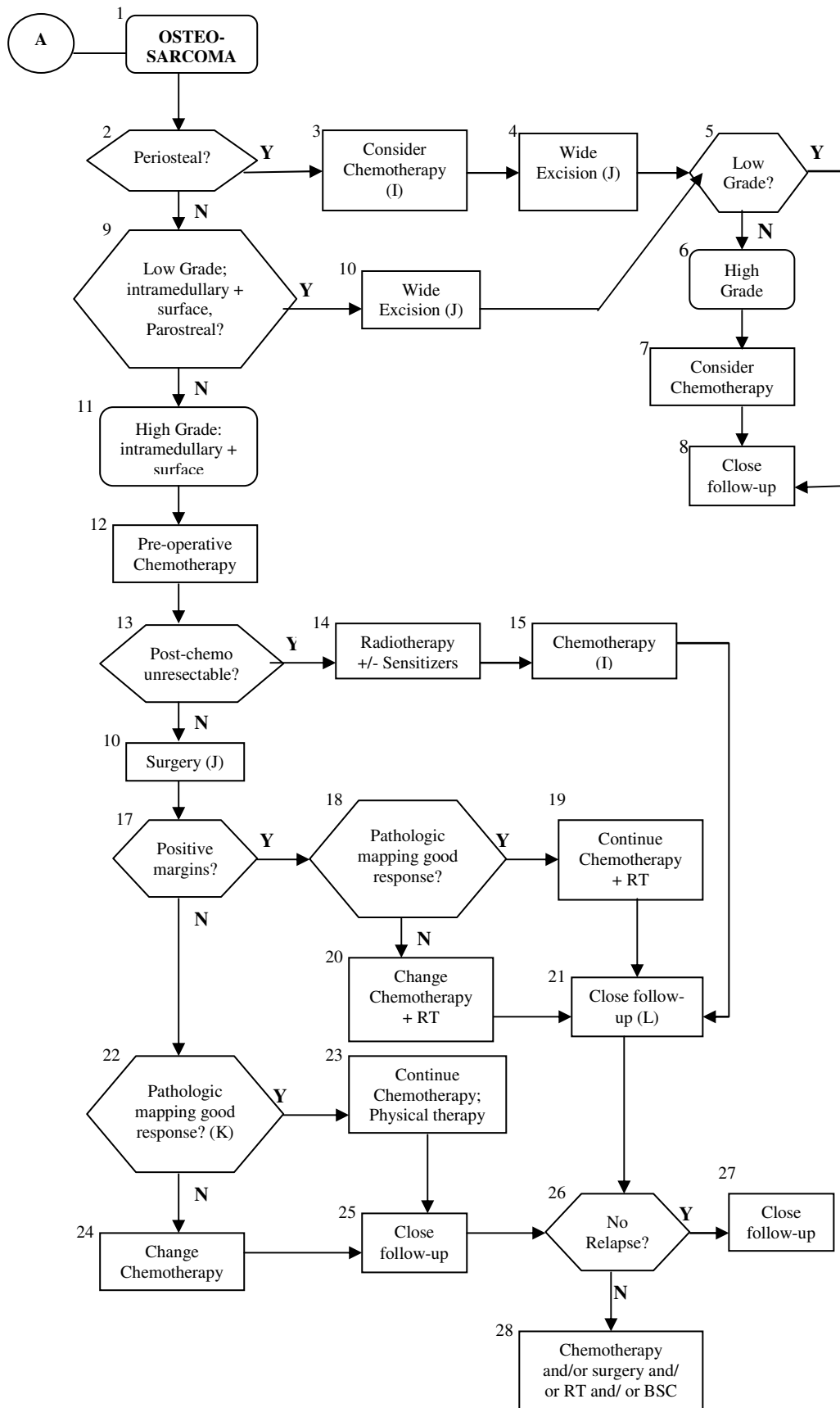
T1 – intracompartmental or within cortex; T2 – extracompartmental or beyond cortex
 Histopathologic Grade (G):

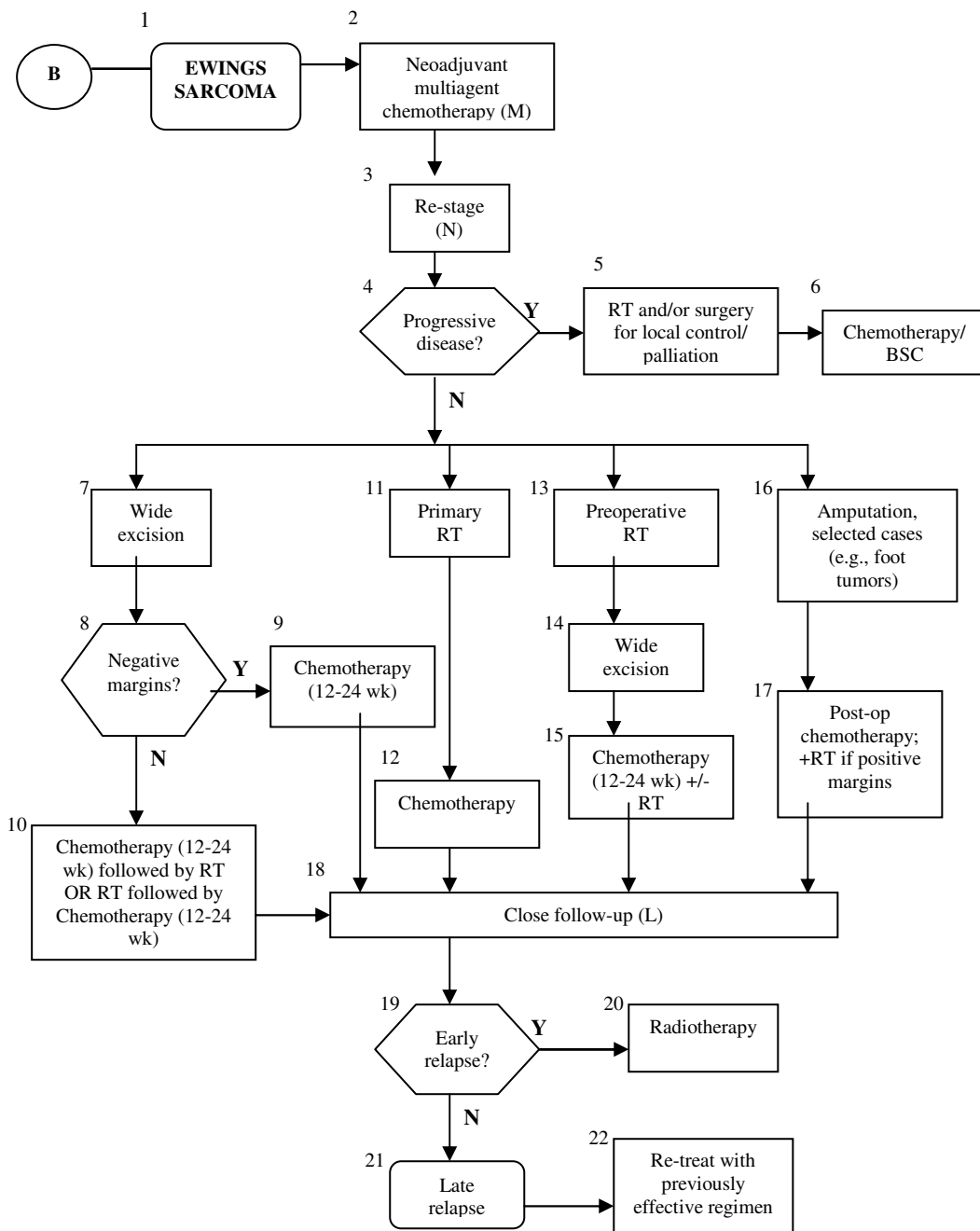
- Gx – grade cannot be assessed
 - G1 – well differentiated – Low Grade
 - G2 – moderately differentiated – Low Grade
 - G3 – poorly differentiated – High Grade
 - G4 – undifferentiated – High Grade
- Note: Ewing's sarcoma is classified as G4;

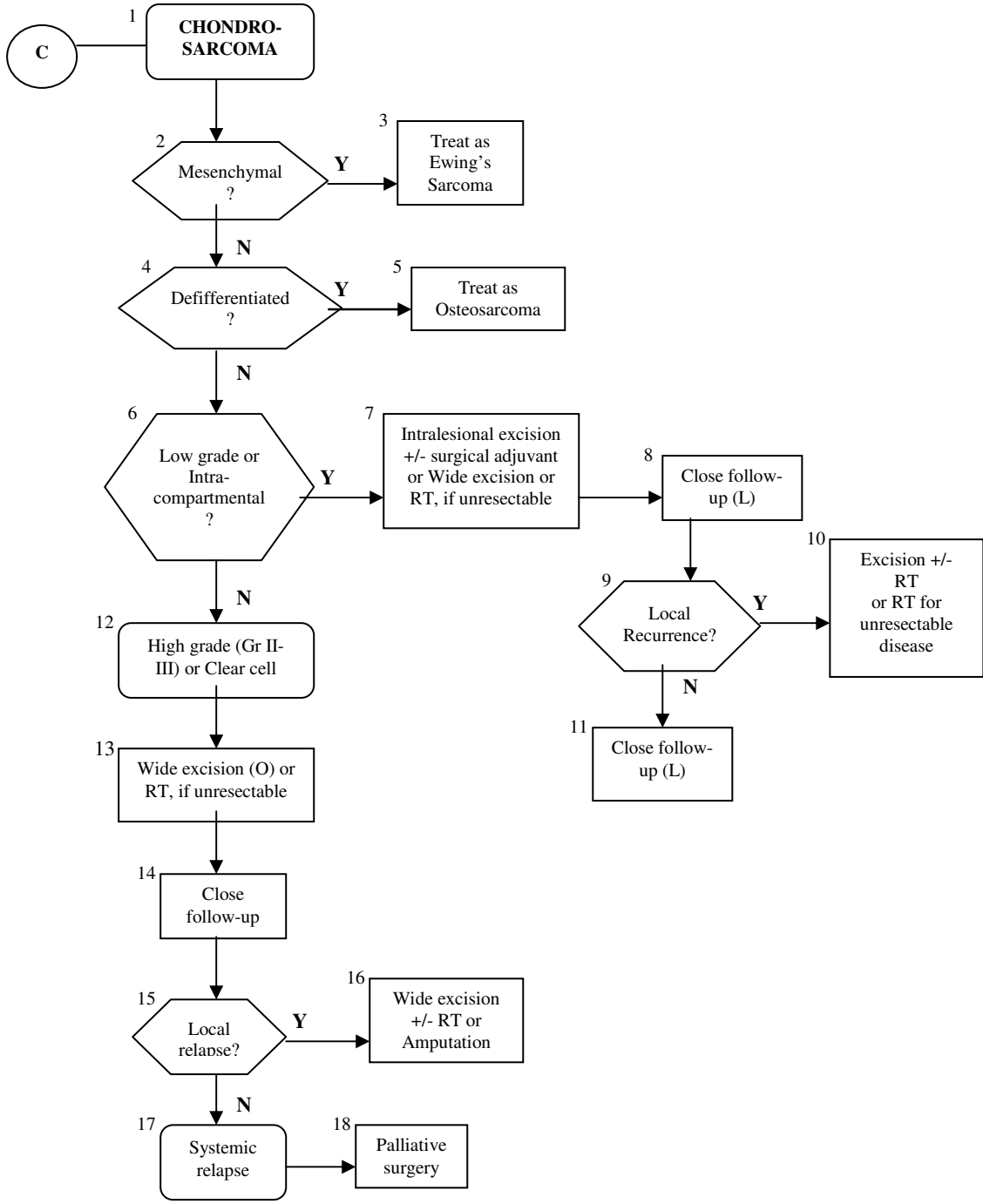
Spread of bone sarcoma to LNs is rare; usual pattern is heterogenous to pulmonary and other sites. Prognosis is similar whether metastasis to LN or other sites. Chest x-ray is routine. CTscan can detect small metastasis to lung.

- (I) Chemotherapy may be IV or intra-arterial, given for 2-6 cycles, and include at least 2 of – doxorubicin, cisplatin, ifosfamide, high-dose methotrexate, and growth factors
- (J) Wide excision implies histological negative margins and is necessary to optimize local control. Limb preservation is desirable, where possible, without compromising satisfactory oncologic outcome. Surgical margins should be negative, wide enough to minimize potential local recurrence and narrow enough to maximize function. In the individual case, either amputation or limb sparing surgery may be the most appropriate. Selected elderly patients may benefit from immediate surgery
- (K) Response defined by pathologic mapping is either good (pathological complete response or no residual disease) or poor (pathological positive residual disease)
- (L) Osteosarcoma - Close follow-up schedule is every 3 months for years 1-2, every 4 months for year 3, every 6 months for years 4-5 and yearly thereafter, looking at PE, chest imaging, CBC, bone scan or local primary site imaging, with reassessment of function every visit.
Ewing's sarcoma – PE, chest x-ray, and local primary site imaging every 2-3 months, CBC annually, MRI every 6 months for 2 years, bone scan as indicated; increase intervals for PE, chest and local imaging after 24 months; annually after 5 years (indefinitely).
Chondrosarcoma – PE, chest and primary site imaging every 3-6 months for 5 years, then yearly for a minimum of 10 years; reassess function at every visit for high-grade lesions. PE, chest and lesion x-ray every 6 months for 2 years then yearly as appropriate for low-grade lesions.
- (M) Chemotherapy should include the following – ifosfamide and or cyclophosphamide, etoposide, doxorubicin, vincristine – treat for 12-24 weeks
- (N) Restage with chest x-ray, local imaging, bone scan (optional), and repeat other at-baseline abnormal studies
- (O) Negative margins in surgery should be obtained. Wide excision may include radical resection and/ or amputation; and may be required to achieve negative margins.







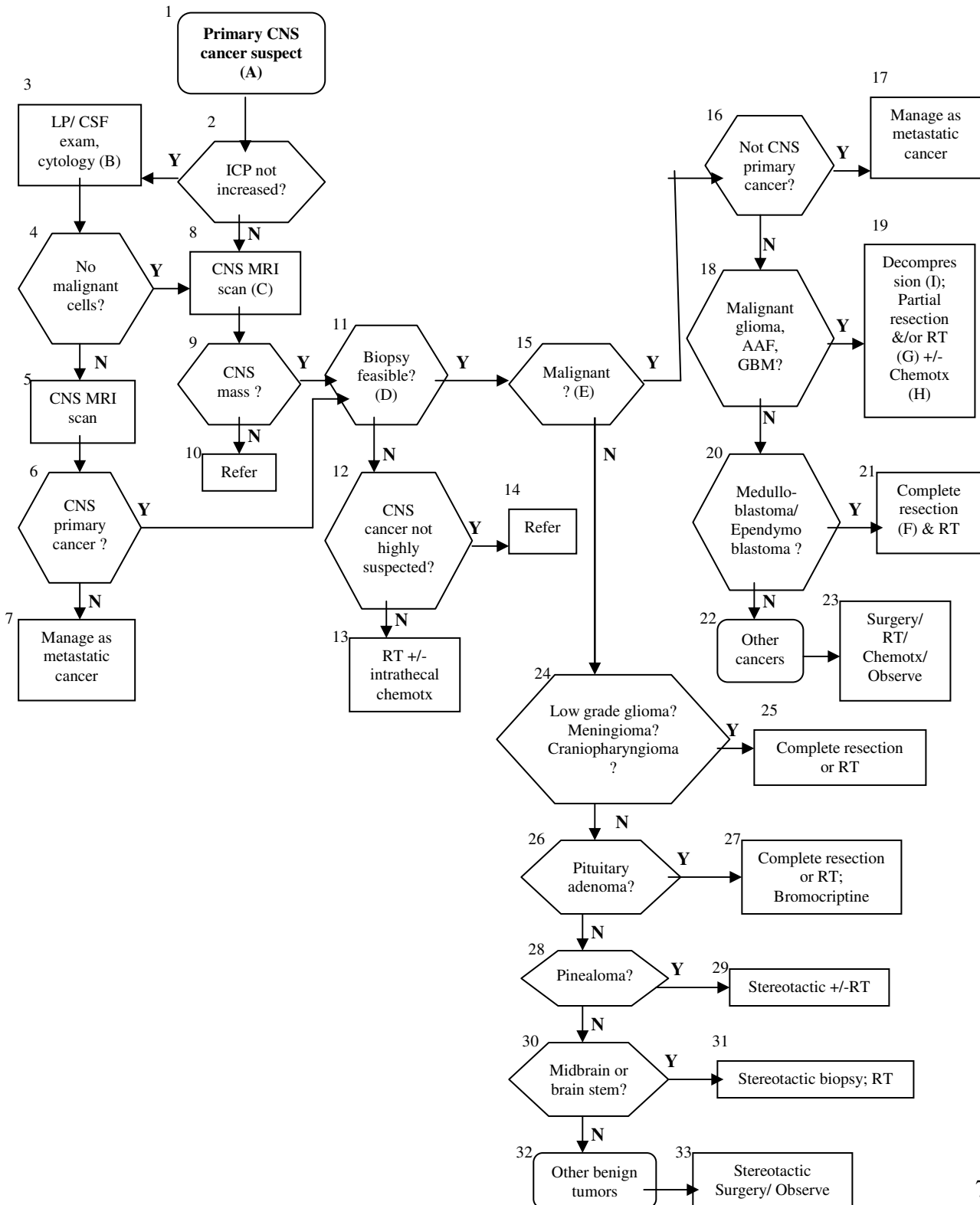


PRIMARY CNS TUMORS

The management of CNS tumors must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

- (A) Increased intracranial pressure (ICP) due to increasing tumor mass and/ or associated edema or hemorrhage/ infarction within the tumor, inside an enclosed rigid compartment (i.e., skull and spinal canal), can cause symptoms such as headache, nausea and vomiting, and later depression of mental status (somnia, lethargy, disorientation). Epileptic seizures in an adult who has never had them are high suspects. Suboccipital tenderness is common with posterior fossa tumors. Degrees of aphasia or apraxia, asymmetry of CN function, incoordination, musculature weakness, and loss of extremity sensation can occur. Always do fundoscopic and visual field (VF) exam to detect increased ICP or VF alterations, respectively.
- (B) Lumbar puncture (LP) is avoided when there is obvious evidence of increased ICP. LP can be useful to determine whether ICP is elevated and to be able to get CSF for exam. CSF protein is elevated approximately 1/3 of the time if with intracranial tumor and almost always in presence of a spinal cord tumor. CSF glucose may be low in presence of highly malignant tumors or metastatic meningeal deposits. CSF cytology is (+) in meningeal carcinomatosis and in tumors that involve the meninges or are situated in a subependymal location. Cerebral spinal fluid cytology should be evaluated in primitive neuronal tumors (PNET) and primary non-Hodgkin's lymphoma.
- (C) MRI is non-invasive, safe, painless, highly sensitive and efficient technique, and can detect neoplasia which is <1 cm in largest diameter. It is the screening procedure of choice in diagnosing and localizing tumors of the brain stem, posterior fossa and spinal cord, and for defining the extent of low-grade gliomas. It can differentiate between intrinsic and extrinsic spinal cord problems and metastatic disease versus disc problems. It can provide 3-dimensional tumor imaging and with contrast agent gadolinium, can identify regions of the tumor where the blood-brain barrier is altered. It does not need iodinated contrast. It will replace myelogram as an initial procedure for evaluating spinal cord tumors and discs.
- CT scanning can be performed if MRI is not available or affordable. CT complements the information available from MRI. CT can detect intracranial calcification and separate them from acute hemorrhage. MRI cannot detect calcifications and can only demonstrate acute hemorrhage with special techniques. CT is more economical in following progress of patients in post-op period.
- (D) Biopsy is required for most CNS tumors. Biopsy can be done with MRI or CT stereotactic guidance. In absence of stereotactic biopsy, a high index of suspicion based on clinical picture can suffice to treat the tumor as malignant.
- (E) Histopathology is more important than staging in determining the clinical behaviour and prognosis of primary brain tumors and their treatment. Astrocytomas are divided into low-grade or benign gliomas, astrocytomas with foci of anaplasia (AAF), and glioblastoma multiforme (GBM), which has the worst prognosis. Medulloblastomas are primitive neuronal tumors (PNET) which are rapidly growing, infiltrative, with marked tendency to spread throughout the subarachnoid space and to produce disseminated meningeal foci. Meningiomas and neurilemmomas are tumor of supporting structures of the nervous system and they can cause compression of spinal cord and spinal roots. Meningiomas are almost always histologically benign, but recur quite commonly. Developmental tumors arising from cells that have developed abnormally and persisted throughout post-natal growth include craniopharyngiomas (an expanding lesion), pituitary tumors (benign, slow-growing, encapsulated but can increase ICP and be actively causing endocrinopathy).
- (F) Initial treatment for all intracranial tumors is surgical excision. Removal is limited by the tumor location and invasiveness of the particular lesion, or, in the case of some benign lesions, by technical problems at the time of operation. Working with a unique computer-guided stereotactic coupled laser system with use of magnified vision and microscopic instrumentation, neurosurgeons are able to eradicate a large number of varying types of cortical tumors with relatively benign post-op courses.
- (G) Most malignant brain tumors respond to external irradiation. Radiation therapy is the most important treatment modality; it produces cures in certain tumors and prolonged survival in others. Radiation therapy is generally indicated when the tumor is: 1) malignant (AAF, GBM, gliosarcomas, meningiosarcomas, medulloblastomas, ependymomas, ependyoblastomas, pinealoma, pinealoblastomas, and germinomas); 2) incompletely excised or recurrent low grade tumors; 3) centrally located and involves critical structures so that surgical intervention is not possible, such as tumors in the midbrain, 3rd ventricle, brain stem; 4) pituitary tumor; and 5) metastatic deposit.
- (H) Unfortunately, when the tumors are malignant, recurrence of the tumor has not been prevented, even when it appeared to have been destroyed radiologically. For malignant brain tumor, chemotherapy is given concomitantly with radiation therapy or for recurrence after radiation. Lipid-soluble drugs (nitrosureas, lomustine, carmustine, semustine, procarbazine, and vincristine) remain the mainstay of therapy, together with temozolamide. For pituitary adenomas, bromocriptine is used to lower prolactin levels.

(I) Corticosteroid therapy (dexamethasone at 16 mg daily dose) will control edema around a brain tumor, providing dramatic relief of symptoms often within a day, and making it easier to prepare patients for surgery. Corticosteroid therapy has proven considerable benefits in palliative care of brain cancer patients.

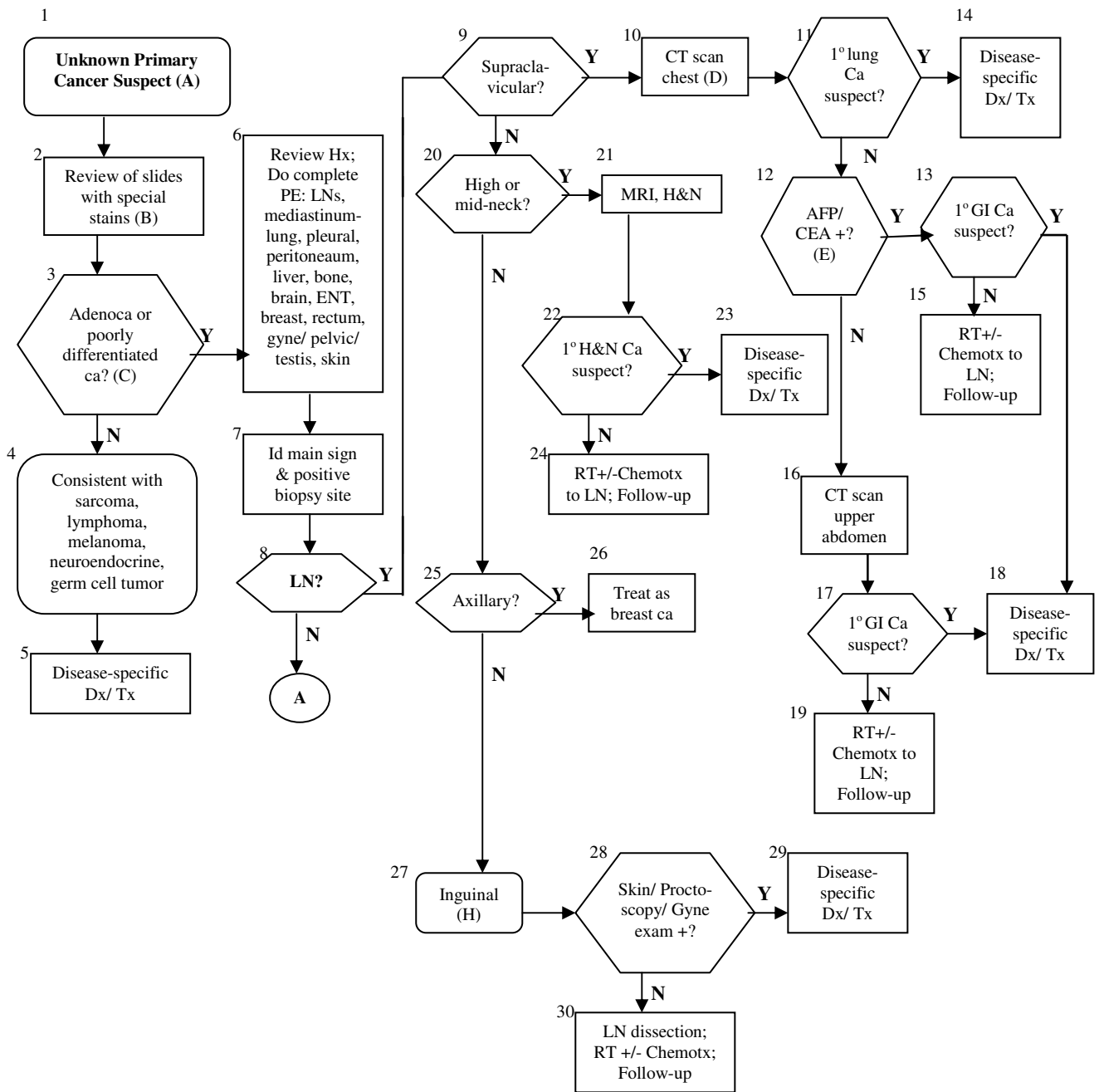


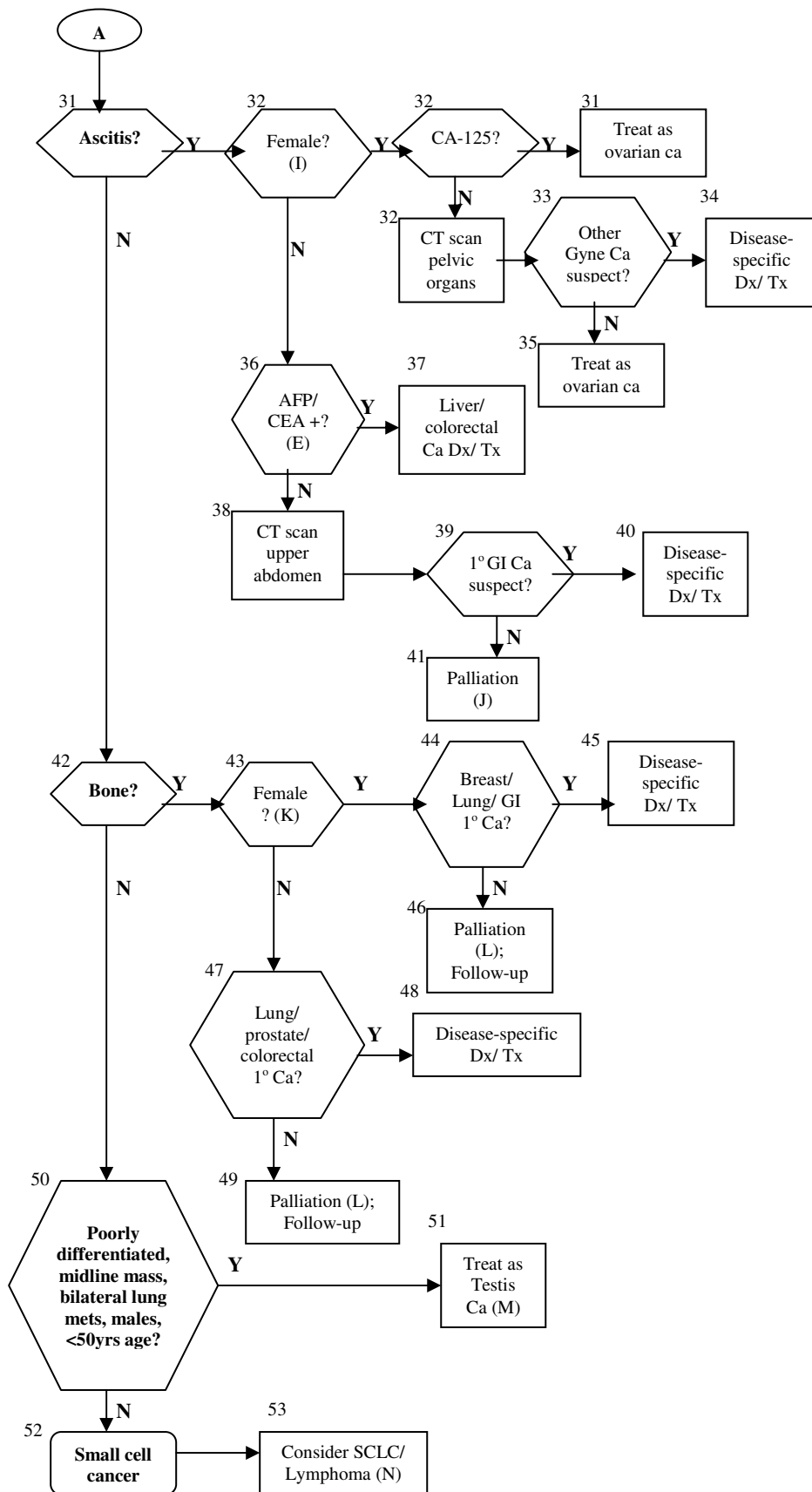
CARCINOMA OF UNKNOWN PRIMARY SITE

The management of cancer of unknown primary site must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

- (A) Carcinoma of unknown primary is defined as a histological diagnosis of carcinoma with no apparent primary site after complete history and physical examination, basic laboratory studies (including urinalysis, CBC, occult blood in stool), chest x-ray, and ultrasound/ CT scan of abdomen & pelvic organs. Additional studies are done only as suggested by detectable abnormalities. For example, PET scan is not recommended for routine use, but may be done in some situations when considering local/ regional therapy. The goal of additional studies is to identify the primary site, particularly in clinical situations in which potentially curative or effective therapy is available. An extensive "blind" work-up is not cost-effective and therefore not recommended. Palliation of symptoms takes priority in these patients, particularly since this is advanced disease by stage.
- (B) The pathologic examination is the single most important step in determining the primary site. In any situation wherein cancer is highly suspected, adequate tissue samples should be provided to experienced pathologists. Aids in identifying primary sites include electron microscopy and histochemical and immunohistochemical staining. At the time of biopsy/ surgery, the biopsy specimen should be divided into 3 portions: 1 portion snap frozen without fixation for immunohistochemical studies, 1 placed in glutaraldehyde for electron microscopy, and 1 into formalin for routine processing.
- (C) Once the results of pathological slide review are known, the clinical history and a complete physical examination which includes careful and thorough evaluation of the lymph-node-bearing areas, skin, and breast, and internal examination of the ENT, gynaecologic/ pelvic organs and testis. If the pathology evaluation does not suggest a primary site and labels the specimen as adenocarcinoma or poorly differentiated carcinoma, identify the patient's main or predominant presenting sign and/ or where the biopsy specimen turned out positive for cancer.
- 3 major histopathological types are commonly associated with unknown primary site: 1) adenocarcinoma or carcinoma, NOS, 2) squamous cell carcinoma, and 3) small cell, anaplastic carcinoma.
- (D) The most common presenting sign of patients with carcinoma of unknown primary site is lymphadenopathy. Supraclavicular lymphadenopathy is usually associated with cancers of the lung (particularly in men with a background of heavy cigarette smoking), gastrointestinal tract, and breast (in women). If lung cancer is suspected, CTscan can detect lung lesions missed out by chest x-ray.
- (E) Colorectal carcinomas account for 89% of gastrointestinal cancers and CEA is the preferred marker. A combination of CA 72-4 and CEA achieves the highest specificity (95%) in case gastric cancer is suspected. Liver cancer occurs commonly in the Philippines, and alpha-fetoprotein (AFP) is a particularly useful marker (relatively high in primary liver cancer; relatively low AFP in combination with high CEA usually occurs in metastatic liver cancer).
- If tumor markers for gastrointestinal tumors are not useful, CT scan of upper abdomen may be able to detect lesions not detected by ultrasound of the hepatobiliary system. PET scan may also be done.
- If still no primary site is identified, radiotherapy+/- chemotherapy against the enlarged LN may be done. Usually GI-active and/or radiosensitizer chemotherapeutic agents can be used – e.g., FU, cisplatin, capecitabine.
- (F) Squamous cell carcinoma is found in >70% of patients whose involved nodes are high in the neck or midneck. The most common occult primary sites include the nasopharynx, tonsil, base of the tongue, and hypopharynx. An MRI of the head and neck is done followed by direct laryngoscopy with random biopsies from suspected lesions in the tonsils, nasopharynx, and base of the tongue.
- If still no primary site is identified, radiotherapy+/- chemotherapy can be given to enlarged LNs/ site. Usually H&N-active and/or radiosensitizer chemotherapeutic agents can be used – e.g., FU, cisplatin, capecitabine, gemcitabine.
- (G) The most common cause of adenocarcinoma or poorly differentiated carcinoma confined to the axillary nodes is occult breast cancer, with or without supraclavicular lymph adenopathy. Biopsy material should be analyzed for estrogen and progesterone receptors, and also HER-2/neu. For women, a mammography may be done; if still with negative results, treat the patient as a breast cancer. For men, particularly >40 years of age, do PSA; consider also testicular ultrasound/ tumor markers.
- (H) Inguinal LN metastasis of unknown origin is a rare clinical presentation. Careful inspection of the skin, endoscopic evaluation of the anal canal and rectum, and gynecologic examination are of major importance. Patients in whom the primary tumor cannot be identified should undergo LN dissection of the affected areas.

- (I) In female patients with ascitis, ovarian carcinoma is highly suspected. A positive CA-125 is an important marker for ovarian cancer. AFP and B-HCG can be positive in germ cell tumors of the ovary. CT scan can detect lesions in the pelvic area. Even in the absence of detectable ovarian disease, treat women who present with peritoneal carcinomatosis according to guidelines for Stage III ovarian cancer disease.
- (J) Ascitis may be due to cancers of the ovary and GI tract, carcinomas that can be palliated with cisplatin-containing chemotherapeutic regimens. Supportive care with/ without cytotoxic chemotherapy can be done for poor performance status patients.
- (K) Bone metastasis can be from breast, lung, or GI (particularly colorectal) cancers among female patients; among males, common primary sites are lung, prostate, and colorectal cancers. A thorough evaluation of these possible sites should be done. Elevated PSA and acid phosphatase (prostatic fraction) is suggestive of prostate cancer.
- (L) If primary site is still unknown, palliative RT to symptomatic and weight-bearing affected bone areas can be done; pain relief can also be achieved by analgesics and osteoclast-inhibiting agents, such as bisphosphonates (e.g., ibandronate, zoledronate, clodronate).
- (M) A special clinical subset includes males <50 years old with rapidly growing, poorly differentiated carcinomas involving predominantly midline structures (mediastinum, retroperitoneum) with or without bilateral pulmonary nodules. This clinical presentation is termed "extragonadal germ cell cancer syndrome". Approximately 10-15% of these patients may be cured with cisplatin-containing chemotherapy.
- (N) Small cell carcinomas of unknown primary site may be lung (SCLC) or lymphoma-related; these cancers have common chemotherapeutic agents – cyclophosphamide, vincristine, doxorubicin – which can be given.





GENERAL GUIDELINES FOR PALLIATIVE MANAGEMENT OF ADVANCED CANCER

The management of patient with advanced cancer must be multi-disciplinary interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

The Medical Oncologist heads the Palliative Care of a cancer patient; in his her absence the Internist or the Family Medicine practitioner with hospice care expertise.

- (A) At some point, a person's cancer may start growing and spread to vital organs. This is called *advanced cancer*. As the cancer progresses and choices for further cancer treatment become limited, palliative care increases and becomes the major focus of care for the patient and the family. Symptoms increase and more attention is needed to help control them. As an example, the person with advanced cancer receiving medicines to control his/her cancer pain near the end of life is receiving palliative care.

Although palliative care is given throughout all stages of the cancer to some degree, this general guideline focuses on care given during the last year of life.

Palliative care is care that relieves suffering and improves the quality of a patient's life. It is care that treats symptoms caused by the cancer treatment or symptoms caused by the disease. Some health workers call this *supportive care*.

Common symptoms that are treated and controlled or relieved by palliative care include:

- Pain
- Difficulty of breathing
- Lost of appetite and weight loss
- Fatigue
- Weakness
- Sleep problems
- Depression& anxiety
- Confusion

The purpose of screening is to determine if palliative care is needed. The health care team does this screening. Palliative care is considered for patients who:

- Have advanced cancer that cannot be cured.
- Are expected to live less than a year.
- Request palliative care.
- Have other serious medical problems.

- (B) The cancer care team considers several factors to help them determine if the patient is expected to live a year or less. These factors include:

- How well the person can care for him or herself and carry out daily activities.
- The presence of complications of advanced cancer such as:
 - Too much calcium in the blood (hypercalcemia)
 - Liver or kidney problems
 - Other serious medical conditions
 - Involvement of the central nervous system (brain and spinal cord)
 - Superior vena cava syndrome

- (C) The cancer care team will determine if any symptoms or any other serious medical condition/s (e.g., NIDDM, hypertension, CHF, etc) are present. Symptoms include - pain, difficulty of breathing, fatigue and weakness, loss of appetite and weight loss, sleep problems, confusion, depression or anxiety. Infection may also occur. The treatment is directed at the specific symptoms.

The patients may develop advance care plans. This includes a living will, power of attorney, CPR preference and readiness for hospice or special palliative care.

- (D) Considerations for definitive treatment of cancer will include:

- Typical history of the cancer type
- Likelihood of a response to treatment
- Effect of cancer on vital organs
- The patient's ability to take care of self and do daily activity

Plus the life expectancy of the patient:

- Years-months – may do disease-specific definitive treatment
- Months-weeks – consider no further definitive cancer treatment
- Weeks-days – symptom control only

- (E) Considerations of definitive treatment of cancer will include:

- Patient's wishes and family needs

- Spiritual and religious needs
- Cultural needs
- Readiness for hospice or special palliative care services

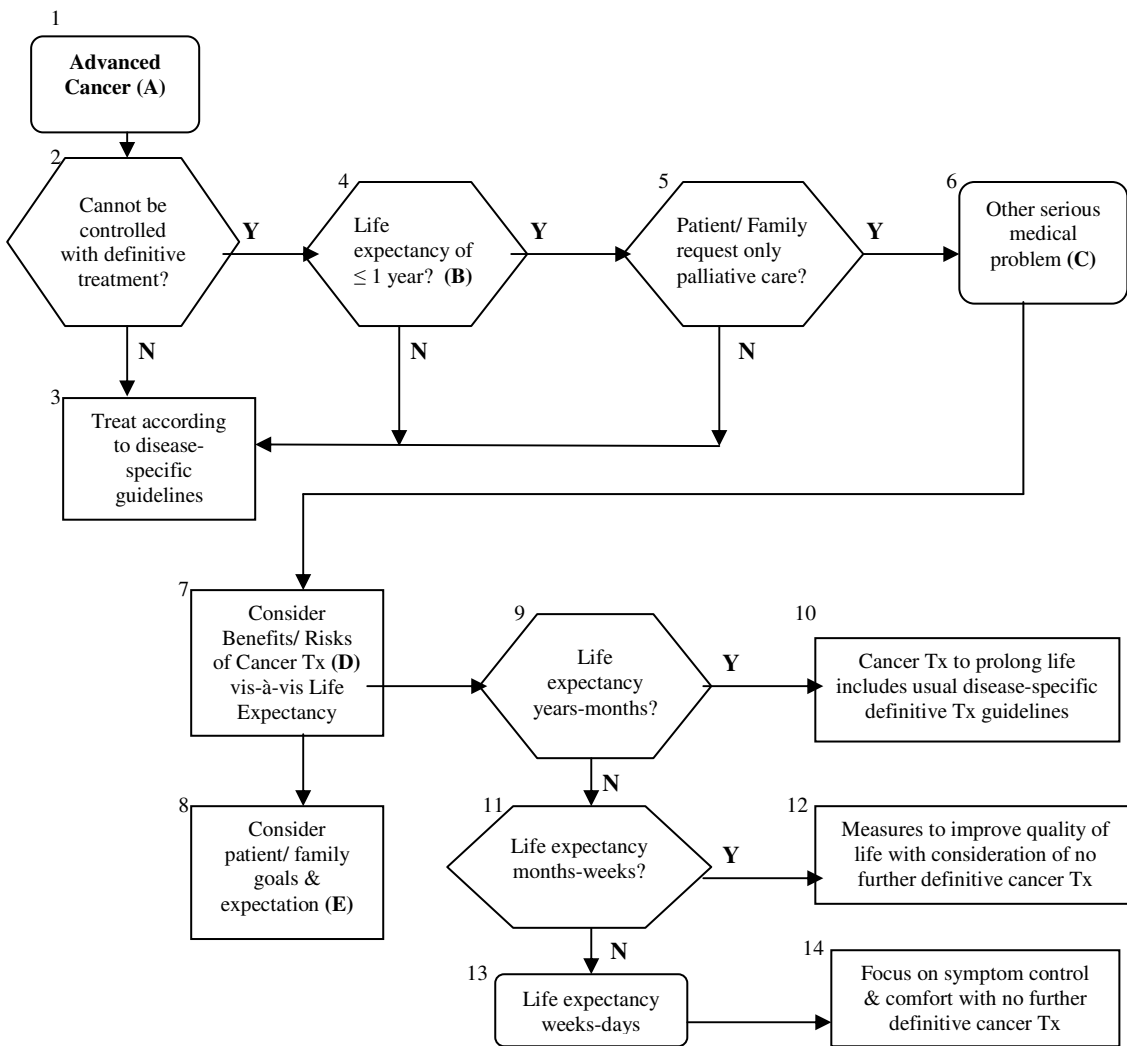
For those with life expectancy of years-weeks, the doctor will:

- Determine how much information the patient wishes to have
- Determine how much information the patient wishes his family to have
- Determine how the patient and his family make decisions and help resolve any conflicts between the patient's goals and expectations with those of his family
- Determine the patient's ability to make decisions for himself
- Determine the patient's desires with respect to quality of life
- Encourage the patient to review and revise his priorities, identify unfinished business, resolve personal relationships, and put affairs in order
- Determine the patient's readiness for hospice/specialized palliative care
- Provide clear, consistent discussion with the patient and the patient's family about prognosis on an ongoing basis
- Make arrangements to ensure that the patient do not die alone.

For those with life expectancy of weeks-days, the doctor will:

- Help the patient and his family prepare for the end of the patient's life
- Facilitate anticipatory grief work
- Help the patient and his family understand what is happening
- Ensure that the patient do not die alone

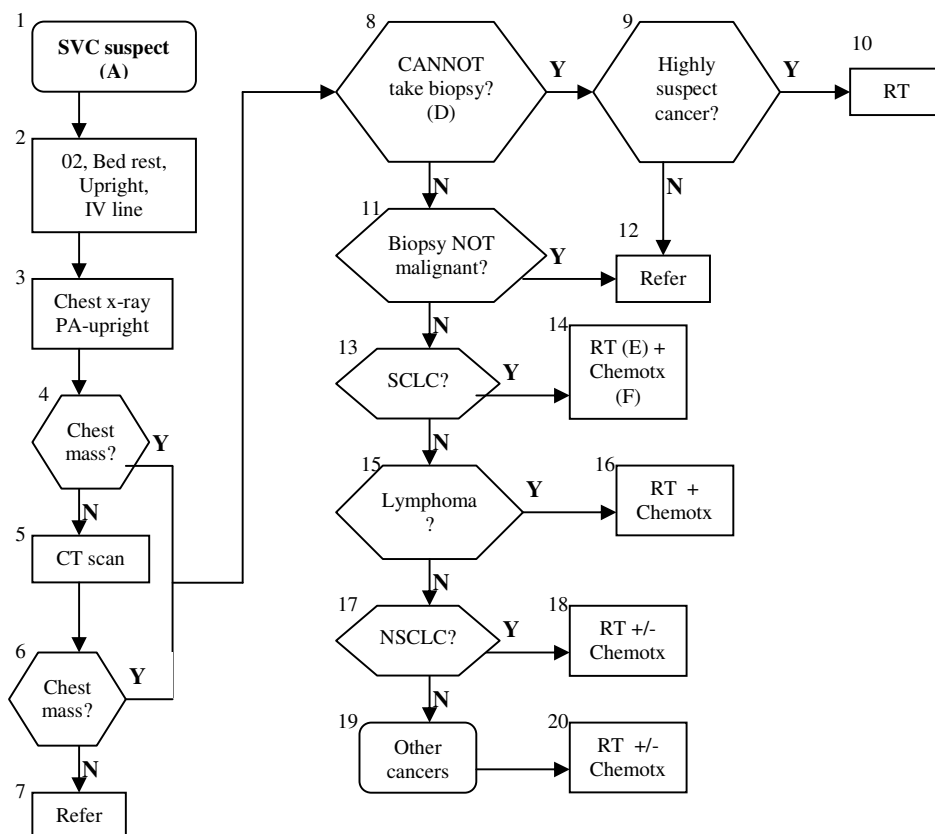
Social support given to patients by people who care about them is also necessary. This might include someone to talk to and discuss goals and plans with, someone to hold their hand or take them for a walk, or someone to help with buying groceries. This support can be provided by family, community, cultural, spiritual or religious groups. The patient's past coping abilities, strengths, and vulnerabilities will be considered.



SUPERIOR VENA CAVA SYNDROME (SVC)

The management of SVC must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

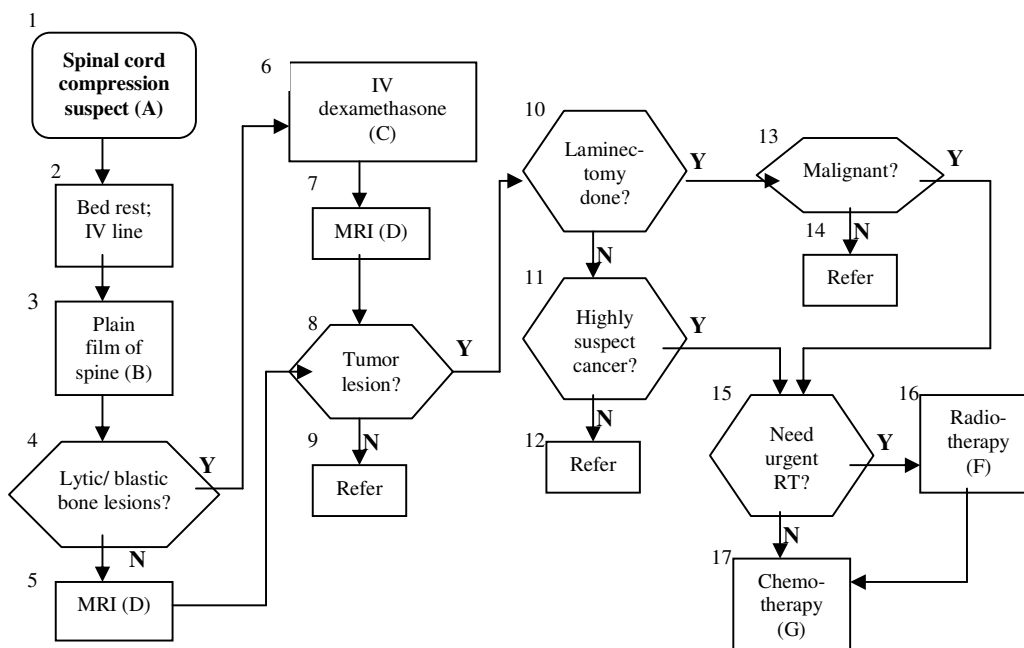
- (A) Obstruction of the superior vena cava is usually caused by lung cancer, but it can also be due to lymphoma and other mediastinal tumor and metastatic tumors. Headache, nausea, vomiting, visual disturbances, and syncope are presenting complaints. Symptoms of vocal hoarseness, dyspnea, dysphagia, back pain suggest involvement of other mediastinal structures. Upper body venous distention, edema, and cyanosis are prominent physical findings.
- (B) Chest film may reveal a right-sided paratracheal or mediastinal mass.
- (C) CT scan of the chest is diagnostic and helpful in defining disease extent, guiding biopsy attempts, differentiating extrinsic caval compression from intrinsic obstruction, and planning radiation therapy.
- (D) Tissue diagnosis may be pursued during the treatment of the severely symptomatic patient. Attempts at tissue diagnosis must be deferred in favor of urgent therapy.
- (E) Emergency treatment usually prompts administration of radiation therapy to the obstructing mediastinal mass. Symptoms are ameliorated in 70% of cases.
- (F) Chemotherapy is given for patients with lymphoma or small cell lung cancer (SCLC), and simultaneously treats overt or suspected metastatic disease. Radiotherapy can be given with chemotherapy for bulky tumors.



SPINAL CORD COMPRESSION (SpCC)

The management of SpCC must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

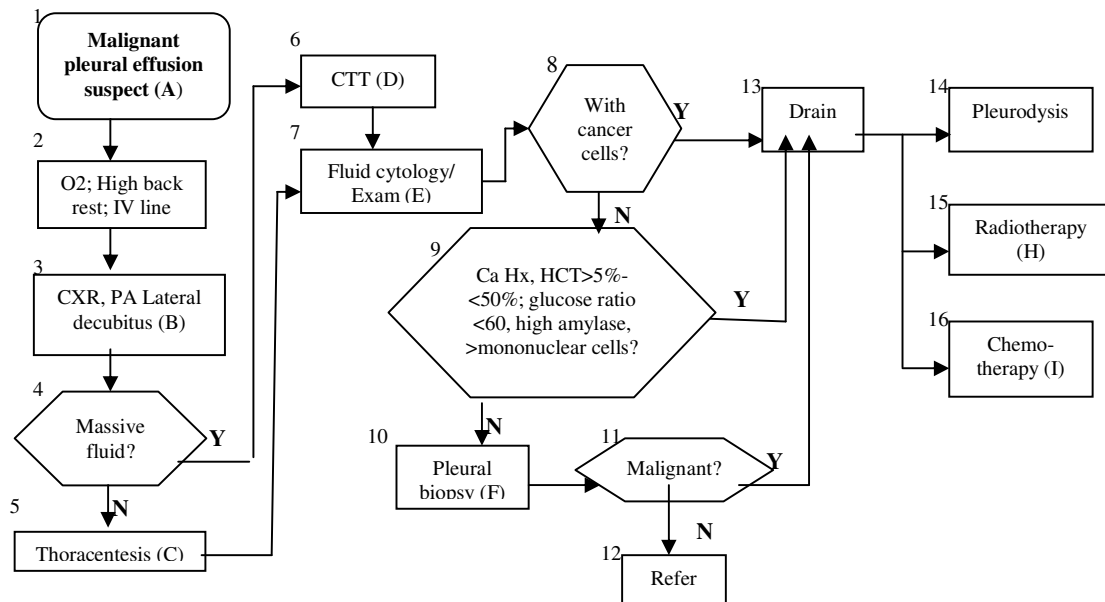
- (A) Recognition of incipient cord compression is essential because expeditious treatment at this stage prevents irreversible neurologic injury. Neoplastic cord compression is almost always secondary to extramedullary, extradural metastasis (most frequently from breast, lung, prostate, lymphoma, or kidney). In 70% of cases, the thoracic spinal cord is most often involved. Almost all patients present initially with neck or back pain, which may be central or radicular. Leg weakness, numbness, and paresthesias follow; loss of sphincter control is a late event. Spine tenderness is common and neck flexion or straight leg raising may provoke radicular pain. The specific neurologic findings depend on the level of the cord lesion.
- (B) Plain film of the spine frequently demonstrates associated vertebral blastic or lytic lesions.
- (C) Corticosteroids are administered promptly to reduce peritumoral edema. Traditionally, dexamethasone 16 mg/day in divided doses is given.
- (D) MRI of the spine is the procedure of choice for detection and localization of cord compression. Myelography may be employed if MRI techniques are not available. At the time of myelography, CSF should be obtained for cytology.
- (E) Decompression laminectomy is indicated initially if: 1) a tissue diagnosis is required, 2) the cord compression is in a previously irradiated area, 3) neurologic deterioration occurs during radiation therapy, 4) with radioresistant tumor, and/ or 5) with rapid evolution of paraplegia.
- (F) Radiation therapy alone is used for patients with: 1) radiosensitive tumors, 2) lesions below conus medullaris, 3) slow onset of compression, 4) medical contraindications to surgery, 5) surgically unapproachable disease. Patients treated initially with decompression laminectomy should also receive post-radiation radiotherapy.
- (G) Chemotherapy may be considered for patients with chemosensitive tumors who can no longer benefit from surgical intervention or radiotherapy.



MALIGNANT PLEURAL EFFUSION

The management of malignant pleural effusion must be multi-disciplinary & interdisciplinary, with each discipline respecting the specialty expertise of the other, all for the benefit of the cancer patient.

- (A) Malignant pleural effusions are exudative processes usually related to the presence of tumor cell implants in the visceral or parietal pleura. Metastatic breast and lung cancer and lymphoma account for more than 75% of malignant pleural effusions. Sometimes the effusion is due to impairment of pleural lymphatic drainage by mediastinal tumor. Symptoms of dyspnea, unproductive cough, and dull chest discomfort are reported. PE includes decreased breath sounds and percussion dullness on the area of effusion. A significant fraction of effusion is asymptomatic, however.
- (B) Significant pleural effusions are visible on chest radiographs. Lateral films confirm free-flowing fluid. Ultrasonography differentiates fluid portion from tumor mass.
- (C) Diagnostic thoracentesis is required to confirm a malignant etiology. Large-volume thoracentesis can also evaluate minimal to moderate fluid flow from the pleura.
- (D) For significant pleural effusions, a chest tube thoracostomy is done to drain fluid and for pleurodesis. Do pleurodesis when drainage is <100 cc/day. If drainage is persistently >100 cc/day, indwelling chest drainage tube may be maintained by the thoracic surgeon.
- (E) A large volume of fluid should be sent for cytologic analysis, pleural fluid chemistries (lactate dehydrogenase, protein, glucose, pH levels), blood cell count, and cultures if needed.
- (F) In patients with negative cytology and in isolated exudative effusion (pleural fluid LDH>200, a pleural fluid-to-blood LDH ratio>0.6, or protein ratio>0.5), high amylase, glucose >60, HCT >5% but <50% ratio, predominantly small lymphocytes and mononuclear cells, pleural biopsy may not be indicated, particularly if patient has history of cancer (Ca Hx).
- (G) In the absence of effective anti-neoplastic treatment, fluid accumulates a few days. Lasting control of effusion is achieved by pleurodesis in 70-85%. Agents used for pleurodesis are tetracycline, doxorubicin, or bleomycin.
- (H) Radiotherapy can be done for NSCLC, and for bulky chest tumors (lymphoma, malignant thymoma, germ cell tumor).
- (I) Pleural effusions due to lymphoma, breast cancer, SCLC, malignant mediastinal germ cell tumor or thymoma, often respond to chemotherapy.



PAIN IN CANCER

Pain in cancer is a major problem in cancer management.

- (A) Pain assessment should include a complete neurologic examination and the patient's description of –
- Site of pain
 - Quality of pain
 - Temporal pattern
 - Exacerbating and relieving factors
 - Exact onset
 - Associated signs and symptoms
 - Interference of activities
 - Impact on patient's psychological state
 - Response to previous treatment and present treatment
- (B) Somatic pain results when nociceptors are activated in cutaneous/ deep tissues. It is typically well localized and described as dull or aching. Examples are metastatic bone pain, post-surgical incisional pain, musculoskeletal pain.

Visceral pain results from activation of nociceptors from infiltrates, compression, extension or stretching of thoracic, abdominal or pelvic viscera. It is usually poorly localized, usually described as deep, squeezing, pressure-like.

These two types of pain account for about 80% of pain problems in cancer patients.

- (C) Neuropathic pain results from injury to the peripheral or central nervous system as a consequence of tumor compression or infiltration of peripheral nerve or spinal cord. It is usually intermittent and described as burning or electric-shock-like sensation.

The adjuvant analgesic drugs are particularly useful in the treatment of this type of pain.

- Trial of tricyclic antidepressant: Start with low dose and increase every 3-5 days if tolerated or lengthen interval up to 14 days (e.g., nortriptyline 10-100 mg/day) AND/ OR
- Trial of anticonvulsant: Start with low dose and increase every 3-5 days if tolerated or lengthen interval up to 14 days (e.g., gabapentin 100-1200 mg tid; pregabalin 75 mg bid-tid up to 600 mg/day; carbamazepine 100-400 mg bid) AND/ OR
- Consider topical anaesthetics or capsaicin
- If results are unsatisfactory after a 2-3 week trial, consider referral to pain expert or anaesthesiologist/ neurosurgeon for an appropriate invasive procedure.

- (D) Drug therapy should be given to provide pain relief to patient as the cause of pain is being sought after or when the pain is being treated by radiation/ chemotherapy/ surgery and has not yet produced the pain-free state for the patient. When/ If the cause of pain is resolved thru radiotherapy, chemotherapy/ surgery, analgesic drug therapy may be discontinued.

The general principles of drug therapy for pain relief are:

- 1) The drug should be given *per orem*, unless patient cannot take oral medication.
- 2) The drug should be given around the clock, not on '*pro re nata*' basis.
- 3) The drug should be given by the analgesic ladder recommended by WHO:

Non-opioid analgesic (paracetamol or NSAID) with or without adjuvant drug → If no relief, Give weak opioid analgesic (codeine or tramadol HCl) +/- NSAID +/- adjuvant drug → If no relief, Give strong opioid analgesic (morphine, oxycodone, fentanyl) +/- NSAID +/- adjuvant drug.

- (E) Paracetamol 650 mg every 4 hours; caution for liver toxicity. NSAID equivalent to ibuprofen 400 mg qid; caution for renal/ GI toxicity and hypersensitivity. Selective COX-2 inhibitors are with lesser renal/ GI toxicity.

Patients high risk for renal toxicity – age >60 years, compromised renal function/ concomitant renal pathology, use of other nephrotoxic drugs; high risk for GI toxicity – age >60 years, history of peptic ulcer disease, > alcohol intake, major organ dysfunction, high dose NSAID intake for long periods. Monitor for toxicities – BP, BUN, creatinine – every 3 months. Discontinue NSAID if with toxicity.

If two NSAID are tried in succession and no pain relief – discontinue; use weak opioid.

- (F) Short acting Tramadol HCl 50 mg every 6-8 hours; may shift to long acting Tramadol HCl 100-300 mg every 12 hours with short acting form as rescue dose.

- (G) The appropriate opioid dose is the dose that relieves the patient's pain throughout its dosing interval without causing unmanageable side effects.

Calculate increase based upon total opioid dose (around the clock/ scheduled and as needed) taken in the previous 24 hour.

Increase both around the clock and as needed doses. The rapidity of dose escalation should be related to the severity of the symptoms:

For example:	Pain 7-10	Consider increasing dose by 50-100%
	Pain 4-6	Increase by 25-50%
	Pain 1-3	Increase by 25%

If patient is experiencing unmanageable side effects and pain is <4, consider downward titration by approximately 25% and re-evaluate.

The following are approximate dose equivalents of opioids based on single dose data;

Opioid analgesic	Oral dose	Parenteral dose	Duration of action
Codeine	100 mg	50 mg	q 3-4 hours
Oxycodone	7.5-10 mg	N/A	q 3-4 hours
Morphine	15 mg	5 mg	q 3-4 hours
Transdermal fentanyl	N/A	50 mcg/h	q 48-72 hours

Consider converting from short-acting opioids to sustained release opioids for control of chronic persistent pain when 24 hour opioid requirement is stable:

- Sustained-release morphine sulfate tablet/ capsule every 8-24 hours.
- Sustained-release oxycodone HCl tablet every 8-12 hours
- Transdermal fentanyl patch every 48-72 hours

Provide rescue doses of short-acting opioids for pain not relieved by sustained-release opioids including acute exacerbations of pain, activity, or position related pain or pain at the end of dosing interval:

- Use short-acting form of the sustained release opioid whenever possible
- Allow immediate-release rescue doses of 10-20% of 24-hour oral dose (mg) every 1 hour *prn*
- The 24-hour adult morphine dose equivalent of transdermal fentanyl is 2 x ug/hour dose.

Increase dose of sustained release opioid if patient persistently needs doses of as needed opioids or when dose of around the clock opioid fails to relieve pain at peak effect or at end of the dose.

Common side effects of opioid analgesics are:

- Constipation – Start stimulant laxative + stool softener (senna + docusate, 2 tablets every morning) when opioids are started; increase dose if opioid dose is increased; increase fluids, dietary fiber, exercise as appropriate. If constipation persists – add bisacodyl 2-3 tabs po daily or 1 rectal suppository daily/ lactulose 30-60 mL daily.
- Nausea/ Vomiting – Make antiemetics available with opioid prescription. If nausea develops, give metoclopramide 10-20 mg po every 6 hours *prn* or around the clock for 1 week then change to *prn*. Consider adding granisetron 1-2 mg IV then 1-2 mg po daily or ondansetron 8 mg IV then 8 mg po tid or ramosetron 300 mcg IV then 100 mcg tab daily or tropisetron 5 mg IV then 5 mg po daily. Consider ice chips, sour candies. Consider reduce opioid dose and add another analgesic.
- Sedation – Consider a lower dose of opioid given more frequently. Consider add caffeine 100-200 mg po every 6 hours. Consider co-analgesic to reduce opioid dose.
- Delirium – Consider changing the opioid or coanalgesic to reduce opioid dose.

Assure patient side effects may happen during the first 3-5 days of initial opioid use, but to persevere as this can be transient.

(H) The adjuvant analgesic drugs are used to increase the analgesic effects of the opioids to counteract their side effects or to act as analgesics themselves. They include:

- Antidepressants – if depression persists despite improved pain control; the tricyclic anti-depressants may be the most useful in pain management.
- Anti-convulsants – e.g., carbamazepine, pregabalin, clonazepam. The anti-depressants and anti-convulsants are not use only for their anti-depressant/ anti-convulsant effect, respectively, but they in smaller doses also have primary analgesic effect, particularly for neuropathic pain.
- Oral local anesthetics – considered as second line drugs (with anti-depressants and anti-convulsants) for neuropathic pain that has proven to be resistant to treatment
- Try glucocorticoids for pain-associated with inflammation and or nerve compression.
- For diffuse pain consider bisphosphonates.
- Other adjuncts are the anti-histamines, anti-psychotics, amphetamines, laxatives, and anti-emetics.

Reassess the patient regularly and consider adjuvant therapy when patient's pain is unrelieved by non-opioid or opioid analgesics.

(I) The pathologic process responsible for pain can be altered with radiotherapy, chemotherapy, hormonal therapy, and even whole-body hyperthermia. It is important to note that palliative anti-tumor measures have definite limitations related to efficacy, patient acceptance, side effects, and complications. The decision to pursue anti-tumor therapy does not imply that analgesic drugs and other supportive treatment should be discontinued.

(J) Almost 80-90% of pain in cancer patients can be adequately controlled with drug therapy. The remainder may be controlled with alternative modes of treatment, like psychological approaches (e.g., cognitive-behaviour therapy, psychotherapy), anaesthetic and neuro-surgical approaches (e.g., nerve blocks, trigger point injection, neuroablative procedures). All these need to be done by specialists. Consider local radiation therapy or nerve block for local bone pain. For resistant pain, consider anesthetic, orthopedic, or neuro-surgical approaches.

- (K) Intensity of pain can be assessed clinically by the following tools:
- Categorical scales in which patients are asked to describe their pain as mild, moderate, severe or excruciating.
 - Numerical scales in which patients are asked to rate their pain between 0-10, where 0= no pain and 10=worst pain.
 - Visual analogue scales in which patients are shown a 10-cm straight horizontal line. The line is anchored on either end by two points – no pain and worst possible pain – and the patient is asked to work on the line the intensity of the pain.

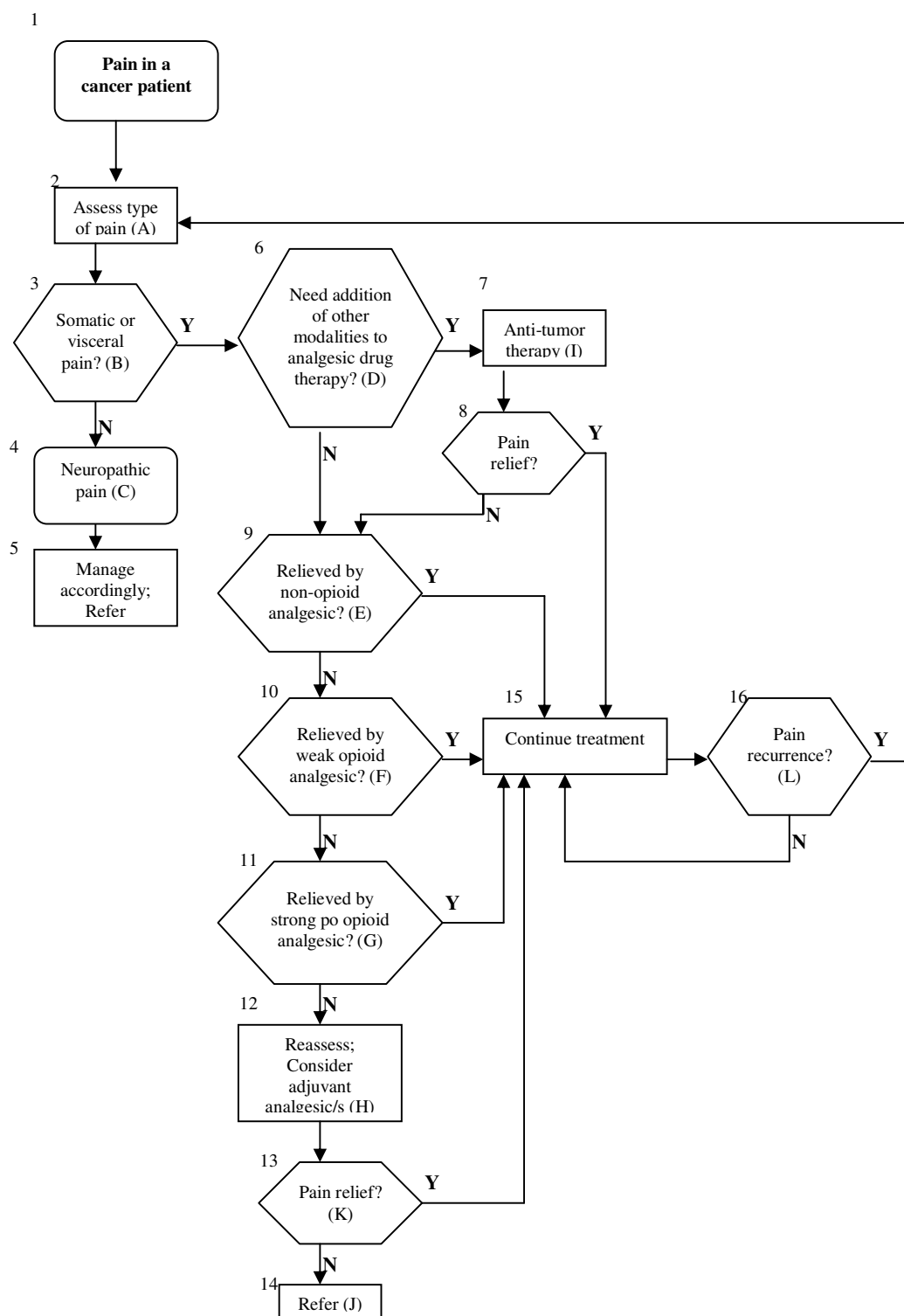
No pain /-----/ Worst possible pain

Relief of pain is measured by using a visual analogue scale, wherein a 10-cm straight line is anchored on either end of two points – no relief of pain and complete relief of pain. The patient is asked to mark on the line the degree of pain relief.

No relief of pain /-----/ Complete pain relief

- (L) When there is pain recurrence after adequate control, two major considerations are:
- Patient has become tolerant to drugs being given to him/ her.
 - There is progression of disease and/ or appearance of new causes of pain.

Careful and thorough reassessment is imperative. Constant reassessment of both diagnosis and treatment is a must in the treatment of pain in cancer patients.



ANEMIA IN CANCER

Anemia is a major occurrence among cancer patients.

- (A) Anemia is defined as Hb <11 g/dL. Do CBC with indices, reticulocyte count, iron studies (serum iron, total iron binding capacity, serum ferritin), B12/ folate, stool guaiac, LDH, fractionated bilirubin, bone marrow examination, direct Coombs, Hb electrophoresis, creatinine and or creatinine clearance. Review peripheral smear as needed.
- (B) Anemia can either be:
- Non-cancer or non-cancer-treatment-related – bleeding, hemolysis, nutritional deficiency, hereditary, renal dysfunction, iron deficiency
 - Cancer or anti-cancer treatment related – severity maybe:
 - Mild: Hb 10-11 g/dL
 - Moderate: Hb 8-10 g/dL
 - Severe: Hb <8 g/dL
- (C) Anemia may be symptomatic – cardiac symptoms (chest pain, dyspnea on exertion, peripheral edema, sustained tachycardia, orthostatic lightheadedness/ near syncope, syncope) and fatigue. Symptoms may be more pronounced in presence of co-morbidities such as cardiac history/ decompensation, chronic pulmonary disease, and cerebral vascular disease.

In symptomatic moderate to severe anemia, immediate correction with blood transfusion may be required, particularly in frank bleeding. RBC transfusion is an option depending upon severity of anemia or clinical circumstances.

Consider epoetin therapy to maintain Hb levels after BT.

In symptomatic Hb 10-11 g/dL, consider epoetin therapy;

In symptomatic Hb <10 g/dL, strongly consider epoetin therapy:

Epoetin	Initial dosing	Titration for response	Titration for no response
Epoetin alfa	150 units/kg 3x weekly SC	If Hb increase by > 1 g/dL in a 2 week period, dose should be reduced by 25% If Hb exceeds 12 g/dL, hold therapy. Re-initiate therapy if Hb falls <12 g/dL at 25% dose reduction of the prior dose.	Increase dose to 300 units/kg 3 x weekly SC
Epoetin alfa	40000 units q week SC	-as above-	Increase dose to 60000 units q week SC
Epoetin alfa	60000 units loading dose SC than 120000 units q 3 weeks maintenance SC	-	-
Epoetin beta	450 units/kg weekly SC (~10000 units per week for a 70 kg person)	If after 4 weeks, no response, double the dose. If Hb increases by > 2 g/dL in a month's period, dose should be reduced by 50%. If Hb exceeds 14 g/dL, hold therapy, until <=12 g/dL. Re-initiate therapy if Hb falls <12 g/dL at 50% reduction of the prior dose. If Hb falls by > 1g/dL during 1 st cycle of chemotherapy, then epoetin therapy may be effective	Double initial dose

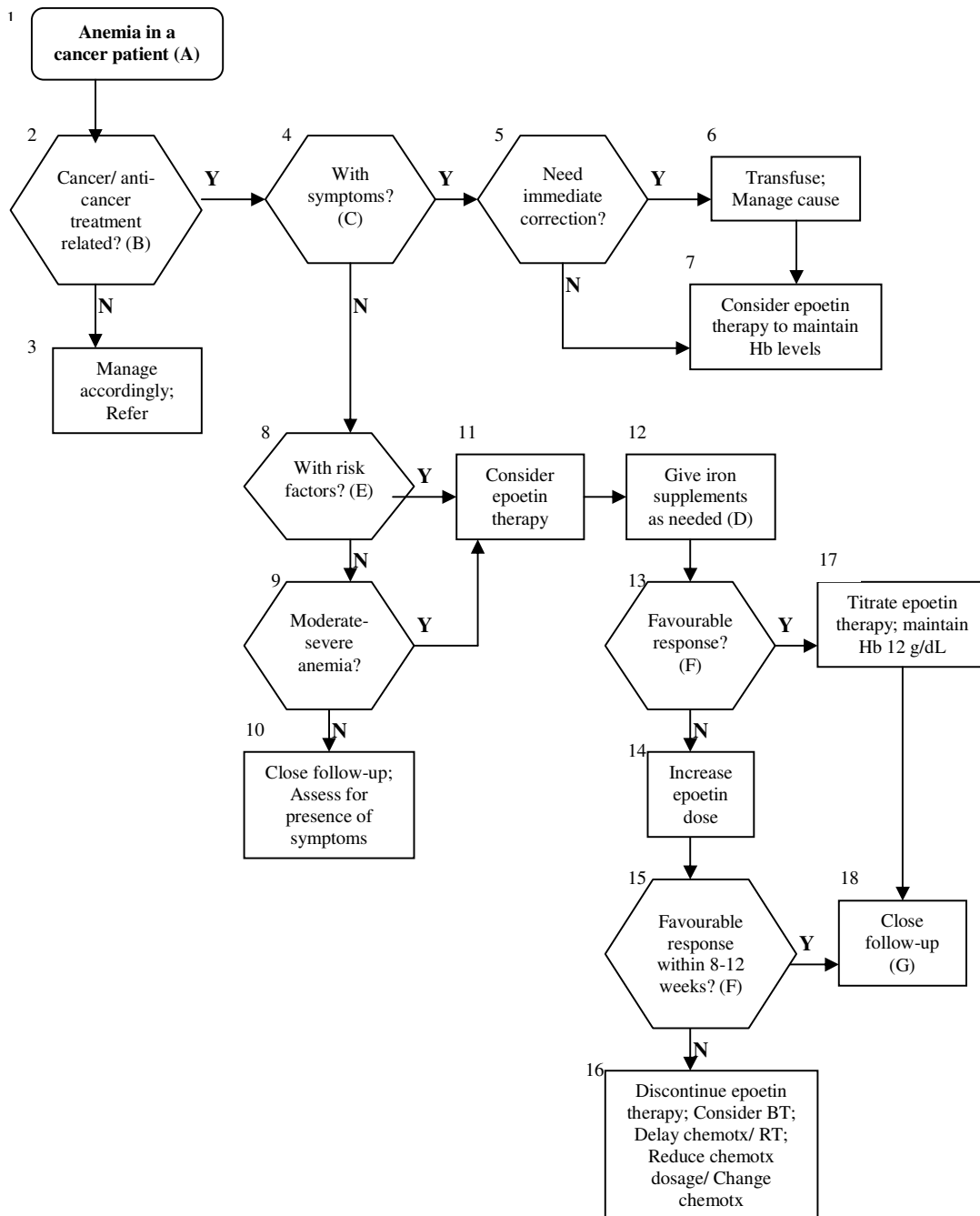
- Epoetin is recommended as treatment option for patients with chemotherapy-associated anemia and Hgb concentration that has declined to ≤ 10 g/dL level
- For patients with declining Hgb levels but less severe anemia (Hgb <12g/dL but never <10g/dL) – decision whether to use epoetin immediately or to wait until Hgb levels fall closer to 10g/dL should be determined by clinical circumstances. Usually start epoetin when Hgb <10g/dL
- Recommended starting dose is 150 U/kg 3xwk (~10,000 U for a 70 kg patient) for a minimum of 4 weeks, with consideration given for dose escalation to 300 U/kg for an additional 4-8 weeks in those who do not respond to the initial dose (Hgb has not risen by at least 1-2g/dL). An alternative weekly dosing regimen (30,000 U/wk epoetin B) can be given; dose escalation similar to 3xwly regimens.

- Continuing epoetin tx beyond 6-8 weeks in absence of response (e.g., <1-2 g/dL rise in Hgb), assuming appropriate dose increase has been attempted in non-responders does not appear to be beneficial. Patients who do not respond should be investigated for underlying tumor progression or iron deficiency. Discontinue medication.
- Hg levels can be raised to (or near) a concentration of 12g/dL (10,11,12g/dL) at which time the dosage of epoetin should be titrated to maintain that level or restored when the level falls to near 10g/dL. Decrease wkly dose or hold dose until Hgb drops to target range & reinstitute at that time. Insufficient evidence to date supports the 'normalization' of Hgb levels to >12g/dL. Epoetin should be titrated once Hgb increase to >12g/dL – reduce dose or frequency of injections according to clinical situation. Baseline and periodic monitoring of iron, total iron-binding capacity, transferrin saturation or ferritin levels and instituting iron repletion when indicated may be valuable in limiting the need for epoetin, maximizing symptomatic improvements for patients, and determining the reason for failure to respond adequately to epoetin.

	EPOETIN β (40)	EPOETIN α (42)
Mean days of observation	114	103
Mean changes in max Hgb levels	3.3g/dL	2.8g/dL
% achieving ≥1g/dL Hgb increase	87.5%	85.7%
% achieving >2g/dL Hgb increase	77.5%	66.7%
Route of administration	SC/ IV	IV/ SC

*Pujade-Lauraine E et al, Onco Reports, 2005

- (D) Give oral iron supplementation if ferritin <100, transferrin saturation <20%. Iron will be needed as long as epoetin therapy is being given.
- (E) Anemia may be asymptomatic. Risk factors for developing symptomatic anemia are:
- Transfusion in past 6 months
 - History of prior myelosuppressive therapy (e.g., BMT)
 - History of radiotherapy >20% of skeleton
 - Myelosuppression potential of current therapy – duration, schedule, agents
 - Age (>= 65 years)
 - Hemoglobin level
- If asymptomatic with no risk factor present, particularly in mild anemia, do close follow-up.
If asymptomatic with presence of risk factors, particularly in moderate to severe anemia, consider epoetin therapy.
- (F) Favourable response from epoetin therapy is seen when Hb increases by 1 g/dL within 4 weeks. Titrate dosage to maintain optimal Hb at 12 g/dL. If HB exceeds 12 g/dL, hold therapy. Re-initiate if Hb falls <12 g/dL at 25% dose reduction of the prior dose.
- If there is no initial response is seen, increase dose of epoetin (+/- iron supplementation as indicated) aiming a Hb increase by 1 g/dL at 8-12 weeks, then titrating dosage to maintain optimal Hb at 12 g/dL. If Hb level stays within 1-2 g/dL of baseline while receiving chemotherapy, continue epoetin therapy. If there is no Hb response at 8-12 weeks, discontinue epoetin therapy, give BT as needed, delay chemotherapy cycles/ radiotherapy, and reduce next chemotherapy dosages accordingly or consider change chemotherapy regimen.
- (G) Periodic re-evaluation for symptoms and risk factors for anemia development at every visit. If Hb levels decreases, check for iron stores and evaluate for development of other anemia specific causes.



CHEMOTHERAPY-INDUCED NEUTROPENIA

Neutropenia can occur among cancer patients receiving chemotherapy and radiotherapy.

- (A) Chemotherapy for cancer particularly high dose, dose dense, as well as standard dose therapy) can cause neutropenia. Neutropenia of significant medical concern is neutrophils/mcL of <500 or <1,000 neutrophil/mcL and a predicted decline to <=500 mcL over the next 48 hours.

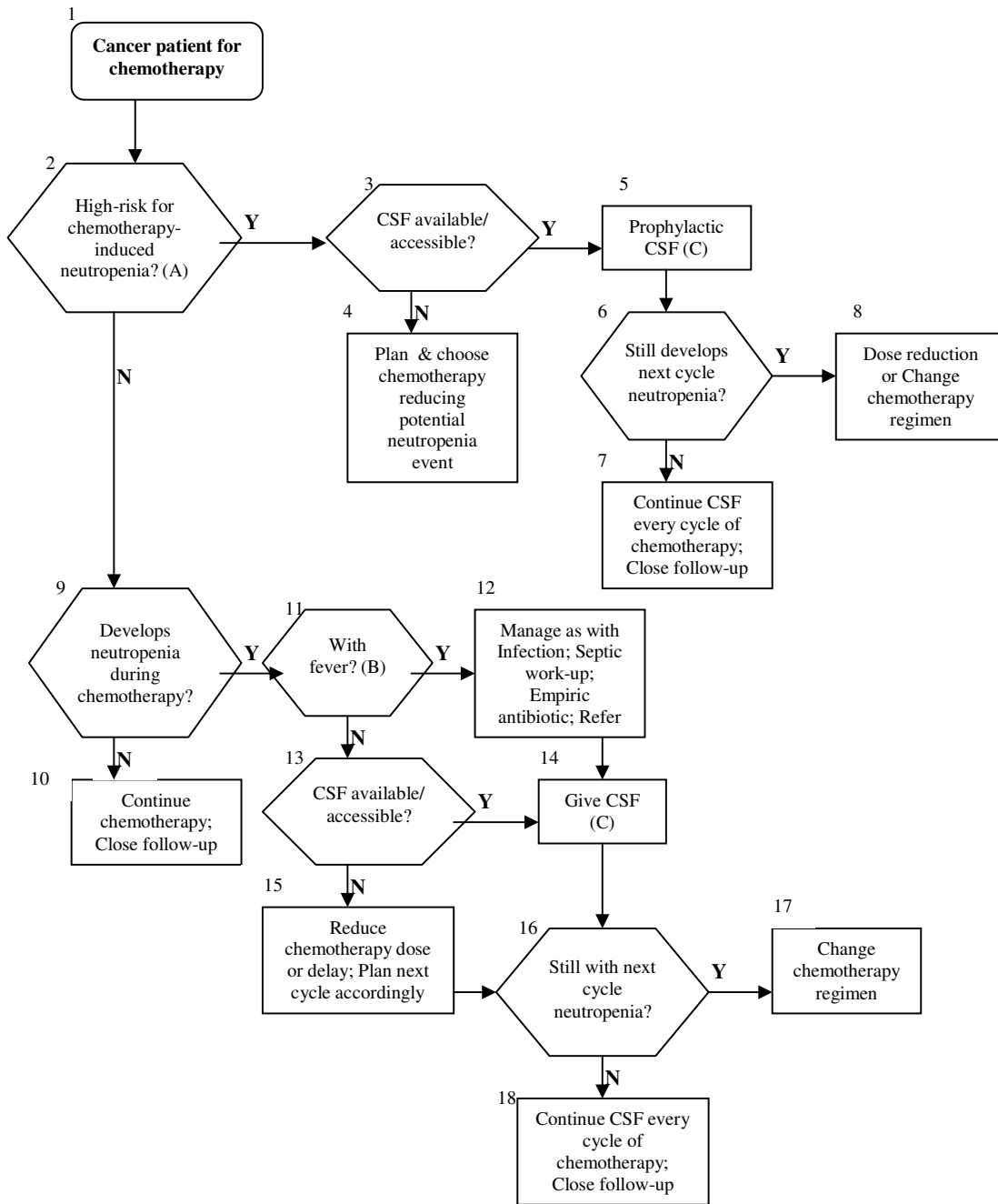
There are patient risk factors for chemotherapy-induced neutropenia (in adult patients with solid tumors and non-myeloid cancers), wherein prophylaxis with myeloid growth factors can be considered, so that the scheduled chemotherapy cycle will be given on time on planned dose:

- Treatment-related:
 - Previous history of severe neutropenia with similar chemotherapy
 - Type of chemotherapy (e.g., anthracycline)
 - Planned relative dose intensity >80%
 - Pre-existing neutropenia (<1000) or lymphocytopenia
 - Extensive prior chemotherapy
 - Concurrent or prior radiation therapy to marrow containing bone
- Patient-related:
 - Age (>65 years)
 - Female gender
 - Poor performance status (ECOG >=2)
 - Poor nutritional status (e.g., low albumin)
 - Decrease immune function
- Cancer-related:
 - Bone marrow involvement with tumor
 - Advanced or uncontrolled cancer
 - Elevated lactate dehydrogenase (Lymphoma)
 - Lymphoma
 - Lung cancer
- Conditions associated with risk of serious infection:
 - Open wounds
 - Active tissue infection
- Co-morbidities:
 - COPD
 - Cardiovascular disease
 - Liver disease (elevated bilirubin, alkaline phosphatase)
 - Diabetes mellitus
 - Low baseline haemoglobin

Give prophylaxis myeloid growth factors in the presence of the above risk factors particularly when the treatment intent is curative/ adjuvant, prolonging survival/ QoL.

If myeloid growth factors are not available accessible then chemotherapeutic dose is reduced and or delayed for 1 week upon re-evaluate of WBC counts.

- (B) Such neutropenia can be accompanied by fever – single temperature $\geq 38.3^{\circ}\text{C}$ orally or $\geq 38.0^{\circ}\text{C}$ over 1 hour (so-called febrile neutropenia). In presence of fever, evaluation is focused on determining potential sites of infection and causative organisms – septic work-up and referable to an infectious disease expert.
- (C) There is level 1 evidence to support the CSF or myeloid growth factor filgrastim or pegfilgrastim for the prevention of febrile neutropenia; these can also be used for maintenance of scheduled dose delivery:
- Filgrastim – daily subcutaneous dose of 5 mcg/kg (rounded to nearest vial size) until post-nadir ANC recovery to normal or near-normal levels by laboratory standards
 - Pegfilgrastim – 1 dose of 6 mg per cycle; start 1-3 days after completion of chemotherapy and treat through post-nadir recovery. This is for chemotherapy given every 3 weeks.



CHEMOTHERAPY-INDUCED EMESIS

Emesis is a common and bothersome complication of chemotherapy.

- (A) From the cancer patient's point of view, nausea and vomiting are the most distressing complications of chemotherapy.

Three types of chemotherapy-induced emesis are: 1) acute emesis –occurs soon after drug administration, 2) delayed emesis – begins about 24 hours after chemotherapy administration and may persist for 6-7 days, and 3) anticipatory emesis – occurs in anticipation of a subsequent course of treatment usually when there has been poor emetic control during previous course/s.

The principles of emesis treatment are:

- Assess for and treat underlying cause
- Use of anti-emetics
- If unresponsive – assess for psychological factors, reassess for missed physical causes, and try different anti-emetics and/ or combinations.

Commence anti-emetic drug use before the vomiting starts:

- in adequate doses,
- in combination if necessary and
- by parenteral or rectal route if necessary.

The patient should eat only lightly; treatment environment should be quiet and reassuring.

- (B) Antineoplastic drugs differ quantitatively and qualitatively in their emetogenic potential: 1) High (e.g., cisplatin), 2) Moderate (e.g., cyclophosphamide), and 3) Low (e.g., methotrexate). Emetogenic potential increases in combination therapy.

Emesis can begin 4-6 hours post-chemotherapy and can last up to 5 days, or can also begin 3-4 days post-chemotherapy and can last up to 5 days, or can occur bi-phasicly hours after and then again days after.

- (C) 5-HT₃ receptor antagonists are more effective anti-emetic agents than metoclopramide. These are granisetron, ondansetron, and ramosetron. Choose an agent wherein the per orem and the parenteral forms are both available and accessible; in instances wherein frank vomiting occurs, the parenteral form is the preferred drug.

Adjunct anti-emetic drugs such as diphenhydramine, lorazepam, and dexamethasone can be used particularly in highly emetogenic drug/s administration, moderate-severe emesis, and anticipatory emesis.

Start parenteral anti-emetic pre-medication 1-2 hours (not less than 30 minutes) prior chemotherapy administration in all anticancer chemotherapy administration sessions.

Delayed nausea and vomiting occurring more than 24 hours after therapy is treated with anti-emetics for a further 2 or more days. Maintenance anti-emetic can be in the per orem form.

Conditioned or anticipatory emesis is managed by giving pre-medications with anti-emetics and anxiolytics (e.g., lorazepam), starting the night before chemotherapy, either given per orem (when at home) or parenteral (when in hospital).

Relaxation and distractions such as television may be of benefit. Ice chips, mentholated or sour candies may be of benefit.

- (D) Emesis in a cancer patient can also be caused by a variety of other conditions that one should always consider before beginning anti-emetic treatment and when reassessing the patient for persistent emesis. The majority of patients with advanced disease will suffer nausea and vomiting at some stage of their illness. The anti-cancer drugs can also be stopped and the patient given time to recover. Then alternative drugs can be chosen with less emetogenic potential.

