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Diagnostic terminology for reporting thyroid fine needle aspiration cytology: European Federation of Cytology Societies thyroid working party symposium, Lisbon 2009

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Diagnostic terminology for reporting thyroid fine needle aspiration cytology: European Federation of Cytology Societies thyroid working party symposium, Lisbon 2009

A European Federation of Cytology Societies (EFCS) working party of 28 members from 14 European countries met at the European Congress of Cytology in Lisbon in September 2009, with two observers from the USA, to discuss the need for standardising thyroid FNA nomenclature in the light of the National Institute of Cancer (NCI) recommendations resulting from the State of the Science conference in Bethesda in 2007. The data

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were obtained through two questionnaires sent by email and a transcript of the live discussion at the congress, which is presented in full.
The surveys and discussion showed that there were currently no national terminologies for reporting thyroid FNA in the different European countries except in Italy and the UK. Personal, 'local', surgical pathology and descriptive terminologies were in use. All but one of the working party members agreed that thyroid FNA reporting should be standardised. Whilst almost a third would adopt the NCI Bethesda terminology, which offers the advantages of a 'risk of cancer' correlation and is linked to clinical recommendations, more than half favoured a translation of local terminology as the first step towards a unified nomenclature, as has been done recently in the UK. There was some disagreement about the use of: a) the six-tiered as opposed to four or five-tiered systems, b) the use of an indeterminate category and c) the 'follicular neoplasm' category, which was felt by some participants not to be different from the 'suspicious of malignancy' category.
The conclusions will be passed to the different national societies of cytology for discussion, who will be asked to map their local terminologies to the Bethesda classification, observe its acceptance by clinicians and audit its correlation with outcome.

Keywords: thyroid, fine needle aspiration, cytology, classification, european guidelines

Thyroid is the organ currently most sampled by fine needle aspiration (FNA) cytology. This is partly due to the fact that the use of core biopsy in this vascular area is hazardous and partly to the more widespread diagnostic use of positron emission tomography for non-thyroid disease, thus highlighting unexpected thyroid lesions. Most importantly, continuing use of thyroid FNA is due to the fact that it can make a real difference to the management. By using FNA, 70–80% of FNA thyroid can be classified as benign or malignant[1] with 92% negative predictive value for a benign diagnosis and 100% positive predictive value for malignancy. However, despite its widespread use, thyroid FNA currently suffers from a reporting confusion: multiplicity of category names, descriptive reports without categories, variable surgical pathology terminology. This confusion in diagnostic terminology and clinicians' perception of its inconsistency is shown by Redman *et al.*[2] who found that pathologists use diagnostic categories variably. The effect of this on patient management is shown when clinicians repeat 98% of 'non-diagnostic' FNAs, send to surgery 96% of patients with 'suspicious' reports and, for 'indeterminate' reports, either repeat 58% of FNAs or send 32% of patients to surgery. In the 'atypical' category, 37% of FNA are repeated and 52% go to surgery. Looking only at the 'indeterminate 'category, Yoder *et al.*[1] found that, although it represents 13% of the workload, 41% of these patients undergo thyroid surgery, 18% of which are malignant. Given the published evidence, and following the National Cancer Institute Bethesda conference for Terminology in Thyroid Cytology,[3] the European Federation of Cytology Societies (EFCS) formed a working party, chaired by Drs B. Cochand-Priollet (France) and G.Kocjan (UK), in order to confirm the need for a unified terminology and to discuss the options of using one of the existing national or international classifications (see Table 1, Cross and Poller[4]).

Questions 1–4 were sent to the working party prior to the EFCS conference and discussed at the conference where American colleagues were invited as observers: Z. Baloch (ZB) and E. Cibas (EC). After the conference, supplementary questions were sent to the interested participants. The majority of participants were from European countries. The following is the transcript of the discussion at the EFCS conference, followed by replies to the supplementary questionnaire (Questions 5–7).

Question 1. Do you use a national or 'local' terminology or one of the international terminologies?

Question 2. What are your main comments on the Bethesda classification?

AD (UK) Until recently, we did not have a national terminology in England or the UK but in our hospital in London we use one that is almost identical to the recently published British Thyroid Association (BTA)/Royal College of Pathologists classification[5] with the exception of 'Thy1c' and 'Thy2c'.

TS (Norway): There is no national terminology in Norway, neither for thyroid nor in other FNA areas. I use my own and think the different institutes might do the same. The terminology is not very different from one institution to another, and the one that it is mainly comparable with is the Bethesda nomenclature.

GF (Italy): I support 'local' terminologies because in Italy we have just devised a new classification in

agreement with the endocrinologists, which has been published in the official journal of the Italian Endocrinological Society as part of the Italian guidelines for the management of nodular thyroid lesions. It is similar to the BTA classification; it is a 5-tiered classification based on the use of five diagnostic categories, each using an appropriate cytological terminology.

PV (France): We have started discussion of the Bethesda terminology. However, I still do not use this international classification. I use a 'local' one, which is based on the four categories: 'insufficient', 'suspicious', 'malignant' or 'benign'. I will use the Bethesda terminology as soon as it is published, because I think that the main advantage is that it encompasses not only morphology but also the risk of malignancy the patient may have. I think that one of the basic problems is in the perception of the risk: in the USA you can say to a patient what is the risk and a patient may accept to have a 5% risk of having a cancer and have no action taken. We, in Europe, are probably much more conservative and find it difficult to accept the 5% risk of cancer and not to act on it.

ET (Sweden): We are just now working and writing general rules for thyroid for the Cytology and the Pathology Societies. So far, we use a descriptive report but lately, a suggestion was made to use the British classification.[5] However with the Bethesda classification available, we are now to choose between two. This discussion today is therefore very appropriate and we would like to follow the EFCS recommendation.

DP (UK): The Royal College of Pathologists in the UK set up a working group on thyroid cytology terminology.[4] The working group made a generic decision to adopt the principles of the Bethesda classification. However we had the problem of modifying our old system, which is the BTA classification, so we tried to squeeze the old BTA 'Thy' categories into the new Bethesda categories. We have succeeded.[4] It is perhaps not perfect but our old Thy1-5 terminology is now mapped to the Bethesda classification.[4] If you use a national ('local') terminology, you can still map it onto Bethesda if you choose to do so. It makes sense because patients travel between different countries and want a system that is transferable. We did not want to reinvent the wheel when the Bethesda group have looked at all the categories. They have now also done a reproducibility study.[6] Britain has a habit of driving on the 'wrong' side of the road. Let's just do what everyone else is doing for a change.

JD (Czech Republic): With Professor Ryska, we have just organised a national thyroid working group. We agree in principle with a question whether to use a 'local' or international terminology. Currently, we are used to communicating with our clinicians by using the surgical pathology terminology, but there would be no problem in using the Bethesda classification as a coding system. We support the need for the comparison of international studies and therefore a unified system of nomenclature. The choice of this unifying nomenclature should be the one the majority agree with.

CE (Turkey): We do not have national terminology for reporting thyroid FNAs but recently in some centres we have been using the Bethesda terminology including my university in Addana. Before we started to use the new terminology, we educated clinicians and pathologists; we gave lectures for the clinicians, endocrinologists and others involved in thyroid care. Turkish Society of Cytopathology conducted a 2-day course for thyroid cytology. As Philippe (Vielh) said, after the publication of the Bethesda classification, it will be more widely used in Turkey.

LV (Hungary): We do not have any national reporting system for thyroid. Most of those who are dealing with thyroid cytology write a descriptive diagnosis as a rule in this country. It has to be defined as 'benign', 'malignant', 'unsatisfactory'. Specific entities, such as inflammations are defined by name (Hashimoto, giant cell thyroiditis, etc.). We are also using 'follicular neoplasia' as a diagnosis. We would be very happy to adjust ourselves to any kind of classification. My criticism of the Bethesda classification is that I am not very happy with the 'non-diagnostic' category. If the material is acellular, I believe that there is cytology beyond the cells; sometimes absolutely acellular preparations are nevertheless diagnostic.

US (Germany): We use four categories (statistical groups). In addition, we use a description and a cytological diagnosis. For all cases that are not 'normal' we always make a management recommendation towards the next diagnostic step. In addition to normal and abnormal, we have an 'indeterminate' or, as we call it, 'repeat suggested' category. A cyst without cells or just a few cells is of course a 'normal/negative' case. There is nothing more normal in Bavaria, an endemic goitre region, than to have 'water in the thyroid'.

CB (Belgium): We do not have a national nomenclature in Belgium. Each centre uses its own nomenclature. In our centre we use a classification very

similar to what Philippe Vielh mentioned (4-tier). We have weekly multidisciplinary meetings. This is very important, not so much for benign or malignant, which are not disputed, but for 'follicular lesion of indeterminate significance'. I believe we should decide on a proportion of cases in total that should be put into that category, similar to the Bethesda classification for cervical cytology. If you report each lesion with a few atypical follicular cells as an 'AUS' you will end up with a non-category.

NM (Croatia): We use categories very similar to the Bethesda categories. In my opinion, it is not very important to link morphological diagnoses with clinical management because the clinician should be aware of the diagnostic uncertainties in cases where we are not sure whether the lesion is benign or malignant. 'Benign' and 'malignant' diagnoses are separate categories as well as the 'non-diagnostic' but the 'indeterminate' category should be only one category without further splitting. How many specific cytological diagnoses should be 'indeterminate lesions'? The question is how to define these categories. We do not know exactly what is the risk of malignancy in these cases and the management considerations should include other factors, such as the size of the nodule, age of the patient and the results of other investigations.

YD (Iran): We do not use the international terminology in Iran and we are receiving maybe 10–15 thyroid fine needle aspirations daily, performed by a pathologist under ultrasound guidance.

AR (Czech Republic): Here, we are trying to oversimplify the very broad spectrum of lesions of thyroid gland into just five categories. It is important to distinguish between different types of malignancy such as papillary or medullary carcinoma because of different management considerations. I agree with Fernando Schmitt that we should try to follow the histopathological classification used in surgical pathology and try to adapt our cytology diagnosis as close as possible to surgical pathology.

ZB (USA): The Bethesda classification was made to be very flexible and adaptable to one's own practice of thyroid FNA cytology. As David (Poller) stated, so that you can match the other classifications with this classification. I want to make a comment about malignancy, which was the comment just made. Malignancy is a major category and then you can comment: 'papillary carcinoma', 'medullary carcinoma' or 'lymphoma'; so these are the subcategories. Whenever you write a report you are not just stating: 'Thyroid FNA, 3 cm nodule: Malignant'. You are reporting 'malignant' as a lead diagnosis and then followed by 'papillary carcinoma' or a 'medullary carcinoma'. This is clearly stated in the articles published after the NCI meeting and in the Bethesda book.[7]

AD (UK): Comparing the BTA and Bethesda[4], cyst fluids, in England, are currently suggested as a special category of an insufficient diagnosis as well as a subcategory of benign diagnosis. The former will engender a huge amount of work, which you are unlikely to improve on. Sometimes, cyst fluids that are 'negative' turn out to be papillary carcinoma or other differentiated tumours. It is wrong to put cyst fluids into an unsatisfactory category. This encourages clinicians to ask for renewed assessments which you as cytopathologists know are not able to improve upon.

PV (France): I have a problem with the categories of 'indeterminate significance'. If it is not very well defined we may be end up with a large percentage of lesions being put in this diagnostic category. Ed Cibas told us that we shouldn't put more than 7% of the samples in this category. How do we define it? I would say quantitatively, not qualitatively.

MT (Germany): We report about 4 000 thyroid FNAs per year and have less than 10% diagnoses reported as 'indeterminate'. We have combined both these categories 'follicular lesion of indeterminate significance' and 'follicular neoplasm' because we believe that we cannot separate them cytologically. I also believe that the idea concerning the risk of malignancy, in the first category 5–15% and in the second category 15–30% of, is something that is difficult to convey to the patient. For me, 'indeterminate' is one common category, and the indications for surgery must be decided by the clinician. I just recommend in the report that, according to the experience in our centre, the probability of malignancy is approximately 22%. I am strictly against separating these two entities, for practical reasons.

GF (Italy): Even if we make a perfect diagnosis, we do not treat the patient so we should aim to convey to the endocrinologists a clear message so that they are able to understand it. It is very important to use the categories to give the correct message to the clinician and to the patient, which can be understood locally and around the world. In my institution, the clinicians understand perfectly when I say 'follicular neoplasm' but I am not sure if this report would be understood by the clinicians in the nearest hospital in the same

way. In addition we, as cytopathologists, also need to make our cytological diagnosis. For example, 'Thy2' is a non-neoplastic lesion but there is a difference, within this same category, between a goitre or a thyroiditis or a hyperfunctioning nodule. It is potentially dangerous that we say only 'Thy5' because it might mean papillary carcinoma, medullary carcinoma, lymphoma or anaplastic carcinoma, all requiring different treatments.

AR (Czech Republic): Do the categories imply clinical recommendations as well or do we have to add a recommendation to each diagnosis? If the recommendation can be tailored, then I can agree with the principle of diagnostic categories.

Question 3. What do you not appreciate in the TBS? For example, concerning the 6-tiered system and the atypical cells of undetermined significance (AUS)/follicular lesion of undetermined significance (FLUS) category: (a) would it be better to include this in the benign category (with same risk of cancer), (b) does it include cells not only of follicular origin, (c) is it not well defined cytologically and (d) is there a risk of it being used as 'waste basket' category?

Question 4: Should the 'follicular neoplasm' category be (a) included in the AUS category, (b) included in the lesion suspicious for malignancy (LSM) category and (c) may we consider Hürthle cells as a misnomer?

EC (USA): I thank the organizers for inviting us (Drs. Baloch, Faquin, Layfield, Cibas) to participate as observers here. Regarding the questions you have raised about the Bethesda/NCI terminology, there was not much controversy about distinguishing 'suspicious for malignancy' from the 'follicular neoplasm category'. There is a different risk of malignancy associated with those two cytological patterns. 'Suspicious for malignancy' is usually 'suspicious for papillary carcinoma,' and the risk of malignancy for that diagnostic category is around 60–75%. For the category 'follicular neoplasm' or 'suspicious for follicular neoplasm' (the two terms are synonymous), the risk of malignancy is significantly lower (around 15–30%). Regarding the term 'Hürthle cell', we acknowledge that it's a misnomer. We use that term more often than we use 'oncocyte' or 'Ashkenazy cell' because it's familiar to us and we continue to use the term 'Hürthle cell type' as a subcategory of follicular neoplasm. Regarding the category AUS (or, alternatively, FLUS), it was the most controversial category at the NCI conference, and we spent a lot of time talking about the rationale in favour of and against it. After much discussion, we took a vote. The vote was relatively close, but the majority agreed that there was some value in separating out that category from the other categories. It is defined rather specifically in the atlas.[7] There are about seven or eight rather well defined scenarios that fall into this category. It is correct to think of it (AUS/FLUS) as a bit of a 'waste basket' category, but that is not necessarily a bad thing. The reason is this; the other categories are quite familiar to everybody. Every now and then we come across a case, however, that doesn't fit those criteria exactly. Not every case can always be easily placed into one of those five categories. It was the acknowledgment of that reality that led us to a majority agreement on the sixth category: the AUS category. Segregating AUS/FLUS cases into their own category helps keep the other categories as pure as possible, thus preserving their predictive value for malignancy.

ZB (USA): I know the category AUS appears relatively vague, but the participants must know that in USA thyroid nodule FNA is on the rise and often they include patients who are 75 years old with a 1 cm thyroid nodule with questionable calcification. On review, the majority of the slides look benign and it is only one slide with one cell or a group of atypical cells that you are not comfortable diagnosing as benign. We all deal with it, as Ed (Cibas) said, and that was the main reason we all supported this category.

FS (Portugal): Any classification needs to be discussed with the endocrinologists. The endocrinologists should be in agreement with the system of classification that we use. The clinicians that we work need to understand the report. They are often victims of fashion and are likely to hear about the new nomenclature in the United States, probably at the next American Congress of Endocrinology. After this, they will ask us to use a new nomenclature. Until this moment we prefer to use the same terminology that we use in surgical pathology for thyroid and if we change it in the future, this has to be agreed with the clinicians. The same occurred with the gynaecological terminology. I think that our aim is to offer a good report and for the patients to have the right treatment. We need to use the system that works for the patient.

AF (Italy): The dark side of the moon; there is also a medicolegal aspect of this discussion. If one of our cases ends up in the court, I would like to tell the judge that I am following the Italian terminology or an international classification. Since they understand the internal and external quality control, I think that using an internationally approved terminology is important.

AR (Czech Republic): For me there are two weak points of the Bethesda classification. The first is that a category which I call 'I don't know' is too vaguely defined and the second, the separation of 'suspicious' and 'malignant' is highly artificial. For the clinician, it is irrelevant whether the report is 'suspicious of papillary carcinoma' or 'papillary carcinoma'. He will operate to remove it. I think that the separation of 'follicular/oncocytic' category is wise in order for the clinicians to realise that we have no means of separating benign from malignant cases and call it simply 'follicular lesion', due for excision.

CB (Belgium): I believe we should be extremely cautious in adding 'AUS' diagnostic categories. These categories merely reflect the uncertainty and limitations of cytology in making a diagnosis of a follicular lesion and do not correspond to a real diagnostic entity. Extrapolation of the 'ASC' categories we use in gynecological cytology cannot be done without thorough validation. Efforts should be made in improving the diagnostic accuracy rather than adding 'uncertain' categories. A new classification has to be evaluated in each lab with regard to its diagnostic performance.

FS (Portugal): First of all, I would like to congratulate Gabrijela and Beatrix for organizing this session during the EFCS congress, giving European cytopathologists the opportunity to discuss thyroid classification systems. In my opinion, standardization of nomenclature in cytology is timely, making way for a universal language in this area. We all seem to agree that there is a need for standardizing thyroid cytology reporting. However, there is no consensus between us as to which of the existing classifications we should adopt. We do not have to accept the Bethesda classification without discussion but we know that it is evidence-based and should be given a serious consideration. I hope that, as a result of this discussion, European cytopathologists will meet and define the morphological criteria, study their reproducibility and suggest improvements to this nomenclature.

Following Professor Schmitt's closing remarks, a supplementary questionnaire was sent to the participants who attended the discussion and who wanted to make further comments. The following questions were selected by the moderators of the working party:

Question 5: Do you confirm the need to standardise reporting of thyroid FNA cytology in Europe?

Question 6: Common thyroid reporting categories need (a) adhering to Bethesda, (b) 'translating' national nomenclature into Bethesda or (c) none of the suggested categories?

Question 7: In cases of a 'translation template', has it been validated by your national cytology society?

A response was received from 21 cytopathologists, most of whom attended the original discussion, originating from 14 European countries. All except one participant (95%) agreed about the need for standardization of thyroid FNA reporting. The majority of participants (52.5%) considered that a 'translation template' between the existing (national, local) and the Bethesda nomenclature should be the first step to standardization. Six participants (28.5%) supported the idea of adopting the Bethesda classification immediately. For two participants (9.5%), both options were considered acceptable (to adopt the Bethesda nomenclature or to use a 'translation template'). Two participants (9.5%) did not accept any of the proposals. In cases of 'translation template', these are at the moment not validated by any of the national cytology societies, except in the UK where the template between the BTA and the Bethesda classification has been validated by the Royal College of Pathologists and there is pending validation by the College of American Pathologists.[4] Of note is that, at the time of publication, the Bethesda classification has already been recommended as the national terminology by the national societies of cytology in two European countries: France and Greece.

Summary and conclusions

1. Almost all working party members from 14 European countries agree about the need for standardization of thyroid FNA.
2. Currently, there are no national terminologies for reporting thyroid FNA in the different European countries except in Italy and Great Britain; the USA (Bethesda) and British (BTA/RCPath) terminologies are not universally applied; personal, 'local', surgical pathology and descriptive terminologies are currently used by the cytopathologists.
3. Whilst almost a third would adopt the Bethesda terminology, which offers the advantages of a 'risk of cancer' correlation and is linked to clinical recommendations, the majority favoured a translation of the local terminology to Bethesda as the first step towards a unified nomenclature, as has been done recently in the UK.[4]

4. Some disagreement amongst the working party members persists regarding the use of (i) the 6-tiered categories (several cytopathologists support a 4-tiered system), (ii) the AUS/FLUS category, which does not seem well defined and (iii) the 'follicular neoplasm' category which is felt by some participants not to be different from the 'suspicious of malignancy' category.

The conclusions of the working party will be passed to the different national societies of cytology for discussion. They will be asked to map the local terminologies to the Bethesda terminology and to observe its acceptance by the clinicians.

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The moderators thank the General Secretary of the EFCS, Philippe Vielh, who has launched the idea of a thyroid working party as well as the President of the European Congress in Lisbon, Fernando Schmitt, who has organized it. We thank our colleagues from the USA, Edmund Cibas and Zubair Baloch, who have accepted to come as observers. They have helped a better understanding of the Bethesda terminology. We thank all the participants for their lively and constructive contribution.

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