multicentric and are often advanced at the time of diagnosis. Most patients are white men with an average age of 57 at the time of diagnosis.

Mutation and over expression of p53, apoptosis-related genes, myc amplification, mutations of the cadherin/catenin membrane complex, microsatellite instability and expression of CD44 are included in the molecular alterations already identified in BO containing dysplastic/carcinomatous changes.[13]

The primary treatment of carcinoma is surgical resection, combined with chemotherapy and radiation.

The prognosis of adenoncarcinoma arising from BO is poor, with a 5-year survival rate of 14.5%. The prognosis is, however, similar to that of conventional squamous cell carcinoma of the oesophagus.

Unusual malignancies arising from BO include adenosquamous carcinoma, squamous cell carcinoma, sarcomatoid carcinoma, neuro-endocrine carcinoma, choriocarcinoma and yolk sac tumours.[14]

### The future

In the future, non-biopsy endoscopic methods including chromo-endoscopy and narrow-band imaging may be used, allowing a reduction in the number of biopsies. Other possibilities include light-induced fluorescence endoscopy, light-scattering spectroscopy and spectroscopy. However, further evaluation is necessary before clinical application will be possible.[1,9]

**References available at www.cmej.org.za**

## Lymph node biopsy: Some aspects revisited

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Lymph node biopsy, if performed correctly, is likely to yield an optimal diagnostic result.[1-3] However, in view of the invasive nature of the procedure, biopsy should only be undertaken in patients with a definitive clinical indication. Less invasive investigations, such a full blood count and serology, and fine needle aspiration (FNA), may indeed provide a conclusive diagnosis especially if a careful medical history/examination reveals the most likely clinical cause for the lymphadenopathy, which is subsequently confirmed.

FNA as a tool to allow for a reliable diagnosis has gained increasing acceptance.[2-5] Larger/referral laboratories have access to additional specialised investigations, including immunophenotyping, flow cytometry, cytogenetics and other techniques that can be performed as part of FNA sampling aiding in/allowing for a conclusive diagnosis.[1,2] Unfortunately, of the latter depend on 'on site' sampling. As a very significant percentage of the population is, at least initially, managed at peripheral healthcare units, lacking readily accessible specialised work-up. More complicated cases in need of ancillary techniques cannot optimally be assessed in this way.

Guidelines for lymph node biopsy are provided in various surgical, medical and pathology textbooks.[1,2,4,5] In a clinical scenario where other means of arriving at a conclusive diagnosis have failed some of the more important indications for biopsy include:

- Persistent, unexplained lymph node enlargement. Decisions on further management will have to be based on other relevant considerations, i.e. age, general health, findings of clinical examination (site of involvement and whether lymphadenopathy is localised or generalised).
- Confirmation of clinically suspected diagnosis. Medical history and/or findings on examination may indicate that malignant disease is most likely, but conclusive histological diagnosis in most cases remains mandatory to allow for further management. Examination of draining nodes involved by metastatic disease of a primary tumour (i.e. where the latter is far less readily accessible for biopsy) may yield a definitive diagnosis.
- Assist in the investigation of a patient with a lymphadenopathy with associated clinical symptoms/signs that are difficult to explain conclusively (on the assumption that other relevant investigations have failed to provide a diagnosis). In this category conditions inducing non-neoplastic lymphadenopathy, which may have been overlooked, including infections, connective tissue disease and drug-related reactions may be relevant. Lymph node biopsy in these cases may indeed also be indicated to exclude the possibility of malignancy, including lymphomas with unusual presentation or unexpectedly widespread involvement by metastatic disease.
- Localised lymphadenopathy, especially of superficial nodes which are only moderately enlarged and soft, particularly in paediatric patients, may indeed be

due to reactive lymphadenopathy at a site draining a focus of infection. In our setting tuberculous lymphadenitis/HIV-related lymphadenopathy remains a relatively common cause for lymph node enlargement and can very often reliably be diagnosed by FNA.

- All non-invasive means should be used to arrive at a reliable diagnosis, and biopsy should only be performed if results of, for example, FNA remain worrisome but inconclusive or if other clinical indications, such as a lack of response to instituted antibiotic therapy, complicate the case.
- Hard or rubbery nodes generally need sampling for an urgent diagnosis.
- Additional indications include lymph node dissection as part of staging procedures as well as monitoring of response to treatment. The latter are largely part of specialist/tertiary management and therefore less relevant in general/primary care practice.

## Lymph node biopsy technique[1,2]

Lymph node biopsy represents an invasive procedure which may require significant surgical expertise, depending on the site of involvement, general condition and age of the patient, nature of diseased nodes, etc. While optimally biopsies should be performed by surgical specialists, with the overall profound shortage of specialist medical professionals it is not feasible in the South African context. In peripheral/rural settings lymph node biopsies are indeed performed by non-specialist medical practitioners; in most cases with a sound clinical judgement as to feasibility and safety of the procedure. Less experienced staff need adequate training/supervision before an intervention of this nature. More complicated cases, however, may have to be referred to tertiary centres/specialists for sampling.

In cases where prior less invasive procedures have not provided a conclusive answer but the findings on, for example, FNA/needle biopsy remain very worrisome, needle or preferably excisional biopsy is indicated. While larger centres have ready access to ultrasound/CT-guided needle biopsies, this is unfortunately not the case at peripheral smaller medical units. If needle biopsy is performed numerous representative cores of diseased, viable tissue need to be submitted. For optimal histological assessment especially of unusual cases an intact node with minimal traumatisation artefact is preferred. Artefact is related largely to surgical procedure. A markedly traumatised biopsy may indeed not allow for a reliable morphological evalua-tion, therefore rendering a diagnosis impossible.

The optimal diagnostic yield also relates to choice of node for biopsy. If the patient presents with a single diseased node, this will obviously be the node to sample and submit. With more widespread disease additional considerations become relevant. Inguinal nodes should, more specifically in adults or patients with previous lymphadenitis at the site/persons known to often go barefooted, be avoided as changes related to previous lymphadenitis may significantly complicate interpretation. Axillary and cervical nodes are preferred.

In general the largest diseased node is likely to yield the most optimal tissue. Please note that easily accessible superficial/small nodes may not be representative and relevant disease may then be missed. If aggregates/matted nodes are identified, removal of several nodes may result in a more accurate final assessment (variability of involvement).

Biopsies of abdominal nodes, i.e. during laparotomy where lymphadenopathy was an unexpected finding, should be performed after diligent inspection to allow for most optimal sampling including, for example, retroperitoneal nodes. Note should also be taken of other relevant findings, e.g. regional pathology, organomegaly, or possible metastatic involvement.

Cases where lymph node biopsies need to be taken from sites that are technically difficult to sample, e.g. mediastinum/deep locations, should be referred for specialist management.

## Specimen handling

For optimal tissue preservation intact lymph nodes need to be bisected without delay and fixed in 10% buffered formalin. Tissue cannot be 'kept' in saline as the latter has no fixative properties and profound autolytic change, rendering the tissue useless, will result.

(Requirements for MC&S are different and need to be discussed with the relevant laboratory prior to sampling.)

For surgical bisection of nodes good-quality instruments in optimal condition must be used to limit traumatisation artefact.

If specialised other techniques are indicated/desired, e.g. imprint cytology/electron microscopic assessment, the case needs to be discussed with the referral laboratory/pathologist to allow for optimal handling of the specimen. Prior to dispatching a specimen due care must be taken to check patient identity and appropriate labelling of the specimen. Full clinical information/findings of available investigations and possible pending results should be provided. While diagnosis in more straightforward cases may be readily forthcoming, other difficult cases may

## More about...

be significantly delayed and discussion between the attending clinician and pathologist is then indicated. In such cases, patients should also be informed of the reason for the delayed diagnosis, e.g. the need for ancillary laboratory investigations, to lessen the distress for the patient and the family.

**References available at www.cmej.org.za**