Praca oryginalna *Original paper*

Enlarged prostate lesions of pure-bred and mongrel dogs

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Summary

The purpose of the study was: to evaluate the incidence of benign prostate hyperplasia in dogs; to estimate the changes of prostate size and histomorphological features during the dog's lifetime; to evaluate the BPH ratio with other prostate pathologies and their relation to the dog's age and breed.

The study examined 104 cadavers of dogs aged between 0,3-16 years. Changes in the prostate glands were determined during macroscopic and microscopic examinations. Slides from the prostate glands were stained with H–E, PAS, AB and Sirius red. The most frequent pathologies of the prostate glands were epithelial and epithelial–cystic hyperplasia. The latter are more characteristic for older dogs, but can also be found in young dog's prostates (in this case in a 1,5 year-old dog). It is also common to find mixed lesions in the prostate, such as hyperplasia as well as inflammations, hyperplasia and intraepithelial neoplasia and carcinoma, metaplasia and focal fibrosis. Generally, the most predominant pathology is hyperplasia (epithelial and epithelial–cystic) (91,3 %). Epithelial cystic hyperplasia with inflammation foci and epithelial hyperplasia alone are more often found in German sheep dogs, Rottweilers and Dobermans. Epithelial cystic hyperplasia with IN foci is more common in Scotch sheep dogs, Irish setters and Poodles.

Keywords: dogs, prostate, benign hyperplasia, neoplasia

Benign prostate hyperplasia (BPH) is not common disease in animals. Associated with age spontaneous prostate hyperplasia develops only in human, monkey (13) and dogs (2, 11, 12). Hyperplasia macroscopically is found in 60% of six-year-old dogs, while already in 85-95 % of nine-year-old dogs. (2, 11, 22). Prostatic volume in affected dogs is 2 to 6.5 times greater than in normal dogs of similar weight (14).

Supposedly because of different tissues sensitiveness of sexual hormones and various growth factors BPH in canine prostate involves more peripheral region (12). It was not established strong relationships between some pathologies and prostate regions (8). There are not nodules in canine hyperplasia, and appears to be of pure proliferation of epithelial cells (12, 13). Hyperplasia is supposedly related with acinar basal cells and neoplasia – with ducts basal cells. Sensitiveness of them for factors, influencing hyperplastic or neoplastic growth, is unequal (15). The role of androgens in BPH remains unclear, and it is supposed, that the main ethiological factor in development of hyperplasia may be platelet – derived growth factor (PDGF) (7).

The criterions, that are used for canine BPH diagnosis, are enlarged prostate index and other, the earliest – is the rise of papilliation of epithelium into ductal and acinar lumen due to proliferation of epithelium (12, 17). Cytological feature of prostatic epithelium does not differ from cytological feature of normal gland epithelium. Another change seen in canine hyperplasia is cystic dilatation of acini and small ducts (22). Although it is generally considered to be part of the disease (the later stage of BPH), the possibility remains that this is an independent process (13).

The purpose of the was: a) to evaluate the incidence of benign prostate hyperplasia in dogs, b) to estimate the changes of prostate size and prostates histomorfological features in dogs lifetime run, and c) to evaluate the BPH ratio with others prostate pathologies and their dependence on dogs age and breeds.

Material and methods

The study was performed on 104 cadavers of 0.3-16 year age both pure-bred and mongrel dogs. We have examined dogs of German Shepard (n=15), Rottweiler (n=11), Doberman Pinscher (n=6), Poodle (n=5), Boxer (n=6), Scotch Collie (n=6), French bulldogs (n=3), Irish Setters (n=3) and Scotch Terriers (n=3). From other breed were taken one or two dogs. The dogs were divided into groups: under 1 year of age, 1-5 year of age (I group), 6-10 year of age (II gro-

up), 11 year and older (III group) (17). The were only 4 dogs under 1 year of age. The prostatic glands were examinated macroscopically: the consistence, the colour, midline, the uniformity of lobes and the appearance in section. The enlargement of prostate was calculated using this formula – body weigth divided from prostate weigth (prostate index). For microscopically examination the prostates were fixed in neutral buffered 10% formalin, embedded in paraffin and sectioned at 2-4mm. The slides were stained with haematoxylin – eosin (H-E), Sirius red for connective tissue, PAS, AB for mucins – acid and neutral both. From H-E slides, proliferation and papiliation of epithelium in to ducts and acinar lumen, cysts formations were estimated. Where used control slides from normal dogs prostates.

PIN criterions were: secretory cells crowding and heaping up, loss of polarity, nuclear and nucleolar enlargement, hyperchromasia, overlapping nuclei. Criterion for prostate tumor was: atypical cell (of cytoplasma and nucleus, nucleolus), invasion in stroma, formation intraluminal or intraductal architectural patterns, with adjacent inflammation foci.

In cases of inflammation, tissues sample of prostates were selected in sterile Petri plates and microbiological tests was performed using different simple and selective nutritical medium (Mac – Conkey, Levin) for *Staphylococcus spp., Streptococcus spp., Escherichia spp., Actinomyces spp., Pseudomonas spp.* at 37°C for 24-48 hours in aerobic and facultative anaerobic conditions.

The relationships between age or body weight and prostate weight were tested by means of correlation analysis in all dogs of all groups, using spreadsheet 'EXCEL2000 for Windows'.

Results and discussion

Those were examined 78% pure-bred and 22% mongrel dogs. The enlargement of prostate was found in 70% dogs. The enlargement of prostate in pure-bred and mongrel dogs was found 67% and 83% respectively. The changes of prostatic index are show in 1 Table.

The most frequent pathologies of canine prostates, which are found during our examination, are epithelial cystic hyperplasia, epithelial hyperplasia and inflammations. Often these pathologies are mixed: hyperplasia – inflammation, hyperplasia – inflammation and metaplasia, hyperplasia and tumour. Various pathology distributions in all groups are shown in Fig. 5.

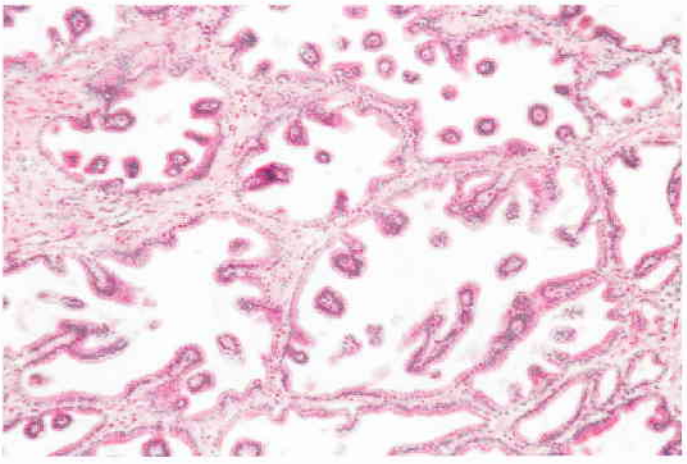

Fig. 1. Epithelial hyperplasia (×200)

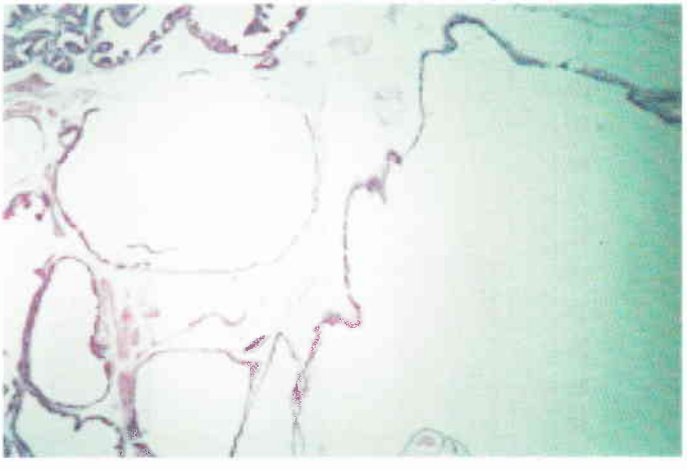

Fig. 2. Epithelial cystic hyperplasia (×50)

The normal growth of dog prostate happens from 1 to 5 years of age. Though, even from three years of age, when the index of the gland is still normal, the beginning of hyperplasia (papillations and tufts of epithelium) rather often is confirmed in histological examination. Hyperplastic growth occurs in 6-10 year old dogs. Increased index and changed histological features of the gland are characteristic for this growth. Uncomplicated BPH is therefore regarded as a normal aging process (1). It begins to develop rather early: hyperplasia already can be found in 2.5 year old dogs (4). Histological, prostate's hyperplasia is found in 50% of 4-5 year old dogs (2).

The prostate enlargement was detected in 51%, 86% and 71% of dogs in I, II, III groups accordingly (pure-bred and mongrel both) (Fig. 3, 4). Only 6% of dogs from I group had not enlarged prostate and without histopathologic changes. Histologically hyperplasia (epithelial and epithelial cystic) was found in 91,3% dogs of all groups. The highest percent of epithelial hyperplasia was in I group (Fig. 5). The youngest one, which had histolo-

Tab. 1. The relathionship between dogs body weight and prostate weigth

Age groups and number of dogs	Weight of prostate g		Body weight of dogs kg		Index of prostate	
	Mean X	Sd	Mean X	Sd	Mean X	Sd
I (n=27)	22.88	14.48	25	13.38	1.04	0.65
II (n=50)	40.93	31.20	27.87	16.39	1.83	1.51
III (n=23)	51.73	44.58	22.52	10.41	2.43	2.25

The was good correlation between body weight and prostate weight in I, II and III groups ($P < 0.01$), but not in group of dogs under 1 year age ($P > 0,05$).

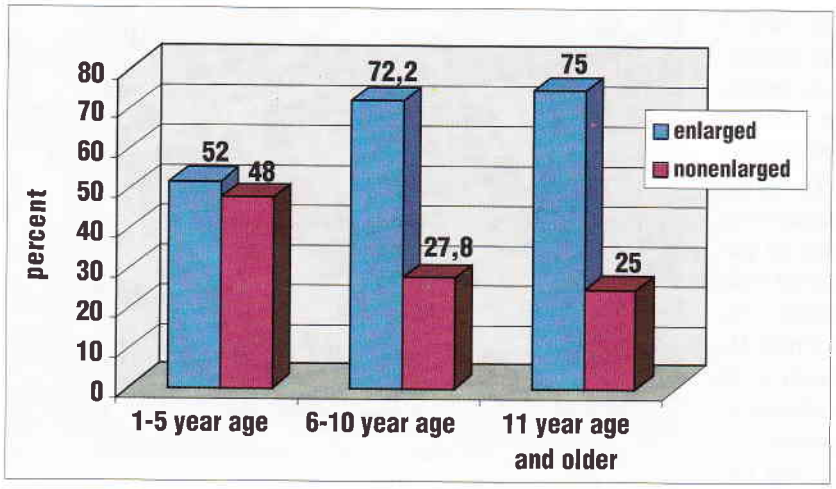

Fig. 3. Incidence of prostate enlargemant in pure-breed dogs

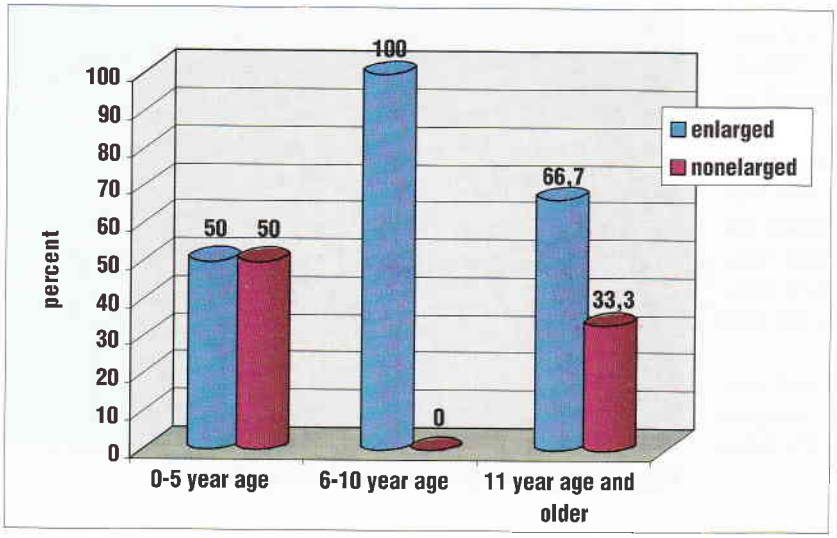

Fig. 4. Incidence of prostate enlargement in mongrel dogs

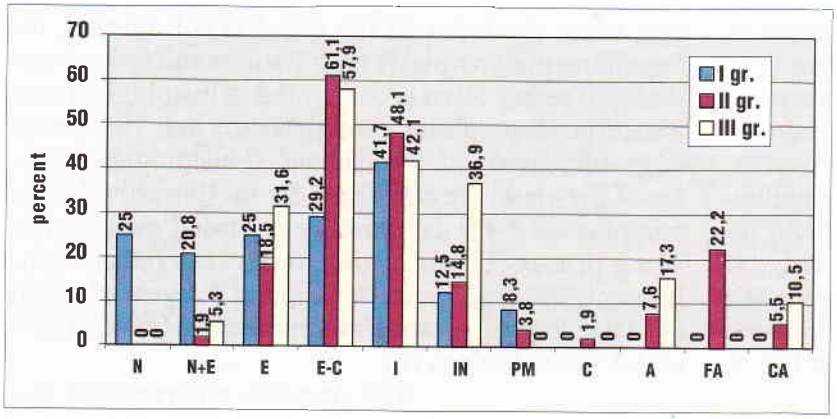

Fig. 5. Incidence of prostate histopathology in all dogs

N – normal histological feature, N+E – beginning of hyperplasia – the acini with papillation in neighbourhood with normal acini, E – epithelial hyperplasia, C – polycystosis, EC – epithelial cystic hyperplasia, Ca – carcinoma, I – inflammation, IN – intraepithelial neoplasia, A – focal atrophy and fibrosis, PM – platenepithelial metaplasia.

gical diagnosed hyperplasia, was 1.5 year old. Generally, the most frequent pathology was epithelial cystic hyperplasia, especially in old dogs.

Our data showed that BPH and other pathologies are characteristic for many 11 years of age and older dogs. Some scientists explain, that hyperplasia of prostate is normal process of ageing. With age, in dogs testis the number of spermatogoni decreases, and together with it decreases the amount of inhibin that they produce. This stimulates producing of GTH, with acts on testis and increases producing of testosterone (16, 18). With age tissues of prostate becomes more sensitive to androgens, which are necessary for maintaining abnormal size of the gland. It considered that unnormal size of senile gland is kept on not by the level of increased cell replication, but more by the decreased level of cell death (apoptosis) (5). Other scientist make hypothesis, that exists a population of androgen independent basal cells and they can cause senile hyperplasia (10).

The inflammation and BPH in the same prostate was found in 42% of cases. It was frequently similar in all groups. In 7.7% animals of all groups were observed epithelial cystic hyperplasia and suppurative inflammation with forming pus filled cyst 2-3 cm in diameter. Such cysts were found 1-4 in all the glands. Very big cysts (500-1000 ml volumes) were found in 2 glands. The rupture of one gland was caused the death of dog. For evaluating the index of prostates (0.8-2.9) only weight of pure prostates was used. In glands of other dogs were found lymphocytic (22%) and lymphocytic – plasmocytic (12%) inflammation. During microbiological examination, *Staphylococcus spp., Streptococcus spp., Escherichia spp., Actinomyces spp.* were found. Following microorganisms are commonly found in cases of dogs prostates inflammation (2, 16).

In addition to hyperplasia, there is a bigger possibility to find intraepithelial neoplasia (IN) and carcinomas in those prostates, which are extremely enlarged and are of older dogs, according our study. The percent of epithelial cystic hyperplasia and intraepithelial neoplasia was highest in 11-year-old dogs and older (in III group). In this group, 37% dogs prostates (11 dogs) had epithelial cystic hyperplasia. 54% of those with epithelial cystic hyperplasia (6 dogs) showed also intraepithelial neoplasia, and the 18% of them showed also carcinoma. Index of prostates with intraepithelial neoplasia was 2.03-5.9. Some authors indicate that even intraepithelial neoplasia can be found even in 2 or 3-year-old dogs (6). Significant changes in the expression of oncogenes, growth factor receptors occur during the transition from bening epithelium to PIN, but

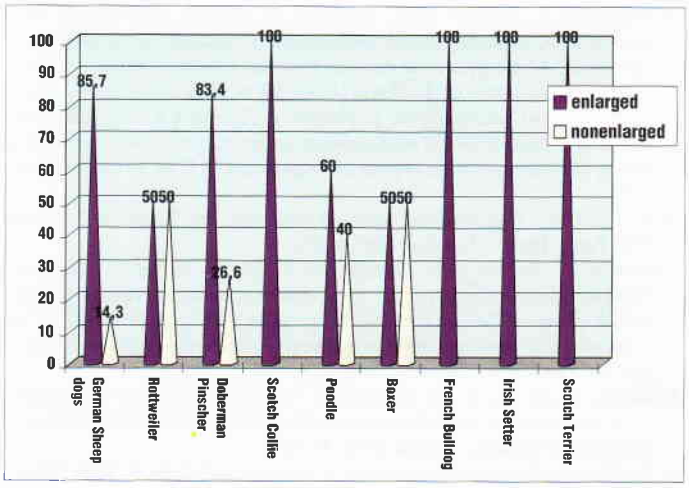

Fig. 6. Incidence of prostate enlargement in dogs of different breeds

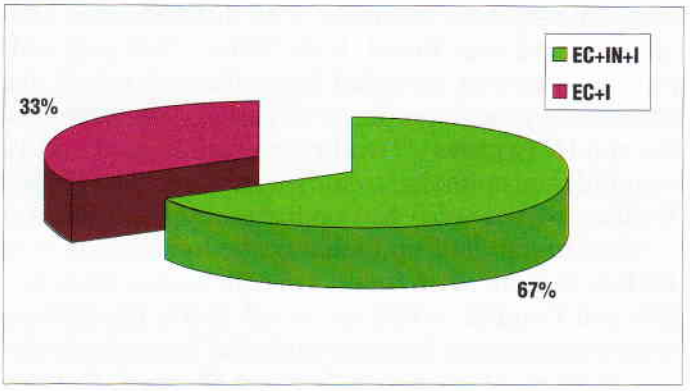

Fig. 7. Histopathological changes in Scotch Collie dogs prostates

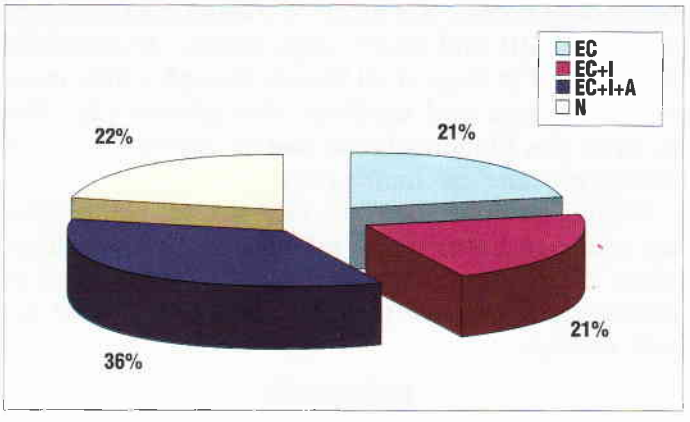

Fig. 8. Histopathological changes in German Sheep dogs prostates

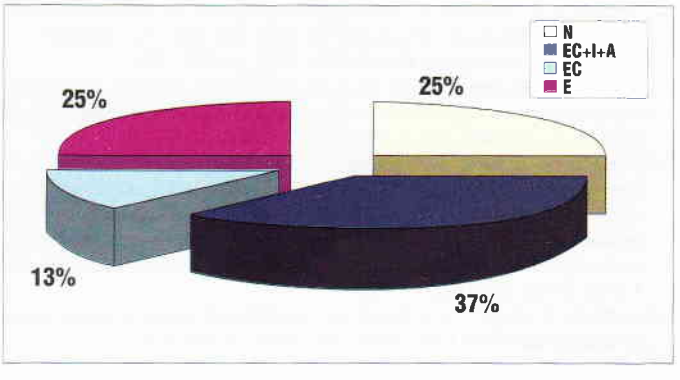

Fig. 9. Histopathological changes in Rotweiller dogs prostates

N – normal histological feature, N+E – beginning of hyperplasia – the acini with papillation in neighbourhood with normal acini, E – epithelial hyperplasia, C – polycystosis, EC – epithelial cystic hyperplasia, Ca – carcinoma, I – inflammation, IN – intraepithelial neoplasia, A – focal atrophy and fibrosis, PM – platenepithelial metaplasia.

causes are unclear (22). One possible cause – changed response of epithelial cells to sex-steroide (6, 22).

The tumours of canine prostate often do not reveal themselves clinically for a long time, they forms metastases into regional lymph nodes, vertebrae of the waist, and long bones of limbs (2, 6, 11). We have found the metastases of prostate's carcinoma in one from five dogs, which had diagnosis of this pathology. In our case the metastases of carcinoma were found in spleen, lungs and lymphatic nodules of abdomen cavity.

In the case of mixed pathology, sometimes arises the question, which of them is primary, and which is secondary. The foci of carcinoma, which are found in hyperplastic glands, are secondary. It is considered that these processes can develop in such sequence: benign hyperplasia – intraepithelial neoplasia – carcinoma. If the chronic inflammation is found in hyperplastic prostate, we can make a premise, that this inflammation could have been a primary process. It is observed that in humans benign prostate's hyperplasia often develops at the same time with chronic inflammation (7). It is suggested that it can be connected with PDGF, which can be an etiological factor of hyperplasia. This factor releases from inflammation cells in the process of inflammation. It can be a potential mitogen for the cells of epithelium and stroma (21). Chronic inflammation can cause and increase the growth of fibromuscular tissue, in a similar way, as in wound healing (9), but other authors (10) draw a conclusion, that hormone induced BPH is preceding cells mediated and humoral immune response.

The relations between dogs breed and pathology are shown in Fig. 6. We have observed gross incidence of epithelial cystic hyperplasia and intraepithelial neoplasia (IN) in Scotch Collie (10-12 years age) (Fig. 7). The ratio of their prostates was noticeably elevated 1.33-5.9 (3.4). In 78% hyperplasic prostates of German Shepard dogs (1.5-14 year old) intraepithelial neoplasia foci were not found, but there were found foci of inflammation and post inflammation fibrosis and atrophy (Fig. 8). The index of their prostates was 0.6-3.6 (2.6). Prostates of Rottweilers (2-7 year old) were not enlarged distinctly, the index of them was 0.45-1.37 (1.97) and epithelial cystic hyperplasia was the most frequent pathology. In Poodles we found epithelial hyperplasia (2 cases) and epithelial cystic hyperplasia (2 cases). In bigger prostate IN foci were found. In all Dobermans prostates epithelial cystic hyperplasia was found. In Scoth Terriers the epithelial

cystic hyperplasia, sqamous, well differenciated adenocarcinoma was found. Irish Setters (5-9 year old) prostates showed epithelial hyperplasia (3 cases), the epithelial cystic hyperplasia (2 cases), adenocarcinoma and IN (2 cases). Two French Bulldogs (9 and 10 year old) had epithelial cystic hyperplasia. The French Bulldog (4 year old) had epithelial hyperplasia. According to our data, epithelial cystic hyperplasia with IN foci is more often found in Scoth Collie, Irish Setters and Poodles, while epithelial cystic hyperplasia with inflammation foci and epithelial hyperplasia alone are more often met in German Shepard, Rottweilers and Doberman Pinchers. We have not found date about of prevalence of some prostate pathology in different dogs breeds. Not much date about relathionships between BPH and single dogs breeds. Hyperplasia shows itself in dogs of all breeds, though a little more often in large and medium size breeds (2). The Bouvier des Flandres breed had an increased risk of having prostate carcinoma (20).

Having in mind that fact, that several pathologies are found in hyperplastic prostate at the same time, when examining the material taken by the method of prostate's biopsy, the obtained diagnosis can be not very precise.

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STAN ZAKAŹNYCH CHORÓB ZWIERZĄT W POLSCE,

według danych Głównego Inspektoratu Weterynarii w maju 2003 r.*)

1) **Wścieklizna zwierząt domowych** – wystąpiła w 2 województwach: lubelskim (1-1) i warmińsko-mazurskim (1-2). Stwierdzono ją u 1 psa i 2 kotów.
2) **Wścieklizna zwierząt dzikich** – wystąpiła w 9 województwach: kujawsko-pomorskim (1-1), lubelskim (3-3), małopolskim (1-1), pomorskim (1-2), śląskim (1-1), świętokrzyskim (1-1), warmińsko-mazurskim (3-4), wielkopolskim (7-8), zachodniopomorskim (1-1). Zanotowano ją u 16 lisów, 4 jenotów, 2 kun i 1 nietoperza.
3) **Zgnilec amerykański pszczół** – wystąpił w 4 województwach: dolnośląskim (1-1), lubelskim (1-1), podlaskim (1-1) i warmińsko-mazurskim (1-1).

*) W nawiasach podano liczbę powiatów i miejscowości, w których choroba została stwierdzona w okresie sprawozdawczym.