

I. TITLE

**VALUE OF FINE NEEDLE ASPIRATION
CYTOLOGY IN DIAGNOSIS OF THYROID
NODULES AT KENYATTA NATIONAL
HOSPITAL**

**A dissertation submitted in part fulfillment for the degree of Master of
Science in Clinical Cytology in the Department of Human Pathology,
University of Nairobi.**

University of NAIROBI Library



0393269 6

By

**Rose F. Odhiambo
BSc (Poona)
2001**

UNIVERSITY OF NAIROBI LIBRARY

II. DECLARATION

This work is original and has not to my knowledge been submitted for a degree in any other university.



ROSE F. ODHIAMBO

This dissertation has been submitted for examination with my approval as the university supervisor.



DR. FARZANA RANA

III. DEDICATION

To the memory of my father J.R. Odhiambo who never lived to see me complete my undergraduate course.

UNIVERSITY OF NAIROBI
LIBRARY

IV. ACKNOWLEDGEMENTS

I am indebted to all persons who helped with useful ideas and who by their encouragement made the production of this work possible. I am especially indebted to the following:

1. My Supervisor Dr. F.S. Rana without whose assistance this dissertation might never have been written.
2. Prof. D. Penner et al (Canada) and Prof. Erick Van Mark of Belgium for their support in terms of literature and finances.
3. Gloria Thompston and Danielle Beathiaume of Canada for instilling in me Superb screening skills.
4. Prof. A Nyongo for much useful advice and suggestions in preparing the Proposal for the study.
5. Mrs. Rose Kiathe for providing published material from the Healthnet.
6. Nancy Kisia, Cytology-in-charge and her Section for the assistance in data and slide retrieval from their archives.
7. Mr. Peter Mbone of Histology Section, Department of Pathology for his assistance in collection of histologic data.
8. Mr. Kariuki of Nairobi Hospital for his assistance in photography.
9. My Loving husband Parmenus for his patience.
10. My children Robert, Nora and especially Jason who was born during the Completion of this work.
11. The previous and present cytology class for their encouragements.
12. Lily, Kagia, and Lydia Nafula for their invaluable assistance in Computation of this work.

V. CONTENTS

I.	Topic	(i)
II.	Declaration	(ii)
III.	Dedication	(iii)
IV.	Acknowledgements	(iv)
V.	Table of Contents	(v)
VI.	List of Abbreviation	(vi)
VII.	List of Tables and Figures	(vii)
VIII.	List of Plates	(viii)
IX.	List of Appendices.....	(x)
X.	Abstract.....	1
XI.	Introduction and Literature	3
XII.	Justification of the Study.....	14
XIII.	Aims and Objectives.....	15
XIV.	Material and Methods	16
XV.	Results	19
XVI.	Discussion	25
XVII.	Constraints	32
XVIII.	Recommendations	33
XIX.	Plates.....	34
XX.	Appendices.....	45
XXI.	References.....	53

VI. LIST OF ABBREVIATIONS

FNA	Fine needle aspiration
KNH	Kenyatta National Hospital
U/S	Unsatisfactory
FN (c)	Follicular Neoplasm favouring cancer
F.A	Follicular Adenoma
BFC	Benign Follicular cells
S	Suspicious
H	Hyperplastic
M	Malignant
F.N.	Follicular Neoplasm
UN	Unknown
H&E	Hematoxylin and Eosin stain
Pap	Papanicolaou stain
AIDS	Acquired Immunodeficiency Syndrome

VII. LIST OF TABLES AND FIGURES

- Table I:** Age distribution of patients whose thyroid nodules were diagnosed by FNAC.
- Table II:** Summary of Cytology and Histology results.
- Table III:** Comparison of Cytology and Histology diagnosis.
- Table IV:** Summary of consistence of Cytology diagnosis in comparison with Histologic analysis.
- Table V:** Statistical analysis.
- Figure I:** Role of FNA in the sequential approach to the cold thyroid Nodule.
- Figure II:** Algorithm for management of thyroid nodules.
- Figure III:** Histogram of age distribution of patients whose thyroid nodules were diagnosed by FNAC.

VIII. LIST OF PLATES

Plate I	Benign follicular cells
Plate II	Benign follicular cells
Plate III	Benign follicular cells
Plate IV	Benign follicular cells
Plate V	Benign follicular cells
Plate VI	Benign follicular cells
Plate VII	Thyroid cyst contents
Plate VIII	Foamy macrophages
Plate IX	Nodular goitre
Plate X	Nodular goitre
Plate XI	Acute thyroiditis
Plate XII	Acute thyroiditis
Plate XIII	Hashimoto's thyroiditis
Plate XIV	Hashimoto's thyroiditis
Plate XV	Follicular Neoplasm
Plate XVI	Follicular Neoplasm
Plate XVII	Follicular Neoplasm
Plate XVIII	Hurthle cell Neoplasm

Plate XIX	Papillary carcinoma
Plate XX	Papillary carcinoma
Plate XXI	Anaplastic carcinoma
Plate XXII	Anaplastic carcinoma

IX. LIST OF APPENDICES

- Appendix I** Formulae used to calculate sensitivity, specificity, accuracy, Positive and negative predicitive values.
- Appendix II** Sample size calculations
- Appendix III** Papanicolau staining procedure.
- Appendix IV** Hematoxylin and Eosin staining procedure
- Appendix V** Cytomorphology of thyroid nodules (main features)
- Appendix VI** Approved letter from KNH Research and ethics committee.

X. ABSTRACT

Thyroid nodules are common at Kenyatta National Hospital. About five new cases are seen weekly. The results of 398 consecutive Fine Needle Aspiration Cytology (FNAC) of thyroid from 383 patients performed and interpreted by different pathologists between 1st January and 30th June 1997 were retrospectively reviewed and compared with their histologic findings. The objective of the study was to assess the value of FNAC in the diagnosis of thyroid nodules with emphasis on consistency and accuracy using histology as the "Gold Standard". The study population consisted of 347 (90.6%) females and 36 (9.4%) males. The age of the study population ranged from 15 – 78 years. A total of 318 (87.1%) FNAC had sufficient material for Cytologic diagnosis. Of these 249 (78.3%) were benign hyperplastic lesions. Only seven (1.83%) of the population studied were diagnosed as cancers. Surgical confirmation of the Cytologic diagnosis was obtained in 75 of the cases, of which 60 (80%) were accurately called benign or malignant. A further 9 (15%) cases who had unsatisfactory FNAC were found to be benign. In 48 (64.00%) of the cases the cytologic diagnosis was consistent with the histologic diagnosis. The calculated sensitivity was 80%, specificity 100%, accuracy 98.6%, positive and negative predictive values were 100% and 98.8% respectively. There was one false negative and no false positives.

The study shows that FNAC is a sensitive, specific, accurate and cost-effective technique in the management of patients with thyroid nodules. It should be used along with clinical assessment as the first diagnostic technique to determine the management of thyroid nodules at K.N.H. . This would assist in selecting patients for surgery and a reduction in cost of management of patients with thyroid nodules.

XI. INTRODUCTION AND LITERATURE REVIEW

Thyroid nodules are extremely common in iodine – deficient areas but occur in other geographic locations as well [1] A 5 to 10% lifetime risk, exists for developing a palpable thyroid nodule [2]. With sensitive imaging studies, more than a third of all women will be found to have at least one thyroid nodule [2]. Clinically palpable thyroid nodules are present in more than 5% of the adult population. The annual incidence of thyroid cancer in U.S. is approximately 25 to 35 cases per million population accounting for about 0.4% of cancer death [3]. It follows therefore that only a few clinically palpable nodules of the order of one to two per 1000 are cancers [3]. At Kenyatta National Hospital an average of 12,580 patients with thyroid nodules were seen annually between January 1997 and December 1999, out of these only 0.1% were diagnosed as cancers. A total of 5 new cases are seen weekly. Given this large population requiring evaluation and the relatively low incidence of malignancy, we need reliable criteria to identify patients with thyroid nodules who are likely to have a neoplasm.

For years the cornerstone of clinical appraisal of a nodular thyroid has been the scintiscan, following administration of radioiodine [3]. Most thyroid cancers and many adenomas, cannot accumulate significant quantities of radioiodine and so appear as nonfunctioning “cold” nodules. Although, most adenomas and carcinomas are “cold” nodules; so are nonfunctioning nodules in multinodular goiter and focal enlargement in Hashimoto’s thyroiditis, 80% of all the thyroid nodules are cold. It is estimated that only

about 20% of cold nodules prove to be malignant [3]. Moreover, some adenomas and a rare cancer may be 'hot', i.e. may take up radioiodine. Thus although scintiscan suggest probabilities they are not definitive [3].

Apart from scintiscan, abnormalities of the thyroid may be evaluated by a sophisticated array of biochemical assays, clinical assessment and ultrasonography. The latter method is used to determine whether a thyroid lesion is cystic or solid. These techniques aim at selecting patients for surgery [1,2,4,5]. They have been poor parameters for assessing solid nodules. Incidence of neoplasm at surgery have only been 10-35% [6]. In spite of considerable progress in assessing the status of the thyroid, there remains a substantial group of patients in whom precise diagnostic determination cannot be made by clinical means and who therefore become candidates for surgical exploration or Fine Needle Aspiration Cytology FNAC [1].

The thyroid is richly vascularized and has a high rate of blood flow, which may interfere with surgical biopsy [4]. Conventional excisional biopsy has therefore never achieved significant popularity in the diagnosis of thyroid disorders. The essentially non-traumatic nature of FNAC, therefore has made it an attractive procedure for routine use in this field [4]. Unlike excisional biopsy, FNAC require minimal equipment, comprising of a needle, syringe, slides and a fixative. Thus FNAC can be done in the physicians office, which obviates the need for admission.

The purpose of FNAC is to obtain diagnostic material for cytological study from organs that do not shed cells spontaneously [4]. The aspiration cytology as a diagnostic technique has been practiced now for more than

half a century. The bone marrow, spleen, liver, breast, thyroid gland and lymph nodes were initially the targets of this diagnostic procedure [4]. FNAC is a highly effective diagnostic procedure, which is now appreciated, and practiced in most large hospitals worldwide, yet many pathologists are still doubtful about the details of the procedure, who should perform the aspiration? How should the specimen be stained? What can and cannot be safely diagnosed [7].

FNAC of thyroid is a simple and safe procedure which provides the most information of all procedures available excluding surgical biopsy investigation. Its introduction has meant that morphological diagnosis of thyroid can be obtained without resorting to open surgery for tissue [8]. The procedure can be done with ease in the clinicians office because thyroid nodules are usually palpable nodules and rarely require sophisticated radiologic guidance. For the most part however, the clinician is able to secure the nodule with one hand and proceed with the FNAC procedure. Only in cases where the nodules are not palpable or are less than one centimeter in size is aspiration with guidance required [1]. The aspiration is performed with the patient supine. To avoid inadvertent displacement of the gland during aspiration, the patient is instructed to refrain from swallowing and speaking. Aspirate is always collected from different parts of the palpable gland. The actual aspiration is performed as quickly as possible, in about 1-2 seconds, to avoid flooding the syringe with blood [4]. A drop of the aspirated sample from the thyroid nodules is expelled onto a clean glass slide and smears are prepared. Preferably, 21 to 23 gauge needles are used, but some authors [9] recommend 25 gauge. A 25G needle is recommended [9] to reduce the amount of blood in smear preparations. It has been shown

to produce cell rich preparations while minimizing blood seen in the background of smear. When draining cysts a larger needle is required.

In certain centers, fine needle sampling without aspiration (cytopuncture) has been reported to yield results as good as or better than conventional FNAC. This technique, based on the principle of capillary action, is seen to be particularly useful in highly vascularized organs or in tumours in which tissue sampling may lead to contamination by abundant fresh blood. The sample is obtained by directly inserting the needle, held between the thumb and forefinger of one hand, into the mass and moving the needle rapidly in and out of the nodules, as with the conventional FNA method. The biopsy material is recovered by attaching the syringe and expressing the needle contents onto a glass slide.

FNAC of thyroid causes little discomfort to the patient and practically no complication except on rare occasions. In more than 10,000 aspiration cytologies of the thyroid at Radiumhemmet, no untoward complications have arisen, apart from occasional haematomas, which caused no major discomfort [4]. At the Karolinska Hospital, more than 20,000 FNAC of thyroid have been performed with excellent results.

Routinely there are two fundamental methods of processing thyroid aspirates. Fixation (in 95% alcohol) and staining with either papanicolaou (pap) or hematoxylin-eosin (H&E) or air-drying of smear followed by haematologic stains. Both methods have their advantages and disadvantages [4]. In general fixed material allows better comparison with histology and is favoured by many Histopathologists. On the other hand air dried smears in

expert hands yields excellent results. Special stains commonly used in histopathology laboratory may provide additional evidence for specific diagnosis. For example, Congo red may be used to demonstrate amyloid in medullary carcinoma of the thyroid.

It must be stressed that interpretation of the cytologic material from the thyroid is by no means simple. Except in some obvious situations, the identification of diagnostic cell pattern is difficult and requires excellent material and a great deal of experience [1]. The Cytologic Study of the smears should be carried out keeping in mind other ancillary data. Certain lesions (e.g Colloidal goitre) yield specimens with few cells and abundant colloid. Although this material would be considered as cytologically non-diagnostic, it is consistent with the clinical impression. It follows therefore that the training and experience of a Cytopathologist is important in weighing clinical information to avoid bias. Whatever the clinical information may be, the cells on the slides are still the crux of the matter. [15] The success of this procedure depends upon examination of lesion to be aspirated, experience of the person performing the aspiration, person preparing and staining the smear and one interpreting the smear.

The diagnostic accuracy of FNAC has been extensively and convincingly documented [1]. Many studies have been done and have shown that FNAC of thyroid has a sensitivity ranging from 68% - 100% [2,6,9-12] and specificity ranging from 72% - 100% [2,6,9-12]. False negative and positive rates have been low. Despite this data the role of FNAC of thyroid is still somewhat controversial [8]. A major problem diminishing the potential of FNAC is the unskilled physician performing the aspiration or the

inexperienced cytopathologist interpreting the smears [2]. Poor needle technique leads to a high proportion of unsatisfactory cytology specimens and probably a higher rate of surgical procedures [2]: Inexperienced cytopathologists may report a very big proportion of follicular lesions or suspicious cytology specimens, perhaps from lack of confidence in interpreting those nodules that are benign [2]. Another concern is the report of “no malignant cells seen” in a smear that is hypocellular or acellular, the result is a false conclusion of a benign FNAC cytology. To guard against this error, the cytopathologist should adhere to appropriate criteria for smear adequacy including at least six to eight cells clusters smeared on the slide [2].

Evaluation of follicular neoplasms by FNAC remains a “gray” area. Frable [8] believes that the diagnosis of follicular adenoma from well differentiated follicular carcinoma is the most difficult differential in FNAC but notes that it also can be difficult histologic diagnosis. The cytology of many well-differentiated encapsulate carcinomas may closely resemble cellular follicular adenoma [5]. The diagnosis of carcinoma in such instances rests on the histologic demonstration of capsular invasion or angioinvasion. Unfortunately these findings are not observed in FNAC specimens. Despite this limitation, classification of follicular neoplasm can be made with some accuracy. Frable [8] aspirated 17 follicular neoplasms in which he favoured adenoma, 14 of which were confirmed by histologic studies. The remaining three cases were hyperplastic nodular goiters. It has been suggested that perhaps newer techniques such as planimetric studies of mean projected nuclear areas and DNA evaluation for aneuploidy might prove helpful in separating the follicular neoplasms in the future [11].

There are few series of thyroid aspirated wherein errors of omission or commission have not been made [4]. Thus, the principal role of FNAC of the thyroid (see figure I & II) is to assist in the management and selection of patients for surgery [1,4,5]. Used in this manner, FNAC is primarily a screening rather than a diagnostic procedure, and a conclusive cytologic diagnosis is not always required [5]. Since the introduction of this method at Montefiore medical center [4] the number of surgical procedures on the thyroid has been reduced by 48% and percentage of cancers in the surgical material rose from 11.0% to 31% in 7 years, a change consistent with the experience of other centers. Miler et al [9] reported surgery reduction by 50% and doubled percentage of cancer at surgery. Not only has the preoperative use of FNAC reduced the number of thyroidectomies, but it has also uncovered many clinically unsuspected cancers that would otherwise have been followed medically.

FNAC is an extremely cost effective procedure. It should be used as a first procedure for diagnosing thyroid nodules to avoid unnecessary expenses [11]. Some institutions [11] have already abandoned the use of scan and ultrasound as a first diagnostic procedure due to the expensive cost. Medical costs have greatly been reduced in management of thyroid nodules in many institutions [11]. At Fitzumman Army Center costs declined by 25% per patient. Hamburger et al believed that the wide spread application of FNAC of thyroid could result in \$15,000,000 annual reduction in the total cost for management of patients with thyroid nodules in the U.S.

FNAC of thyroid is able to give definitive diagnosis on the following conditions:-

- Hashimoto's thyroiditis
- Subacute (granulomatous) thyroiditis
- Colloid nodule (nodular goiter)
- Papillary carcinoma
- Follicular carcinoma
- Medullary carcinoma
- Anaplastic carcinoma
- Malignant lymphoma
- Metastatic carcinoma to thyroid

Sufficient criteria exists in the majority of these entities to establish the type of lesion. Apart from follicular neoplasms, nodular goiter with atypical fibroblasts, Hurthle cell tumors and Hashimoto's thyroiditis with atypical oncocytes (Hurthle cell) may give diagnostic problem.

Cystic nodules, representing 10 to 25% of all thyroid nodules, present additional diagnostic challenges [2]. The incidence of malignancy in cysts is probably less than that of solid nodules, nonetheless, complex cystic nodules may be malignant[2]. Few are thin-walled cysts that collapse completely with needle evacuation. Most have partially solid components. Cyst when encountered are completely evacuated and fluid sent to laboratory for cytologic analysis. FNAC is then done in residual solid mass [2]. In most instances smears from cysts do not meet the criteria for adequacy. Caution

should be exercised when interpreting cystic nodules so as not to miss tumors like papillary carcinomas.

FNAC enables the clinician to decide for or against surgery with more accuracy than other methods of evaluation. Negative Cytologic findings can support long term medical management for the clinically nonsuspicious multinodular goitre, simple thyroid cyst, thyroiditis, functioning nodule or nonfunctioning nodules that are small and respond to thyroid suppression. Repeat FNAC can be used for follow-up evaluations. FNAC can identify malignancies such as malignant lymphoma or undifferentiated carcinoma, which are better treated with irradiation or chemotherapy and do not need surgery. The procedure can be applied to the inoperable patient or elderly. FNAC complements the surgical evaluation of the patient since the surgeon can be knowledgeable preoperative about the nature of the neoplasm. By using specific diagnostic terminology, FNAC of the thyroid bridges the gap between clinical evaluation and final surgical pathologic diagnosis in the majority of the cases.

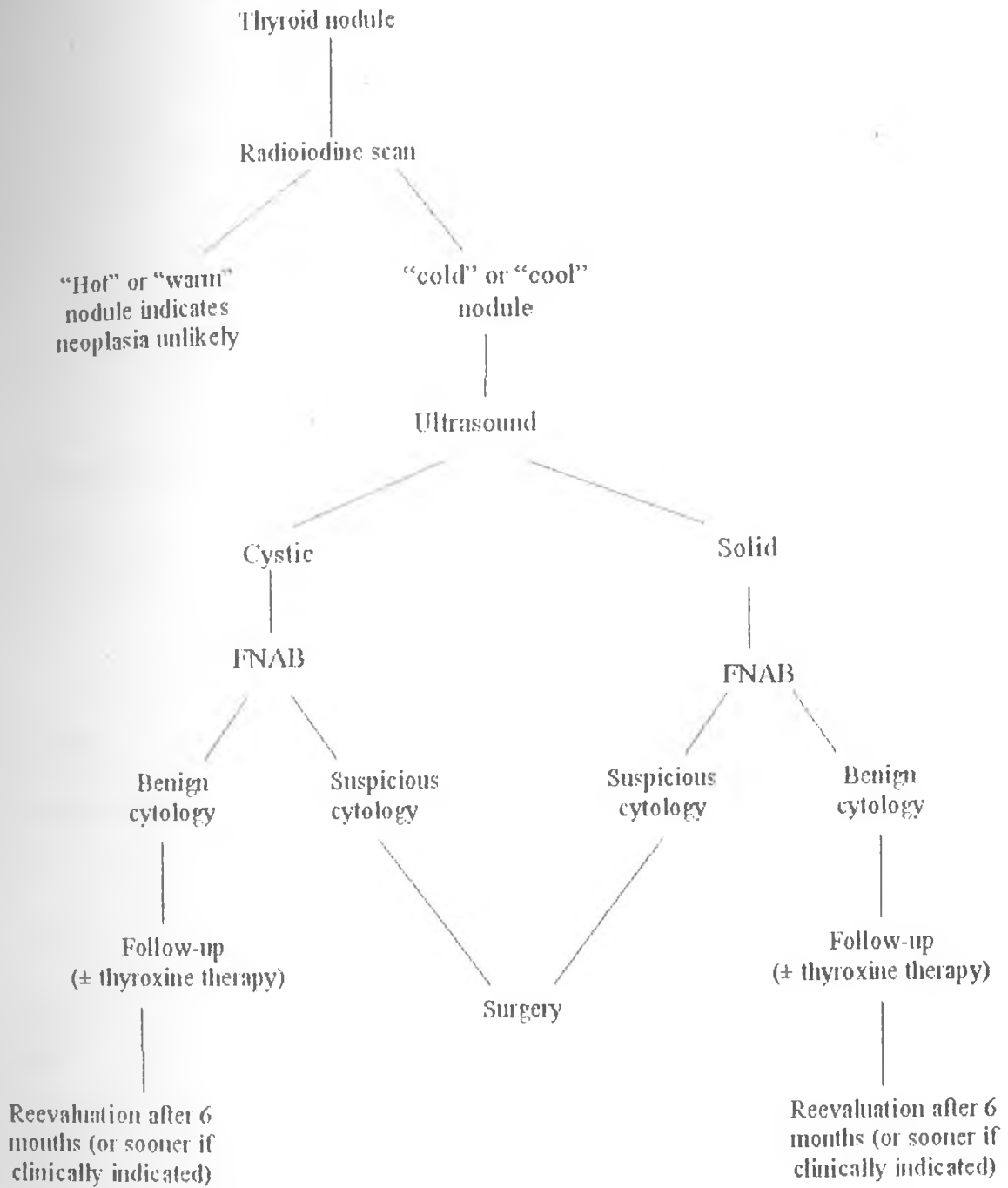


FIGURE 1: Role of the needle aspiration biopsy (FNAB) in the sequential approach to the cold thyroid nodule. [5]

THYROID

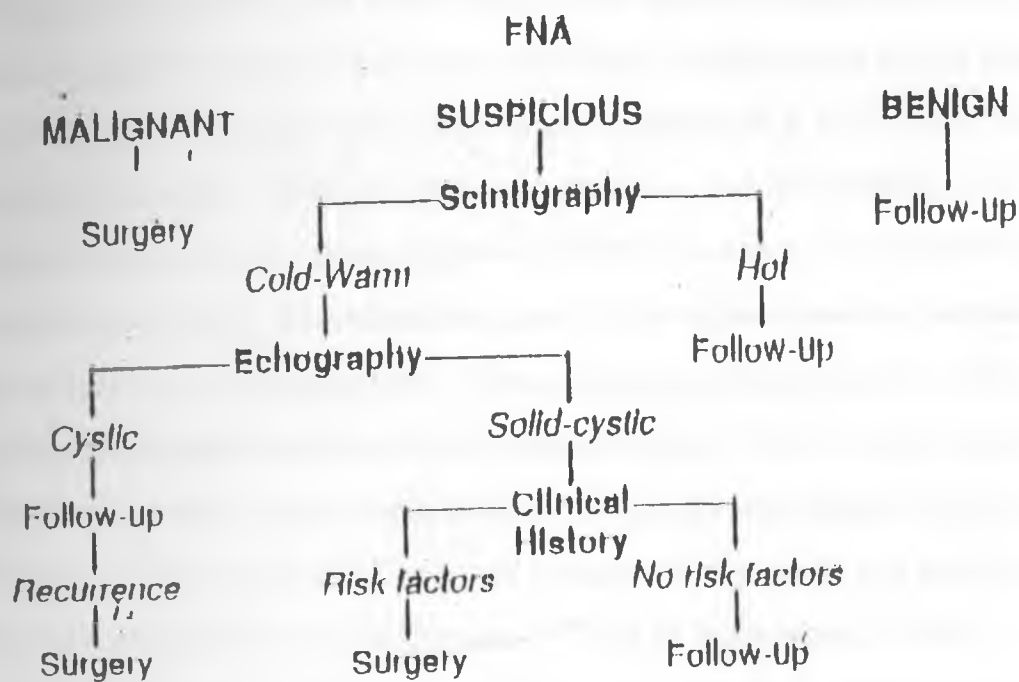


FIGURE II. Algorithm for management of thyroid nodules. (13)

XIII. JUSTIFICATION OF THE STUDY

F.N.A.C. was introduced as a routine diagnostic procedure at K.N.H in 1989. A previous prospective study has established that it has an overall high sensitivity (84%) and specificity (87%) in evaluating tumour from all anatomic sites. The study also brought to light the fact that sensitivity and specificity of the technique varies from one anatomic site to the other. In view of this, it is necessary that more specific and detailed studies focussed on specific sites be done. A previous such study has been done on the breast. The thyroid is the third most common site aspirated at K.N. H. after breast and lymph nodes. Thyroid nodules are common, but the incidence of thyroid cancer is low. Abnormalities of the thyroid may be evaluated by a sophisticated array of biochemical assays, clinical assessments, scanning technique and ultrasonography. These techniques lack sensitivity, they cannot distinguish malignant from benign nodules. FNAC is the single most sensitive, specific and cost-effective method in the investigation of thyroid nodules. The role of FNAC is to aid in selection for surgery of nodules that have a high probability of malignancy. Used in this manner, FNAC is primarily a screening rather than a diagnostic procedure, and a conclusive cytologic diagnosis is not always required. Preoperative FNAC may also help uncover unsuspected cancer and in planning surgery. This study will increase our understanding and awareness on use of FNAC in diagnosing thyroid nodules, identify its limitations and give recommendations on how to improve it. In a busy national hospital like K.N.H., it is important to embrace a technique that would make thyroid surgical procedures more selective, reduce unnecessary thyroidectomies and at the same time improve on patient care in terms of quality and cost.

XII. AIMS AND OBJECTIVES

1. To assess the value of FNAC in the diagnosis of thyroid nodules at K.N.H with emphasis on consistency and accuracy.
2. To determine sensitivity and specificity of FNAC of thyroid nodules at KNH.

SPECIFIC OBJECTIVES

1. To determine the false Negative and Positive rates of FNAC of thyroid.
2. To determine the Positive and Negative predictive values of FNAC of thyroid.
3. To compare the percentage of neoplasms in patients who had undergone FNAC and in those who had surgery after FNAC.
4. To document the frequency of different lesions encountered by FNAC of thyroid.

XIV. MATERIAL AND METHODS

Study Design

This was a retrospective study in which 383 consecutive FNAC slides and reports were reviewed and compared with their histologic report where applicable.

Study Site

Department of Human Pathology (Cytology and Histology sections).

Study Population

All F.N.A.C done between January 1996 and June 1999 at the KNH FNAC clinic.

Inclusion Criteria

1. Patient with palpable thyroid nodules in which there is a corresponding histologic report who have had the benefit of F.N.A. at K.N.H will be included in the study.
2. If F.N.A.C report is inadequate/unsatisfactory, the Repeat FNAC will be considered if available.
3. Only reports bearing Inpatient/outpatient number will be included in the study.

Exclusion Criteria

1. All reports without Inpatient/Outpatient number
2. Reports with improperly filled request form.

Sample Size

(See appendix II)

Control

Histologic reports were considered the 'gold standard

Method

The reports and slides of 398 consecutive FNAC of thyroid from 398 patients performed between January 1996 to June 1999 were retrieved.

There were results of nodule aspirated by different pathologists.

FNAC had been performed using disposable 5 ml or 10 ml syringe and a 21 – 23 gauge disposable needle. Aspiration had been performed using multiple passes, while negative pressure was maintained. The aspiration material had been expelled onto a glass slide and smear prepared by pressing the material on the slide with another slide and spreading this material over a small area (similar to preparation used in bone marrow aspirate). The smears had been fixed in 95% alcohol immediately and later stained by Hematoxylin and eosin (H/E) and papanicolaou stains. If a cystic lesion was encountered the aspirated fluid was totally removed and palpation repeated to rule out residual mass. Residual mass if present was aspirated.

The smears were interpreted by a Cytologist with the benefit of a Pathologist. Different Pathologists and Cytologists had done the interpreting and reporting of the smears.

From the request forms, personal numbers, name, age, sex and clinical data were noted. Records in histology were retrieved and checked if FNAC was followed by surgical biopsy. In all the applicable cases the histology reports were recorded. For all cases with both FNAC and surgical biopsy of the same lesion a comparison were made. In all cases with discrepancy slides were retrieved and reviewed by the investigator and confirmed by the pathologist (supervisor).

Data Analysis

The data was entered into the computer utilizing statistical package for Social Science (SPSS)/PC (personal computer system) and analyzed.

Ethical Consideration

Before embarking on the study, permission was sought and granted from the KNH ethical review committee. All patient reports were treated with strict confidentiality.

XV. RESULTS

TABLE I

Age Distribution of patients whose thyroid nodules were diagnosed by FNAC.

Age Group	Male	Female	Total	Percentage
10 – 19	0	12	12	3.13
20 – 29	7	85	92	24.02
30 – 39	9	100	109	28.45
40 – 49	6	62	68	17.75
50 – 59	4	28	32	8.36
60 – 69	5	15	20	5.22
70 – 79	1	4	5	13.05
Unknown	4	41	45	11.75

Out of 383 patients in the study, 347 (90.6%) were female and 36 (9.4%) were male. The age of the patients ranged from 15 – 78 years. The majority of the patients (46.21%) were in the age group of 20 – 40.

Histogram I: Age distribution of patient whose thyroid nodules were diagnosed by FNAC

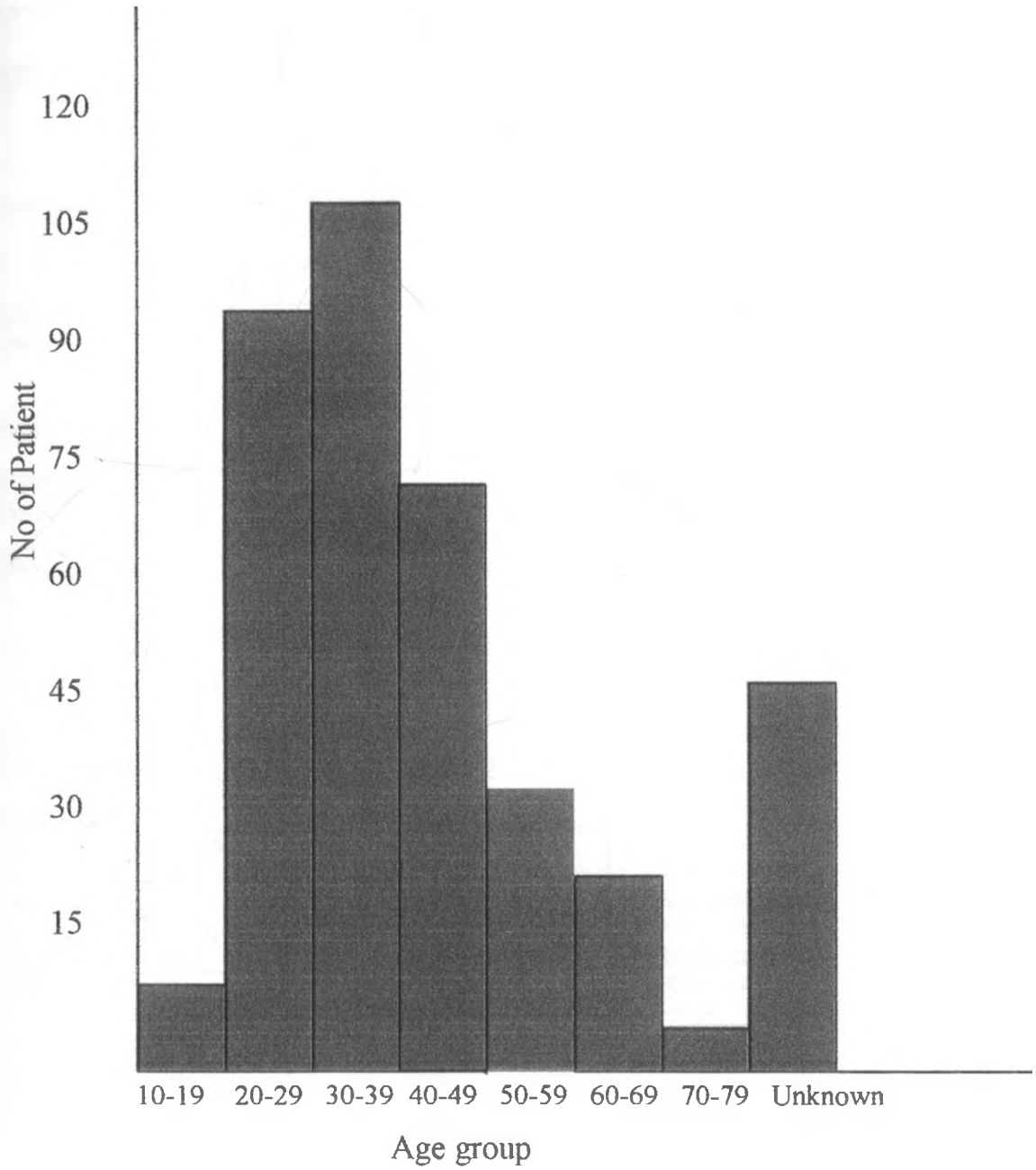


TABLE II

SUMMARY OF CYTOLOGY AND HISTOLOGY RESULT

Cytology Diagnosis	No. of Patients	Percentage %	Histology Diagnosis	No. of Patients	Percentage %
NON NEOPLASTIC	344	89.92	NON NEOPLASTIC	58	77.33
Hyperplasia	249	65.01	Hyperplasia	57	76.00
Cyst	4	1.04	Benign follicular Cells not further Classified	1	1.33
Thyroiditis. (i) Acute (ii) Subacute	2 2	0.52 0.52			
Benign follicular cells not further classified.	22	5.74			
Unsatisfactory	65	16.97			
NEOPLASM	39	(10.18%)	NEOPLASM	17	(22.66%)
Benign	32	8.35	Benign	12	16.0
Follicular adenoma	2	0.52	Follicular Adenoma	11	12.0
Follicular Neoplasm	14	3.66	Atypical follicular Adenoma	1	1.33
Follicular neoplasm favouring cancer	1	0.26			
Hurthle cell tumour	1	0.26			
Atypical/possible malignant	14	3.66			
Cancer (malignant)	7	1.83	Cancer (Malignant)	5	6.66
Follicular carcinoma	1	0.26	Follicular carcinoma	2	2.67
Papillary carcinoma	1	0.26	Papillary carcinoma	1	1.33
Malignant not otherwise specified/poorly differentiated carcinoma	5	1.31	Medullary carcinoma	1	1.33
			Poorly differentiated carcinoma	1	1.33
TOTALS	383	100%		75*	100%

* 2 cases (2.78%) of mixed follicular adenoma and simple colloid goitre.

The cytology diagnosis are summarized in table II. 318 (83.03%). Out of 383 had adequate material for diagnosis. 39 (10.18%) cases were diagnosed as neoplasm. The remainder (89.32%) were non-neoplastic with approximately 65% hyperplasias. 4 cysts were encountered and collapsed after aspiration leaving no palpable nodule. Surgical confirmation of the cytology diagnosis was obtained in 75 (19.58%) of the patients, of these 17 (26.66%) were neoplastic, 12 (16%) of which were follicular adenomas and 5 carcinomas. The remainder 58 (77.33%) were non-neoplastic of which 57 (76.00%) were hyperplastic. There were two cases, which were diagnosed as having areas of both follicular adenoma and hyperplasia.

TABLE III
COMPARISON OF CYTOLOGY AND HISTOLOGY DIAGNOSIS

Cytology Diagnosis	Histology diagnosis								Total
	U/S	B.F.C	H	F.A	F.N	F.N (c)	S	M	
U/S	-	-	7	2	-	-	-	-	9
B.F.C.	-	-	1	1	-	-	-	-	2
H	-	1	43	6	-	-	-	1	51
F.A	-	-	1	-	-	-	-	-	1
F.N.	-	-	4	2	-	-	-	-	6*
F.N.(c)	-	-	1	-	-	-	-	-	1
S	-	-	-	1	-	-	-	-	1
M	-	-	-	-	-	-	-	4	4
TOTAL		1	57	12	-	-	-	5	75

U/S – Unsatisfactory

F.N (c) – Follicular Neoplasm favouring cancer

F.A – Follicular Adenoma

B.F.C. – Benign Follicular Cells

S – Suspicious

H – Hyperplasia

M – Malignant

F.N. – Follicular Neoplasm

* 2 cases called F.A with areas of Hyperplasia.

TABLE IV

**SUMMARY OF CONSISTENCE OF CYTOLOGY DIAGNOSIS IN
COMPARISON WITH HISTOLOGIC DIAGNOSIS**

Cytology diagnosis	Number of cases	Percentage %
Diagnosis consistent with surgical results	48	64.00
Benign but diagnosis not consistent	10	13.30
Unsatisfactory but benign histologically	9	12.00
Suspicious or neoplasms but surgically benign	5	6.66
Benign but malignant histologically	1	1.33
Malignant cytological and histologically but inconsistent with histology results	2	2.66

XVI. DISCUSSION

As mentioned earlier, there are very few reported series of Thyroid aspirates where error of omission or commission have not been made. There is no doubt that FNAC of Thyroid is a valuable tool in diagnosis of Thyroid Nodule. In spite of its limitations, their advantage outweighs the limitations. However it is important to know when and how to use the Cytologic Technique.

There were 398 consecutive FNAC from 383 patients in the study. The age of the patient ranged from 15-78 years, however 82.3% were in the age group 20-60 years (See table 1 and figure 111). The percentage of female was 90.6% and males 9.4%. Thomas et al (6) in a similar study carried out in Columbia reported a range of 14 – 80 years, 84% female, 16% males and 60% patients between 30 – 60 years. Studies done by Hawken et al (10) in Spain reported a range of 9-84 years, 89.5% female and 10.5% male. These findings are in agreement with those in the study and confirm that Thyroid nodules are more in females than in males.

A major problem diminishing the potential of FNAC is the difficulty in sampling. Fifteen FNAC were repeated due to an initial unsatisfactory attempt. Sixty-five (16.9%) cases had a final diagnosis of unsatisfactory. Silverman et al (11) report 11.7% specimen as insufficient for definitive diagnosis, although many of these were consistent with benign cysts. The

main reasons for insufficiency in the study includes: Lack of adequate cytologic material, too much blood and poor technical preparation. There is need to perfect the aspiration technique at K.N.H. to reduce the number of unsatisfactory reports. Elaborate procedure on the technique is given by many authors (1-8,13,15). Sampling of the thyroid requires skill and practice. The percentage of unsatisfactory reports have been known to decrease with experience (14)

According to Stanley et al (2) the Cytopathologist report should contain of reference to the Cellularity of the specimen. With all but the smallest nodules, different areas should be aspirated. The gauge of the needle varies from 22-29 depending on the vascularity or fibrous consistency of the nodule. Care should be taken to avoid blood dilution, crush artifacts or air drying of wet fixed material. When feasible microscopic evaluation during the procedure, provides information on adequacy of the aspirate and results in lower rate of unsatisfactory specimens. Thomas et al (6) in his study of 300 consecutive cases was able to attain sufficient material in all his cases.

The types of nodules encountered in the thyroid in this study are summarized in Table 11. According to the findings, Non-neoplastic nodules constituted 89.82% and neoplastic 10.18% of the nodules. Majority of the non-neoplastic nodules, 57 (65.01%) were hyperplasias (nodular/adenomatous goitre and colloid goitre) when FNAC was followed by surgical exploration non-neoplastic nodules decreased to 77.33% and neo-plastic nodule increased to 22.66%

These results reflect minimal changes in percentage of neo-plastic and non neoplastic nodules compared to a similar study by Silverman (11). He reported 74% non-neoplastic and 26% neoplastic nodules. When surgery followed FNAC non-neoplastic decreased to 28% and neoplastic increased to 74%. From the finding we can conclude that the number of unnecessary surgery being done in own institute is still high in comparison to other centers. Occasionally, a surgical procedure will be appropriated despite clearly benign FNAC findings in an anxious or cancer-phobic patient with progressively growing or initially very large nodules (2).

MEDICAL LIBRARY
UNIVERSITY OF MALAYA

Surgical confirmation of cytologic report was possible in 75 cases. Out of these 57(76.00) were hyperplasia. This trend was attributed to the fact that in the majority of hypercellular hyperplasia a comment was given after the diagnosis to the effect that it was difficult to differentiate follicular adenoma, well differential carcinoma and nodular goiter cytologically. This statement should be avoided as much as possible and used only when the situation is compelling.

Indeed it is difficult to differentiated Hypercellular nodule goitre, follicular adenoma and well differentiated follicular carcinoma. In the study 6 follicular adenoma were diagnosed as hyperplasia and on the other hand, 6 hyperplasia were diagnosed as follicular neoplasm (see table 111). This was attributed to the fact that too much emphasizes was laid on cellularity to give diagnosis. Hypercellularity of smear does not always indicate neoplasm, it may be derived from a hyperplastic (adenomatous goitre) Likewise, hypocellularity of smears does not necessary mean nodular goitre, rather it

may be a reflection of poor skills of the aspirator or desmoplastic nature of the tumour. More important the pathologist must carefully evaluate the cellularity of a tissue fragment because this reflects the cellularity of the nodule more accurately and hence is a more dependable criterion (13).. Other refined criteria that may assist include; studying the uniformity of the follicular units, nuclear details of individual cells and amount of colloid in the background.

Using the criteria in the appendix (v) it was possible to give cytologic diagnosis consistent with histologic diagnosis in 48 (64%) of the nodules. In 60 patients FNAC was able to establish whether the nodules were malignant or benign. Due to this FNAC should be used as a screening procedure to select patients for surgery as emphasized by some authors (2,5,20,25,27). Each FNAC report pathology report should be individualized as in surgical pathology reporting so that the clinician who receive the report, will have a clear understanding of the pathologic certainty, or doubts regarding the nature of the nodules.

The calculated sensitivity, specificity and accuracy were 80%, 100% and 98.6% respectively. This was in agreement with those in other studies (2,12,20,27). Only 4 ;out of the 7 cases diagnosed as cancer had traceable histologic reports. The question as to whether this limited data on positive cases was sufficient to calculate sensitivity still lingers in the author's mind. The author presumes that with more positive cases, the sensitivity would drastically change. These points to the importance of having an efficient follow up system such that the positive cases are given first priority in further surgical exploration. The cytologist and pathologist must stress the

need for urgent surgery in such cases. On the other hand K.N.H being a referral hospital the possibility of the patient being followed up in a different institution cannot be ruled out, due to the long theatre waiting lists.

There was no false positive report in this study, unlike some authors (11,18,20) cases that were diagnosed as suspicious, atypical and follicular neoplasm and turned out to be benign were not considered as false positives. This is because FNAC should not be used in isolation. Other available techniques (see figure I & II) should be employed to investigate such nodules further, before a decision for surgery is made. Only outright malignant nodules should warrant surgical exploration on the basis of FNAC alone.

False negative reports are primarily due to inadequate or unrepresentative material and not misinterpretation by the pathologist. Low false negative rates have been reported in most studies (2,6,26,27). There was one false negative in the study. Although the morphological feature did not suggest malignancy, the clinical information given on this particular case was very suspicious. The patient had a recurring nodule after thyroidectomy done five months earlier. In Bouvet et al's study, (26) two out of 17 patients who had negative FNAC but underwent thyroidectomy based on other factors were found to have cancer. Due to this the presence of other findings suspicious of malignancy should preclude clinical decision-making based on FNAC alone. Thus stressing the need for proper clinical observation and history in the diagnosis of thyroid nodule.

FNAC is the therapeutic in case of cysts. Four cysts were encountered and completely evacuated. Frable (8) aspirated 23 thyroid cysts and followed the patient up for a period of six months to four years. Only four cysts recurred.

The need for experienced pathologist to interpret the FNAC of thyroid has led to hesitance in accepting FNAC of thyroid (2,10,12). Experts suggest therefore that FNAC is properly confined to centres in which each operator obtains no fewer than 500 specimens each. This study rebuts this.

According to the finding, several well-trained pathologists are able to attain acceptable accuracy. Further more, cytopathologists are made by training, experience, attending workshops and liberally using internal consultation in interpreting FNA. Better interpretation of results are achieved when the cytopathologist who aspirates the nodule interpret the material.

FNAC is cheaper than the other technique available in evaluation of thyroid nodules. It is not a replacement to surgery nor any other technique. For one to achieve maximum benefits from it, it should be used as the first procedure in investigating thyroid nodules together with clinical assessment. This way, many expensive techniques will be avoided resulting to better management of thyroid nodule.

KNH is a referral hospital that serves the whole country. For Nairobi and its environs, it also serves as a provisional hospital. Due to this, the demand for health care at the hospital is great. The AIDS pandemic has even worsened

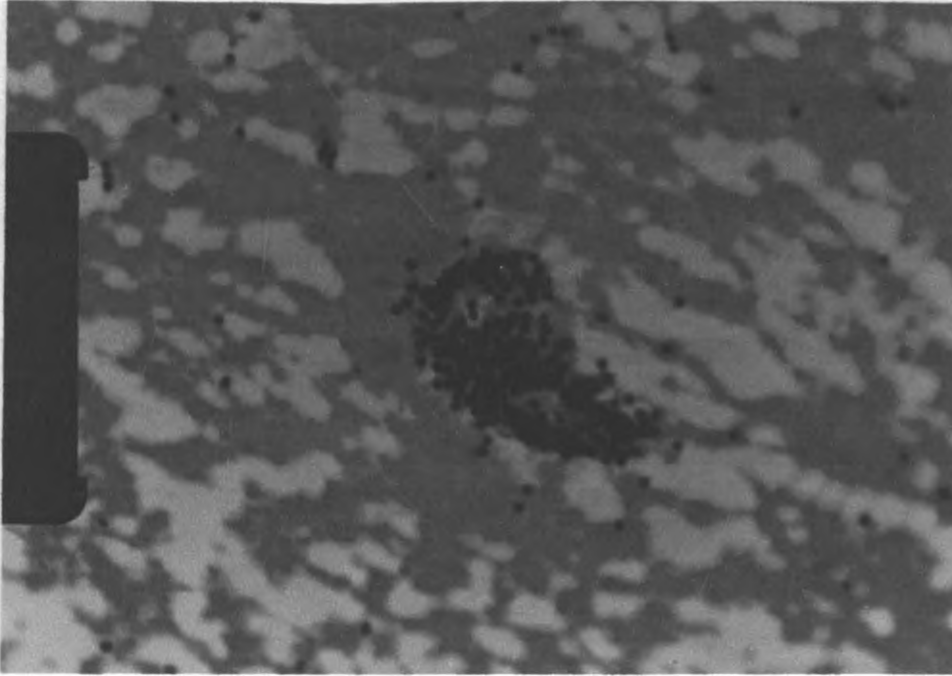
the situation. It is therefore very important that priorities are set out in managing thyroid nodules. FNAC, if used in the proper manner, can play a significant role in easing the congestion at the hospital. Theatre time will be reduced, bed shortage eased and costs cut done for the patients and the hospital.

XVII. CONSTRAINTS

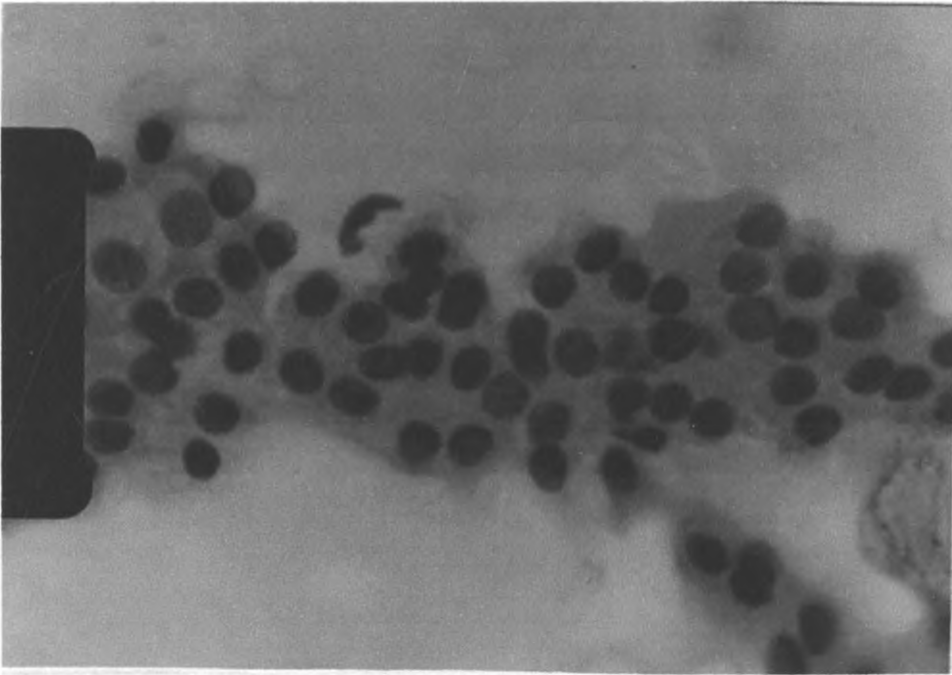
1. Since the histology and cytology sections work as two independent bodies, it was difficult to correlate histology and cytology results.
2. There were many forms with insufficient history and clinical data. In some cases, the names of the patient used changed, others had no personal number, age or sex.
3. The follow-up system in the hospital is poor. At the Registry, some reports were missing from the files and some personal numbers in the request forms did not correspond to the files.

XVIII. RECOMMENDATIONS

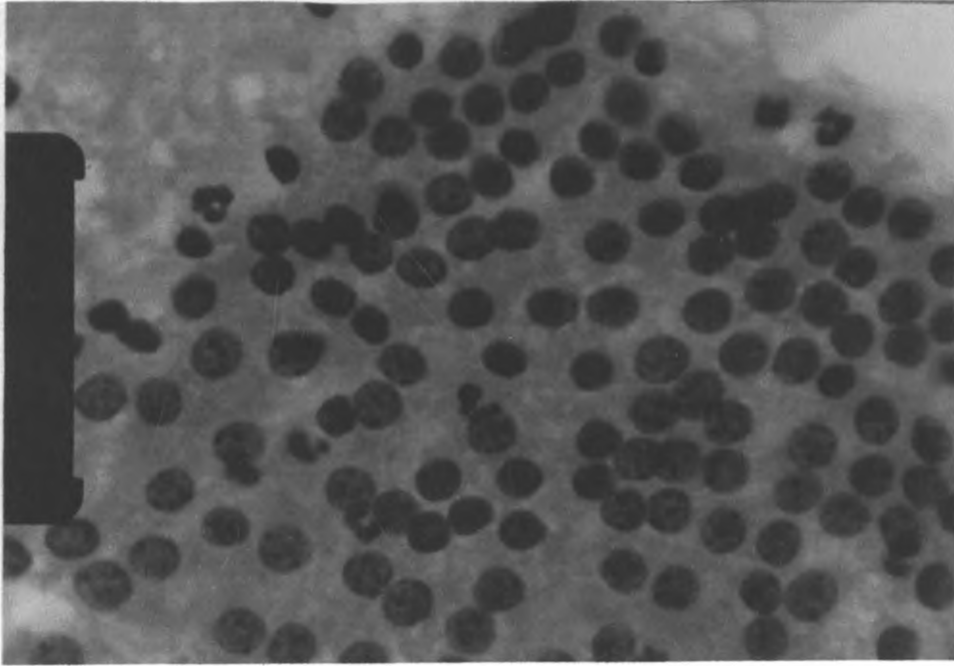
1. FNAC along with clinical assessment should be the first diagnostic test to determine the management of thyroid nodules at KNH.
2. The Clinician and Pathologist should work as a team with bi-directional feedback on difficult cases. They should also come up with a consensus guideline on the management of thyroid nodule at K.N.H.
3. To ease the burden on the few Pathologists available at K.N.H, the Clinicians should be trained on the technique. The need for properly filled request forms should also be emphasised to them.
4. Continuous correlation between cytology and histology reports should be maintained as a quality control measure.
5. There is need to carry out a prospective study on the thyroid to establish further the value of FNAC in the diagnosis of thyroid nodules with respect to effect on surgery, complications and cost effectiveness.

XIX. PLATESPlate I

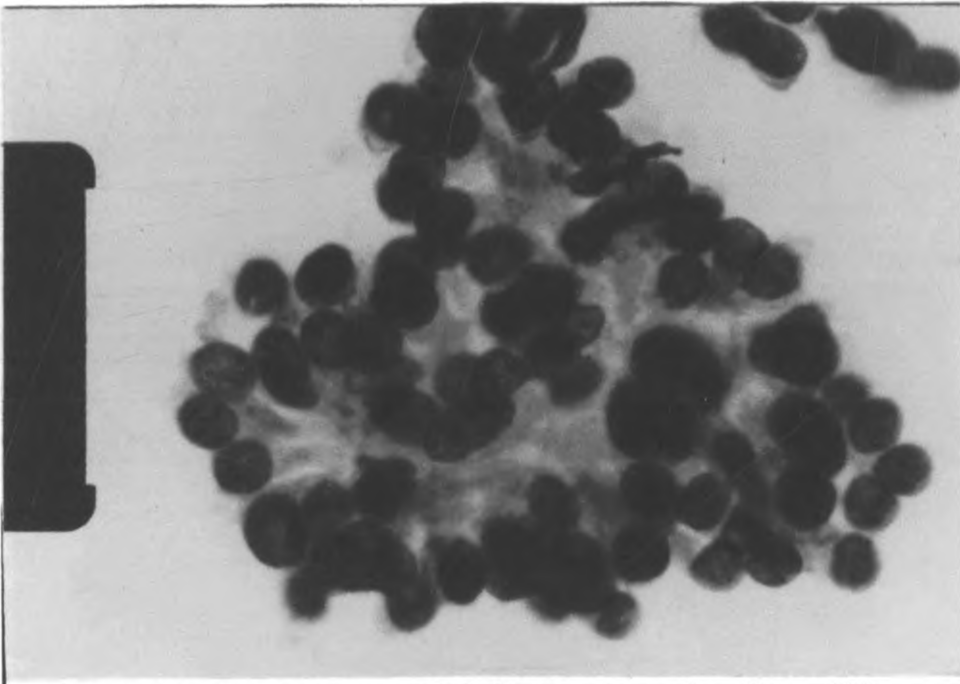
Benign sheet of uniform follicular cells in an hemorrhagic background. (H&E x 100).

Plate II

Uniform follicular cells with well-rounded nuclei (H&E x 400).

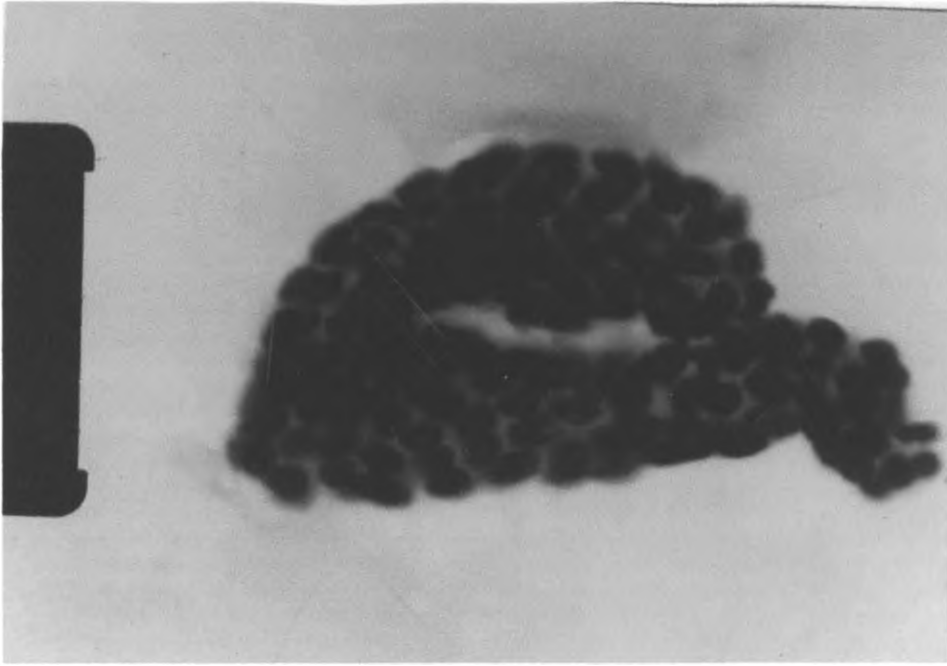
Plate III

Large sheet of uniform follicular cells (Pap x 200)

Plate IV

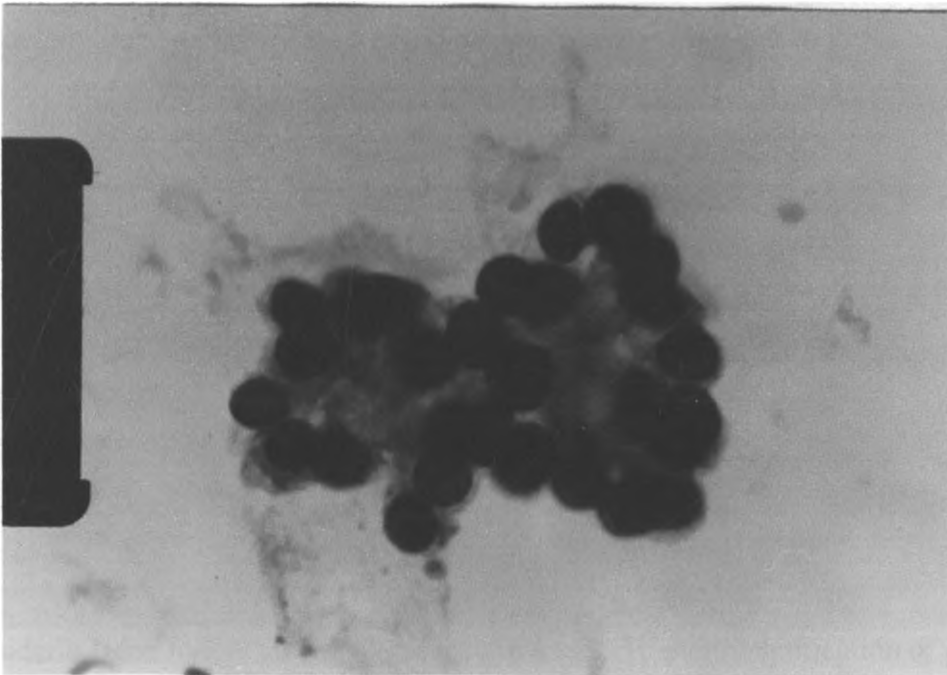
High power view of benign follicular cells in Rosette formation (Pap x 400).

Plate V

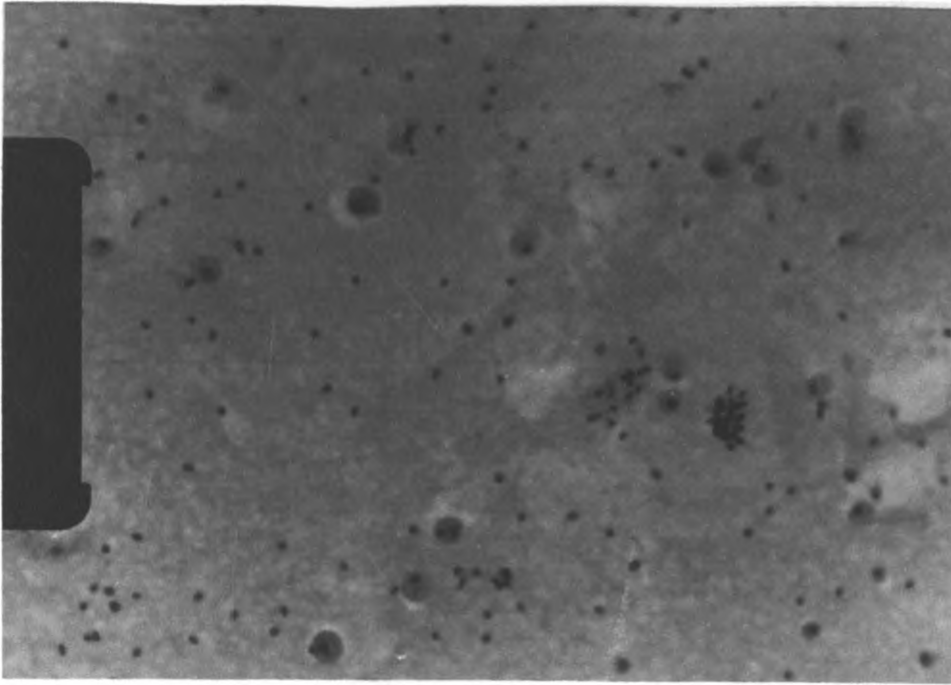


Three dimensional sheet of benign follicular cells (Pap x 400)

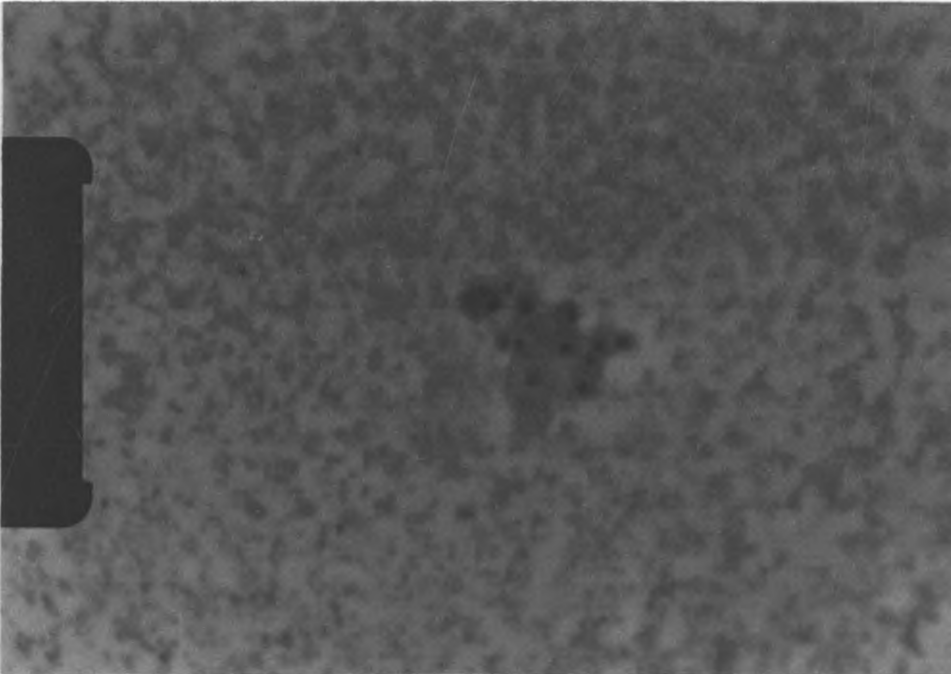
Plate VI



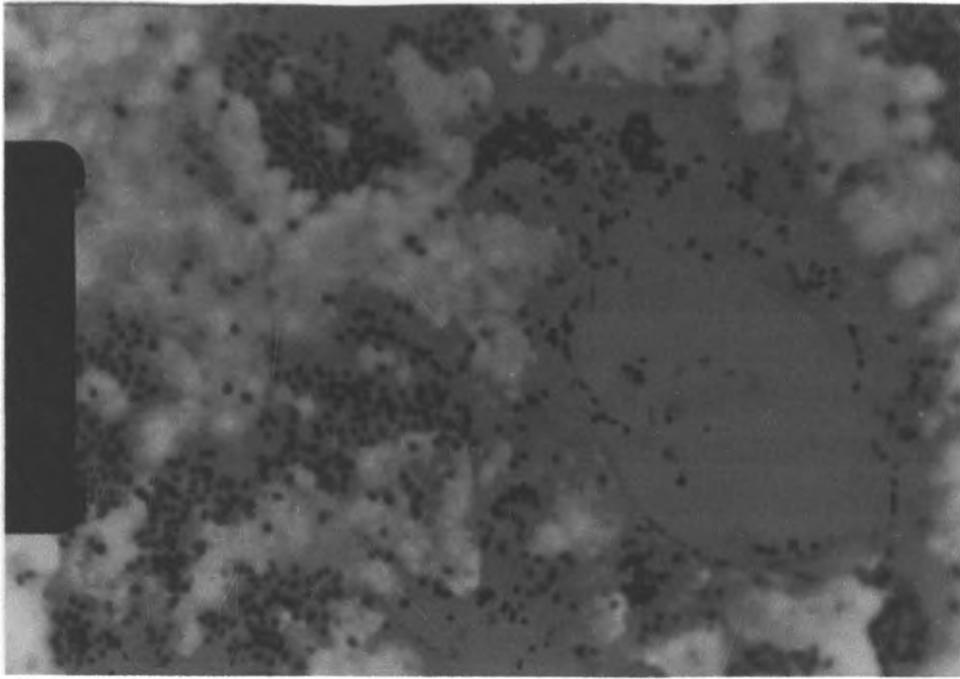
Classical Rosette formation a characteristic of follicular cells (Pap x 400).

Plate VII

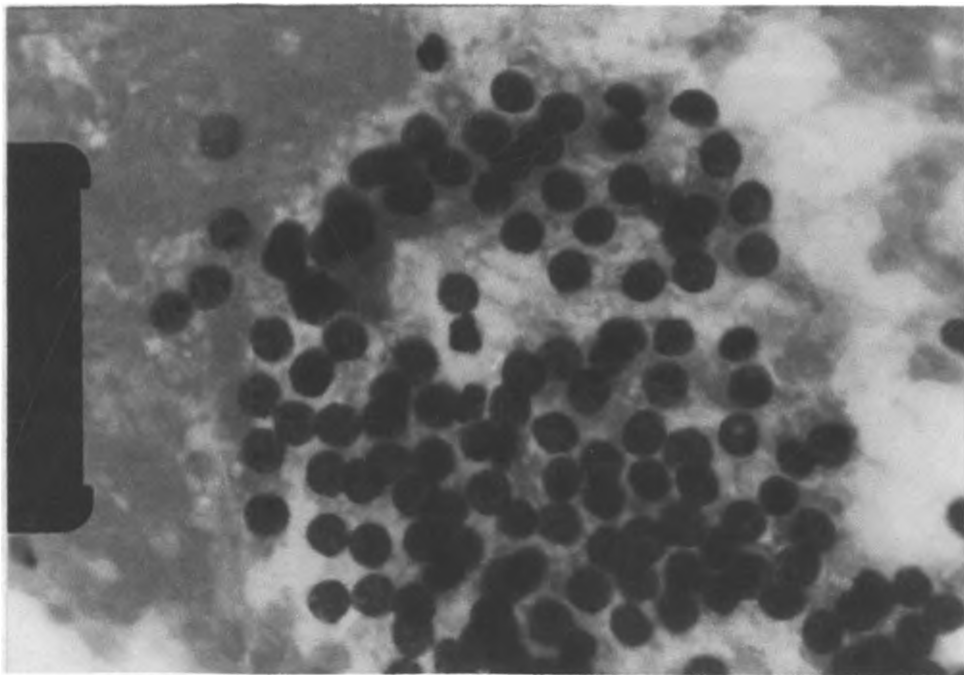
Cyst: A small sheet of follicular cells and macrophage with foamy cytoplasm, some haemosiderin laden and bloody background (Pap stain x 100).

Plate VIII

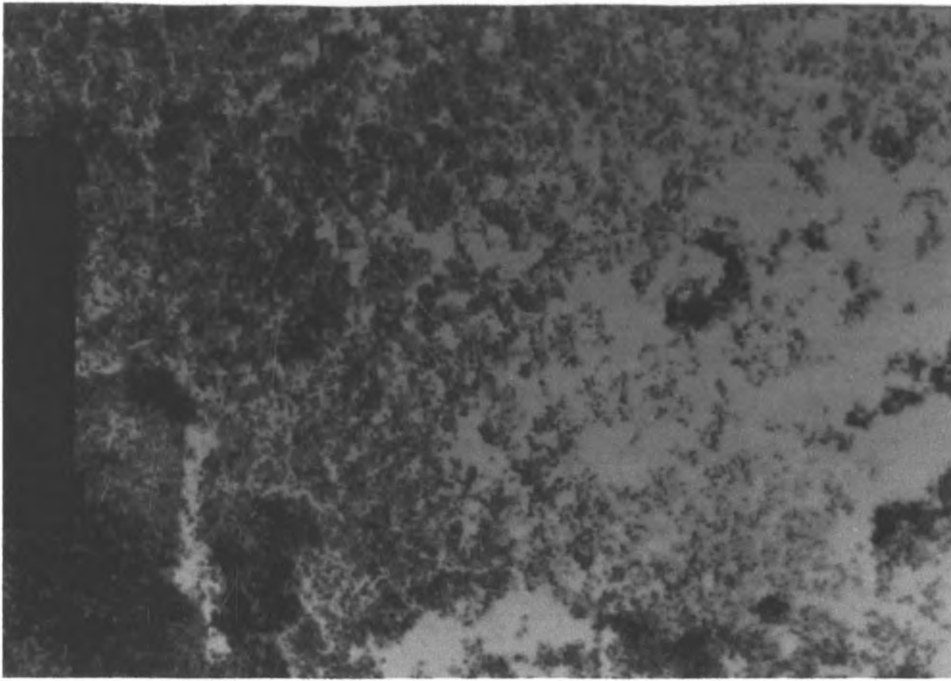
Haemosiderin laden foamy macrophages seen in a cyst (Higher magnification of plate I (Pap stain x 400).

Plate IX

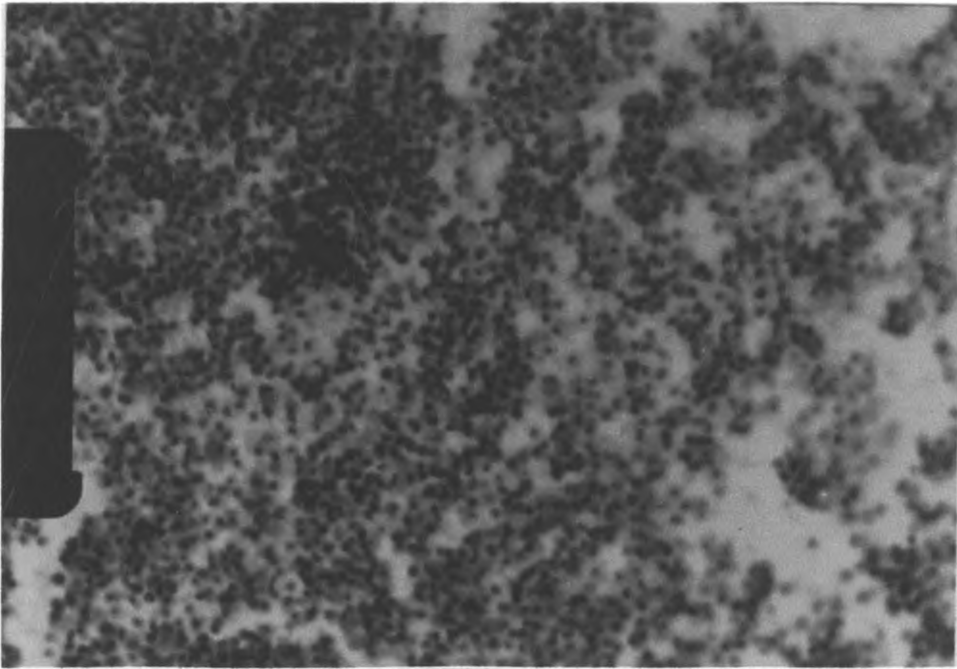
Nodular goitre: Uniform sheets of follicular cells, some naked nuclei and abundant colloid.

Plate X

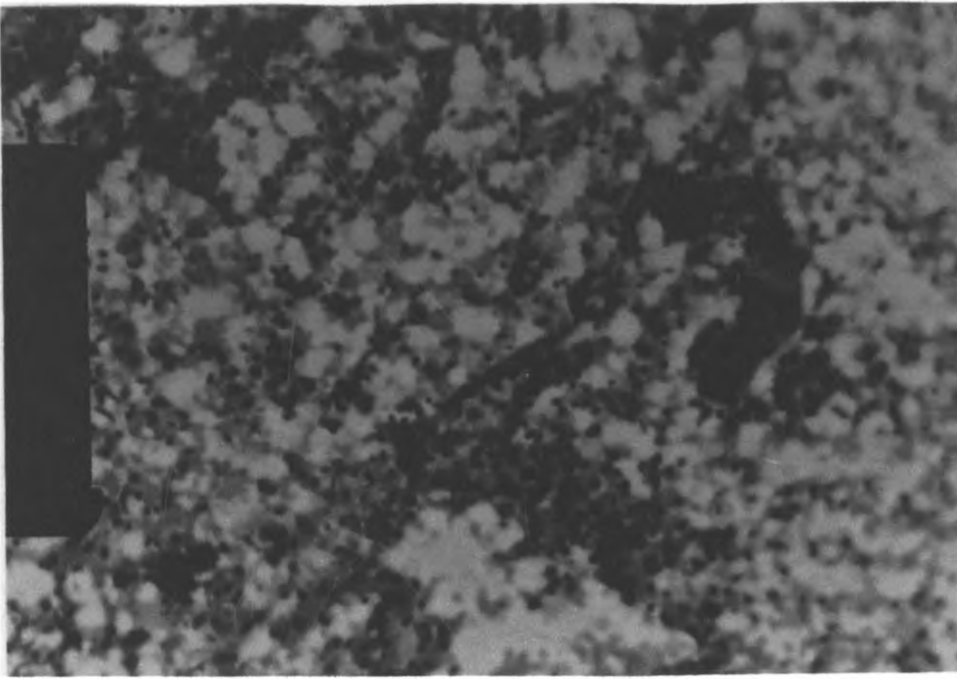
(Pap stain x 400) Higher magnification of follicular cells.

Plate XI

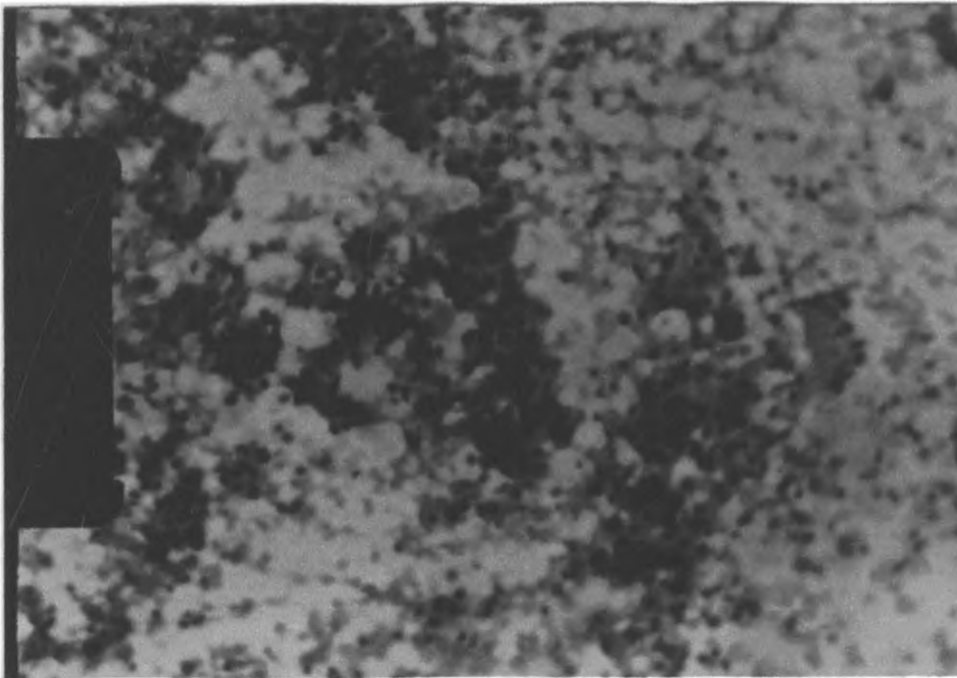
Acute thyroiditis: Numerous neutrophils, macrophages in a background of cellular debris. (x 100).

Plate XII

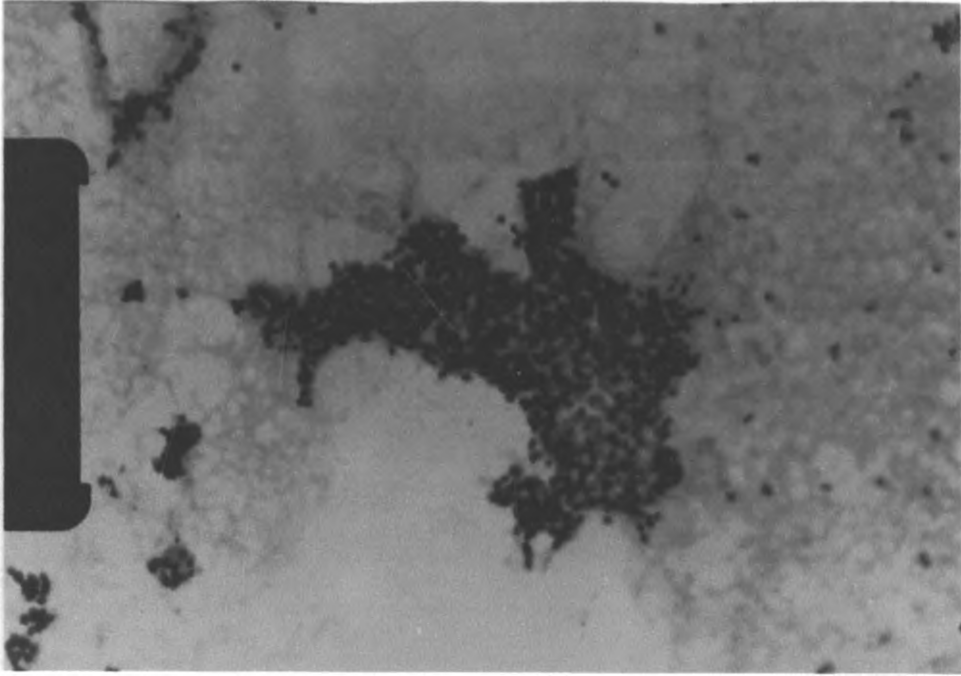
Acute thyroiditis (x 400).

Plate XIII

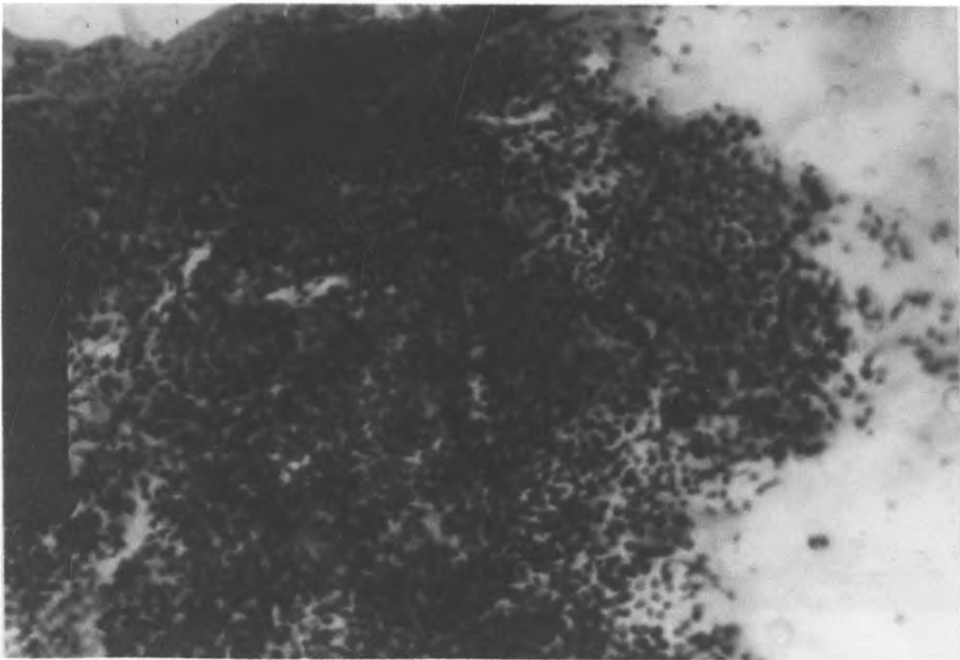
Hashimoto's thyroiditis: Background of lymphocytes, follicular cells and Hurthle cells (Pap x 100).

Plate XIV

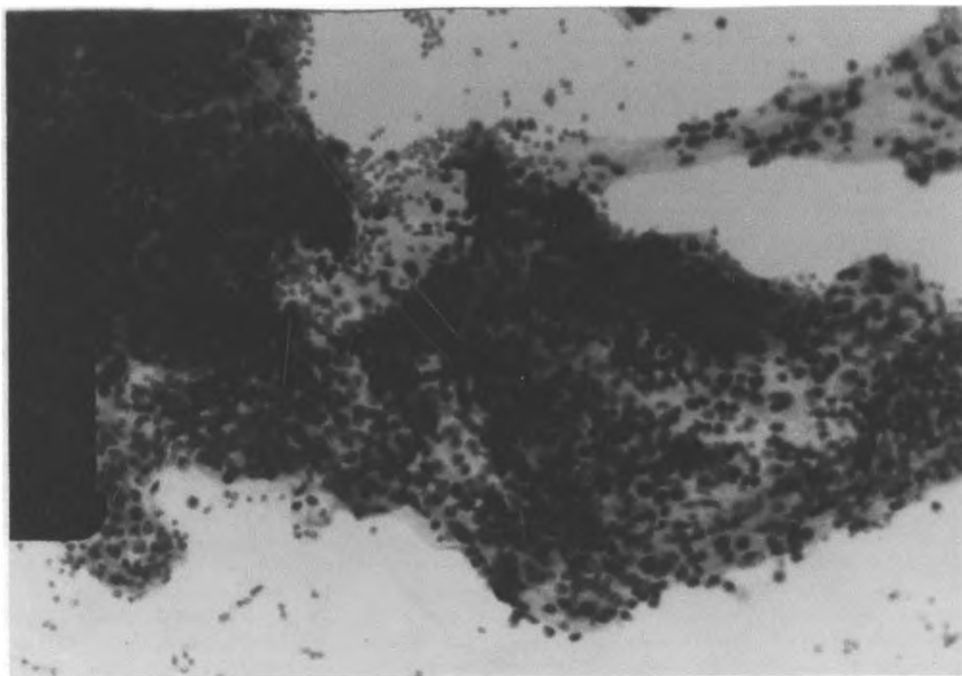
Hashimoto's thyroiditis (Pap x 400)

Plate XV

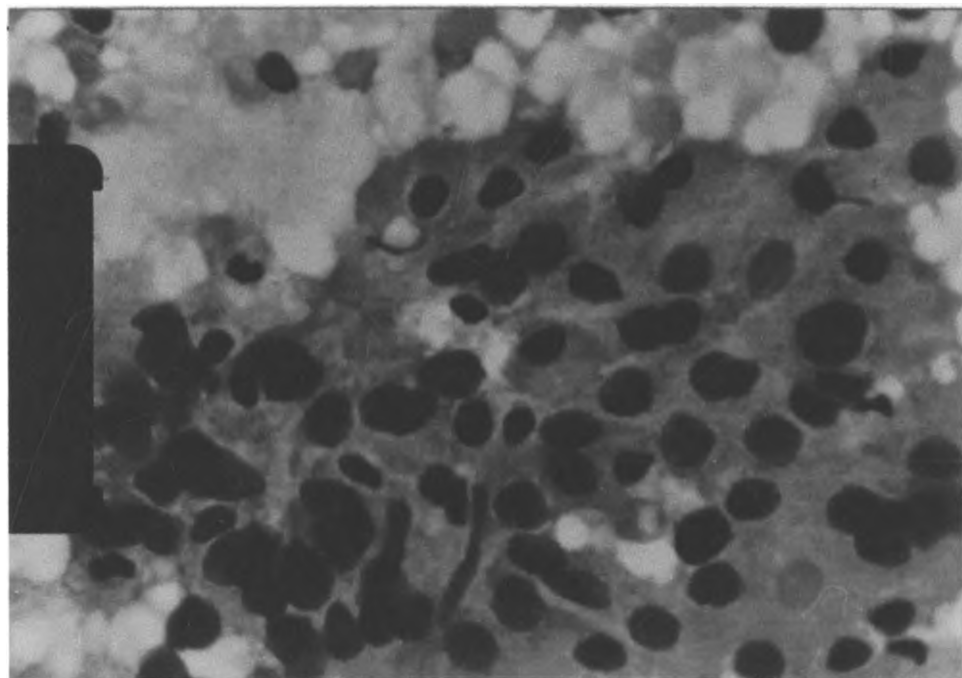
Follicular Neoplasm (Pap x 100)

Plate XVI

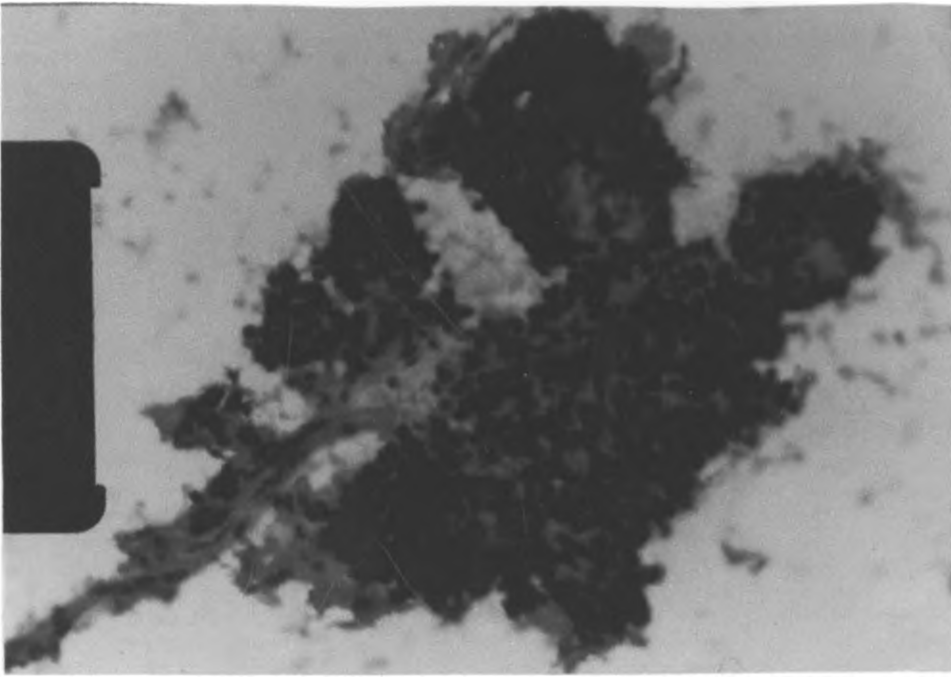
Follicular Neoplasm (Pap x 400) sheets of cells in microfollicle formation.

Plate XVII

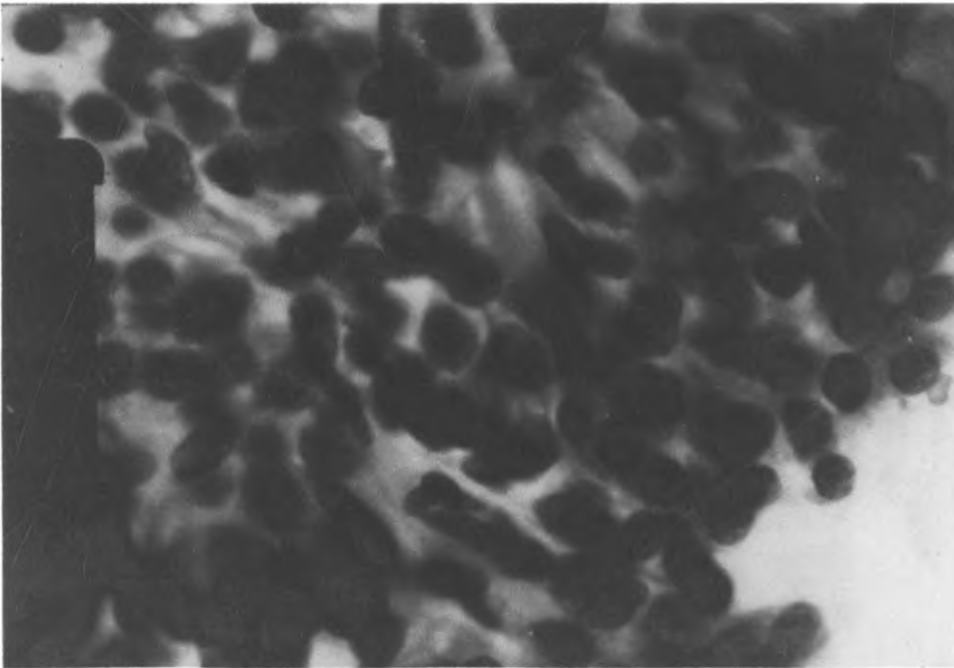
Follicular Neoplasm: tight sheets of follicular cells. (Pap x 400)

Plate XVIII

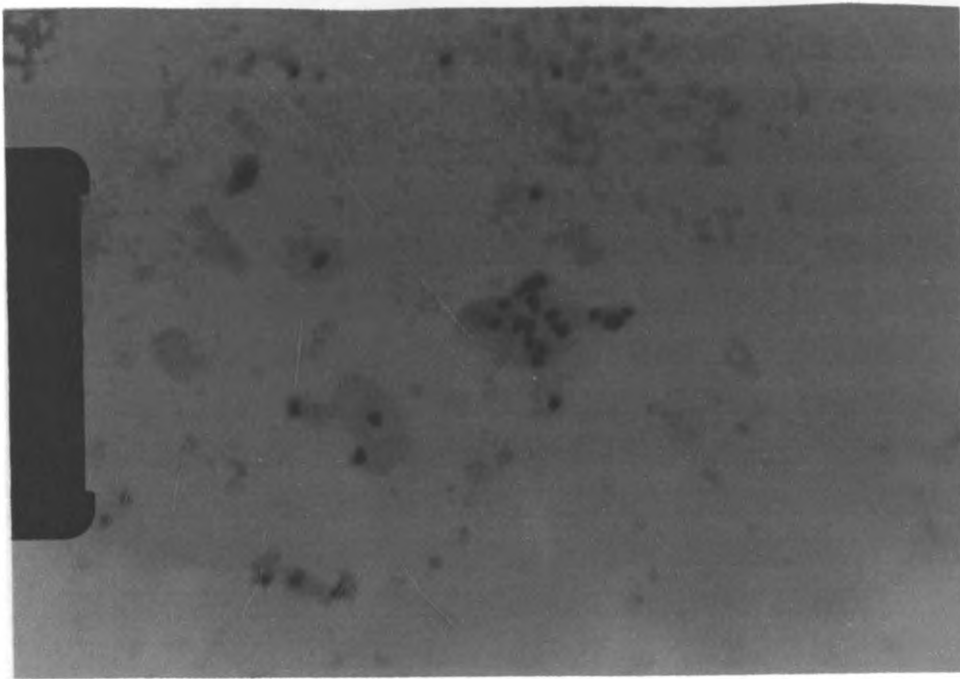
Hurthle cell Neoplasm: Cells with abundant eosinophilic granular cytoplasm, Large round to oval and frequently binucleated (Pap x 400).

Plate XIX

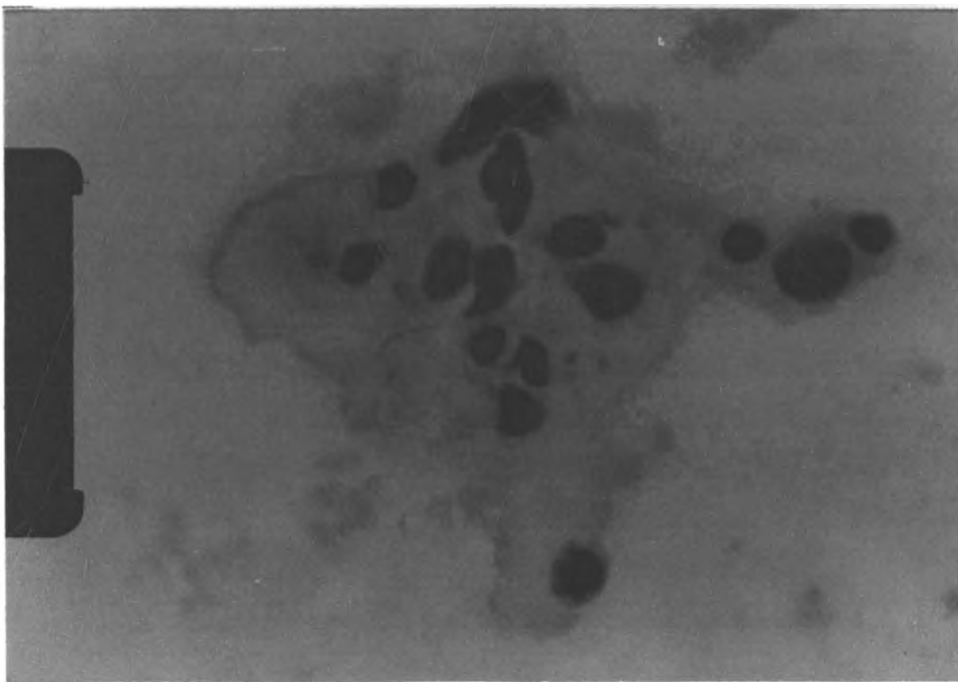
Papillary carcinoma: Tight sheet of follicular cells in papillary formation (H&E x 100).

Plate XX

Higher power view of papillary carcinoma: (H & E x 400).

Plate XXI

Anaplastic carcinoma (Pap x 100).

Plate XXII

Anaplastic carcinoma (Pap x 400).

XX. APPENDICES

APPENDIX I

Formulae used:

$$\text{i) Sensitivity} = \frac{\text{True positive}}{\text{True positive} + \text{False negative}}$$

$$\text{ii) Specificity} = \frac{\text{True negative}}{\text{True negative} + \text{False positive}}$$

$$\text{iii) Accuracy} = \frac{\text{True positive} + \text{True negative}}{\text{True positive} + \text{False positive} + \text{True negative} + \text{False negative}}$$

$$\text{iv) Positive predictive value} = \frac{\text{True Positive}}{\text{True positive} + \text{False positive}}$$

$$\text{v) Negative Predictive value} = \frac{\text{True Negative}}{\text{True Negative} + \text{False Negative}}$$

TABLE V

Sensitivity	80%
Specificity	100%
Accuracy	8.69%
Positive Predictive Value (PPV)	100%
Negative Predictive Value (NPV)	98.8%

APPENDIX II

Sample size

The sample size was estimated using the formula

$$n = \frac{Z_{\alpha/2}^2 \cdot p \cdot q}{d^2} = 199$$

where n = size of the minimum sample acceptable to the study.

$Z_{\alpha/2}$ = value of the Standard Gaussian variable Z such that a proportion $\alpha/2$ of the values exceed it (in this case $Z_{\alpha/2} = 1.96$ for 95% confidence interval).

p = the success or the sensitivity of the test (sensitivity of 84.7% of Audi-Rogena (25) was used).

q = $1-p$ or expected proportion

d = width (level of significance) in this case it is 5% (0.05) for 0.025 above and 0.025 below the mean.

APPENDIX III

Papanicolaou Stain

1. 80% ethanol – (10 dips)
2. 70% ethanol – (10 dips)
3. 50% ethanol – (10 dips)
4. Distilled water – (10 dips)
5. Harris Hematoxylin – (10 dips)
6. Distilled water – (10 dips)
7. 1% acid alcohol – (3 dips)
8. Distilled water – (10 dips)
9. Scotts tap water – (10 dips)
10. Distilled water – (10 dips)
11. 70% ethanol – (10 dips)
12. Orange – G stain – (1¹/₂ min)
13. 95% ethanol – (10 dips)
14. 95% ethanol – (10 dips)
15. 95% ethanol – (10 dips)
16. Eosin – Azure (EA 36) - (3 min)
17. 95% ethanol – (10 dips)
18. Absolute ethanol – (10 dips)
19. Absolute ethanol – (10 dips)
20. Xylene - (10 dips)
21. Xylene - (10 dips)
22. Xylene - (10 dips)
23. Mount - (10 dips)

APPENDIX IV

Hematoxylin and Eosin Stain

1. Xylene - (5 min)
2. Xylene - (5 min)
3. Absolute ethanol - (10 dips)
4. 95% ethanol - (10 dips)
5. 80% ethanol - (10 dips)
6. 70% ethanol - (10 dips)
7. Distilled water - (10 dips)
8. Harris's hematoxylin - (3 – 4 min)
9. Distilled water - (10 dips)
10. 1% acid alcohol - (3 dips)
11. Distilled water - (3 dips)
12. Scotts tap water - (1 min)
13. Distilled water - (10 dips)
14. 70% ethanol - (10 dips)
15. 1% Eosin - (30 sec)
16. Distilled water - (10 dips)
17. 95% ethanol - (10 dips)
18. Absolute ethanol - (10 dips)
19. Absolute ethanol - (10 dips)
20. Xylene - (10 dips)
21. Xylene - (10 dips)
22. Xylene - (10 dips)

NB: For smear step 1 and 2 are omitted.

APPENDIX V

CYTOMORPHOLOGY OF THYROID NODULES (main features)**I. NON-NEOPLASTIC****(I) Cyst**

- Numerous macrophage (with or without haemosiderin) with foamy cytoplasm.
- Rare follicular cells.
- Occurs mainly due to haemorrhage, degeneration or necrosis within an oedematous nodule.

(ii) Nodular Goitre

- Uniform sheets of follicular cells.
- Abundant colloid
- Haemosiderin laden macrophages.
- Occasional fibroblasts.
- Naked nuclei of follicular cells.
- Very rare Hurthle cells.

(iii) Graves disease (diagnosis made clinically rarely requires cytologic confirmation)

- Rich in blood
- Very little colloid.
- Enlarged follicular cells with enlarged nuclei.
- Cytoplasm contains round vacuoles containing thin deposits of colloid.

(iv) Acute thyroiditis (Very rare)

- Caused by bacterial infection.
- Very cellular
- Numerous neutrophils, macrophages, some multinucleated in a background of cellular debris.

(v) Subacute thyroiditis (de Quervain's)

Pseudotuberculous, giant cell thyroiditis or viral thyroiditis.

Etiology may be viral (adenovirus)

- Foreign body giant cells/multinucleated histiocytes.
- Langan's giant cell may also be seen.
- Epithelioid cells
- Background inflammatory cells (lymphocytes, neutrophils, plasma cells)
- Few follicular cells, hurthle cells and colloid.

(vi) Hashimoto's (lymphocytic thyroiditis)

- Sheets/groups or Hurthle cells
- Some follicular cells (Singly, small cluster)
- Colloid rare
- Numerous dispersed lymphocytes and plasma cells.

2. (a) NEOPLASTIC (Benign)(i) Follicular Neoplasm

- Very cellular , less colloid
- Cells present in follicular arrangements which show nuclei crowding/overlapping

(ii) Hurthle cells neoplasm

- Very cellular
- Cells lie singly or in loose cohesive groups.
- Cells appear monomorphic, have abundant eosinophilic granular cytoplasm round.
- The nuclei are large, round or eccentric.
- Some cells are binucleated.
- The nuclei have one large round, well defined, single nucleoli.

2. (b)NEOPLASTIC (Malignant)

(i) Papillary carcinoma

- Cellular with monolayered sheets of cells in papillary formations.
- Nuclei of well differentiated show only slight variation in size and shape.
If less differentiated then more variation is noted.
- Intranucleoli clear zones representing intranuclear cytoplasmic invaginations or inclusions are seen (orphan Annie).
- Occasionally ground-glass nuclei are seen.
- Psammoma bodies are seen in 20% of smears.

(ii) Follicular carcinoma

- Cells are arranged in rosette or acinus-like clusters with crowding and overlapping of nuclei.
- Irregularly outlined nuclei with coarse chromatin and prominent nucleoli.
- Intranuclear cytoplasmic inclusions may also be seen.

(iii) Medullary Carcinoma

- Cells occur singly or in small clusters
- Plasmacytoid cells with abundant cytoplasm wherein neurosecretory granules can be demonstrated.
- Bi or multinucleated cells are common.
- Homogenous deposits of amyloid are present in the background.
- Intranuclear cytoplasmic inclusion may be observed.

(iv) Anaplastic carcinoma

- Smear composed of both giant and spindle cells.
- Cells are pleomorphic occurs singly or in groups.
- Cells exhibit bizarre shapes and sizes.
- Cytoplasm appear dense or vacuolated
- Nuclei are large and contain coarsely clumped chromatin, large nucleoli, intranuclear inclusions and bizarre mitotic figures.
- Background composed of tumour diathesis and inflammation.

XII. REFERENCE

1. Koss L.G., Woykes S., Olszewski W. Aspiration biopsy cytologic interpretation and histologic bases. IGAKU-SHOIN, New York. Tokyo. 1992: 271 - 317.
2. Stanley Feld. AACE Clinical Practice Guidelines for the Diagnosis and Management of Thyroid Nodules. AACE. 1996.
3. Kumar V, Ramzi. S, Stanley L.R. Pathologic Basis of disease. Saunders, Philadelphia. 1991: 1203-1216
4. Koss L.G. and Zajicek J. Aspiration biopsy. In: cytology and its Histopathologic bases. Lippincott, Philadelphia. 1992: 1269 - 1279.
5. Suen K.C. Thyroid. In: Scatterfields S.T. Ed, Atlas and Text of aspiration biopsy cytology, William and Wilkins. 1990: 16-40.
6. Calacchio J.A., Lo-Gerjo P., Feind C.R. FNAC diagnosis of thyroid nodules. Review and report of 300 cases. AM J Surg. 1980; (140): 568 - 581.
7. Greg F., Sterrett and Srante R. Orele. In: Fine needle aspiration cytopathology. Edited by Young J.A., Blackwell scientific publications, London. 1993: 41 - 48.
8. Lowhagen T., Willems J.S. Aspiration biopsy cytology in diseases of the thyroid. In Advanced Clinical Cytology. Edited by Koss L.G., Coleman A. London Butterworth. 1981: 201 - 231.
9. Miller J.M., Hamburger J.I., Kini S. Diagnosis of thyroid nodules use of fine needle aspiration and needle biopsy. JAMA. 1979; (241): 481 - 84.

10. Howkins F., Bellido D., Bernak, Rigopoulows S. Valdepenas M.P.R., Lazaro E, Perez-Barrios A. and De Augustin P. FNAB in thyroid cancers and disease. *Cancer*. 1987; (59): 1206 - 1209.
11. Silverman J. West R.E., Larkin E.W. et al. The role of FNAB in the rapid diagnosis and management of thyroid neoplasm. *Cancer*. 1986; (57): 1164 - 70.
12. Georgitis A., Waldrom W., Sims E.J. and Kield G.S. FNA of thyroid use in an average health care facility. *AM J Med*. 1987; (83): 489 - 493.
13. Frable W.J.; Thyroid. In: Thin needle aspiration biopsy, Saunders, Philadelphia. 1983: 152 - 181.
14. Al-Sayer H.M., Kvukowski Z.H., Williams V.M., Matherson N.A. FNAC in isolated thyroid swellings. A prospective two year evaluation. *Br Med J*. 1985; (290): 1490 - 1492.
15. Davidson H.G., Compora R.G. In: Comprehensive cytopathology Edited by Bibo M, Saunder, Philadelphia. 1991: 649 - 666.
16. Suen K.C. How does one separate cellular follicular lesions of the thyroid by fine needle aspiration biopsy. *Diagnostic cytopathology*. 1987; Vol. 4 No. 1: 78 - 81.
17. Ramzy I.M.D. Aspiration of Head, Neck and subcutaneous masses. In seventh annual cytopathology review course. Houston Texas. 1989: 112 - 115.
18. Rifat S.F., Ruffin M.T. Management of thyroid nodules. *AM Fan physician (U.S.A.)*. Sept. 15, 1994; (50) 4: 785 - 90.

19. Danese D., Sciaechitano S. The thyroid nodule. Diagnostic consideration. *Minerva Endocrinol (Italy)*. Sept. 1993; 18 (3): 129 - 37.
20. Piromallic D., Marlelli G., Del Prato I., Collini P., Pillotti S. The role of fine needle aspiration in the diagnosis of thyroid nodules analysis of 795 consecutive cases. *J Surg Oncol (U.S.A.)*. Aug. 1992; 50 (4): 247 - 50.
21. Loy T.J, Saindrum F.X. Diagnostic management of solitary thyroid nodules. *Ann Acad Med Singapore (SINGAPORE)*. Nov. 1989; 18 (6): 658 - 64.
22. Havsoulis P., Leontsevi M., Economou A., Gerasimidis T., Smbarounis C. Fine needle aspiration biopsy cytology in the diagnosis of thyroid cancer. *Br. J Surg (England)*. June 1986; 73 (6): 461 - 4.
23. Liel Y, Zirkin H.J., Sobel R.J. Fine needle aspiration of the thyroid. Five years experience with 183 patients. *Isr J Med Sci (ISRAEL)*. Sep 1985; 21 (9): 719 - 21.
24. Griffies W.S., Donegan E., Abel M.E. The role of fine needle aspiration in the management of thyroid nodules *Laryngoscope (U.S.A.)*. Sep 1985; 95 (9 pt 1): 1103 - 6.
25. Audi – Rogena E.A. Evaluation of Fine Needle Aspiration as a means for diagnosis on accessible tumours at Kenyatta National Hospital, Kenya. A dissertation for Masters in Pathology, University of Nairobi. 1996.
26. Bouvet M, Feldman J.I., Gill C.N., Dillmann W.H, Nahum A.M, Russack V., Robbins K.T. Surgical management of the thyroid

nodules: Patient selection based on the results of FNAC.

Laryngoscope (U.S.A.). Dec, 1992; 102 (12pt.): 1353 - 6.

27. Bapat R.D., Shah S.H., Relekur R.G., Pandit A. Analysis of 105 uninodular goitres. J Post graduate Med (India). Apr - June 1992; 38 (2): 60 - 1.

Tel: 726300 - 19
726550 - 9
726562 - 6
726450 - 9
726581 - 2
Fax: 725272



KENYATTA NATIONAL HOSPITAL
P.O. Box 20723,
NAIROBI.

Email: knh@healthnet.or.ke

Ref: KNH-ERC/01/995

12 April 2001

Ms Rose F. Odhiambo
Dept. of Human Pathology/Clinical Cytology
Faculty of Medicine
University of Nairobi

Dear Rose,

**RE: RESEARCH PROPOSAL "VALUE OF FINE NEEDLE ASPIRATION CYTOLOGY IN THE
DIAGNOSIS OF THYROID NODULES AT KENYATTA N. HOSPITAL" (P939/11/2000)**

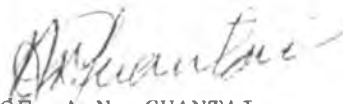
This is to inform you that the Kenyatta National Hospital Ethical and Research Committee has reviewed and **approved** the revised version of your above cited research proposal.

On behalf of the Committee I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of data base that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Thank you.

Yours faithfully,


PROF. A.N. GUANTAI
SECRETARY, KNH-ERC

c.c. Prof. K.M. Bhatt,
Chairman, KNH-ERC,
Dept. of Medicine, UON.
Deputy Director (CS),
Kenyatta N. Hospital.

Supervisor: Dr. F. Rana, Dept. of Human Pathology, UON
The Chairman, Dept. of Pathology, UON
The Dean, Faculty of Medicine, UON