ORIGINAL ARTICLE

AGE-WISE HISTOLOGICAL CHANGES IN ADULT HUMAN PARATHYROID GLANDS

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ABSTRACT: CONTEXT (BACKGROUND): Increasing problems of calcium deficiency with advanced age, it becomes the need of time to focus attention towards parathyroid glands as one of the essential entity. Hence the present study has been undertaken to have an idea about normal variation in the gland as per age. **MATERIAL AND METHODS**: Parathyroid glands from 25 autopsied cases of 20 to 59 years were studied after staining with Hematoxylin and Eosin, Masson's Trichrome and Gomori's Reticulin stains. **RESULTS**: Stroma composed of short often branching reticular fibers along with blood vessels and fat cells. By statistical examination, it was revealed that as age advances amount of stromal fat increased, reaching a peak in age groups between 40-49 years and then slightly decreased irrespective of sex. Oxyphil cells being less numerous than chief cells were distinguished by their dark eosinophilic, granular cytoplasm and arranged mostly in closely packed groups. Oxyphil cells also found as placed singly among chief cells and as continuous masses or anastomosing columns. The number of oxyphil cells increased as age advances irrespective of sex. **CONCLUSIONS:** The amount of stromal fat increased as age advances and it reached to a peak in the middle of the 5th decade thereafter it slightly decreased and also the number of oxyphil cells increased as age advances irrespective of sex.
KEYWORDS: Oxyphil cells, Stromal fat, Quantitative assessment.

INTRODUCTION: The endocrine system is most essential for body regulations and control. Parathyroid gland is formed by four nodules derived from the third and fourth branchial arches. The two pairs of small glands anatomically situated in posterior border in upper and lower pole of the lateral lobe of thyroid gland. It is oval in shape measure 6x4x2 mm. The gland secrets parathoromone to maintain optimal level of calcium in the blood acting in harmony with calcitonin secreted by 'C' cells by the thyroid gland.

Our knowledge of the parathyroid glands has greatly increased since they were first discovered by Richard Owen (1850)[1] as a small, compact yellow glandular body attached to the thyroid gland of an Indian rhinoceros. These glands were unknown to the medical profession until it was rediscovered, named and for the first time adequately described by a Swedish anatomist, Ivar Sandstrom (1880).[2]

Garven H.S.D.(1957)[3] described meaning of parathyroid from Greek word 'para' means beside and 'thyreos' means shield & 'eidos' means like.

Welsh D. A. (1898)[4] examined the parathyroid glands from 40 human autopsies, published an accurate description of the histology of the normal gland and to which little of fundamental importance has been added. He recognized for the first time the "oxyphil" cell, which he distinguished clearly from the predominant "principal" or "chief" cell.

Erdheim J. (1903)[5] published his first paper on the relationship of parathyroid activity and bone diseases including rickets.

Increasing problems of calcium deficiency with advanced age, it becomes the need of time to focus attention towards these glands as one of the essential entity. Accidental removal of these glands during thyroidectomy may cause decreased blood calcium level. Hence the present study has been undertaken to have an idea about normal variation in the gland as per age. This study is of immense help in the field of medicine like biochemistry, pathology, surgery, gynecology and obstetrics etc.

MATERIAL & METHODS: In the present study parathyroid glands from 25 autopsied cases of age between 20 to 59 years, having no hormonal dysfunctions (from death certificates and history from medical records) were collected within 10 to 12 hours after death with consent of the relatives from autopsy room of Department of Forensic medicine and Toxicology, Government Medical College, Nagpur. To reveal age-wise differences, specimens of glands of both male and female have been divided into 4 age groups, i.e. 20 to 29, 30 to 39, 40 to 49 & 50 to 59.

The specimens were fixed in formalin for 24 hours. After proper preservation and fixation, parathyroid tissues were processed for routine histology procedure for paraffin sections and trimmed for expose the tissue. Then serial transverse sections of 5 to 7 µm thickness were taken on Spencer rotary microtome. Sections were stained with Haematoxylin and Eosin (H & E), Masson's Trichrome and Gomori's reticulin stains. All the sections were studied under binocular compound light research microscope and microphotography was done with Karlzeiss photomicrographic unit low power to oil immersion.

Calculation of percentage of stromal fat: Stromal fat was determined with the aid of net micrometer of 20x20 squares (400 points) (Fig. no. 9) in a 10 x focusable wide field eye piece of binocular microscope using a 4x objective, similar to the point counting method by Weibel E.R. (1973).[6] The percentage of stromal fat was calculated as per number of points on fat divided by number of points on parenchyma or interstitial tissue.

$P = h / h+m$

p= Percentage of stromal fat

h = Number of points on stromal fat

m = Number of points over other components

Calculation of average oxyphil scores: A quantitative assessment was made of the number of oxyphil cells by measuring the diameter in microns of each group of oxyphil cells in sections taken through the maximum diameter of each gland and summating the areas thus obtained by the formula $\prod ab$, where 'a' & 'b' represent one half of each major & minor axis respectively, as stated by Christie A. C. (1967)[7]

Statistical Analysis: Data is analysed on stastistical software intercooled STATA version 8.0. Data was presented in mean± standard deviation and categorial variables are expressed in percentages. Chi-square test for linear trend was used to show linear trend between age and oxyphil scores. $P < 0.05$ was taken as statistical significance.

Statistical formulae for calculations:

1) Mean $\rightarrow \bar{x} = \sum x/n$
Where $\rightarrow \bar{x}$ = mean
x = individual value
n= number of observations
$\sum x$= sum of all measurements

2) Standard deviation → S. D. = $\sqrt{\sum(X-\bar{X})^2/n}$

OBSERVATIONS: Entire specimens of parathyroids used in the present study were normal. Quantitative assessment of tissues was also done.

Fibro-elastic vascular connective tissue capsule of collagen and elastic fibers (Fig. no. 2) surrounding parathyroid gland was observed (Fig. no. 1 and 2). Delicate connective connective tissue septa (Fig. No. 1) extends into the parenchyma from capsule carrying blood vessels and fat cells (Fig. no. 2) which divide the parenchyma into incomplete and irregular lobules (Fig no. 1). Parenchyma of gland revealed chief and oxyphil cells (Fig. no. 5).

Observations were done mainly under following headings:

1) Stromal fat 2) Oxyphil cells

Stromal fat: Stroma composed of short often branching reticular fibres (fig. 3) along with blood vessels and fat cells in it (fig 2) was observed.Parathyroid gland enclosed in capsule showing collagen fibres with Masson's Trichrome stain and from which vascular septa carrying fat cells in the substance of gland was observed (Fig no. 4). Stromal fat cells were observed (Fig. No. 5 and 6) and quantitative assessment of stromal fat in different age groups of both sexes was done and by statistical examination, it was found that the amount of stromal fat increased with increased age and reached a peak in the middle of the 5th decade thereafter it slightly decreased as shown in Table no 1.

Oxyphil cells: Oxyphil cells were observed and quantitatively studied. Oxyphil cells, being less numerous than chief cells were distinguished by their dark eosinophilic, granular cytoplasm (Fig. no. 7). They were arranged mostly in closely packed groups without interstitial fat in between the cells (Fig. no. 2). A large encapsulated mass of oxyphil cells seen at the periphery of the gland near its capsule (Fig. no. 8). Oxyphil cells were also seen as placed singly among chief cells (Fig. no. 5), as continuous masses (Fig. no. 2) and anastomosing columns (Fig. no. 6). Average oxyphil scores were calculated and shown in Table no. 2. It was observed by statistical analysis that number of oxyphil cells increased in number as age advances irrespective of sex.

DISCUSSION: Erdheim J. (1903)[5] showed the presence of fat in the stroma. He noted the appearance of fat after 3rd decade with gradual increase with increasing age. Castleman B. and Mallory T.B. (1935)[8] observed that following puberty large fat cells appear in the stroma and increase in number until about 40 years of age. The fat tissue remains fairly constant during

middle age and does not increase with old age. According to Roth S. I. (1962)[9] around puberty fat cells appear in the stroma which increase in amount with advancement of age. He further stated that this increase continues until the middle of 5th decade and thereafter fat slightly decreases. Maximow A. A., Bloom W. (1949)[10], Garven H.S.D. (1957)[3], Kelly D. E., Wood R. L. and Enders A. C. (1984)[11] stated that the parathyroids are infiltrated by large number of fat cells as age advances. Roth S. I. (1996)[12] stated the first appearance of adipocytes in the stroma in 1st decade and reaching to a peak in 3rd to 5th decade.

Bloom W. and Fawceet D. W. (1962),[13] Khan A. A., Osman H.AE and Ahmed M. (2001)[14] stated that adipocytes increase with age. In the present study only adults were included and it was observed that stromal fat increased with increasing age and reached peak in middle of 5th decade thereafter it slightly decreased. Hence the present study partially correlated with the above mentioned authors.

Garven H. S. D. (1957)[3], Kelly D. E., Wood R. L. and Enders A. C. (1984)[11] stated that because of fat cells solid appearance of gland is lost. The present study revealed the same.

With advanced age stromal fat increased which causes a division of parenchyma into thinner cords and masses which in part responsible for extreme structural variations seen in the normal parathyroid glands.

Sandstrom I. (1880)[2] stated that the granular cells undoubtedly oxyphils have the tendency to lie near the surface. Leeson T. L., Leeson C. R. and Paparo A. A.(1988),[15] Pal G.P. (2005)[16] quoted oxyphil cells are less numerous than the chief cells. Fawcett D. W. and Ronald P. J. (2002)[17] stated that oxyphil cells which are few in number, are larger than chief cells and they stain more deeply with eosin. According to Anthony L. M. (2010)[18] oxyphil cells, larger than principal cells which are characterized by acidophilic cytoplasm. The present study revealed the same.

Maximow A. A., Bloom W. (1949)[10] quoted that oxyphil cells are arranged as continuous masses and anastomosing columns.. Fawcett D. W. and Ronald P. J. (2002)[17,] Gilmour J. R. (1939)[19,] Young B. and Heath J.W. (2000)[20] stated arrangement of oxyphil cells in groups or as continuous masses or singly in between the chief cells. These findings correlated with the present study. Castleman B. and Mallory T. B. (1935)[8] studied parathyroid tissues extensively in 150 autopsied cases and observed sharply circumscribed, unencapsulated, the large islands of oxyphil cells after 40 to 50 years.

He observed increase in number of oxyphil cells with increasing age. Gilmour J.R.(1939)[19] studied parathyroid tissues in great details from 428 autopsied cases and observed oxyphil cells having acidophilic granular cytoplasm increases in number with increasing age. He further observed tendency of oxyphil cells to lie near the surface of gland with rare interstitial fat cells in between. He also observed the oxyphil cells arranged in groups. Current findings revealed the same.

Castleman B. and Mallory T. B. (1935)[8], Gilmour J. R. and Martin W. J. (1937),[21] Christie A. C. (1967)[7], Gray H. (2008),[22] Gunasegran J. P.(2010)[23] reported increase in number of oxyphil cells with increase in age. The present finding revealed the same.

Comparison of average oxyphil scores for each decade in both sexes was done with study of Christie A. C. (1967)[7] and shown in Table no. 3. It was observed that both scores were somewhat similar.

EM study by Munger B. L. and Roth S. I. (1963)[24] suggested that oxyphil cells are not involved in hormone synthesis or secretion though abundant mitochondria suggest a high metabolic activity. They further showed the lack of organelles necessary for protein synthesis and secretion in normal oxyphil cells. It can be predicted from the above that oxyphil cells are degenerating cells and with their increased number with advanced age activity of gland decreased.

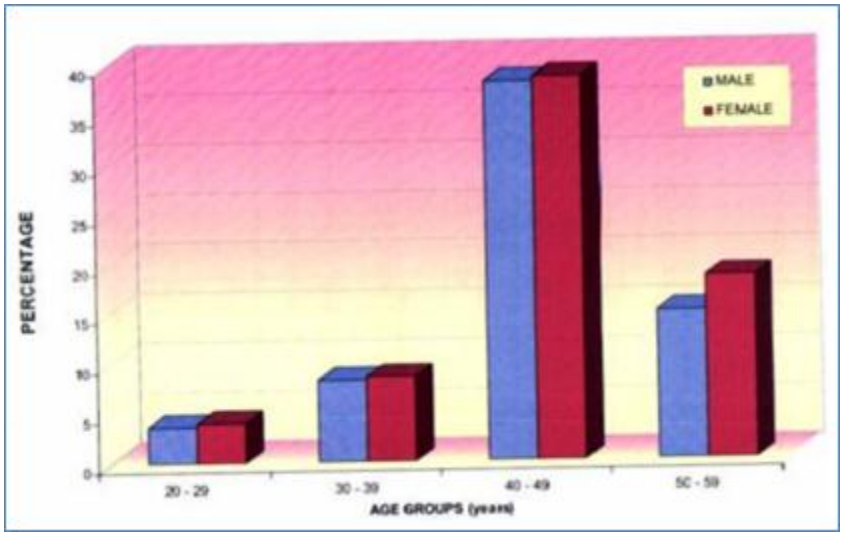
CONCLUSIONS:

1. By statistical analysis it was revealed that the amount of stromal fat (fat cells in connective tissue) increased as age advances and it reached to a peak in the middle of the 5th decade thereafter it slightly decreased and also the number of oxyphil cells increased as age advances irrespective of sex.
2. An increase of stromal fat and the number of oxyphil cells with advanced age causes reduced activity of gland resulting in decreased levels of calcium in blood, suggesting the need of supplementary calcium with vitamin D_3 as age advances. This study is of immence help in field of medicine like Bio-chemistry, pathology, surgery, gynaecology and obstetrics etc.

Age groups (years)	Male	Female
20-29	3.66	4.0
30-39	8.2	8.5
40-49	38.13	38.56
50-59	14.9	18.3
Overall mean± S.D.	17.06±14.28	19.57±15.74

Table no. 1: Showing average percentage of stromal fat in each decade of both sex

In the present study average percentage of stromal fat in males was 3.66 and in females it was 4.0 in age group between 29-29 years. The average percentage of stromal fat in males was 8.2 and in females it was 8.5 in age group between 30-39 years. The average percentage of stromal fat in males was 38.13 and in females it was 38.56 in age group between 40-49 years. The average percentage of stromal fat in males was 14.9 and in females it was 18.3 in age group between 50-59 years. The overall mean in males was 17.06±14.28 & in females was 19.57±15.74.



Graph 1: Average percentage of stromal fat in each decade of both sexes

Age groups (years)	Male	Female
20-29	6.0	15.0
30-39	18.0	85.50
40-49	35.25	199.33
50-59	150.0	308.33
Overall mean±S.D.	55.40±16.02	172.40±118.13

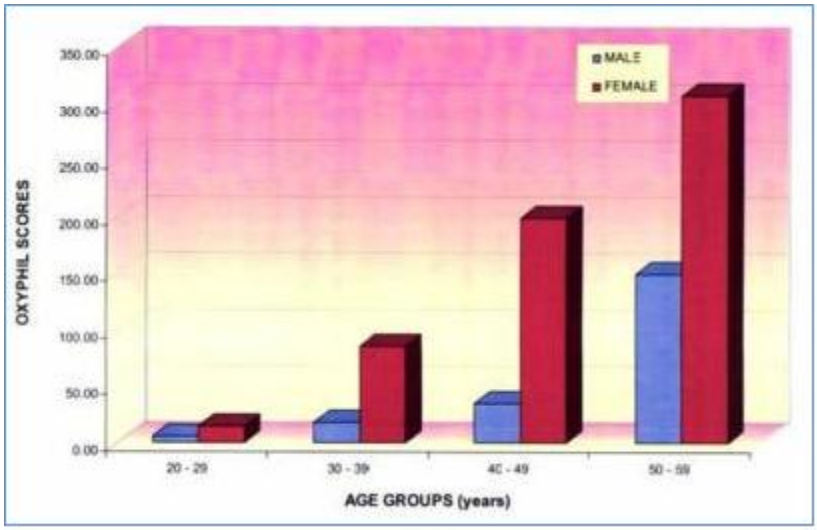
Table no 2: Showing average oxyphil scores for each decade in both sex (x10^3square microns/gland)

For linear trend,

P value for males $\Rightarrow$ $P < 0.001$

P value for females $\Rightarrow$ $P < 0.001$, Highly significant

In the present study average oxyphil scores in males was 6 x10^3 square microns/gland and in females it was was 15 x10^3 square microns/gland in age group between 29-29 years. Average oxyphil scores in males was 18 x10^3 square microns/gland and in females it was 85.50 x10^3 square microns/gland in age group between 30-39 years. Average oxyphil scores in males were 35.25 x10^3 square microns/gland and in females it was 199.33 x10^3 square microns/gland in age group between 40-49 years. Average percentage oxyphil scores in males were 150 x10^3 square microns/gland and in females it was 308.33 x10^3 square microns/gland in age group between 50-59 years. The overall mean of average oxyphil scores in males was 55.4 ± 16.02x10^3 square microns/gland) and in females it was 172.4± 118.13 x 10^3square microns/gland.



Graph 2: Average oxyphil scores for each decade in both sexes

Age Groups (years)	Christie A. C.(1967)		Present Study	
	Male	Female	Male	Female
20-29	6.4	16.0	6.0	15.0
30-39	19.0	86.6	18.0	85.5
40-49	35.0	201.0	35.25	199.33
50-59	151.0	315.0	150.0	308.33

Table No. 3: Comparison of average oxyphil scores for each decade in both sex (x 10^3 square microns/gland)

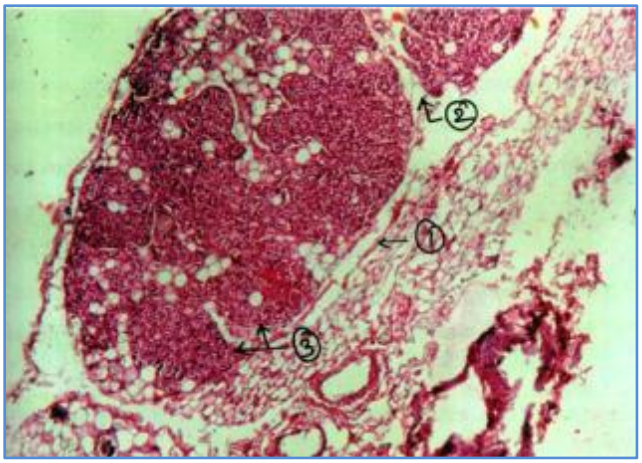


Fig. 1: 52 yrs/F, H&E stain, x 40

1) Capsule 2) Septa 3) Incomplete and irregular lobules

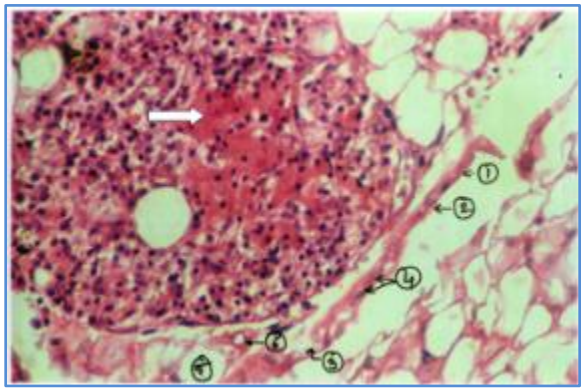


Fig. 2: 52 yrs/ F, H & E stain, x200, showing oxyphil cells in group indicated by white arrow

1) Capsule 2) Collagen fibres 3) Elastic fibres 4) Nuclei of connective tissue cells 5) Fat cells 6) Blood vessels

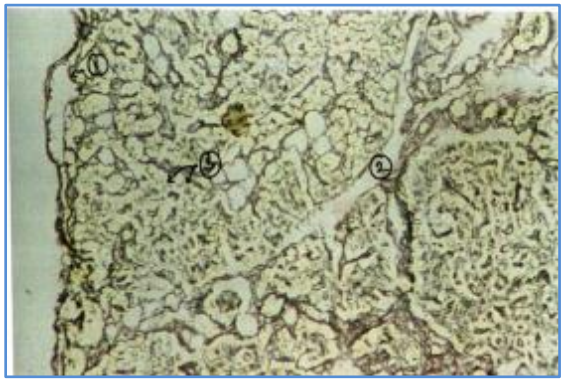


Fig. 3: 25 yrs/F, Reticulin stain, x100

1) Collagen fibres 2) Septa 3) Reticular fibres

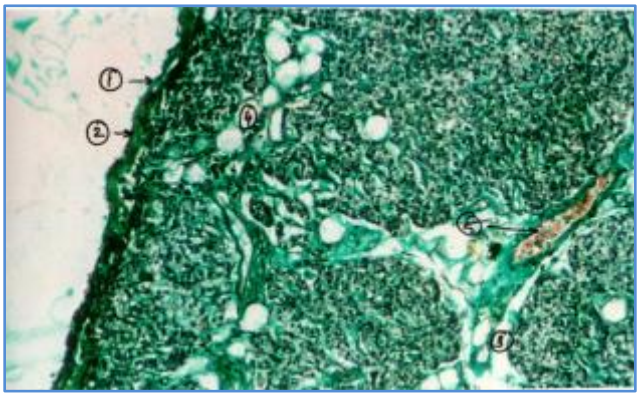


Fig. 4: 23yrs /M, Masson's Trichrome stain, x100

1) Capsule 2) Collagen fibres 3) Septa 4) Fat cells 5) Blood vessel

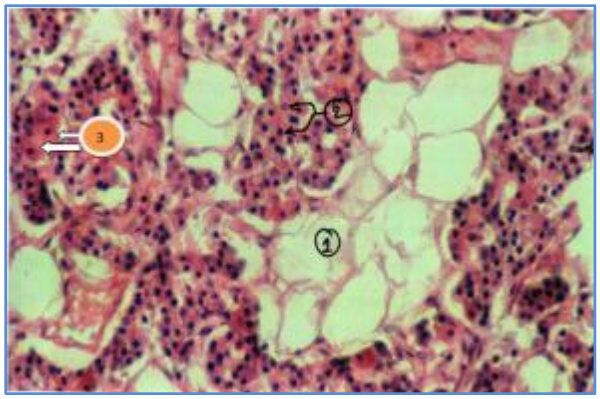


Fig. 5: 44 yrs/ F, H & E stain, x200

1) Fat cells 2) Chief cells 3) Oxyphil cells

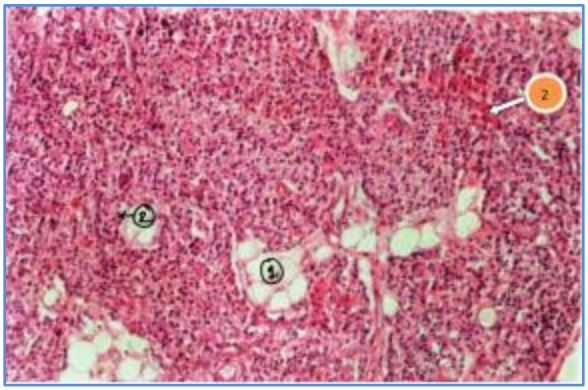


Fig. 6: 35yrs /M, H & E stain, x100

1) Fat cells 2) Oxyphil cells in anastomosing cords

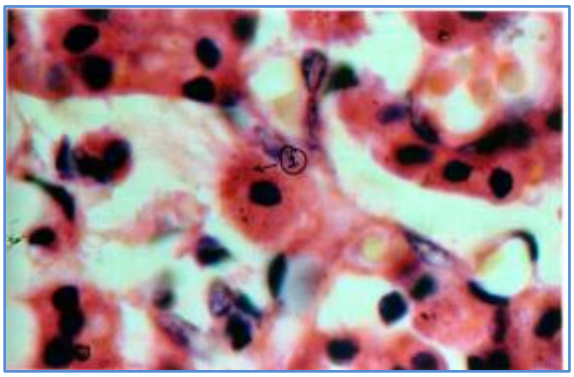


Fig. 7: 33yrs/ M, H & E stain, x1000

1) Granules of oxyphil cells

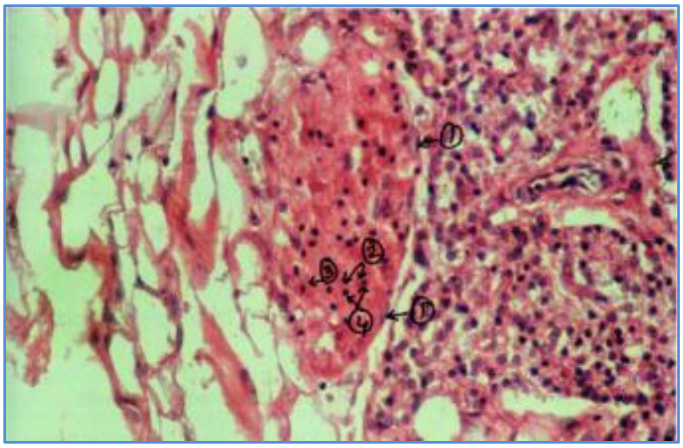


Fig. 8: 59 yrs/F, H & E stain, x 200

1) Nuclei of connective tissue cells 2), 3) & 4) Oxyphil cells in groups at the periphery

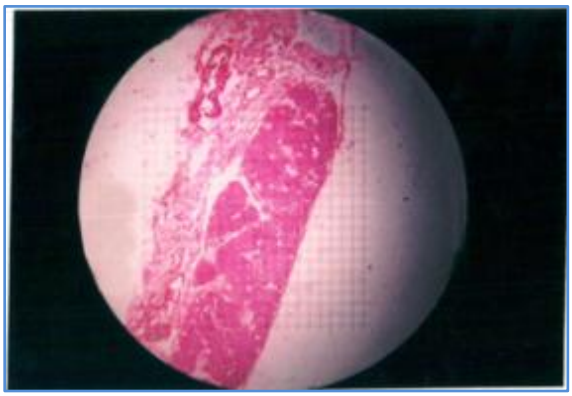


Fig. 9: Net micrometer of 20 x 20 squares (400 points)

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