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Bilateral Dysgenetic Polycystic Parotid Glands

Morphological Analysis and Differential Diagnosis of a Rare Disease of the Salivary Glands *

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Summary. Dysgenetic (bilateral) polycystic parotid glands present a rare pathological picture which has not yet been described in detail. In the Salivary Glands Register (Institute of Pathology, University of Hamburg) 360 non-tumourous cysts were registered (from a total of 5739 cases of disturbances of the salivary glands for the years 1965–1979). Among them there were 2 cases of polycystic parotid glands. The analysis of the observations in these cases led to the following conclusions concerning polycystic parotid glands:

1. The disease may be unilateral or bilateral. The cysts, which are not uniform in size, are bounded by duct epithelia exhibiting various sorts of differentiation (striated duct and intercalated duct epithelium, primitive epithelial buds) and containing secretion products, spheroliths and microliths. Regressive focal epithelial alterations with desquamation occur. The remains of the glandular parenchyma can be found among the cysts.

2. The cystic change is due to a developmental malformation of the duct system, in particular a disturbance of ramification and canalization. Evidence for this conclusion can be found in the spur-like septation of the cysts and the hourglasslike indentations.

3. Polycystic parotid glands can be compared with cystic malformations of the pancreas (cystic pancreas) or the lung (cystic lung).

4. This disease must be distinguished from congenital sialectasias of the parotid glands, from cysts of the salivary ducts and from lymphoepithelial cysts. The criteria for differential diagnosis are presented.

Key words: Polycystic parotid glands – Cystic lesions of the salivary glands – Differential diagnosis – Comparison with other cystic malformations.

Introduction

Primary, dysgenetic cysts must be distinguished from secondary, acquired cysts in the salivary glands (Lit.: Seifert 1966; Gorlin 1970; Rauch et al. 1970; Ri-

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chardson et al. 1978). Secondary cysts arise as a result of obstruction of the ducts (sialolithiasis, inflammation, tumours, trauma) and occur as mucoceles, particularly in the small salivary glands of the lower lip and as retention cysts of the salivary ducts in the parotid glands (Lit.: Harrison 1975; Seifert et al. 1980b). It is necessary to differentiate between these non-tumourous cysts and primary tumours of the salivary glands which include cystic structures, especially cystadenolymphomas, mucoepidermoid tumours, cystadenocarcinomas and pleomorphic adenomas (Thackray and Lucas 1974; Seifert and Donath 1976).

Primary dysgenetic congenital salivary gland cysts are very rare (Lit.: Seifert 1966). Ranula of the sublingual gland, sialectasias of the parotid glands and – less often – sialectasias of the submandibular gland belong to this group. The congenital origin of salivary gland cysts and the lymphoepithelial cysts of the parotid glands is still controversial (Lit.: Bhaskar 1966; Acevedo and Nelson 1971; Giunta and Cataldo 1973; Weitzner 1973; Seifert 1980). In an individual case such cysts cannot be distinguished with certainty from cysts developed postnatally.

The congenital dysgenetic (bilateral) cystic parotid gland presents an extremely rare pathological picture amongst the primary dysgenetic cysts. Of the 5739 salivary gland cases registered between 1965 and 1979 in the Institute of Pathology of the University of Hamburg, 360 exhibited non-tumourous cyst formations. Only 2 of these 360 cases show dysgenetic cystic parotid glands, a disease which, according to the literature at our disposal, has not as yet been described in detail. Reports on this subject to date are limited to an incorrect interpretation (Moore 1940) and an unsatisfactory documentation of findings (Mihalyka 1962). The goals of the present paper are therefore: 1. to define the pathohistological characteristics of polycystic parotid glands; 2. to attempt to define differential diagnostic criteria from other parotid gland cysts and 3. to make pathogenetic comparisons with analogous cysts in other organs (kidney, liver, pancreas, lung).

Material and Methods

The cases registered in the salivary gland files were assessed and documented according to a uniform pattern of findings. Of a total of 5739 cases between 1965 and 1979, 360 (=6%) fell into the category of non-tumourous cystic alterations of the salivary glands. The classification of the material is shown in Table 1.

For all the cases examined paraffin slides were available; for some there were also semi-thin slides embedded in synthetic material. The following stains were routinely used: Masson-Goldner, Azan, Giemsa, Best's Karmin, silver staining according to Gomori.

We would like to take this opportunity to thank the Throat-Nose-Ear Clinic of the Düsseldorf University for making available to us the clinical data regarding the first case of cystic parotid glands and Prof. Dr. J. Ormós of the Institute of Pathology of the University of Szeged (Hungary) for the second case. Further details of the casuistics can be found in Thomsen (1980).

Results

Case 1 (J.-No. 10944/75 and 13520/75)
A 6-year-old girl (G.E.).

Clinical Data. Conservative treatment for generally painless, recurrently swollen parotid glands (both sides). In sialography cystic foamy alterations in both

Table 1. Classification of the non-tumorous cystic lesions of the salivary glands ($n=360$). Salivary Glands Register 1965–1979 ($n=5739$)

Type of cyst	Main localization	Number	
		n	%
Mucoceles	Minor salivary glands	273	76
Extravasation mucocele (=Mucus granuloma)	Lower lip	240	67
Retention mucocele	Lips, cheek palate, floor of the mouth	33	9
Salivary duct cysts	Parotid gland	32	9
Lymphoepithelial (branchiogenic) cysts	Parotid gland Floor of the mouth	26	7
Ranula	Sublingual gland	22	6
Congenital sialectasias	Parotid gland	5	1.5
Dysgenetic polycystic parotid glands	Parotid gland	2	0.5
Sum		360	100

her salivary glands were seen. Palpation revealed tenderness. No pathological abnormality was revealed by blood analysis, intestinal biopsy or numerous laboratory investigations (tests of liver and pancreatic function, blood sugar, etc.). The level of immunoglogulin A in the saliva and a sweat test were normal. The history revealed that the girls father allegedly experienced identical changes in the parotid glands until 12 years of age.

Morphological Findings. In the first biopsy (0.5 cm in diameter) of the left parotid gland (J.-No. 10944/75) the gland lobules are largely permeated by salivary duct cysts of varying sizes which are, for the most part, bounded by a flat epithelium and which occasionaly contain some lumps of secretory material (Fig. 1). Between the duct cysts remains of glandular acini and a modest amount of connective tissue can be found (Fig. 1) including isolated histiocytes and lymphocytes. The secretory inclusions in the duct cysts form concentric and radial patterns, similar to spheroliths and microliths (Fig. 2) and consist of acid and neutral mucopolysaccharides (Astrablue-staining and PAS-reaction). At some points there are transitions from cylindrical, oncocytically differentiated duct epithelium to flat epithelium, generally with a single layer (Fig. 3). In some areas the flat duct epithelium exhibits button-like elevations with apocrine secretions or signs of desquamation. There is often hydropic transformation of the cytoplasm and large darkly staining nuclei which form spherical arches towards the duct openings (Fig. 4).

In the second biopsy (1 cm in diameter) from the right parotid gland, a low power view showed that cyst formation in the individual gland lobules had proceeded to varying extent (Fig. 5). Some cyst structures showed indentations similar to hourglasses (Fig. 5) and exhibited differing epithelial linings.

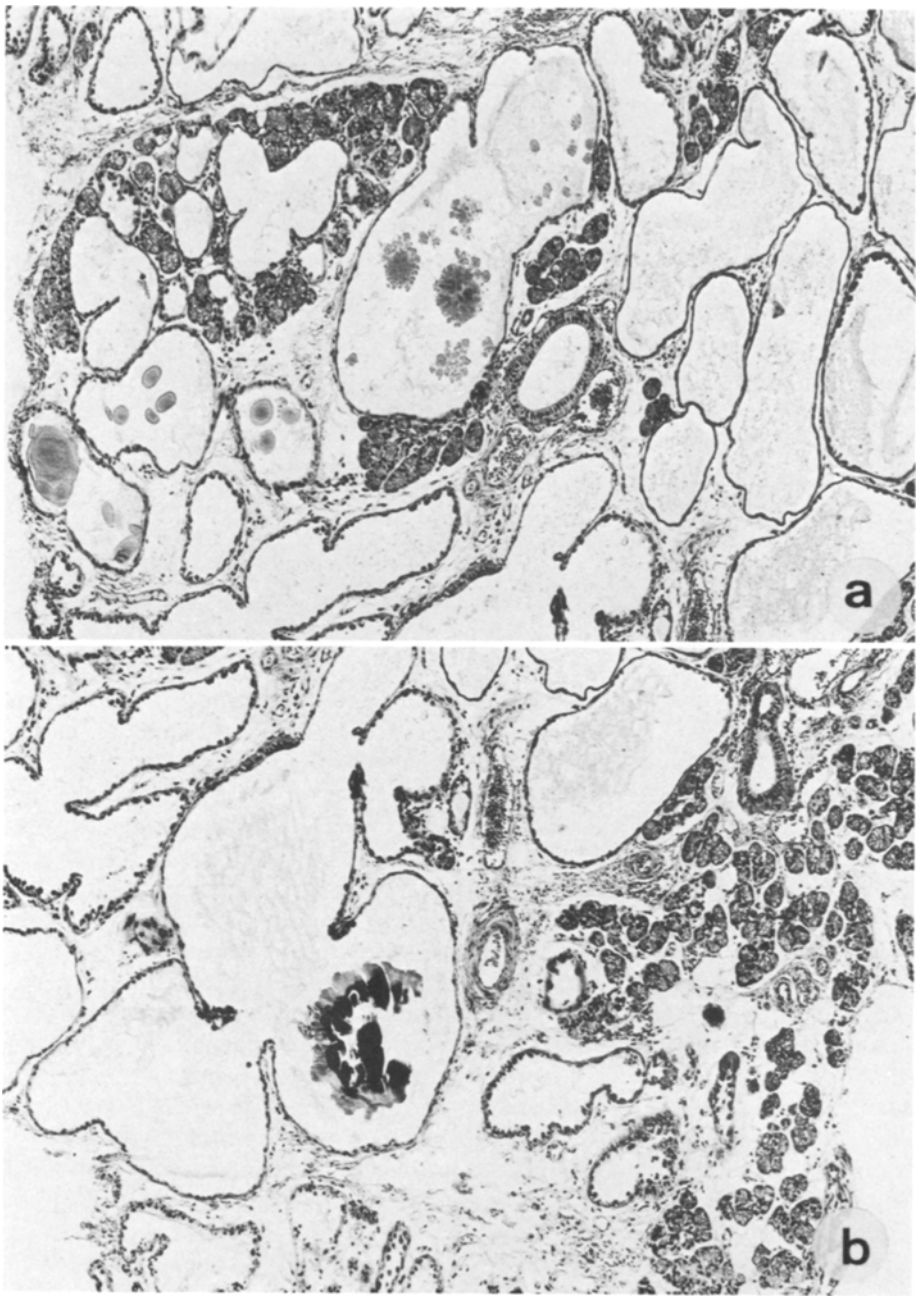

Fig. 1a and b. Polycystic parotid glands (J.-No. 10944/75; left parotid gland). **a** Multiple epithelial cysts of varying size; rests of glandular parenchyma between the cysts. No inflammation. **b** Microlith in a cystic ramification. Haematoxylin-eosin. **a** and **b** × 63

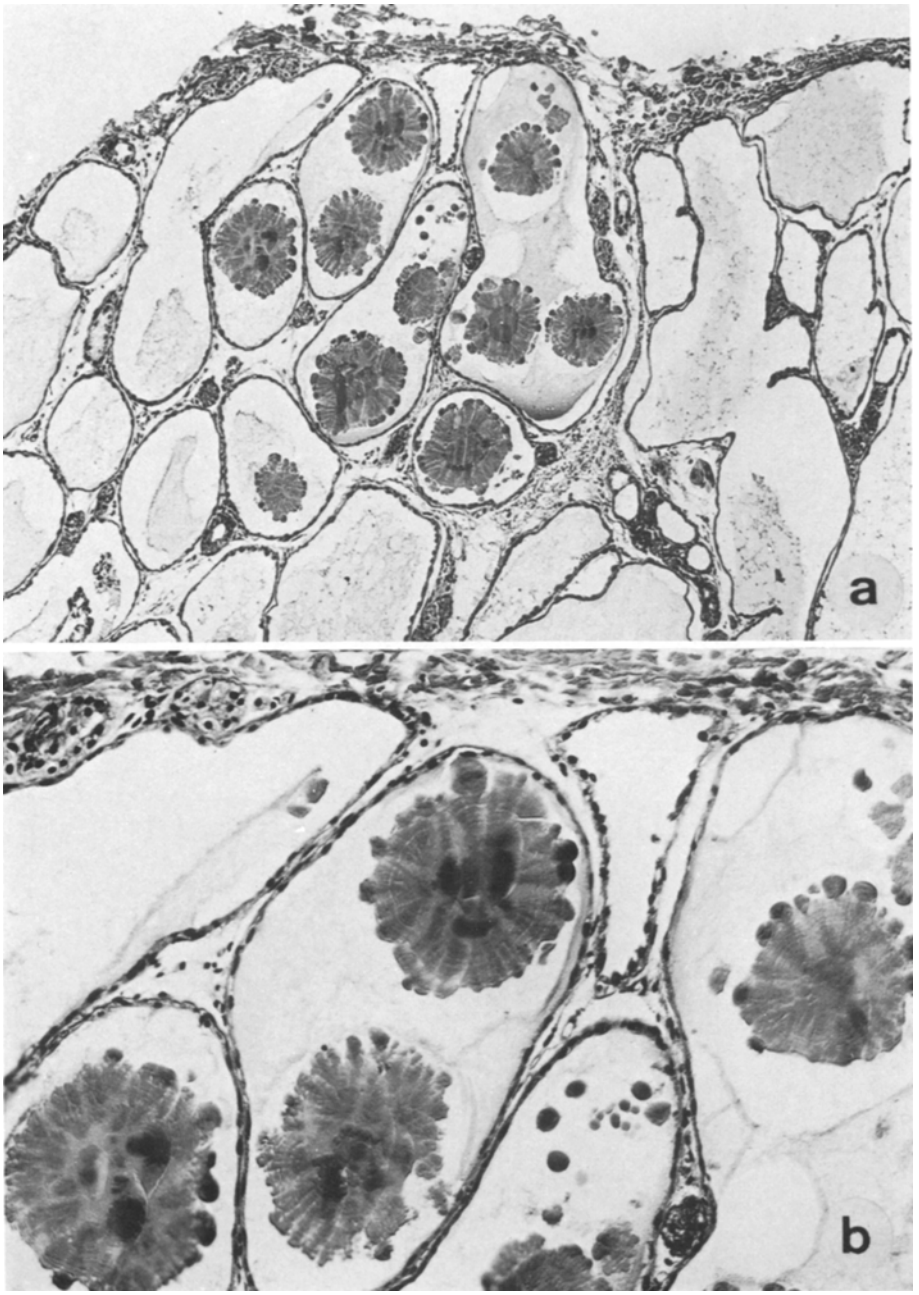

Fig. 2a and b. Polycystic parotid glands (J-No. 10944/75). **a** Multiple spheroliths with concentric and radial patterns in the lumens of the cysts. **b** Higher magnification of **a**; cysts lined with flat epithelial cells. Haematoxylin-eosin. **a** × 63, **b** × 160

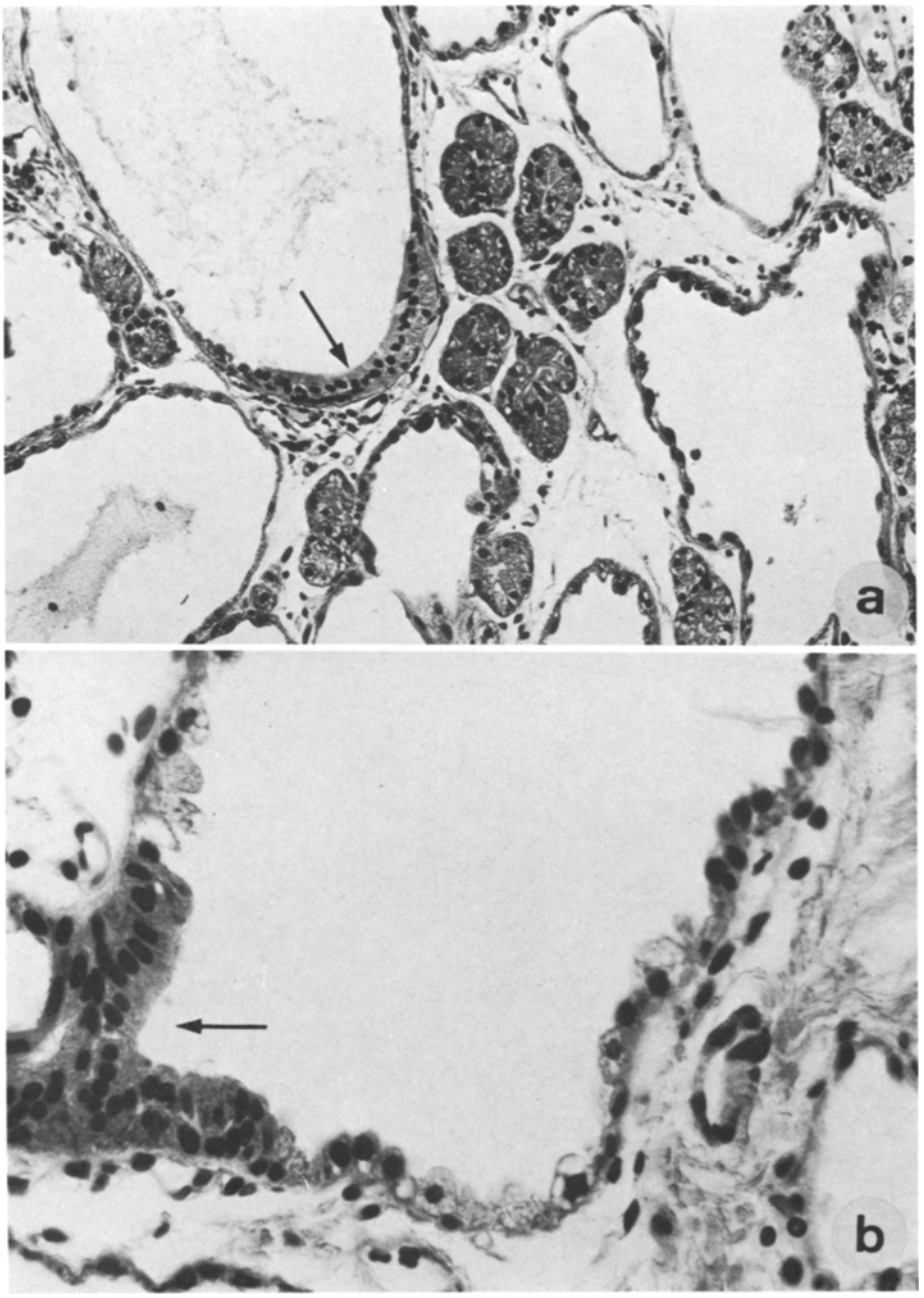

Fig. 3a and b. Polycystic parotid glands (J-No. 10944/75). **a** Differing epithelial lining of the cysts; transition from oncocytic epithelial cells (*arrow*) to a single-lining flat duct epithelium. **b** Transition of striated duct epithelium (*arrow*) to a single-lining epithelium. **a** Haematoxylin-eosin, ×160. **b** Masson-Goldner, ×400

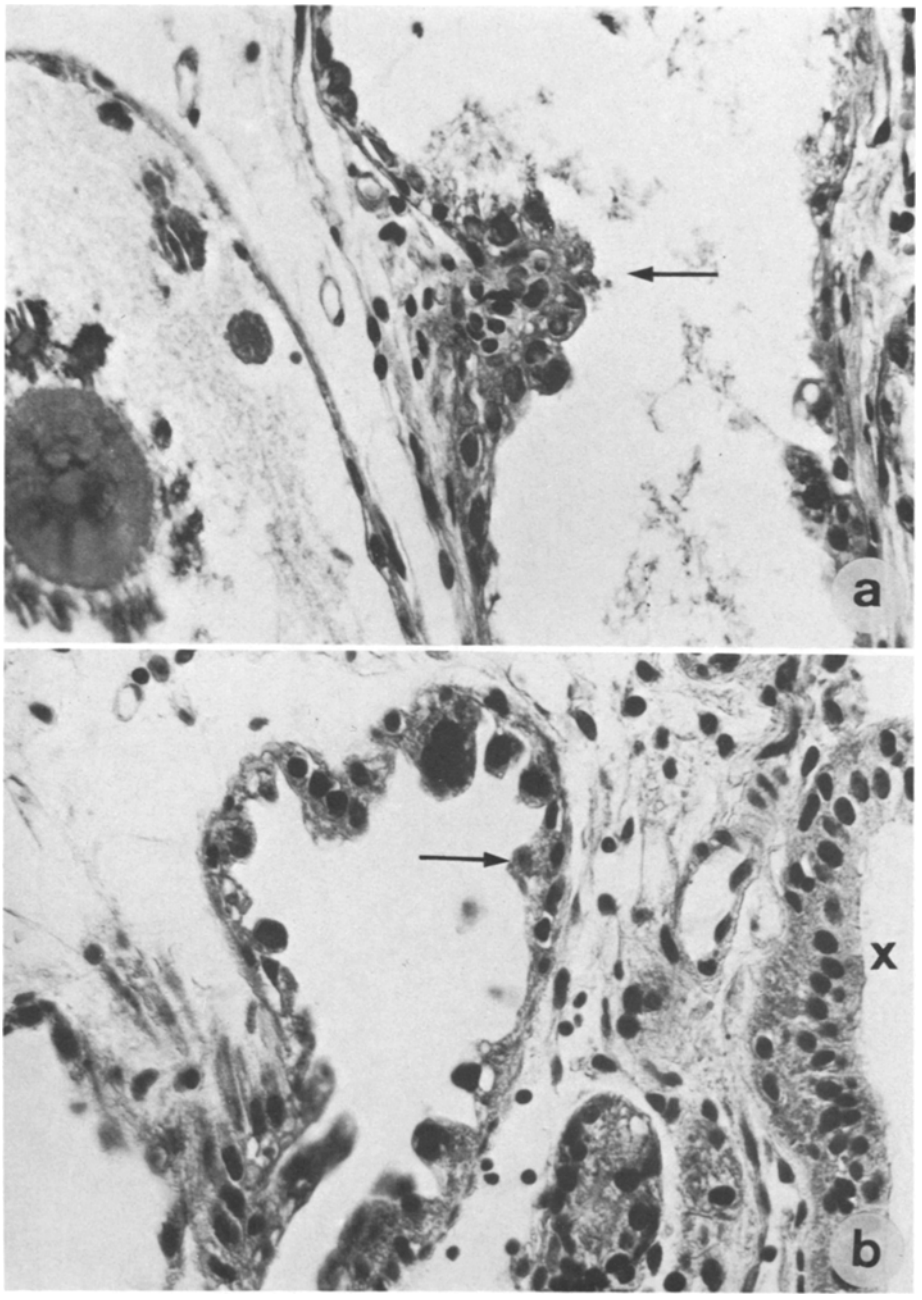

Fig. 4a and b. Polycystic parotid glands (J-No. 10944/75). **a** Polypoid bud-like epithelial cell proliferation (*arrow*) in the lumen of a cyst. **b** Degenerative changes of the epithelial cell (vacuolization of cytoplasm, pyknosis of the nuclei; *arrow*) of a cyst; oncocytic differentiation in another cyst (*cross*). **a** PAS reaction, ×400. **b** Masson-Goldner, ×400

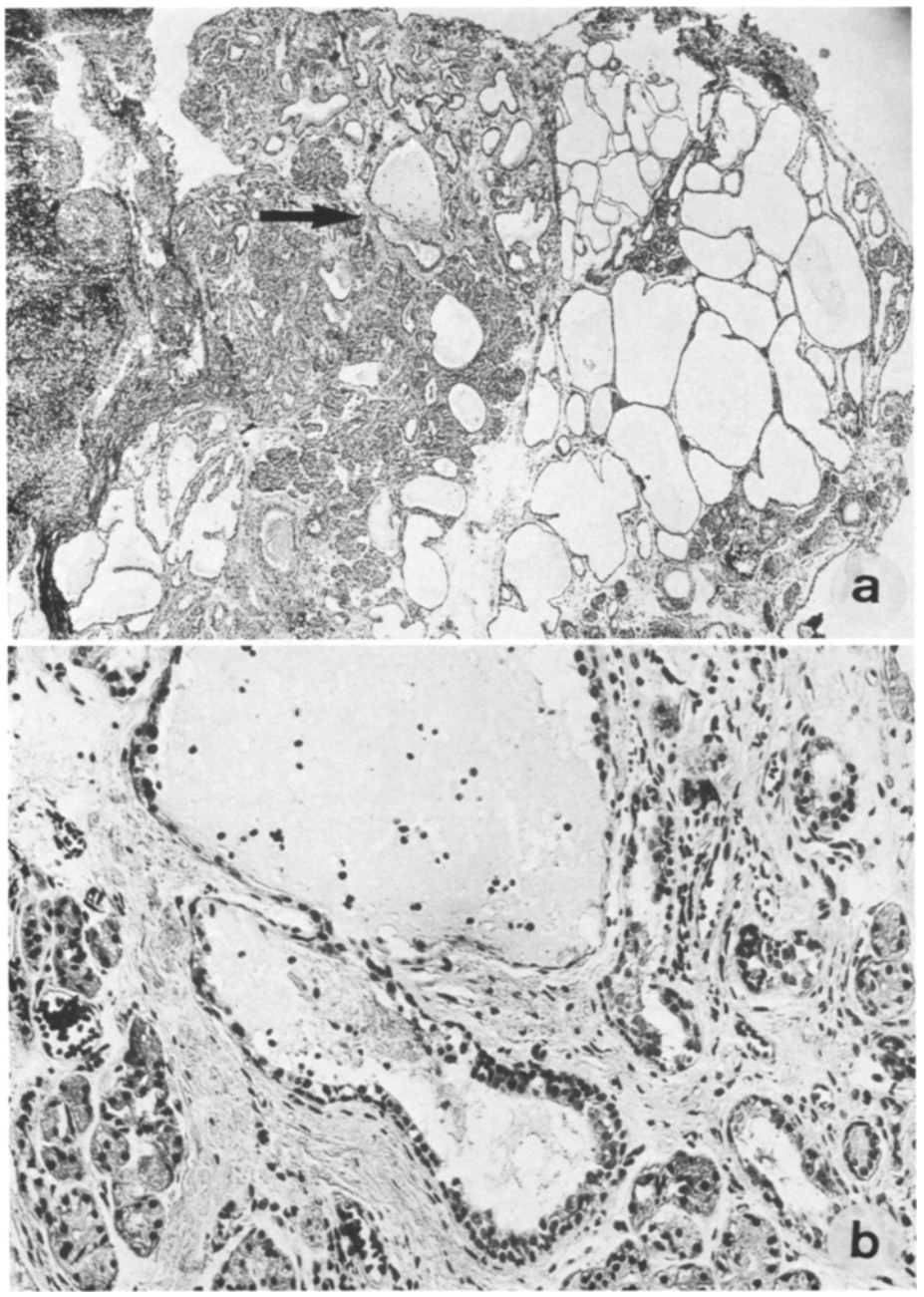

Fig. 5a and b. Polycystic parotid glands (J-No. 13520/75; right parotid gland). **a** Multiple cysts in a partly lobular arrangement; paraglandular lymph node (*left side*); hourglass-like formation of a cyst (*arrow*). **b** Higher magnification of the cyst with hourglass-like structure. Masson-Goldner. **a** ×25, **b** ×160

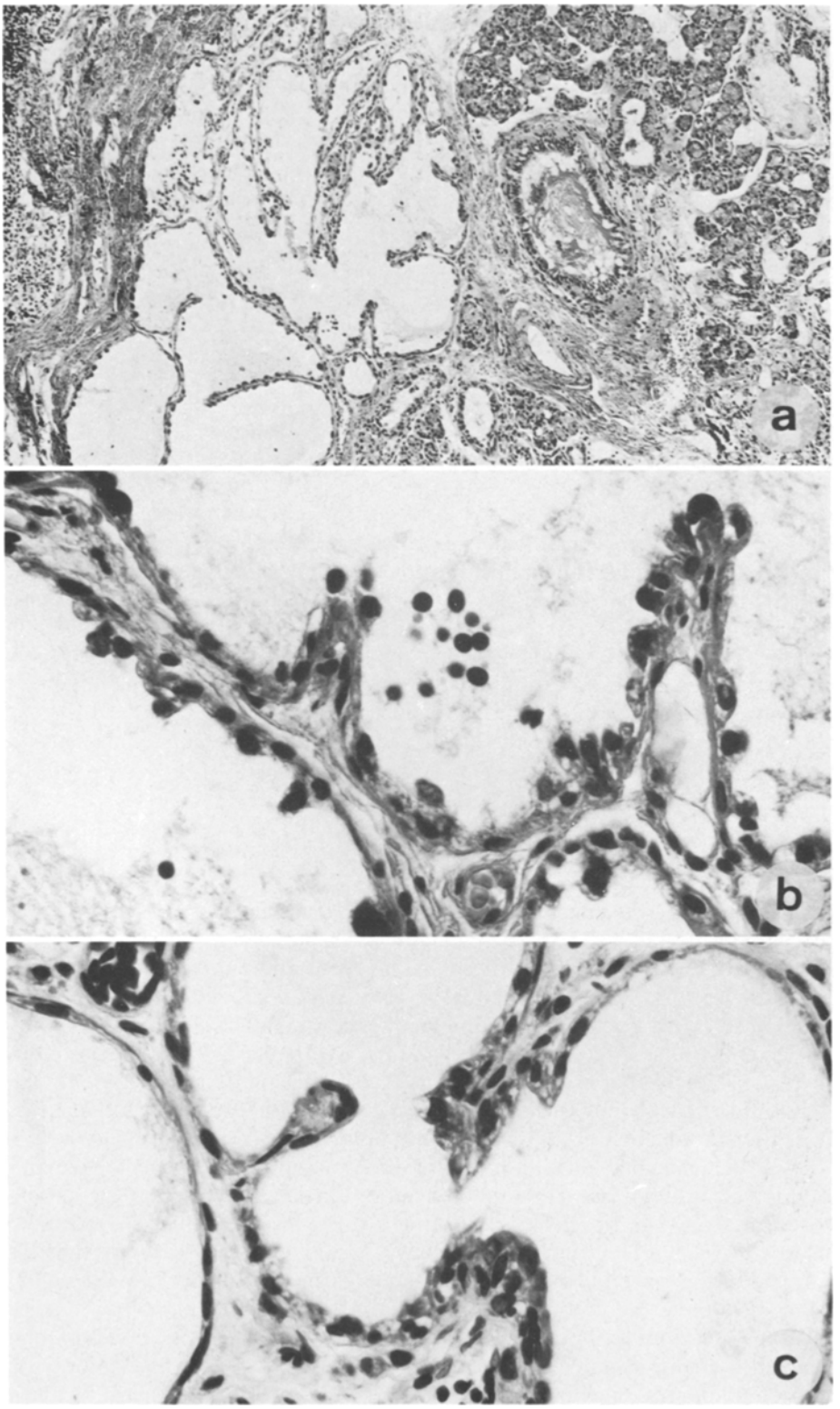

Fig. 6a–c. Polycystic parotid glands (J-No. 13520/75). **a** System of partly subdivided cysts with spur-like septa. **b** and **c** Higher magnification of some cysts with incomplete septa. Haematoxylin-eosin. **a** ×63, **b** and **c** ×400

Some cysts are subdivided into chambers, where the septations extend into the cyst openings like spurs (Fig. 6). In a very few instances microcysts can be found in the immediate vicinity of larger cysts and they resemble intercalated ducts in structure. Beside them further transitions can be seen from striated duct epithelium to a flat epithelium.

Case 2 (J-No. 18882/76)
A 65-year-old woman (J.J.)

Clinical Data. Conservative treatment for an indolent swelling of the right parotid gland which had existed for 9 years and had recently increased. Sialography revealed extended spherical ectasias in the vicinity of the peripheral duct segments. Scintigraphy (Gamma camera $3mCi^{99}TcO_4$) showed a decrease in the activity of the entire parotid gland.

Morphological Findings. In the operative specimen of the right parotid gland (size: 15×8 cm) the gland lobules are interspersed with duct cysts which are primarily bounded by flat epithelium and contain flaky lumps of secretory material (Fig. 7). Remains of gland acini can be recognized among the cysts. No inflammatory infiltrations are present. In some places the cystic epithelium is almost as flat as endothelium, so that the cyst structures resemble lymphatic cysts; in some spots, however, they are swollen (Fig. 8). The epithelium of the cystic coating exhibits secretory disturbances (Fig. 9), including hydropic and finely vesicular cytoplasmic changes, together with swelling, vacuoles and pyknosis of the cell nuclei.

Discussion

The dysgenetic cystic parotid gland is a polycystic malformation of the salivary duct system which can occur unilaterally or bilaterally. The lining of these ductal cysts may be a cylindrical epithelium with apocrine secretion (striated duct type); or there may be cuboidal or flattened endothelium-like epithelium of the intercalated duct type. Finally, undifferentiated duct buds can be found. The cysts contain altered salivary secretions with spheroliths and microliths. In some places there are also distinct regressiv epithelial alterations to be found, with cytoplasmic and nuclear vacuoles, nuclear pyknosis and cell desquamation. The cysts are sometimes subdivided into chambers by means of spur-like projections, or they may take on an hourglass-form. Among the duct cysts the remains of gland acini and a moderate amount of vessel-rich mesenchyme can be observed, but there is no chronic inflammatory infiltrate or other reference to a secondary cause for duct obstruction. The sialographic findings, showing a multicystic permeation of the gland tissue, is in agreement with the pathohistological tissue picture.

In the literature we have found no description of a dysgenetic cystic parotid gland with changes comparable to our own. Mihalyka (1962) reports only on the sialography findings on a patient who had a symptomless parotid gland

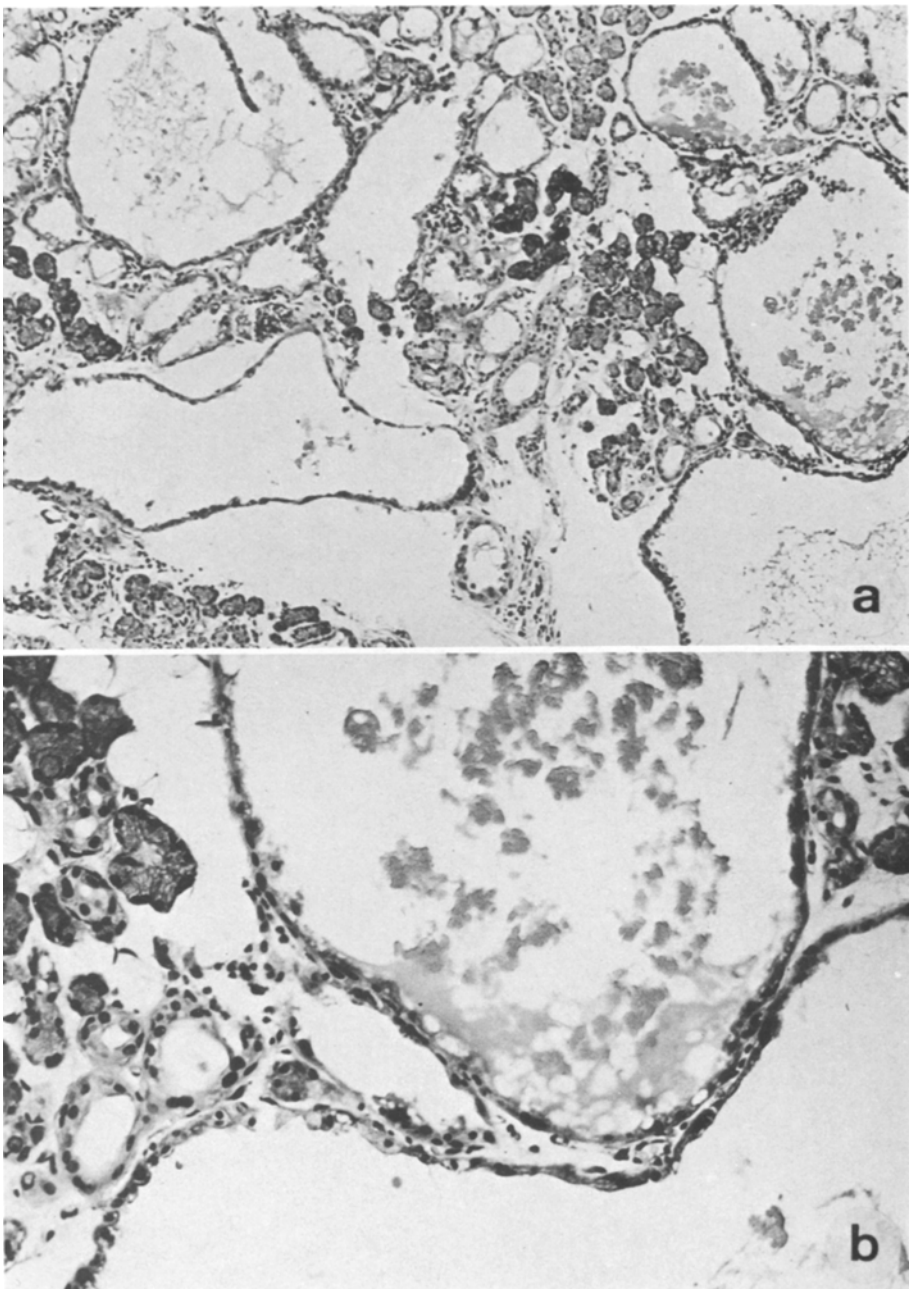

Fig. 7a and b. Polycystic parotid glands (J-No. 18882/76; right parotid gland). **a** Multiple cysts with a flat epithelium as boundary; rests of glandular parenchyma between the cysts. **b** Section of a cyst with boundary consisting of flat epithelial cells; flaky secretion particles in the lumen of cyst. Haematoxylin-eosin **a** × 63, **b** × 160

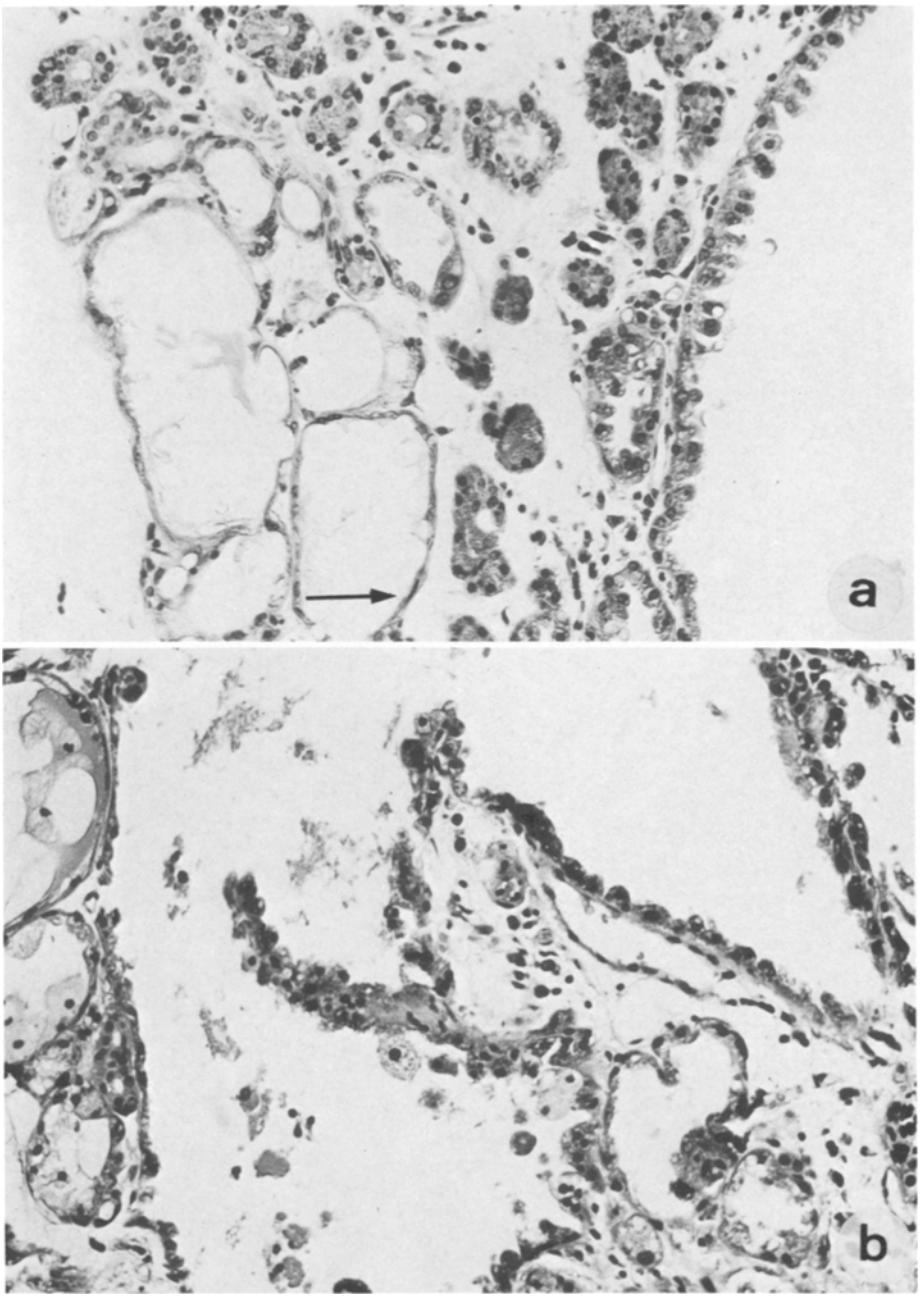

Fig. 8a and b. Polycystic parotid glands (J-No. 18882/76): Varying lining of the cysts. **a** Endothelial cell-like structure similar to lymph cysts (*arrow*) or single-layer pattern in a polypoid arrangement. **b** Spur-like incomplete septa with swollen epithelial cells. Haematoxylin-eosin. **a** and **b** × 160

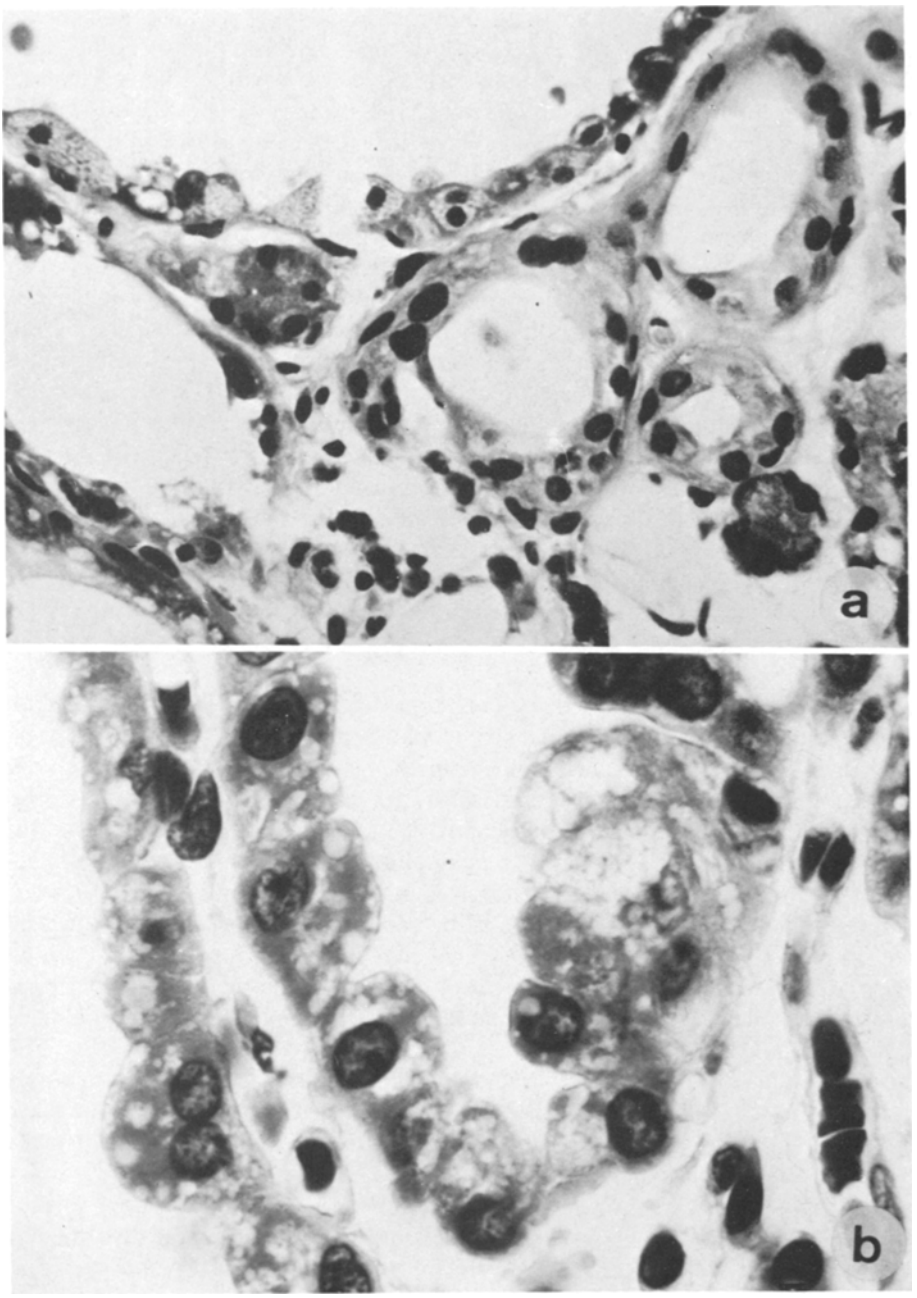

Fig. 9a and b. Polycystic parotid glands (J-No. 18882/76). **a** Cysts with partly hydropic swelling of the cytoplasm and pyknosis of the nuclei. **b** Higher magnification with intensive vacuolization of the cytoplasm and degenerative changes of the nuclei. **a** Haematoxylin-eosin, ×400. **b** Masson-Goldner, ×1,000

swelling for over 40 years. The small multiple cysts seen by sialography were interpreted as sialectasias. There is no patho-histological analysis of this case, but the classification "congenital bilateral polycystic parotid glands" chosen by Mihalyka may nevertheless be accurate. The description by Moore (1940), however, does not represent a congenital cystic parotid gland but rather either a lymphoepithelial cyst or a metaplastic cystadenolymphoma. The cysts were lined with a multilayered epithelium and a lymphoid stroma including lymph follicles.

From comparison of the structure of the cystic parotid gland with the pattern of development of the parotid gland (Becker et al. 1978; Young and van Lennep 1978, Donath et al. 1978) it follows that it is probably disturbances in the ramification and canalization of the terminal salivary duct buds which are responsible for the development of cystic parotid glands. Differentiation of the parotid gland tissue proceeds according to the developmental principle that initially the primary epithelial bars move into the mesenchyme, subsequently branching off dichotomously. They are transformed from solid epithelial branches into narrow tubular formations. The process of canalization of the parotid gland is completed in the 22nd development week. The further, functional, development of the gland tissue with the formation of the acini takes place from the 34th embryonal week and continues after birth. Therefore this period must be regarded as that in which a disturbance of canalization with resulting cyst formation may take place.

The cystic parotid gland can be compared with the developmental process resulting in cystic malformations of the pancreas or lung. Parallels can be drawn with the embryonal development in the process of budding and lumen formation in the duct systems, and with the further differentiation of the acini and the alveolae. In the dysgenetic cystic pancreas (Lit.: Seifert 1956; Becker 1973), malformations in the duct system with closing of the ducts, disturbances in canalization and inhibition of acinar buddings have been discussed. In cystic lung (Lit.: Giese 1960) there is disturbed development of the bronchial tree. In this disorder, the extent to which the individual forms of cystic lung malformation develop is also dependent on the teratogenic period of determination and entodermal/mesodermal interactions, which play an additional role (Lit.: Östör and Fottune 1978).

The cystic liver (Bolck and Machnik 1978) and the cystic malformations of the kidneys (Zollinger 1966; Potter 1972) present a special problem, since different "anlagen" become united in the course of the organ development (metanephrogenic blastema and ureter bud in the kidney; primary and secondary biliary duct plate in the liver). Therefore, Potter (1972) distinguishes the various types of cystic kidney on the basis of the time of developmental disturbance. The fact that cystic malformations can occur in kidney, liver and pancreas indicates that the period of determination is protracted, suggesting a generalised effect dependent upon the differing development of these organs. The question of whether cystic parotid glands occur in connection with dysgenetic cysts of the kidney, liver, lung or pancreas – and if so, how often – cannot yet be answered.

In the differential diagnosis of cystic parotid glands from other parotid

gland cysts the following 2 cystic forms must be primarily considered: salivary duct cysts and lymphoepithelial cysts.

Salivary duct cysts (Seifert and Waller 1981) are usually located in the border area of the parotid gland and contain a mucous secretion. Generally there is a coating of ductepithelium with single or multiple layers consisting partially of flat, cubical epithelial cells, and partially of oncocytically differentiated cylindrical epithelium. In the cyst wall there is a scanty collagenous connective tissue, occasionally a moderate lymphocytic infiltration also. The bordering parotid gland shows ectasia of the ducts, congestion of secretory material and interstitial inflammation. The salivary duct cysts usually result from retention of secretion, but may also be due to a dysgenetic cause, particularly when they arise in early youth.

Lymphoepithelial cysts (Bernier and Bhaskar 1958) are bounded by a squamous epithelium (sometimes keratinized) containing desquaminated squamous lamellae and cell detritus. A lymphoid stroma with lymph follicles may develop in the wall of the cysts. The close contact between epithelium and lymphoid stroma corresponds to the structure of the lymphoepithelial tissue of the pharynx ring, so that the lymphoepithelial cysts located in the parotid glands are derived from the 1st branchial arch and can be classified with the "branchiogenic cysts". The fact that they may also occur on the floor of the mouth as well as in other oral regions has led to the interpretation that these cysts arise by envelopment and non-neoplastic proliferation of ductal or oral epithelium within lymph nodes, perhaps induced by stimuli such as chronic inflammation or trauma (Seifert 1980). The distinction of lymphoepithelial cysts from cystadolymphomas with epithelial metaplasia (metaplastic cystadenolymphomas) will not be discussed further here (Seifert et al. 1980a)

Congenital sialectasias of the parotid gland occasionally exhibit spherical extensions of the parotid duct system of both sides and generally contain secretions of lumpy material. The sialectasia, in contrast to cystic parotid glands, are in direct and continuous relationship to the duct system and may represent the basis of the chronic sialectatic parotitis of the infant and small child (Lit.: Becker et al. 1978; Haubrich 1976).

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