MANAGEMENT OF NASOPHARYNGEAL CARCINOMA
ALGORITHM B: MANAGEMENT OF PERSISTENT DISEASE OR RECURRENT NASOPHARYNGEAL CARCINOMA

1. In Malaysia, nasopharyngeal carcinoma (NPC) is the fourth most common cancer. NPC is predominant among Chinese, followed by natives of Sabah and Sarawak (especially Bidayuh) and Malay.

2. Tobacco smoking is one of the important risk factors for NPC.

3. NPC is usually diagnosed late due to trivial presentation which leads to poor survival outcome.

4. In patients presenting with cervical lymphadenopathy, full head and neck assessment and fine needle aspiration cytological examination of the nodes should be done.

5. NPC should be diagnosed by histopathological examination of the nasopharynx.

6. Staging of NPC is by using the tumour node metastasis (TNM) system American Joint Committee on Cancer or AJCC Cancer Staging Manual 2010 (7th Edition).

7. Primary treatment for NPC is radiotherapy. Intensity modulated radiotherapy is the preferred radiation technique.

8. Concurrent chemoradiotherapy should be offered in Stage II, III, IVA and IVB.

9. In recurrent NPC, nasopharyngectomy or re-irradiation may be offered.

10. Multimodality treatment including dental, supportive and palliative care should be considered in the management of NPC.

This Quick Reference provides key messages and a summary of the main recommendations in the Clinical Practice Guidelines (CPG) Management of Nasopharyngeal Carcinoma.

Details of the evidence supporting these recommendations can be found in the above CPG, available on the following websites:

Ministry of Health Malaysia : www.moh.gov.my
Academy of Medicine Malaysia : www.acadmed.org.my
Malaysian Society of Otorhinolaryngologists : www.msohns.com
Head & Neck Surgeons

Also available as a mobile app for Android & IOS platform: MyMaHTAS

CLINICAL PRACTICE GUIDELINES SECRETARIAT
Health Technology Assessment Section
Medical Development Division, Ministry of Health Malaysia
4th Floor, Block E1, Parcel E, 62590 Putrajaya
Tel: 603-8883 1229 E-mail: htamalaysia@moh.gov.my
CLINICAL PRESENTATIONS AND REFERRAL

• Patients presenting with any of the following symptoms should be referred to Otorhinolaryngologists as soon as possible to rule out NPC:
  ○ painless neck lump (unilateral/bilateral)
  ○ blood-stained nasal discharge/saliva
  ○ unilateral ear block or hearing loss
  ○ headache
  ○ facial numbness
  ○ diplopia

RISK FACTORS OF NASOPHARYNGEAL CARCINOMA

• Ethnicity (especially Chinese and natives of Sabah & Sarawak)
• Gender (male to female ratio is 3:1)
• Family history of NPC
• Lifestyle and environment
  ○ Tobacco smoking
  ○ Consumption of salted fish
  ○ Exposure to domestic wood cooking fires
  ○ Exposure to occupational solvents
  ○ Occupational exposure to wood dust
## AJCC CANCER STAGING MANUAL 2010 (7TH EDITION)

### Nasopharynx

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tumour characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Tumour confined to the nasopharynx, or tumor extends to oropharynx and/or nasal cavity without parapharyngeal extension*</td>
</tr>
<tr>
<td>T2</td>
<td>Tumour with parapharyngeal extension*</td>
</tr>
<tr>
<td>T3</td>
<td>Tumour involves bony structures of skull base and/or paranasal sinuses</td>
</tr>
<tr>
<td>T4</td>
<td>Tumour with intracranial extension and/or involvement of cranial nerves, hypopharynx, orbit, or with extension to the infratemporal fossa/masticator space</td>
</tr>
</tbody>
</table>

*Note: Parapharyngeal extension denotes posterolateral infiltration of tumour.

### Distant Metastasis (M)

<table>
<thead>
<tr>
<th>M0</th>
<th>No distant metastasis</th>
<th>M1</th>
<th>Distant metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
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### Follow-up Schedule of NPC without recurrence

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<thead>
<tr>
<th>Year after completion of treatment</th>
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### Toxicities of Radiation Therapy on Head and Neck

**Acute Toxicities**

- Tumour confined to the nasopharynx, or tumor extends to oropharynx and/or nasal cavity without parapharyngeal extension*
- Tumour with intracranial extension and/or involvement of cranial nerves, hypopharynx, orbit, or with extension to the infratemporal fossa/masticator space
- Tumour with parapharyngeal extension*
- Tumour involves bony structures of skull base and/or paranasal sinuses

*Note: Parapharyngeal extension denotes posterolateral infiltration of tumour.

**Late Toxicities**

- Lethargy
- Radiation dermatitis
- Mucositis
- Dysphagia
- Taste changes
- Nausea and vomiting
- Haematological toxicities (neutropaenia)

### Prognosis of Different NPC Stages

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<tr>
<td>T1-2 N0-1</td>
<td>Relatively good treatment outcome</td>
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<tr>
<td>T3-4 N0-1</td>
<td>Mainly local failure</td>
</tr>
<tr>
<td>T1-2 N2-3</td>
<td>Mainly regional and distant failure</td>
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<tr>
<td>T3-4 N2-3</td>
<td>Local, regional and distant failure</td>
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### AJCC Cancer Staging Manual 2010 (7th Edition)

**Note:** Parapharyngeal extension denotes posterolateral infiltration of tumour.

**Note:** Midline nodes are considered ipsilateral nodes.

**Note:** Supraclavicular zone or fossa is defined by three points:
1. The superior margin of the sternal end of the clavicle,
2. The superior margin of the lateral end of the clavicle,
3. The point where the neck meets the shoulder.

All cases with lymph nodes (whole or part) in the fossa are considered N3b.
### PROGNOSIS OF DIFFERENT NPC STAGES

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### FOLLOW-UP SCHEDULE OF NPC WITHOUT RECURRENCE

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*interval of follow-up may be adjusted based on clinical judgement

### TOXICITIES OF RADIOTHERAPY ON HEAD AND NECK

#### ACUTE TOXICITIES

- Lethargy
- Radiation dermatitis
- Mucositis
- Dysphagia
- Taste changes
- Nausea and vomiting
- Haematological toxicities (neutropaenia)

#### LATE TOXICITIES

**Neurological Complications**

- Temporal lobe injuries
- Cranial nerve palsies
- Lhermitte’s syndrome

**Non-neurological Complications**

- Tinnitus
- Hearing loss
- Otorrhea
- Trismus
- Dysphagia
- Endocrinopathy
- - primary hypothyroidism
- - hypopituitarism
- Xerostomia
- Second cancer within radiotherapy fields
ALGORITHM A : MANAGEMENT OF NASOPHARYNGEAL CARCINOMA

- History taking
- Complete physical examination
- Nasopharyngeal examination & biopsy
- +/- FNAC of regional lymph nodes
- Baseline investigations (FBC, renal profile, random blood sugar, liver function test, chest X-ray and electrocardiogram)
- MRI of nasopharynx & neck (from base of skull to thoracic inlet) or CT with contrast
- PET-CT or CT thorax/abdomen or ultrasound and bone scan, as indicated
- Pre-treatment dental assessment
- Nutritional evaluation

**Stage I (T1N0M0)**
Treatment with definitive radiotherapy (RT) to nasopharynx & elective RT to neck

- Definitive RT: -
  - Primary site: total of 66-70 Gy for 33-35 fractions, treated one fraction/day for 6-7 weeks (1.8-2.0 Gy/fraction)
  - Prophylactic neck: 54-60 Gy for 30 fractions, treated one fraction/day for 6 weeks (1.8-2.0 Gy/fraction)
- IMRT recommended to minimise dose to critical structure

**Stage II, III, IVA and IVB**
Concurrent chemoradiotherapy

- Cisplatin + RT
- Conventional fractionation:
  - Primary site: total of 66-70 Gy for 33-35 fractions, treated one fraction/day for 6-7 weeks (1.8-2.0 Gy/fraction)
  - Neck: 54-70 Gy for 30-35 fractions, treated one fraction/day for 6-7 weeks (1.8-2.0 Gy/fraction)
- IMRT recommended to minimise dose to critical structures

**Stage IVC (distant metastasis)**
Palliative treatment

- Consider clinical trial if available
- Palliative chemotherapy to be considered in patients with good ECOG performance status (0-2)
- RT to palliate symptoms
- Referral to palliative care/palliative home care

**Follow-up and Surveillance**
- Multidisciplinary team involvement (ENT specialist, oncologist, speech therapist, audiologist, etc)
- Head & neck and systemic examination (including nasopharyngoscopy):

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- Cross-sectional imaging in the initial 5 years
- Speech/swallowing assessment as clinically indicated
- Hearing evaluation & rehabilitation as clinically indicated
- Post-treatment dental management every 3 to 4 months by trained and experienced dental specialist
- Weight assessment on follow-up
- Annual thyroid function test (TFT) screening
ALGORITHM B : MANAGEMENT OF PERSISTENT DISEASE OR RECURRENT NASOPHARYNGEAL CARCINOMA

Options include:
- Nasopharyngectomy OR
- Re-irradiation with external beam RT or brachytherapy

Options include:
- Neck dissection
- Re-irradiation
- Chemotherapy

Options include:
- Consider clinical trial if available
- Palliative chemotherapy to be considered in patients with good ECOG performance status (0-2)
- RT to palliate symptoms
- Referral to palliative care/palliative home care

Follow-up and Surveillance
- Multidisciplinary team involvement (ENT specialist, oncologist, speech therapist, audiologist, etc)
- Head & neck and systemic examination (including nasopharyngoscopy):
  - First year: Every 1 to 2 months
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### CHEMOTHERAPY DRUGS AND COMMON SIDE EFFECTS

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<th>COMMON SIDE EFFECTS</th>
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</table>
| Cisplatin           | • Nausea and vomiting  
|                     | • Myelosuppression   
|                     | • Renal toxicity     
|                     | • Electrolyte imbalance (hypomagnesaemia, hypocalcaemia, hypokalaemia)  
|                     | • Auditory (tinnitus; with or without hearing loss) |
| Carboplatin         | • Myelosuppression  
|                     | • Nausea and vomiting  
|                     | • Hypersensitivity reaction  
|                     | • Alopecia  |
| Fluorouracil        | • Diarrhoea and stomatitis  
|                     | • Myelosuppression  
|                     | • Angina, myocardial infarction, arrhythmia, acute pulmonary oedema (special precaution)  
|                     | • Alopecia  |
| Docetaxel           | • Myelosuppression  
|                     | • Fluid retention  
|                     | • Alopecia, cutaneous reaction, nails changes  
|                     | • Stomatitis, diarrhoea, nausea and vomiting  
|                     | • Hypersensitivity reaction  |