Dr Alison J Marker

#### **Patterns**

- Oncocytic
- Spindle cell
- Cystic
- Lymphocyte-rich
- Basaloid

#### Oncocytic pattern

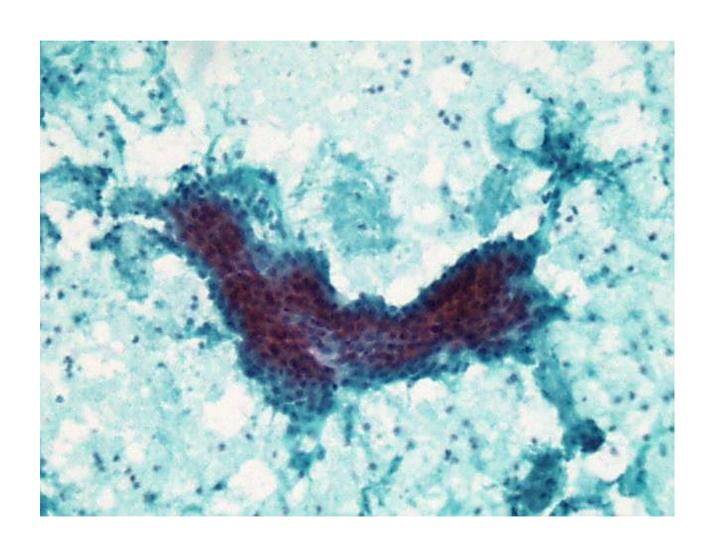
#### Neoplastic

- Warthin tumour
- Oncocytoma or oncocytic carcinoma
- Oncocytic metaplasia
  - -PA
  - Mucoepidermoid carcinoma
  - Acinic cell carcinoma
- Metastatic renal cell carcinoma

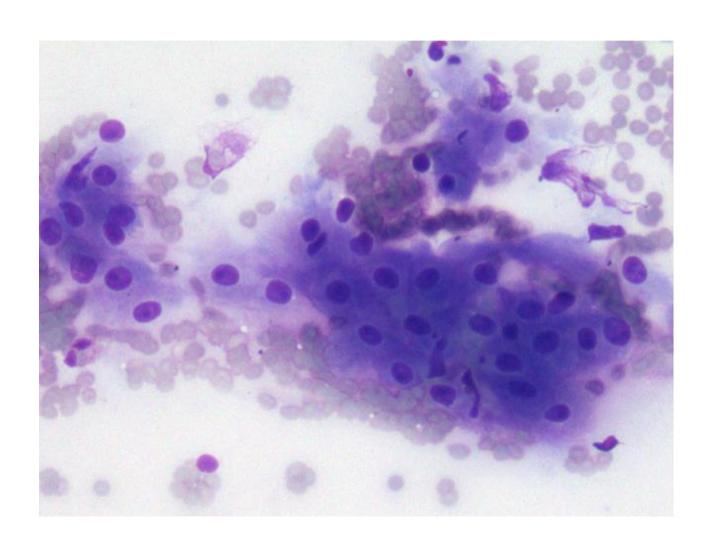
#### Non-neoplastic

Oncocytosis

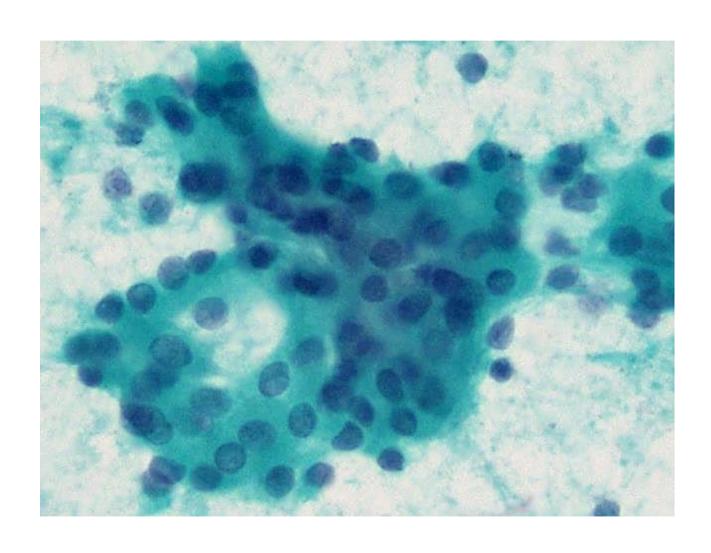
### Warthin's tumour cytology



### Warthin's tumour cytology



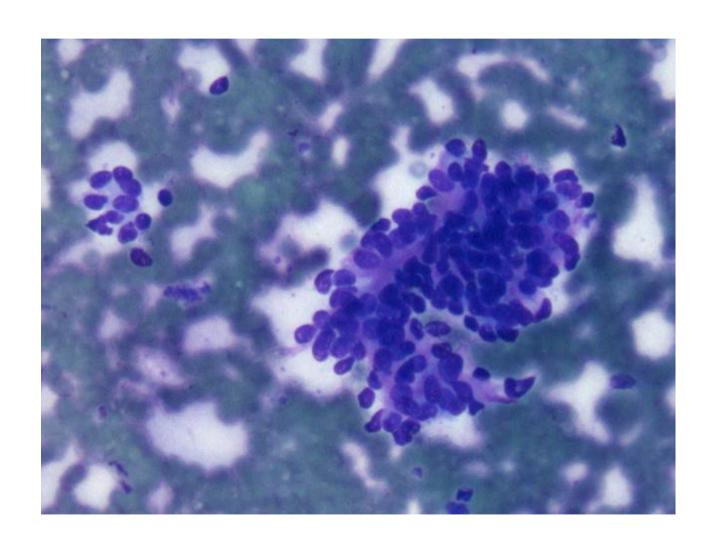
### Warthin's tumour cytology



#### Spindle cell pattern

- Myoepithelial-rich neoplasms
  - Myoepithelial rich pleomorphic adenoma
  - Myoepithelioma
  - Myoepithelial carcinoma
  - Epithelial myoepithelial carcinoma
- Schwannoma
- Metastatic melanoma

### Myoepithelial-rich pattern



#### Cystic pattern

Cyst fluid only present

- State whether mucinous or non-mucinous
- Interpret in context of clinical and radiological findings

### Lesions yielding "cystic" fluid

#### Intrinsic

- Non-neoplastic
  - Obstructive sialadenopathy
  - Salivary duct cyst
  - Lymphoepithelial (HIV-associated) cyst
- Neoplastic
  - Warthin tumour
  - PA
  - Mucoepidermoid carcinoma
  - Acinic cell carcinoma
  - Cystadenoma/cystadenocarcinoma
  - Secretory carcinoma

#### **Extrinsic**

- Non-neoplastic
  - Branchial cleft cyst
- Neoplastic
  - Necrotic metastatic carcinoma in intraparotid or periparotid lymph node

### Lymphocyte-rich pattern – differential diagnosis Intrinsic

- Non-neoplastic
  - Chronic sialadenitis
  - Granulomatous sialadenitis
  - Lymphoepithelial sialadenitis (LESA)
  - Lymphoepithelial (HIV-associated) cyst
- Neoplastic
  - Warthin tumour
  - Mucoepidermoid carcinoma
  - Acinic cell carcinoma
  - Malignant lymphona

#### **Extrinsic**

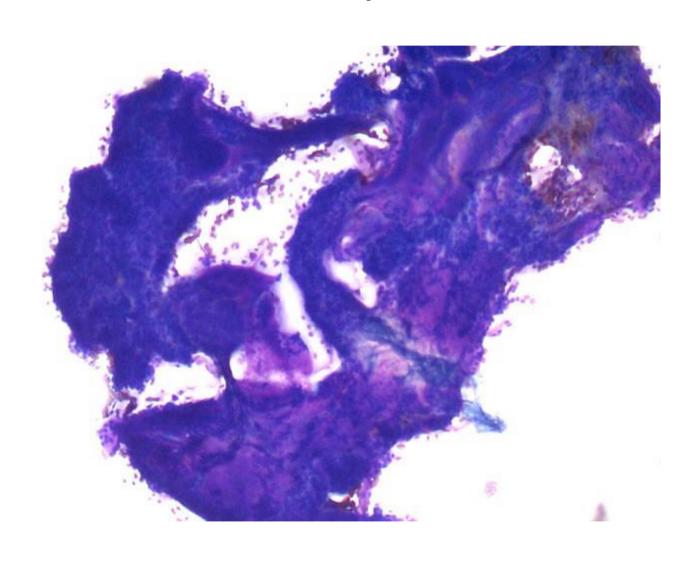
- Non-neoplastic
  - Reactive lymph node hyperplasia
- Neoplastic
  - Malignant lymphoma of nodal origin

#### Basaloid pattern

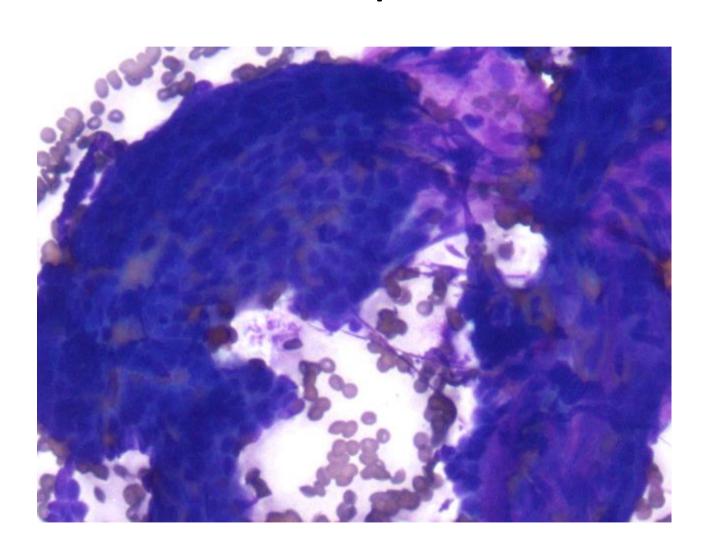
Broad differential diagnosis

- Non-neoplastic
  - Chronic sialadenitis
- Neoplastic
  - Basal cell adenoma/adenocarcinoma
  - Adenoid cystic carcinoma, solid variant
  - Non-salivary gland neoplasms

### Basaloid pattern



### Basaloid pattern



- Is it adequate?
- Is it non-neoplastic or neoplastic?
- If neoplastic
  - Specific diagnosis possible?
    - Benign
    - Malignant
      - Low grade or high grade
  - Specific diagnosis not possible?
    - Low grade or high grade

# Milan System for Reporting Salivary Gland Cytopathology (MSRSGC)

Diagnostic category	Risk of Malignancy (%)	Management
I. Non-diagnostic	25	Clinical and radiological correlation/repeat FNA
II Non-neoplastic	10	Radiological correlation/ clinical follow up
III. Atypia of undetermined significance	20	Repeat FNA, core biopsy or diagnostic excision
IV. Neoplasm		
Neoplasm: Benign	<5	Surgery or clinical follow up
Neoplasm: SUMP	35	Surgery
V. Suspicious for malignancy	60	Surgery
VI. Malignant	90	Surgery

#### II. Non-neoplastic

- Sialadenitis
  - Acute/chronic/granulomatous/ lymphoepithelial (LESA)
- Lymph node
  - Reactive lymphoid hyperplasia
- Other
  - Sialadenosis
  - Oncocytosis

#### III. Atypia of undetermined significance

- FNA lacking either qualitative or quantitative cytomorphological features to be diagnosed with confidence as non-neoplastic or neoplastic
- FNA shows atypical cytology that excludes possibility of classifying as non-diagnostic

#### Atypia of undetermined significance (AUS)

Use in the following scenarios

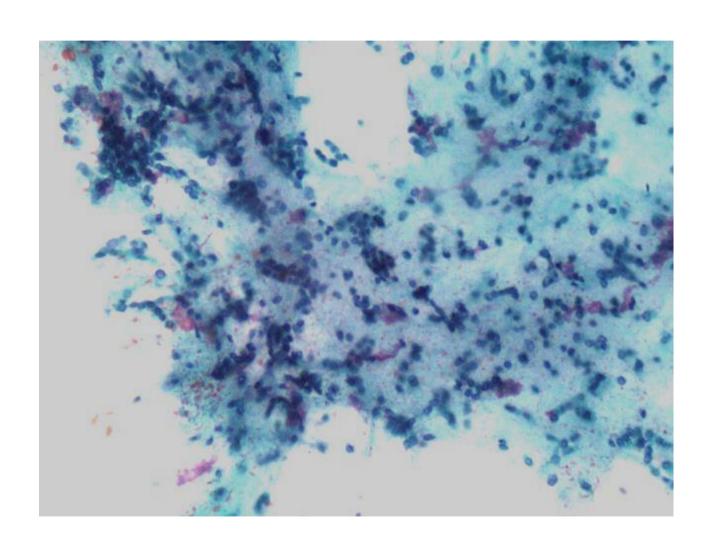
- Reactive and reparative atypia indefinite for a neoplasm
- Squamous, oncocytic or other neoplastic changes indefinite for neoplasia
- Low cellularity specimens suggestive of but not diagnostic of a neoplasm
- Specimens with preparation artefacts hampering distinction between a non-neoplastic and a neoplastic process
- Mucinous cystic lesions with absent or very scanty epithelial component
- Salivary gland lymph nodes or lymphoid lesions that are indefinite for a lympho-proliferative disorder

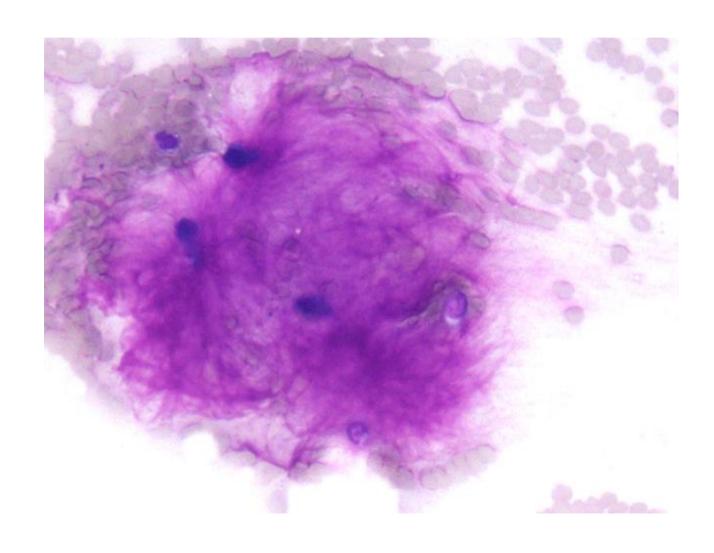
#### IV. Neoplastic

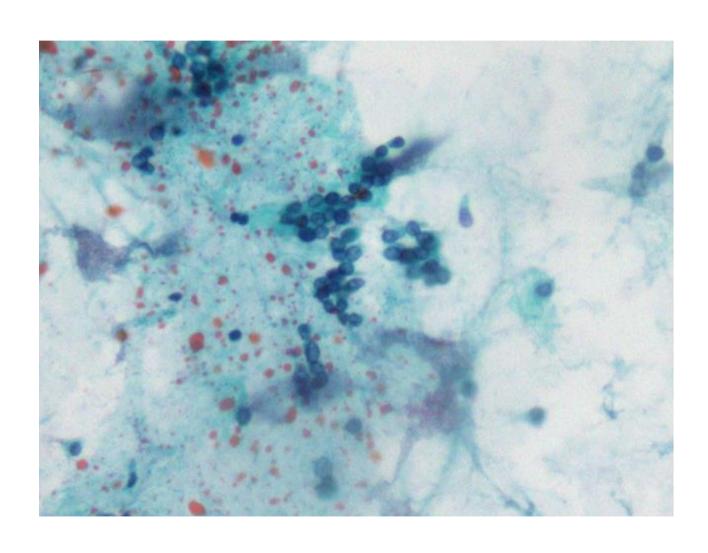
Benign

FNA shows characteristic features of specific benign epithelial or mesenchymal salivary gland neoplasm. Commonest are pleomorphic adenoma (PA) and Warthin's tumour (WT):

- 1. Epithelial origin
  - Pleomorphic adenoma
  - Warthin's tumour
- 2. Mesenchymal origin
  - Lipoma
  - Schwannoma







#### IV. Neoplastic

Salivary gland tumour of uncertain malignant potential (SUMP)

- Cytology cannot distinguish between a benign and malignant neoplasm
- 1. Cellular basaloid neoplasm
- 2. Cellular oncocytic neoplasm
- 3. Cellular neoplasm with clear cell features

#### V. Suspicious for malignancy

- Some but not all criteria for diagnosis of malignancy are present
  - Should qualify in report whether suspicious of primary salivary gland malignancy, metastasis or lymphoma
  - Features
    - Markedly atypical cells but showing poor preservation/fixation artefact/obscured by inflammation or blood
    - Cytological features suggesting specific malignant lesion but sparsely cellular
    - Markedly atypical and/or suspicious cytological features in subset of cells but admixed with features of a benign salivary gland lesion

#### VI. Malignant

- Shows features that, either alone or in combination with ancillary studies, are diagnostic of malignancy
- Low grade carcinoma
  - Acinic cell carcinoma
  - Adenoid cystic carcinoma
  - Mucoepidermoid carcinoma (low grade)
  - Secretory carcinoma
  - Epithelial myoepithelial carcinoma
  - Myoepithelial carcinoma

## IHC in differential diagnosis of low grade salivary gland malignancies

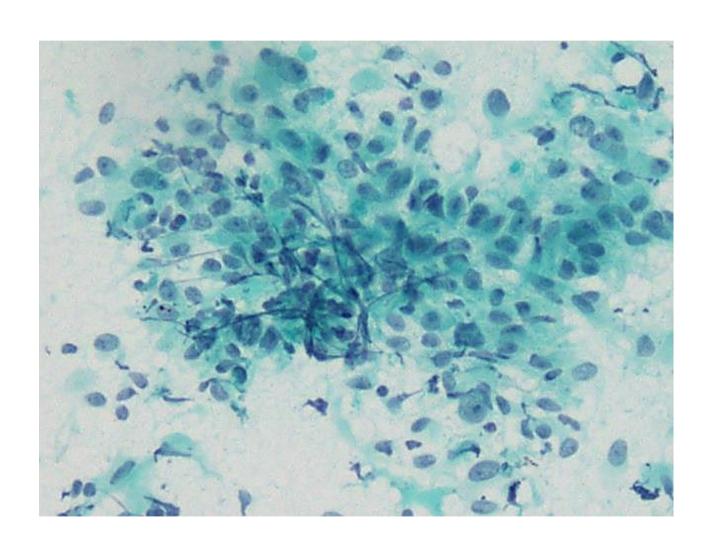
Key: me=myoepithelial cells, ep=epithelial cells, sq=squamous cells, muc=mucin producing cells

	P63/p40	SMA/ SMMHC calponin	S100	CK8/18	CK5/6	CD117	DOG1	Mucin	PASD
ACC	-	-	-	+	-	-	+	-	+
AdCC	+ (me)	+(me)	+	+(ep)	+(me)	+	-	-	-
MEC, LG	+ (sq)	-	-	+(muc)	+(sq)	-	-	+	+
SC	-	-	+++	+	-	-	-	+	+/-
EMC	+ (me)	+(me)	+(me)	+ (ep)	+(me)	-	-	-	-
MC	+	+	+	-	+	-	-	-	-

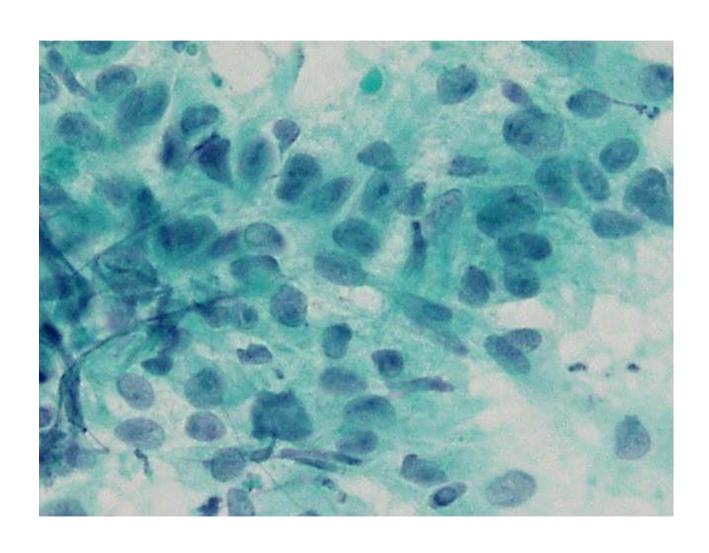
#### VI. Malignant

- Shows features that, either alone or in combination with ancillary studies, are diagnostic of malignancy
- High grade carcinoma
  - Mucoepidermoid carcinoma, high grade
  - Salivary duct carcinoma
  - Poorly differentiated carcinoma, neuroendocrine type
  - Squamous carcinoma
  - Metastatic carcinoma

### High grade malignancy



### High grade malignancy



# IHC in differential diagnosis of high grade salivary gland malignancies

	P63/p40	SMA, SMMHC, calponin	CK8/18	CK5/6	СК20	Synapto, chromo, CD56	AR	Mucin
MEC, HG	+	-	focal	+	_	-	_	focal
SQCC	+	-	-	+	-	-	-	-
SDC	_	-	+	-	-	-	+	-
PDC, NE	-/+	-	+(dot)	-	+	+	-	-
Metast atic	-	-	+	-/+	-/+	-	_	-/+

### Ancillary techniques

Tumour type	Gene fusion
Pleomorphic adenoma	PLAG1 HMGA2
Mucoepidermoid carcinoma	CRTC1-MAML2 CRTC3-MAML2
Adenoid cystic carcinoma	MYB-NFIB
Secretory carcinoma	ETV6
Hyalinising clear cell carcinoma; myoepithelial carcinoma, clear cell variant	EWSR1-ATF

Tumour type	Chromosomal translocation
Polymorphous adenocarcinoma	PRKD1 E710D mutation

### Summary

- Accurate, sensitive and specific technique
- Optimal sample taking and preparation is essential to minimise non-diagnostic samples and facilitate interpretation
- Broad categorisation into non-neoplastic and neoplastic benign or malignant (low or high grade) is usually sufficient for patient management
- Findings should be discussed with the clinician and radiologist in a multidisciplinary team setting to ensure optimal treatment planning
- Milan system has been published to standardise salivary gland FNA reporting with risk of malignancy for each category

#### Pleomorphic adenoma

#### **Description**

- Cellular sample containing variably-sized sheets and groups of myoepithelial cells including spindle-shaped, epitheloid and plasmacytoid forms. The cells are arranged in variably-sized sheets and groups and are interspersed with abundant metachromatic fibrillary stroma
- Scanty groups of possible epithelial cells are identified

#### **Conclusion**

Warthin's tumour

<u>Description</u>: Moderately cellular sample containing scattered small cohesive groups of oncocytic cells in a background of lymphocytes

**Conclusion:** Warthin's tumour

Metastatic SCC

<u>Description</u>: cellular sample containing atypical keratinising and non-keratinising squamous cells in a necro-inflammatory background

**Conclusion**: metastatic squamous carcinoma

<u>Comment</u>: please correlate with the clinical and radiological findings at MDT meeting

Metastatic malignant melanoma

<u>Description</u>: cellular sample containing a population of epitheliod and spindle-shaped cells with eccentrically placed nuclei showing binucleation and occasional intranuclear inclusions. Finely granular dark brown pigment is evident in the cytoplasm of some cells\*. Small lymphoid cells are present in the background consistent with lymph node sampling

**Conclusion**: metastatic malignant melanoma

<u>Comment</u>: please correlate with the clinical and radiological findings at MDT meeting

\* Melanin pigment is seen in <50% of aspirate smears

Reactive lymph node

<u>Description</u>: cellular sample consisting of a heterogeneous population of lymphoid cells predominantly small lymphocytes. A few immunoblasts and tingible body nacrophages are identified. No granulomatous inflammation or evidence of malignancy is seen.

**Conclusion**: reactive lymph node

Comment: please correlate with the clinical and radiological findings. Rarely, partial involvement of a lymph node by a neoplastic process can result in a false negative result. If the lymph node enlargement persists or increases, repeat sample (including excision biopsy) should be considered.