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Usefulness of post mortem determination of serum tryptase, histamine and diamine oxidase in the diagnosis of fatal anaphylaxis

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ABSTRACT

The diagnosis of fatal anaphylaxis can be difficult for clinical features may not always be evident in necropsy. Therefore post mortem determination of tryptase and other blood parameters can be helpful in verifying the diagnosis. We compared post mortem tryptase, histamine and diamine oxidase (DAO) serum levels of two patients who had died after a Hymenoptera sting and one patient who died of bronchospasm during anaesthesia with data obtained from 55 control subjects who had died from other causes than anaphylaxis.

In the three anaphylactic cases, serum tryptase level was 880, 68 and 200 $\mu\text{g/l}$ (normal range in living subjects: $<11.4 \mu\text{g/l}$), histamine was 37.5, 8.5 and 23.2 ng/ml (normal range: $<0.3 \text{ ng/ml}$) and DAO was 1, 30 and 4 U/ml (normal range 10–30 U/ml), respectively. Values in the control group were as follows: tryptase 1–340 $\mu\text{g/l}$ (mean 24.2 ± 58.2), histamine 5.0–22.0 ng/ml (mean 14.7 ± 3.9) and DAO 0–114 U/ml (mean 21.1 ± 27.8). 19/55 (34.5%) of the controls had elevated tryptase levels $>11.4 \mu\text{g/l}$, with four of them showing values $>45 \mu\text{g/ml}$. Significantly higher histamine levels were seen in blood samples taken more than 24 h post mortem ($p < 0.05$), whereas the timing of blood collection had no effect on tryptase and DAO levels.

While moderately elevated tryptase levels are common in post mortem sera, values above 45 $\mu\text{g/l}$ may support the diagnosis of fatal anaphylaxis. Strongly elevated histamine levels might give an additional clue on fatal anaphylaxis, whereas DAO does not seem to be helpful.

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1. Introduction

Anaphylaxis is the most severe form of an acute IgE-mediated allergic reaction. Resulting in the systemic degranulation of effector cells, anaphylaxis can cause variable clinical manifestations, such as nausea, vomitus, diarrhea, pruritus, urticaria, bronchospasm, edema of larynx and pharynx and finally anaphylactic shock. The most common agents causing anaphylactic reactions are Hymenoptera venoms, foods and drugs [1].

While the diagnosis of allergic reactions in living patients is based on the patient's history, skin tests, determination of specific IgE and sometimes provocation tests, it can be difficult to diagnose an anaphylactic reaction post mortem. Macroscopic as well as microscopic findings are not specific and in many cases not present in necropsy [1,2]. Obvious sting sites or the presence of the causing food allergen in the gastrointestinal tract are unusual findings [3] and a history of sensitization or former allergic reactions can rarely

be obtained. In many cases death due to shock can appear so quickly, it leaves no time for other features to appear [1]. Therefore additional use of post mortem determined serum parameters has been discussed.

Tryptase is a serine protease mainly synthesized and released by mast cells. It can be used in living patients as a marker for mast cell number (α -tryptase) and the grade of mast cell activation (β -tryptase) [4]. Due to its high stability tryptase can be assessed even days post mortem [5]. Values above 11.4 $\mu\text{g/l}$, which is the upper normal limit in living subjects, have been found in anaphylactic deaths by several authors [1,6–9]. However, elevated values have also been observed in non-anaphylactic deaths, like sudden infant death syndrome (SIDS) [10–12], trauma [5], atherosclerotic cardiovascular disease [3], and after heroin injection [13]. Some authors described an increase of tryptase levels with increasing post mortem interval [3] while others found no such effect [8].

Histamine is the most important inflammatory mediator released by mast cells and basophils during an allergic reaction. Causing various effects like vasodilatation, bronchoconstriction and pruritus, histamine plays a crucial role in anaphylaxis and the cause of death. However, its short half life and the possibility of non-specific histamine release during blood drawing diminish the

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validity of histamine as a marker for anaphylactic reactions in living patients [14].

Diamine oxidase (DAO) is a major histamine-degrading enzyme. Pharmacologic blocking of DAO together with a high exposure to histamine-rich food can lead to severe shock in animals [15]. To our knowledge, DAO has not been measured in post mortem blood before.

In this study, we obtained sera from three anaphylactic deaths and 55 control subjects to assess the post mortem levels of tryptase, histamine and DAO. Additionally, we investigated if the time point of blood sampling has an effect on either parameter and we compared our findings with published data, reviewing the literature available in PubMed.

2. Methods

Blood samples were collected from three cases of anaphylactic death and compared to samples from 55 consecutive control bodies (35 m, 20 f, mean age 67.6 ± 16.8 years) drawn during necropsy at the Department of Forensic Medicine in Vienna between January 2006 and May 2007. Inclusion criteria for all cases were adequate information about the cause and the time point of death as well as availability of a blood sample drawn from the femoral vein (including knowledge of the time point of collection) for the determination of tryptase, histamine and diamine oxidase (DAO).

Anaphylaxis case 1 was a 57-yo male with a well-known history of venom allergy treated by specific immunotherapy ten years before. After a honeybee sting into the shoulder he developed acute shortness of breath and hypotension and died within 1 h. Necropsy revealed laryngeal edema. Post mortem determination of allergen-specific IgE antibodies was positive for honeybee venom (2.2 kU/l), and negative for wasp (*Vespula*) venom. Case 2 was a 48-yo male without a history of venom allergy who developed an anaphylactic shock after multiple wasp stings when disturbing a wasp's nest during lawnmowing. Death occurred within 30 min. Post mortem determination of allergen-specific IgE was positive for *Vespula* venom (9.8 kU/l) and also for honeybee venom (1.68 kU/l). Case 3 was a 59-yo male who developed fatal bronchospasm during the initiation period of anaesthesia after receiving succinylcholin, which is known as a histamine releaser.

The causes of death of the control bodies were divided into four groups: (1) cardiac ($n = 41$), (2) cerebral haemorrhage ($n = 4$; one case following gunshot), (3) trauma ($n = 5$; mostly polytrauma after fall from heights), and (4) bleeding to death ($n = 5$; 4× thoracic or abdominal aortic aneurysm rupture, 1× gastrointestinal haemorrhage).

In all cases, blood was collected from the femoral vein. Serum tryptase was assessed using an immunofluorescent enzyme assay (ImmunoCAP, Phadia, Sweden) measuring both α - and β -tryptase. Histamine concentrations were determined using a radioimmuno assay with a lower sensitivity cut-off of 0.1 ng/ml (Immunotech, Marseilles, France). DAO activity was determined by a commercial radioimmuno assay using radio-labeled putrescine as a substrate (Scitech, Vienna, Austria). All parameters were analyzed using two sided *t*-test. A *p*-value of <0.05 was considered statistically significant.

To compare the results obtained in the three anaphylaxis cases with published data on post mortem tryptase, a literature search was performed in PubMed using "anaphylaxis" and "tryptase" as key words.

3. Results

3.1. Tryptase, histamine and DAO levels

Normal tryptase levels in living subjects are $<11.4 \mu\text{g/l}$. The three anaphylactic cases showed values of 880, 86, and 200 $\mu\text{g/l}$,

respectively. Levels in the control group varied between 1 and 340 $\mu\text{g/l}$ (mean $24.2 \pm 58.2 \mu\text{g/l}$, median 9.0 $\mu\text{g/l}$) (Table 1, Fig. 1). 19 control samples (34.5%) showed values above 11.4 $\mu\text{g/l}$, with four of them exceeding 45 $\mu\text{g/l}$ (1 in the cardiac group, 2 in the trauma group, and 1 in the bleeding to death group).

Normal histamine levels in living subjects are $<0.3 \text{ ng/ml}$. All post mortem sera had strongly elevated histamine concentrations. The anaphylactic cases showed values of 37.5, 9.0 and 23.2 ng/ml . In the controls, values varied between 5 and 22 ng/ml (mean $14.7 \pm 3.9 \text{ ng/ml}$, median 15.0 ng/ml) (Table 1, Fig. 2).

DAO standard values in living people are around 10–30 U/ml. We found an unexpected high variation in post mortem DAO levels. Subjects having died of anaphylaxis showed values of 1, 30 and 4 U/ml, while those of the controls varied between 0 and 114 U/ml (mean $21.1 \pm 27.8 \text{ U/ml}$; median 10.0 U/ml) (Table 1, Fig. 3).

3.2. Time point of blood sampling

Blood samples were drawn between 4 and 110 h post mortem with a mean of $29.1 \pm 19.8 \text{ h}$. No significant influence on tryptase or DAO levels could be found while histamine concentrations showed a tendency to rise with increasing post mortem interval. Blood taken within 24 h post mortem had significantly lower histamine levels than samples taken later than 24 h ($p = 0.035$) (Fig. 4). Values below 10 ng/ml were restricted to sera collected not later than 40 h post mortem. Except for a weak positive correlation between histamine and tryptase, no significant correlations were found in the control group between tryptase, histamine and DAO levels.

3.3. Review of literature

Searching the key words "anaphylaxis AND tryptase" in PubMed revealed 25 reports of post mortem assessed tryptase in a total of 91 anaphylactic death cases (Table 2).

The causes of anaphylaxis could be divided into insect stings ($n = 19$), contrast media ($n = 6$), antibiotics ($n = 8$), induction agents in anaesthesia (muscle relaxants, propofol, fentanyl, $n = 5$), substances described as 'iatrogenic' ($n = 8$), foods ($n = 18$), analgetics ($n = 1$), and other rather unexpected causes like hair dye, loperamid (opiate-receptor blocker), sotradecol (sodium tetradecyl sulfate, a sclerosing agent), psyllium (natural hydrophilic mucilloid of the genus *Plantago* [16]), mites and pollen (natural exposure) as well as unknown causes ($n = 19$). Tryptase has not been measured in one case [17].

Fifty-two of the 91 described fatal anaphylactic cases (57.1%) showed tryptase levels $>45 \mu\text{g/l}$. Fineschi and colleagues found a mean tryptase value of $>45 \mu\text{g/l}$ in 32 anaphylactic death cases [13]. Pumphrey and colleagues reported elevated tryptase levels $>11.4 \mu\text{g/l}$ in 14 of 16 anaphylactic deaths but did not provide data for single patients [1].

Among insect sting victims, 16 of 19 displayed tryptase levels $>45 \mu\text{g/l}$, as was the case in 4 of 5 patients deceased after receiving contrast media and in 3 of 5 during the induction of anaesthesia. In

Table 1
Post mortem tryptase, histamine, and DAO levels in anaphylactic cases and controls. Figures for tryptase, histamine and DAO refer to mean values $\pm$ SD and range of variation (in parenthesis).

Cause of death	<i>n</i>	Age (a)	Tryptase ($\mu\text{g/l}$)	Tryptase $>11.4 \mu\text{g/l}$	Tryptase $>45 \mu\text{g/l}$	Histamine (ng/ml)	DAO (U/ml)
Anaphylactic deaths (all)	3	54.7 ± 5.9	388.7 ± 429.3	3/3 (100%)	3/3 (100%)	23.1 ± 14.5	11.7 ± 15.9
Honeybee sting	1	57	880			37.5	1
Multiple wasp stings	1	48	86			9	30
Bronchospasm during anaesthesia	1	59	200			23.2	4
Controls (all)	55	67.6 ± 16.8	24.2 ± 58.2 (1–350)	19/55 (34.5%)	4/55 (7.3%)	14.7 ± 3.9 (5–22)	21.1 ± 27.8 (0–114)
Cardiac	41	69.2 ± 16.6	16.8 ± 40.1 (1–262)	13/41	1/41	14.6 ± 4.0 (5–22)	23.4 ± 28.9 (0–114)
Cerebral haemorrhage	4	51.5 ± 17.5	8.8 ± 3.8 (5–14)	1/4	0/4	14.5 ± 1.3 (13–16)	33.0 ± 42.3 (3–94)
Trauma	5	65.0 ± 17.9	90.8 ± 143.1 (5–340)	3/5	2/5	11.8 ± 2.7 (10–16)	6.6 ± 2.6 (4–10)
Bleeding to death	5	69.6 ± 13.4	30.8 ± 52.3 (2–124)	2/5	1/5	18.0 ± 3.9 (13–22)	7.6 ± 7.4 (0–17)

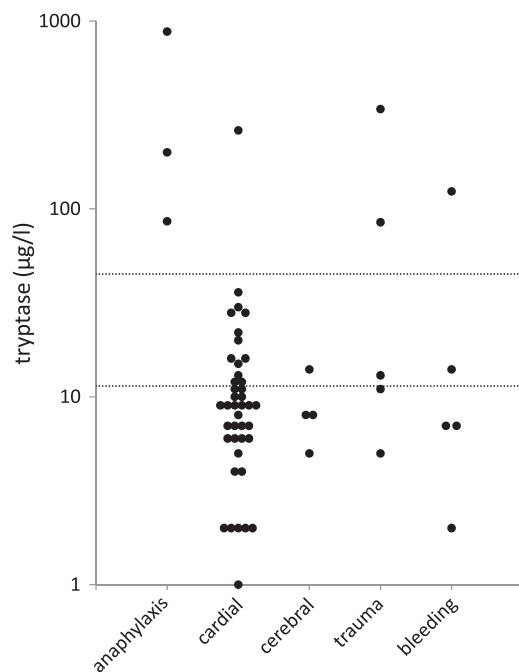


Fig. 1. Post mortem tryptase levels in anaphylactic deaths and control groups. Dotted lines indicate cut-off levels of 11.4 µg/l and 45 µg/l.

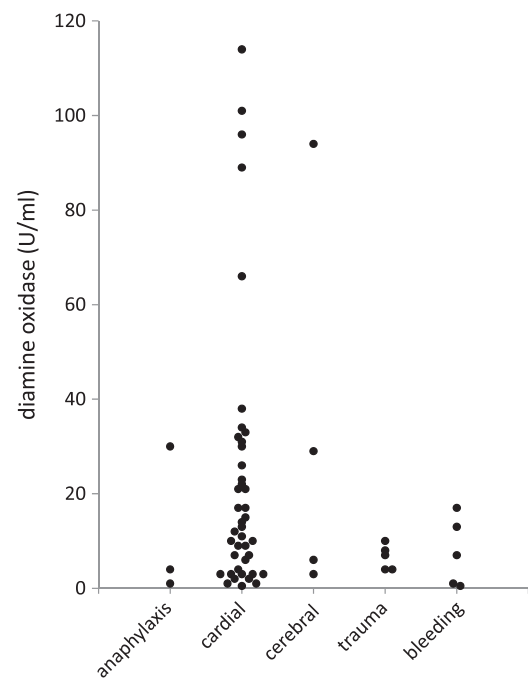


Fig. 3. Post mortem diamine oxidase (DAO) levels in anaphylactic deaths and control groups.

contrast, in only 3 of 8 fatalities after receiving antibiotics, 7 of 19 cases of food-induced fatal anaphylaxis and 11 of 19 unknown causes of anaphylaxis were tryptase levels >45 µg/l. Including the anaphylactic cases described in this study, 18 of 21 insect sting victims and 4 of 6 subjects with fatal anaphylaxis during anaesthesia displayed strongly elevated tryptase levels beyond 45 µg/l.

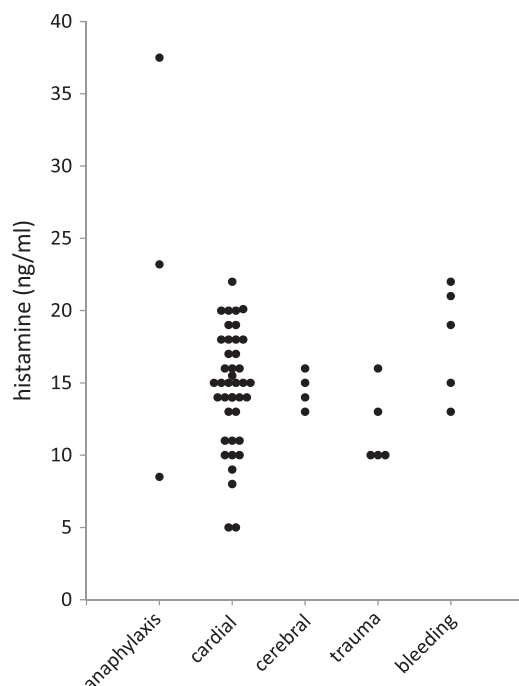


Fig. 2. Post mortem histamine values in anaphylactic deaths and control groups.

4. Discussion

Anaphylaxis is often difficult to diagnose in autopsy, for morphologic changes are nonspecific, if present at all. The most common pathological findings are pulmonary congestion with or without edema, intra-alveolar haemorrhage, increased tracheo-bronchial secretion, visceral congestion [2], mucus plugging and hyperinflated lungs, pharyngeal and/or laryngeal edema and petechial haemorrhages indicating asphyxia [1]. However, many cases do not exhibit these changes. Pumphrey et al. examined 56 cases of fatal anaphylaxis and found no macroscopic changes in 23 of them. It was suggested, that in some cases cardio-respiratory shock is leading to death so quickly, there is no time for pathological changes to develop [1]. Therefore the determination of certain blood parameters has been a main topic of recent investigations [1,3,6–8]. The best-reviewed parameter is tryptase,

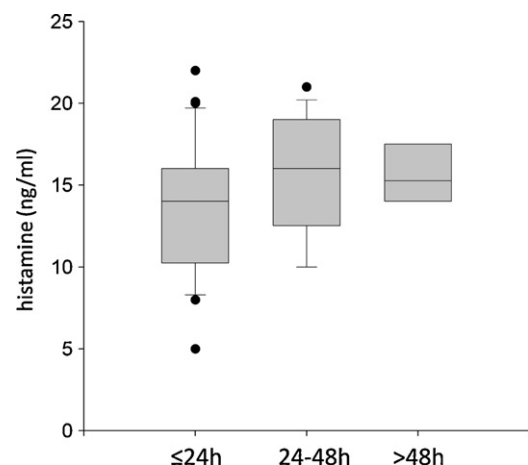


Fig. 4. Relationship between post mortem serum histamine levels and time point of blood collection.

Table 2

Overview about published data on tryptase levels in post mortem sera.

Author	n	Causing agent	Tryptase $\mu\text{g/l}$	α/β	Sample source
Yunginger et al. [9]	19	Wasp sting	50	Unknown (presumably β only)	Unknown
		Wasp sting	494		
		Wasp sting	55		
		Wasp sting	125		
		Wasp sting	41		
		Wasp sting	150,000		
		Fire ant sting	131		
		Fire ant sting	700		
		Honey bee sting	5041		
		Soybean	10		
		Peanut	<2.5		
		Peanut	29		
		Peanut	61		
		Pecan	<3.4		
		Crab	74		
		Codfish	17		
		Codfish	159		
		Hexabrix	1038		
		Sotradecol	6000		
Ansari et al. [6]	1	Honey bee sting	51	$\alpha + \beta$	Cardiac chambers
Fisher and Baldo [28]	2	Induction with thiopentone	50	Unknown (presumably β only)	Unknown
		Induction with suxamethonium	36		
Edston et al. [29]	2	Food (oriental kebab)	5.5	Unknown (presumably $\alpha + \beta$)	Femoral veins
		Penicillin V	2		
Edston and Van Hage-Hamsten [5]	7 ^a	Unknown	11-16-17-33-37	β only	Femoral vessels
Prahlw and Barnard [19]	1	Fire ant stings	12	Unknown (presumably $\alpha + \beta$)	Unknown
Brockow et al. [30]	1	Contrast medium	621		
Fineschi et al. [31]	1	Fluorescein angiography	194	Unknown (presumably $\alpha + \beta$)	Cardiac cavity
		14 of 16 anaphylactic deaths with levels >11.4 $\mu\text{g/l}$			
Pumphrey and Roberts [1]	16	Unknown, mean tryptase level		Unknown	Unknown
		Induction with propofol and fentanyl			
Fineschi et al. [13]	32	Induction with propofol and fentanyl	148.6 $\pm$ 160.8	$\alpha + \beta$	Femoral veins
Konarzewski et al. [32]	1	Mold in pancake mix	185	Unknown (presumably $\alpha + \beta$)	Unknown
Bennett and Collins [33]	1	Amikacin	14		
Shen et al. [34]	3	Cephadrine	52	Unknown (presumably $\alpha + \beta$)	Cardiac chambers
		Lincomycin	121		
Riches et al. [35]	3	Honey bee sting	0.73	Unknown (presumably $\alpha + \beta$)	Unknown
		Honey bee sting	174		
		Honey bee sting	>2000		
Khalili et al. [16]	1	Honey bee sting	>200	Unknown (presumably $\alpha + \beta$)	Unknown
Flannagan and Wolf [36]	1	Psyllium	15.7/25 ^b		
		Food-dependent exercise-induced anaphylaxis	56	Unknown (presumably $\alpha + \beta$)	Unknown
		Fluorescein angiography			
Hitosugi et al. [37]	1	Induction of anaesthesia	33.4	Unknown (presumably $\alpha + \beta$)	Unknown
Fernandez-Galinski et al. [38]	1	Honey bee sting	285		
Low and Stables [39]	13	Honey bee sting	>200	Unknown (presumably $\alpha + \beta$)	Unknown
		Honey bee sting	5–9.9		
		Seafood	>200		
		Seafood	50–99.9		
		3 latrogenic ^c	5–9.9		
		1 latrogenic ^c	10–19.9		
		1 latrogenic ^c	20–49.9		
		3 latrogenic ^c	50–99.9		
		1 Undetermined	50–99.9		
Edston et al. [7]	5	Unknown	13 ¹ /18 ²	$\alpha + \beta$	Femoral veins ¹ /cardiac chambers ²
		Unknown	72 ¹ /37 ²		
		Unknown	200 ¹ /170 ²		
		Unknown	320 ¹ /–		
		Unknown	180 ¹ /390 ²		
Perkskvist and Edston [17]	9 ^a	Honey bee sting	180	β only	Femoral blood
		Mite	200	$\alpha + \beta$	
		Pollen	320	$\alpha + \beta$	
		Penicillin V	29	$\alpha + \beta$	
		Diagnostic agent	480	$\alpha + \beta$	
		Unknown	3300	$\alpha + \beta$	
Srinivasa and Phelan [40]	1	Loperamid	51.8	Unknown (presumably $\alpha + \beta$)	Unknown
Greenberger et al. [41]	4	Unknown	63-78-101-200		
Osawa et al. [42]	3	Contrast agent	182	Unknown (presumably $\alpha + \beta$)	Cardiac chambers

Table 2 (Continued)

Author	n	Causing agent	Tryptase $\mu\text{g/l}$	α/β	Sample source
Shen et al. [43]	14	Analgesics	395	$\alpha + \beta$	Unknown
		Antibiotics	433		
		Honey bee sting	>200		
		Honey bee sting	>200		
		Seafood	8.5		
		Seafood	8		
		Chinese food	7.3		
		Peanut	15		
		Chinese food	3.3		
		Uncertain (ice cream?)	200		
		Anaesthesia	3.9		
		Recephin	27.1		
		Penicillin	18		
		Hair dye	18		
		Unknown	16.2		
This paper	3	Unknown	26.9	$\alpha + \beta$	Femoral veins
		Honey bee sting	880		
		Wasp sting	68		
		Induction of anaesthesia	200		

^a Two patients already described in Edston et al. [29].^b Two subsequent measurements in the same patient.^c During anaesthesia or antibiotic treatment.

but there is also one study discussing mast cell chymase as an additional marker for fatal anaphylaxis [18].

A relationship between fatal anaphylaxis and elevated tryptase levels ($>11.4 \mu\text{g/l}$) was reported by many authors [1,6,8,19]. Schwartz et al., finding higher tryptase levels in 9 of 68 sudden unexpected deaths, concluded that anaphylaxis may be underdiagnosed in necropsy [20]. Other authors, however, found tryptase levels $>11.4 \mu\text{g/l}$ also in cases not associated with anaphylaxis [3,10–13], indicating that moderately elevated tryptase levels may be a common finding in post mortem sera. Based on the data from 44 control subjects, Edston et al. proposed a value of $45 \mu\text{g/l}$ as a new cut-off point for the post mortem diagnosis of anaphylaxis [7].

Our results agree with these previous observations as moderately increased tryptase values were present in 35% of the control samples, presumably resulting from autolysis of mast cells and passive diffusion [5], whereas all anaphylactic cases displayed markedly elevated levels beyond $45 \mu\text{g/l}$ ($86\text{--}880 \mu\text{g/l}$). Anyhow, also four of the control samples showed levels above $45 \mu\text{g/l}$ despite no evidence of anaphylaxis, indicating that strongly elevated tryptase levels, though suggestive of, do not proof anaphylaxis with certainty. Remarkably, three of the four control bodies with strongly elevated tryptase levels were encountered in the trauma and the bleeding to death group (fall out of window, gun-shot wound, abdominal aortic aneurysm rupture), while just one case came from the cardiac group (myocardial infarction). Although no definite conclusions can be drawn from these observations due to the small sample size, it fits well to previous studies also describing elevated tryptase levels in trauma cases, possibly resulting from unspecific degranulation of pulmonary and gastrointestinal mast cells due to the massive physical stimulus [5]. In atherosclerotic cardiac death, high tryptase levels might be explained by stress-dependent non-specific degranulation of mast cells often found in high numbers near atherosclerotic plaques [3].

Histamine has previously been studied during anaphylactic reactions in the living. Because of its short half life of minutes, it can only be detected for a short time period. Histamine is not stored exclusively in mast cells but also in basophil granulocytes [14]. For this reason, histamine in post mortem sera is most likely released from basophils during haemolysis. In accordance with this, histamine levels were consistently elevated in all control sera in our study with a relatively small variability of $5\text{--}22 \text{ ng/ml}$. Again, the highest values (23.2 and 37.5 ng/ml) were found in two of the anaphylaxis cases, suggesting that exceedingly high

histamine concentrations may indicate precedent mast cell activation and thus might give some additional clues in the diagnosis of fatal anaphylaxis.

Because DAO catabolizes histamine and other biogenic amines [21], it could be another factor relevant for the outcome of systemic allergic reactions. Low DAO levels might signify low histamine-degrading capacity favoring more severe and prolonged anaphylaxis. However, in the present study, DAO levels showed a unexpectedly wide range of variation within all groups, with DAO activity hardly detectable in some samples while in others being as high as in the serum of pregnant women. Therefore, this parameter is currently difficult to interpret. Since very low DAO levels were quite common in control sera, low levels do not seem to be specifically associated with anaphylaxis and DAO measurement therefore does not seem to be helpful in the diagnosis of fatal anaphylaxis.

Analyzing the influence of the time point of blood sampling on the studied parameters, only histamine showed a tendency to rise with increasing time point of blood sampling. This is in line with the assumption of successive release from blood basophils during autolysis. We found no such effect on tryptase and DAO levels. Although there seems to be a correlation between histamine and tryptase in the living [14], we found only a modest non-significant correlation between those two parameters in post mortem samples. There was no correlation of DAO with either tryptase or histamine.

Reviewing the literature revealed 25 articles dealing with post mortem obtained tryptase. In many reports there is no clear information about whether α and β tryptase or only the β form was measured. Since the widely used Phadia UniCAP method measures both α and β tryptase and the RIACT method detects only the β form, the method described in the article gives indirect information about which tryptase form was measured. Although the majority of authors determined total tryptase, a few authors only mention the β form, which makes it difficult to compare the results in some cases. In all available reports, including our study, tryptase levels $>45 \mu\text{g/l}$ were common in fatal anaphylaxis from insect stings (18/21), diagnostic agents (4/5), and drugs used in the induction of anaesthesia (4/6), but less common in anaphylactic deaths caused by antibiotics (3/8), foods (7/19) and unknown causes (11/19).

This stands in line with the experience of some authors, who describe no relevant increase of serum tryptase during non-fatal anaphylactic reactions to foods [22,23] and anaphylactoid reac-

tions to vancomycin [24]. In contrast, a rise in tryptase has been consistently observed after (non-fatal) insect sting challenge [14]. It has been suggested, that these differences might be related to the route of allergen administration. Parenteral allergen administration seems to be associated with a more pronounced increase in serum tryptase levels, possibly due to the preferential triggering of tryptase- and chymase-containing (TC) mast cells, which contain approximately threefold more tryptase than human tryptase-containing chymase-negative (T) mast cells [9].

Some cases of elevated post mortem tryptase levels, especially those found in fatal anaphylaxis, might be attributed to mastocytosis, which is a well-established risk factor for severe anaphylaxis in insect venom-allergic patients [26,27]. In living subjects, a tryptase level $>20 \mu\text{g/l}$ is considered a diagnostic criterion of systemic mastocytosis [25]. It cannot be ruled out that the extremely high tryptase level of $800 \mu\text{g/l}$ observed in one of our anaphylaxis cases was associated with mastocytosis, however, no anamnestic data were available for this subject substantiating this assumption.

In summary, our study confirmed that post mortem tryptase can be a helpful parameter in the diagnosis of fatal anaphylaxis in addition to autopsy and patient's history. As moderately elevated tryptase levels appear to be common in post mortem samples, only strongly elevated values, e.g. $>45 \mu\text{g/l}$ as suggested by Edston and colleagues [7], should be considered indicative of anaphylaxis. However, in some cases similarly high values may be found also in non-anaphylactic deaths, and according to published data just moderately elevated tryptase does not rule out anaphylaxis. Thus, post mortem diagnosis of fatal anaphylaxis should not be based on determination of serum tryptase alone.

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