

Grading of the prostate carcinoma: cyto-histological correlations on 100 cases

P. Della Palma¹, S. Dante¹, G. Costantin², A. Rebuffi², F. Zattoni³ and R. Piazza³

¹Istituto di Anatomia Patologica dell'Università di Padova, Italy;

²Centro Tumori ULSS, Padova, Italy;

³Clinica Urologica dell'Università di Padova, Italy

Summary. From January 1980 to December 1983, 154 patients underwent prostatic FNAB and histological control. The sensitivity of cytology was 85%, the specificity 68% and the predictive value of positive cases 83%.

The cyto-histological correlation of the grading of the 100 prostatic carcinomas histologically confirmed (85 cytologically positive for carcinoma and 15 negative or uncertain) showed a predictive value of positive results of 58%, ranging from 42% for G3, 50% for G1 and 69% for G2.

The usefulness of cytological grading is stressed to monitor the follow-up of those patients treated for prostatic carcinoma who, because of the advanced stage or age, were not surgically treated.

Key words: Prostate cancer - FNAB - Cytohistological grading correlation

Introduction

Cytological studies are essential in the diagnosis of prostate carcinoma (Zattoni et al., 1983). Cyto-histological statistics show that fine needle aspiration biopsy (FNAB) allows us to obtain an accurate diagnosis in 75% (VonReuter and Schuck, 1971) to 91% of cases studied (Esposti, 1982). These results are much better than those obtained with cytological studies following prostatic massage (Garret and Jassie, 1976).

In addition, FNAB permits us to grade prostate carcinoma into well, moderate and scarcely differentiated forms (Esposti, 1971, 1982). Several authors (Ekman et al.,

1967; Alfthan et al., 1970; Epstein, 1976; Ackermann and Muller, 1977; Kaufman et al., 1982; Kline et al., 1982; Kline, 1985; Yatani et al., 1985; Carter et al., 1986) have referred to the possibility of obtaining a reliable cytological grade when compared **histologically**, but unfortunately they reported only a limited number of cases. For this reason, we have considered it useful to report our experience in this field.

Materials and methods

Between January 1980 and December 1983, 154 patients underwent prostatic FNAB and histological control. FNAB was carried out with **Franzen's** needle (1960), performing 3-5 aspirations, not only on the suspected sites but also the rest of the gland. The aspirated material was smeared and fixed with a spray (Merckofix); the slides were then stained with **Papanicolaou's** method. All samples diagnosed positive for carcinoma were subsequently graded as G1, G2 or G3, according to the morphologic aspect, tendency of cells to isolate and grade of atypia (Esposti, 1971, 1982; Zattoni et al., 1983). Where cells were arranged in **acinar-like** aggregates and were smaller than normal, with scarce granular cytoplasm and a uniform round or oval, hyperchromatic, rarely nucleolated nucleus, a presumed diagnosis of "**atypical** hyperplasia" (in this work "suspicious") was accepted (Gaetani and Trentini, 1978; Helpap, 1980).

Histological material, obtained from prostatic fragments following biopsy with TRUCUT, after transurethral resection or after radical prostatectomy, was prepared and stained by the usual methods. **Cases** of carcinoma were subsequently classified according to the W.H.O. system (Mostofi et al., 1980).

The cyto-histological grading was independently diagnosed by cytologists or pathologists.

Offprint requests to: Paolo Della Palma, Istituto di Anatomia Patologica, via A. Gabelli 61, 35100 Padova, Italy

Results

In 154 patients (subjected to both types of study) who underwent both types of control, we diagnosed histologically 100 carcinomas, 45 nodular hyperplasias and 9 prostatites whereas, cytologically, 102 showed malignant cells and 52 were considered negative for carcinoma (unsatisfactory, suspicious or true negative).

Table 1 shows the cyto-histological correlation of the 154 patients: the sensitivity of cytology was 85%, the specificity 68% and the predictive value of positive cases 83%. Nevertheless, these values did not reflect the real accuracy of prostatic FNAB, since they excluded 76 patients with positive cytological diagnosis for neoplasias where no histological control had been performed. These

cases must be considered true positive, as they presented a hard fixed prostate, high serum levels of acid phosphatase and a positive bone scan for metastasis. Considering all these patients, the diagnostic accuracy increases to 90%.

Table 2 reports the correlation between the cytologic and histological grading in 100 cases of carcinomas histologically diagnosed. The distribution of the 85 cytologically positive cases was 12 G1, 61 G2 and 12 G3, respectively. The predictive value of cytologic grading was 58% when considered globally, varying from 42% for G3, 50% for G1 and 60% for G2. The table also includes 15 cytologically false negatives, which were redistributed as G1 and G2. Only one case, already classified as unsatisfactory, for the presence of numerous seminal vesicles cells, was re-evaluated as G3.

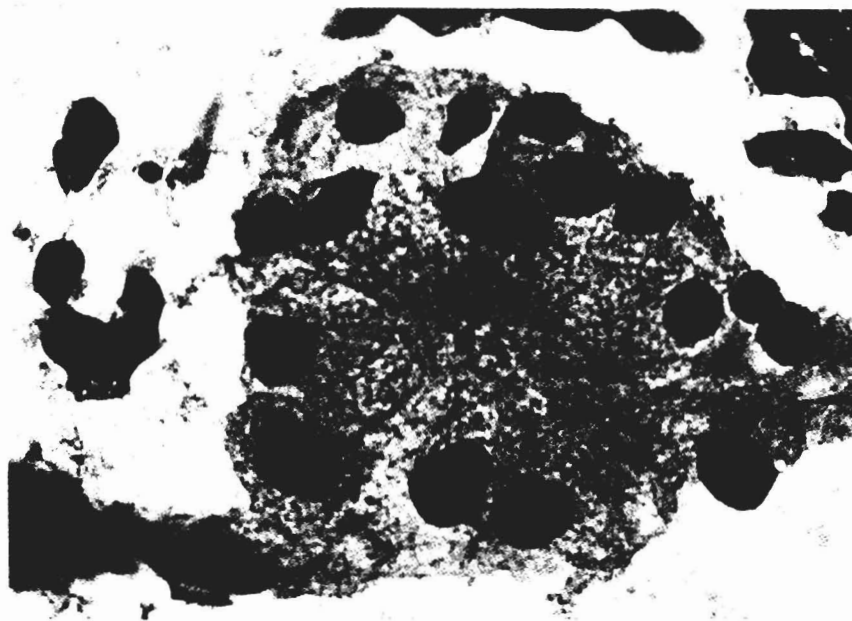


Fig. 1. Well-differentiated carcinoma, G1: microacinar formations due to fusion of single cytoplasmic in a central eosinophilic "core", around which somewhat-atypical nuclei are arranged radially. Pap. x 1000



Fig. 2. Moderately-differentiated carcinoma, G2: cells with moderate polymorphism and evident nucleoli. Pap. x 1000

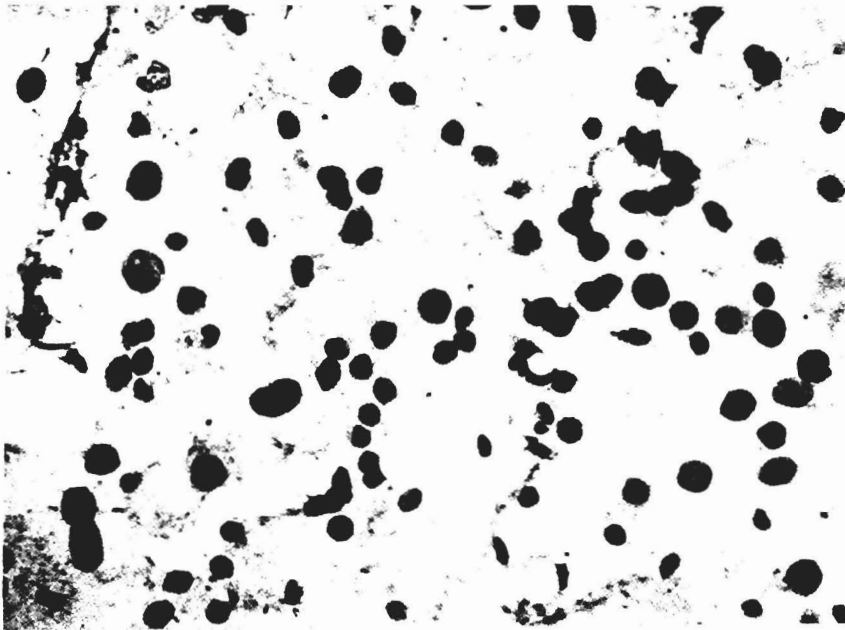


Fig. 3. Scarcely-differentiated carcinoma, G3: isolated cells with marked polymorphism and macro-nucleolated bizarre nuclei. Pap. x 400

Table 1. Cyto-histological correlation in 154 patients

	CARCINOMA	HISTOLOGY HYPERPLASIA	PROSTATITIS	TOTAL
CYTOLOGY POSITIVE	85	11	6	102
CYTOLOGY NEGATIVE*	15	34	3	52
TOTAL	100	45	9	154

*"suspicious" considered as "negative".

Table 2. Correlation between cytological and histological grading

CYTOLOGY	HISTOLOGY			TOTAL
	(G I)	(G II)	(G III)	
CARCINOMA G I	6	6	—	12
CARCINOMA G II	11	38	12	61
CARCINOMA G III	—	7	5	12
SUSPICIOUS	1	2	—	3
NEGATIVE	4	1	—	5
UNSATISFACTORY	2	4	1	7
TOTAL	24	58	18	100

Discussion

The results obtained by cyto-histological correlation were very encouraging and followed that reported in literature. Histological examination of the 17 cytologically false positive cases revealed 11 nodular hyperplasias and 6 prostatites. Since this last type of pathology is frequently

associated with carcinoma and since, in these patients, radical prostatectomy was obviously not performed, they must be considered "dubious false positive", as they could be microcarcinomas not observed by biopsy. In these cases, only an adequate follow-up can give us the answer. Two cases, previously diagnosed negative by biopsy, subsequently developed an evident clinical carcinoma.

Fifteen cytologically negative cases were histologically diagnosed as "carcinomas". In fact, the limitation of FNAB, as also histology, consists in the impossibility of always obtaining samples from the suspected site, even if 3 to 5 aspirations of the same nodule are usually performed. However, in 3 out of 15 cases, the cytologic diagnosis was "suspicious". The major problem of the cytologist is to distinguish cells of a well-differentiated carcinoma from those of a hyperplasia with atypia, since the two morphological aspects can co exist (Gaetani and Trentini, 1978). The cyto-histological correlation of the grading is very difficult, as various histomorphological classifications of prostatic carcinoma have been reported in literature (Gleason, 1966, 1977; Murphy and Whitmore, 1979; Mostofi et al., 1980; Gaeta, 1981; Brawn et al., 1982). According to the authors, each of these classifications should show a correlation between tumoral differentiation and prognosis. VACURG's classification, better known as Gleason's (1966, 1977), considers only the grade of glandular differentiation and type of growth, but not the cytological grading; Gaeta's (1981) classification considers 4 different structural and cytological grades. Finally, the W.H.O. (Mostofi et al., 1980) considers 3 cytological grades independently from the histological pattern. We consider that only this last classification can be utilized for a cyto-histological correlation.

Doubts on the reliability of cytological grading as a basic parameter in the prognosis of prostate carcinoma arise from this evaluation being subjective, hardly reproducible and, especially, too variable from site to site. However, we consider that the cytologist should specify if positive cells for carcinoma show scarce, intermediate or marked atypias, since the cytological grading can represent an objective and reliable parameter to evaluate medical and/or radio-therapy in non-operable patients not histologically evaluated (Kline, 1982). In these cases, therefore, prostatic FNAB is the only diagnostic method which is reliable, inexpensive, simple to perform and easily repeated, a map of the neoplastic extension being obtained when, in addition to the suspected nodule, other samples have been studied.

Acknowledgements. We wish to thank Francesco Gallo, M.D., for having translated the paper and for his suggestions.

References

- Ackermann R. and Muller H.A. (1977). Retrospective analysis of 645 simultaneous perineal biopsy punch biopsies and transrectal aspiration biopsies for diagnosis of prostatic carcinoma. *Eur. Urol.* 3, 29-34.
- Alfthan O., Klintrup H.E., Koivuniemi A. and Taskinen E. (1970). Cytological aspiration biopsy and Vim-Silvermann biopsy in the diagnosis of prostatic carcinoma. *Ann. Chir. Gynaecol. Fenn.* 59, 226-229.
- Brawn P.N., Ayala A.G., von Eschenbach A.C., Hussey D.H. and Johnson D.E. (1982). Histologic grading study of prostate adenocarcinoma: The development of a new system and comparison with other methods. A preliminary study. *Cancer* 49, 525-532.
- Carter H.B., Riehle A.R., Jr., Koizume H.J., Amberson J. and Vaughan E.D., Jr. (1986). Fine needle aspiration of the abnormal prostate: A cytohistological correlation. *J. Urol.* 135, 294-298.
- Ekman H., Hederg K. and Persson P.S. (1967). Cytological versus histological examination of needle biopsy specimens in the diagnosis of prostatic cancer. *Brit. J. Urol.* 39, 544-548.
- Epstein N.A. (1976). Prostatic biopsy. A morphologic correlation of aspiration cytology with needle biopsy histology. *Cancer* 38, 2078-2087.
- Esposti P.L. (1971). Cytologic malignancy grading of prostatic carcinoma by transrectal aspiration biopsy. *Scand. J. Urol. Nephrol.* 5, 199-209.
- Esposti P.L. (1982). Aspiration biopsy and cytological evaluation for primary diagnosis and follow-up. In: *Prostate cancer*. Jacobi G.H. and Hohenfellner R. (eds). Williams and Wilkins. Baltimore. pp 71-92.
- Franzen S., Giertz G. and Zajicek J. (1960). Cytological diagnosis of prostatic tumours by transrectal aspiration biopsy: a preliminary report. *J. Urol.* 32, 193-196.
- Gaeta J.F. (1981). Glandular profiles and cellular patterns in prostatic cancer grading. *National Prostatic Project System. Urology (suppl.)* 17, 33-37.
- Gaetani C.F. and Trentini C.P. (1978). Atypical hyperplasia of the prostate. A pitfall in the cytologic diagnosis of carcinoma. *Acta Cytol.* 22, 483-486.
- Garret M. and Jassie M. (1976). Cytologic examination of post prostatic massage specimens as an aid in diagnosis of carcinoma of the prostate. *Acta Cytol.* 20, 126-130.
- Gleason D.F. (1966). Classification of prostatic carcinoma. *Cancer Chemother. Rep.* 50, 125-128.
- Gleason D.F. (1977). Histologic grading and clinical staging of prostatic carcinoma. In: *Urologic Pathology: The prostate*, Tannenbaum M. (ed). Lea and Febiger. Philadelphia. pp 171-198.
- Helpap B. (1980). The biological significance of atypical hyperplasia of the prostate. *Virchows Arch. A.* 387, 307-317.
- Kaufman J.J., Ljung B.M., Walther P. and Waisman J. (1982). Aspiration biopsy of the prostate. *Urology* 19, 587-591.
- Kline T.S., Kohler F.P. and Kelsey D.M. (1982). Aspiration biopsy cytology (ABC); its use in diagnosis of lesions of the prostate gland. *Arch. Pathol. Lab. Med.* 106, 136-139.
- Kline T.S. (1985). *Guides to clinical aspiration biopsy. Prostate. Igaku-shoin*, New York.
- Mostofi F.K., Sesterhenn I. and Sobin L.H. (1980). *Histological typing of prostate tumours*. W.H.O., Geneva.
- Murphy G.P. and Whitmore W.F. (1979). A report of the workshops on the current status of the histologic grading of prostate cancer. *Cancer* 44, 1490-1494.
- VonReuter H.J. and Schuck W. (1971). Die Nadelbiopsie der Prostata zur Zytologischen Karzinom-diagnostik Erfahrungen an 1500 Fallen. *Z. Urol. Nephrol.* 64, 857-862.
- Yatani R., Shiraishi T., Soga T., Yabana T., Chigusa I. and Shibata H. (1985). Reliability of cytological grading of prostatic carcinoma compared with histological grading. *Path. Res. Pract.* 180, 68-73.
- Zattoni F., Pagano F., Rebuffi A. and Costantin G. (1983). Transrectal thin-needle aspiration biopsy of the prostate: Four years' experience. *Urology* 22, 69-72.

Contents

Aguilar, E., s. Martín de las Mulas, J., et al.	93	Figols, J., Cervós-Navarro, J. and Wolman, M.: Encephalopathy with astrocytic residual bodies. Report of a case and review of the literature	59
Ainsworth, D.M., Keith, I.M., Lobas, J.G., Farrell, P.M. and Eicker, S.W.: Oxygen toxicity in the infant rhesus monkey lung. Light microscopic and ultrastructural studies	75	Fiore-Donati, L., s. Bonetti, F., et al.	391
Akay, F., s. Kadota, E., et al.	219	Gerritsen, G.C., s. Sawada, G., et al.	1
Akay, F., s. Nishida, S., et al.	69	Gherzi, N., s. Guzman de Fleury, M., et al.	227
Al-Bagdadi, F.K., s. Henry, R.W.	355	Gómez-Bezares, M.C., s. Marigil, M.A., et al.	297
Andersen, A., s. Eker, R., et al.	255	Greenberg, S.R.: The association of medial collagenous tissue with atheroma formation in the aging human aorta as revealed by a special technique	323
Apaja-Sarkkinen, M., s. Jalovaara, P., et al.	377	Guerini, A., s. Facchetti, F., et al.	181
Ballesta, J., s. Zuasti, A., et al.	139	Guzman de Fleury, M., Tapia, F.J., Soto, J., Gherzi, N. and Convit, J.: Density of epidermal Langerhans cells in psoriasis patients treated with an aromatic retinoid (RO 10-9359). An immunoperoxidase study using anti-T6 and anti-la monoclonal antibodies	227
Bani-Sacchi, T., Bartolini, G. and Biliotti, G.: A multihormonal tumor of the pancreas producing neurotensin associated with the WDHA syndrome. Histology, histochemistry and origin	187	Haensly, W.E. and Lee, J.C.: Metaplasia of the parietal layer of Bowman's capsule: a histopathological survey of the human kidney	363
Baradi, A.F., Heslop, J.H. and Rao, N.S.: Peritoneal fine structure of inguinal hernia: a scanning electron microscope study	89	Hansen, J.T., s. Chen, I-li, et al.	203
Bartolini, G., s. Bani-Sacchi, T., et al.	187	Hashimoto, S., s. Kadota, E., et al.	219
Bhasin, Y., s. Breathnach, A.S., et al.	235	Hashimoto, S., s. Nishida, S., et al.	69
Biliotti, G., s. Bani-Sacchi, T., et al.	187	Hashimoto, S., Nishida, S., Hiruma, S., Takahashi, M., Enomoto, Y. and Sakatani, K.: Immunohistochemical reaction of myocardial fibers with actin antiserum in autopsy cases of myocardial infarction	241
Blanks, M.C., s. Sawada, G., et al.	1	Hattori, T., s. Takada, M.	271
Bonetti, F., Chilosi, M., Menestri, F., Lestani, M., Scarpa, A., Todeschini, G., Pizzolo, G. and Fiore-Donati, L.: Blastic OKT6-positive proliferation preceding malignant histiocytosis	391	Henry, R.W. and Al-Bagdadi, F.K.: Duodenal microanatomy of the domestic cat (<i>Felis catus</i>) ..	355
Bonetti, M.F., s. Facchetti, F., et al.	181	Heslop, J.H., s. Baradi, A.F., et al.	89
Breathnach, A.S., Robins, E.J., Bhasin, Y., Ethridge, L., Nazzaro-Porro, M., Passi, S. and Picardo, M.: Observations on cell kinetics and viability of a human melanoma cell line exposed to dicarboxylic acids in tissue culture	235	Hiruma, S., s. Hashimoto, S., et al.	241
Callea, F., s. Facchetti, F., et al.	181	Hiruma, S., s. Kadota, E., et al.	219
Carstens, P.H.B., s. Swartz, F.J.	111	Hiruma, S., s. Nishida, S., et al.	69
Cervós-Navarro, J., s. Figols J., et al.	59	Hiscock, J. and Straznicky, C.: The development of the neurons of the glossopharyngeal (IX) and vagal (X) sensory ganglia in chick embryos	129
Chen, I-li, Yates, R.D. and Hansen, J.T.: Substance P- like immunoreactivity in rat and cat carotid bodies: Light and electron microscopic studies	203	Holm, R., s. Lunde, S., et al.	27
Chilosi, M., s. Bonetti, F., et al.	391	Idoate, M.A., s. Marigil, M.A., et al.	297
Convit, J., s. Guzman de Fleury, M., et al.	227	Imahayashi, T., s. Shimada, M., et al.	327
Costantin, G., s. Palma, P. Dalla, et al.	399	Imai, Y., Dobashi, M. and Terashima, K.: Postnatal development of dendritic reticulum cells and their immune complex trapping ability	19
Cortesini, C., s. Faussone-Pellegrini, M.S.	119	Imai, Y., s. Dobashi, M., et al.	277
Cuesta, B., s. Marigil, M.A., et al.	297	Imai, Y., Yamakawa, M., Masuda, A., Sato, T. and Kasajima, T.: Function of the follicular dendritic cell in the germinal center of lymphoid follicles	341
Dante, S., s. Palma, P. Dalla, et al.	399	Jalovaara, P., Rämö, J. and Apaja-Sarkkinen, M.: Occurrence of pancreatic ductal cell dysplasia in rats fed with a high fat diet and ethanol	377
Diani, A.R., s. Sawada, G., et al.	1	Johannessen, J.V., s. Eker, R., et al.	255
Dobashi, M., s. Imai, Y., et al.	19	Johannessen, J.V., s. Lunde, S., et al.	27
Dobashi, M., Yuda, F., Masuda, A., Terashima, K. and Imai, Y.: Electron microscopic study on amyloid fibril formation in human lymph nodes	277	Kadota, E., Tanji, K., Nishida, S., Takahashi, M., Maeda, M., Hiruma, S., Enomoto, Y., Hashimoto, S. and Akay, F.: Lectin (UEA-1) reaction of capillary endothelium with reference to permeability in autopsied cases of cerebral infarction	219
Eicker, S.W., s. Ainsworth, D.M., et al.	75	Kamo, S., Takeuchi, H. and Yamada, M.: Comparative cytospectrophotometry of Wright-stained erythroid cells of vertebrates	103
Eker, R., Nesland, J.M., Andersen, A. and Johannessen, J.V.: Prognostic factors in renal cell carcinoma ..	255	Karzel, K., s. Weischer, C.H., et al.	303
Enomoto, Y., s. Hashimoto, S., et al.	241	Kasajima, T., s. Imai, Y., et al.	341
Enomoto, Y., s. Kadota, E., et al.	219	Kasuga, T., s. Kitagawa, M., et al.	335
Ethridge, L., s. Breathnach, A.S., et al.	235	Keith, I.M., s. Ainsworth, D.M., et al.	75
Facchetti, F., Tardanico, R., Bonetti, M.F., Guerini, A. and Callea, F.: HBsAg, HBeAg and Delta-Ag in liver tissue: simultaneous visualization in a single tissue section by triple immunostaining	181		
Farrell, P.M., s. Ainsworth, D.M., et al.	75		
Faussone-Pellegrini, M.S. and Cortesini, C.: Ultrastructure of striated muscle fibers in the middle third of the human esophagus	119		
Ferrer, C., s. Zuasti, A., et al.	139		

Contents

Kitagawa, M., Matsubara, O. and Kasuga, T.: Effects of Friend leukemia virus (FLV) inoculation in F ₁ mice and differentiation of FLV-induced leukemia	335
Kitagawa, T., Okamura, K., Sohma, M., Namiki, M. and Ono, K.: Ultrastructural changes in pancreatic acinar cells of rats after administration of 4-hydroxyaminoquinoline-1-oxide	369
Kitagawa, T. and Ono, K.: Ultrastructure of pancreatic exocrine cells of the rat during starvation	49
Köpf-Maier, P.: Dying and regeneration of human tumor cells after heterotransplantation to athymic mice	383
Krisinger, J., s. Weischer, C.H., et al.	303
Lapis, K., s. Timár, J., et al.	43
Lee, J.C., s. Haensly, W.E.	363
Leeson, R., s. Leeson, T.S.	33
Leeson, T.S. and Leeson, R.: Close association of centroacinar/ductular and insular cells in the rat pancreas	33
Lestani, M., s. Bonetti, F., et al.	391
Lindop, G.B.M., Mallon, E.A. and MacIntyre, G.: Atrial natriuretic peptide in the heart and pancreas	147
Livne, E. and Silbermann, M.: Further characterization of spontaneous arthritic changes in murine squamomandibular joint: histopathological aspects	161
Lobas, J.G., s. Ainsworth, D.M., et al.	75
Lunde, S., Nesland, J.M., Holm, R. and Johannessen, J.V.: Primary malignant fibrous histiocytoma of the breast	27
Luzi, P., s. Miracco, C., et al.	9
MacIntyre, G., s. Lindop, G.B.M., et al.	147
Maeda, M., s. Kadota, E., et al.	219
Maeda, M., s. Nishida, S., et al.	69
Mallon, E.A., s. Lindop, G.B.M., et al.	147
Marani, E., s. van Rijn, C.M., et al.	291
Marigil, M.A., Pardo-Mindan, F.J., Cuesta, B., Rocha, E., Idoate, M.A. and Gómez-Bezares, M.C.: Non Hodgkin's lymphomas following chemoradiotherapy for Hodgkin's disease. Two new cases and a review of the literature	297
Martin de las Mulas, J., Aguilar, E. and Sánchez-Criado, J.E.: Immunohistochemical localization of prolactin in functioning and regressing <i>corpus luteum</i> of pituitary autotransplanted rats	93
Masuda, A., s. Dobashi, M., et al.	277
Masuda, A., s. Imai, Y., et al.	341
Matsubara, O., s. Kitagawa, M., et al.	335
Menestri, F., s. Bonetti, F., et al.	391
Metcalf, W.K., s. Tarburton, J.P.	213
Miracco, C., Sensini, I., Vessio, G. and Luzi, P.: Oncocytic adenoma of the nasal cavity. A case report	9
Miragall, F., s. Paz, P. de, et al.	197
Mitchell, O.G., s. Steinberg, B., et al.	155
Murakami, T.H., s. Shimada, M., et al.	327
Nagayo, T.: Gastric cancer preceded by severe dysplasia	171
Nagy, K., s. Timár, J., et al.	43
Namiki, M., s. Kitagawa, T., et al.	369
Nazzaro-Porro, M., s. Breathnach, A.S., et al.	235
Nesland, J.M., s. Eker, R., et al.	255
Nesland, J.M., s. Lunde, S., et al.	27
Nishida, S., Akai, F., Hiruma, S., Maeda, M., Tanji, K. and Hashimoto, S.: Experimental study of WGA binding on the endothelial cell surface in cerebral ischemia	69
Nishida, S., s. Hashimoto, S., et al.	241
Nishida, S., s. Kadota, E., et al.	219
Okamura, K., s. Kitagawa, T., et al.	369
Ono, K., s. Kitagawa, T.	49
Ono, K., s. Kitagawa, T., et al.	369
Ozaki, H.H., s. Shimada, M., et al.	327
Palma, P. Dalla, Dante, S., Costantin, G., Rebuffi, A., Zattoni, F. and Piazza, R.: Grading of the prostate carcinoma: cyto-histological correlations on 100 cases	399
Pardo-Mindan, F.J., s. Marigil, M.A., et al.	297
Passi, S., s. Breathnach, A.S., et al.	235
Pastor, L.M., s. Zuasti, A., et al.	139
Paz, P. de, Zapata, A., Renau-Piqueras, J. and Miragall, F.: Morphological differentiation of mitochondria in the early chick embryo: a stereological analysis	197
Persaud, T.V.N., s. Ross, C.P.	13
Piazza, R., s. Palma, P. Dalla, et al.	399
Picardo, M., s. Breathnach, A.S., et al.	235
Pizzolo, G., s. Bonetti, F., et al.	391
Râmö, J., s. Jalovaara, P., et al.	377
Rao, N.S., s. Baradi, A.F., et al.	89
Rebuffi, A., s. Palma, P. Dalla, et al.	399
Renau-Piqueras, J., s. Paz, P. de, et al.	197
Rietveld, W.J., s. van Rijn, C.M., et al.	291
Robins, E.J., s. Breathnach, A.S., et al.	235
Rocha, E., s. Marigil, M.A., et al.	297
Ross, C.P. and Persaud, T.V.N.: Early embryonic development in the rat following <i>in utero</i> exposure to alcohol and caffeine	13
Rush, R.A., s. Smet, P., et al.	315
Sakatani, K., s. Hashimoto, S., et al.	241
Sánchez-Criado, J.E., s. Martín de las Mulas, J., et al.	93
Sato, T., s. Imai, Y., et al.	341
Sawada, G., Wyse, B.M., Blanks, M.C., Vidmar, T.J., Gerritsen, G.C. and Diani, A.R.: Morphometric evaluation of capillary basement membrane thickness in the quadriceps muscle of diabetic and nondiabetic Chinese hamsters	1
Scarpa, A., s. Bonetti, F., et al.	391
Sensini, I., s. Miracco, C., et al.	9
Shimada, M., Shimono, R., Imahayashi, T., Ozaki, H.H. and Murakami, T.H.: Diazo-reaction positive substance observed in the cortex of <i>Chattonella antiqua</i>	327
Shimono, R., s. Shimada, M., et al.	327
Silbermann, M., s. Livne, E.	161
Singh, I.J., s. Steinberg, B., et al.	155
Smet, P., Rush, R.A. and Straznicky, C.: The thoracic sympathetic neurons of the chick: normal development and the effects of nerve growth factor	315
Sohma, M., s. Kitagawa, T., et al.	369
Soto, J., s. Guzman de Fleury, M., et al.	227
Steinberg, B., Singh, I.J., and Mitchell, O.G.: An autoradiographic study of the uptake of tritiated proline by osteoblasts during hibernation	155
Straznicky, C., s. Hiscock, J.	129
Straznicky, C., s. Smet, P., et al.	315
Swartz, F.J. and Carstens, P.H.B.: An islet of Langerhans located within the epithelium of a human pancreatic duct	111
Takada, M. and Hattori, T.: Fine structural changes in the rat brain after local injections of gliotoxin, alpha-amino adipic acid	271
Takahashi, M., s. Hashimoto, S., et al.	241
Takahashi, M., s. Kadota, E., et al.	219
Takeuchi, H., s. Kamo, S., et al.	103
Tanji, K., s. Kadota, E., et al.	219
Tanji, K., s. Nishida, S., et al.	69
Tapia, F.J., s. Guzman de Fleury, M., et al.	227

Contents

Tarburton, J.P. and Metcalf, W.K.: The kinetic differences between sodium nitrite, amyl nitrite and nitroglycerin oxidation of hemoglobin	213	Wilson, D.B. and Wyatt, D.P.: Growth hormone and prolactin immunoreactivity in the pituitary gland of postnatal little <i>lit</i> mice	309
Tardanico, R., s. Facchetti, F., et al.	181	Wolman, M., s. Figols, J., et al.	59
Terashima, K., s. Dobashi, M., et al.	277	Wyatt, D.P., s. Wilson, D.B.	309
Terashima, K., s. Imai, Y., et al.	19	Wyse, B.M., s. Sawada, G., et al.	1
Timár, J., Nagi, K. and Lapis, K.: Morphologic and immunoelectronmicroscopic identification of human T-cell lymphotropic virus type III(HTLV-III)	43	Yamada, M., s. Kamo, S., et al.	103
Todeschini, G., s. Bonetti, F., et al.	391	Yamakawa, M., s. Imai, Y., et al.	341
van Rijn, C.M., Marani, E. and Rietveld, W.J.: The neurotoxic effect of monosodium glutamate (MSG) on the retinal ganglion cells of the albino rat	291	Yates, R.D., s. Chen, I-li, et al.	203
Vassio, G., s. Miracco, C., et al.	9	Yuda, F., s. Dobashi, M., et al.	277
Vestfrid, M.A.: The ovarian lobule: a histoembryological unit	251	Zapata, A., s. Paz, P. de, et al.	197
Vidmar, T.J., s. Sawada, G., et al.	1	Zattoni, F., s. Palma, P. Dalla, et al.	399
Weischer, C.H., Krisinger, J and Karzel, K.: Effects of mellitic acid (MA) and sodium fluoride (NaF) on the histological appearance of murine fetal tibiae cultured <i>in vitro</i>	303	Zuasti, A., Ferrer, C., Ballesta, J. and Pastor, L.M.: Ultrastructure of the renal corpuscle of <i>Testudo graeca</i> (Chelonia). A comparison between hibernating and non-hibernating animals	139

Indexed in
 CURRENT CONTENTS
 EXCERPTA MEDICA
 SCIENCE CITATION INDEX