For 5-FU-related diarrhoea,consider the following:

I. Evaluation

1. Onset and duration of diarrhoea: for a duration of >12 h,collect a stool sample
2. Number of stools and stool composition (watery, blood)
3. Assessment for fever, neutropenia, abdominal pain, dizziness, and weakness
4. Medication profile (diarrhoeatic e.g. bulk agents, softeners, and prokinetics) to be stopped

II. Management

1. Consider oral rehydration solution as part of fluid intake
2. Drink 8–10 large glasses of clear fluids per day (water, clear soup, non-carbonated soft drinks)
3. Consume frequent small meals as tolerated
4. Administer antibiotics as appropriate (fluoroquinolones)
5. Admit neutropenic patients with grade 3 diarrhoea or worse

III. Treatment

1. Initially, loperamide, 4mg followed by 2mg after every loose stool up to 16mg daily, or codeine phosphate 30–60mg QDS
2. Reassessment after 12 h

   After 12–24 h

Diarrhoea resolved

1. Stop loperamide administration after a 12-h diarrhoea-free interval
2. Check that the patient is eating small frequent meals

Persistent diarrhoea: grade 1–2

1. Continue with loperamide, 2mg every 2 h up to16mg for the first 24 h and then re-review.
2. Administer antibiotics as appropriate

Persistent diarrhoea: grade 3–4

1. Admit the patient
2. Budesonide, 9mg PO once a day (OD) until diarrhoea is resolved (all patients with a positive response to budesonide should receive prophylactic budesonide, 9mg PO OD, for 3–5 days, with subsequent courses)
3. IV fluids, antibiotics as appropriate
4. If diarrhoea is unresolved: octreotide 100–150mcg SC thrice a day (TDS) for 5 days, increased by 50mcg up to 200mcg TDS if necessary

Irinotecan-associated late-onset diarrhoea:

This may occur approximately 1 week after treatment (and may therefore coincide with neutropenia). There are specific instructions for patients to follow, which should be given on an information sheet to all patients receiving irinotecan.

These are as follows:

- Take loperamide, 4mg, once after the first liquid stool then 2mg every 2 h. Continue for 12 h after the last liquid stool (do not continue beyond 48h).
- If diarrhoea has not resolved within 24 h, start ciprofloxacin, 250mg PO BD, for 7 days.
- Patients should contact the hospital for advice as soon as diarrhoea is experienced.

If diarrhoea is severe, continues for more than 48 h, or is associated with nausea, vomiting or fever, the patient needs to be admitted to the hospital

- Examination on admission:
    - Stool culture, microscopy
    - Patients should be closely monitored: daily urea and electrolytes, abdominal radiography (as required), and urine output monitoring.
    - Ciprofloxacin should be continued for a total of 7 days, unless pyrexia develops, in which case, appropriate IV antibiotics should commence.
    - Loperamide should continue at 16 mg daily.
    - If diarrhoea persists, consider octreotide and other possible causes.

Chest pain whilst receiving fluoropyrimidines

Fluoropyrimidine agents (capecitabine/5-FU) are known to rarely cause a syndrome of angina-like chest pain, which is thought to relate to coronary artery spasm. If patients develop angina-like pain whilst receiving 5-FU or capecitabine, treatment should be discontinued immediately. Electrocardiography must be performed to exclude myocardial infarction and cardiac enzymes including troponin should be measured. Patients should be admitted overnight if significant pain has occurred within the previous 24 h. If electrocardiography or blood abnormalities are noted or the patient redevelops chest pain whilst off chemotherapy, referral for a cardiology opinion should be considered.

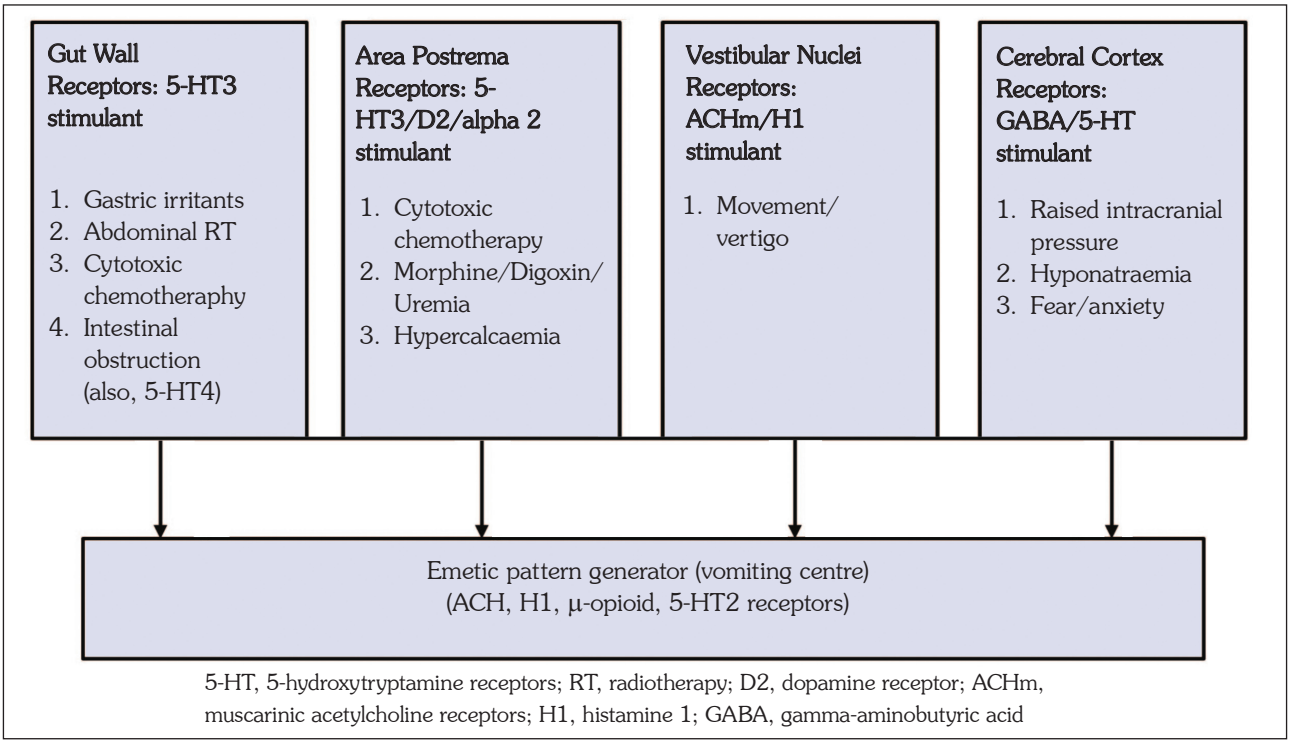
Patients should not recommence treatment, but their case should be discussed and alternative chemotherapy should be considered (oral tegafur-uracil). In some cases, in discussion with a cardiologist, fluoropyrimidines may be recommenced with anti-anginal cover (Ca^{++} channel antagonist and nitrate).

Nausea and vomiting

It is important to assess the cause of vomiting in order to be able to treat it appropriately.

- Comprehensive history and physical examination
- Minimum investigations
- Consider 'holistic' assessment

The receptors shown below are stimulated to induce vomiting. Drugs are chosen for specific receptors.



5-HT, 5-hydroxytryptamine receptors; RT, radiotherapy; D2, dopamine receptor; ACHm, muscarinic acetylcholine receptors; H1, histamine 1; GABA, gamma-aminobutyric acid

Commonly used drugs acting on specific receptors							
Drug	**Dosage**	**D2**	**H1**	**ACHm**	**5-HT2**	**5-HT3**	**5-HT4**
Metoclopramide	10–20 mg q4–6h PO/SC/IV	++	0	0	0	+	++
Domperidone	10–20 mg q4–8h PO	++	0	0	0	0	0
Haloperidol	0.5–2 mg q6–12h PO/SC/IV	+++	0	0	0	0	0
Ondansetron	4–8 mg q8–12	0	0	0	0	+++	0
Chlorpromazine	25–50 mg q6-8h PO/IV	++	++	+	0	0	0
Diphenhydramine	50–100 mg q4–6h PO/IV	0	++	++	0	0	0
Prochlorperazine	10–20 mg q6h PO/IV or 25 mg q6hPR	++	+	0	0	0	0
Olanzapine	1.25–2.5 mg PO OD	+	++	++	++	+	0
Dexamethasone	4–20mg qAM PO/IV/SC	0	0	0	0	?	0

Measures other than medication include consuming small tasty meals, a variety of foods, or cold food; a break from cooking; and home ventilation.

Before the administration of oxaliplatin, dexamethasone and ondansetron is recommended.

For the prevention of delayed nausea and vomiting, use corticosteroids and metoclopramide (and ondansetron, if required).

Hand-foot syndrome or palmar-plantar erythrodysesthesia

Capecitabine and 5-FU can both cause hand-foot syndrome or palmar-plantar erythrodysesthesia. This side effect can be prevented by advising patients as follows:

- Modify some of the normal daily activities to reduce friction and heat exposure to the hands and feet for a period of time following treatment (approximately 1 week after IV medication and as long as possible during the time tablets are being taken).

- Avoid prolonged exposure of hands and feet to hot water while, for example, washing dishes, taking a shower, or taking a tub bath.
- Take short showers in tepid water.
- Do not wear dishwashing gloves, as the rubber will hold heat against the palms.
- Avoid increased pressure on the soles of the feet or palms of the hands.
- Do not jog, do aerobics, perform power walking, or jump. Avoid long days of walking.
- Avoid using garden tools, household tools such as screwdrivers, and other tools that require squeezing the hand on a hard surface.
- Do not use knives to chop food as this may also cause excessive pressure and friction on the palms.
- Place the palms of the hands or soles of the feet on an ice pack or a bag of frozen peas (anything cold),as this may be very comforting. Alternate between placement on the cold surface and removal from the surface for 15–20 min at a time. Avoid rubbing lotion on the palms and soles during this period, although it is very important to keep these areas moist between treatments.
- Use emollients to provide excellent moisturizing to the hands and feet.
- Take paracetamol as this may be helpful in relieving the discomfort associated with hand-foot syndrome. Celecoxib also may be used for this purpose.
- Take vitamin B6 (pyridoxine), as this may be beneficial in preventing and treating hand-foot syndrome.

Skin rash associated with cetuximab

Management: the STEPP protocol[72]

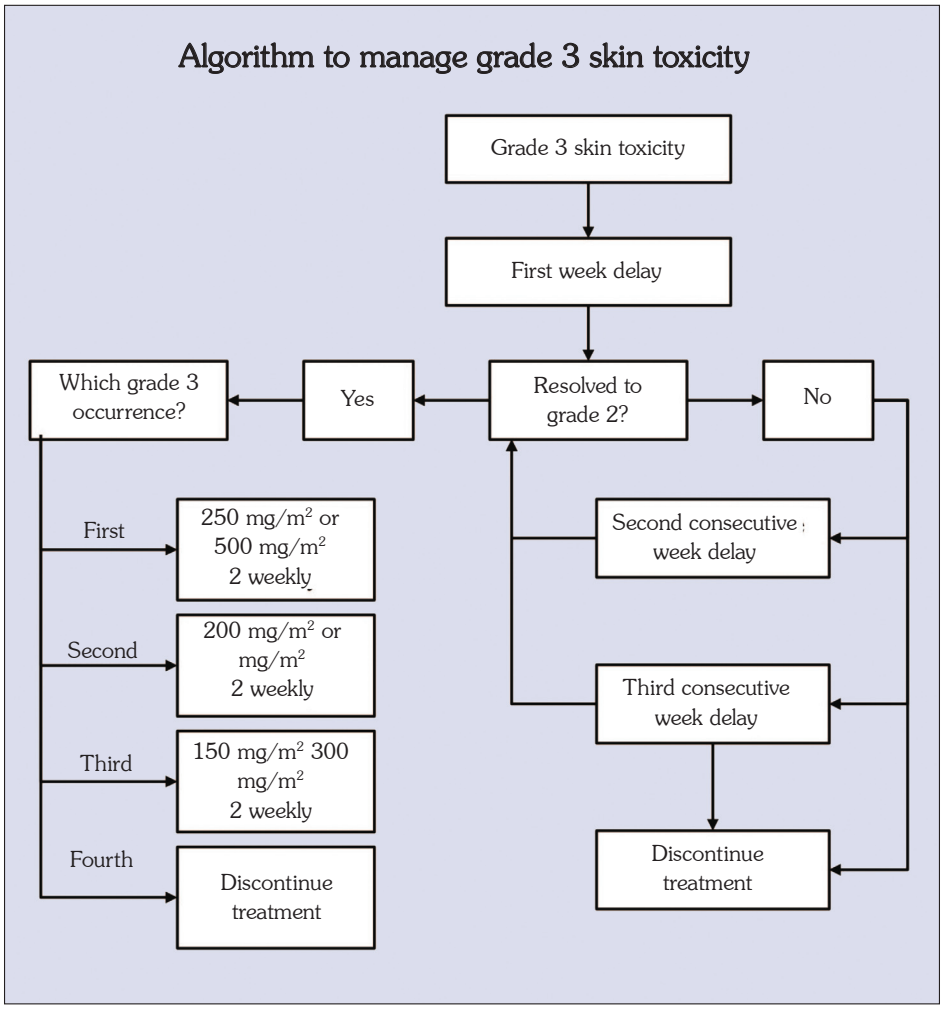
Prophylactic skincare reduces the number of skin reactions by 50% compared with reactive treatment.

All patients should receive the following:

- Emollient cream applied to the face, hands, feet, neck, back, and chest, once daily at bedtime
- Hydrocortisone 1% cream applied to the face, hands, feet, neck, back, and chest, at bedtime
- Lymecycline 408 mg OD
- Sunscreen, sun protection factor 15 or higher (with ultraviolet A and ultraviolet B protection), applied to exposed skin areas before going outdoors

In case of grade 3 skin toxicity, delay infusion.

Algorithm to manage grade 3 skin toxicity:



Vaccination during chemotherapy

Where possible, patients may receive vaccines such as the influenza vaccine before commencing chemotherapy. Immunization should be postponed if a patient is suffering from an acute illness. Minor infection, in the absence of fever or systemic symptoms, is not itself a contraindication to vaccination.

Live vaccines such as mumps and rubella, Bacillus Calmette–Guérin,and yellow fever should never be administered to immunocompromised patients, including those receiving chemotherapy, within 6 months after receiving chemotherapy.

Vaccines that are killed such as the influenza vaccine or protein subunits such as hepatitis B may be given, but the immunological response may be impaired by chemotherapy. These vaccines should be given at the end of the cycle when the degree of immunosuppression is at its lowest.

Vaccine	Live	Suitable for immunocompromised patients
Bacillus Calmette–Guérin Heaf Mantoux test	Yes No	No Yes
Hepatitis B	No	Yes

The decision to vaccinate should always be made on an individual patient basis.

CHAPTER 7

FOLLOW UP AND SURVIVORSHIP

Colerectal Cancer (CRC)

Follow-up after adjuvant chemotherapy or NACT

Year	Time from start of chemotherapy (months)	Clinical examination	Elevated tumour marker levels, CEA or CA19.9, at diagnosis	CT CAP	Discharge
0	0	✓	✓	✓	
1	3	✓	✓		
	6	✓	✓		
	9	✓	✓		
	12	✓	✓	✓	
2	18	✓	✓		
	24	✓	✓	✓	
3	30	✓	✓		
	36	✓	✓	✓	
4	48	✓	✓		
5	60	✓	✓		✓

Ensure that colonoscopic surveillance continues:

- Every 1 year after surgery and every 3 years thereafter
- If polyps are noted,every 6–12 months until polyp-free status is achieved

Follow-up after liver/lung resection

Year	Time after surgery (months)	Clinical examination	Elevated tumour marker levels, CEA or CA19.9	CT CAP	Discharge
0	0	✓	✓	✓	
1	3	✓	✓		
	6	✓	✓	✓	
	9	✓	✓		
	12	✓	✓	✓	
2	18	✓	✓	✓	
	24	✓	✓	✓	
3	30	✓	✓		
	36	✓	✓	✓	
4	48	✓	✓	✓	
5	60	✓	✓	✓	
6	72	✓	✓		
7	80	✓	✓		✓

Advanced disease

- Following completion of chemotherapy, review the case every 3 months (may be extended if the patient is stable).
- Measure CEA or CA19.9 levels (whichever was raised at diagnosis) at each clinic visit.
- Routine imaging is not indicated unless symptom driven.
- Consider CT if signs/symptoms suggest disease progression or if rising levels of tumour markers are noted.
- Ensure all patients have palliative care support if possible (desirable).
- If no further treatment can be offered following evidence of disease progression, the patient should be discharged from the clinic with adequate psychological/palliative support if possible.

CHAPTER

8 PALLIATIVE CARE

Palliative care is aimed at providing comfort to the patient in all possible scenarios. Patients should receive physical, psychological, spiritual, and social support, if feasible. Quality of life should be the main focus of care. Care should be offered for each suffering by a multidisciplinary professional team in the hospital, home, or hospice—the choice of the patient and family in concurrence with the treating physician.

Goals

- Relief from suffering
- Treatment of pain and other distressing symptoms
- Psychological and spiritual care
- Support system tohelp the patient live as actively as possible
- Support system to sustain and rehabilitate the patients' family

Aims

- Provide relief from pain, shortness of breath, nausea, and other distressing symptoms
- Affirm life and regard dying as a normal process
- Intend neither to hasten nor postpone death
- Integrate the psychological and spiritual aspects of patient care
- Offer a support system to help patients live as actively as possible
- Offer a support system to help the family cope
- Use a team approach to address the needs of patients and their families
- Improve quality of life
- Be applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy

Holistic Care

Patients should receive appropriate care for physical (e.g. pain, nausea and vomiting, constipation, dyspnoea, bowel obstruction, and fungating wounds), social (e.g. finance, education, job, and social environment), psychological (grief, helplessness, hopelessness, lack of self-worth, despair, and family collusion), and spiritual (e.g. address questions such as 'why me?', 'what is the meaning of disease', and 'what comes next?") suffering.

Psychological care

Psychological care and emotional support is an extremely essential part of palliative care. It offers a support system to help patients live as actively as possible until death and help the family cope during the patient's illness and in their own environment.

Principle guidelines for psychological care in the palliative care setting are as follows:

- At the time of initial consultation: assess psychological wellbeing, reactions to current losses, the support system and coping of patients and caregivers. Privacy and confidentiality should be maintained at all times.
- Assessment will include mood, feelings, concerns, family relationships, social support, and impact of illness on day-to-day life and work.
- Patients and caregivers both should be evaluated during assessment.
- All staff are directly responsible for patient care and should offer general emotional support based on skilled communication, effective information provision, genuineness, and respect.
- Psychological support should be provided through intimate care and positive communication skills during difficult situations
- Need based interventions should be planned, for example, from self-help to specialized psychological interventions for patients.
- Patients and caregivers with a significant level of psychological distress and premorbid psychiatric issues should be promptly referred to specialist psychiatric services.
- Psychological needs and problems of the staff caring for patients should be explicitly assessed and adequately met to improve the quality of care.

On-going psycho-social assessment is a fundamental need in palliation to assess the emotional, social, and economic status of patients and their families in order to help them be sustained during the advanced phase of cancer.

Interventions

- Facilitating respite care (if feasible): counselling, telephonic help, and material and emergency aid such as free medicines, monthly ration, education fees for dependents, fulfilling last wishes of children, and providing stay and food while the patient is on short-duration medical interventions like radiotherapy.
- Advocacy and referral networks: address economic and existential concerns of families when the patient is the primary source of income in his family and link families with local resources and various government schemes
- Empowering and educating families: help them combat fear of contagion, stigma, and isolation.
- Community outreach: create awareness amongst medical and paramedical health care professionals at the grass-root level.

CHAPTER 9

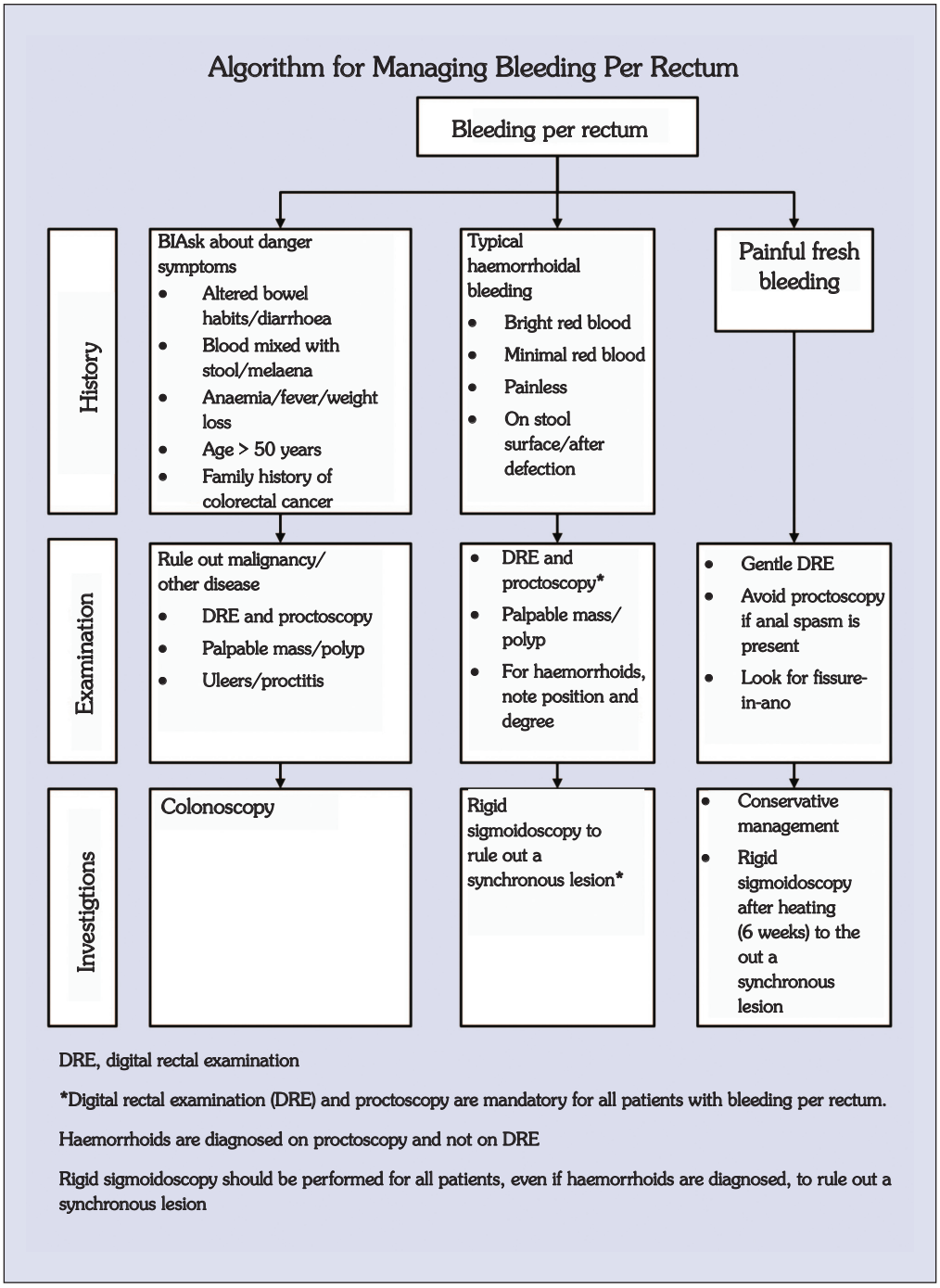
RESEARCH AVENUES

- Genetics, epidemiology, and lifestyle study of familial and non-familial CRC.
- Molecular diagnosis and characterisation including genomic sequencing
- Duration and role of chemotherapy in adjuvant setting
- Role of targeted therapies
- Role of radiotherapy in rectal cancers
- Role of surgery in colorectal liver metastases
- Training and credentialing of surgeons, pathologists, radiologists, medical oncologists and radiation oncologist in site-specific areas
- Role of new techniques for diagnosis and management – endoscopy, MRI and PET CT, IMRT, Radio gold nanospheres

CHAPTER

10 APPENDICES

Appendix A: Algorithm for Managing Bleeding Per Rectum



Computed Tomography of the Abdomen and Chest: Colon Cancer Staging Report Template

Primary tumour morphology: Annular/Ulcerating/Polypoidal/Villous/Mucinous

Border: Nodular/Smooth/Infiltrating

Site:Caecum/Ascending colon/Hepatic flexure/Transverse colon/Splenic flexure/Descending colon/ Sigmoid

Advancing edge of the tumour (border): Mesenteric/Peritoneal

The tumour is [confined to/extends through] the bowel wall

Peritoneal infiltration:No evidence/Evidence

Tumour extension:<5mm/>5mm

Tumour spread:___ mm

Tumour diameter: ___ mm

Tumour thickness:___ mm

Lymph nodes in colonic mesentery: Benign/Reactive/Malignant

There is [evidence/no evidence] of extramural venous invasion

There is [evidence/no evidence] of peritoneal dissemination

Retroperitoneal lymphadenopathy is [absent/present]

Incidental note is made of [intra-abdominal pathology/pelvic pathology]

There is [evidence/no evidence] of metastatic disease in liver:

Details: There is segmental sparing/There is no segmental sparing

Incidental note is made of [cysts/haemangiomas/equivocal low-density lesions]

[requires/does not require FNA]
[for follow-up]
[likely/unlikely to represent metastatic disease]

Pulmonary metastatic disease:No CT evidence/CT evidence

Details: Unilateral/Bilateral/Number/Lobes

Summary:Overall stage:T[ ]N[ ]M[ ]

Appendix C: Pathology Reporting of Colorectal Carcinoma and Staging

Surgical Anatomy of the Colorectum with Respect to the Visceral Peritoneum

A small part of the posterior surface of the caecum can be retroperitoneal. The ascending colon and descending colon are retroperitoneal posteriorly. The upper third of the rectum is invested by a peritoneal covering on its anterior and lateral aspects and is bare or non-peritonealised on its posterior aspect. The middle third is draped by the peritoneum only on its anterior aspect, leaving the lateral and posterior surfaces bare or non-peritonealised,whereas the lower third is completely devoid of peritoneal covering or is entirely non-peritonealised.

Clinical Relevance of the Anatomical Relationship of the Colorectum with the Visceral Peritoneum

In general, the prognosis of rectal tumours is poorer than that of tumours occurring in other parts of the colon. Within the rectum itself, tumours situated below the anterior peritoneal reflection have a poorer prognosis because of the high chances of local recurrence. This is especially true of the tumours located in the anterior and lateral quadrant of the rectum. The non-peritonealised surfaces (NPS) (previously referred to as the circumferential resection margin or CRM) of all parts of the colon as described above are dissected by the surgeon, and hence conceptually, they are surgical resection margins, or more precisely, surgical surfaces. The serosal surface on the other hand is not a surgical margin. It is the outer most barrier to the tumour formed by a layer of mesothelial cells and their basement membrane. When the serosa is invaded by the tumour, it gains unrestricted access to the peritoneal cavity. Thus, despite their close anatomic proximity, the serosa and NPS represent 2 conceptually different anatomic entities with entirely different connotations on the management of colorectal cancer (CRC).

Types of Surgical Specimens

1. Polypectomy: A polyp can be sessile or pedunculated
2. Right hemicolectomy, left hemicolectomy, transverse colectomy, descending colectomy, and sigmoid colectomy
3. Anterior resection (AR): AR is performed for high rectal tumours where preservation of the anal sphincter is easy.
4. Abdominoperineal resection (APR):APR involves en bloc resection of the rectosigmoid, the rectum, and the anus along with the surrounding sigmoid mesentery, mesorectum, and perianal soft tissues. APR is performed for low rectal and anal canal tumours where the anal sphincter cannot be saved.
5. Total proctocolectomy: Total proctocolectomy is usually performed in the setting of familial adenomatous polyposis syndrome.

Step-wise Technique and Principles of Grossing of Colorectal Oncology Surgical Specimens

1. Receipt of specimen: Receive the unopened specimen in formalin along with the proper clinical history. Check the specimen identification.Surgeons should refrain from opening the specimen because such practice could result in distorting important structures such as the serosa or NPS with respect to the tumour.
2. Note the nature of surgical procedure.
3. Record the length of the entire specimen. Record the length of the terminal ileum and appendix separately if present in the specimen.

4. Palpate the tumour from the outer aspect of the specimen. This will help re-enforce the ink on the bare area in relation to the tumour.
5. Assess the quality of total mesorectal excision (TME) before the application of ink or opening the APR and the AR specimens.

The concept of TME

The rectum is encased by a thick blanket of fatty tissue known as the mesorectum,which contains the blood vessels and lymph nodes that drain the rectum. The mesorectum is in turn enclosed by a fascia known as the endopelvic fascia. Removal of the mesorectum en bloc with the rectal tumour, referred to as TME, forms the current surgical 'gold standard' for rectal tumours. The goals of TME for rectal cancer resection are achieving adequate lymphadenectomy and a maximum lateral resection margin. TME of good quality reduces the possibility of locoregional relapse. Thus, the NPS is conceptually a surgical resection margin created to deliver the rectum together with its mesorectum. Involvement of the serosa by the tumour represents a pT4 stage, whereas involvement of the NPS (CRM/radial margin) implies pT3.

Pathological assessment of the quality of TME

TME of good quality improves local recurrence rates and corresponding survival by as much as 20%. The quality of mesorectal excision is assessed as follows:

A. Complete TME (grade 3):

The plane of surgery is the mesorectal fascial plane. The mesorectum is intact and bulky with a smooth surface. Only minor irregularities are noted on the mesorectal surface, with no surface defects greater than 5 mm in depth. Coning is not observed towards the distal margin of the specimen. The CRM is smooth on transverse slices.

B. Nearly complete TME (grade 2):

The plane of surgery is through the mesorectum. The bulk of the mesorectum is moderate.The mesorectal surface is irregular, with defects greater than 5 mm, but none extending to the muscularis propria. No areas of visibility of the muscularis propria except at the insertion site of the levator ani muscles. Moderate coning is seen towards the distal margin of the specimen. Moderate irregularity of the CRM is seen in transverse slices.

C. Incomplete TME (grade 1):

The plane of surgery is through the muscularis propria. The bulk of the mesorectum is slight. Defects in the mesorectum expose the muscularis propria.The circumferential margin in transverse sections appears very irregular. A very irregular CRM is seen in transverse slices. For AR specimens, only a single plane, i.e. the mesorectal plane, is evaluated. However, for an APR specimen, gross evaluation of the surgical plane of the anal canal is also evaluated. Surgical planes evaluated for the anal canal include the following:

a. The levator plane: the surgical plane lies outside the levators, which are removed en bloc in the APR specimens. The specimen is cylindrical.
b. The sphincteric plane: the surgical plane lies on the surface of the sphincter.
c. The intra-sphincteric plane: the surgical plane passes through the sphincter.

6. Photograph the specimen from both aspects for recording purposes.

7. Look for the presence of tumour site perforation before inking.

   Tumour site perforation is a poor prognostic factor, which results in high morbidity and mortality due to peritonitis and sepsis. Serosal perforation at the tumour site also gives tumour cells access to the peritoneal cavity. Therefore, when present, the tumour is classified as pT4 according to the TNM classification system. This is irrespective of the actual presence of tumour cells at the serosal surface on microscopy.

8. Paint the NPS with ink, with special reinforcement to the NPS associated with the tumour. The serosa is histologically identifiable by the presence of mesothelial cells and its basement membrane; hence, it should not be painted as the ink obscures the mesothelial cells.

9. Upon inking, open the specimen from the anterior aspect starting from either end of the tumour up to 1 cm above and below the tumour, thereby, keeping the segment containing the tumour intact. This ensures that the association of the tumour with the serosa is intact as is the NPS/CRM.

10. Note the distances of both longitudinal resection margins from the tumour. Record the distance from the pectinate line in the APR specimen. In APR specimens for rectal carcinoma, the distance from the pectinate line and from the anal verge will justify the surgical procedure,which results in permanent loss of the anal sphincter.

11. Record the location of the tumour in relation to the anterior peritoneal reflection in the rectosigmoid, AR, and APR specimens.

    Tumours located above the anterior peritoneal reflection are covered by peritoneum anteriorly and laterally while they are related to the NPS on the posterior aspect. Tumours at/astride the peritoneal reflection are covered by peritoneum only anteriorly while they are non-peritonealised on the lateral and posterior aspects. Tumours lying below the anterior peritoneal reflection are not at all related to the peritoneum and are entirely related to the NPS or the CRM.

12. Insert a cotton wick soaked in formalin into the lumen of the intact segment containing the tumour and fix the entire specimen in an appropriate volume of formalin overnight or for 48 h. Ideally, the colon should be pinned down onto a cork board and immersed in formalin.

13. Upon adequate fixation, sample longitudinal mucosal resection margins. If the tumour is less than 1 cm from the longitudinal mucosal resection margin, then sample the margin in a radial manner (perpendicular to the long axis of colon) after inking the resected end of the segment or anal verge. Otherwise, a 'shave' margin (parallel to long axis of colon) should suffice.

14. Document the size of the tumour in 2 dimensions. Tumour size has no prognostic relevance. However, it is important to correlate the actual size with imaging findings. It is especially important in patients who have received neoadjuvant chemotherapy and/or radiotherapy.

15. Sampling from the tumour

    Technique of tumour sampling

Cut serial slices,not more than 5mm in thickness, of the segment containing the tumour (which is kept intact and inked appropriately) in a transverse manner starting from 1 cm above and ending1cm below the limits of the tumour. Place the circular intact slices thus obtained sequentially, one below the other. Identify the deepest invasive parts of the tumour with respect to both serosa and the NPS/CRM (if applicable). Sample 4 to 5 sections of the deepest invasive parts of the tumour, each containing the most relevant anatomical surface (serosa and/or NPS/CRM). Document the distance between the tumour and NPS as well as the serosa.