Acta neuropath. (Berl.) 20, 110—121 (1972)

A Histochemical Study of Meningiomas

I. Lolova and A. Ivanova

Research Group on Brain Functions Localization,
Bulgarian Academy of Sciences, Sofia

S. Bojinov

Department of Neurology at the Faculty of Medicine, Sofia

Received June 24, 1971/August 2, 1971

Summary. The results of a histochemical study of biopsies of 30 meningiomas are reported. The study includes the demonstration of oxidative and hydrolytic enzymes, lipids and glycogen and examines the relationship between the histological and histochemical characteristics of the structural elements of the various types of meningiomas and of their malignant varieties. The data obtained are compared with those of other workers which often present conflicting findings. The possibilities offered by the histochemical methods of investigation are discussed with regard to the problems of histogenesis, the signs of malignancy, the processes of hyalinosis and destruction, the vascular involvement and the role of the mast cells.

Key words: Meningiomas — Enzyme Histochemistry — Malignancy — Vascular Changes — Mast Cells.

The histological features of meningiomas have been known for a long time. Recent research has been directed towards clarification of the histogenesis of these tumours, their comparative characteristics, their proclivity to recidivism towards a further refinement of the criteria of malignancy, investigations of the mechanisms of calcification, hyaline and mucoid degeneration, etc. The newer morphological methods of study including histochemical methods, offer additional approaches to the solution of these problems.

The aim of this study was to arrive at a more comprehensive histochemical characterization of the various histological types of meningioma and their structural elements and to compare the results of the study with the existing data in the literature many of which seem to us controversial.

Material and Methods

The material studied consisted of 30 meningiomas extirpated at operation. Depending on the methods applied the material was used fresh or fixed in a chilled solution of 4% formol-calcium, Rossmann's fixative or Carnoy's solution.

The following methods were used: *Histological methods:* hematoxylin-eosin, van Gieson, Gomori (for reticular fibres), toluidine-blue, Bismarck brown. *Histochemical methods* for identification of: *oxidoreductases*—succinic dehydrogenase (SDH) (Nachlas *et al.*, 1957), isocitric—(IDH), malic—(MDH), glutamic—(GDH), glycerophosphate—NAD/GIDH (NAD), β-oxibutyrate—(β-OBDH), lactic—(LDH) dehydrogenases (Hess *et al.*, 1958), glycerophosphate dehydrogenase with menadion/GIDH(M)/ (Kultas, 1964), glucoso-6-phosphate dehydrogenase (G-6-PDH) (Wegmann and Gerzeli, 1961), NAD- and NADP-diaphorases (NADH-D, NADPH-D) (Novikoff, 1963); hydrolases—alkaline phosphatase (ALP-ase) (Burstone, 1965), acid phosphatase (AcP-ase) (Barka and Anderson, 1962), non-specific esterase (NEs-ase) (Davis and

Ornstein, 1959), β-glucuronidase (β-glu-ase) (Hayashi *et al.*, 1964), N-acetyl-β-glucosaminidase (N-acetyl-β-glu-ase) (Hayashi, 1965), adenosinetriphosphatase (ATP-ase) (Padykula and Herman, 1955; in Pearse, 1962), phosphorylase (Guha and Wegmann, 1960); *glycogen* (Shabadash, 1949), lipids (Sudan III and Sudan black) (Romeis, 1954).

Results

1. Oxidoreductases

The character, distribution and intensity of the reactions depend to some extent on the histological structure of the meningioma. The diformazan granules fill out the cellular bodies and the processes. The highest level of activity is found in the whorls, and especially in those consisting of fewer cells (Fig. 1 A). Generally speaking, the reactions for oxidative enzymes are more intensive in the *meningothelial* structures than in the fibroblastic ones. If some degree of hyalinazition is present, the reaction of these cells is weaker and the granules are coarser. In the *psammoma bodies* in various stages of hyalinization and calcification there are usually some cells with processes which show a marked and very intense fine-granular reaction for oxidoreductases (Fig. 1 B). *Xanthomatous cells*, occupying large areas in some meningiomas, are represented by a few course granules in the form of a ring at the periphery of the cell. The picture of the oxidative enzymes in angioblastic meningiomas is more variable, depending on the extent of representation of vascular and meningothelial elements and the morphological alterations of vascular walls and dystrophy. In two biopsies the H.-E.-picture was to some extent reminiscent of the haemangiopericyte type of angioblastic meningioma recently reviewed in detail by Pitkethly *et al.* (1970). The pattern of oxidoreductases was similar to that of the meningothelial structures. However, in spite of the large number of mitosis, no cellular histochemical polymorphism was found (Fig. 2) as is usual with malignant meningiomas.

The histochemical picture of reactions for oxidoreductases in *malignant meningiomas* is characterized by variability between areas and between individual tumour cells, especially in the large bi- and polynuclear cells and syncytial structures of bizarre appearance (Fig. 3 A).

In the zone of *infiltration* of malignant meningiomas into the adjacent cerebral substance the reactions in the tumour cells are very intense. There is an increased number of large monstrous cells and cellular bizarre syncytial structures.

The perivascular lymphocyte clusters manifested themselves only with a ring of diformazan granules around the nuclei in all reactions for oxidative enzymes.

Regardless of the histological type of the meningioma, the reaction for SDH is weaker in comparison with the other two dehydrogenases of the Krebs cycle. The reaction for NADPH-D is weaker than that for NADH-D although no difference is found in the character and distribution of the reaction products. The reaction for G6PDH is comparatively weak.

The oxidative enzymes reactions in the blood vessels of the meningiomas show considerable variability, conditioned by the increased activity and histochemical polymorphism in the proliferation endothelium (Fig. 3 B) or by the gradual diminishing activity in cases of hyalinization and sclerosis.

In *areas of destruction* the reaction product is in coarse granules, few in quantity.

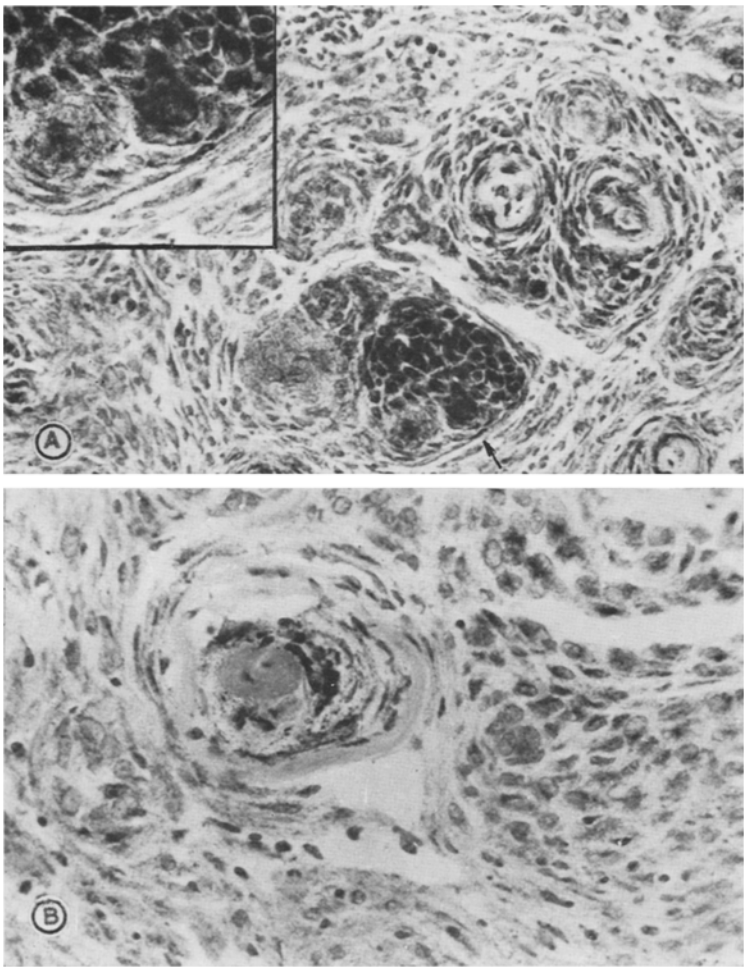

Fig. 1. A NAD-diaphorase (×80). Big cells with a very intense reaction in the whorls. Activity decreases in sites of hyalinization (indicated by arrow). Detail (×160). B Succinic dehydrogenase (×160). Cells with intense reaction in the psammoma bodies

2. Hydrolytic Enzymes

ALP-ase. In 22 of the meningiomas irrespective of histological type and anaplastic signs, we found positive reaction for alkaline phosphatase in the *parenchyma*. The reaction was uniform among the cells and delineated well the peripheries of the cell bodies in the meningothelial structures, especially those near the stroma, and the cell processes in the fibroblastic type. Higher activity was found in the whorls and in their periphery. The cells in the peritheliomatous structures of the haemangiopericyte type of angioblastic meningioma and the vessels localized in the centres of the these structures lacked ALP-ase activity.

With advance hyalinization and calcification the reaction becomes weaker and limited to peripheral concentric circles. In completely calcified psammoma bodies there is no activity.

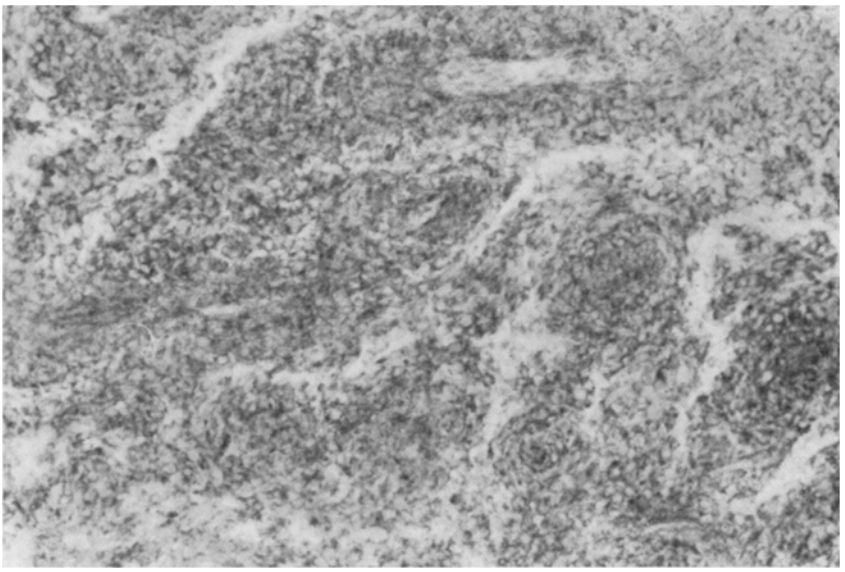

Fig. 2. A haemangiopericyte type of angioblastic meningioma. NAD-diaphorase (×80)

In most meningiomas the reaction for ALP-ase in the vessels is extremely variable: from intense to negative. There is a tendency toward an inverse relationship between the intensity of the reaction in the parenchyma and the vessels. This is demonstrable even in different areas of one and the same preparation. Tumour cells surrounding negative vessels frequently show a higher activity.

Lysosome enzymes (AcP-ase, NEs-ase, β-glu-ase, N-acetyl-β-glu-ase). The character and intensity of reactions are contingent upon the type of meningioma and upon the lysosome enzyme studied. In the *fibroblastic* type it is moderate and comparatively uniform. In *meningothelial* meningiomas the reaction is again finely-granular but more varied, regardless of its intensity. The reaction is more intense with AcP-ase and NEs-ase than β-glu-ase and N-acetyl-β-glu-ase. (Fig. 4 A). Some small, spindle-shaped cells possessing a very intense finely-granular NEs-ase reaction are particularly prominent, especially in the meningothelial areas The *whorls* have a somewhat higher activity than the surrounding tumour cells. The character of the reaction is the same. The psammoma bodies in initial stages of development possess some concentric-located cells with very intense reactions. The wholly hyalinized and calcified psammoma bodies have no activity. In meningiomas, rich in psammoma bodies, the cells lying immediately next to the latter form a zone of intense NEs-ase reaction which is wider than the analogous zone with AcP-ase.

In malignant meningiomas the intensity of the reaction varies in the individual cells, especially the AcP-ase reaction, as was pointed out for the oxidoreductases.

The haemangiopericyte type of angioblastic meningioma had an intense AcP-ase reaction and a uniform moderate NEs-ase reaction. There are no cells possessing a very intense NEs-ase reaction as in the other histological types (Fig. 4 B).

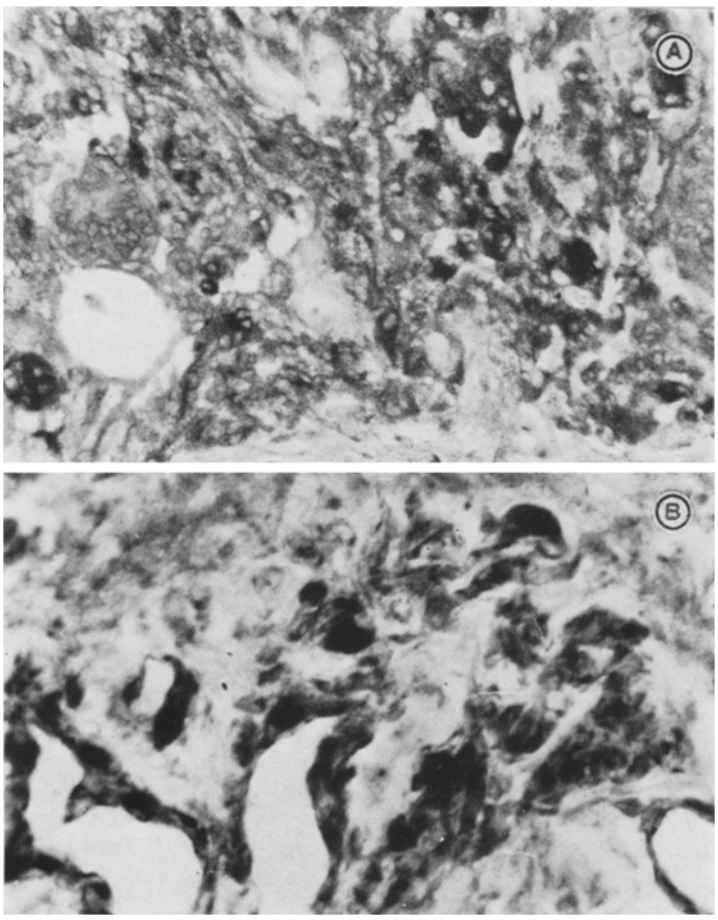

Fig. 3. A NAD-diaphorase (×80). Malignant meningioma. Marked polymorphism: big polynuclear cells and bizarre syncytial structures with intense reaction; B lactic dehydrogenase (×160); big endothelial cells with a very intense reaction

The *xanthomatous* cells showed a fairly intense granular reaction, in the form of clusters, at certain places.

The perivascular lymphocyte clusters have no activity.

In the vascular *endothelium* the reaction is weak and diffuse. It is more intense in proliferating vessels. In hyalinized vessels some large endothelial cells retain their high activity.

In *areas of destruction* the reaction is intense and coarsely-granular, both in tumour cells and in the vessels.

ATP-ase. The parenchyma of meningothelial, fibroblastic and psammoma meningiomas shows moderate or intense reaction. The reaction product is fairly evenly distributed and its intensity varies little, except in cells lying closer to the stroma and having slightly higher activity. The reaction in the *whorls*, particularly the small ones, is more intense. *Psammoma bodies* in intial stages of hyalinization

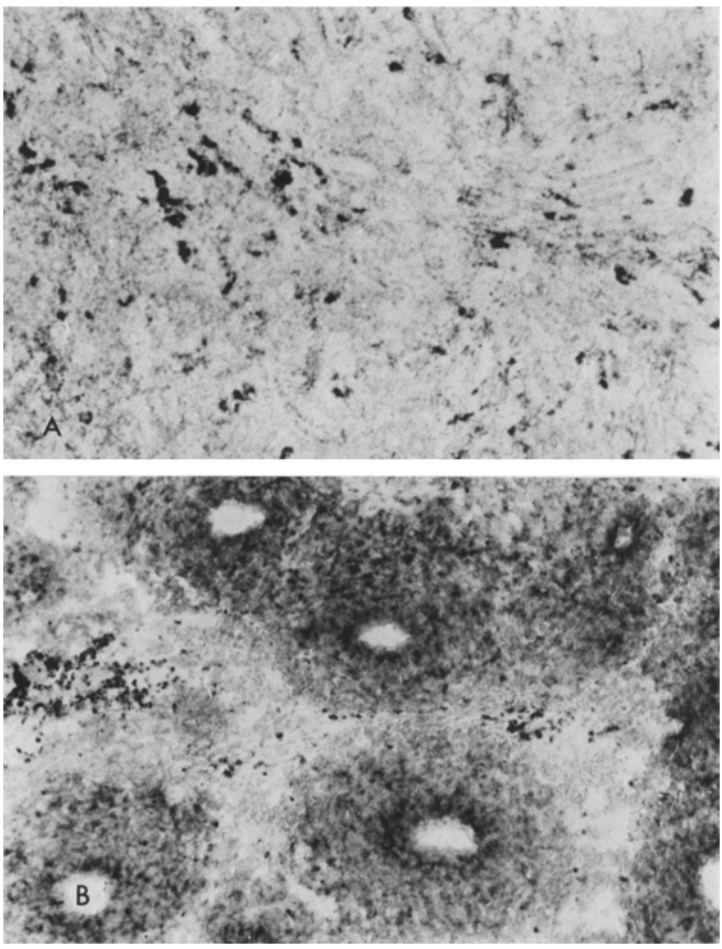

Fig. 4. A N-acetyl-β-glucosaminidase. Scattered cells with processes and intense finely granular reaction ($\times 80$). B A haemangiopericyte type of angioblastic meningioma. A very intense AcP-ase reaction in the cells around blood vessels. Additional methyl green staining for nuclei ($\times 32$)

have a more intense ATP-ase reaction in comparison with the other tumour cells. Completely calcified bodies show no reaction. In the peritheliomatous structures of the haemangiopericyte type of *angioblastic* meningioma the reaction was uniformly weak. The centrally located vessels had a weaker reaction than the interstitial tissue. *Xanthomatous* cells have only single granules at the periphery of the cell body. In malignant meningiomas activity increases in areas of polymorphism.

The reaction in the vessels is uneven, regardless of the size of the vessels (Fig. 5).

3. Glycogen and Phosphorylase

The reactions for the identification of glycogen and phosphorylase show almost identical pictures. The *parenchyma* of the various meningiomas exhibits

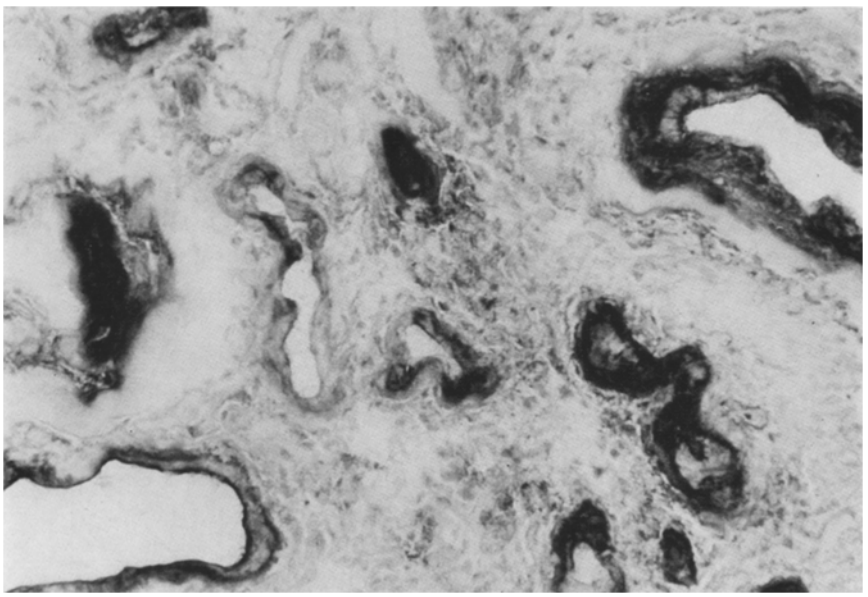

Fig. 5. Adenosinetriphosphatase. Varying reaction in the vessels, regardless of their size (×80)

an intense granular PAS-positive reaction. The *fibroblastic* areas have a more uniform and slightly more intense reaction. In meningothelial areas some lobules and especially the whorls, rich in glycogen are found along with lobules of weak reaction. Phosphorylase is more evenly distributed. With advanced hyalinization the granular reaction for glycogen and phosphorylase decreases while the diffuse PAS-positive reaction increases (the latter resists α-amylase). Malignant meningiomas contain a large and variable amount of glycogen and show a tendency for more intense reactions in sites with fibroblastic structure.

4. Lipids

The staining for lipids with Sudan III and Sudan black demonstrates limited foci of destruction in which the cells are loaded with sudanophil substance. Rarely, in the centres of whorles with some hyalinization may be seen cells containing large lipid granules. The xanthomatous cells are loaded with large lipid granules or globules. There is a gradual transition from small cells with short processes and fine granules to cells without processes with round enlarged bodies and large lipid granules.

Mast cells were found in all types of meningiomas, including malignant ones and the haemangiopericyte type of angioblastic meningioma. Mast cells are found usually around the vessels and occasionally in lobules of connective tissue. In areas containing whorls and psammoma bodies the number of mast cells in the stroma is large but they are found within the whorls and psammoma bodies in exceptional cases only. There are mast cells with rounded outlines, without processes and with pale granules. Granules may also be seen outside the cell bodies.

Discussion

Our data suggest certain differences in the oxidative enzyme activity of meningothelial and fibroblastic areas in the meningiomas differing from other reports which stress that the reaction in both area is uniform (Osske and Jänisch, 1967; Viale and Andreussi, 1965).

Our results of a more intense reaction for NADH-diaphorase than for NADPH-diaphorase are in agreement with the report of Viale and Andreussi (1965) and Udvarhelyi *et al.* (1962), but disagree with Schiffer *et al.* (1964) who found low levels of activity of both diaphorases in meningiomas.

Our findings suggest that the proliferation of the vascular endothelium, especially in angioblastic and malignant meningioma, is associated with very high oxidoreductase activity.

The literature on hydrolytic enzymes (Bingas, 1966; Fabiani *et al.*, 1967; Feigin and Wolf, 1959; Hanefeld, 1966; Lehrer, 1962; Nasu, 1964; Osske and Jänisch, 1967; Schiffer *et al.*, 1964, 1968, 1969) is confusing. Most of the discrepancies are related to the activity of the AlP-ase which is one of the most widely studied enzymes in meningiomas, due to its role in the processes of calcification, anaplasia and vascular permeability. Our study failed to demonstrate a clear-cut distribution of meningiomas into three groups, on the basis of the localization of AlP-ase, as has been suggested by Nasu (1964) and later by Osske and Jänisch (1967). We believe that an inverse relationship exists between the intensity of the reaction in the parenchyma and the vessels. Taking into account Meier-Ruge's theory (1966) about the participation of the AlP-ase in the processes of active transport in the vascular wall, our finding may be indicative of some general and contrasting patterns of change in the metabolism of the parenchyma and the vessels. This finding is not limited to a special group of meningiomas, as Osske and Jänisch insist.

The histological types of meningioma vary in their AlP-ase activity only to a certain degree. In spite of what has been reported in the literature however, in some areas of meningioblastomas we found high activity. We agree with Feigin and Wolf (1959) and Osske and Jänisch (1967), who, contrary to Nasu (1964), hold that no relationship exists between intensity of the AlP-ase activity and malignancy in meningiomas. Our data support the suggestion that the AlP-ase in meningiomas is related to the process of calcification.

Some discrepancies exist in the literature concerning the AcP-ase and NEs-ase activity in meningiomas (Bingas, 1966; Osske and Jänisch, 1967). Regarding the character and localization of the reaction in the individual cellular elements of the meningiomas, our findings are similar to those of Fabiani *et al.* (1967).

The number of scattered cells with a more intense NEs-ase reaction is greater than that of scattered cells with high AcP-ase activity. These cells were characteristic of our preparations as well, but we could not find their analogues with reactions for oxidoreductases. Contrary to Takao *et al.* (1965) we found an increased AcP-ase activity in malignant meningiomas.

The authors who have studied the AcP-ase and NEs-ase activity in meningiomas give no characteristics of the angioblastic type. We should note the increased activity of the proliferating vascular endothelium. Very intense reactions are also

observed in the parenchyma of the haemangiopericyte type of angioblastic meningioma.

In comparison with the other lysosome enzymes investigated, the β-glucuronidase activity is weaker in the tumour parenchyma. Our findings in the haemangiopericyte type of angioblastic meningioma are similar to Hanefeld's (1966) data on the mesodermal angioblastoma where β-glucuronidase is well represented.

Our results on the N-acetyl-β-glucosaminidase activity cannot be discussed comparatively, as we were unable to find literature data on this enzyme in cerebral tumours.

The histochemical picture of the whorls and psammoma bodies merits special attention. In our study, the whorls showed the most intensive reaction for all oxidative enzymes, some hydrolases, glycogen and phosphorylase. In the course of the formation of psammoma bodies the activity of these enzymes decreases, together with a changing localization and character of the reaction product. However, some cells continue to exhibit a high activity for a long time. These latter cells are probably identical to what Napolitano *et al.* (1964) have described as persisting cytoplasmatic residues among the homogenous and laminar masses of well-formed psammoma bodies. However, it is difficult to explain why these dying cellular elements have more intensive oxidoreductase reaction than the remaining parenchyma. It is not clear whether this is the effect of some compensatory function or of damaged lipoprotein membranes which facilitate the entry of substrates.

Although meningiomas are generally regarded as relatively benign tumours, the question of malignancy in them has aroused considerable interest in recent years, in association with their radical removal, tendency to recidivism and effects of radiotherapy (Crompton and Gautier-Smith, 1970; Earle and Richany, 1969; Tytus *et al.*, 1967).

This raises the question of the histochemical characteristics of malignant meningiomas. Data on the enzyme activity in these are scarce (Takao *et al.*, 1965; Viale and Andreussi, 1965). Our results show that the most general characteristics of these tumours is their histochemical polymorphism demonstrable both in areas and individual cells. It is much more apparent in histochemical preparations than with H.-E.-staining. On the on hand, polymorphism is associated with higher incidence of regressive tissue and cellular changes in malignant growths, as has been emphasized by Schiffer *et al.* (1969). On the other hand, however, in areas with apparent anaplasia the oxidative enzyme activity is increased mostly in the large polynuclear cells and in the bizarre syncytial structures. The reactions for lysosome enzymes and lipids show no regressive changes in them.

The histochemical characteristics of the individual cellular elements in the meningiomas bear upon the important but undecided problem of the origin of these components (Penfield, 1957; Wolman, 1952; Kernohan, 1941; Courville, 1950; Crompton and Gautier-Smith, 1970). Modern morphological methods such as tissue cultures and electron microscopy (Napolitano *et al.*, 1964; Cervós-Navarro and Vasquez, 1969) give more and more evidence for the identical fine structure of tumour cells, regardless of the cellular type and the histological differences between the various types of meningiomas. Our results support this, both with regard to oxidative and hydrolytic enzymes, because the observed differences

between meningothelial and fibroblastic structures are not essential. These differences pertain above all to the intensity of reactions and may be indicative of varying degrees of functional and structural differentiation in one and the same cellular type.

The question of the presence and role of the mast cells in the meningiomas and tumours in general has not been solved. Their incidence, distribution and function in meningiomas are discussed in detail by Schiffer *et al.* (1968) and Olsson and Sjöstrand (1969). Our results are in agreement with some of their data.

There are, however, some differences in localization. Schiffer *et al.* (1968) found a proportion of the mast cells in the centres of hyalinized and calcified whorls and attribute this to the process of calcification. We failed to find such a localization although we studied meningiomas at various stages of psammoma bodies formation. There are hypotheses and some evidence of a participation of mast cells in many and different processes (Combs *et al.*, 1965; Kon, 1964; Olsson and Sjöstrand, 1969; Fischer and Fischer, 1965; Sawicki, 1967). It seems that the function of mast cells in meningiomas should not be regarded as related to calcification only.

We suppose that they are nonspecific reaction of the stroma with tumour growth. Our considerations were that mast cells may are found in all histological types of meningiomas despite the existing calcification, the features of rapid growth and malignancy.

References

Barka, T., Anderson, P. J.: Histochemical methods for acid phosphatase using hexazonium pararosanilin as coupler. J. Histochem. Cytochem. **10**, 741—754 (1962).

Bingas, B.: Enzymhistochemische Befunde an intrakraniellen Tumoren. Naturwissenschaften **53**, 87 (1966).

Burstone, M. S.: Enzyme histochemistry and its application in the study of neoplasms, pp. 214, 247. V. V. Portugalov, Moskva 1965.

Cervós-Navarro, J., Vasquez, J. J.: An electron microscopic study of meningiomas. Acta neuropath. (Berl.) **13**, 301—323 (1969).

Combs, J. W., Lagunoff, D., Benditt, E. P.: Differentiation and proliferation of embryonic mast cells of the rat. J. Cell Biol. **25**, 577—585 (1965).

Courville, C. B.: Pathology of the central nervous system; a study based upon a survey of lesions found in a series of 40,000 autopsies. 3rd ed. Mountain View, Calif. Pacific Press Publishing Association 1950.

Crompton, M. R., Gautier-Smith, P. C.: The predicition of recurrence in meningiomas. J. Neurol. Neurosurg. Psychiat. **33**, 80—87 (1970).

Davis, B. J., Ornstein, L.: High resolution enzyme localization with a new diazoreagent "Hexazonium pararosanilin". J. Histochem. Cytochem. **7**, 297—298 (1959).

Earle, K. M., Richany, S. F.: Meningiomas: A study of the histology, incidence and biological behaviour of 243 cases from the Frazier Grant collection of brain tumours. Med. Ann. D.C. **38**, 353—356 (1969).

Fabiani, A., Monticone, G. F., Schiffer, D.: Histochemical study of hydrolytic enzymes in meningiomas. Psychiat. et Neurol. (Basel) **154**, 95—105 (1967).

Feigin, I., Wolf, A.: The alkaline phosphomonoesterase activities of brain tumors. Arch. Path. **67**, 670—678 (1959).

Fischer, E. D., Fischer, B.: Role of mast cells in tumor growth. Arch. Path. **79**, 185—191 (1965).

Guha, S., Wegmann, R.: La mise en évidence histochimique de l'activité phosphorylasique dans le foie et dans d'autres organes. I. Technique. Bull. Soc. Chim. biol. (Paris) **42**, 115—121 (1960).

Hanefeld, F.: Nachweis und Verteilung der hydrolytischen Enzyme β-D-Glucosidase und Arylsulfatase in intracraniellen Tumoren. Naturwissenschaften **53**, 230—231 (1966).

Hayashi, M.: Histochemical demonstration of N-acetyl-β-glucosaminidase employing naphthol AS-BI N-acetyl-β-glucosaminide as substrate. J. Histochem. Cytochem. **13**, 355—360 (1965).

— Nakajima, Y., Fishman, W. H.: The cytologic demonstration of β-glucuronidase employing naphthol AS-BI glucuronid and hexazonium pararosanilin. J. Histochem. Cytochem. **12**, 293—297 (1964).

Hess, R., Scarpelli, D. G., Pearse, A. G. E.: Cytochemical localization of pyridine nucleotide-linked dehydrogenases. Nature (Lond.) **181**, 1531—1532 (1958).

Kernohan, J. W.: Tumors of spinal cord. Arch. Path. **32**, 843—883 (1941).

Kon, Huh: A study of the incidence of calcification in a histological survey biopsies of meningiomas. J. Neurosurg. **21**, 751—757 (1964).

Kultas, K. N.: A cytochemical study of the distribution of succinic dehydrogenase and α-glycerophosphate-dehydrogenase in the Deiters' nucleus of the rabbit (Russ.). Citologiya **6**, 452—457 (1964).

Lehrer, G. M.: The quantitative histochemistry of human glial tumors. In Proc. IV Intern. Congress Neuropath, vol. 1, pp. 66—70. H. Jacob (ed.), Stuttgart: G. Thieme 1962.

Meier-Ruge, W.: Das Gliom und seine Differentialdiagnose im enzymhistotopochemischen Bild. Z. Krebsforsch. **68**, 276—283 (1966).

Nachlas, M. M., Tsou, K. C., Souza, E. D., Cheng, C. S., Seligman, A. M.: Cytochemical demonstration of succinic dehydrogenase by the use of a new p-nitrophenil substituted ditetrazole. J. Histochem. Cytochem. **5**, 420—436 (1957).

Napolitano, L., Kyle, R., Fischer, R. E.: Ultrastructure of meningioma and the derivation and nature of their cellular components. Cancer **17**, 233—241 (1964).

Nasu, H.: Fermenthistochemische Untersuchungen an Meningeomen. Acta neuropath. (Berl.) **3**, 627—637 (1964).

Nepveux, P., Wegmann, R.: Les aldolases—notions biochemiques et histochemiques. Techniques histoenzymologiques. Ann. Histochim. **10**, 177—188 (1965).

Novikoff, A.: Electron transport enzymes. Biochemical and tetrazolium staining studies. In: First Intern. Congr. Histochem. Cytochem., pp. 465—481. Oxford-London-New York-Paris: Pergamon Press 1963.

Olsson, Y., Sjöstrand, J.: Proliferation of mast cells in peripheral nerves during Wallerian degeneration. Acta neuropath. (Berl.) **13**, 111—121 (1969).

Osske, G., Jänisch, W.: Zur Enzymhistochemie der Meningiome. Acta neuropath. (Berl.) **9**, 290—297 (1967).

Pearse, A. G. E.: Histochemistry. Theoretical and applied, 2nd ed. pp. 805—805. Moscow: V. V. Portugalov ed., Intern. Publ. House 1962.

Penfield, W.: Encapsulted tumors of nervous system; meningeal fibroblastomata, perineurial fibroblastomata and neurofibromata of von Recklinghausen. Surg. Gynec. Obstet. **45**, 178—188 (1957).

Pitkethly, D. T., Hardman, J. M., Kempe, L. G., Earle, K. M.: Angioblastic meningiomas. Clinicopathologic study of 81 cases. J. Neurosurg. **32**, 539—544 (1970).

Romeis, B.: Mikroskopische Technik, pp. 249, 252. I. I. Sokolov ed., Moscow: Intern. Publ. House 1954.

Sawicki, W.: Mitotic activity of mast cells in precancerous mouse skin. Experientia (Basel) **23**, 460—461 (1967).

Schiffer, D., Cognazzo, A., Fabiani, A., Monticone, G. F.: The mast cells in meningiomas and their relationship with calcifications. Arch. Suisses Neurol. Neurochir. Psychiat. **101**, 72—78 (1968).

— Fabiani, A., Cognazzo, A., Monticone, G. F.: A histochemical study on the distribution and localization of beta-glucuronidase activity in cerebral tumors. Acta neuropath (Berl.) **13**, 91—106 (1969).

— — Vesco, C., Glabella, G.: Studio istochimico di alcune attivita enzimatiche, ossidative e idrolitische nei tumori cerebrali. Acta neurol. (Napoli) **19**, 287—307 (1964).

Shabadash, A. P.: Problems of the histochemical study of glycogen in the normal nervous system (Russ.). Moscow: Publ. House for Med. Literature, Medgiz 1949.

Takao, K., Kisaburo, T., Masato, N., Takuro, O.: The relationship between histochemical enzyme activities of brain tumors and chemical features of the patients. Acta med. Okayama **19**, 293—306 (1965); ref. J. Biol. (Oncologia) **53**, 100 (1967).

Tytus, J. S., Lasersohn, J. T., Reifel, E.: The problem of malignancy in meningiomas. J. Neurosurg. **27**, 551—557 (1967).

Udvarhelyi, G. B., O'Connor, J. S., Walker, A. E., Laws, E. R., Kranin, S. A.: A histochemical study of tumors of the central nervous system. In: Proc. IV. Intern. Congress Neuropath., vol. 1, pp. 95—102. H. Jacob (ed.), Stuttgart: G. Thieme 1962.

Viale, G. L., Andreussi, L. G.: Histochemical study of the oxidative activity in tumors of the nervous system. Acta neuropath. (Berl.) **4**, 538—558 (1965).

Wegmann, R., Gerzeli, G.: Le glucose-6-phosphate des hydrogenases et ses correlations avec des substrats voisins du glucose-6-phosphate. Role de l'hexokinase. Ann. Histochim. **6**, 111—124 (1961).

Wolman, L.: Role of arachnoid granulation in development of meningioma. Arch. Path. **53**, 70—77 (1952).

Dr. I. Lolova
Research Group on Brain
Functions Localization
Bulgarian Academy of Sciences
Georgi Sofijski Str., 1
Sofia 31, Bulgaria