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Artikel: Influence of social stress on incidence and extent of amyloidosis in the Syrian golden hamster

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THE INCIDENCE OF MALIGNANT NEOPLASMS OF THE DOG IN A 40-YEAR PERIOD (1950 – 1989) IN MUNICH

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Between 1950 and 1989 a total of 27,959 dogs were autopsied at the Institute of Veterinary Pathology, University of Munich. 4,839 dogs (17.3%) had malignant tumours, excluding those of the central nervous system.

The frequency of malignant neoplasms between 1950 and 1954 had an average of 6.4%, increased to 16.4% in the next five years and had a level between 13.4 and 22.9% in the following study period without any significant tendency. The changing frequency was correlated positively with the average age of the dogs necropsied.

The average age of all dogs with tumours was 9.7 years, while that of the dogs without tumours was 5.4 years.

Breed disposition ranged from the more frequently affected breeds German Shepherd dog, Boxer and Airdale Terrier to the less frequently affected breed Dachshound and mixed breeds, these results were statistically proven.

Male dogs showed a higher incidence of haemangioendotheliomas and malignant perianal gland tumours than the female dogs, indicating a sex disposition for these neoplasms.

The incidence of the malignant tumours of the thyroid gland decreased from an average level of 26.5% in the period 1950–55 to 3.0% in the period 1985–89. This tendency is perhaps most likely caused by the effect of the addition of iodine to the dog's food.

The incidence of liver tumours was highest in the late fifties and the beginning of the sixties (up to 16% in 1957). After that a decrease was recognized and at the end of the study period it was on average between 3 and 4%. The causes of this tendency are unknown.

Haemangioentheliomas were not found until 1955. After that their occurrence increased from 3.5% to 20.8%, computed in five-year periods. The reasons for the increasing incidence are unknown so far.

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INFLUENCE OF SOCIAL STRESS ON INCIDENCE AND EXTENT OF AMYLOIDOSIS IN THE SYRIAN GOLDEN HAMSTER

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Amyloidosis in the Syrian hamster (SGH) was reported as an age-dependent change (1). The significance of social stress for spontaneous amyloidosis was demonstrated for the SGH (2) and for other species (3). The latter authors (3) defined a 'gradient of stress', characterized by various combinations of space and number of animals (crowding) per cage. This paper reports the relationship of amyloidosis in the SGH to social stress patterns which were induced by crowding the animals by up to 7 animals per cage.

Material and methods

A total of 220 SGH, 110 animals each sex, were kept under standardized laboratory conditions and were subdivided into four experimental groups: 20 animals (of each sex) were housed individually; 30 animals were housed with 3 animals per cage, 25 animals were housed with 5 animals and 35 animals with 7 animals per cage, respectively. A complete necropsy was performed on each animal which died spontaneously or which was killed when moribund. Tissues were prepared for histological examination, using H.E. stain. Sections showing hyalin deposits were recorded as positive when Congo Red preparations (4) were positive in conventional and polarized light microscopy. Amyloidosis was graded in five selected organs (thyroid, adrenals, liver, spleen, kidneys) using a semiquantitative 0 to 3+ scale. The statistical data were evaluated using the 'Kruskal-Wallis'-test and the 'Wilcoxon-2-sample'-test.

Table 1: Incidence (%) of amyloidosis in the Syrian hamster related to the number of animals per cage

organ	thyroid		liver		spleen		adrenals		kidneys	
sex	m	f	m	f	m	f	m	f	m	f
group										
1	55	63	50	80	47	65	25	74	45	60
3	67	88	64	93	60	89	63^{c}	93	60	96^{c}
5	58	80	59	96	67	96^{B}	65	91	44	87^{B}
7	86^{AF}	87	88^{ADF}	97	84^{AF}	90^{A}	96^{ADF}	96^{AD}	92^{ADF}	96^{A}

Significant difference between the experimental groups: A: 7 to control (1), B: 5 to 1, C: 3 to 1, D: 7 to 3, E: 5 to 3, F: 7 to 5; $p \leq 0.05$, ('Wilcoxon-2-sample-test')

Results

The most striking differences in the incidence of amyloidosis were seen among the controls and the hamsters of the 7-animal group (Tab. 1). The significant results in the kidneys and the adrenals between the different groups indicates that these organs are possible target-organs for amyloidosis. The comparison of the experimental groups with regard to the other organs was generally not significant. Table 2 shows the significance of the stress-influenced amyloidosis in

Table 2: Probability of significant differences for incidence of amyloidosis classified by animals per cage, p-values:

organ	thyroid	liver	spleen	kidneys	adrenals
males	0.01	0.03	0.02	0.001	0.0001
females	0.40	0.18	0.02	0.02	0.07

('Kruskal-Wallis-test', chi-square approximation)

different organs for the sexes. For the male hamsters the amyloidosis in all organs was related to social stress, whereas in the female hamsters this was only true for the spleen and kidneys. The analysis of variance for age dependency of these lesions showed no correlation between age and amyloidosis (data not shown).

Discussion

This study indicates an influence of social stress patterns on the development of amyloidosis in the SGH. Several authors have presented data with large differences in incidence and extent of amyloidosis (1, 5, 6, 7, 8). This can probably be explained in part by the number of animals housed per cage. Page and Glenner (2) discussed a predisposing influence of chronic inflammation on amyloidosis. This inflammation could result from wounding due to social fights. They excluded crowding of the animals as a directly influential factor. In contrast, our data which are in agreement with the data of Cowan and Johnson (3), suggest a more direct influence of crowding on amyloidosis. The authors did not recognize extensive wounding due to social fights. In our experiment such animals were excluded from statistical data evaluation. Furthermore, we could not establish a correlation between 'chronic inflammation' in various organs (whole organ spectrum examined) and amyloidosis. In contrast to other studies (1, 6) the results presented here also showed no clear age-dependence of amyloidosis, neither in the individually housed animals nor in the other groups.

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CONTRIBUTION TO THE HISTOGENESIS OF GRANULAR CELL TUMOURS

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Granular cell tumours (GCT) are rare tumours in humans and some domestic animal species. They are usually benign, rarely malignant. Most canine GCT occur within the tongue, whereas the equine cases have been described in the lung. They consist of round to spindle shaped cells, which contain diastase-resistant eosinophilic granules in their cytoplasm. The histogenesis is not established with certainty. In humans, current evidence suggests a neural source, which is assumed for animals as well. One author reported basal cell tumours in three dogs showing locally features of GCT. In this study we report four tumours classified as GCT because of their PAS-positive eosinophilic granules, which were demonstrated additionally by electronmicroscope. The tumours were investigated immunohistochemically with antibodies against keratin, desmin, vimentin, GFAP and S-100. The results are summarized in the following table:

	GCT 1	GCT 2	GCT 3	GCT 4
Species:	horse	dog	dog	dog
Localization	lung	tongue	tongue	lip
Antibodies:				
Keratin:	–	–	–	+
Vimentin:	–	+	+	–
Desmin:	+/–	–	–	–
S-100:	+	–	–	–
GFAP:	–	–	–	–

+: most of the tumour cells with positive reaction
–: no reaction of the tumour cells with the antibody
+/–: reaction of few tumour cells with the antibody

The GCT examined immunohistochemically reacted differently: GCT 1 showed positive reaction against S-100 only. In humans GCT are frequently stained by S-100. This, and the fact that human GCT contain most often neuron-specific enolase and myelin basic protein led to the conclusion, that GCT are of neural origin and probably derive from Schwann cells. This might be true for our GCT 1. Both canine tumours of the tongue (GCT 2, GCT 3) only contained vimentin. This supports a histogenesis of both tumours from a nonmuscular mesenchymal cell. GCT 4 only reacted with the keratin antibody. This fact, its histomorphologic appearance, and its localization in the lip favoured a histogenesis from epidermal basal cells, which has been discussed in humans and dogs by other authors.
As far as conclusions can be drawn from the small number of cases, the findings suggest that the histogenesis of GCT in domestic animals is not uniform. The hypothesis is supported that GCT show similar appearance despite different histogenesis, possibly because of an unknown metabolic defect of the tumour cells.