The University of Oregon

STUDIES IN CHRONIC PARANASAL SINUSITIS

VI.

OBSERVATIONS ON THE NORMAL HISTOLOGY OF THE MUCOUS MEMBRANE LINING THE VARIOUS PARANASAL SINUSES OF MAN

A Thesis Submitted to the Faculty of the Graduate School in Partial Fulfillment for*

A Master of Arts Degree.

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P R E F A C E

A brief period of but 50 years, an interval within the memory of living men, covers our knowledge of the paranasal sinuses. There is still much to be learned and gained in a study of the sinuses.

Infection and gross disease in one part of the body is just as important as in another. Pathogenic bacteria draw no distinctions. And yet, even today, physicians not only fail to treat sinusitis, but what is more devastating, they fail to diagnose it.

The preparatory scientific era has just been entered in rhinology, and the uncontrolled swing of blind work, early exaggeration, and clinical devastation has passed unchecked.

Further advance must be along the lines of histology, physiology, microbiology, histopathology, and metabolism in the sinus mucous membranes.

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This manuscript is the fruit of two years of research. Five previous clinical reports have been made in collaboration with Drs F.B.Kistner and Noble Wiley Jones.

For more than two years we have observed the pathological in all of its various aspects. A wealth of histological information has accumulated.

Thus little by little we have stored a fund of knowledge concerning the basic principles of the healthy reactions and pathological deviations in the course of sinus inflammations.

Concerning sinusitis a mass of opinions has been accumulating for years. Every day the problem instead of becoming simpler becomes more complex.

Careful work is found in the German and Italian Literature, but nowhere in the American Literature is there an account of the histology and pathology of these important mucous membranes.

It seemed to us that the time has arrived to look at the essential facts in great detail. The confusions of terminology and disputes of observers have lead us to induce photographs -- because these speak a universal language.

Certain individuals will perhaps think that it would have been preferable to have been more analytical and less documentary, to have confined ourselves to one phase of the problem, thus arriving at one conclusion or another.

We are frankly uncertain about many microscopic changes. Having tried to penetrate the meaning in thousands of microscopic slides, we have observed a multitude of variations and a contradiction to any absolute conclusions.

We marvel in our curiosity, how a film of tissue, of cigarette-paper thinness, holds in its delicate meshes life and health, struggling to protect the organism in a multitude of ways-- and finally overwhelmed by its physical weaknesses, it falls under the onslaughts of pathogenic bacteria.

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OUTLINE OF THESIS

ANATOMICAL AND PATHOLOGICAL OBSERVATIONS IN SINUS MEMBRANES

OBSERVATIONS ON THE NORMAL HISTOLOGY OF THE MUCOUS MEMBRANE LINING THE VARIOUS PARANASAL SINUSES OF MAN

INTRODUCTION

The recent recognition of chronic sinusitis as a possible focus of infection has stimulated interest in the pathology of sinus disease. Questions now arise concerning the normal histological appearance of the mucous membrane lining the maxillary, frontal, ethmoidal, and sphenoidal sinuses. In the past the more minute anatomic structure of the mucous membrane lining these various paranasal air cavities of man has received scant attention.

It has been established that the mucous membrane of the nasal cavity extends into the paranasal accessory sinuses, but there is every reason to believe that it is greatly modified in these rudimentary cavities. Zuckerkandl (1) remarked that the mucous membrane becomes thinner as soon as it enters the sinus. Schiefferdecker (2) observed that there are many square centimeters of sinus mucous membrane that are devoid of glands. Schaeffer (3), comparing the nasal respiratory with the sinus mucous membrane, states that

the mucous membrane lining the paranasal sinuses is much thinner, contains fewer glands, and does not assume the characteristics of an erectile tissue.

Rugani (4) considered the maxillary sinus mucous membrane more fully developed than either the frontal, ethmoidal, or sphenoidal mucous membranes. He observed that the blood vessels and glands are relatively small and scarse in the latter sinuses.

Cutore (5) in a careful study of the mucous membranes from the maxillary sinuses of man and domestic animals, observed that the lining from the antrum of man has a characteristic structure. He considered the conflicting observations of all the previous writers and concluded from his studies of human materkal that glands are present on the medial wall where the submucosa is slightly thicker and that they become progressively fewer as one proceeds in any direction from the vicinity of the ostium. He stained fat and mitachondria in the epithelial cells and noted a special broad columnar cell in the epithelium.

In the dog he found an excessive number of glands and a greater thickness of the entire mucous membrane. While human sinus linings are only 0.1 to 0.89 mm. in thickness, those of the dog are from 0.45 to 1.34 mm. Bast (6) presented a valuble

description of the so-called maxillary sinus of the dog and demonstrated nerves going to the glands and epithelium. In the latter he demonstrated special sensory cells. That conclusions drawn from the mucous membranes in dogs may not apply to human sinuses is a conceded fact among investigators. The maxillary mucous membrane in the dog is probably a part of the respiratory nasal mucosa.

INCIDENCE OF SINUSITIS --- At the very outset, we desire to call attention to the vulnerable character of the human paranasal sinuses. These rudimentary structures appended to the respiratory tract bear a close biological resemblance to the vermiform appendix, the rudimentary structure of the gastro-intestinal tract. Both the mucosa of the appendix and that of the paranasal sinus are susceptible to infection. Appendicitis reflects itself in gastro-intestinal disturbances while sinusitis manifests itself in rhinitis and bronchitis.

Inflammation is exceedingly common in the various paranasal sinuses. Carmody (7) states that there is hardly an infant who has reached the age of one year without an acute infection in the sinuses. Persistent infection is favored by the adverse situation of the ostia augmented by edematous obstruction. Proetz (8) states that once infection sets in and exudation occurs, ciliary action becomes ineffective

and evacuation becomes a physical problem.

The common colds and various upper respiratory inflammations associated with acute infectious diseases always involve the paranasal sinuses and frequently terminate in chronic degenerative changes so that routine autopsies disclose many cases of gross sinusitis.

Disease of the paranasal mucous membranes is found in approximately fifty per cent of individuals coming to necropsy. In a series of 146 post mortem examinations, Fraenkel (9) found only 73 with negative sinuses. Oppikofer (10) found 94 out of 200 cases to have sinusitis, and Tunis (11) described 47 cases of sinus desease in a series of 100 necropsies.

Because sinus inflammation is so common and subsequent morphological alteration is so apt to follow, it is not accurate to describe sinus mucous membranes without a previous thorough clinical record. This knowledge was available in the study herewith presented, and our anatomic and histo-pathologic deductions were considered in the light of a preceeding clinical history and prolonged period of observation.

We have arrived at a concept of the normal appearance of the sinus mucous membrane by the study of, (A) the healthy and,(B) the proven diseased, taking into consideration: (1) the Previous History of health or diseases, (2) the functional capacity of the tissue under observation, (3) the complete resolution of acute inflammations, (4) the clinical course of inflammatory processes, and (5) the subsequent macroscopical and microscopical appearance of the mucous membrane.

The following demonstrations of the normal histological structures and disease processes in the paranasal sinus mucous membranes may make these relations clear.

MATERIALS AND METHODS

MATERIAL STUDIED

The present study is chiefly based on an extensive collection of surgical specimens * , augmented by necropsy specimens chisled from the skulls of new-born infants and healthy adults who had met sudden death. In this material every possible aspect of the mucous membrane in the various paranasal sinuses was observed. The collection consists of the complete mucous membranes of 20 frontal, 76 sphenoidal, 68 ethmoidal, and 612 maxillary sinuses. There are 42 pieces from the nasal wall of the antrum and 53 specimens from the mucous membrane lining the nasal cavity and its turbinates. The collection was started in 1924 by Professor R. L. Benson of the Department of Pathology and F. B. Kistner, Clinical Professor of Otolaryngology of the University of Oregon Medical School.

SURGICAL TECHNIC EMPLOYED IN SECURING SPECIMENS

The various paranasal cavities were entered in a number of ways and in general Kistner's approach was similar to that outlined by Sewall (12,13). The antra were opened through the canine fossa of the maxilla according to the Caldwell-Luc principle. (Fig. 1). The frontal sinuses were opened by the external operation. The

* The majority of our specimens are from patients who have been under observation at The Portland Clinic for many years. Some significant clinical features were presented in previous reports, Kistner (14), Kistner and Semenov (15), Semenov and Kistner (16), Jones and Kistner (17), and Kistner and Semenov (18). Each patient was thoroughly studied by rhinoscopic, radiographic, and laboratory procedures prior to surgical intervention. At the time of operation, the exact status and duration of disease was known. During the operation, cultures were made from the mucous membranes; and bacteria, pathogenic for experimental animals, were frequently found in the pathologic tissues.

The sphenoidal and posterior ethmoidal sinuses were usually exposed through the antrum by the so-called "transantral-ethmosphenoidectomy"; but when the frontal sinuses were opened, the ethmoidal and sphenoidal cavities were approached by the so-called "frontal ethmosphenoidectomy operation".

When the bone is removed and the periosteal aspect of the maxillary mucous membrane is exposed, one may see, associated with respiration, tambour-like pulsations of the sinus membrane as it responds to positive and negative fluctuations of air pressure in the antrum.

The surgical methods of obtaining and manipulating the sinus specimens merit special description. Most operators scrape the mucous membranes from the bony walls by curettement, this forbids careful histological study and is in reality more difficult than sub-periosteal exenteration according to Kistner's method. The entire sinus membrane is removed in one whole piece (Fig. 1). The mucous membrane of all the sinuses is loosely attached to the bone by means of a few blood vessels, nerves, and small strands of connective tissue. The medial wall of the maxillary sinus is fused with the nasal mucosa at one point, the membraneous wall, and the portion, including the ostium is cut out by a circular dissection. In this manner contact with the infected surface of the mucosa is minimized and an untraumatized, complete specimen is secured. An incision is sometimes made into the antrum lining for purposes of inspection. This is always on the anterior aspect. This was the method employed in securing most of the specimens for this study. Occasionally an

unopened, unmounted specimen was preserved and sectioned en masse.

LABORATORY TECHNIC

The linings were immediately mounted on cardboard (Fig. 2) or everted on a ball of cotton (Fig. 3) and then quickly immersed in fixing fluid. The paper or cotton support preserved the characteristic features of the mucous membrane and expedited the penetration of the fixing fluid into the epithelium.

(In orienting maxillary sinus specimens, it is merely necessary to indicate the side from which it was taken. The central portion of the flat mount or dome of the cotton mount (Figs. 2 & 3) is of necessity the posterior wall as exposed by the anterior incision. The medial wall contains the ostium; hence the antero-medial and antero-lateral quadrant are recognized. The periphery of the specimen is from the anterior area of the mucous membrane.)

With an extensive series of specimens, a number of laboratory procedures may be tried, and in this study we have employed various methods of sectioning and staining.

GROSS STUDY -- A number of specimens were studied while still warm. Ciliary action was demonstrated by immersing the membrane in normal saline solution.

The majority of gross specimens, however, were studied after fixation and hardening. Formalin fixation (10%) retains the characteristic form and consistency of a specimen. Cystic contents are preserved and the whole is handled with greater ease. In 100 instances Zenker's fixation was used where better microscopic detail was desired.

Each mucous membrane was measured and carefully described as it appeared after fixation in formalin. Typical areas were cut from such specimens. Those membranes that merited special

consideration were cut into narrow serial ribbons 3-4 mm. in width, and each segment carefully blocked and cut in serial sections.

Tissues were routinely dehydrated in alcohol, cleared in xylol, or cedar oil, and embedded in hard paraffin. The rapid acetone-xylene method was tried and found to give good preparations for paraffin sections. FROZEN SECTIONS for fat stains were readily made on pathologically thickened specimens but proved difficult with normally thin membranes.

METHODS OF STAINING. -- Staining with hematoxylin and eosin (Harris) gave excellant results for general structures. Mallory's Eosin Methylene-blue was only good for leucocytic infiltrations. Van Gieson's stain gave beautiful results and differentiated the important connective tissue structures better than hematoxlyn eosin. Weigert's elastic tissue stain gave good results on the sinus mucous membranes. Phosphotungstic acid brought out no noteworthy detail. Scharlach R was used to demonstrate lipoid in the epithelium. The Golgi technic on formalin material, mentioned by Bast, was tried without success.

GENERAL COMMENTS

It is beyond the scope of this investigation to consider the anatomic location and configuration of the various paranasal cavities. Schaeffer (3) has already presented a comprehensive monograph concerning the embryology and gross anatomy of the nose and its accessory cavities. In this paper we are required to call attention to a simple relationship between the nasal wall and the peri-

pheral walls of the sinuses.

If one looks into the various paranasal cavities, he is impressed by the fact that the walls are asymmetrical and variable. Generally one can recognise a nasal wall, (in the antrum the medial) and several peripheral walls, the posterior, anterior, superior, inferior, and lateral. For all practical purposes we may consider all the walls except the nasal wall as being peripheral inasmuch as they are distal, i.e., beyond the nasal wall. In the maxillary sinus we shall speak of these as the lateral walls; this is possible because the antrum is of pyramidal shape with its base as the medial wall.

Our observations lead us to believe that the maxillary sinus mucous membrane embodied all the characteristics of the various other paranasal sinuses. This cavity differed from the ethmoidal, sphenoidal, and frontal sinuses only on its medial wall, where it was more complex owing to its greater proximity to the ancestral respiratory nasal mucosa. The lateral walls were progressively less developed the farther one moved from the medial (nasal) wall. The apical portion, under the zygoma, was found least developed and here resembled the frontal sinus in many respects. The frontal sinus mucous membranes were the most rudimentary of all the paranasal sinuses. Thus it resembled the most distal portion of the maxillary mucous membrane.

In order to avoid confusion in the mind of the reader, we shall speak of the maxillary first, and only refer to the frontal, ethmoidal, and sphenoidal membranes as they differ from that of the maxillary (Antrum of Highmore).

MORPHOLOGY OF THE PARANASAL MUCOUS MEMBRANES

Study of the various specimens listed above, led to the following observations and conclusions concerning the gross and microscopic appearance of sinus linings in health and disease: --

MACROSCOPIC OBSERVATIONS:

When peeled from the bone, the normal sinus membrane is a thin film of pale pinkish-grey mucosa. It resembles a layer of moist lens paper in appearance and reminds one of a delicate web. Around the ostium it appears slightly more robust.

Measurement of several hundred specimens gives the following information: --

AREA OF MUCOUS MEMBRANES

Sphenoid	2 - 28 sq. cms.	Average 14 sq. cms.
Frontal	2 - 32 sq. cms.	" 13 sq. cms.
Maxillary	8 - 52 sq. cms.	" 28 sq. cms.

* THICKNESS OF MUCOUS MEMBRANES

	Normal Variations Mm.	Usual Measurement Mm.	Common Hypertrophic Ability Mm.
Maxillary Sinus			
Medial Wall	0.3 - 1.0	0.6	5.0
Lateral Wall	0.1 - 0.5	0.2	5.0
Frontal Sinus ...	0.07 - 0.5	0.1	1.5
Ethmoidal "	0.03 - 0.4	0.1	2.0
Sphenoidal "	0.07 - 0.5	0.1	2.0

* Relative normal thicknesses, comparitive tendency and degree of pathological hypertrophy inherent in each mucous membrane. The antrum mucous membrane is more likely to undergo marked thickening.

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From these measurements we may conclude that the MAXILLARY mucous membrane has the greatest area and generally is twice as extensive as the sphenoidal mucous membrane. It varies a great deal in size and thickness. The nasal (medial) and postero-lateral walls are covered by a thicker mucous membrane than the orbital, alveolar, and antero-lateral walls. This membrane may undergo extreme hypertrophy, usually triple that found in the ethmoidal and sphenoidals.

The SPHENOIDAL mucous membrane is less variable than the frontal sinus in regard to area. It is larger than the frontal, but usually half the size of the maxillary mucous membrane. It is also thicker than the frontal and ethmoidal cell membranes, and stands second to the maxillary in all respects.

The Frontal mucous membrane is exceedingly variable in area and unusually thin. Even hypertrophy is less pronounced in this membrane. We have observed less pathologic degeneration in the frontal sinuses and beleive that resolution takes place with greater facility. Edema is always pronounced; the membrane shrinks very rapidly after removal from its bed.

The ETHMOIDAL membranes are extremely variable and may resemble the frontal, sphenoidal or maxillary linings. They are usually smaller in size.

The EPITHELIAL SURFACE of the normal mucous membrane is smooth and displays no folds, nodules, papillae or irregularities except those associated with undulations of the underlying bone. The PERIOSTAL SURFACE is uneven and in the antrum displays on the posterior wall branches of a nerve and artery which enter through the alveolar canal in the infratemporal (posterior) bonny wall.

EPITHELIUM

A layer of pseudo-stratified ciliated columnar epithelium covers the mucous membranes of all the paranasal cavities. (Figs. 4,5,& 6). Three types of cells appear in the epithelium: (1) Basal Cells; (2) Ciliated columnar cells; (3) Goblet cells. By far the most conspicuous is the ciliated columnar. The basal cells are prominent on account of the orderly arrangement of their nuclei; goblet cells are rare under normal conditions and apparently are mucus changes in the columnar cells.

The epithelium varies from 25 to 50 micra in thickness, but usually it is about 35 micra in height. When it exceeds 50 micra, there is every reason to believe that hyperplasia is present. The frontal, ethmoidal, and sphenoidal sinuses are lined by a relatively low lying epithelium. In these cavities it approaches the ciliated cuboidal form and measures from 25 to 40 micra in height. The maxillary sinus epithelium is taller and varies from 30 to 50 micra. By contrast the epithelium of the respiratory nasal mucous membrane is about 70 micra in height. The height of sinus mucous membrane epithelium rarely exceeds 100 micra. Naturally, the thicker epithelia have a stratified character with five or six layers of nuclei (Fig. 22).

Under normal conditions all of the cells composing the epithelium are attached to the basement membrane and the columnar cells extend from their attachment through the entire thickness to the surface of the epithelium. Two or three rows of nuclei appear under normal conditions (Fig. 5). The basal cells form a deep row of round nuclei arranged in linear order near the

basement membrane. An irregular layer of oval nuclei situated above the basal cells constitutes the nuclei of the columnar cells. Beyond the nuclear region of the epithelium is the cytoplasmic border. (Figs. 4 & 5). The free cytoplasmic zone terminates in cilia. This portion of the epithelium contains considerable lipoid when stained by Scharlach R. The cytoplasm takes a pale hematoxylin stain and during catarrhal sinusitis shows mucoid degeneration. The cilia are frequently destroyed.

CILIATED COLUMNAR CELLS

When fresh surgical specimens are immersed in normal saline tinged with methylene blue, cilia can be seen rapidly beating and agitating the fluid. They measure from 5 to 12 micra in length and arise from the outer thickened cuticular borders of the columnar cells. According to Chambers and Renyi (19) it is only at this cuticular border that ciliated cells have an attachment with each other. The injury of one cell causes swelling and coagulation of that cell but does not extend to the adjoining cells.

The proximal portion of the ciliated columnar cell is narrower than the free end. It is attached to the basal membrane by a tapering extremity or a number of forked tentacles that pass between the basal cells.

The bulky end of the ciliated columnar cell contains a considerable quantity of cytoplasm and it is in this free cytoplasmic border that mucoid degeneration begins as a clear pale-staining mass (Figs 57 & 59). The nucleus is oval in form and

elongates or widens in association with the changes of the cell. During inflammation, the nuclei of the columnar cells are flattened and compressed into a thin spindle form by the swelling and parenchymatous degeneration of the cells (Fig. 9). Under normal conditions the ciliated columnar cells adhere to the basement membrane but during acute and chronic inflammations there is considerable exfoliation. The columnar cells are the first to separate and break away from the epithelium (Fig. 8). During purulent sinusitis they are replaced by an unciliated cuboidal cell. Heteroplasia is prominent in sinusitis (Fig. 9).

BASAL CELLS

The basal (stellate) cells are low lying irregular cuboidal cells, frequently of a pyramidal form, found close to the basement membrane (Figs. 4 & 5). They are firmly attached by a broad base and are seldom dislodged in the desquamations of chronic sinusitis. The pointed free end of the cell lies wedged in between the columnar cells and does not reach to the surface of the epithelium. The cytoplasm is dense and relatively scant. The nucleus is round, comparatively large, and surrounded by a pale rim of cytoplasm (Figs. 5 & 7). Considerable chromatin is present in the nucleus. The basal cells give rise to intermediate cells which later develope into columnar and goblet cells.

The Intermediate Cells are fusiform and have an oval nucleus with a spindle-shaped cell body. The cytoplasm contains considerable mucinogen according to Schafer (20) and gives rise

to the mucus of goblet cells. From our observations in paranasal sinusitis, it would seem that basal cells proliferate rapidly and have all the potentialities of a primitive epithelial cell. Division can occur in such a manner that an area of total desquamation is rapidly regenerated (Fig. 14). Sometimes cells are seen subdividing so that they come to lie one above the other (Figs. 12 & 13). Drasch (21) has observed this process in the tracheal epithelium. Chronic irritation frequently creates metaplasia of the epithelium in the paranasal sinuses.

GOBLET CELLS

Goblet cells are distinguished from the neighboring cells by the fact that their free ends are clearer and more vesicular, while their basal portions, containing the nuclei, are narrow and pointed.

Goblet cells indicate pathologic activity in the sinus epithelium. They seldom are seen under normal conditions, but increase in direct proportion to the pathological activity. Goblet cells are most abundant in chronic catarrhal sinusitis with mucoid discharge. In the allergic sinusitis of hay fever, the entire epithelium can be seen undergoing mucoid degeneration into goblet cells. (Figs. 7 & 8). These discharge massive quantities of mucous and cellular debris. Mucoid degeneration of the epithelium usually leaves a single layer of basal cells covering the tunica propria.

These mucous secreting cells often have an outline which

may be compared to that of a goblet or chalice (Fig. 7); but their morphology can vary enormously in different functional states as a result of pressure from surrounding cells (Fig. 21). The typical goblet cell is usually surrounded by a number of firm columnar cells that maintain its form, but when an extensive area of epithelium is involved, the cytoplasm degenerate into a formless mass. (Fig. 58).

Goblet cells are attached to the basement membrane at their lower end and extend through the entire thickness of the epithelial layer. The nuclei are situated at the same level as those of the neighboring ciliated columnar cells, but as the amount of mucus increases in the cell, they become distorted and flattened.

EPITHELIUM OF THE SINUSES AND MAIN BRONCHI

In general, it might be said that the epithelium of the paranasal sinuses bears a close resemblance to that of the trachea and main bronchi.

HYPERPLASIA AND METAPLASIA

The formation of stratified epithelium is characteristic of chronic sinusitis (Fig. 12). Young (22) has shown that hyperplasia is the result of epithelial trauma. Six or seven layers of poorly outlined cuboidal cells can often be seen in chronic hyperplastic sinusitis. Metaplasia as a result of chronic irritation is observed in the trachea and main bronchi (Miller-23). Inhibition of ciliated columnar cells with proliferation of the cuboidal cells is due to persistent infection with repeated ciliary injury.

accumulated debris, and inflammatory secretions. Epithelial hyperplasia is also present in vitamin deficiencies as shown by Dr. Manville of the Department of Physiology (Figs. 15 & 16). Here the mechanism is obscure.

GLANDS

In general, the glands of the sinus mucous membrane resemble those of the respiratory nasal mucous membrane. They vary, however, a great deal in appearance and quantity. The glands of the sinus mucous membrane are relatively few and their distribution is limited to certain regions of the sinus (Figs. 20 & 26).

DISTRIBUTION--In the antrum the glands are most abundant around the ostium which lies on the medial (nasal) wall (Fig. 56). The presence of the glands in the mucous membrane of the medial wall is constant. By comparison, the glands are more complex in this region. Around the ostium are small compound tubo-alveolar glands (Fig. 26). As the radial distance from the ostium is increased, the glands become thinner, more scattered, and simpler (Fig. 27). They are found along the medial margins of the various walls but never are as large or numerous as those around the ostium. Alveoli are practically absent from the antero-lateral, postero-lateral and lower portions of the mucous membranes (Fig. 20). Those glands seen on the periphery of the gland bearing area are usually simple tubular glands as opposed to the compound glands of the area around the ostium. In the region opposite the ostium, glands are absent altogether.

In the ethmoidal sinuses a few branched tubular glands occur (Fig. 19). Glands in the frontal sinus, however, are extremely rare and simple. The same is true for the sphenoidal sinus. Although our specimens would seem to indicate that glands are usually more numerous in the ethmoidal sinuses, nevertheless, they are so inconstant, and simple, that no definite conclusions can be reached. In general, there may be simple tubular glands located near the ostia of the various sinuses.

POSITION--The position of the glands in the submucous connective tissue is variable and worthy of consideration. The acini are usually deposited in the deeper portion of the loose layer of connective tissue (Fig. 26). Gland clusters can frequently be seen lying below the periosteal layer of compact connective tissue, between the mucous membrane and the bone (Fig. 25). The deep alveoli are often harbored in small boney lacunae or osseous depressions. A large cluster is sometimes found to be spread under the mucous membrane and portions of gland alveoli can cling to the bone when the membrane is peeled away from its attachments. The bulk of the glands, however, lie in the intermediate zone of connective tissue between the loose and compact layers. Cystic dilatation of the glands is common due to the poor mechanical support afforded by the periacinar connective tissue (Figs. 31 & 32). The individual gland acini are surrounded by a delicate web of connective tissue fibrils and large tissue spaces. The complete gland lobule is usually buried in the spongy tissue of the mucous

membrane and as a result is involved in the variety of edematous and inflammatory degenerative processes that destroy its walls. Periglandular infiltrative of leucocytes is evidence of infection in the glands (Fig. 34).

MORPHOLOGY -- Small excretory ducts arise from the gland alveoli and open on the free surface (Fig. 34) of the epithelium. The predominating gland acini are lined by the serous type of secreting cells. Mucous glands, however, are frequently encountered and some of the mucous tubules have definite crescents of Gianuzzi or demilunes of Heidenhain (Fig. 26). Mucous glands are conspicuous in the allegic membranes (Fig. 29). The distance between the gland clusters and individual acini varies in different individuals. There are many simple tubular glands and there is a great amount of loose connective tissue between the tubules of the sinus mucosa.

The acini are relatively far apart and are not as closely packed as those of the respiratory nasal mucosa. The lumen of the acini is quite large. The cells are pyramidal in shape. The nuclei of the serous cells are round and placed near the base of the cell. Those of the mucous cells are oval and are compressed against the basement membrane of the acinus. The nuclei are rich in chromatin and take a heavy stain with hematoxylin. The cytoplasm of the serous cells is granular and of a uniform density. Mitachondria are seen in the glandular cytoplasm. The normal secretion of the sinus glands is a thin serous fluid. The cytoplasm

of the mucous cells is abundant and takes a pale stain. It encroaches on the lumen of the acinus. When a demilune is present, the acini have an ovoid form.

The ducts are usually short and run through the mucous membrane at an inclined angle to reach the surface. Sometimes a long excretory duct can be traced for several millimeters as it runs toward the region of the ostium. Usually several alveoli lined by secretory epithelium can be seen opening into a common lumen. This empties into an intercalcary duct with low flattened cuboidal epithelium. The intercallery ducts open into the main duct which is lined with tall cuboidal cells of a pyramidal shape. The cuboidal cells are uncilinated at first but as they approach the surface of the epithelium, they acquire cilia and become taller. The terminal portion of the excretory duct is lined by ciliated columnar epithelium and appears to be part of the surface epithelium. Deep tunnels and submucous pockets of surface epithelium appear to be related to the gland ducts (Figs. 28 & 29).

CYSTIC DILATATION -- Cystic dilatation of the submucous glands is very common in chronic sinusitis. The presence of cysts is characteristic of previous inflammatory processes. (Fig. 34). Here obstruction of the excretory dust is not sufficient to cause cystic distension of the glands. The weak support of the periglandular stroma and the pull of the edematous distension, augmented by increased glandular pressure, favors the formation of cysts.

The loose layer of superficial spongy connective tissue usually harbors many cysts (Fig. 59). Those acini buried in the compact connective tissue seldom become cystic. McGregor (24) considers the inflammatory paralysis of the excretory duct cilia as an important factor in the formation of cysts. As Kistner and Semenov (15) have shown, the cysts may attain a large size and over 50% of sinus cysts are infected.

As each acinus becomes cystic, it encroaches on the adjacent acini and eventually the individual dilated tubules rupture into each other (Fig. 33). The epithelial lining of a cyst is variable. Usually there are areas devoid of epithelium bordering on areas of flattened cells which gradually pass over into columnar cells and finally one may find mucus or goblet cells. It is probable that the epithelial variations represent stages in the cystic evolution. The contents of the cysts may contain a thick granular mucoid material mixed with concentric deposits of epithelial debris and leucocytes.

MEMBRANA PROPRIA

The epithelium is separated from the loose connective tissue by a thin membrane which is usually continuous, sometimes interrupted, and which has longitudinal nuclei scattered here and there upon it (Fig. 4). Intimately joined with the underlying connective tissue , the basement membrane itself takes the connective tissue stains and is found to consist of delicate bundles of white fibers intermingled with numerous elastic fibrils. Un-

der normal conditions it is extremely thin and web-like. Hypertrophy and hyalinization, however, is frequently present and is a sign of pre-existing inflammation (Fig. 20). Hyalin hypertrophy of the basement membrane is characterized by the appearance of a clear homogeneous subepithelial layer from 1 to 10 micra in thickness.(Fig. 22). The elastic fibrils lie under the hyalinized zone and apparently do not partake in the hypertrophic changes. (Fig. 36). In chronic hyperplastic sinusitis, hyalinization is pronounced and the basal membrane may exceed 20 micra in thickness; being greatest where repeated epithelial desquamation and inflammation is most prolonged (Fig. 22). Small channels penetrate the hyalinized membranes and pass by a devious course from the underlying tissue space to the overlying epithelium. Blood cells and leucocytes in various processes of diapedesis can be seen in these channels. In general, the basal membrane of the paranasal sinuses resembles that of the nasal and bronchial mucous membranes.

TUNICA PROPRIA

Morphologically the tunica propria constitutes the bulk and framework of the sinus mucous membrane. The entire submucousa is made up of two layers of connective tissue, a loose subepithelial and a compact periosteal (Fig. 35).

It varies in thickness and structure with each person but tends to be constant in character in all the paranasal sinuses of the same individual. The loose layer plays a significant part

in the mesenchymal reactions to sinus infections and as a result is profoundly altered by chronic sinusitis (Figs. 53 to 67).

THICKNESS — Normally the entire thickness of submucous connective tissue is less than 0.6 mm. in thickness, and often is less than 0.2 mm. on all but the medial aspect of the antrum. It may show considerable variation in various parts of the same cavity. The lining of the maxillary sinus varies from 0.1 mm. to 1.0 mm., being thinnest on the lateral walls and thick on the medial wall. (Fig. 23). The sphenoidal and ethmoidal membranes are slightly thinner than the maxillary and contain less connective tissue. The frontal is uniformly thin and its delicate structure resembles the lateral wall of the antrum. The normal thickness in these cavities varies from 0.07 mm. to 0.5 mm. and seldom is over 0.3 mm.

Hypertrophy of the submucous connective tissue is characteristic of chronic sinusitis. Hypertrophy of the maxillary mucous membrane commonly attains a thickness of 5 millimeters or more. Hypertrophy of the frontal, sphenoidal, and ethmoidal mucous membranes rarely exceeds 1.0 mm.

LOOSE SUPERFICIAL SPONGY LAYER

Morphologically, the subepithelial layer of connective tissue is a delicate web-like structure, composed of thin lamina which join with each other leaving small interstices or spongy spaces. These areolae intercommunicate throughout the extent of the mucous membrane and hence it happens that edematous infiltra-

tion by tissue fluid or serum may spread from one space to another and involve a considerable mass of tissue (Fig. 58).

In some individuals the laminae are less tenacious and softer (Fig. 35) so that a semi-fluid or jelly-like tissue is present, in others a more fibrous and harder structure is present (Fig. 19). This difference is due to the fact that there is a greater developement of ground substance in one and a better development of fibers in the other. Generally the softer tissues degenerate into polypi (Fig. 66) when inflamed and the firm tissue becomes more fibrous (Fig. 6). The latter is less apt to undergo degeneration. The former is more common and is especially conspicuous in allergic individuals.

The areolae are larger and the tissue is looser as one passes deeper into the submucosa, but, eventually, they become more compact as one approaches the periosteum. They are small and the tissue more firm just below the epithelium. The subepithelial condensation of tissue is largely due to the presence of elastic tissue at this point. (Fg. 37). The denser variety, deep in the mucous membrane, passes by gradual transition into the periosteal layer of connective tissue which is more fibrous (Fig. 39).

The function of the loose areolar layer of connective tissue is intimately linked with local immunity and is an important defensive process.

PERIOSTEAL COMPACT LAYER

This layer is not a typical periosteum but is called

the periosteal layer because this term best describes the general character and location of the deep compact layer of connective tissue. All the sinus mucous membranes have a fairly thick condensation of firm connective tissue near the bone. This layer is fused with the overlying loose tissue and consists of a denser membrane of white fibrous tissue as revealed by the Van Gieson and Weigert preparations. The inner, bonny aspect, sometimes contains a few elastic fibrils and is sometimes covered by cubical or flattened cells (Fig. 4). Occasionally a cluster of glands can be seen below the periosteal connective tissue interposed between the bone and connective tissue.

The deep layer of connective tissue is passive in its responses to infection whereas the upper loose layer plays an active part. We have seldom seen the degenerative processes involve this deep tissue.

PATHOLOGIC CHANGES IN LOOSE SUPERFICIAL SPONGY LAYER

The primary characteristic of the upper loose layer of connective tissue is its tendency to become extremely edematous. There are vast pockets of tissue fluid in chronic inflammatory cases. The essential degenerative changes associated with edema in connective tissue are all seen. Degeneration is commonly due to inflammatory edema, associated with subsequent hydrolic effects on the connective tissue.

Acute edema of the mucous membrane is a spectacular phenomenon and is frequently seen. Recently Proetz (25) reported

the X-ray study of such a process associated with an allergic attack. Within a few hours the sensitised maxillary mucous membrane was observed to increase in thickness from its usual measurement (0.1 mm.) to an edematous distension more than a centimeter in thickness. We have observed many such specimens microscopically; they show wide tissue spaces containing an enormous amount of fluid (Fig. 38). The epithelium is wrinkled and folded due to shrinking of the inner surface by expansion of the mucous membrane in a closed cavity. These folds give rise to polypi in those individuals who have the softer type of loose connective tissue (Fig. 63).

Another characteristic of the loose layer is its tendency to harbor all the degenerative changes associated with chronic sinusitis. In this layer we see the dense infiltration of purulent sinusitis (Fig. 34 & 39) and the myxomatous degeneration of the polypoid type of sinusitis. Gland cysts and mesothelial cysts appear here.

That destruction of the connective tissue cells takes place in sinusitis is evident in the sections where the rupture of strands appears and a proliferative activity of the fixed tissue cells follows. Areas of active fibrosis are often seen (Fig. 66). During acute inflammation altered connective tissue cells seem to be undergoing a transitional stage from the fixed tissue type to the free type.

Maximow (26) considers the monocytes to have their origin in a multipotential cell which is present in connective tis-

sue.

Mononuclear leucocytes from the connective tissue, the so-called large macrophages appear as irregularly round or oval cells with single eccentrically placed curved or indented nuclei. The young connective tissue cells are large and distinct, usually appearing to be spindle shaped but not infrequently being branched or stellate in form. Their nuclei areround or oval, but occasionally are irregularly indented. With the haematoxylin stain their cytoplasm acquires a faint bluish tint and in general shows no structure other than a faint reticulum. Such cells are not infrequently seen in the process of indirect division and mitotic figures are not rare.

The endothelial cells of the blood vessels in these areolar tissues were sometimes actively multiplying. Such endothelial cells often become rounded up so that they project into the lumen of the vessel.

Prolongations of connective tissue blood vessels, lymphatics, etc. pass into the bone and sometimes can travel through the entire thickness of the sphenoidal wall and come to rest against the dura mater as shown by Turner (27).

THE LYMPHATICS

Lymphatic channels ramify and form a rich plexus in the deeper portions of the tunica propria. They are seen accompanying the blood vessels and appear relatively large on the nasal wall of the antrum. Elsewhere there are smaller vessels. Andre

(28) in an injection study of the lymphatics in two children describes an extra-ordinarily fine network in the sphenoidal and ethmoidal sinuses and believes these thin vessels penetrate the honey wells to drain into the parameningeal spaces. Grunwald (29) injected the antrum of a man and concluded that the lymphatics of all the paranasal sinuses communicate with each other thru a plexus of channels in the nasal mucous membrane. Mullin and Ryder (30) demonstrate the functional course of lymphatic drainage from the accessory sinuses and conclude that a system of ramifying lymphatics joins the paranasal sinuses so that infection in one may spread to the others. They also observe drainage into the parameningeal spaces.

Sinusitis is associated with cervical lymphadenitis and there is sufficient post-mortem evidence to show that infections in the frontal, ethmoidal, and sphenoidal membranes metastasize to the pericerebral spaces with serious intracranial consequences. In view of the multiplicity of cerebral and pulmonary complications associated with sinusitis, Mullin's and Ryder's experimental considerations of lymphatic drainage are significant.

LYMPHATIC TISSUE

Lymphatic tissue is never seen in a healthy sinus mucous membrane. When present, it is a manifestation of an infectious or toxic process.

As far as we have been able to determine, this is the first time that lymphoid follicles have been described in the

mucous membranes of the paranasal sinuses. These structures are seen in specimens from outspoken clinical cases of subacute and chronic sinusitis with marked histopathologic inflammatory activity. Many are from allergic patients. Some show a chronic pyogenic and others a chronic hyperplastic mucous membrane.

The lymphatic nodules are generally found in the loose layer of connective tissue; more often in the depths of the tunica propria than in the upper layers and occasionally in juxtaposition to the periosteal layer (Fig. 4). The principle morphological variety presents a solitary follicle with a light center surrounded by a dark marginal rim of cells (Fig. 40).

The light center consists of pale cells of equal size and a diameter about double the size of small lymphocytes. The nuclei are irregular in form and contain nucleoli, karyokinetic figures, and a pale staining basophilic protoplasm. The centers vary in size and in some specimens are absent. There is a clear demarcation between the light central zone and the heavy marginal zone in many specimens. In others a gradual transition is seen (Fig. 44).

The dark marginal zone appears as a well defined ring around the central pale area. Sometimes a narrow rim of lymphocytes can be seen and at others a preponderant accumulation of marginal cells with no definite peripheral boundaries appears. Occasionally, only a few lymphoid cells form around the central pale area (Fig. 45).

Plasma cells and eosinophils in concentric peripheral

arrangement sometimes augment the geographical accumulation of cells around the lymphoid nodules. Definite arterioles and capillaries seem to approach these lymphoid follicles. (Fig. 42). Not infrequently the perivascular lymphatics are seen filled with lymphocytes (Fig. 41).

Recently Ehrich (31) investigated pseudo-secondary lymph nodules, Flemming's secondary nodules (germinal centers), and transition forms of lymphatic tissue. His studies lead him to believe that interstitial accumulations of lymphocytes, plasma cells, and in extreme cases, reticulo-endothelial cells, can be regarded as primary reactions of the organism to bacteria and their products (32).

We are not prepared to say whether or not the structures observed in our sections are germinal centers, but we are certain that they appear as a consequence of infection and inflammation in the sinuses. There is every reason to believe that a local proliferation of lymphocytes and plasma cells occurs in the membranes of chronic sinusitis. Emigration of these cells through the blood vessel walls is rare in the presence of a relative tissue lymphocytosis with active neutophilic diapedesis.

LEUCOCYTIC INFILTRATIONS

Normally the mucous membrane is not invaded by leucytic elements. There may be an occasional lymphocyte in the loose layer of connective tissue but more than eight or ten cells per square millimeter under low power is abnormal. Infiltration in

the sinus mucous membranes is to be considered a manifestation of inflammation and the same histopathologic criteria apply to the sinuses that apply to the lungs and branchi.

Sinusitis is characterized by plasma cells and lymphocytes in all types of infection. Polymorphonuclear neutrophils increase in the purulent cases. Eosinophilic granulocytes predominate in allergic cases and are common in non-specific chronic sinusitis, usually hyperplastic. All leucocytic accumulations are most dense in the sub-epithelial region and progressively less dense in the deeper areas of the mucous membrane. The periosteum is seldom infiltrated. Emigration of neutrophils through the epithelium creates pus. Plasma cells and lymphocytes also emigrate but not in as great a flow as the neutrophils. Eosinophilic exudation occurs in the severe allergic specimens. Periglandular infiltration is evidence of deep seated glandular infection and is very common. This type of infection is unusually resistitive to ordinary conservative sinus treatment as shown by Kistner and Semenov (15).

BLOOD VESSELS

The sinus mucous membrane is not as rich in blood vessels as that of the nasal cavity. Capillary nets are seen most commonly in the superficial portion of the mucous membrane, larger arterioles and venules are found in greater frequency in the deeper portion of the tunica propria; here they ramify to a large extent.

Microscopical sections from a sinus mucous membrane always show an organized syst tem of arterial branching. One can divide the vessels into three layers.

The three vascular orders are as follow:

1. Periosteal Arteries, between the bone and mucous membrane, entering the latter at a slant and rapidly passing through the periosteal layer to the intermediate layer of connective tissue. They are never seen entering the mucous membrane at right angles. These vessels are fairly large.

2. Intermediate Arterioles, ramifying just above the periosteal layer in a definite manner and showing a clear-cut tendency to form a vascular plexus beneath the loose layer of connective tissue. Sometimes appearing as erectile tissue channels on the medial wall of the antrum but never on the lateral walls. (Figs. 4, 46-49)

3. Capillary Circulation, offshoots of the intermediate layer of blood vessels, ramifying throughout the sinus mucous membrane and reaching the lower margin of the basement membrane.

In some cases of chronic sinusitis the arterial walls show definite arteriosclerotic tendencies in young subjects. This may have some relation to the conception of infectious arteriosclerosis.

NERVE SUPPLY

We have already referred to a large nerve that enters through the alveolar canal of the antrum. This trunk is large and entirely confined to the mucous membrane. When the lining is being withdrawn from the cavity, the nerve can be stretched for several centimeters before it breaks. Its ramifications have been observed in the deeper layers of the mucous membrane but our attempts to stain the terminations have been unsuccessful, chiefly due to technical inexperience. Various investigators have studied the nerves in experimental animals. As early as 1872, Insani (33) observed nerve fibres in the maxillary and frontal sinuses. Calamida (34) later demonstrated small ganglia and trunks ramifying in the submucous connective tissue of the

various paranasal sinuses . As revealed by the Golgi technic, in the dog, they seem to form a plexus just beneath the epithelium. Some fibres were traced accompaning blood vessels, others were found independent of blood vessels. Branches were given off to the glands and formed a basket or network of fibrils around the acini and ducts. Other branches reached the epithelium and gave off fibrils that penetrated the mucous membrane and terminated in the epithelial cells. Bast (6) has differentiated two types of cells in the epithelium of dogs antra and believed that they have an important part in the sensory function of the sinus. The first of these cells was considered an ordinary olfactory cell because of its structure, position and nerve connection. The second type takes the Golgi nerve stain and is a broad cell with branched processes. It has intimate nerve connections. Bast concluded that cells of the latter type may be regarded as sensory end organs.

REGENERATION OF THE MUCOUS MEMBRANE ... THE CHARACTER OF THE HEALED ANTRUM AND ITS RELATION TO SURGICAL TECHNIC

The post operative healing and replacement of tissue in the sinuses has been observed clinically but only one case had been studied histologically by Theandorf (54) prior to our report. Variable post operative results have been obtained. In some cases the new lining is thick and in others it is thin. It always consists of scar tissue and only resembles the original lining in a general way. We shall attempt to present the important features of the repaired linings according to the manner of operation.

Our observations in repair and regeneration are based on tissues secured from 15 individuals: 7 cases reoperated after apprevious Caldwell-Luc operation had been done, 6 biopsies obtained from antra through the counter opening, 1 specimen from an antrum through a large permanent opening in the canine fossa, and 1 from an healed ethmoidal sinus. In general we have found that a biopsy specimen gives meager information. Conclusive evidence was only obtained from the reoperated cases where the whole regenerated lining was removed and a complete series of sections made.

On casual inspection the regenerated sinus lining seems to resemble the normal mucous membrane originally present but on microscopical analysis with Weigert's, Van Geison's and Mallory's stains shades of difference appear. The new formed submucosa is true scar tissue.

That the histologic findings in healed sinuses will vary according to the type of operation or the thoroghness of exenteration is manifested by an analysis and comparison of the tissues we have removed. For instance, in reoperated cases in which we know that the first operation was not thorough, we have found fragments of the original mucous membrane still attached to the bone or merged with the surrounding scar tissue. Tonndorf (35) made the same observation in a case that came to autopsy four weeks after a Caldwell-Luc operation in w hich curretage was employed. As we have already shown, it is possible for clusters of subperiosteal glands to remain and cling to the bone even after radical exenteration -- these may then appear in the scar after repair.

We beleive that the Schneiderian nasal mucous membrane plays an important part in the regeneration of tissue in the paranasal cavities. It is of particular significance as a source of the epithelium that will cover the scar.

When the source of the new epithelium is in the nose it will be found that the regenerated sinus epithelium retains to some extent the character of nasal epithelium. But where there is a possibility of epithelium extending in from some other sources, such as the buccal cavity, it will be found that the new epithelium has the character of stratfied squamous epithelium.

When fragments of sinus epithelium remain in the cavity we find an actual regeneration from these cells. In all events the new epithelium is subject to the variation of pathologic hyperplasia or atrophy.

The spread of nasal epithelium into the granulating sinus is fairly constant. In sections made from the medial half of the operated sinus cases we often find the

characteristic structure of nasal mucous membrane. We believe that this is nasal mucous membrane transplanted into the antrum either intentionally or accidentally; for its characteristic appearance disappears abruptly when we reach the new formed tissues lining the rest of the cavity.

Examination of the tissues at the opening in the canine fossa in reoperated cases, where we could be sure the original mucous membranes had been destroyed, has always shown a dense scar covered with a variable cuboidal or columnar epithelium and a complete absence of glands.

REPAIR IN A SMALL AREA

Approximately one square centimeter was cut from the nasal wall of the antrum in the usual glandbearing portion of the mucous membrane. Four months later the healed area with some adjacent membrane was removed. Microscopic sections show a layer of ciliated columnar pseudo-stratified epithelium resting on white fibrous scar tissue. No submucous glands are found.

REPAIR OF A LARGE AREA (Fig. 68.)

About one-third of the mucous membrane was removed from 2 cases. Two years later the sinuses were reoperated and the entire antrum lining removed. Microscopic sections show the original portion of the membrane containing thenormal histologic structure as follows: (1) A layer of pseudo-stratified ciliated columnar epithelium; (2) a superficial spongy layer of areolar connective tissue with large tissue spaces; (3) tubo-alveolar mucous

and serous glands in the layer of loose connective tissue; (4) an orderly arrangement of branching arteries and arterioles in definite layers; (5) a definite periosteal layer of compact connective tissue. While the repaired portion of the lining consists of a thick mass of fibrous scar tissue, covered for the most part by an indifferent layer of cubical epithelium which is stratified in some areas and entirely absent in others, an irregular vascularization of scar tissue is present. The usual histological structure of antrum mucous membrane is entirely absent. No glands are seen. No loose areolar tissue with large tissue spaces is seen (Fig. 68).

EPITHELIZATION FROM THE NASAL MUCOUS MEMBRANE

After complete subperiosteal exenteration of the lining through the canine fossa a counter-opening is made in the nasal wall of the antrum to permit drainage. A flap of nasal mucous membrane several millimeters in width is usually brought into the antrum to cover the floor of the counter-opening. Two cases were examined, one 8 months and the second 18 months after the primary operation. Repair produced a great deal of bony thickening in the walls of the sinuses. Whereas the original antrum lining is easily peeled from the bone, the new lining is only torn away with difficulty. Spicules of bone are found imbedded in the scar tissue of the new lining. The healed antrum is lined by a thick, dense, firm layer of scar tissue covered by stratified columnar epithelium. The normal antral membrane contains only a few glands on the nasal wall, but the membranes obtained after repair with

the nasal flap contain many more mucous and serous glands than the original lining. The glands are derived from the nasal flap and are buried in the firm scar tissue. The white fibrous scar tissue contains fibroblasts in the superficial portion, and dense wavy strands deeper in the lining. There is no loose areolar connective tissue.

Recently, Knowlton and McGregor (36), working on 3 dogs curetted portions of the mucous membrane from the recess in the nasal cavity and observed complete epithelial regeneration in one dog at 3 months and gland regeneration in another dog at 5 months.

EPITHELIZATION FROM THE ORAL MUCOUS MEMBRANE

In one case, after sub-periosteal exenteration, the opening through the canine fossa was kept patent. After 6 months the antrum was lined with a firm membrane composed of stratified squamous epithelium. This lining is similar to that of the oral cavity from which it was derived.

VALUE OF THE NEW TISSUE

We are not certain that the new tissue is better than the old original mucous membrane. We believe that the rudimentary structure and loose character of the usual sinus mucous membrane certainly offers bacterial harbors. The glandular infection, the tissue space cysts, the thin connective tissue, the ready absorption from the capillary bed, and the thin bony walls are all weaknesses that are altered by Subperiosteal Dissection, when all the infected tissue is removed. Repair is a remarkable phenomenon. Sometimes bone replaces the entire sinus cavity. Nothing could be more desirable.

S U M M A R Y

1. The paranasal sinus mucous membranes have a characteristic appearance and cannot be considered the same as the nasal mucosa.

2. In general, all the mucous membranes of the various paranasal sinuses are similar. The medial (nasal) wall of the antrum is well developed and is unique in this respect. The frontal and sphenoidal sinus membranes are least developed and unusually thin. Hypertrophy is evidence of pathologic activity.

THICKNESS OF MUCOUS MEMBRANES

	Normal Variations Mm.	Usual Measurement Mm.
Maxillary Sinus:		
Medial Wall	0.5 - 1.0	0.5
Lateral Wall	0.1 - 0.5	0.2
Frontal Sinus	0.07 - 0.3	0.1
Ethmoidal Sinus	0.08 - 0.4	0.1
Sphenoidal Sinus	0.07 - 0.5	0.1

3. Sinusitis is exceedingly common; the inflammatory changes of the mucous membranes should be recognized. Leucocytic infiltration is as abnormal here as it is in the lungs.

4. A single layer of ciliated columnar (pseudo-stratified) epithelium covers the surface of themembrane. It measures from 25-50 micra in thickness. More than 5 layers of nuclei is evidence of pathologic irritation with subsequent hyperplasia.

5. The basal cells are the embryonic ancestors of the ciliated cells and are active in regeneration and hyperplasia.

6. The cytoplasmic zone, distal borders, of the columnar cells contain lipoids. This may have some relation to the cholesterin crystals washed from sinuses with chronic degeneration.

7. Goblet cells are rare. In large numbers they indicate catarrhal sinusitis.

8. A basement membrane is present; normally it is very thin. After inflammation, it becomes hyalinized and this change is evidence of previous disease in a thin membrane that may be normal.

9. Glands are rare. In the maxillary sinus they occur on the nasal wall. In the sphenoidal and ethmoidal sinuses they may be seen near the ostia; in the frontal sinuses they are often absent.

10. Cystic degeneration and infection of the glands denotes pathologic degeneration and is favored by the weakness of the surrounding stroma.

11. Glands may occur in bony lacunae, under the periosteum. Such glands are difficult to remove surgically.

12. The tunica propria consists of two layers; an upper loose areolar tissue, and a deep compact tissue. The loose tissue is extremely active during inflammation. The deep layer resembles a periosteum.

13. Lymphatic nodules, probably the so-called germinal centers of Flemming, are described in the loose layer. These lymphatic nodules are absent under normal conditions.

14. Blood vessels emerge through the bony walls and subdivide into three plexuses lying in the plane of the mucous membrane. The paranasal sinus mucous membranes have a relatively poor blood supply.

15. An abundant nerve supply reaches the mucous membrane.

16. Post operative repair does not regenerate the old lining but substitutes firm scar tissue covered with a variable epithelium.

Much new bone is deposited on the surrounding walls.

17. The present study is based on 851 specimens and in such a large series considerable histological variation is noted. Individuals tend to vary in the type of mucous membranes that they carry.

18. The normal appearance of a sinus mucous membrane was determined by a study of the healthy mucosa. By analysis of proven pathological tissues it was possible to define the normal limits and variations.

19. The normal sinus mucous membrane is thin, has a smooth epithelial surface, contains no leucocytic infiltrations, no edema, no gland cysts and no hyperplastic or mucoid changes in the epithelium.

20. An occassional ethmoidal ethmoidal cell is found in the concha and although these are called "cystic turbinates" they are usually normal ethmoidal sinuses.

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At the request of investigators interested in Sinus Studies, we have started to compile our Bibliography on the various phases. This list will be available within a few weeks. It will cover the bacteriology, pathology, and significant clinical aspects of paranasal sinusitis.

F I G U R E S A N D P L A T E S

74 Figures on

31 Plates

4 Drawings and
70 Microphotographs.*

* Microphotography by the writer, conducted in the laboratory of Mr. Walter Johnson with his kind permission.

SURGICAL AND TECHNICAL PROCEDURES

One Plate

Figures: 1, 2, & 3.

DIAGRAM OF TYPICAL SINUS MUCOUS MEMBRANE STRUCTURES.

One Plate.

Figure : # 4 .

Figure 1.

The whole antrum mucous membrane is removed intact through the opening in the canine fossa of the maxilla. The plate shows the periosteal aspect of the mucous membrane with the periosteal vessels as they appear running between the membrane and bone; the epithelial surface of the lining is within. When it is necessary to inspect the epithelial aspect, an incision is made through the anterior portion of the membrane as shown.

All the membranes of the various paranasal cavities are removed in the same manner. After the antrum has been entered through the Caldwell-Luc opening, it is possible to go through the counter-opening in the nasal wall of the antrum and reach the sphenoidal and posterior ethmoidal sinuses, "Transantral-ethmosphenoidectomy."

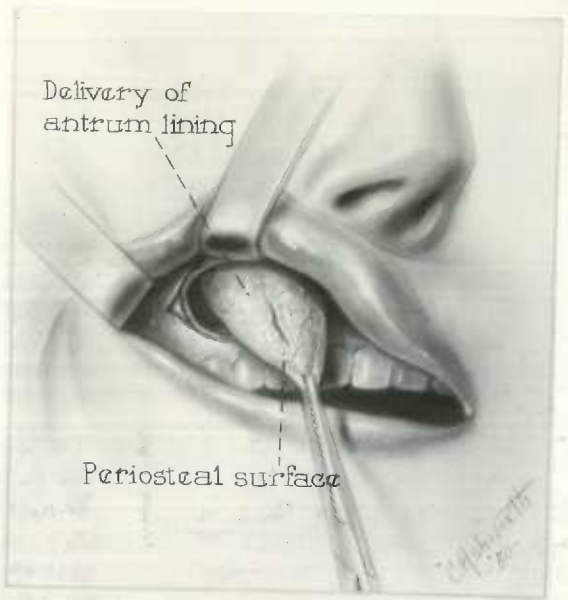
Figure 2.

Thin sinus membranes are immediatly spread with the epithelial surface upward. When fresh, the tissues adhere to the cardboard with sufficient strength to permit rapid fixation and hardening in the fixing fluids without distortion.

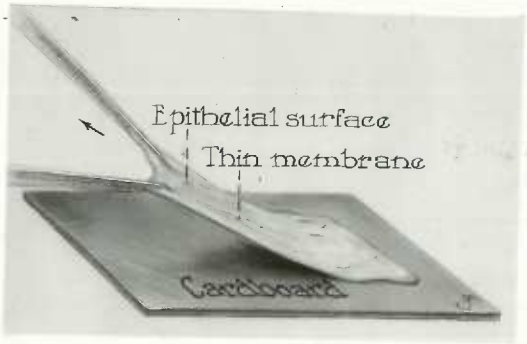
Figure 3.

Here the mucous membrane is shown inverted on cotton and thus the various ridges, crests, folds, cyts, etc. are held in place during fixation and hardening.

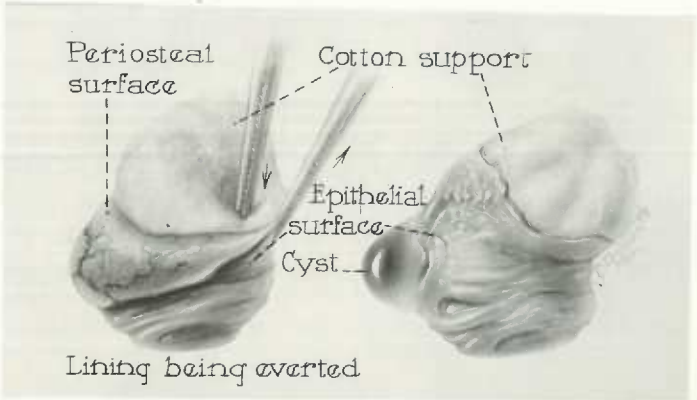
In this manner specimens are mounted and fixed with a minimum of handling. Another rapid and simple method is to drop the entire specimen (unopened) into the fixing fluid, this procedure is not used very often because most specimens are opened in the surgery for inspection.


Delivery of
antrum lining
Periosteal surface

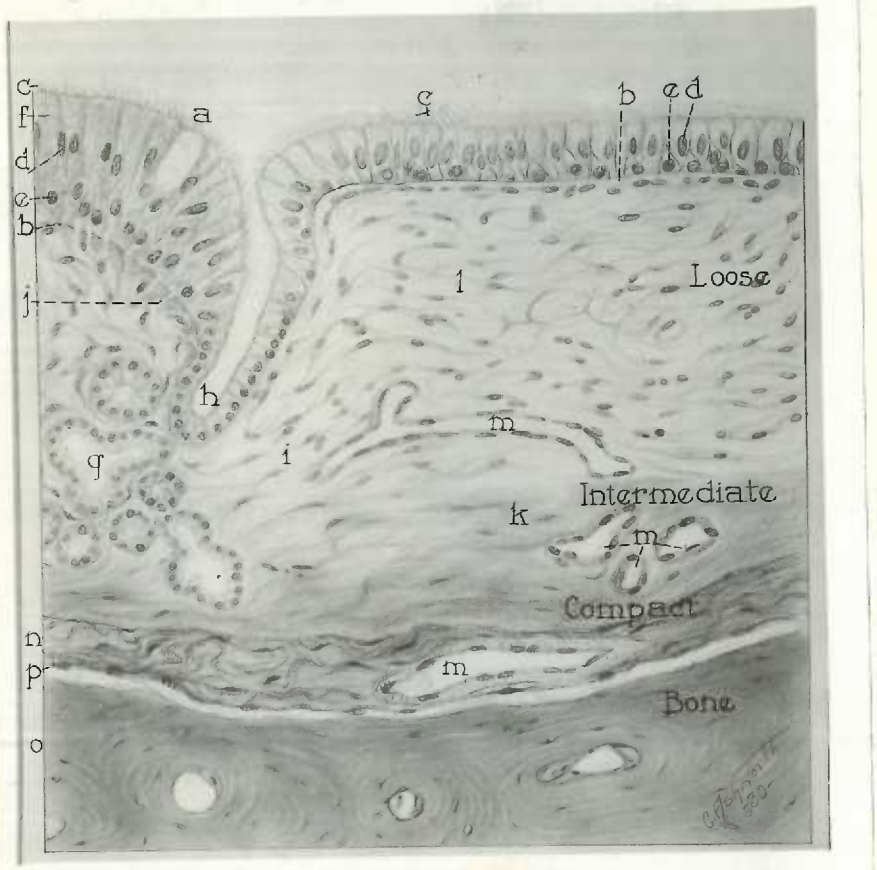
1


Epithelial surface
Thin membrane
Cardboard

2


Periosteal
surface
Cotton support
Epithelial
surface
Cyst
Lining being everted

3


a
g
b
c
d
e
f
d
c
b
j
l
Loose
h
m
q
i
Intermediate
k
m
Compact
n
p
m
Bone
o

4

Figure 4.

DIAGRAMMATIC STRUCTURE OF SINUS MUCOUS MEMBRANES

EPITHELIUM:

a - Rare goblet cell;
b - Basement membrane, thin on right;
c - Cilia of ciliated columnar cells;
d - Oval nuclei of ciliated cells;
e - Round nuclei of basal stellate cells;
f - Free cytoplasmic border of epithelium contains no nuclei;
g - Glands, submucous tubo-alveolar;
h - Gland ducts near surface;

j - Channels in hypertrophied portion of basement membrane;

TUNICA PROPRIA:

i - Intermediate zone of connective tissue;
k - Compact deep layer;
l - Loose subepithelial layer;
p - Periosteal condensation of compact layer connective tissue;

m - Blood vessels;
o - Bone of sinus wall.

E P I T H E L I A L S T R U C T U R E

Eight Plates and

Seventeen Figures.

Figures:

5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16,

17, 18, 19, 20, 21, 22.

Figure 5.

Maxillary sinus mucous membrane showing the character of the ciliated columnar cells; Cil., cilia; F.C.B., free cytoplasmic border; R.N., round nuclei of basal cells under the O.N., oval nuclei of the columnar cells.

Note the clear rim of cytoplasm around the nucleus of the basal cell.

Attention is directed toward the loose layer of subepithelial connective tissue, L.L.; a minute capillary, Cap.; and the thin compact layer of connective tissue, C.L.

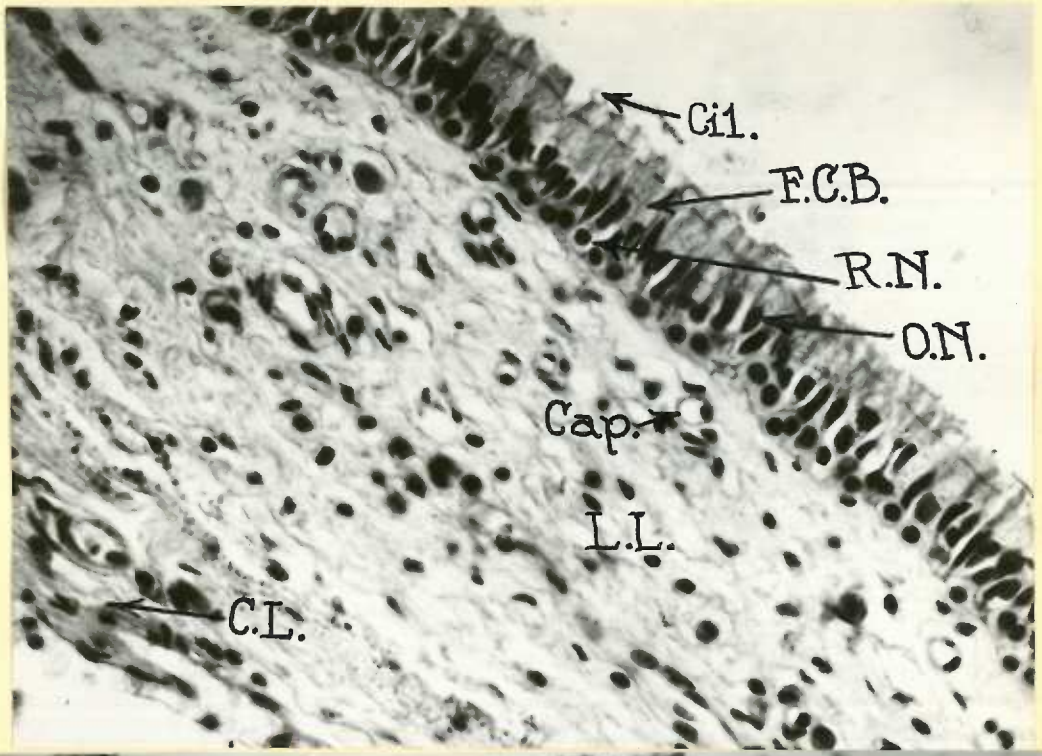
Hematoxylin-Eosin stain, 320 X
Girl 10 yrs.

Figure 6.

Sphenoidal sinus mucous membrane showing the same epithelial structure. Round nuclei of the stellate basal cells are marked-R.; the oval nuclei of the ciliated columnar cells are marked-O.; and the cilia are marked-C.

Note the heavy basement membrane- B.m; this membrane is from a man 50 years old who had had a purulent catarrh for many years which eventually cleared up; clinically absolutely negative as far as his sinuses were concerned; denied having a cold for the last three or four years; histologically all the sinuses had perfect epithelium, the membranes were thick and fibrous -- no loose connective tissue, solid fibrous tissue everywhere, special stains confirm H & E stain.

Microphotograph of Van Gieson's Stain.
320 X. Cilia measure 9 micra.
Epithelium is 36 micra thick.



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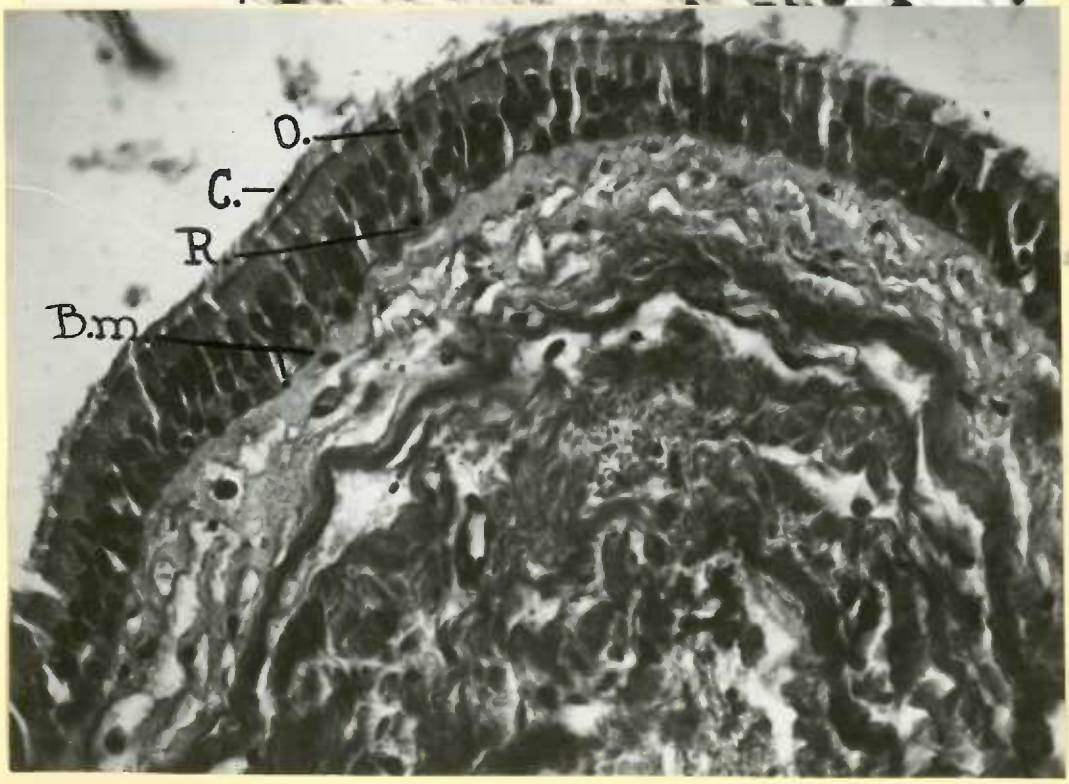


6

Figure 7.

Epithelium during inflammatory reaction showing the massive accumulation of desquamated cells, mucous membrane edema, goblet cells and their by products. Catarrhal Sinusitis.

Note the typical GOBLET CELL - G.C.; with its characteristic beaker form. Observe the hopeless task of the cilia - diminished in numbers and overwhelmed by debris.

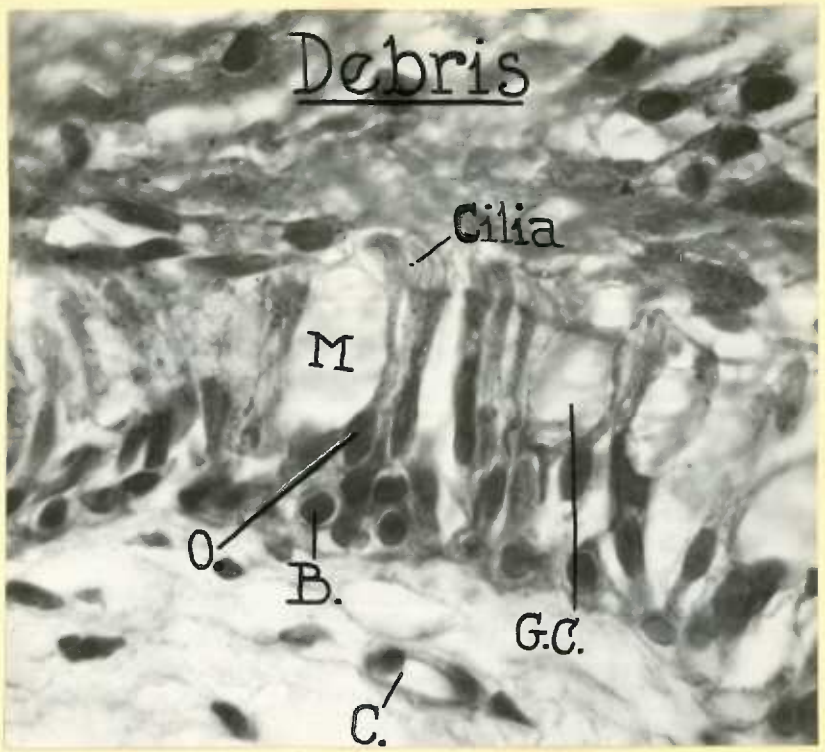
Basal cell nucleus with its pale rim of cytoplasm - B.; Oval nucleus of columnar cell is marked - O.; mucus in cell - M.; capillary is marked -C.; and cilia are so labeled.

Epithelial debris is prominent . A similar but more active catarrhal sinusitis is seen in Figure 60; and a mass of mucus, the result of profound mucoid degeneration is seen in Figure 58. Goblet cells in large numbers are evidence of pathology.

Figure 8.

Simple exfoliation of ciliated columnar cells contrasted with the above. Note that the mucus secretion of these cells is thin and that there are no goblet cells. Goblet cells were extrememly rare in this specimen and apparently the mucous must come from either glands or ciliated columnar cell secretion.

H & E preparations.



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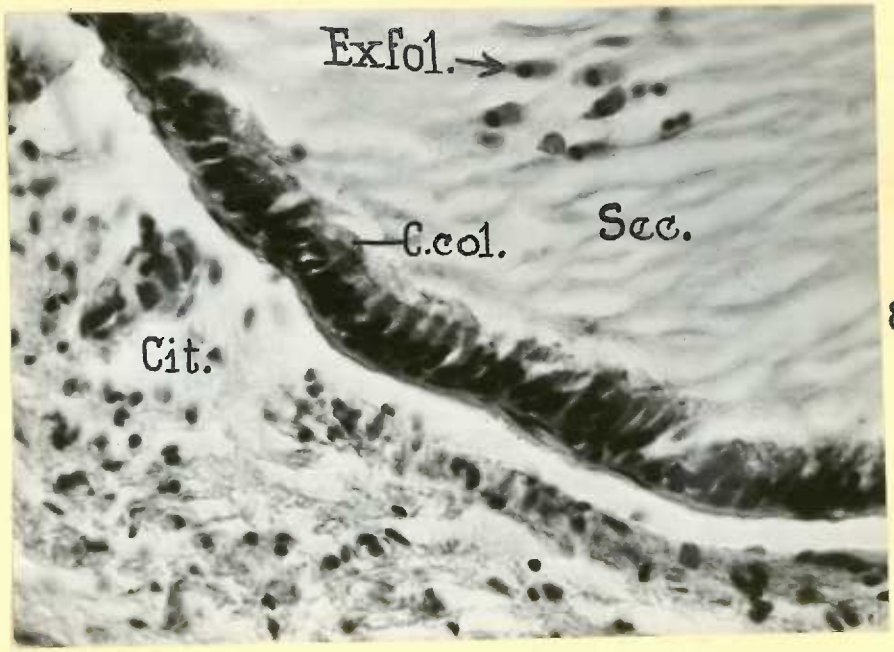


8

Figure 9.

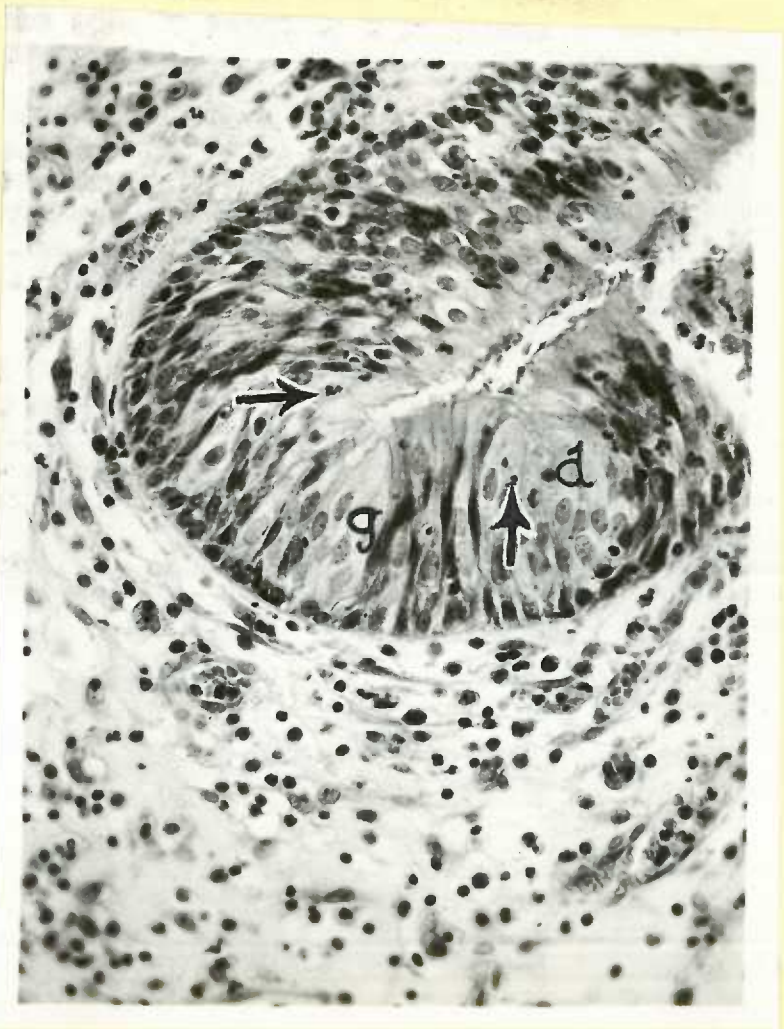
Heteroplasia of epithelium in purulent sinusitis. The oval nuclei are compressed into a spindle-form shape by the edema and coagulation necrosis of adjoining cells.

Note the vesicular nuclei with the great (g) change in chromatin and protoplasmic staining. The arrows point to polymorphonuclear neutrophils emigrating through the epithelium to produce pus. Cilia are degenerated (d) and the entire epithelium is greatly hypertrophied. It measures over 100 micra in height.

See Figures 61 and 62 from this same specimen showing the general appearance of a purulent sinusitis and the incidental epithelial degeneration. The basal cells appear to be proliferating rapidly in all sections.

In 62 there are no cilia. Heteroplasia is most prominent on the surface of papillae and less marked in the crypts.

H & E Stain.



9

Figure 10.

Bacteria on the surface of an infected sinus. This is a specimen of so-called non-purulent sinusitis. It will be seen that the epithelium is hyperplastic and has lost its normal orderly appearance. Cilia are defficinnt.

Epithelial thickness is indicated by the bracket E.; surface mucus is marked S.m.; and the bacteria are B.; Proliferating fibroblasts - F.

Cultural report was Streptococcus of the hemolytic greenish variety.

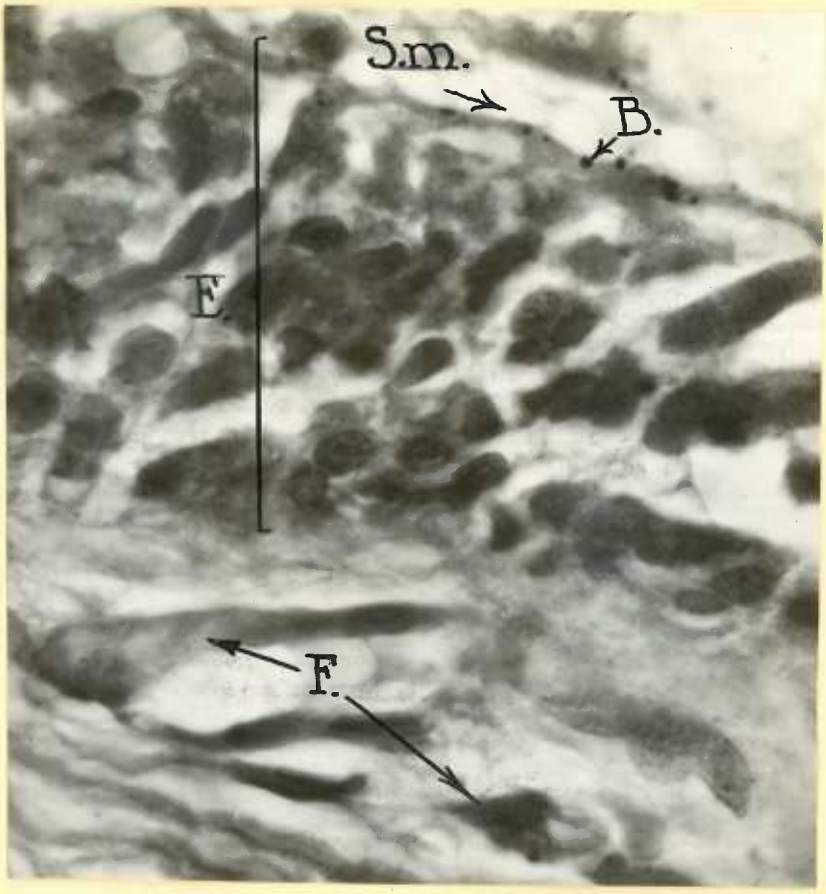
Figure 11.

Staphlococci in purulent sinusitis. The surface epithelium is completely disorganized.

This patient died after 10 months of illness with an empyema of the sphenoidal sinus with subsequent osteomyelitis, meningitis, cavernous sinus thrombosis, etc.

The bacteria were stained in all the tissues around the base of the brain. Cultures gave staphlococcus albus throughout.

Lillie's Modification of the Gram Stain. ---- Safranin Counter Stain.



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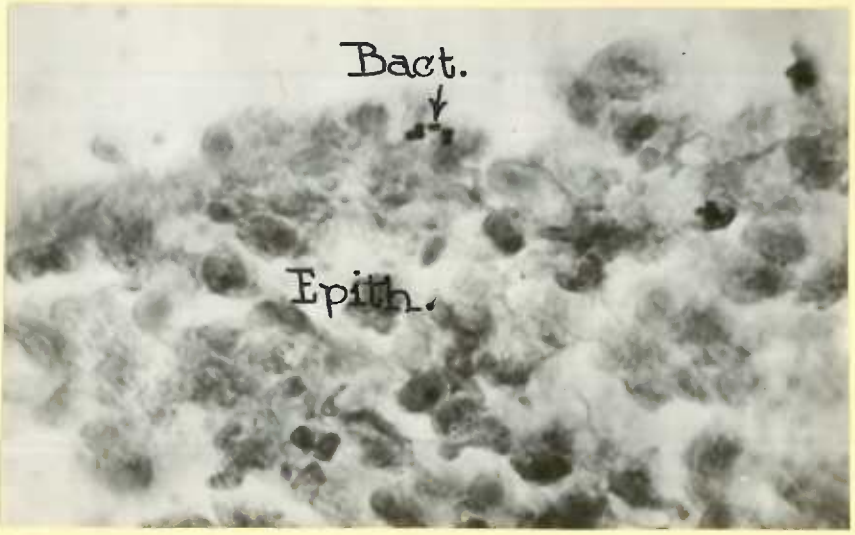


11

Figure 12.

Metaplasia to multilayered cuboidal cells without cilia. This type of epithelial degeneration is common is chronic sinusitis. Contrast this epithelium with that in Figure 6.

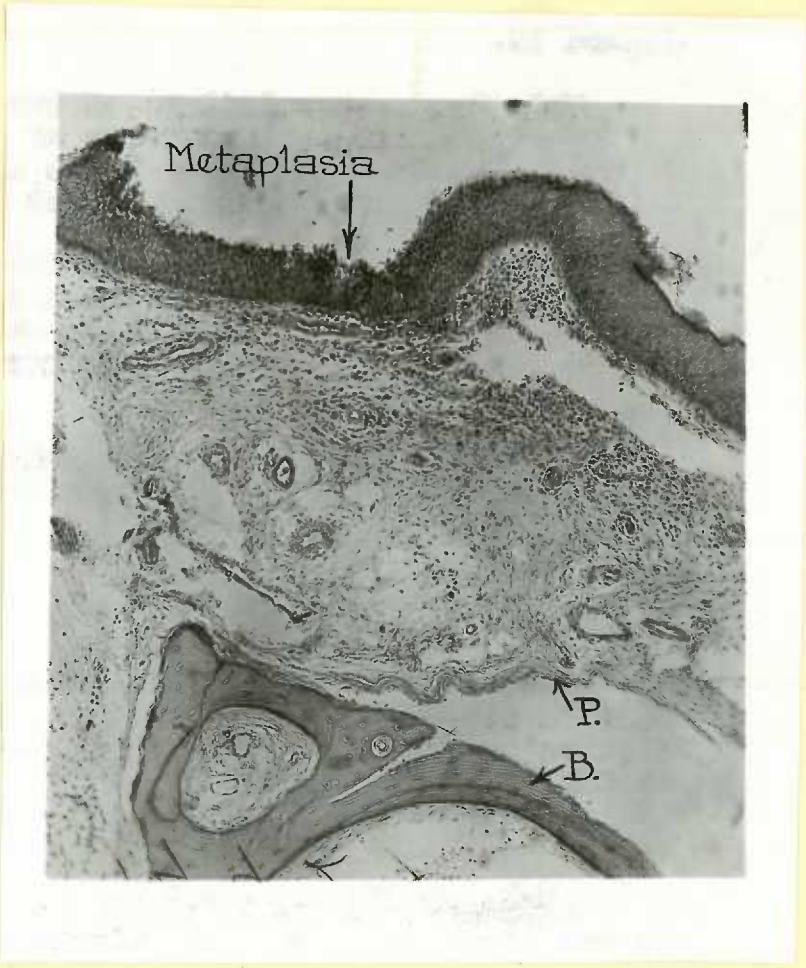
Note the meager changes in the connective tissue, there is a moderate edema and infiltration of leucocytes. The periosteal layer is designated by the letter P; the underlying bone is B.

H & E....Decalcified,
Nitric Acid Formalin.

Figure 13

Note the basal cells apparently giving rise to overlying cuboidal cells that are acquiring cilia. This also is observed in the trachea. (Drasch)

Apology -- This figure is only present in two copies of this ms. The negative is apparently lost.



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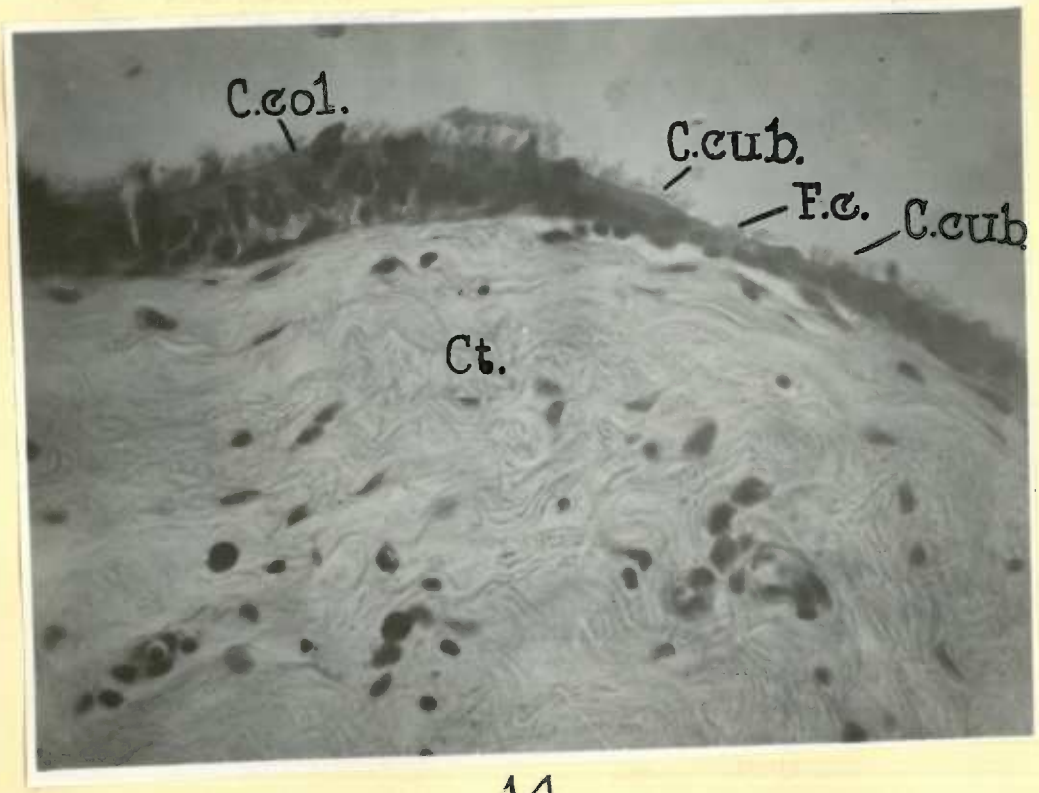


14

Figure 14.

Regeneration of epithelium. A layer of typical pseudo-stratified ciliated columnar epithelium is seen at the point marked, C. Col.; and a layer of cuboidal cells is seen at, F.e.; between the two there is an intermediate type of ciliated cuboidal cells, some approach the columnar in form, marked, C.cub. The underlying connective tissue is, C.T.

Mallory's Methylene-Blue & Eosin Stain.
Magification 320X.

Figure 15

Hyperplasia in the nasal epithelium of a white rat from Dr. Maville's series of Vitamin A & D deficient animals. This hyperplasia is similar to that seen in Figure 22.

Figure 16

Low columnar ciliated epithelium from same animal. Note the contrast in height between the two.

There is no infection present. No leucocytic infiltration or edema is seen. This animal died immediately after birth. Infection is definitely ruled out as the cause of this hyperplasia.

Figures 17, 18, 19, 20, 21, & 22.

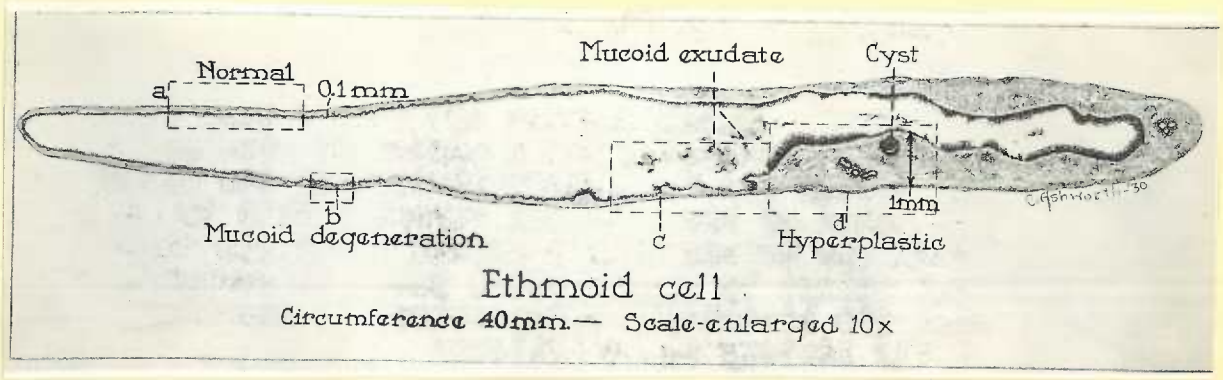
These figures are from a case that was studied clinically for a period of nine months before operation and the interpretation of the specimens is based on his clinical record. This is in accord with our belief that a normal sinus can only be determined by its clinical power to resist infection; that its histological appearance is secondary. A breif history is as follows:

Mr. L.T., a young adult logger, had frequent colds for five years and presented himself with all the clinical and laboratory evidence of a left sided Purulent Pansinusitis with severe pain over the left frontal sinus. Under conservative treatment and continual observation all the evidence of pansinusitis disappeared except some residual distress over the left frontal .(91 days after the onset of the present illness.) It was necessary to do an intranasal frontal drainage operation and as result this was performed. Eight months after the onset of his illness he still had discomfort and purulent discharge.(five months after the intranasal.) Two hundred and sixty days after his attack of pansinusitis an external frontal sinusectomy and ethmoidectomy had to be performed in spite of all the previous treatment. At operation a large frontal sinus filled with muco-pus lined by a thick, soft, rough and dark red membrane was found. The adjacent ethmoid cells were opened and found to be free of secretion but definetly hyperplastic in some places. Now we enter into a consideration of the ethmoid cells in greater detail for here we know that there was a purulent sinusitis at one time. Apparently part of the membrane resolved, normal, and another portion becamehyperplastic, abnormal.

Figure 17.
This shows a cross section drawing of the entire sinus lining. Observe the relationship of the various portions of the membrane. Obviously hyperplasia is confined to the glandular portion where harbored infection is most apt to occur.

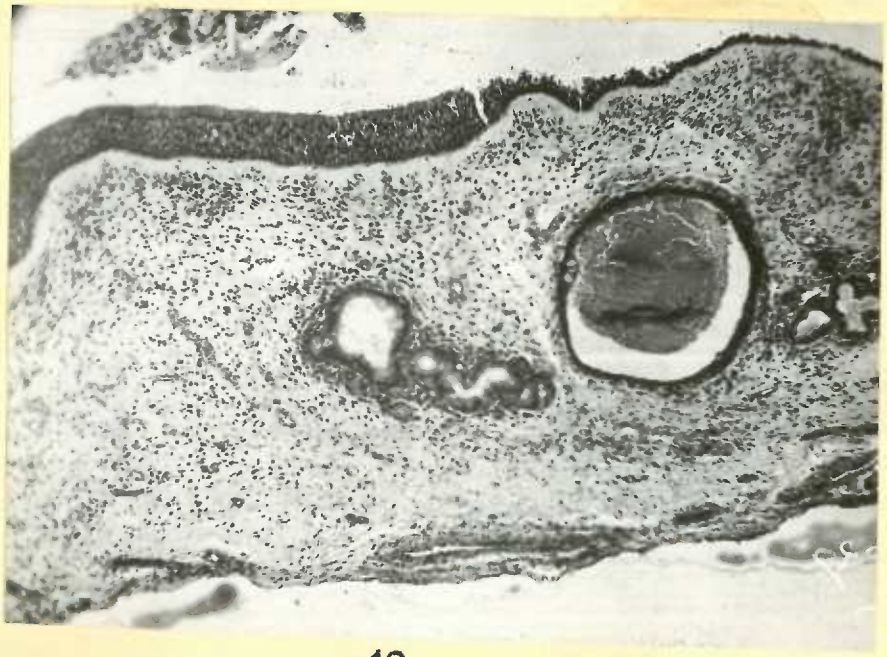
Figure 18.
Taken from point A, fig. 17; a normally thin membrane enlarged 150 X.

Figure 19.
Taken from point B., hyperplastic; same enlargement shown for contrast. Note cysts.


Mucoid exudate
Cyst
Normal
a
0.1mm
1mm
b
Mucoid degeneration
c
d
Hyperplastic
Ethmoid cell
Circumference 40mm.— Scale-enlarged 10x

17

18



19

Figures 20, 21, & 22.

Magnification the same in all three figures --- 250 X normal size.

Hematoxylin-Eosin Stain, Formalin.

Figure 20.

Normal ethmoid mucosa. From A. fig. 17. Ciliated columnar epithelium - C.; Basal cells, B.c.; hyalinized slightly hypertrophied basement membrane, B.m.; capillary, A.; red blood corpuscle on the surface of the cilia, R.b.c.

Note that the slightly hyalinized basal membrane is the only evidence in this area of a preexisting inflammation.

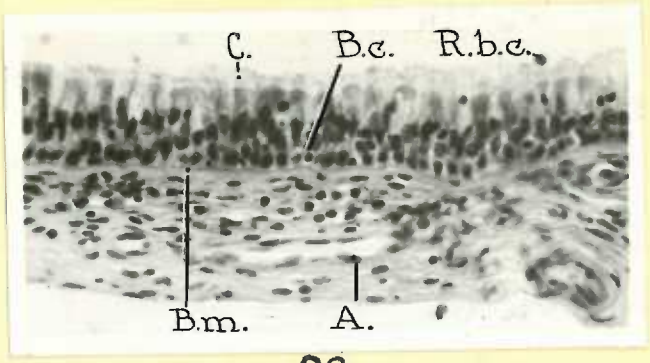
Figure 21.

Catarrhal degeneration, from C. fig 17. Here there is greater hypertrophy of the basement membrane, the epithelium is also taller, goblet cells are seen, compression of the oval nuclei appears and edematous distension of the submucous connective tissue is present. Many eosinophilic leucocytes are present in the submucous infiltration.

Figure 22.

Hyperplastic epithelium, from D. fig. 17. Note the numerous layers of cuboidal cells with a surface layer of columnar cells. Cilia are present but they are very short and feeble. The basal membrane is greatly hypertrophied. Note the channels in the basal membrane containing cellular elements.

From these figures all found in the same cavity we have evidence of a normal portion favored by location and absence of infected glands and an infected hyperplastic portion degenerating as a result of adverse structure.



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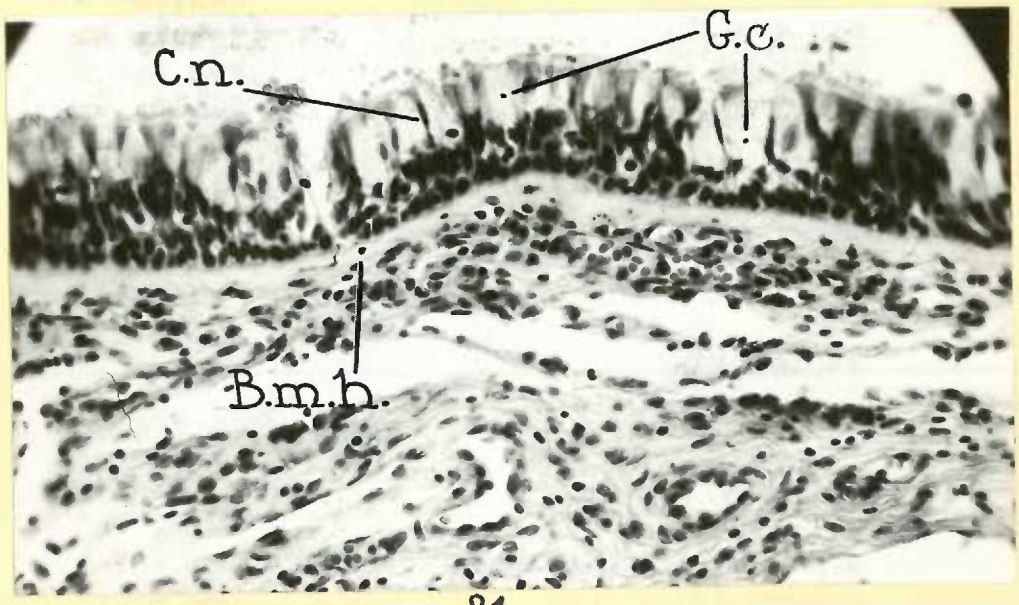

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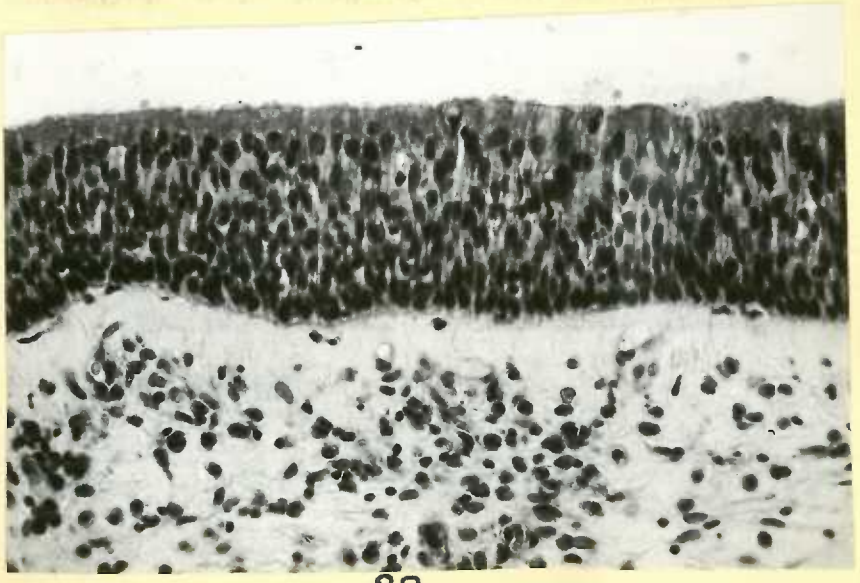


22

G L A N D U L A R S T R U C T U R E

Five Plates

Figures: 23, 24, 25, 26, 27, 28,
29, 30, 31, 32, 33, 34.

Figure 23

The lateral and medial walls of an antrum that was found normally thin in all parts. This is shown to demonstrate the difference between the medial and lateral walls in reference to thickness and the number of glands.

Medial wall is 0.435 mm. thick.
Lateral wall 0.079 mm. thick.

Hematoxylin-Eosin Stain. 80 X.

Figure 24

Lateral wall of a normal antrum shwoing no glands, no leucocytic infiltration, no edema, no goblet cells and a very thin layer of loose tissue - L.l.;but a well formed compact layer - C.l.; with normal ciliated columnar epithelium - E.p.

Total thickness of mucous membrane - 0.136 mm.
Hematoxylin-eosin. 320 X.

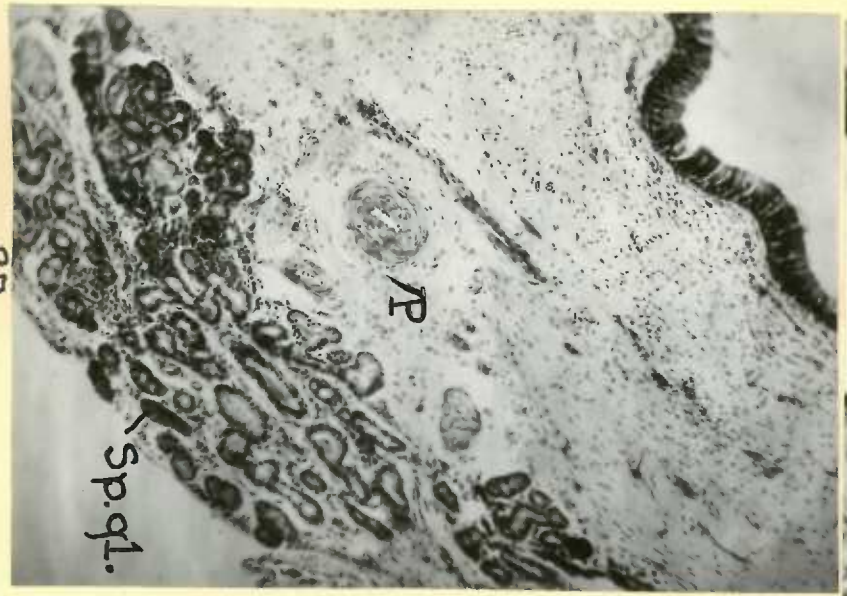
Figure 25

Showing medial wall with many glands lying beneath the periosteal portion of the mucous membrane in such a manner th at they become attached to the bone -- these subperiosteal glands are marked, Sp. gl. . The position of the periosteum is indicated by, P.

Figure 26.

Usual position of mucous and serous glands above the periosteum, P.; note the small connective tissue prolongation from the periosteum into the boney lacuna, L. C., is an erectile tissue channel.

H & E.



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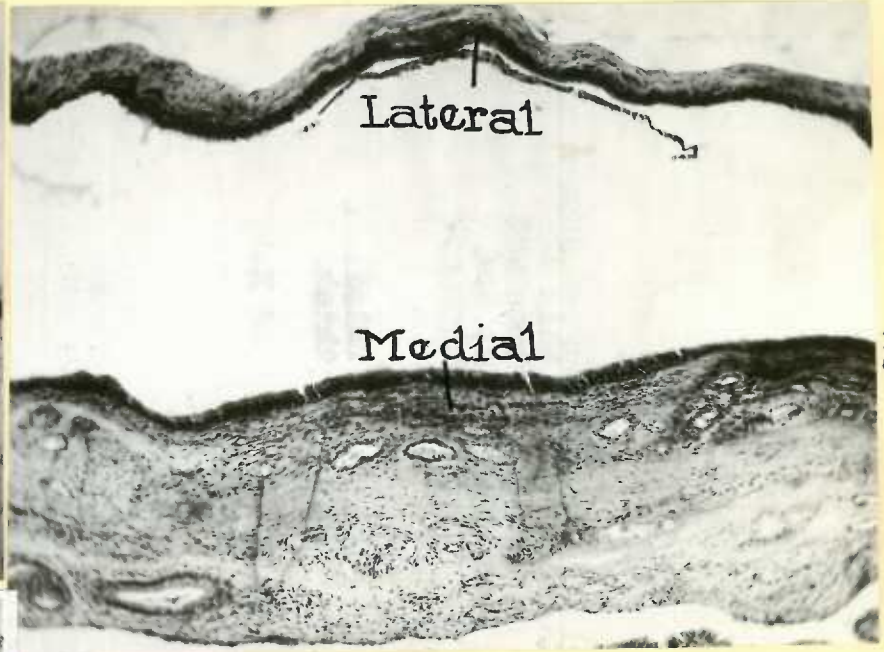

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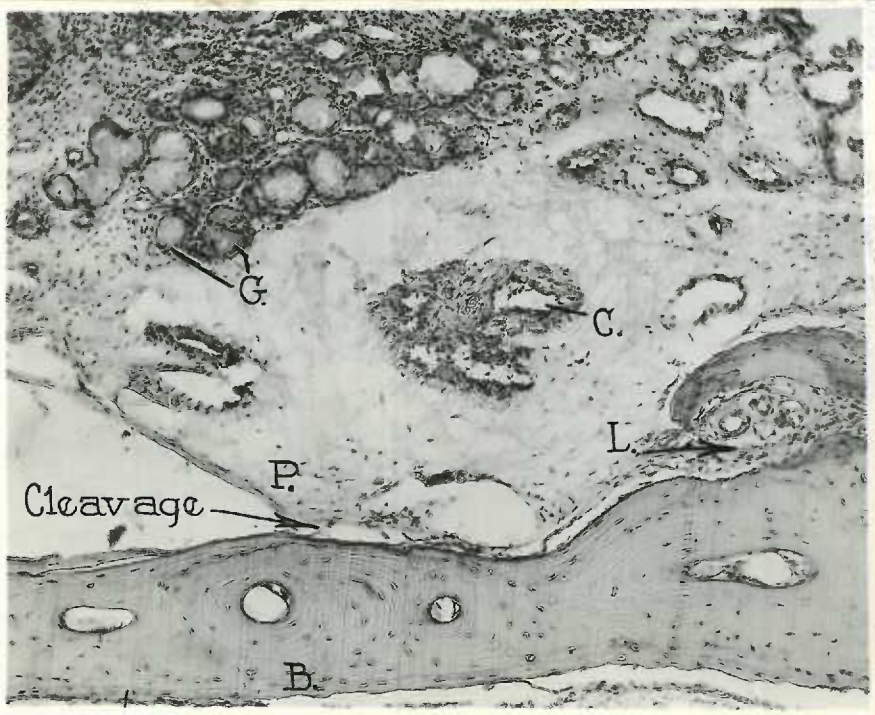

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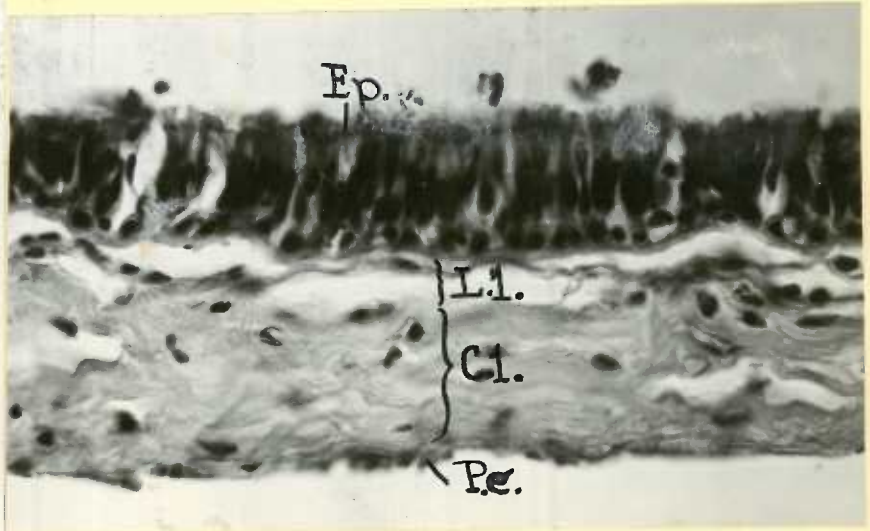

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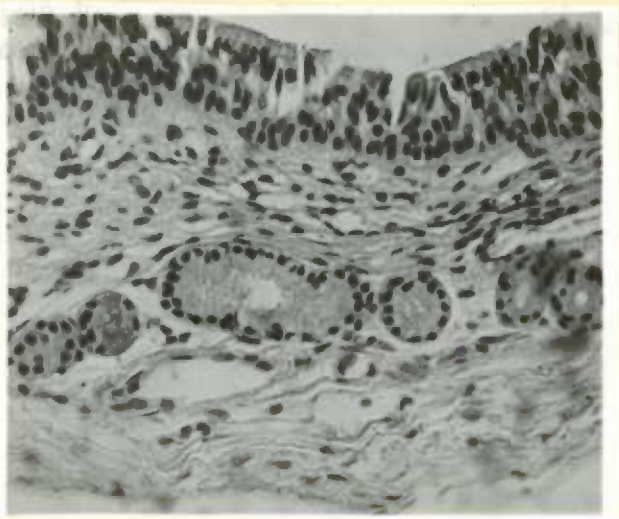


Figure 27

Simple tubular glands lying in a thin portion near the periphery of the medial wall of an antrum mucous membrane.

Figure 28.

Showing surface folds, S.F.: free mucus, M.; definite mucous glands, M.g.; lying at the periosteum, P.; in an active catarrhal sinusitis associated with hay - fever.

The surface folds could easily be mistaken for epithelial tunnels passing through the epithelium.

Figure 29.

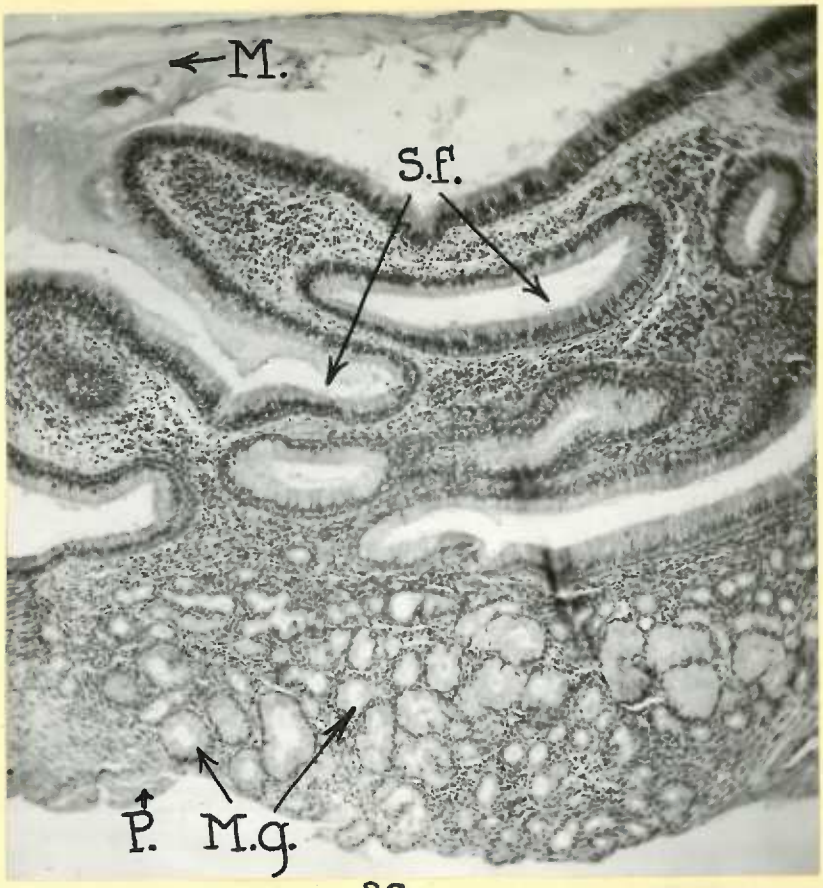
Showing a true epithelial tunnel of ciliated columnar cells acting as an outlet for glands. Tunnel is makked, T..

Figure 30.

The usual glands have a defintie duct and generally lie midway between the upper loose and deep compact layers of connective tissue. The type shown in Fig. 29 is less common.

Gland cluster, Gl.c.; Loose connective tissue, L..

Hematoxylin-eosin preparations.



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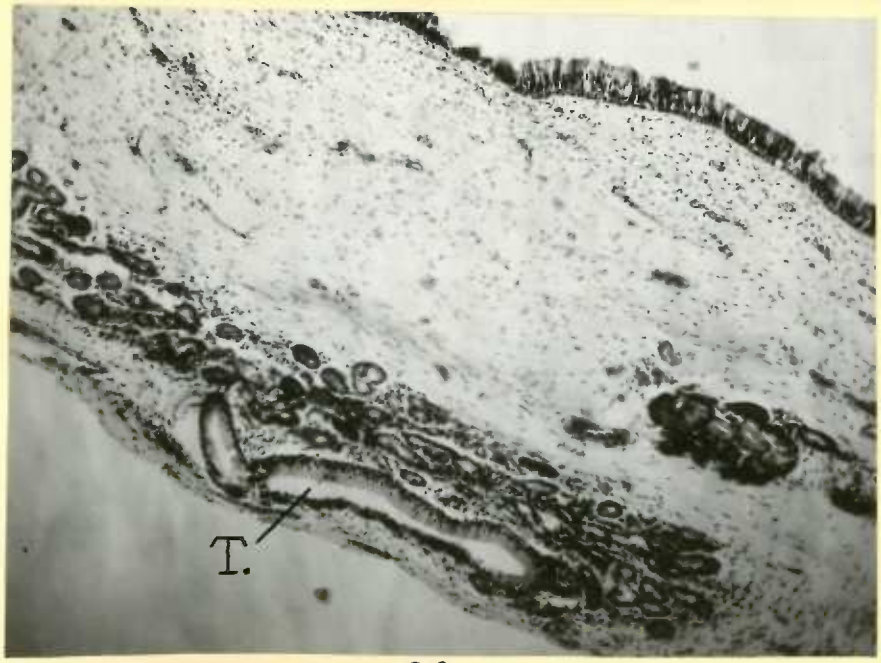

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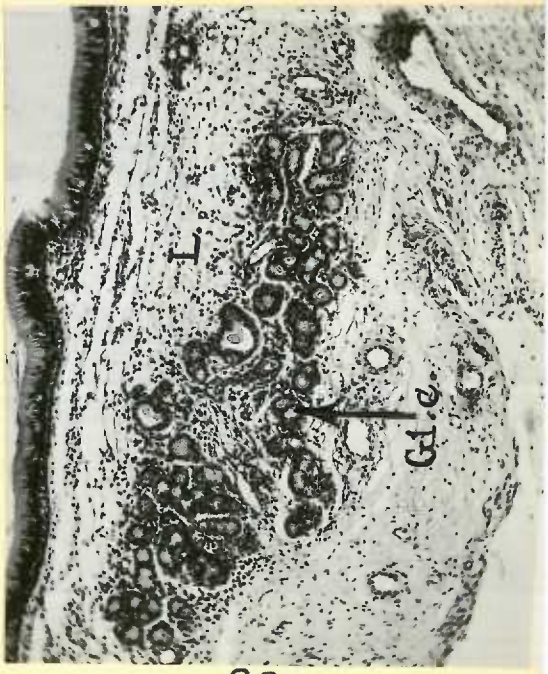


30

Figures 31 & 32:

Hematoxylin-eosin stain, formalin fixation, magnification 320 X normal, taken from same specimen, see figure 35 for general structure of this specimen. This lining is definitely pathologic, there is an early edema and infiltration of the submucosa but the anatomic details are not greatly altered.

Figure 31.

Epithelium, Ep.; gland duct lined with cuboidal cells, D.; simple tubular acinus, lined with columnar cells, A.; note how narrow the duct lumen appears. This bottle-neck type of gland is readily obstructed and favors cystic formation.

Figure 32.

Deeper in the loose spongy layer of connective tissue, typical acinus, A.; surrounded by edematous loose tissue space filled with serum, L.t.; and the glandular nutrient capillary running between the acini is seen.

Attention is called to the absence of stroma and glandular bulwark around the acini. This also favors cystic degeneration.

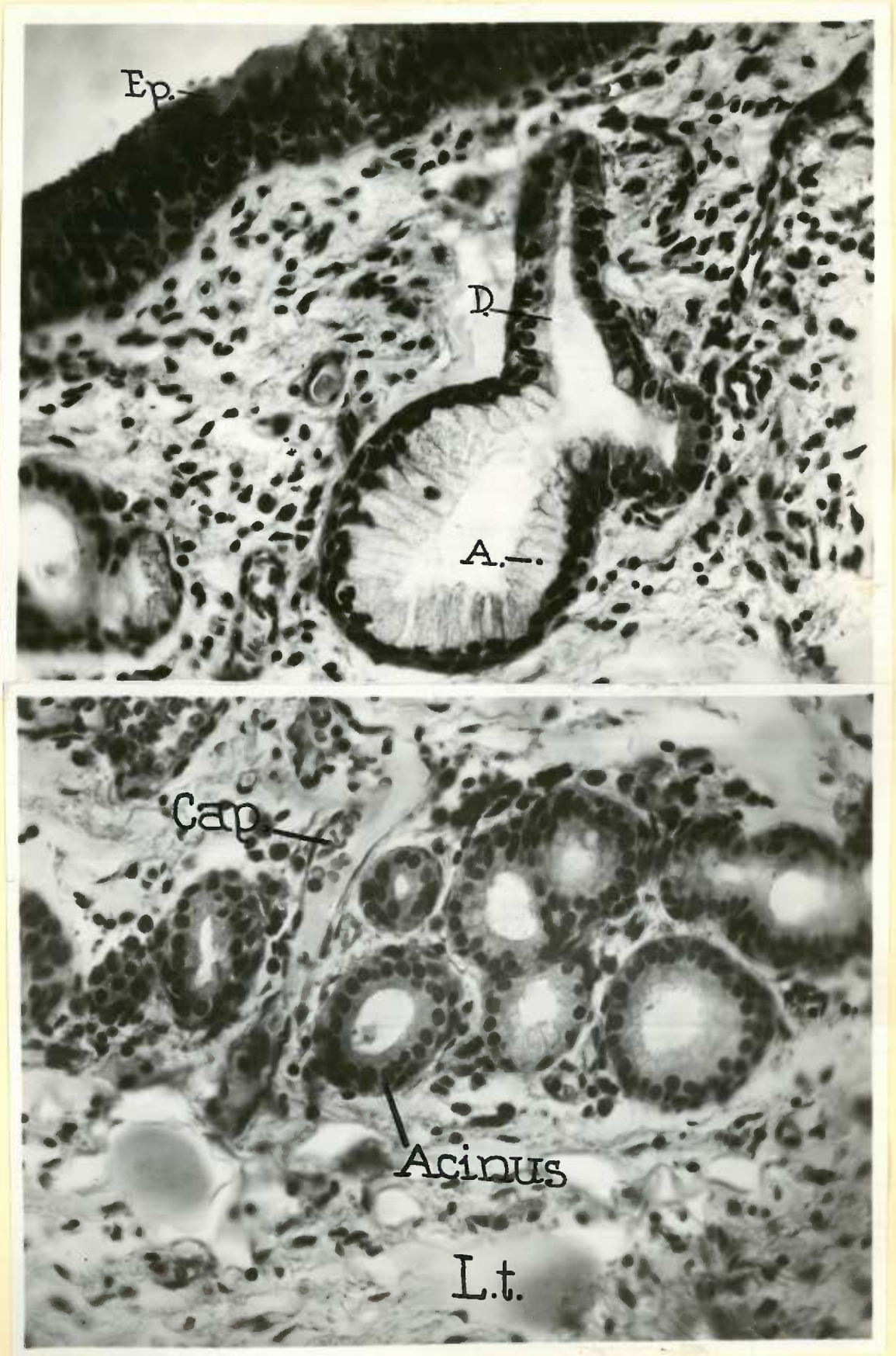

Ep.
D.
A.
Cap.
Acinus
L.t.

Figure 33.

Cystic degeneration of the glands. Note how the distended acini are rupturing into each other and thereby forming large single cysts. This probably accounts for the various types of epithelium found in large cysts. The overlying epithelium is macerated as aresult of the underlying pathology.

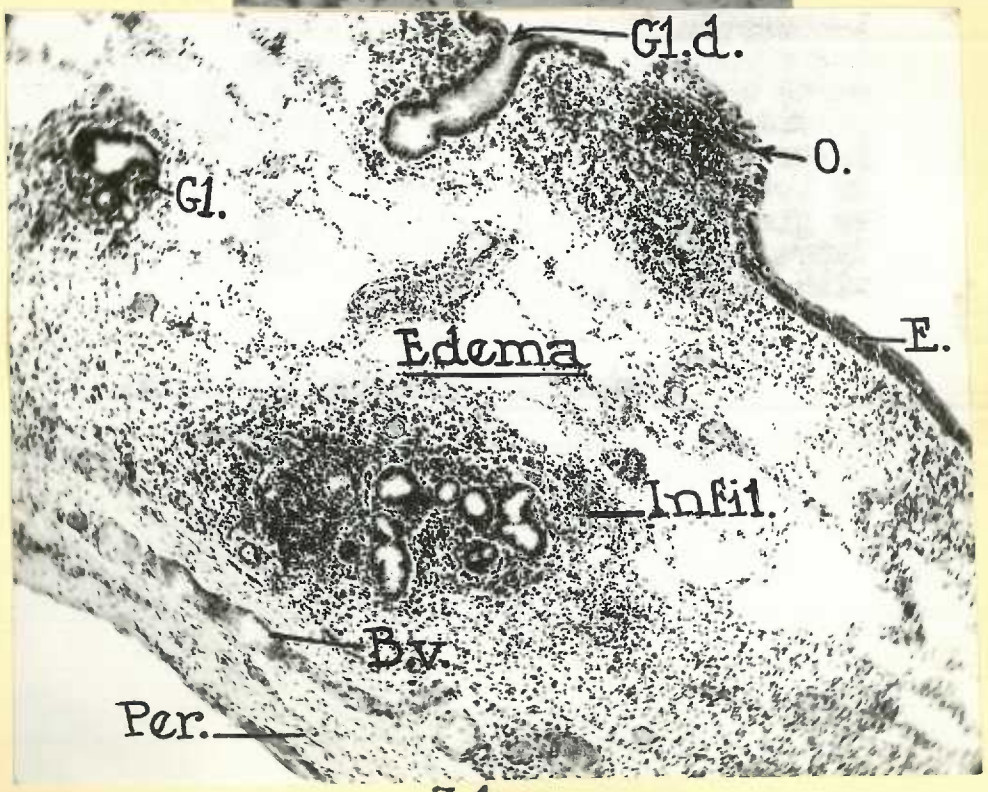
Figure 34.

Periacinar infiltration. The important features of chronic suppurative simusitis are visible in this microphotograph.

Gl.d., gland duct from surface carrying infection down into the acini. U., is and ulcerating area of epithelium with underlying leucocytic infiltration near the duct. E., is the ciliated columnar epithelium. Gl., is an early cyst. Edema of the loose layer of connective tissue is seen. Note that the compact periosteal layer of connective tissue is not invaded by edema or leucocytic infiltration! Here is the mechanism of gland infection, cyst formation and persistant intractable simusitis that refuses to improve with surgical drainage.

Hematoxylin-eosin, formalin.

33



34

STRUCTURE OF TUNICA PROPRIA AND PERIOSTEUM

Three Plates.

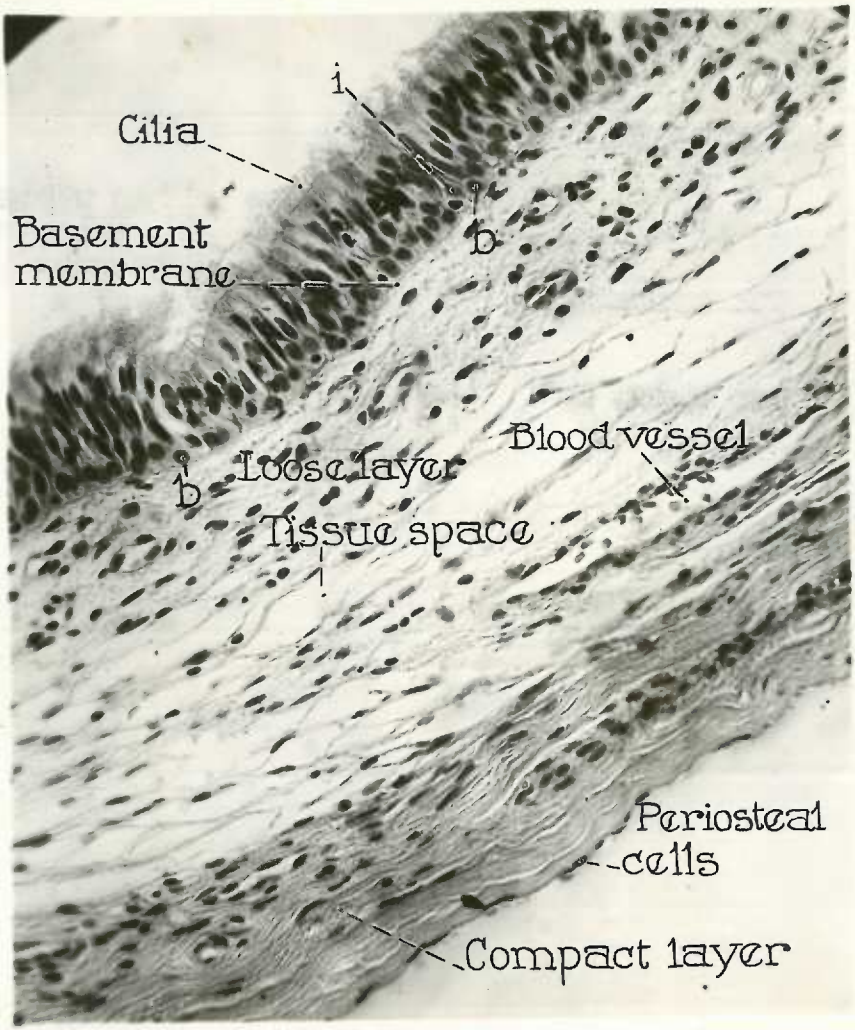
Figures: 35, 36, 37,

38 & 39.

Figure 35.

General structure of the sinus mucous membrane. Microphotograph enlarged 150 X normal size. The total thickness of the membrane is 0.363 mm.

Glands from the same specimen are shown in Figures 31 & 32.


i
Cilia
Basement
membrane
b
b
Loose layer
Blood vessel
Tissue space
Periosteal
cells
Compact layer

Figures 36 & 37.

Elastic tissue in the mucous membranes of the paranasal sinuses.

Figure 36.

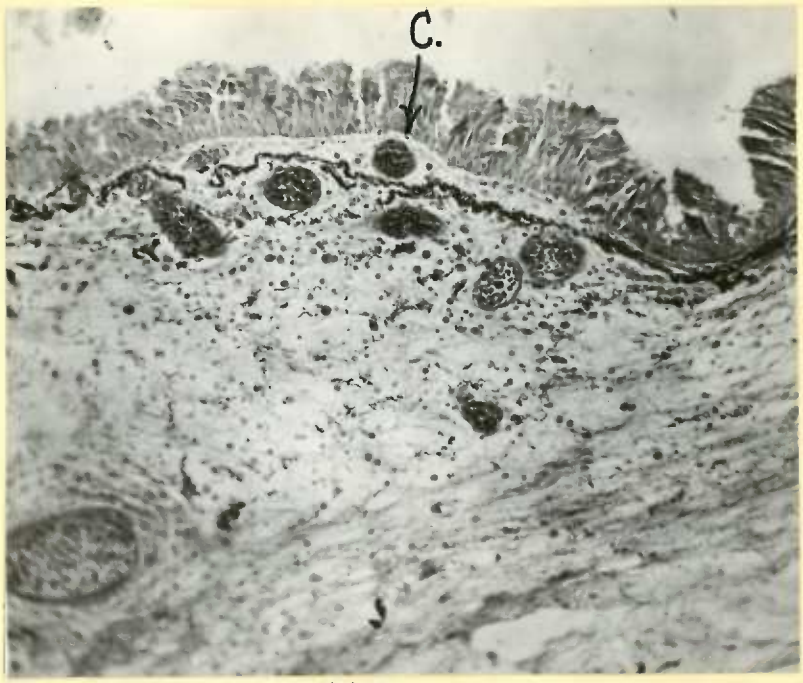
The elastic fibrils lie just beneath the basement membrane and form a definite strata. Some fibrils are incorporated in the basal membrane but the membrane itself consists largely of collagen fibrils.

C., is a capillary lying above the elastic tissue layer but under the basal membrane.

Figure 37.

Ep., epithelial layer; L., loose layer of connective tissue; El.F., elastic tissue fibrils; C., compact tissue of periosteal layer with a few fibrillar elements in the bony aspect.

Weigert's elastic tissue stain.
Formalin fixation.



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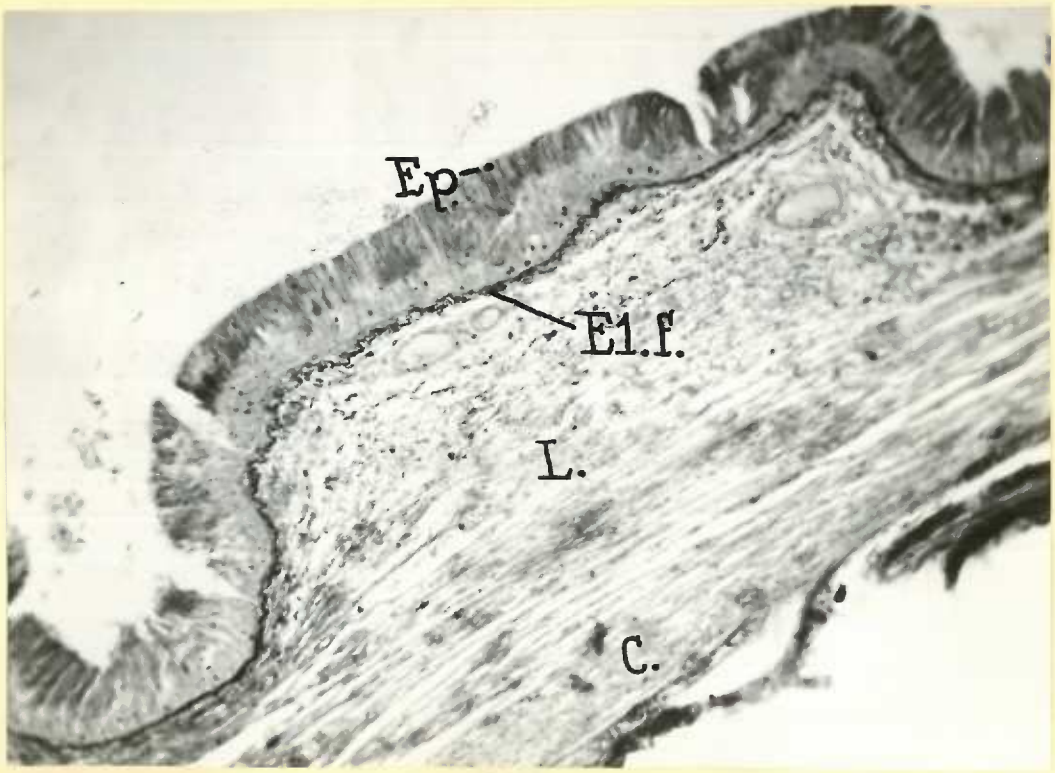

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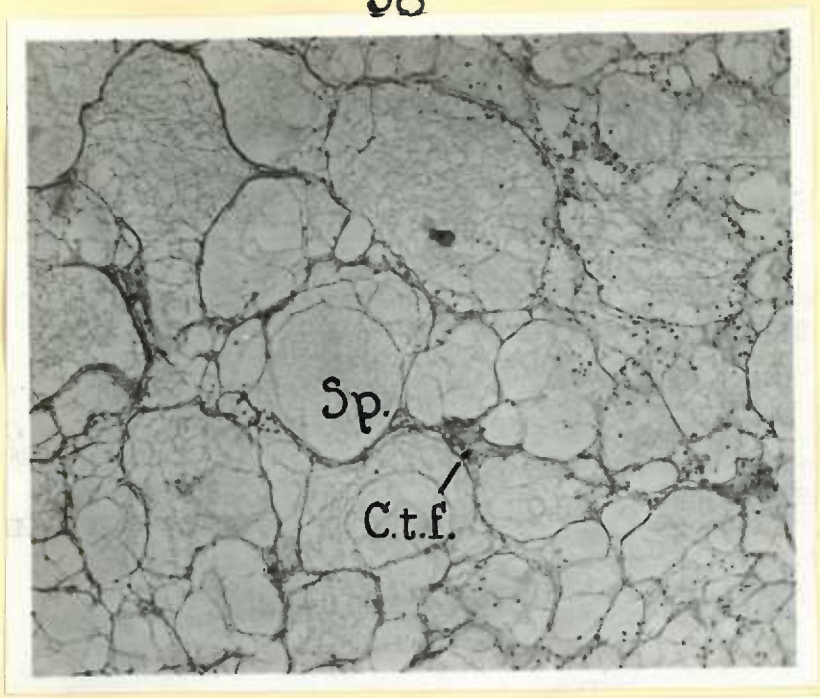
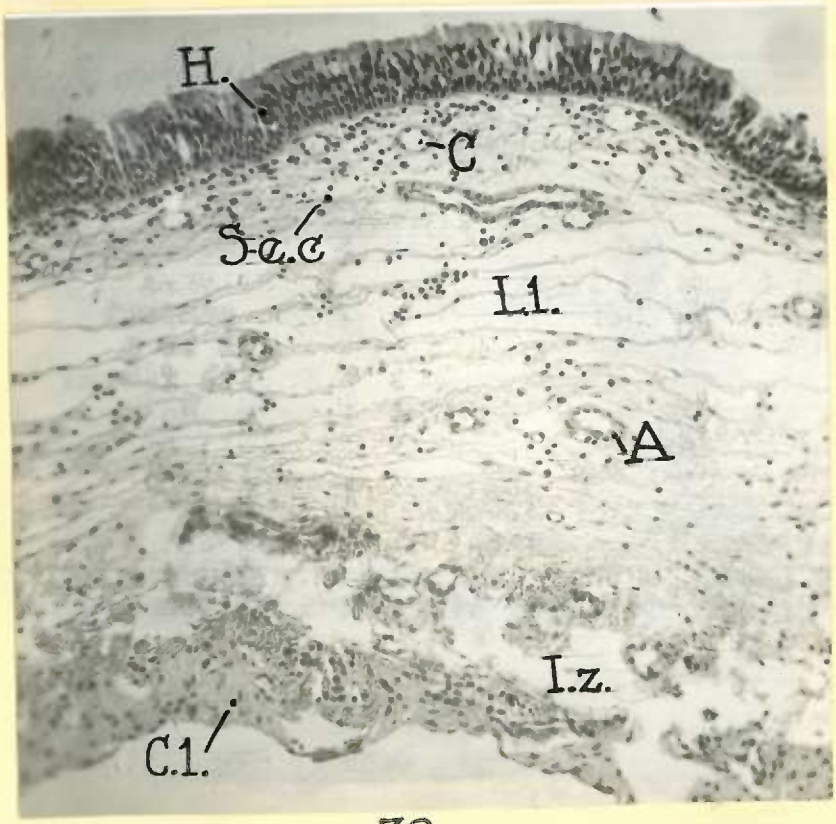




39

Figure 38.

Extreme distension of areolae of loose layer of connective tissue by edematous process. Sp., tissue space filled with serum; C.t.f., connective tissue fibrils. This is the underlying mechanism of polypoid sinusitis and mesothelial cyst formation. When the connective tissue fibrils rupture as a result of tension, the spaces enlarge and a large cyst is formed. This type of cyst usually contains a clear amber fluid and has no epithelial lining. Refer to Fig. 59.

Hematoxylin-eosin, formalin.
250 X

Figure 39.

Mucous membrane showing general structure. This specimen in contrast to that shown in Fig. 35, shows a gradual transition from the loose to the compact layer of connective tissue. There is a double layer of compact tissue with fibres directed in two different planes. E., epithelium; C., capillary near surface; S.c.c., subepithelial condensation of loose connective tissue; L.l., loose layer of connective tissue; A., artery; I.z., intermediate zone of connective tissue; C.l., compact layer of periosteal connective tissue.

Hematoxylin-eosin, formalin,
160 X.

L Y M P H A T I C N O D U L E S

Two Plates

Figures: 40, 41, 42, 43, 44, 45.

Figure 40.

Lymphatic nodule near the surface of a hyperplastic maxillary mucous membrane. M., marginal ring of lymphocytes; C., central zone of large vesicular cells; L., loose layer of mucous membrane; Ep., epithelium.

Figure 41.

Lymphatic nodule just above the compact periosteal layer of connective tissue. Note the lymphocytes apparently gravitating toward the blood vessel.

Figure 42.

Higher magnification of nodules, note the small capillaries supplying the nodule.

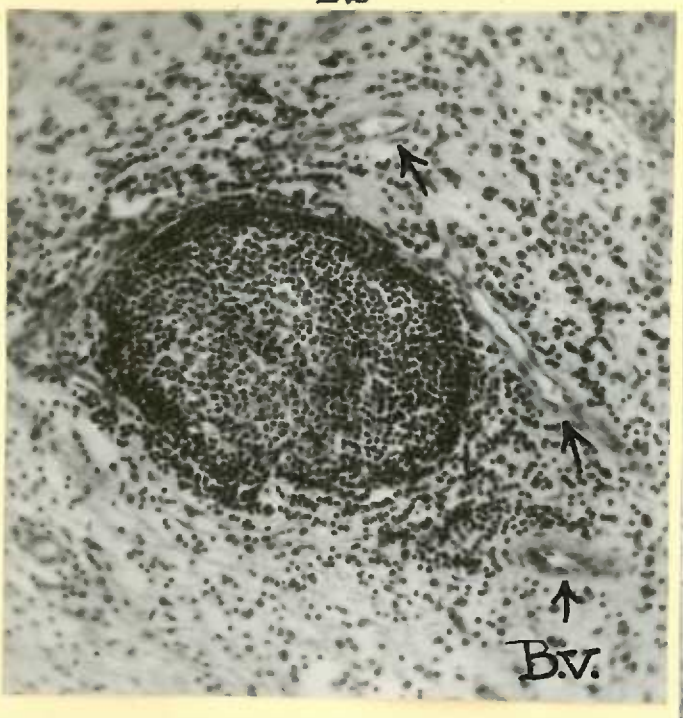
Figure 43.

Showing the central cells, contrast appearance with the marginal cells.

Figure 44 & 45, turn page.

Show variable appearances of nodules, some are small and others are large. One has less lymphocytes than the other.

42



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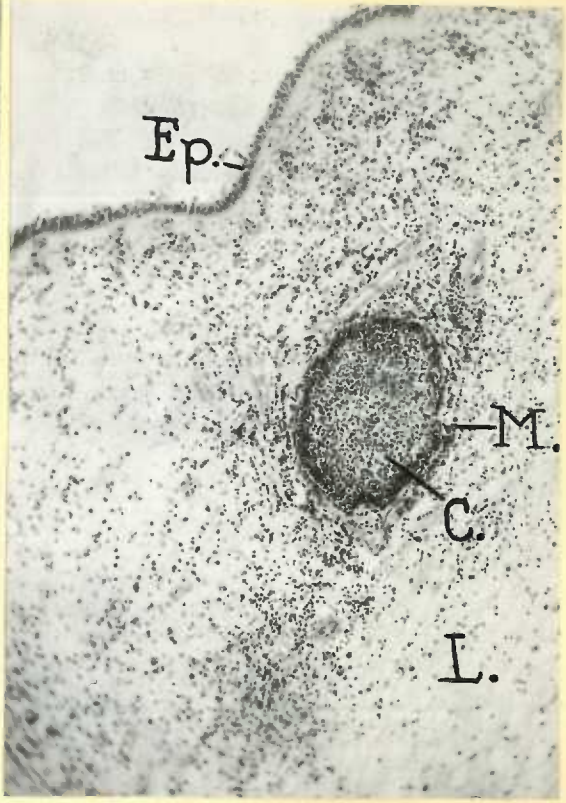

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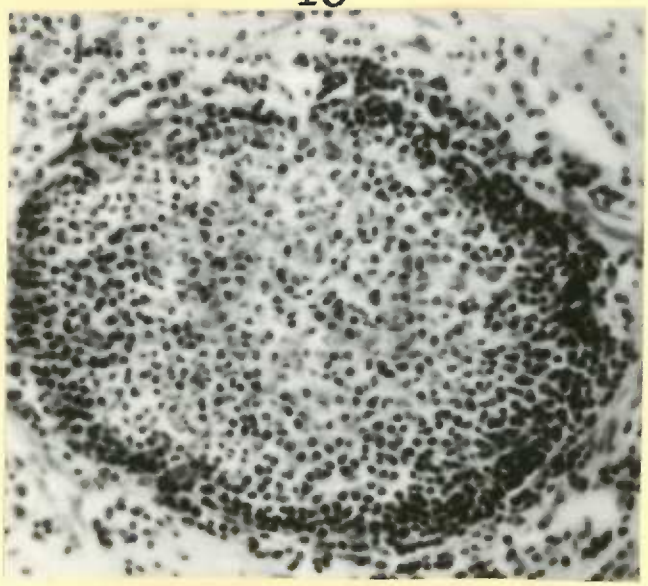

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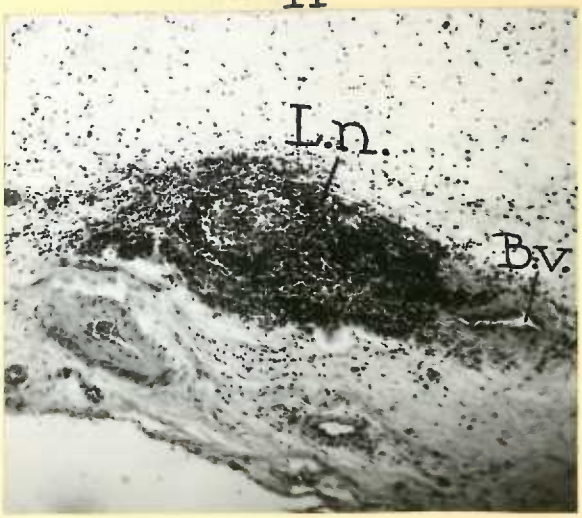

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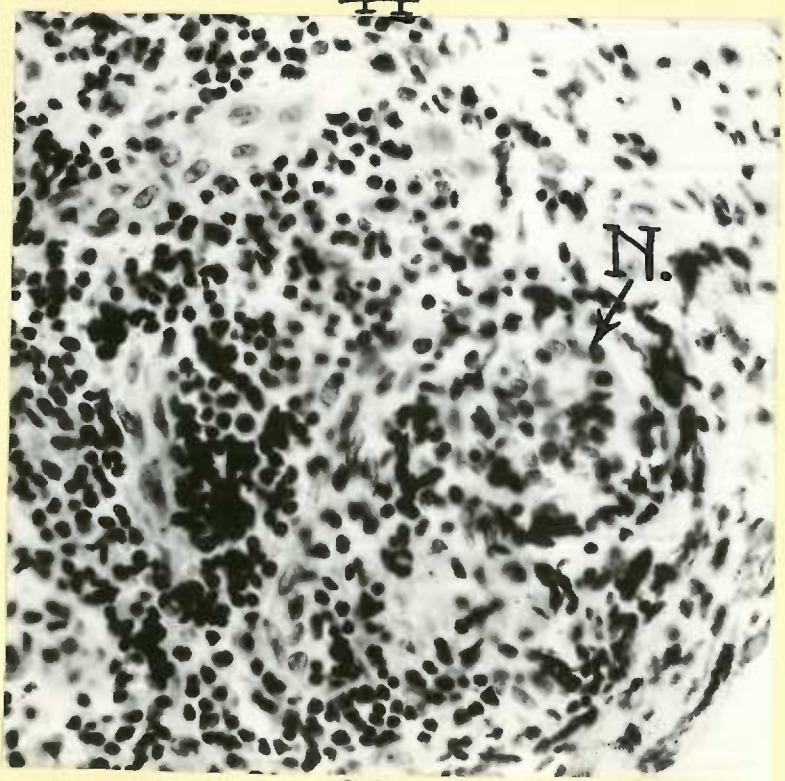


45

B L O O D V E S S E L S

One Plate

Figures: 46, 47, 48, 49.

Figures 46, 47, 48, & 49.

These figures show the blood vessels as they commonly appear in the mucous membranes of the paranasal sinuses.
Hematoxylin-eosin, formalin.

Figure 46.

H., hyperplastic epithelium; P.V. large distended periosteal arterioles and veins giving rise to smaller branches; B.C., blood capillaries in upper loose connective tissue. Note the early edema of the mucous membrane. P.T., periosteal c.t.
90 X.

Figure 47.

L., loose layer of connective tissue; A small arteriole distributing capillaries; P., periosteal layer of mucous membrane. 75 X.

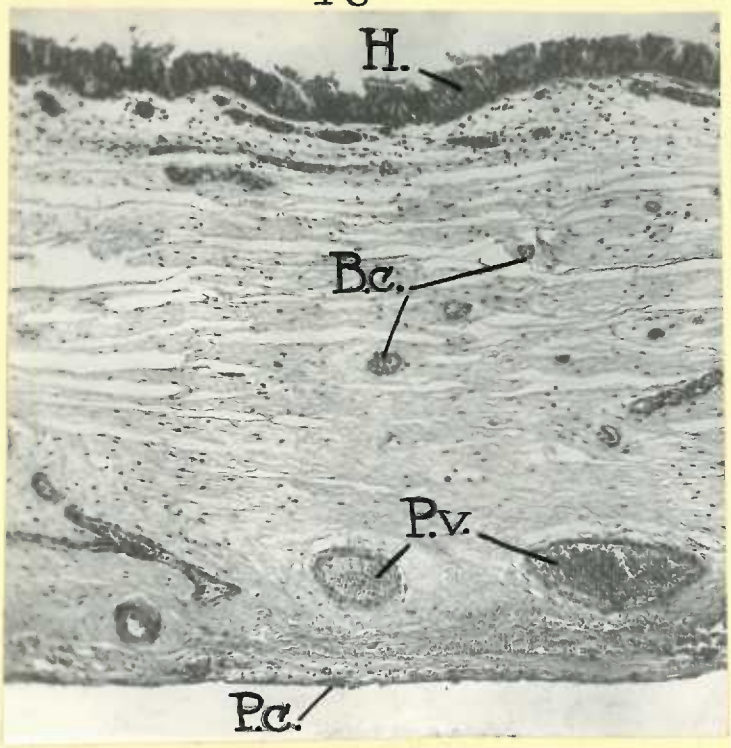
Figure 48.

Loose connective tissue with blood vessel just above the periosteal condensation of connective tissue. In all sections the arteries and trunks ramify just above the periosteal layer. B.V., blood vessel; L., loose tissue; P., periosteal layer. 200 X

Figure 49.

B.V., vessels just above the periosteal layer; P., periosteal layer; N., lymphatic nodules; D.G., deep acini of glands. Note that the infiltration and edema stops just above the periosteal layer. 150 X.

46



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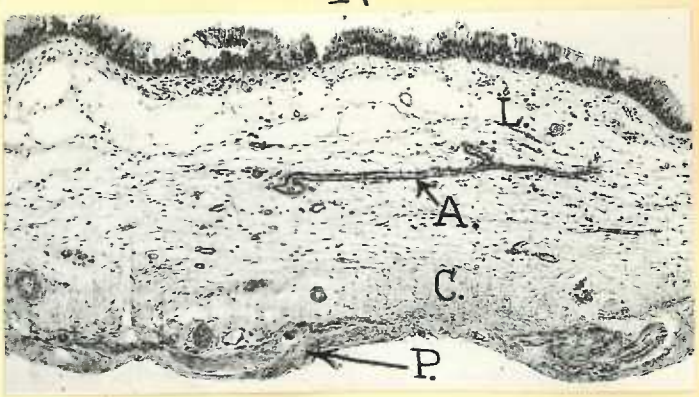

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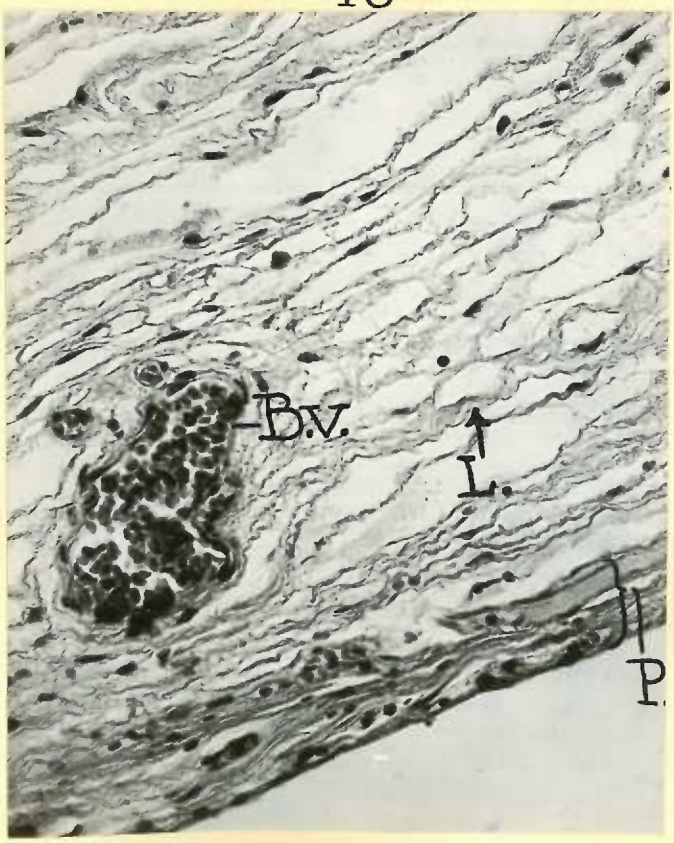


49

AN ANOMALOUS ETHMOID CELL

SHOWING RELATIONSHIP BETWEEN NASAL

MUCOUSA AND SINUS

One Plate.

Figures: 50 & 51.

AN INTERESTING SPHENOIDAL
MUCOUS MEMBRANE WITH PIGMENT GRANULES
IN THE EPITHELIUM.

One Plate.
Figure: # 52.

Figure 50.

Cross section of a middle turbinate showing an Ethmoid Cell in the turbinate. There is every reason to believe that this is an ethmoid cell, but rhinologists have introduced the term "cystic turbinate" for this anatomic anomaly. There is absolutely no evidence of cystic degeneration present. Note the thickness of the respiratory nasal mucous membrane over the concha, N.

NE. - Nasal epithelium ; B. - Bone of turbinate; EE. - ethmoidal epithelium. Contrast the thickness of the two epithelia.

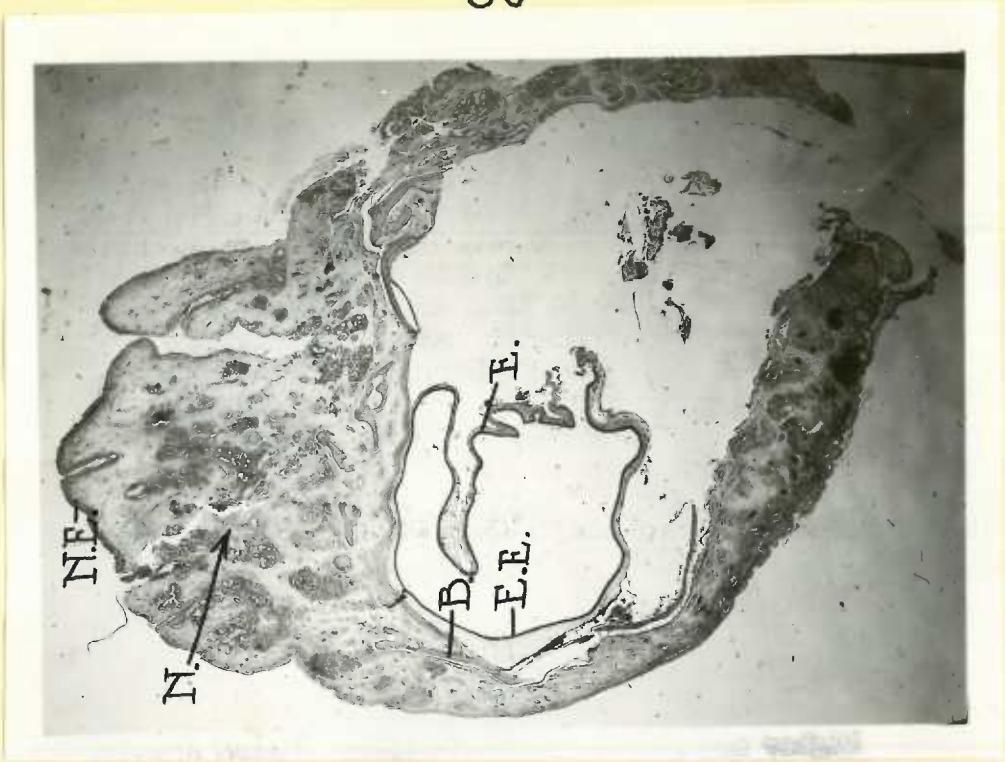
Magnification 8 X. Hematoxlyin-Eosin.

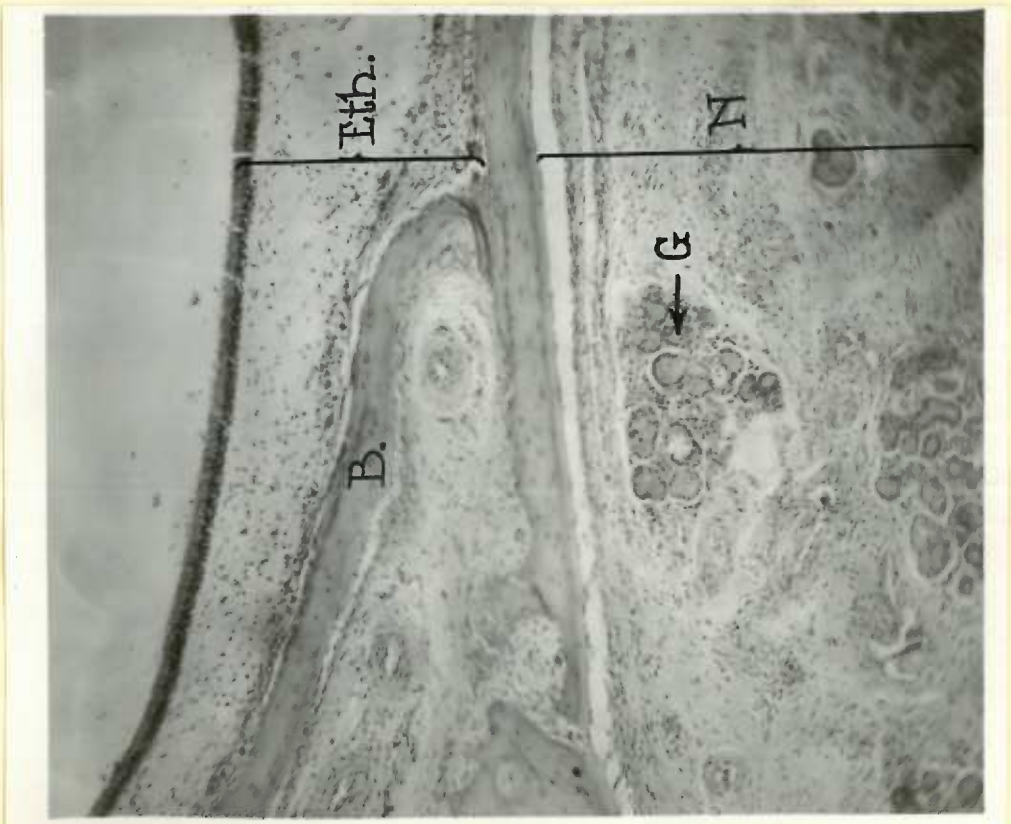
Figure 51.

Higher magnification of ethmoidal mucosa showing the typical sinus epithelium and tunica propria with its upper loose and deep compact layers. Bone is marked B.; Nasal mucosa, N.; glands in nasal mucosa, G. The sinus epithelium measures 0.036 mm. thick, the total membrane is only 0.06 mm. in thickness.

Magnification 60 X. Hem. & Eosin.

50





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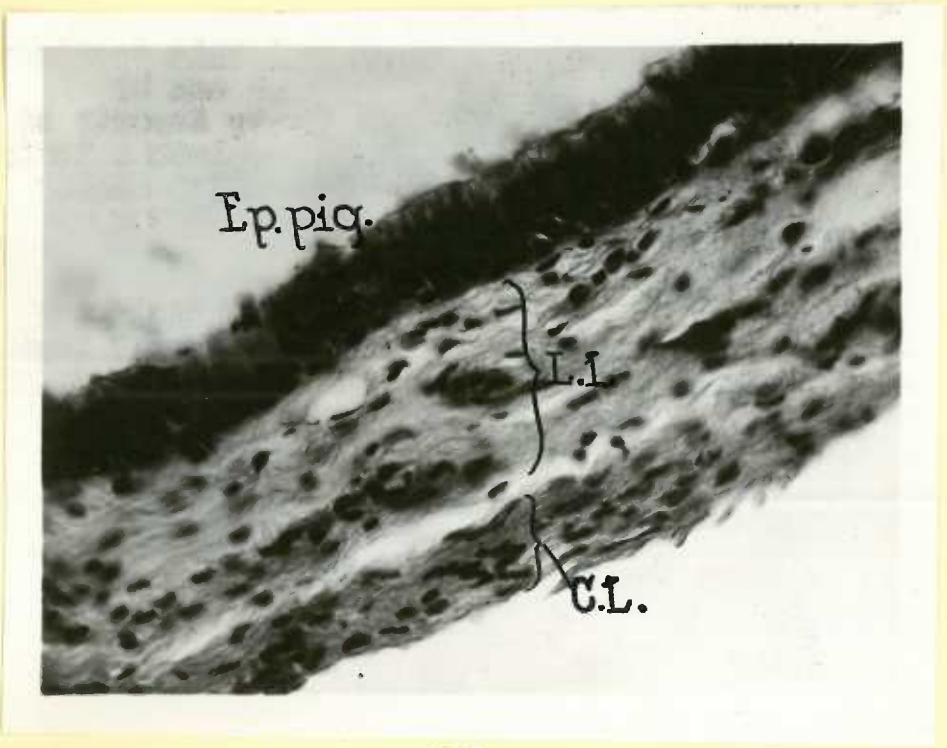

Ep. pia.
L.I.
C.L.

Figure 52.

Sphenoidal mucous membrane removed from a normal sinus. Enlarged 230 X, hematoxylin and eosin stain, formalin fixation.

The unusual feature of this specimen is obscure in this photograph, but can be recognized. It consists of a heavy deposit of brownish granules in the free cytoplasmic border of the columnar cells; these granules appear much like hematoidin particles in the usual mononuclear phagocytes.

The subject fell from a height and was instantly killed as a result of heart rupture. The significance that can be attached to the granules is undetermined.

L.l., loose layer; C.l., Compact.

TYPICAL NORMAL HISTOLOGY AND HISTOPATHOLOGY.

Photographed to the Same Scale so that an Easy and Simple Basis of Comparison between the NORMAL and ABNORMAL is Possible.

EMPHASIS OF THE GENERAL STRUCTURE *
OF THE MUCOUS MEMBRANES :
IN DISEASE AND HEALTH

Five Plates. Figures: 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, & 65.

* Relatively low degree of Magnification --- 8 X Normal.

THE FOLLOWING FIGURES ARE ALL PHOTOGRAPHED WITH THE CAMERA AND MICROSCOPE SET IN THE SAME POSITION. THE MAGNIFICATION IS CONSTANT AND IN THIS MANNER SHADES OF CONTRAST BETWEEN THE NORMAL AND ABNORMAL SINUSES CAN BE READLY OBSERVED. THESE FIGURES ILLUSTRATE THE VARIOUS DEGENERATIVE CHANGES COMMONLY SEEN AS A RESULT OF CHRONIC SINUSITIS.

MAGNIFICATION IS UNIFORMLY 6 X THE NORMAL SIZE.

Figure 53.

An early edema and hyperemia in a borderline hyperplastic sinusitis. This specimen is a good example of very early inflammation.

Figure 54.

Absolutely normal sinus membrane. Note how thin and unifrom the lining is. On the right it is slightly thicker. At this point we are approaching the nasal wall.

Figure 55.

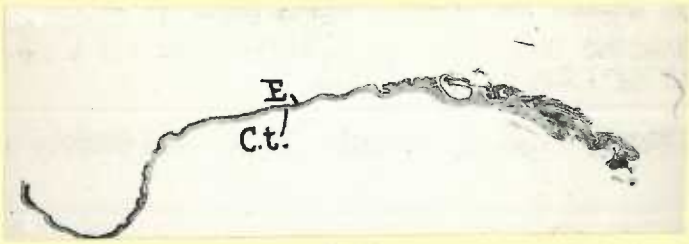
Here is a hyperplastic sphenoidal membrane. Note how much thickening there is in the connective tissue. Very few glands are seen in the entire circumference of the cell. Serial sections disclose only and occassional gland.

Figure 56.

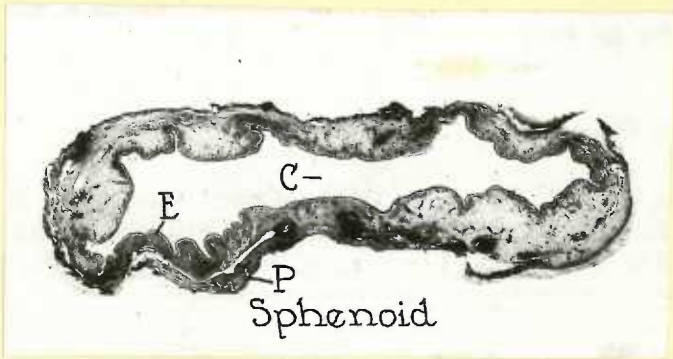
Hyperplastic antrum from the same case as the sphenoid. This illustrates the pansinusitis and uniformity of the changes in the same person. Note that this lining is many times thicker than normal (54) and that gland clusters appear in relatively great numbers only near the ostium. Ep. epithelium; Ln, lymph nodule; o, ostium; per, periosteum; and Bv. blood vessels on the posterior wall of the antrum. Attention is called to the fact thatt the hyperplasia is in the upper loose layer.

Hematoxylin-eosin sections.

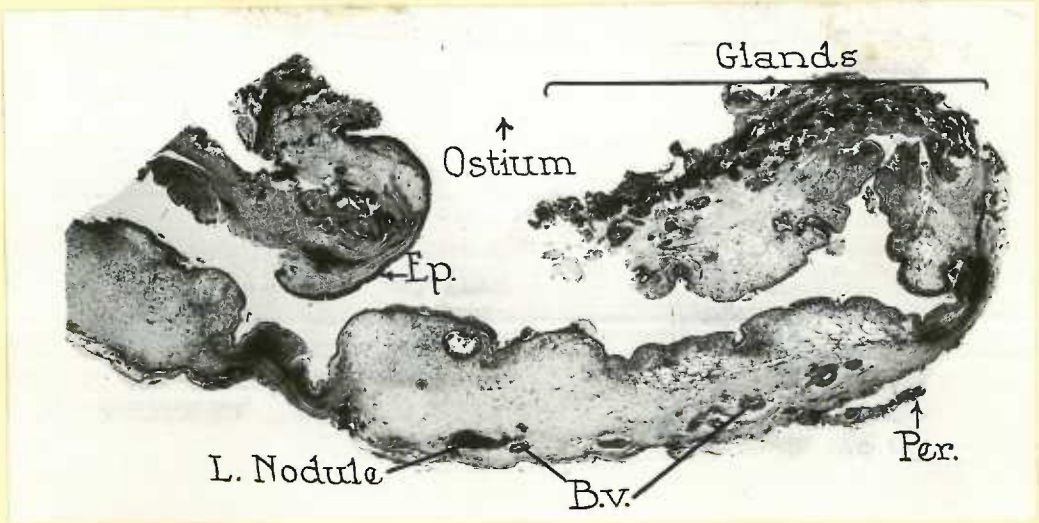
53



54



55



56

Figure 57.

Normal: This shows another maxillary mucous membrane that is normally thin and fairly healthy as far as evidence of degeneration and infiltration are concerned.

Figure 58.

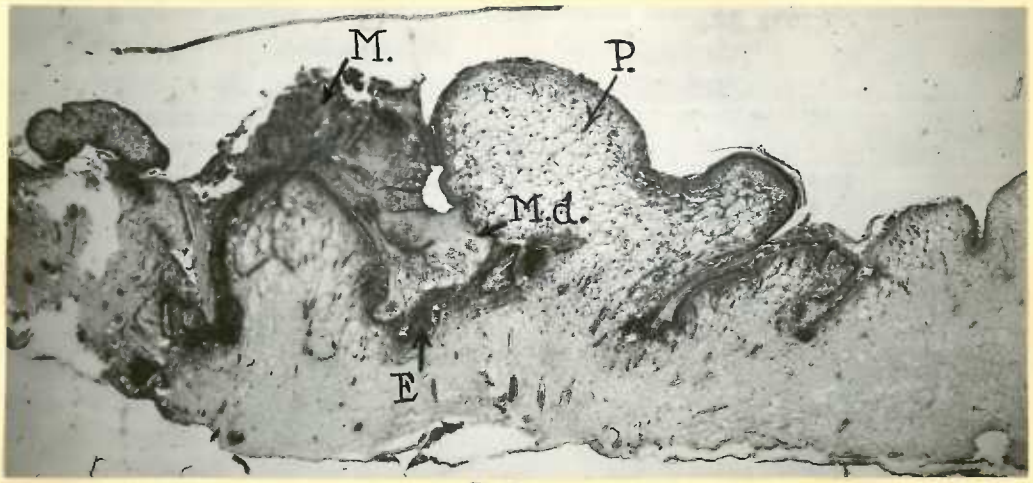
Extremely polypoid and hyperplastic maxillary sinus mucous membrane from an allergic patient: Showing the marked elaboration of mucus, M.; mucoid degeneration of the epithelium, M.d.; edematous polypoid distension of the upper loose layer of connective tissue, P.; and a dense subepithelial infiltration of eosinophils, E. Figure 60 shows the character of the epithelium under high power.

Figure 59.

Cystic hyperplastic sinusitis: M.c., is a mesothelial cyst formed by rupture of the connective tissue fibrils and the union of tissue spaces as a result of edema. G.c., is a large gland cyst filled with the glandular secretion, Mu. Note that these cysts are surrounded by many smaller cysts and that there is considerable edema present. This type of mucous membrane is hopelessly degenerated and can no longer take care of infections.

Magnification in all figures is 8 times normal.
Stain--Hematoxylin-eosin. Formalin fixation.

57



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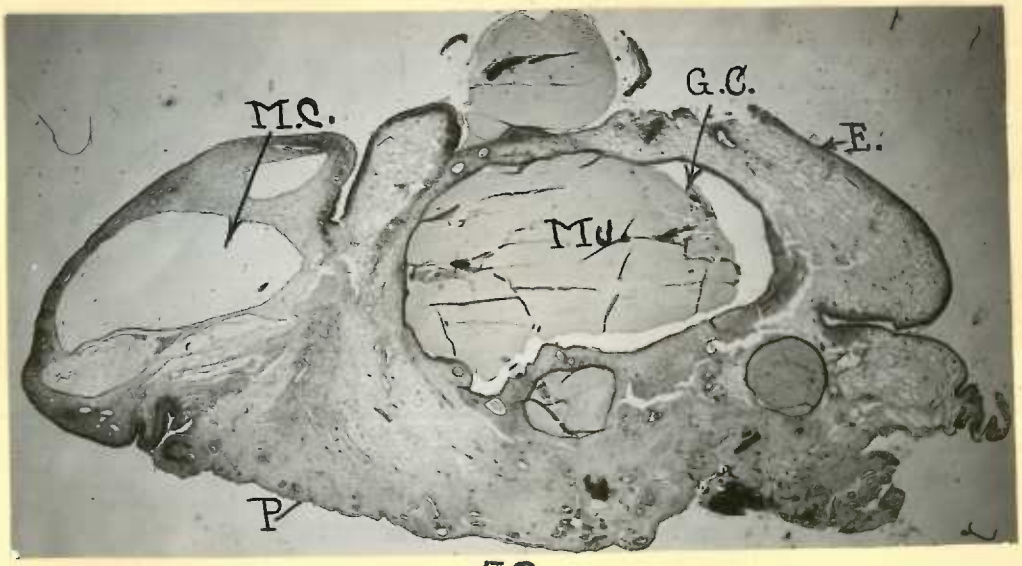

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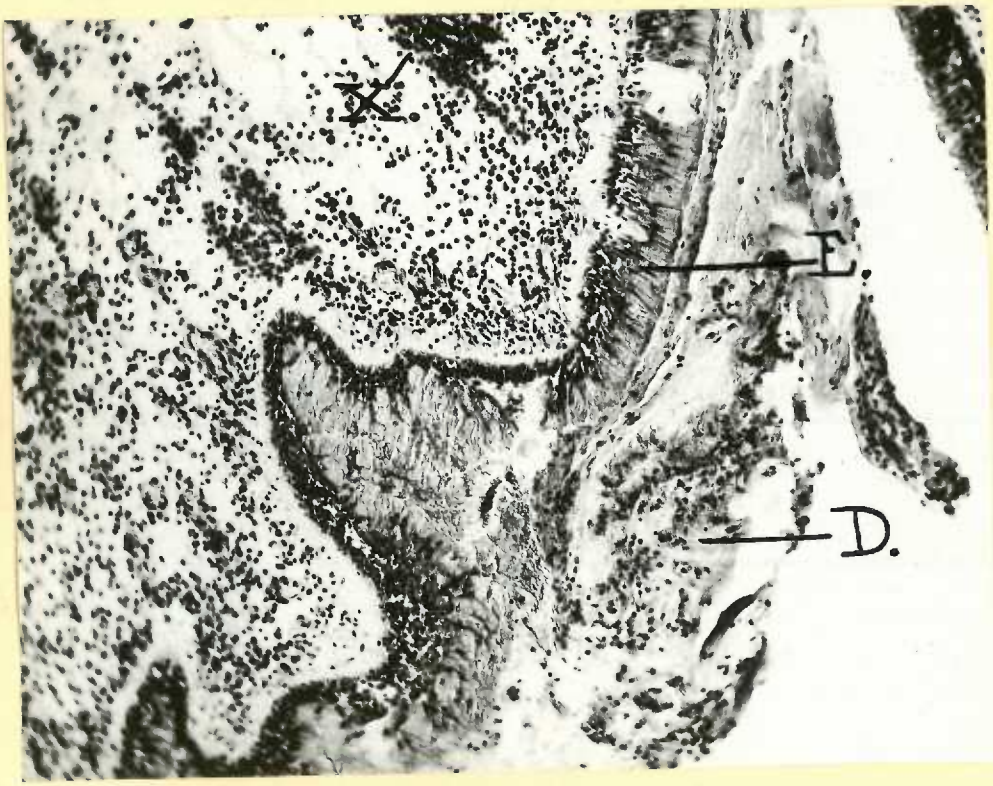

E.
D.

Figure 60

Higher magnification of figure 58 showing the mucoid degeneration of the ciliated columnar epithelium. These cells are over 100 micra in length and show pronounced goblet cell formation. Whole areas of epithelium are breaking off and forming a mixture of mucous and eosinophils. The cellular infiltration is almost entirely eosinophilic. This is a typical hay-fever type of sinusitis. Note the flow of mucous - "Catarrh."

Magnification 150 X
Hematoxylin eosin.

E--- eosinophils in epithelium, emigrating.

M--- debris, mucus, eosinophils, etc.

Figure 61.

From a purulent mucous membrane. Note that edema is not prominent but that there is a definite uniform swelling of the submucosa. This is due to leucocytic infiltration and coagulated serum.

Attention is directed to the papillae and folds, F. seen on the surface of the epithelium, E. This folding is characteristic of purulent sinusitis and is probably a factor in the formation of plicae that eventually become polypi.

The infiltration, I, is most conspicuous in the subepithelial layers. The periosteal portion is relatively free from infiltration but there is considerable swelling. Per.

Magnification -- 8 X.
Hematoxylin-eosin stain.

Compare with the normal antrum Fig.64.

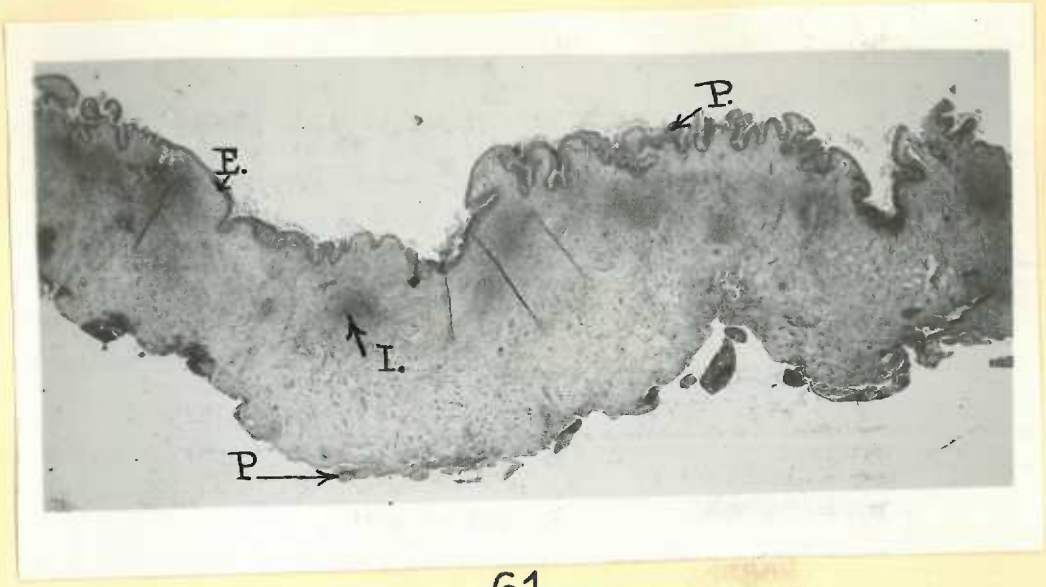
Figure 62.

Higher magnification of the epithelium in chronic purulent sinusitis of this type. Note the absence of cilia and the marked heteroplasia of the cells. Some cells appear round and the nuclei show all the degenerative changes associated with cell degeneration.

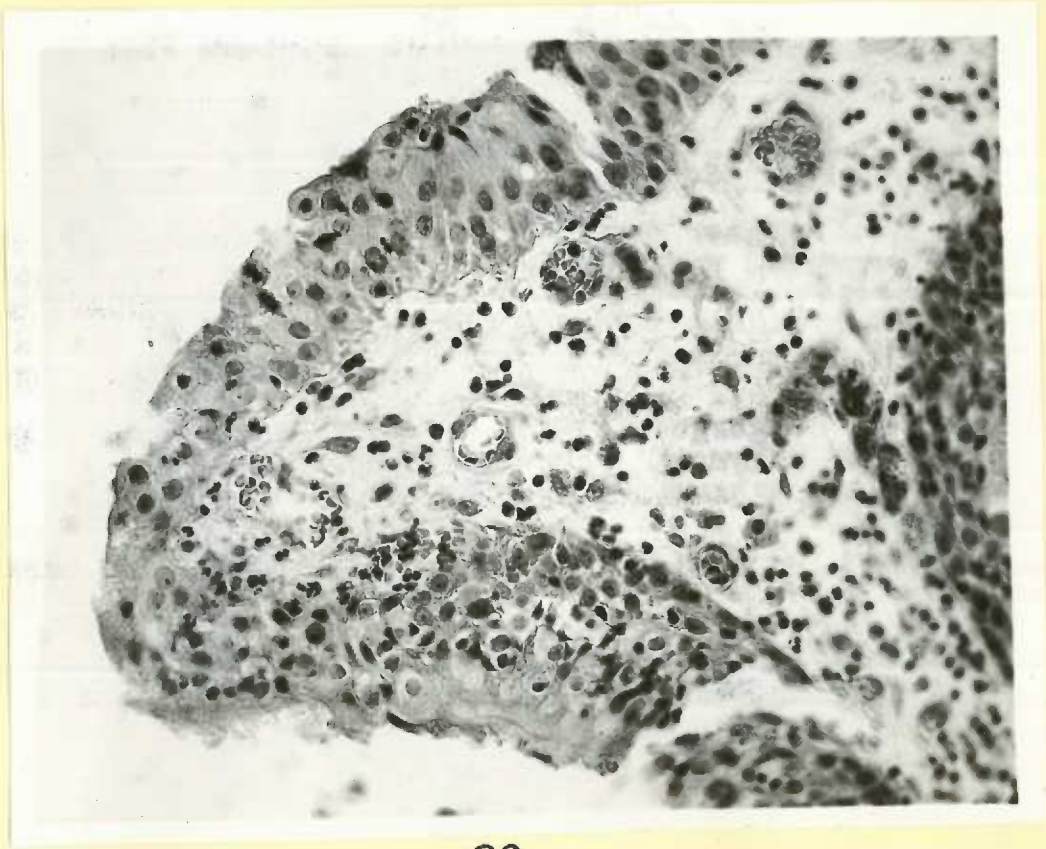
Engorged capillaries, fibroblastic proliferation and polymorphonuclear infiltration is seen. Contrast this submucosa with that of figure 35.

Height of epithelium is 100 micra or more.

Magnification 250 X
Hematoxylin- eosin.



61



62

Figure 63

Chronic pyogenic polypoid sinusitis. This represents a terminal result of the process shown in figure 61. Here there is some resolution but the chronic inflammation and suppuration has degenerated into cystic and polypoid swelling of the mucous membrane. There is much subepithelial infiltration of leucocytes of the pyogenic type. A cyst of the mesothelial type is present on the left. The epithelium is hyperplastic ciliated columnar in type. Apparently heteroplasia terminates in this form of epithelium when the purulency subsides. This case produced a muco-purulent secretion.

Magnification 8 X

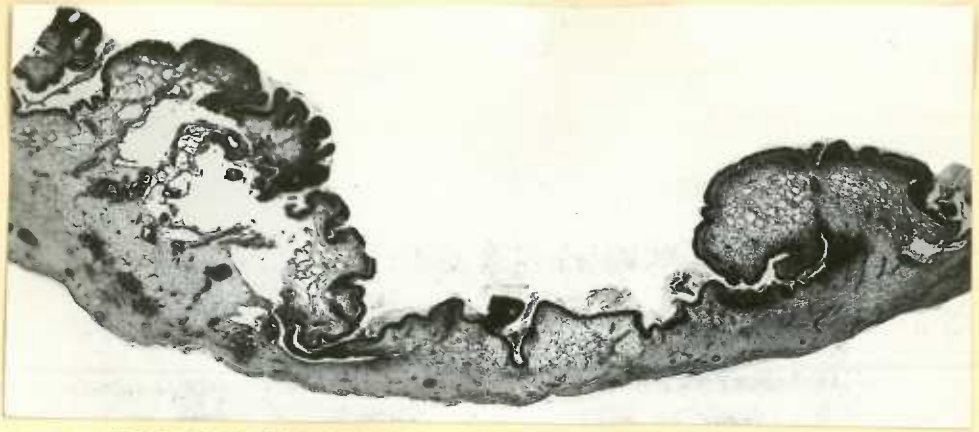
Figure 64

Hyperplastic antrum mucous membrane shown for comparison with the above polypoid lining. Note the lymphatic nodules, Ln. in the submucosa.

Figure 65

A plain polyp photographed with the same magnification. The hyperplastic mucous membrane is shown on the right, Mm.; the polyp consists of an abundent soft intracellular deposit of mucinous character with scant nuclei. Such polypi usually arise from the antrum and project into the nasal cavities where their presence is often considered to be due to an intra-nasal degeneration.

Enlarged 8 X.



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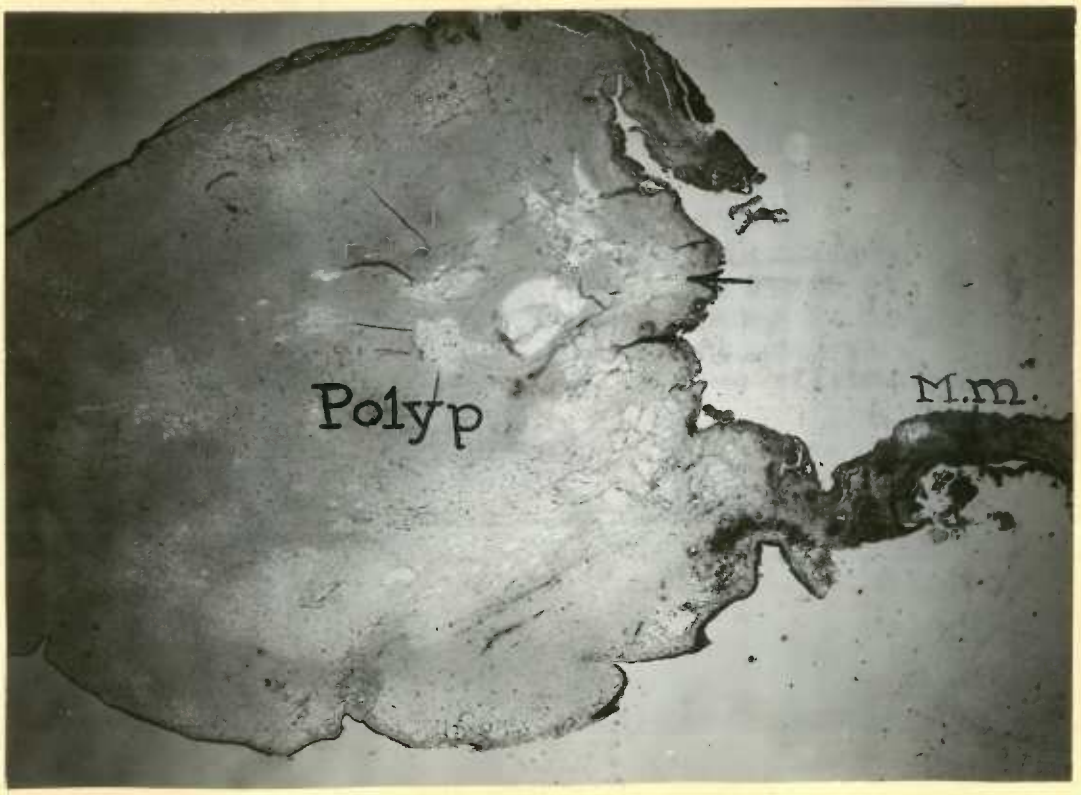
64



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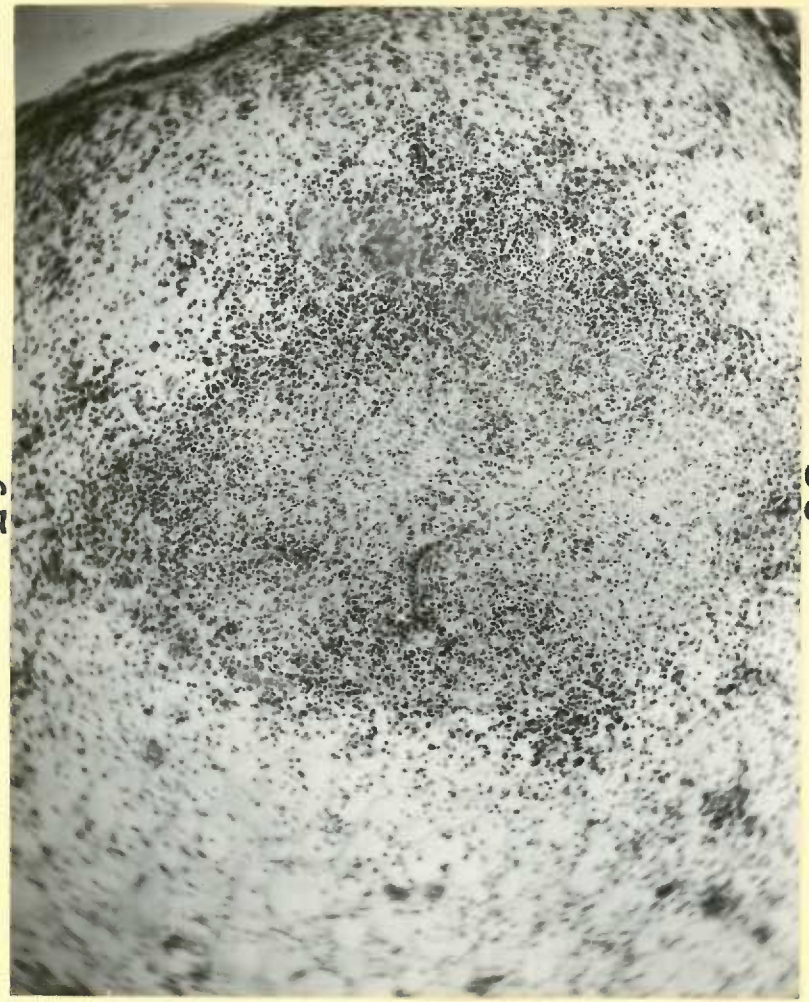

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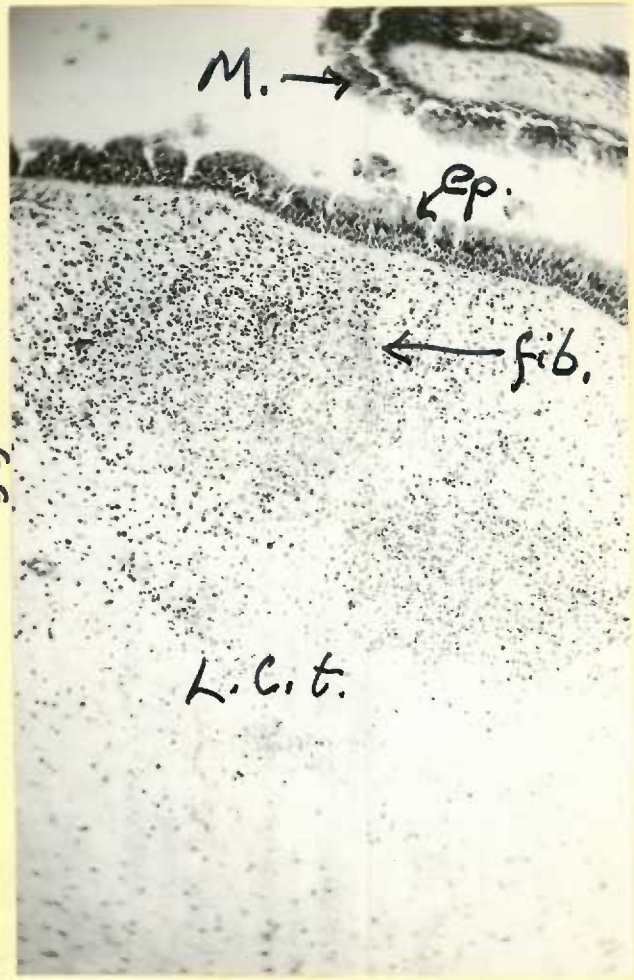


66

Figures 66 & 67.

Fibrosis as a result of proliferation of fibroblasts. In hyperplastic sinusitis one frequently finds areas in which the fibroblasts are condensed and tissue organisation is progressing. Some rhinologists call this process "atrophic sinusitis" but actually the tissue is hypertrophic. The misnomer probably is based on the observation that fibrous areas tend to contract. They never become thin and always are thicker than normal.

Figure 66.

M., mucoid degeneration of epithelium; ep., epithelium; fib., fibroblasts; L.C.T., loose connective tissue.

ON REGENERATION OF THE SINUS LINING AFTER VARIOUS TYPES OF OPERATIONS WITH A DEMONSTRATION OF THE TRANSPLANTED NASAL FLAP AND AN EXAMPLE OF BONE PROLIFERATION.

Two Plates.

Figures: 68, 69, 70, 71, 72, 73, 74.

Figure 68.

Repair in the mucous membrane of the antrum . Duration of healing 2 years. Only the anterior third of the mucous membrane was removed at the first Caldwell-Luc operation. The remaining portion of the membrane was not disturbed and this gave rise to the regenerated epithelium covering the scar. Repair consists of scar tissue characterized by a dense deposit of collagenous fibres and typical small blood channels. A variable epithelium composed of stratified cuboidal and single cuboidal layers is present, e.g.; the transition between the original unoperated mucosa and the new formed lining is shown.

Mag. 8 X ; Zenker's; H & E Stain.

Figure 69.

Repair in the antrum from the mucosa of the nasal cavity. Here the transition between the nasal mucosa, or "nasal flap" as it is called, is shown. The new formed tissue is solid scar tissue and bone. Glands are seen in the nasal flap but do not occur in the scar tissue.

8 x ; H & E; Zenker's.

Figure 70.

Higher magnification of the epithelium and glands in the nasal flap. Attention is directed to these structures because they are normal elements from the nasal cavity introduced into the antrum by the surgeon and should not be mistaken for regenerated structures.

Enlarged 150 X; Zenker's; Hematoxlyin-Eosin.

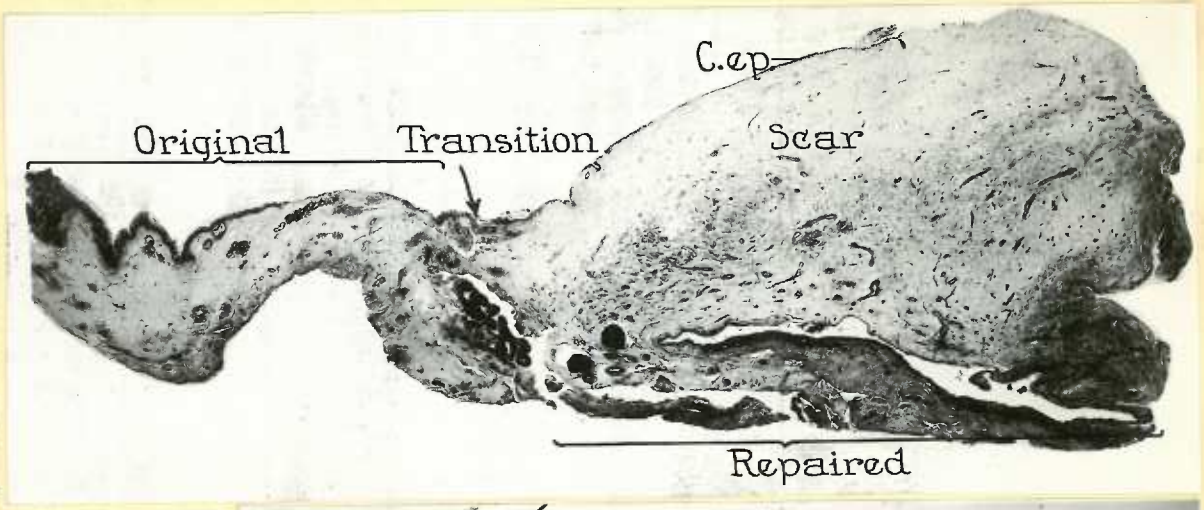
Figure 71.

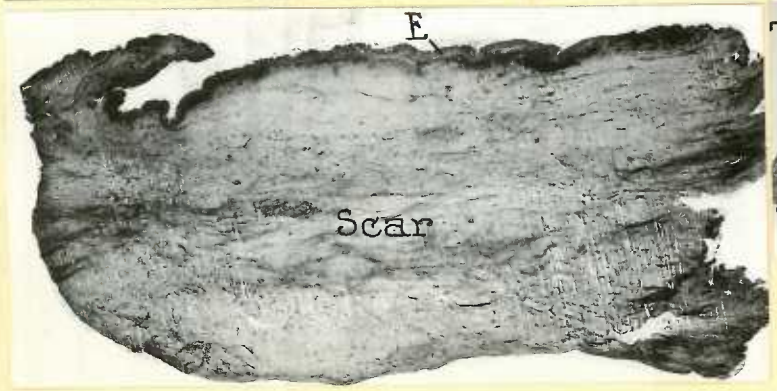
Dense scar tissue covered by ciliated columnar nasal epithelium removed from the anterior wall of a repaired antrum, healing for 20 months. It will be observed how firm and dense the thick scar tissue can become. Compare this structure with the normal lining taken under the same magnification shown in Figure 54 & 57. Obviously the scar is less vulnerable.

Magnification 8 X ; Hematoxylin-Eosin, Zenker's.

70

68

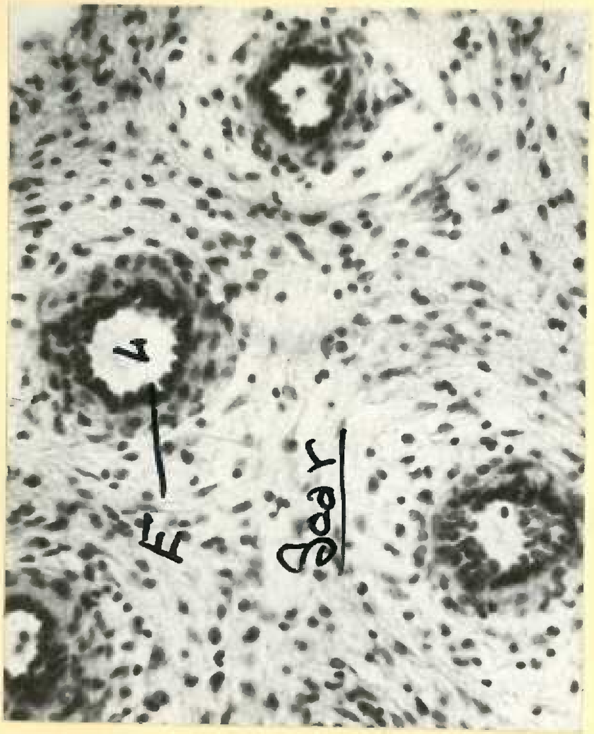

C.ep
Original
Transition
Scar
Repaired


E
Scar

71


Flap
Bone
Scar

69



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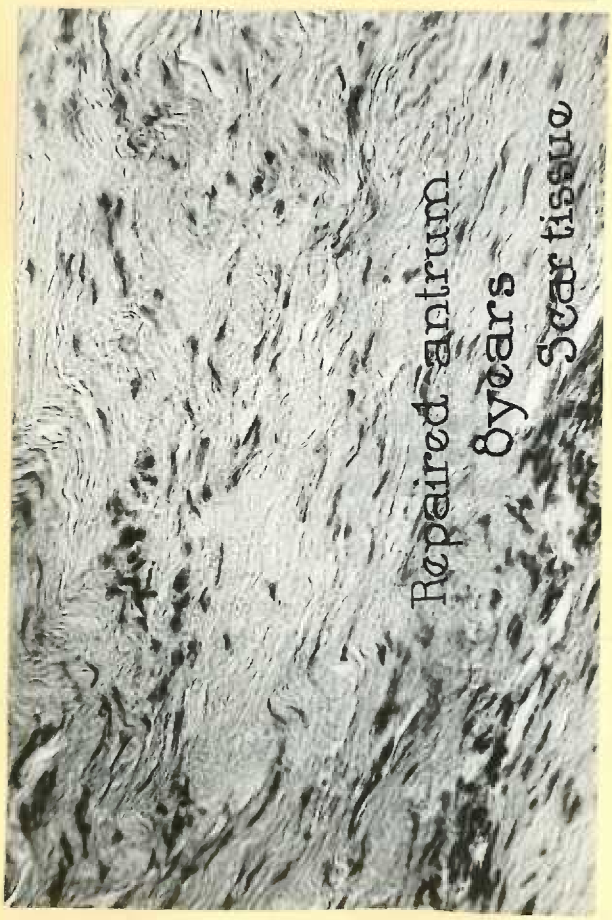

73

Figure 72.

Under higher magnification the young scar tissue of the healing sinuses shows many small blood channels but no definite arteries. There are numerous endothelial cells lining the walls of the channels. The lumen of such a channel is marked, L.; the endothelium is marked, E.; and the young fibrous tissue is labeled Scar. Older scars show more intercellular substance and fewer channels.

Specimen from antrum healing for 30 months, granulation tissue has definitely given way to scar tissue.

Figure 73.

Older scar tissue from the lining of an antrum 8 years after the first Caldwell-Luc operation. Note how firm and dense the scar tissue appears. It is apparent that channels are less numerous and nuclei are less abundant than in the specimen taken a year and a half after operation.

Both specimens are from cases that were reoperated a second time after the first radical exenteration.

Figure 74.

By contrast we again refer to the loose character of the normal and original lining of the antrum. Note the large tissue spaces and delicate connective tissue fibrils. There is greater opportunity in the original lining for edema, bacterial harbors and degenerative changes; the original linigg is very cellular.

An atery is seen on the left. It shows the more orderly nature of the blood vessels in the normal tissue and brings out our chief differential point in recognizing a repaired post operative scar from original mucous membrane.

S U M M A R Y

of

T H E S I S

on

STUDIES IN CHRONIC PARANASAL SINUSITIS

VI

OBSERVATIONS ON THE NORMAL HISTOLOGY OF THE MUCOUS MEMBRANE LINING THE VARIOUS PARANASAL SINUSES OF MAN

By

Herman Semenov

- - - - - -

1. The paranasal sinus mucous membranes have a characteristic appearance and cannot be considered the same as the nasal mucosa.

2. In general, all the mucous membranes of the various paranasal sinuses are similar. The medial (nasal) wall of the antrum is well developed and is unique in this respect. The frontal and sphenoidal sinus membranes are least developed and unusually thin. Hypertrophy is evidence of pathologic activity.

THICKNESS OF MUCOUS MEMBRANES

	Normal Variations Mm.	Usual Measurement Mm.
Maxillary Sinus:		
Medial Wall	0.3 - 1.0	0.5
Lateral Wall	0.1 - 0.5	0.2
Frontal Sinus	0.07- 0.3	0.1
Ethmoidal Sinus	0.08- 0.4	0.1
Sphenoidal Sinus	0.07- 0.5	0.1

3. Sinusitis is exceedingly common; the inflammatory changes of the mucous membranes should be recognised. Leucocytic infiltration is as abnormal here as it is in the lungs.

4. A single layer of ciliated columnar (pseudo-stratified) epithelium covers the surface of the membrane. It measures from 25-50 micra in thickness. More than 5 layers of nuclei is evidence of pathologic irritation with subsequent hyperplasia.

5. The basal cells are the embryonic ancestors of the ciliated cells and are active in regeneration and hyperplasia.

6. The cytoplasmic zone, distal borders, of the columnar cells contain lipoids. This may have some relation to the cholesterin crystals washed from sinuses with chronic degeneration.

7. Goblet cells are rare. In large numbers they indicate catarrhal sinusitis.

8. A basement membrane is present; normally it is very thin. After inflammation, it becomes hyalinized and this change is evidence of previous disease in a thin membrane that may be normal.

9. Glands are rare. In the maxillary sinus they occur on the nasal wall. In the sphenoidal and ethmoidal sinuses they may be seen near the ostia; in the frontal sinuses they are often absent.

10. Cystic degeneration and infection of the glands denotes pathologic degeneration and is favored by the weakness of the surrounding stroma.

11. Glands may occur in bony lacunae, under the periosteum. Such glands are difficult to remove surgically.

12. The tunica propria consists of two layers; an upper loose areolar tissue, and a deep compact tissue. The loose tissue is extremely active during inflammation. The deep layer resembles a periosteum.

13. Lymphatic nodules, probably the so-called germinal centers of Flemming, are described in the loose layer. These lymphatic nodules are absent under normal conditions.

14. Blood vessels emerge through the bony walls and subdivide into three plexuses lying in the plane of the mucous membrane. The paranasal sinus mucous membranes have a relatively poor blood supply.

15. An abundant nerve supply reaches the mucous membrane.

16. Post operative repair does not regenerate the old lining but substitutes firm scar tissue covered with a variable epithelium. Much new bone is deposited on the surrounding walls.

17. The present study is based on 851 specimens and in such a large series considerable histological variation is noted. Individuals tend to vary in the type of mucous membrane that they carry.

18. The normal appearance of a sinus mucous membrane was determined by a study of the healthy mucosa. By analysis of proven pathological tissues it was possible to define the normal limits and variations.

19. The normal sinus mucous membrane is thin, has a smooth epithelial surface, contains no leucocytic infiltrations, no edema, no gland cysts and no hyperplastic or mucoid changes in the epithelium.

20. An occasional ethmoidal cell is found in the concha and although these are called "cystic turbinates" they are usually normal ethmoidal sinuses.

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