

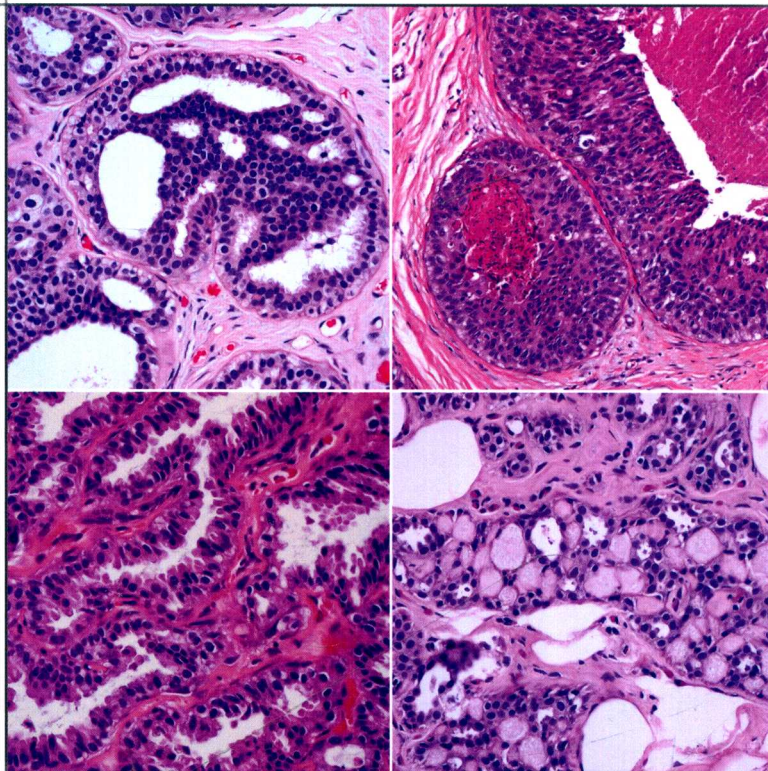


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**DIFFERENTIAL DIAGNOSES IN
SURGICAL PATHOLOGY**

Breast

Jean F. Simpson
Melinda E. Sanders



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Differential Diagnoses in Surgical Pathology: Breast

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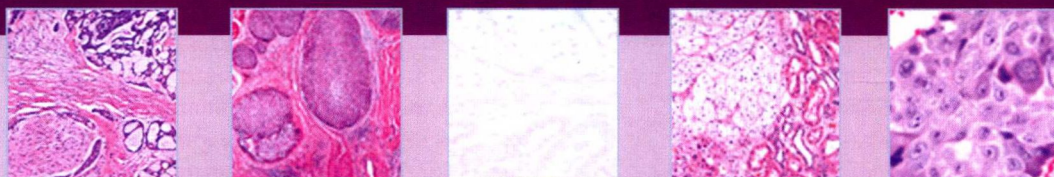
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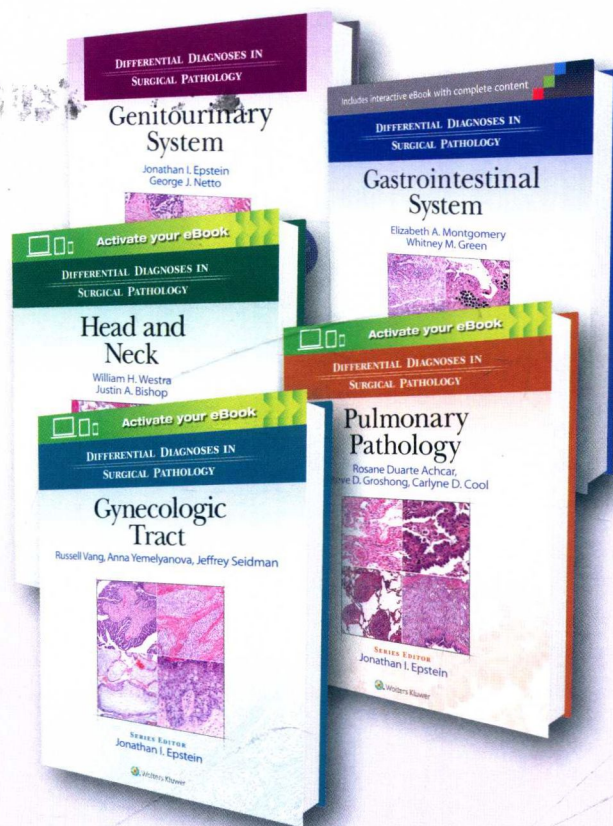
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DEDICATION

In memory of Lowell W. Rogers and J. Allan Tucker, gentle giants who inspired others.

PREFACE

Histopathology remains the cornerstone of the diagnosis and treatment of breast disease. There have been advances in breast imaging techniques, molecular analysis, and immunotherapy of breast cancer, yet the fundamental decisions regarding the need for additional surgery, chemoprevention, radiation, and/or chemotherapy are based on morphologic features.

Histopathology is far from a static or “out of date” discipline. Indeed, specific histologic criteria have been defined that allow for reproducibility in diagnosis; linking these criteria to outcome data for thousands of women through long-term follow-up studies has defined the epidemiology of benign breast disease and helps identify women who may benefit from chemoprevention strategies. These studies also provide concrete evidence that merely undergoing a breast biopsy does not increase risk for later cancer development, a welcome relief for thousands of women.

The widespread use of core needle biopsy has had a major impact on the practice of breast pathology, and many of the images shown in this book are from core needle biopsy specimens. Our approach to the diagnosis of core biopsy specimens is similar to a frozen section, that is, what should the next step be, specifically, should the lesion be formally excised?

We are grateful for the opportunity to have learned breast pathology from Dr. David Page, whose adherence to reproducible criteria and interpretation within the clinical context guide us daily. We also are grateful to pathologists who have trusted us with their difficult cases in consultation. The vast majority of such cases come with a differential diagnosis of one or two entities, underscoring the importance of a textbook that compares and contrasts differential diagnostic partners.

Jean F. Simpson
Melinda E. Sanders

CONTENTS

Preface		vii
Chapter 1	NONPROLIFERATIVE ALTERATIONS OF ACINI	1
Chapter 2	EPITHELIAL PROLIFERATIVE LESIONS, USUAL AND ATYPICAL DUCTAL HYPERPLASIA	17
Chapter 3	LOBULAR NEOPLASIA AND ITS DISTINCTION FROM OTHER EPITHELIAL PROLIFERATIVE LESIONS	31
Chapter 4	DUCTAL CARCINOMA IN SITU	47
Chapter 5	PAPILLARY AND SCLEROSING LESIONS	91
Chapter 6	INVASIVE CARCINOMA: SPECIAL TYPES AND IMPORTANT CONSIDERATIONS	121
Chapter 7	FIBROEPITHELIAL LESIONS	175
Chapter 8	BENIGN AND REACTIVE STROMAL LESIONS	195
Chapter 9	SENTINEL LYMPH NODES	223
Chapter 10	VASCULAR LESIONS	237
Chapter 11	MALE BREAST	257
Index		269

Nonproliferative Alterations of Acini

- 1.1** Columnar cell lesion without atypia vs. Cystically dilated lobular unit
- 1.2** Columnar cell lesion without atypia vs. Columnar cell lesion with atypia
- 1.3** Apocrine change vs. Columnar cell lesion with atypia
- 1.4** Secretory change vs. Columnar cell lesion with atypia
- 1.5** Cystically dilated lobular unit vs. Duct ectasia
- 1.6** Mucocele-like lesion vs. Disrupted cyst

	Columnar Cell Lesion without Atypia	Cystically Dilated Lobular Unit
<i>Age</i>	Adult women	Adult women
<i>Imaging findings</i>	Calcifications, punctuate in clusters	Calcification or lobulated mass, often with septations
<i>Etiology</i>	Unknown	Unknown change in specialized connective tissue results in unfolding of the lobular unit
<i>Histology</i>	<ol style="list-style-type: none"> 1. Lobular unit is enlarged 2. Lined by columnar cells that maintain basolateral polarity (<i>Figs. 1.1.1–1.1.3</i>) 	Unfolded, coalescing acini, lined by a single epithelial cell layer, usually cuboidal or apocrine (<i>Figs. 1.1.4–1.1.6</i>)
<i>Special studies</i>	None	None
<i>Treatment</i>	None	Fine needle aspiration if symptomatic
<i>Clinical implication</i>	No risk implications	No risk implications

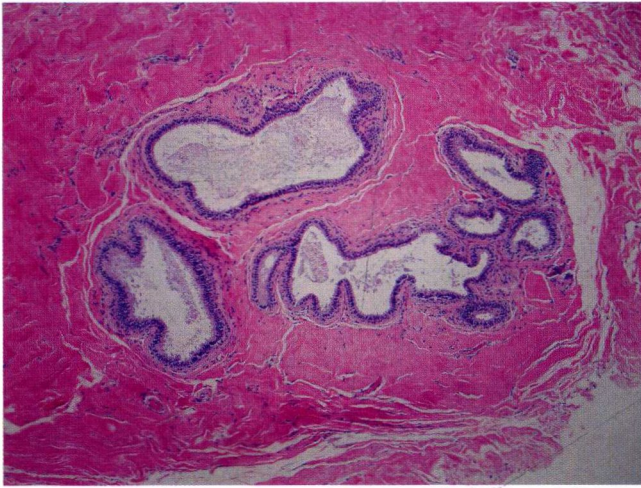


Figure 1.1.1 Columnar cell lesion without atypia: The lobular unit is enlarged and consists of dilated acini with undulating contours. The intra-lobular connective tissue is fibrotic.

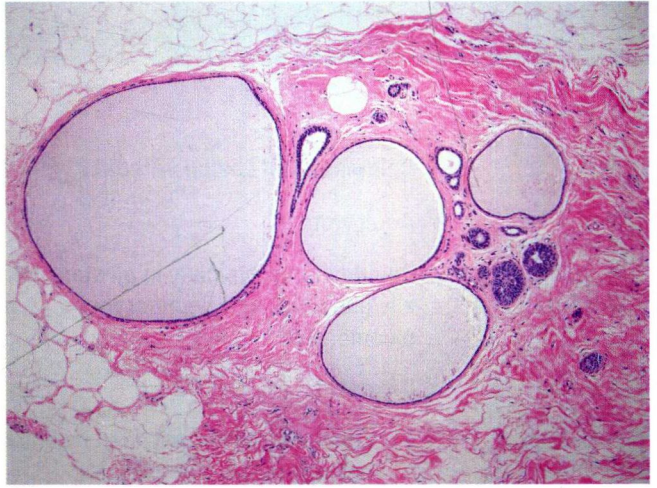


Figure 1.1.4 Cystically dilated lobular unit: Half of the acini of this lobular unit are expanded, but maintain rounded contours.

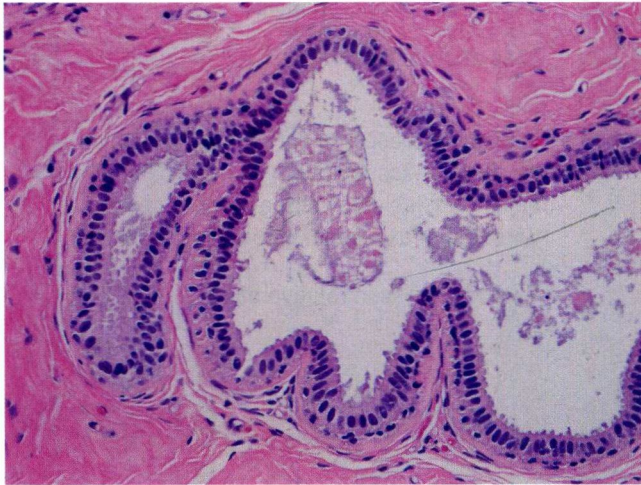


Figure 1.1.2 The dilated acini contain secretions and are lined by a single layer of columnar cells; the relationship with the myoepithelial cell layer is orderly in columnar cell lesions without atypia.

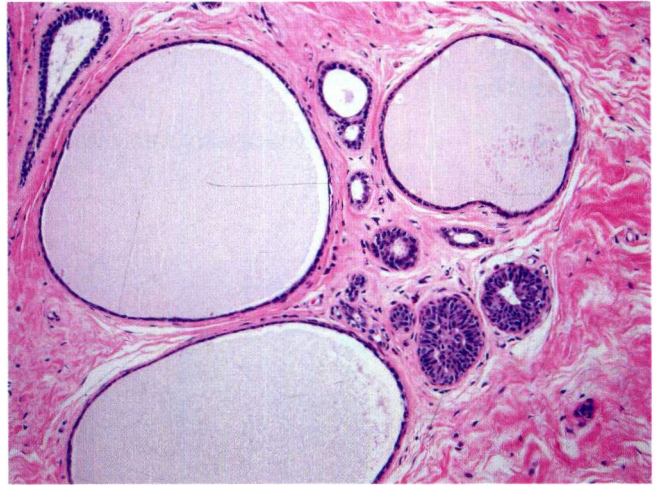


Figure 1.1.5 The dilated acini contain translucent secretions and lack histiocytes or inflammatory cells. Acini of normal size and configuration are present adjacent to the dilated acini.

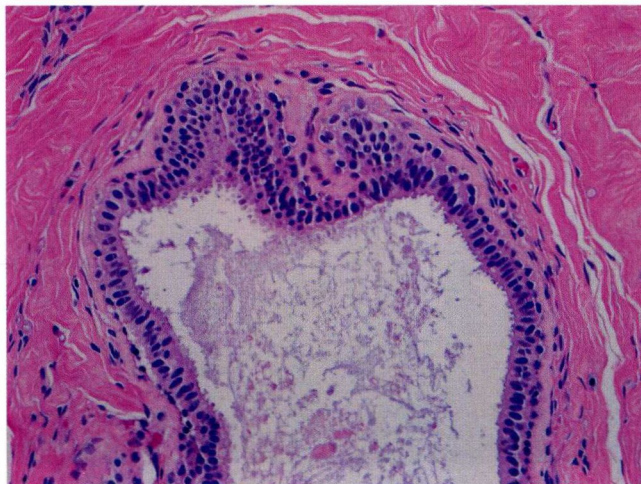


Figure 1.1.3 The columnar cells maintain basolateral polarity. Nuclei are small, without obvious nucleoli. The myoepithelial cells are prominent.

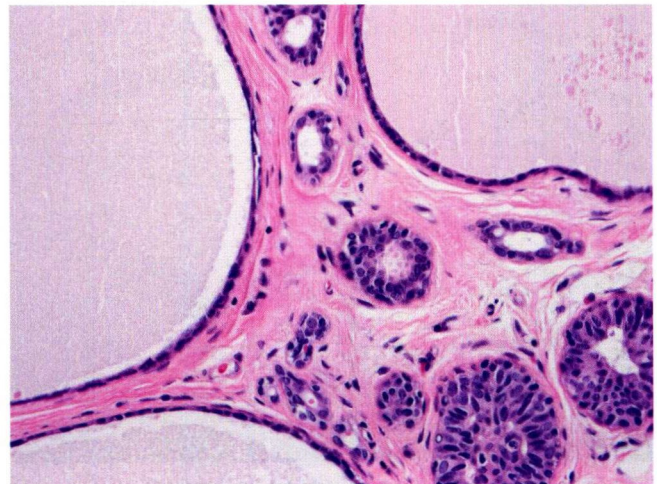


Figure 1.1.6 The cystically dilated acini are lined by a single layer of normally polarized, low cuboidal epithelium, with patchy attenuation.

	Columnar Cell Lesion without Atypia	Columnar Cell Lesion with Atypia
<i>Age</i>	Adult women	Adult women
<i>Imaging findings</i>	Calcifications, typically in clusters, usually punctate, may be amorphous, rarely pleomorphic	Calcifications, typically in clusters, may be punctate or amorphous, rarely pleomorphic
<i>Etiology</i>	Unknown	Unknown
<i>Histology</i>	<ol style="list-style-type: none"> 1. Enlarged lobular unit lined by one or two cell layers 2. Maintenance of basolateral polarity 3. Nuclei lack prominent nucleoli (Figs. 1.2.1–1.2.5) 	<ol style="list-style-type: none"> 1. Enlarged lobular units lined by epithelial cells that have lost basolateral polarity 2. Rounded nuclei often with prominent nucleolus (Figs. 1.2.6–1.2.10) 3. Lacks architectural features of atypical ductal hyperplasia (ADH), e.g., Cribriform spaces or micropapillae
<i>Genetic abnormalities</i>	None	Loss of chromosome 16q
<i>Treatment</i>	Excision unnecessary if detected on core biopsy	Excision if present in core biopsy specimen because of association with more clinically significant lesions; no treatment necessary if detected in excisional biopsy specimen
<i>Clinical implication</i>	None	Slight increase in relative cancer risk (1.5×)

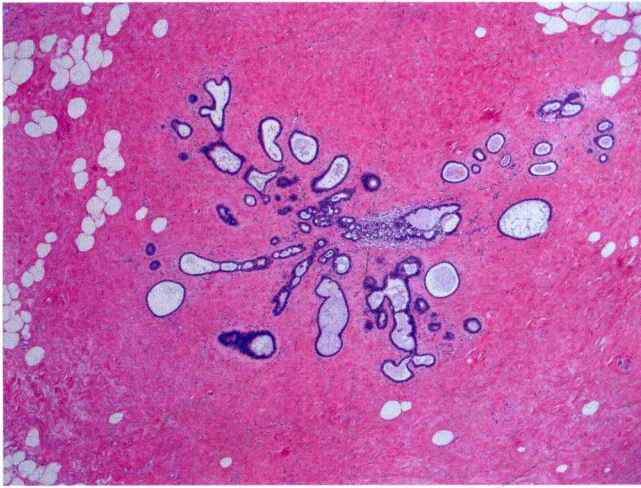


Figure 1.2.1 Columnar cell lesion without atypia. Most acini in the lobular unit are enlarged and have irregular contours.

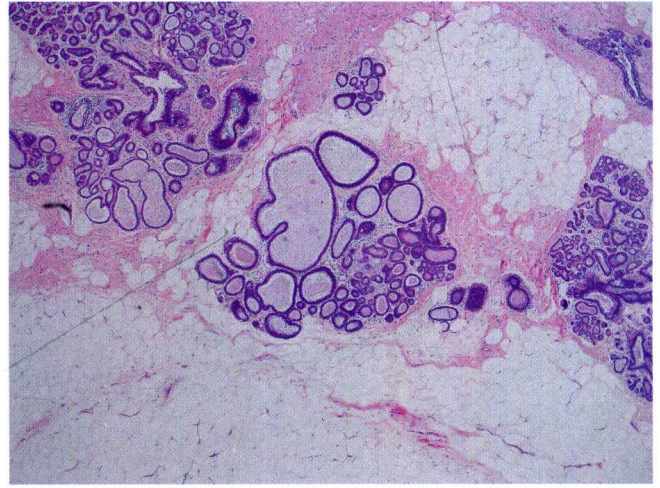


Figure 1.2.6 Columnar cell lesion with atypia: Two adjacent lobular units contain several enlarged, dilated acini. At low power, the character of the lining cells is not evident.

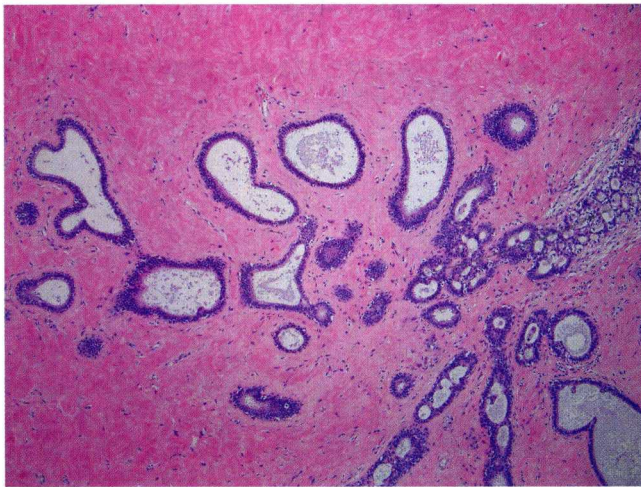


Figure 1.2.2 The enlarged acini contain calcifying secretions and a single columnar luminal epithelial cell layer.

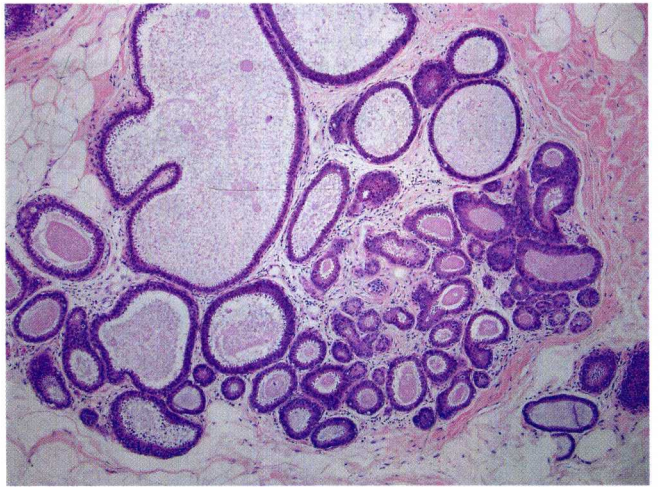


Figure 1.2.7 At higher power, the "globoid" nature of the dilated acini is evident in columnar cell lesions with atypia.



Figure 1.2.3 The acinar cells are distinctly elongated and have prominent apical snouts.

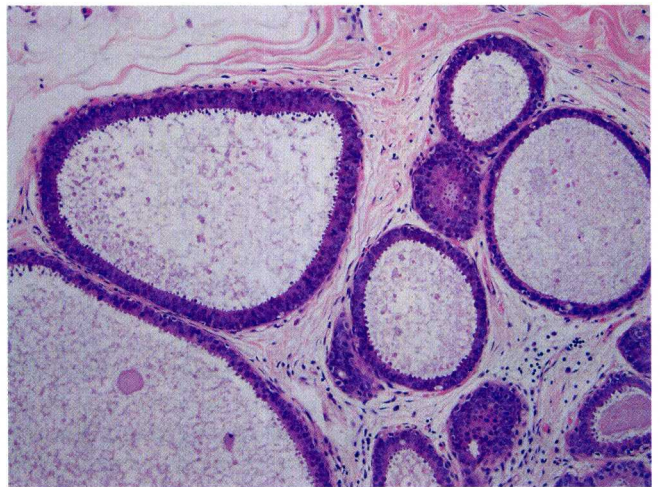


Figure 1.2.8 Columnar cell lesion with atypia: These dilated acini contain secretions and are lined by cells with rounded nuclei with an increased nuclear to cytoplasmic ratio.

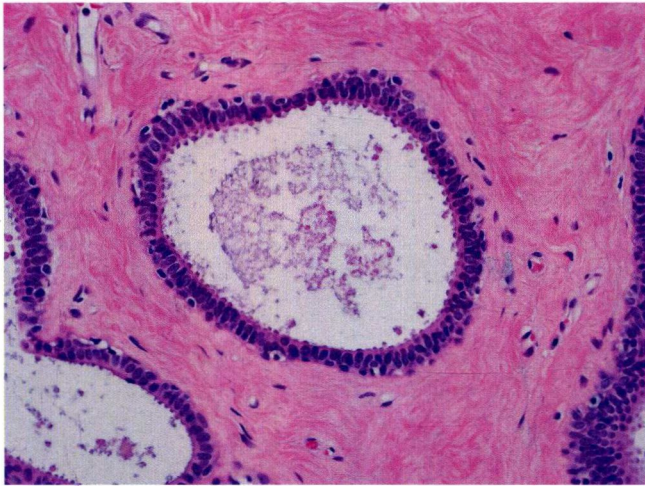


Figure 1.2.4 The columnar lining cells maintain normal basolateral polarity. The myoepithelial layer is regularly identifiable.

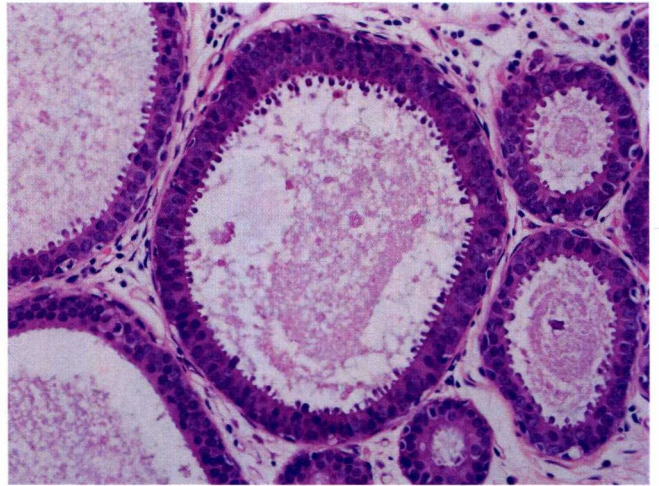


Figure 1.2.9 The acini are lined by several layers of luminal epithelial cells with loss of a polar arrangement. Myoepithelial cells are present, but not prominent. Apocrine snouts are observed in most acini. Note the conspicuous absence of architectural features diagnostic of ADH i.e., cribriform spaces, bars, or bulbous papillae.

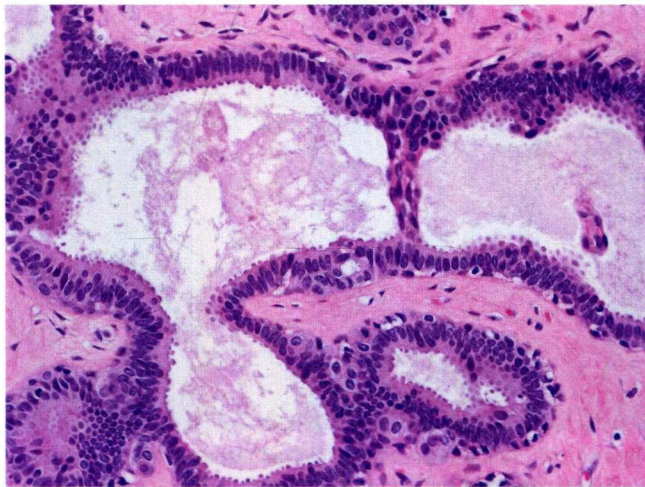


Figure 1.2.5 Although an occasional cellular bridge is noted, the nuclei are overlapping with their long axes oriented parallel with the bar, diagnostic criterion for usual hyperplasia. Focal pseudostratification or tangential sectioning may create the appearance of multiple cell layers and loss of polarity.

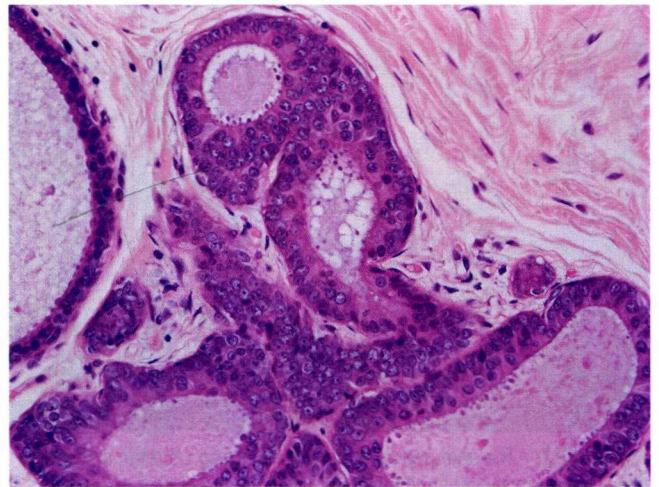


Figure 1.2.10 In addition to loss of polarity, the nuclei have readily apparent nucleoli; compare with the adjacent acinus lined by a single layer of smaller nuclei (left side).

	Apocrine Change	Columnar Cell Lesion with Atypia
Age	Adult women	Adult women
Imaging findings	"Milk of calcium" type calcifications may be present in clusters; aggregated apocrine cysts may form a mass with associated calcifications	Calcifications typically in clusters, may be punctate, amorphous, or rarely pleomorphic
Clinical associations	Often perimenopausal	No specific associations
Histology	<ol style="list-style-type: none"> 1. Dilated lobular unit (<i>Fig. 1.3.1</i>), lined by a single layer of apocrine cells (<i>Fig. 1.3.2</i>) 2. May have apical red cytoplasmic granules 3. Nuclei enlarged with prominent nucleolus (<i>Figs. 1.3.3 and 1.3.4</i>) 	<ol style="list-style-type: none"> 1. Enlarged lobular units lined by epithelial cells that have lost normal basolateral polarity 2. Crowded, rounded, enlarged nuclei, often with a prominent nucleolus 3. Lacks architectural features of ADH, e.g., Cribriform spaces or micropapillae (<i>Figs. 1.3.5–1.3.8</i>)
Genetic abnormalities	None	Loss of chromosome 16q
Treatment	Cyst drainage by fine needle aspiration	Excision if present in core biopsy specimen because of association with other more clinically significant lesions; no further treatment necessary if detected in excisional biopsy specimen
Clinical implication	No increase in cancer risk	1.5× increased relative cancer risk of subsequent breast cancer

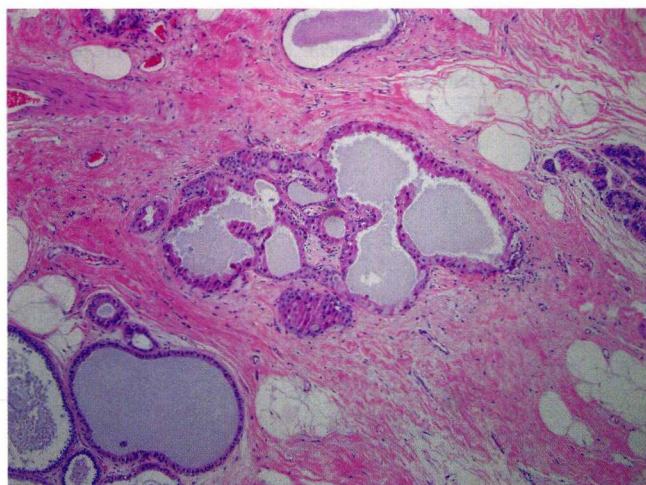


Figure 1.3.1 Apocrine change involving two adjacent lobular units. Acini have partially coalesced, and contain eosinophilic secretory material.

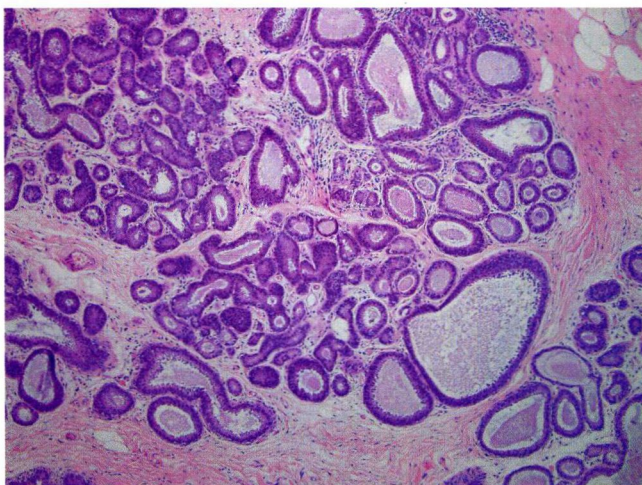


Figure 1.3.5 Columnar cell lesion with atypia: Three adjacent lobular units are expanded with variably sized acini; pronounced basophilia reflects an increased nuclear to cytoplasmic ratio.



Figure 1.3.2 Apocrine change composed of dilated acini lined by a single layer of cuboidal cells.

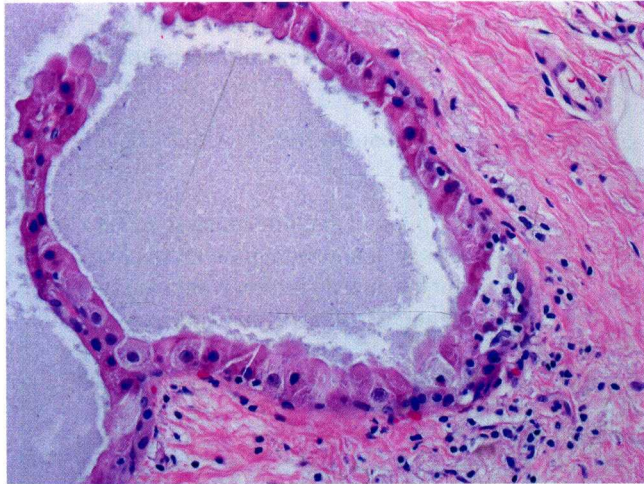


Figure 1.3.3 Apocrine cytoplasm is abundant, pale to eosinophilic, and finely granular. A normal nuclear to cytoplasmic ratio is maintained.

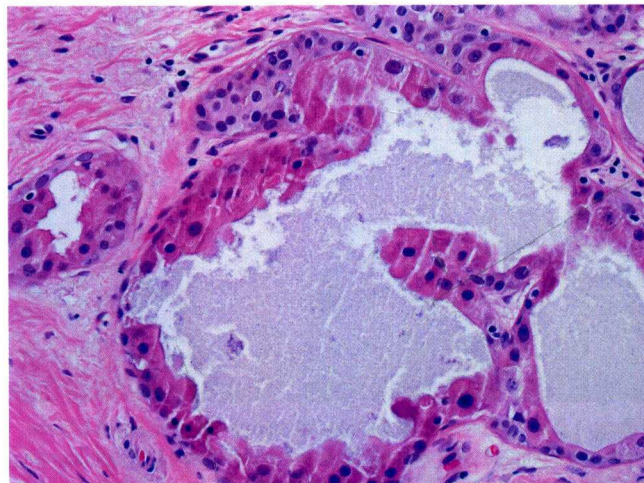


Figure 1.3.4 Bland-appearing, rounded nuclei are characteristic, and normal polarity is maintained. The apical compartment of the cytoplasm contains characteristic red granules.

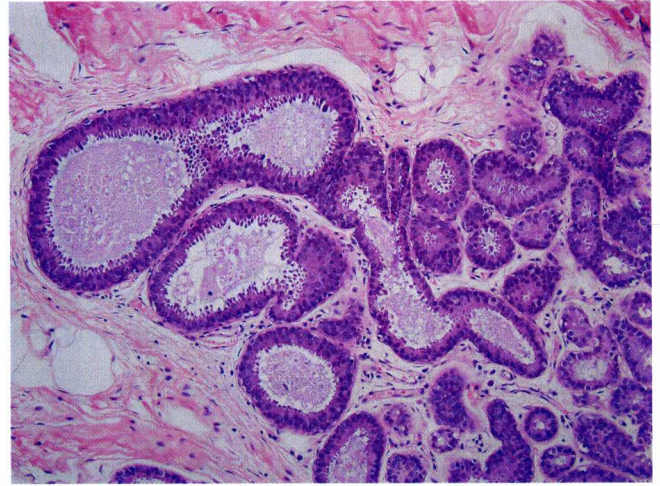


Figure 1.3.6 Dilated acini are lined by columnar cells with prominent apocrine snouts. Nuclear enlargement and lack of the normal basolateral polarity are evident at this magnification.

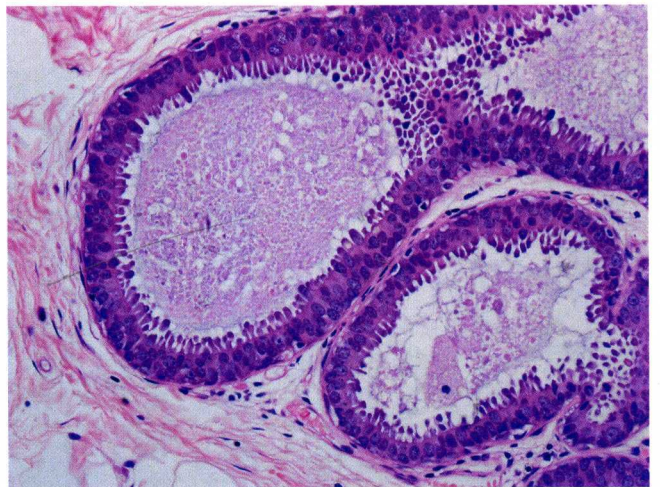


Figure 1.3.7 Columnar cell lesion with atypia: A single pseudostratified cell layer shows "rounding up" of nuclei. Myoepithelial cells are present, but not prominent. There are no complex architectural arrangements to suggest ADH.

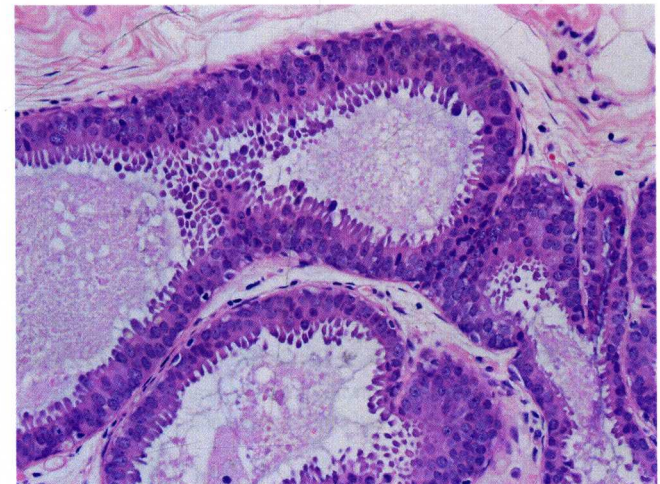


Figure 1.3.8 Tangential sectioning may give the appearance of multilayering. Focally, the apical snouts are apposed, but there are no true arches or bridging.

	Secretory Change	Columnar Cell Lesion with Atypia
Age	Any age, usually women in reproductive years	Any age, predominantly 40–60 y
Imaging findings	Clustered mammographic calcifications, usually spherical	Clustered mammographic calcifications, may be punctate, amorphous or rarely pleomorphic
Clinical associations	Often present postlactation; prolactin-producing pituitary tumors; drugs causing prolactin secretion	Unknown
Histology	<ol style="list-style-type: none"> 1. All or part of a lobular unit may show secretory change (<i>Fig. 1.4.1</i>) 2. Acini are variably dilated (<i>Fig. 1.4.2</i>) and lined by cells that have eosinophilic, bubbly cytoplasm 3. Secretory material is present in lumens (<i>Fig. 1.4.2</i>) 4. Cells contain small dark nuclei with a hob-nail appearance (<i>Fig. 1.4.3</i>) 5. Nuclei are in the apical compartment, similar to the Arias-Stella reaction (<i>Fig. 1.4.3</i>) 	<ol style="list-style-type: none"> 1. Enlarged basophilic lobular units, with a “globoid configuration,” having variably dilated acini (<i>Fig. 1.4.4</i>) 2. Lumens contain secretory material which is frequently calcified (<i>Fig. 1.4.5</i>) 3. Acini are lined by cells lacking basolateral polarity (<i>Figs. 1.4.6 and 1.4.7</i>) 4. Nuclei are round, and have prominent nucleoli (<i>Fig. 1.4.7</i>) 5. Apical snouts are common (<i>Fig. 1.4.8</i>)
Genetic abnormalities	None	Loss of chromosome 16q
Treatment	None	Excisional biopsy if present in core needle biopsy because of association with other clinically significant lesions; no further treatment if present in an excisional specimen
Clinical implication	None	1.5× increased relative risk of subsequent breast cancer

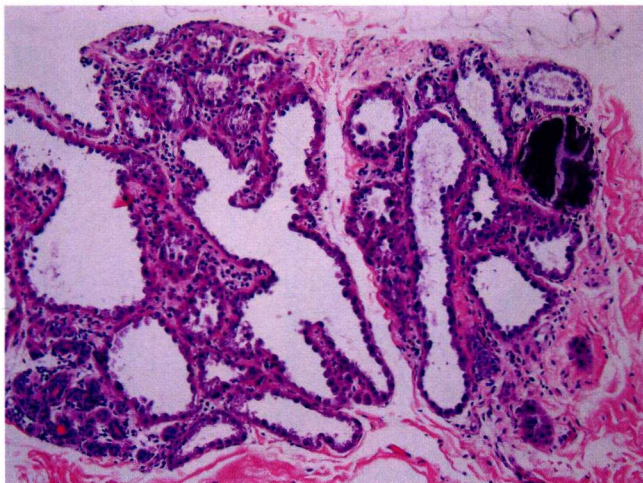


Figure 1.4.1 Secretory change partially involving two adjacent lobular units, characterized by several dilated acini, one of which has undulating contours. Note the spherical calcification (right). The lobular unit in the bottom left contains several normal acini.

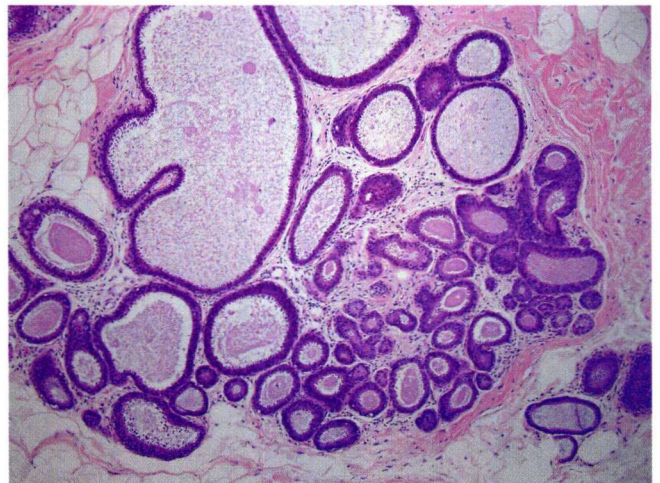


Figure 1.4.4 Columnar cell lesion with atypia: Note the globoid configuration of the acini in this enlarged lobular unit; most contain secretory material within their lumens.