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Morphology, immunohistochemistry and morphometry of the thyroid gland in cases of Sudden Infant Death Syndrome (SIDS)

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Abstract The thyroid glands of 107 SIDS victims (sudden infant death syndrome) have been studied. Controls consisted of 20 thyroid glands from infants who died of other causes (accidents, pneumonia etc.). The thyroid glands were investigated histologically, immunohistologically and morphometrically. Immunohistochemistry (S-100 protein and calcitonin) and morphometry showed no significant results. Histologically, hyperemia (severe: 34 cases = 31.8%; mild: 23 cases = 21.5%), and fibrosis (45 cases = 42.1%; mild: 26 cases = 24.3%) were found. A large number of cases showed depleted follicles (87 cases = 81.3%), little colloid (little: 37 cases = 34.6%; none: 9 cases = 8.4%) and desquamation (severe: 21 cases = 19.6%; abundant: 20 cases = 18.7%). Only fibrosis and depleted follicles were found more often in SIDS than in the controls (conditional logistic regression: rise of incidence for SIDS 2.9 times, $P = 0.028$, and 1.2 times, $P = 0.051$, respectively), a commoner occurrence of hyperemia in SIDS was of limited significance ($P = 0.105$). The alterations found can be taken as stress reactions to current or recurrent hypoxemia and the mild fibrosis indicates recurrent hypoxemia. All alterations indicate that the victims had previously suffered near death episodes. Even though the glands were handled with care, artefacts and autolysis must be taken into consideration. Neither the histological, immunohistological nor morphometrical studies of the thyroid gland gave an explanation as to the cause of death or showed any changes providing explicit help in diagnosing SIDS.

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Key words SIDS · Thyroid gland · Hypoxemia · S-100 protein · Calcitonin

Zusammenfassung In unserer Studie wurden 107 Schilddrüsen von an SIDS (plötzlichem Kindstod) verstorbenen Säuglingen untersucht. Die Kontrollgruppe bestand aus 20 Schilddrüsen von Säuglingen, die aus anderen Ursachen (Unfälle, Pneumonien, etc.) verstarben. Die Schilddrüsen wurden histologisch, immunhistologisch und morphometrisch untersucht. Immunhistologie (Calcitonin und S-100 Protein) und Morphometrie ergaben keine Besonderheiten. Histologisch bestanden eine Hyperämie (34 Fälle = 31,8%; mild: 23 F = 21.5%) und Fibrose (45 F = 42,1%; mild 26 F = 24,3%). In 87 Fällen (81,3%) wurden viele entspeicherte Follikel gefunden. Wenig oder kein Kolloid in über 50% der Follikel (wenig: 37 F = 34,6%; kein: 9 F = 8.4%) und deutliche Desquamationen waren weitere Befunde (übermäßig: 21 F = 19,6%; häufig: 20 F = 18,7%). Im Vergleich zur Kontrollgruppe traten jedoch nur die Fibrose und entspeicherte Follikel in größerem Maße auf (Bedingte logistische Regression: Erhöhte SIDS-Rate bei Fibrose: 2,9fach, $p = 0.028$, bei entpeicherten Follikeln 1,2fach, $p = 0.051$). Das gehäufte Auftreten von Hyperämien war statistisch nur bedingt signifikant ($p = 0,105$). Die gefundenen Veränderungen können als Zeichen von wiederholtem oder länger andauerndem präfinalem Stress gedeutet werden, wobei das Vorhandensein der Fibrose eher auf wiederholte Stressphasen als nur auf präfinalen Stress durch Hypoxämie hindeutet. Dies läßt vermuten, daß die Kinder wiederholt sog. "near death episodes" überlebt hatten. Auch wenn die Drüsen entsprechend vorsichtig behandelt wurden, können Artefakte und Autolyse grundsätzlich nicht ausgeschlossen werden. Weder Histologie noch Immunhistologie oder Morphometrie der Schilddrüse konnten eine Todesursache bei plötzlichem Kindstod erkennen lassen, noch konnten sich eindeutige Veränderungen finden lassen, die bei der Diagnosestellung von SIDS eine wesentliche Hilfe darstellen könnten.

Schlüsselwörter Plötzlicher Kindstod · Schilddrüse · Hypoxämie – S-100 Protein – Calcitonin

Introduction

Even though the estimated incidence of Sudden Infant Death Syndrome (SIDS), at about 1–3 per 1000 live births (Schulte 1988, Keeling 1981) in industrial nations, has dropped significantly within the last years, SIDS is still the major cause of death in infancy after the first week of life (Finlay and Rudd 1993). However the etiology is still unknown.

The definition of SIDS states that necropsy fails to show the cause of death; it is hence of great importance to verify the diagnosis by a thorough pathological examination of such infants that die suddenly and unexpectedly. As Valdes-Dapena (1992) stated, 15% of all sudden infant deaths are ultimately not due to SIDS but to a disease process.

Two organs of the victims have to be examined in detail in greater numbers to assist in delineating mechanisms of death in such circumstances and determine whether other factors, some which are genetic, are present (Krous 1988).

The questions are of importance when examining the thyroid gland: 1) are there any alterations that point to diseases of the thyroid gland for causing death? 2) are there any recurrent changes within the organ that help to diagnose SIDS?

As early as 1975 Beckwith listed 73 attempts to explain SIDS and many have since been added. Some theories aroused greater interest. Krous (1984a, b, 1989) discussed obstruction of the upper airway. Naeye (1976, 1989) discussed central apnea as causing measurable morphological alterations of tissue, which have become known as "hypoxic tissue markers". However most of these "markers" could not be confirmed in later studies. It has long been suspected that the ultimate mechanism involves malfunction of the brain and in particular, the brain stem, since abnormalities in the regulation of cardiac, respiratory and sleep arousal patterns have been observed in infants who subsequently died of SIDS (Valdes-Dapena 1992; Wilske 1993). Despite the great interest in SIDS and any morphological alterations that might help to identify infants at risk, very few studies have examined the thyroid gland.

Risse and Weiler (1984, 1990) and Risse et al. (1986) compared thyroid glands of newborn babies and infants with the glands of SIDS victims. They found highly activated organs with depleted follicles, capillary hyperemia and epithelial desquamation. These results were interpreted as a morphological correlate of a premortal chronic or recurrent stress reaction, possibly caused by chronic or recurrent hypoxemia.

In our study we extended the histological parameters and added morphometrical and immunohistochemical methods for examining the thyroid glands.

Material and methods

The study group consisted of 132 cases, 107 of which died of sudden infant death syndrome; 20 died of other causes and were taken as controls (Table 1). In 5 cases SIDS could not be clearly identified and these were excluded from the study.

Table 1 Control group

Diagnosis	Number of cases
Drowning	3
Suffocation	2
Respiratory diseases	8
Exogenous hyperthermia	1
Myocarditis	2
Respiratory distress syndrome III	1
Congenital heart disease	1
Hypoxemia, brain death	1
Reflex death	1

The autopsies were performed at the Institutes of Legal Medicine in Münster and Essen (Germany).

Histology

The thyroid glands were fixed in formalin and embedded in paraffin for light microscopy. The slides were stained with HE and PAS. The morphometric data of the follicular epithelium were obtained with the eyepiece micrometer scale (Firma Ernst Leitz GmbH Wetzlar).

Immunohistochemistry

Sections were immunohistologically stained for S-100 protein and calcitonin by the avidin-biotin-peroxidase complex technique. The sections were incubated with normal goat serum (1:30, 20 min, room temperature), rabbit anti-S-100 protein (30 min, room temperature, 1:300, polyclonal, Dako, Hamburg, Germany) or rabbit anti-calcitonin (30 min, room temperature (1:30, Dako) antibodies followed by biotinylated anti-rabbit antibodies and preformed avidin-biotin-complex (Vectastain). The visualization was achieved with diaminobenzidine tetrahydrochloride as the chromogen. All sections were counterstained with Mayer's hematoxylin.

Quantification and classification

Using light microscopy, the morphology of the lobules was graded as: regular, partially coarsed, and coarsed; the connective tissue as: normal, mildly fibrotic, and fibrotic; hyperemia as: none, mild, and severe.

The shape of the follicles was classified as: circular and noncircular, the height of the follicular epithelium as: flattened, cuboidal, slighlty enlarged and columnal while the existence of intrafollicular folds or pleats was noted. The shape of the nuclei of the follicular cells was greaded as: involuted, flattened, and round, and the chromatin of the follicular cell nuclei as: light, normal , and dark. The existence of desquamations was noted and graded as: none, low, abundant, and severe.

The amount of colloid storage was graded as: absent, little, medium, and rich, and the occurrence of vesicles, lacunes, and vacuoles within the colloid was documented.

The size of the follicles was determined morphometrically by 20 measurements from differnt parts of the gland and classified semi-quantitatively as: depleted, small, medium, and large. For evaluation of immunohistochemistry, we counted the number of positive cells within 30 microscope fields (magnification 140 times).

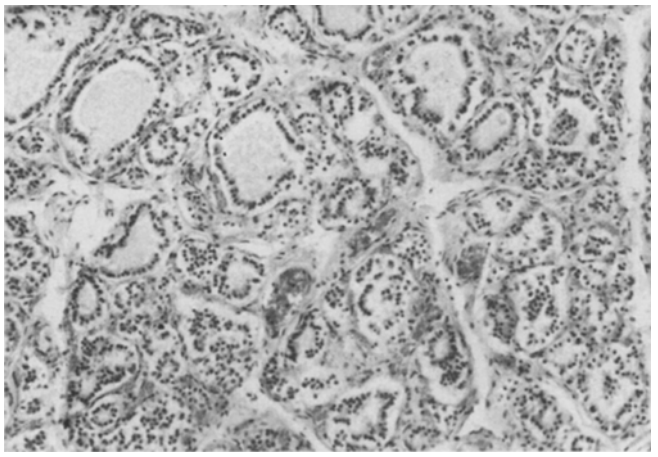

Fig. 1 Case No. N 65/91, 4½ months old female. Depleted follicles, capillary hyperemia. Hematoxyllin-eosin, magnification 90 ×

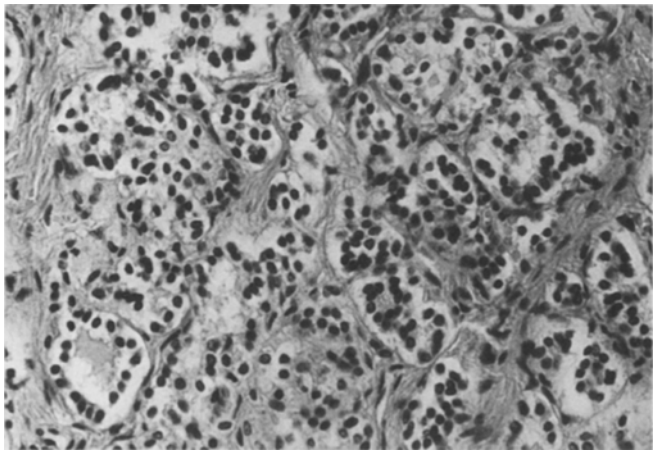

Fig. 2 Case No. N 415/92, 5½ months old male. Strongly depleted follicles, desquamation, many weakly stained follicular cells, mild fibrosis. Hematoxyllin-eosin, magnification 255 ×

Data analysis

For evaluation, 20 pairs of SIDS cases and control group cases were matched by age. While 17 pairs were easily matched, there was quite a discrepancy in age (control/SIDS: 413/378; 559/398; 583/458 days) for the 3 oldest pairs. Since few morphological alterations caused by development in the thyroid are to be expected in children aged about one year within so brief a span, this discrepancy appears to be of no significance. The variables were analyzed by conditional logistic regression using the SPSS statistical package and EGRET ANALYSIS MODULE (SERC and CYTEL) of the Institute of Mathematics and Computer Science of the University of Hamburg and Microsoft EXCEL. The follicle measurements were analysed by the Hotellings T2-test (anaylsis of variance) and conditional logistic regression (Sachs 1984).

Results

Age and sex: In our collective of 107 SIDS cases, the mean age was 5.3 months (range 20 days–15 months), 3 cases (2.8%) were older than one year, 73 (68.2%) were 6 months and younger. Of the 20 cases used for data evaluation, the

Table 2 Morphometry of histological findings

Grading	Number of cases	Percent of cases
Connective tissue		
Fibrotic	45	42.1
Mildly fibrotic	26	24.3
Normal	36	33.6
Size of follicles		
>50% of the follicles depleted	15	14.0
Between 30 and 50% depleted	36	33.6
Between 10 and 30% depleted	36	33.6
<10% of the follicles depleted	16	15.0
No depleted follicles	4	3.7
Hyperemia		
Severe hyperemia	24	22.4
Severe hyperemia in parts of the thyroid	10	9.3
Mild hyperemia in the whole thyroid	18	16.8
Mild hyperemia in parts of the thyroid	5	4.7
No hyperemia	50	46.7
Morphology of lobules		
Coarse in the whole thyroid	11	10.3
Partially coarse	20	18.7
Desquamation		
Severe	21	19.6
Abundant	20	18.7
Low	51	47.7
None	15	14.0
Height of the follicular epithelium		
In all follicles cuboidal epithelium	63	58.9
>50% cuboidal epithelium	41	38.3
Rest: Flat	37	34.6
Slightly enlarged	1	0.9
Flat or slightly enlarged	3	2.8
>50% slightly enlarged epithelium	3	2.8
Intrafollicular folds or pleats		
>60% of all follicles	3	2.8
>30% of all follicles	2	1.9
No folds	41	28.3
Shape of nuclei of follicular cells		
>30% involuted	31	29.0
<30% involuted (<10%)	57 (18)	53.3
>30% flattened	2	1.9
<30% flattened (<10%)	30 (12)	38.3
Chromatin of follicular cell nuclei		
All nuclei normal	33	30.8
>60% normal	52	48.6
>60% fair	5	4.7
>60% condensed chromatin	17	15.9
Weakly stained follicular cells		
Occurrence (>30%)	64 (12)	59.8 (11.2)
Colloid storage		
>50% of the gland little colloid	37	34.6
>50% of the gland no colloid	9	8.4
>50% of the gland medium colloid	46	43.0
>50% of the gland rich colloid	12	11.2
Shape of follicles		
>50% not circular (100%)	57 (13)	53.3 (12.2)
All follicles circular	1	0.9
Vesicles, lacunes, and vacuoles		
Too little colloid	13	12.2
Vesicles (<10%)	71 (16)	66.4 (15.0)
Lacunes (<10%)	77 (49)	72.0 (45.8)
Vacuoles (<10%)	32 (15)	30.0 (14.0)

Table 3 Results of immunostaining

Matched pair	Number of stained cells			
	Calcitonin		S-100 protein	
	SIDS	Control group	SIDS	Control group
1	3	19	5	4
2	6	76	7	36
3	48	53	4	7
4	7	0	4	6
5	129	78	3	3
6	18	39	4	4
7	64	29	8	3
8	7	269	7	14
9	36	1	4	5
10	187	3	11	2
11	2	0	4	2
12	1	59	2	8
13	33	28	3	9
14	28	3	1	6
15	69	6	6	5
16	3	44	1	6
17	1	1	2	4
18	4	15	13	4
19	3	0	0	1
20	307	4	6	7

mean age was 6.7 months; 3 cases (15%) were older than one year, 10 cases were 6 months and younger. The control group showed a mean age of 7.3 months (range 18 days–19 months) and 3 cases (15%) were older than one year and 10 cases were 6 months and younger. The sex distribution in the SIDS group was 58% (62 cases) male and 42% (45 cases) female, for the matched pairs SIDS group 40% (8 cases) male and 60% (12 cases) female, the control group was 60% (12 cases) males and 40% (8 cases) females.

Morphology

Statistically significant differences were found only in very few aspects when comparing 20 SIDS cases with 20 control cases in a matched pair analysis (matched by age). The conditional logistic regression showed a significantly increased incidence of fibrotic connective tissue (Fig. 1) in SIDS cases (2.9 times, $P = 0.028$) and a slight rise (1.2 times) for smaller follicle sizes ($P = 0.051$, Fig. 2).

Of limited statistical significance were increased incidences for hyperemia ($P = 0.105$; 2.3 times, Fig. 1) and irregularity of the lobules ($P = 0.102$; 1.4 times).

No significant differences were found for desquamation, the shape of the follicles, height of the follicular epithelium, and intrafollicular folds or pleats, the shape and tinctorial affinity of the nuclei of the follicular cells and the amount of colloid storage.

The feebly stained follicular cells (Fig. 2) were found just as often in the control cases as in the SIDS groups.

The summarised results of all 107 SIDS cases are listed in Table 2.

Immunohistochemistry

No significant differences between the control group and that of SIDS could be found for calcitonin and S-100 protein (Table 3). The number of calcitonin positive cells show as much variation in the SIDS group as in the controls (range 0 – >300 positive cells), although no explanation for this wide range was found.

Morphometry

The size of the follicles was determined morphometrically by 20 measurements obtained from different parts of the gland (Table 4). No significant difference in follicle size was found ($P = 0.683$).

Discussion

The age distribution of our collective showed similar results to those reported by Lagercrantz (1989) and others. Gibson (1992) and Berry (1992) reported a slightly higher rate (80%) for the first 6 months of life but also described 3% aged above one year. The sex distribution in the SIDS group was 58% (62 cases) male and 42% (45 cases) female which supports the findings of Finlay and Rudd (1993) and Lagercrantz (1989).

In our study, over 60% of the cases showed increased connective tissue. Comparing the SIDS cases with the control group, the conditional logistic regression showed an explicit rise in the incidence of hyperplastic connective tissue in SIDS cases (2.9 times, $P = 0.028$). Fibrosis, generally, is either a sign of previous inflammation or of sustained or recurrent hypoxemia. A former thyroiditis appears unlikely as remnants of cellular infiltrations were lacking.

Sugiyama (1967) and Isenschmid (1910) described relatively abundant septa in the neonatal and infant periods compared to adults so that the reported increase could partly be an age-related discrepancy. An increase of connective tissue in SIDS has not been documented in the studies of Risse and Weiler (1984, 1990) and Risse et al. (1986).

In our study, capillary hyperemia was found in 53%, although it was graded as mild in 21%. In the matched pairs study, increased incidence of hyperemia was found in SIDS cases (2.3 times) but with limited significance ($P = 0.105$). Unfortunately, other organs were not available for comparison of hyperemia. Risse and Weiler (1984, 1990) and Risse et al. (1986) found marked capillary hyperemia in 48%.

Isenschmid (1910) and Wegelin (1926) described the capillary network in thyroids of very young children as being much denser than those in older children and adults.

Table 4 Morphometry of the follicles

Matched pair	SIDS				Control group			
	D^a (μm)		d^b (μm)		D^a (μm)		d^b (μm)	
	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation
1	72.68	40.80	62.71	28.88	100.14	58.74	88.87	37.79
2	65.76	29.61	59.92	22.06	79.07	57.52	56.97	42.80
3	86.85	61.40	77.87	34.70	91.64	57.82	86.75	38.12
4	78.57	45.82	88.90	57.52	115.28	72.89	91.11	79.10
5	71.91	31.04	66.68	27.09	150.93	91.32	132.10	78.72
6	102.29	41.25	85.29	37.53	85.77	43.38	76.59	43.29
7	83.29	48.17	81.62	48.87	73.10	58.62	75.87	61.40
8	102.01	85.29	94.28	76.32	97.11	47.02	79.18	39.96
9	77.44	37.95	66.07	29.66	73.16	48.26	62.61	35.03
10	297.46	737.62	121.64	74.19	73.16	48.26	135.25	77.25
11	70.70	49.78	58.31	34.69	63.44	29.69	58.36	35.61
12	170.64	109.05	154.84	92.96	172.18	104.47	127.92	88.94
13	96.97	55.23	86.48	65.55	102.06	62.12	94.40	45.81
14	94.14	53.67	88.65	42.04	65.76	38.58	84.50	37.98
15	90.48	43.73	89.55	37.51	108.20	88.72	94.44	53.07
16	122.83	74.84	97.29	48.61	135.48	55.69	107.34	41.90
17	56.23	27.50	55.31	21.20	74.19	47.60	61.81	40.45
18	139.82	58.98	134.65	69.69	160.38	124.77	128.02	85.72
19	133.44	74.54	144.87	78.07	52.24	21.69	49.17	27.00
20	114.46	74.77	96.14	59.80	93.57	76.65	75.93	50.10

[a] Longitudinal diameter
[b] Vertical diameter

Hesselberg (1910) found hyperemia in 16 out of 143 cases of infants 6 months and younger. According to these authors, the perfusion of infant glands is higher than of adult glands. Despite this, the perfusion in our cases must still be described as hyperemic.

Conditional logistic regression showed a slight rise in incidence of smaller follicle sizes in SIDS cases (1.2 times, $P = 0.028$). Morphometrically, no significant difference between SIDS and the control group could be found so that the findings could be considered normal for infants. Sugiyama (1967) described the thyroid glands during the suckling period as being of the microfollicular type. Isenschmid (1910) found smaller follicles in infants than in older cases and emphasized their great variability. Depleted follicles have been described in the literature during the first weeks of life only (Gray 1987, Müller and Rämsch 1966, Wegelin 1926).

Approximately 40% of our cases showed abundant or severe desquamation, but desquamation was also found in many of the control cases, statistically significant differences could not be demonstrated. Risse and Weiler (1984, 1990) and Risse et al. (1986) found desquamation in SIDS cases only. It is questionable whether desquamation is more or less physiologically normal in infant glands. Isenschmid (1910) demonstrated abundant or severe desquamation in 53.4% of the investigated glands of infants under 5 years of age, compared to 25.5% of the glands of older children. Krinskaja (1932) described epithelial desquamation in many glands, mostly in those of children who died of asphyxia. Hesselberg (1910) on the other hand found a high amount of desquamation only within the first 3 weeks of life, but later, the epithelium had regenerated and little desquamation was found. Müller and Rämsch (1966) discussed whether desquamation in newborn infants is caused by temperature differences only when an ante finem "distress signal" causes an activation of metabolism. Sugiyama (1967) and others saw the main reason for desquamation as postmortal autolysis (Schulto 1988). Even though the glands were handled with care, artefacts and autolysis must be taken in consideration. In combination with other changes such as hypoxemia and fibrosis, desquamation can be seen as a stress reaction, and therefore possibly as a result of asphyxia.

When investigating the thyroid glands of SIDS victims, Risse and Weiler (1984, 1990) and Risse et al. (1986) found partially depleted follicles in 35% and depleted follicles in 51% of the cases ($n = 176$), and 60% showed a large degree of epithelial desquamation even down to the collapse of most follicles. Marked capillary hyperemia was found in 48%. The authors interpreted these results as highly activated thyroid glands, activated by premortal current or recurrent stress reaction possibly due to recurrent hypoxia. The weakly stained follicular cells, found in the SIDS cases as well as in the control group might be an age-related sign of activity. They have not been described in literature. Artefacts cannot be excluded with certainty. None of the other histological features observed showed any significant alterations.

The immunohistochemical investigations showed very low numbers of calcitonin positive cells in some of cases. Control stains confirmed these low numbers in most cases. Still we tend to consider these low numbers as arte-

facts. There is no difference to be found between the numbers in SIDS and the controls. S-100 protein-positive cells, of significance in idenficiation and prognosis of thyroid papillary and diffuse sclerosing papillary tumors (Schröder et al. 1989, 1990) are not increased in numbers in SIDS cases compared to control cases.

Conclusions

Although histological alterations of the thyroid gland were found in SIDS cases compared to healthy adult glands, few alterations could be found in comparison to infants who died from other causes. It is debatable whether the alterations found are simply age-related since most of the alterations were also found in the control group. However the value of our control group must be questioned as many of these cases died of diseases (eg. pulmonary diseases in 9 cases) which most likely would have caused periods of stress.

Any alterations in desquamation, hyperemia and depleted follicles found can be taken as stress reactions, possibly due to hypoxemia. Mild fibrosis, as found in many of the glands, occurs because of current or recurrent hypoxemia. All alterations found indicate that the victims have suffered near miss episodes before.

No indications for diseases of the thyroid gland as the cause of death have been demonstrated. The minor changes found within the organ might be considered as common features in cases of SIDS but are by no means a proof of it.

No morphological alterations were found within the thyroid gland that could explain the cause of death.

References

Beckwith JB (1975) Sudden infant death syndrome: a new theory. Pediatrics 55:583–584

Berry PJ (1992) Pathological findings in SIDS. J Clin Pathol 45: 11–16

Finlay FO, Rudd PT (1993) Current concepts of the aetiology of SIDS. Br J Hosp Med 49:727–732

Gibson AAM (1992) Current epidemiology of SIDS. J Clin Pathol 45:7–10

Gray ES (1987) The endocrine system. In: Keeling JW (ed) Fetal and neonatal pathology. Springer, Berlin Heidelberg New York, pp 429–452

Hesselberg C (1910) Die menschliche Schilddrüse in der fötalen Periode und in den ersten 6 Lebensmonaten. Frankf Z Pathol 5:322–350

Isenschmid R (1910) Zur Kenntnis der menschlichen Schilddrüse im Kindesalter. Frankf Z Pathol 5:214–254

Keeling JW (1981) Sudden Infant Death Syndrome and non accidental injury. In: Berry CL (ed) Pediatric pathology. Springer, Berlin Heidelberg New York, pp 671–678

Krinskaja VI (1932) Zur Frage der Struktur der Neugeborenenschilddrüse. Frankf Z Pathol 43:41–43

Krous HF (1984a) A necropsy study of petechiae in non-sudden infant death syndrome. Arch Pathol Lab Med 108:75–76

Krous HF (1984b) The microscopic distribution of intrathoracic petechiae in sudden infant death syndrome. Arch Pathol Lab Med 108:77–79

Krous HF (1988) Pathological considerations of sudden infant death syndrome. Pediatrician 15:231–239

Krous HF (1989) The pathology of sudden infant death syndrome. In: Cubertson JL (ed) Sudden Infant Death Syndrome: medical aspects and psychological management. John Hopkins University Press, Baltimore, pp 18–47

Lagercrantz H (1989) Plötzlicher Säuglingstod. In: Bachmann KD, Ewerbeck H, Kleihauer P, Rossi D (eds) Pädiatrie in Praxis und Klinik, Vol. I. Thieme, Stuttgart, pp 362–365

Müller E, Rämsch R (1966) Schilddrüsenbefunde bei Tot- und Neugeborenen. Frankf Z Pathol 75:425–431

Naeye RL (1976) Brainstem and adrenal abnormalities in the sudden infant death syndrome. Am J Clin Pathol 66:526–530

Naeye RL (1989) New brainstem and bone marrow abnormalities in victims of the sudden infant death syndrome. J Perinatol 9: 180–183

Risse M, Weiler G (1984) Histologische Schilddrüsenbefunde beim Neugeborenen und Säugling unter besonderer Berücksichtigung des plötzlichen Säuglingstodes. Z Rechtsmed 92: 205–213

Risse M, Weiler G (1990) Altersabhängige morphologische Schilddrüsenbefunde beim plötzlichen Kindstod. Z Rechtsmed 103:307–312

Risse M, Weiler G, Benker G (1986) Histologische und hormonelle Untersuchungen der Schilddrüse unter besonderer Berücksichtigung des plötzlichen Kindstodes (SIDS). Z Rechtsmed 96:31–38

Sachs L (1984) Angewandte Statistik: Anwendung statistischer Methoden. Springer, Berlin Heidelberg New York, pp 300–344

Schröder S, Dralle H, Bay V, Böcker W (1989) Immunhistologie und Prognose beim Schilddrüsenkarzinom. Bestimmung des Malignitätspotentials papillärer und medullärer Neoplasien durch S-100-Protein und Leu-M1-Antigen-Nachweis. Acta Med Austriaca 16:2–5

Schröder S, Bay V, Dumke K, Kremens B (1990) Diffuse sclerosing variant of papillary thyroid carcinoma. S-100 protein immunochemistry and prognosis. Virchows Arch [A] 416:367–371

Schulte FJ (1988) Sudden Infant Death Syndrome. In: Schulte FJ, Spranger J (eds) Lehrbuch der Kinderheilkunde. Gustav Fischer, Stuttgart New York, pp 211–212

Sugiyama S (1967) Histological studies of the human thyroid gland observed from the viewpoint of its postnatal development. Ergeb Anat Entwicklungsgesch 39:7–72

Valdes-Dapena M (1992) The Sudden Infant Death Syndrome: pathologic findings. Clin Perinatol 19:701–716

Wegelin C (1926) Schilddrüse. In: Henke F, Lubarsch O (eds) Handbuch der speziellen pathologischen Anatomie und Histologie, Vol VIII, Springer, Berlin Heidelberg New York, pp 1–680

Wilske J (1993) Zur Definition und Pathophysiologie des plötzlichen Säuglingstodes. In: Kruse K, Oehmichen M (eds) Plötzlicher Säuglingstod. Hansisches Verlagskontor, Lübeck, pp 7–18