The Lung

The lungs are a pair of large, spongy organs that fill the chest and are either side of the heart.

Each lung consists of several distinct lobes. The right lung has 3 lobes — the superior, middle, and inferior lobes. The smaller left lung only has 2 lobes — superior and inferior. Neuroendocrine cells are present throughout the respiratory tract (lungs) as part of the normal anatomy.

Lung NENs account for up to 20% of all lung cancers. Signs and symptoms may or may not be present. If present they may mimic lung conditions eg asthma or indicate possible airways obstruction / common lung cancer: cough, chest pain, wheezing, etc. Up to 10% may present with symptoms of excess hormone secretion eg Carcinoid Syndrome.

To date 6 types of Lung NEN have been identified:

1. DIPNECH – (Diffuse Idiopathic Pulmonary NeuroEndocrine Cell Hyperplasia) cause unknown and can arise in healthy lungs, without any pre-existing chronic lung disease. Diagnosis is based on microscopic examination: enlarged lung neuroendocrine cells (hyperplasia), multiple tumourlets (<5mm) and associated inflammation and blockage of the smallest airways in the lungs: the bronchioles. DIPNECH is to be suspected if neuroendocrine cell hyperplasia is associated with obliterative bronchiolitis.

2. Typical Carcinoid (TC) low grade neuroendocrine tumour
3. Atypical Carcinoid (AC) mid-grade neuroendocrine tumour. NB DIPNECH/TC/AC are not usually associated with smoking. Approximately 5% of TCs/ACs are associated with MEN1

4. Small cell neuroendocrine carcinoma
5. Large cell neuroendocrine carcinoma
6. MiNEN or mixed cell carcinoma.
Diagnosis for Lung

**Blood / Urine Tests**
- Full blood count
- (B12 + serum Iron)
- Liver and kidney function
- Biochemical :
  - Chromogranin A (and B)
  - Urinary 5-HIAA
  - Calcium
  - Glucose
- If Cushing syndrome present/suspected: serum cortisol, urinary cortisol and ACTH
- If MEN present/suspected: calcium, PTH and consider genetic studies

- Echocardiogram: as a baseline in the presence of carcinoid syndrome / raised U5HiAA and/or elevated NT-Pro-BNP +/- clinical signs of heart valve impairment/R sided heart failure

- Lung/Respiratory Function Tests.

**Endoscopy**
- Bronchoscopy
- Endoluminal Bronchoscopic Ultrasound (EBUS)**

**Scans**
- Chest x-ray
- Contrast or High Resolution chest CT
- CT abdomen/pelvis to exclude secondary disease - or confirm primary if lung NET is secondary.
- *Gallium-Dotatate PET/CT (SRS SPECT/CT if Dotatate PET n/a)
- FDG-PET – if High Grade / rapidly progressing disease.

**Pathology**
- Differentiation and cellular morphology
- Synaptophysin
- Chromogranin
- Ki67
- CD56
- Cytokeratins
- TTF1
- (TTF1, CDX2, Islet1 may be useful to distinguish between primary and secondary lung NET disease.

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Treatment for Lung

For all patients, there are many things to consider in planning treatments. Your treatment will be personalised to you and the type of NEN you have. Even if you have a diagnosis that sounds the same as another patient, your treatment and follow up plan may be different.

Your care team will discuss your treatment options with you - giving you both written and verbal information - to help you make an informed choice. Together you can agree on the most appropriate treatment for you. Information about the treatments that are used in NET and NEC can be found in the NPF Handbook - Your Guide to Living with Neuroendocrine Cancer - www.netpatientfoundation.org

There is consensus agreement that all Neuroendocrine Cancer patients should be reviewed by a Specialist Neuroendocrine Cancer MDT.

Follow-up for Lung

Follow up is dependent on type, tumour extent, histological differentiation and proliferative activity:

**Primary Lung NENs:**
- DIPNECH: No current consensus, but given clinical presentation, impact on quality of life and potential for development of TC, follow up should be clinically driven and ongoing.

**Typical Carcinoid:**
- Following surgery - review at 3, 6 and 12 months for 1st 2 years, then annually (life-long) with Chest X-ray (and bronchoscopy as indicated). CT every 3 years (more frequently if R1 or node positive resection or as clinically indicated). Functional imaging* at 1 year post op, then only if suspicion of recurrence
- EBUS** can be used if there is suspicion of local recurrence, and may be used 5-10 years as surveillance.

**Atypical Carcinoid:**
- Closer monitoring required. Review at 3 months then every 6 months for first 5 years, then annually if all stable/disease free. Functional imaging* at 1 year post op, then only if suspicion of recurrence - in high grade disease FDG-PET may be more accurate than Gallium-Dotatate as functional scan
- EBUS** can be used if there is suspicion of local recurrence, and may be used 1-3 years as surveillance
- If on ongoing therapy: 3 monthly review - If local progression suspected for EBUS**
- Small cell lung neuroendocrine carcinoma and Large cell neuroendocrine carcinoma: follow high grade recommendations.

**High grade follow up:**
- Following surgery: CT every 3 - 6 mths for first 3 years then 6 - 12 monthly. In inoperable/advanced disease: CT every 2 - 3 months if on therapy. Biomarkers repeated if elevated at diagnosis
- Secondary lung NET is dictated by extent of lung involvement, respiratory function and primary site status.
A big part of meeting with your doctors, or specialist nurse, is to make sure you get the information you need to understand what’s happening, so that you can make an informed choice about your care. Asking questions can be difficult, especially if you’re feeling nervous, confused, frightened or struggling to understand what you are being told. You might want to know as much as possible straight away or prefer to take things in small amounts at your own pace.

**Suggestions that may help:**
- Prepare a list of questions that are important to you
- Ask for simple explanations - do not be worried about asking your nurse or doctor to repeat what they have said
- Take someone with you or ask if you can record the conversation. Many mobile phones have a record function or an app you can download
- Ask for a copy of any letters sent to your GP and/or other care team(s)
- If you have a nurse specialist - keep in touch. They can be a great source of information and support for you.

**Example questions:**
- Who can I call if I have any questions? Who is my main point of contact?
- Who will be involved in my care?
- What are the treatment options for me? How might they affect me?
- How often will I need to have scans and tests?
- Are there any flags or warning signs I need to look out for?

Further information about making the most of your consultations can be found in our handbook: www.netpatientfoundation.org

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