



# **RESPIRATORY SYSTEM PATHOLOGY**





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## Regenerative changes in the bronchial epithelium

### ABSTRACT

A histologic examination of the rebiopsy site can reveal the signs of regeneration advanced diversely, depending on the time passed from a former damage. These regenerative changes may be misinterpreted as an epidermoid carcinoma. The material included biopsy specimens obtained by the second bronchoscopy from 145 patients. Depending on the time interval between the first and the second biopsy, ranging from 2-188 days, the analysed samples were classified into eight categories. The histologic parameters of regeneration were analysed by the semiquantitative method. Planocellular metaplasia, cornification, dyskeratosis, nuclear polymorphism, hyperchromatism, multinuclear epithelial cells, nucleoli, mitosis and pseudo infiltration into the fibrin and connective tissue were registered in 5-100% of the cases, with the peak frequency within the 2-14 day interval following the former biopsy. The changes which may be misinterpreted as an epidermoid carcinoma (cornification, dyskeratosis, nuclear polymorphism and hyperchromatism, multinuclear cells, nucleoli, mitosis, pseudo infiltration of the fibrin and connective tissue) can be registered within 2-14 day interval from the former damage of the bronchus. The samples (both cytological and histologic) obtained in this interval should be analysed and correlated to other changes accounting for regeneration.

**KEYWORDS:** Biopsy; Bronch Regeneration; Epithelium

### INTRODUCTION

A damage to the bronchial epithelium can be produced by a variety of agents: biopsy sampling of the bronchus, a foreign body, infections, tumors. On bronchoscopy, the site of bronchus regeneration is seen as altered, most often taking the appearance of an endobronchial excrescence rough in surface and reddish in colour (1,2). A histologic examination confirms the signs of regeneration, the stage of which depends on the time interval passed from the former damage (3,4). These regenerative changes can be misinterpreted as an epidermoid cancer (1-3,5,6).

### MATERIALS AND METHODS

The material of the investigation included 145 patients submitted to a

rebiopsy of the bronchus at the Institute for Lung Diseases in Sremska Kamrnica. The time interval separating the two successive biopsies ranged from 2-188 days. Depending on the length of the time interval, the examined series was classified into eight categories. Each biopsy sample was analysed for the following parameters: the presence of a defect, fibrin, fibrin granulocytes and mononuclears, the presence and thickness of the stratified squamous epithelium in fibrin and on the basal membrane, a break of the basal membrane, surface cornification, dyskeratosis, nuclear polymorphism, hyperchromatism of the nuclei, nucleoli, mitosis, multinuclear cells, intraepithelial granulocytes, the formation of the basal cell layer, presence of goblet cells, formation of the basal membrane, development of the cylindrical epithelium, presence of a pseudo infiltration in fibrin and the connective tissue.

### RESULTS

A surface defect is registered in 134 (92%) patients. The presence of fibrin is established in 141 (97%) patients, registered in the largest quantities within the 2-7 day interval from the former biopsy. Fibrin granulocytes are registered in 126 (86.8%) patients and the micro abscess formation in 4 (2.7%) patients. A mononuclear infiltration is disclosed in 132 (91%) patients. The squamous stratified epithelium is found in all patients, ranging in thickness from 1-6 layers. The squamous epithelium underlying fibrin is found in 4 (2.7%) patients, superimposing it in 124 (85.5%) patients, or within it in 108 (74.48%) patients. The epithelium is registered on the basal membrane in 18 (12%) patients, emerging from the 12th day onwards following the former biopsy sampling. In fact, it is most frequently registered on the 14th day (54% of the patients). A break in the basal membrane is discovered in 106 (73%) patients. Surface cornification is present in 8 (5%) patients and dyskeratosis in 86 (59%) patients. Dyskeratosis most often develops on the 6th day following the former biopsy (47% of the patients). Intraepithelial granulocytes are registered in 121 (83%) patients. The intraepithelial abscess formation is registered in 19 (13%) patients, most frequently seven days after the former biopsy (in 56% of the patients). Nuclear polymorphism is found in 65 (45%) patient over the 2-11 day interval following the former biopsy, most often on the 6th day - in 14 (74%) patients. Nuclear hyperchromatism is registered in 65 (45%) patients, most frequently six days after the former biopsy - in 11 (58%) patients. Nucleoli are found in 134 (92%) patients, commonly within the 5-7 day interval following the former biopsy. The squamous epithelium mitosis is registered in 101 (70%) patients, usually 5-8 days after the former biopsy. Multinuclear cells are disclosed in 75 (52%) patients, most often in the 5-9 day period following the former biopsy. The goblet cells superimposing the squamous epithelium are registered in 59 (40%) patients, emerging from the 6th day onwards, most frequently on the 14th day after the former biopsy. The basal membrane formation is found in 28 (20%) patients, beginning 10 days after the former biopsy, registered on the 14th day in 81% of the patients. The squamous epithelium superimposed by the cylindrical one is found in 19 (13%) patients, from the 11th day onwards, most frequently 14 days after the former biopsy. Hyperplasia of the surrounding cylindrical epithelium is present in 124 (85%) patients. Fibrin pseudo infiltration is registered in 115 (79%) patients, developing within 2-14 day interval following the former biopsy, commonly on the 7th day. Pseudo infiltration of either the granulation tissue or the cellular connective is found in 75 (52%) or 18 (12%) patients respectively.

### DISCUSSION AND CONCLUSION

The analysed changes may be misinterpreted as an epidermoid carcinoma (2,3,5,6). The closest similarity between the regenerative changes and a carcinoma are registered within the 2-14 day period following the former biopsy (3). The samples taken in that interval (both cytological and histologic) should be analysed and correlated to other regeneration-related changes.

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## Luminal alveolitis in pulmonary sarcoidosis

### ABSTRACT

The presence of inflammatory and immunocompetent cells in the lumen of the alveoli in sarcoidosis is termed luminal alveolitis. Material of the study included the transbronchial biopsy samples obtained from 34 sarcoid patients. The quantity of inflammatory and immunocompetent cells was estimated by a stereometric method of the numerical density. In the alveoli far away from a granuloma the mean numerical density of all cell types is 16.873/mm<sup>3</sup>. Macrophages predominate - 8.272/mm<sup>3</sup> (49.02%), followed by lymphocytes - 8.231/mm<sup>3</sup> (48.78%). The mean numerical density of all cell types in perigranulomatous alveoli is 43.140/mm<sup>3</sup>, with predominating lymphocytes 22.814/mm<sup>3</sup> (52.88%), followed by macrophages 19.515/mm<sup>3</sup> (45.23%). Perigranulomatous luminal alveolitis is 2.5 times as intense as alveolitis in the alveoli far away from a granuloma. Perigranulomatous luminal alveolitis is more intense than the one in the alveoli far away from a granuloma. The difference is statistically significant.

KEYWORDS: Sarcoidosis, Pulmonary; Pulmonary Alveoli + pathology; Cell-Count

### INTRODUCTION

Sarcoidosis is a multisystemic granulomatous disorder of unknown etiology characterized by intensified cellular immunology processes at the sites of inflammation. The aim of this study is to determine the intensity of luminal alveolitis in sarcoidosis.

### MATERIALS AND METHODS

Material of the study included the transbronchial biopsy samples obtained from 34 sarcoid patients. The quantity of inflammatory and immunocompetent cells was estimated by a stereometric method of the numerical density. The term „perigranulomatous alveoli“ is used to denote the alveoli surrounding a granuloma at the distance of 100 microns from its external edge. The remaining alveoli are referred to as „the alveoli far away from a granuloma“.

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## RESULTS

Numerical density of all cells found in the lumen of the alveoli far away from a granuloma ranges between 4.575/mm<sup>3</sup> and 30.802/mm<sup>3</sup>, the mean value being 16.873/mm<sup>3</sup>. The following cell elements are found in the lumen of the alveoli:

a. Macrophages, found in all biopsy samples, having the numerical density of 2.353 to 16.634/mm<sup>3</sup>, the mean value being 8.272/mm<sup>3</sup>.

b. Foamy macrophages, present in only one (2.94%) biopsy sample in the numerical density of 0 -51/mm<sup>3</sup>, the mean value being 2/mm<sup>3</sup>.

c. Neutrophil granulocytes, found in 24 biopsy samples (70.58%), having the numerical density of 0 - 833/mm<sup>3</sup>, the mean value being 172/mm<sup>3</sup>.

d. Eosinophil granulocytes, present in 20 (59%) biopsy samples in the numerical density that ranges between 0 and 924/mm<sup>3</sup>, the mean value being 196/mm<sup>3</sup>.

e. Lymphocytes, found in all biopsies, with the numerical density ranging between 2.222 to 12.360/mm<sup>3</sup>, the mean value being 8.231/mm<sup>3</sup>.

Of the total number of all cells found in the lumen of the alveoli, macrophages make 49.02%, foamy macrophages 0.01%, neutrophil granulocytes 1.02%, eosinophil granulocytes 1.16% and lymphocytes 48.78%.

Numerical density of all cells present in the lumen of perigranulomatous alveoli is found to range from 13.744 to 84.974/mm<sup>3</sup>, the mean value being 43.140/mm<sup>3</sup>. Lymphocytes and macrophages are found in all biopsy samples, eosinophil and neutrophil granulocytes in 13 (38%) biopsies, single epitheloid cells (out of a granuloma) in 3 (8.84%), plasma cells in 2 (5.88%) and foamy macrophages in one (2.94%) biopsy. The numerical density of these cell types is reviewed in the Table 1.

## DISCUSSION

The presence of inflammatory and immunocompetent cells on the surface and in the lumen of the alveoli accounts for luminal alveolitis. The presence of these cells in the lumen of the perigranulomatous alveoli accounts for peri-

data are compared to our results, a great correlation is evidenced.

## CONCLUSION

1. The intensity of perigranulomatous luminal alveolitis is found to be 43.092 cells/mm<sup>3</sup>.

2. The intensity of luminal alveolitis in the alveoli far away from a granuloma is found to be 16.873 cells/mm<sup>3</sup>.

3. The intensity of perigranulomatous luminal alveolitis is higher than the intensity of luminal alveolitis in the alveoli far away from a granuloma. The difference is statistically significant.

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**Table 1. Cellular content in the lumen of perigranulomatous alveoli (numerical density in mm<sup>3</sup>)**

	Mean value	Minimum	Maximum	%
Macrophages	19 515	5 966	39 750	45.23
Foamy macrophages	15	0	504	0.03
Neutrophyl granulocytes	259	0	2 570	0.60
Eosinophyl granulocytes	449	0	3 170	1.04
Lymphocytes	22 814	7 778	36 530	52.88
Plasma cells	40	0	1 081	0.09
Epitheloid cells	48	0	1 369	0.11

granulomatous luminal alveolitis which has a significantly higher intensity than the luminal alveolitis in the alveoli far away from a granuloma. Thus the intensity of perigranulomatous luminal alveolitis is found to be 43.092 cells/mm<sup>3</sup>, while the intensity of the luminal alveolitis in the alveoli far away from a granuloma is 16.873 cells/mm<sup>3</sup>. This difference is statistically significant (p`0.01). Polleti (1) analyzes 52 biopsy samples from sarcoid patients and finds luminal alveolitis in 10% of the cases. Aisner (2) examined a biopsy sample from a patient with sarcoidosis and finds macrophages and mononuclear cells giving no precise evidence about their number. Hunninghake (3) examines 6 sarcoid BAL fluid samples and finds 45% of macrophages and 55% of lymphocytes on average. Semenzato (4) examines the BAL fluid simple from 26 patients with sarcoidosis and finds from 12.6% to 51.2% of lymphocytes, depending on the intensity of alveolitis. The percentage of macrophages ranges between 46.9% and 85.2%. Simultaneously, in histologic samples of the same group of patients, in the lumen of the alveoli, he finds lymphocytes in the amount ranging from 14.6% to 43% and macrophages in the amount ranging from 56.9% to 85.3%. If the reported



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## Bronchiectasis

**KEYWORDS:** Bronchiectasis

Bronchiectasis means a permanent, chronic and irreversible dilatation with a deformation of one or more bronchi. The analyses have been done on the autopsy material of 50 lungs from dead patients between 2 and 80 years of age. The taken samples were coloured with many histochemical methods. Both macro- and microscopic examinations were performed. The macroscopic observations at autopsy showed cylindrical, saccular, fusiform, and serpentine acinar bronchiectasis. A cylindrical bronchiectasis was localized in the lower lobes of the lungs. Other forms of bronchiectasis were single or multiple, associated with bronchial obstruction, tumor, fibrosis, enlarged glands and foreign bodies. Its localisation was in different parts of the lung tissue. In chronic tuberculosis, bronchiectasis was situated in the upper lobes. We have found, that bronchiectases were often associated with a collapse and destructive irregular emphysema of the related lung. Complications observed in our cases were abscess, empyema, gangrene, fibrotic pleura, amyloid disease and cerebral abscess. The sign of clubbing fingers was also present. In one case, a carcinoma arising from the metaplastic bronchial epithelium was detected. Congenital bronchiectases take the appearance of cystic lungs. On the microscopical examination of the laterals cut, the bronchi were seen as star-like. The submucous was swollen and extensively infiltrated by neutrophils, lymphocytes, plasma cells and macrophages. The specialised tissue, such as the muscle, epithelium, elastic tissue, glands and cartilage, was progressively destroyed. Lymphoid hyperplasia was also present, especially in follicular bronchiectases. The bronchioles and the alveoli were frequently obliterated. Etiology, pathogenesis and morphology of pathologic bronchiectases are well known, but the prognosis is serious and problematic.

## Catheter biopsy of the lung and its role in early diagnostics

**KEYWORDS:** Lung Diseases + diagnosis; Carcinoma, Squamous Cell; Biopsy; Bronchoscopy

Catheter biopsy of the lung has always been performed when the specimens couldn't be obtained with brush. Every time present when the tissue change was a transbronchial lesion we performed a catheter biopsy. We used a special plastic catheter for an Olympus fiberbronchoscope. We did the cytological findings of 18 transbronchial - catheter biopsies corresponding to 18 cases of carcinoma planocellulare diagnosed in our department during the last two years. Multiple slides were made and stained with hematoxylineosine, PAS and May - Grunwald - Giemsa stains. We examined 18 patients with a suspected shadow in the lung. All patients were examined by a general practitioner and a pulmonologist and sent to a special hospital for lung diseases for bronchoscopy. In all cases clinical, radiographic and cytologic correlations were made. Catheter biopsy of the lung is a very cheap, quick and precise method for cytological diagnosis of a malignancy of the lung. If an urgent diagnosis is needed in severe patients, make a catheter biopsy, which damages the tissue little and induced only small bleeding. After the biopsy all our patients felt well. We strongly recommend this method.



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## Cytologic confirmation of paracentral lung malignancies sampled by transbronchial aspiration biopsy

**KEYWORDS:** Lung Neoplasms; Cytodiagnosis; Biopsy, Needle

With lung malignancies localized paracentrally in the chest, the routine sampling for a cytologic and histologic analysis usually provides negative findings. Objective: to confirm a hypothesis that transbronchial fine-needle aspiration sampling can provide a definite cytologic confirmation of a malignancy with such a localization in the chest. In the course of fiberbronchoscopy of 20 patients with a paracentral tumor mass, besides sputum and catheter aspiration samples, the sample obtained by fine-needle (Olympus Na-1C-1) aspiration biopsy was submitted to a cytologic analysis as well. In 20 examined patients with a paracentral lung malignancy, the following tumor types were diagnosed: 3 squamous, 3 small-cell, 2 adenocarcinomas, 3 Hodgkin's tumors, 3 non-Hodgkin's lymphomas and 2 metastatic carcinomas. The cytologic analysis of a fine-needle aspiration biopsy sample provided a definite diagnosis in 11/20 patients (55.0%), establishing the following tumor types: 2/3 squamous carcinomas, 4/ small-cell cancers, 2/3 Hodgkin's diseases, 2/3 malignant non-Hodgkin's lymphomas, 1/2 metastatic tumors, 0/2 adenocarcinomas. The cytologic analysis of neither the sputum nor the catheter aspiration sample provided a positive finding. The fine-needle aspiration biopsy of paracentral tumor masses in the lungs provides a representative material for a definite cytologic confirmation of a malignancy in 55% of the examined patients, thus significantly reducing the necessity for a diagnostic surgery.

## Pathologic features of the lungs in the immunocompromised host

**KEYWORDS:** Lung; Immunocompromised host; Lung Disease

Catheter biopsy of the lung has always been performed when the specimens couldn't be obtained with brush. Every time present when the tissue change was a transbronchial lesion we performed a catheter biopsy. We used a special plastic catheter for an Olympus fiberbronchoscope. We the citological findings of 18 transbronchial - catheter biopsies corresponding to 18 cases of carcinoma planoepteliale diagnosed in our department during the last two years. Multiple slides were made and stained with hematoxiline-eosine, PAS and May - Grunwald - Giemsa stains. We examined 18 patients with a suspected shadow in the lung. All patients were examined by a general practitioner and a pulmonologist and sent to a special hospital her lung diseases for bronchoscopy. In all cases clinical, radiographic and citologic correlations were made. Catheter biopsy of the lung is a very cheap, quick and precise method for citological diagnosis of a malignancy of the lung. If an urgent diagnosis is needed in severe patients, make a catheter biopsy, which damages the tissue little and induced only small bleeding. After the biopsy all our patients felt well. We strongly recommend this method.



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## Ceruminoma-adenocarcinoma - a case report

**KEYWORDS:** Ear Canal; Ear Neoplasms; Adenocarcinoma

The clinical and pathological features of glandular tumors of the external auditory meatus make the collective term #ceruminoma# ambiguous and misleading. The review of the histology of these glandular tumors classify them as adenoma, cylindroma, adenoid cystic carcinoma or ceruminous adenocarcinoma. The term iceruminoma# should not longer be used unqualified, and those tumors necessitate broader classification. The case of ceruminous adenocarcinoma is reported. Female, sixty seven year old turned to a otorhinolaryngologist with paralysis of the right 7th cranial nerve, and granulations in the auditory canal. The first biopsy was unclear to pathologist and he set up the diagnosis of squamous cell carcinoma with suggestion for repeating it. Second biopsy material was very small (the few micrometers) but undoubtedly it was adenocarcinoma of ceruminous gland origin. Classical histological stains (HE, Sudan black), as well as, immunohistochemical (EMA, CEA, cytokeratine, vimentin, desmin) were performed. This rear tumor, unless partially removed together with the invaded temporal bone, prograded through the tegmentum to the brain. Immunohistochemical staining that was performed is very important because it demonstrate that adenoid cystic carcinoma of the external auditory canal had have dual epithelial and myoepithelial differentiation and could mimic the ceruminous glandes of the auditory canal. Ceruminous adenocarcinoma is more aggressive, with infaust prognosis, so early diagnosis and radical treatment is stressed. We are without knowledge about further course of this patient illness considering that she never turned to the institutions in Nis for further treatment.

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## Primary germ-cell tumor of the mediastinum - a case report

**KEYWORDS:** Mediastinal Neoplasms; Dysgerminoma; Neoplasms, Germ Cell and Embryonal

Primary Germ-Cell tumors have been found in extragonadal sites such as the anterior mediastinum, the retroperitoneum, the presacral region, and the region of the pineal gland. Very few reports concerning the biopsy findings in malignant germ-cell tumors of the anterior mediastinum have been published. Seminomatous germ cell tumors can arise as primary malignancies in the mediastinum without involving the testis. Primary mediastinal seminoma has also been reported in females. The usual location of the tumor is the superior mediastinum and histologically it is identical to testicular seminoma. Mediastinal seminoma most commonly affects young men aged between 20 and 35 years. Most patients are symptomatic with a mass in the mediastinum, but some can be presented without any symptoms and are diagnosed on a routine chest x-ray. A case of 25 year old male is presented. The only symptom was coughing. On chest x-ray a large tumor mass in the anterior mediastinum was detected. The vertebral body was also affected. The open biopsy was performed. The obtained tissue specimen was 1 cm in diameter and histologically, besides histochemical and immunohistochemical stainings, because of the inadequate material, composed of fibrous tissue, the rhabdomyoid element, archiac nerve element, the suspicion of possible teratoma was raised. After that, patient underwent radical tumorectomy and the tumor mass of 1.500 gr. was extracted. In the core of the tumor mass, clearly seminomatous tissue was found. This case is unusual, because of the family history data about the older brother who had a radical orchiectomy due to embryonal carcinoma of the testis.