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Evaluation of the Reid index in infants and cases of SIDS

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Abstract The Reid index is an instrument for the evaluation of chronic bronchitis. The thickness of the mucosa and of its gland layer are measured and the relationship is expressed as a gland/wall ratio. Specimens were obtained from 124 autopsies from the German National Study on SIDS (GeSID). The cases were divided into three groups: group 1 typical SIDS ($n=47$), group 2 SIDS with signs of mild inflammation of the respiratory tract ($n=50$) and group 3 unnatural death controls ($n=23$). The Reid index was measured in sections from the trachea, bifurcation/main bronchi and bronchioli (staining HE and PAS). The Reid index was remarkably constant throughout the different levels of the respiratory tract (standard deviation range 0.06–0.10). A comparison of the three groups did not show statistically significant differences. Group 1: mean Reid index trachea 0.37, bifurcation/main bronchi 0.38, bronchioli 0.39. Group 2: mean Reid index trachea 0.40, bifurcation/main bronchi 0.38, bronchioli 0.38. Group 3: mean Reid index trachea 0.39, bifurcation/main bronchi 0.38, bronchioli 0.41. It can be concluded that the dimensions of bronchial glands do not vary in cases of SIDS as compared to controls. This demonstrates that the Reid index has no significance in the vast majority of SIDS cases and that acute inflammation commonly does not produce an elevated Reid index. In addition, the Reid index was confirmed to be a valid instrument to study the respiratory tract including the trachea due to its stability and it was found that the Reid index is age-dependent: compared to adults, the ratios in infants were higher.

Keywords Reid index · SIDS · Respiratory tract · Chronic bronchitis

Introduction

The Reid index [7] is a well established instrument used for the histological diagnosis of chronic bronchitis. The thickness of the mucosa and of its gland layer are measured and the relationship is expressed as a gland/wall ratio. The Reid index was criticised later [2, 3, 8] but is still considered a useful yardstick in the diagnosis of chronic bronchitis [6, 11].

In addition to dysfunctions of the central nervous system and cardiac dysregulation [1], respiratory insufficiency due to infections or atypical immune reactions have been discussed as possible causes of SIDS. Although chronic bronchitis is very uncommon in this age group, a possible correlation between the dimension of the bronchial glands and the incidence of SIDS could be caused by hypertrophy of the glands or uncommon types of inflammation. Therefore, the Reid index was determined in infants for the first time and the Reid indices in a large number of fatalities from SIDS were compared to those in a control group.

Materials and methods

The material was collected from several German Institutes of Legal Medicine participating in the German National Study on SIDS (GeSID) [4]. In each case a full history, autopsy findings, full histology, toxicology and microbiology were available.

The cases were divided into three different subgroups which were matched for age and show similar distributions concerning gender:

- Group 1 ($n=47$, 16 females, 31 males): cases identified by 3 different pathologists as typical SIDS. The mean age was 128 days, range 10–322 days.
- Group 2 ($n=50$, 24 females, 26 males): the 3 pathologists indicated SIDS as the cause of death but described a mild acute inflammatory disease of one or more sites in the respiratory tract (rhinitis, pharyngitis, tonsillitis, otitis media, tracheitis or bronchitis). The mean age was 134 days, range 8–353 days.
- Group 3 ($n=23$, 9 females, 14 males): control group of unnatural deaths (6 cases of suffocation, 4 of shaken infants, 3 of cranio-cerebral injuries, 2 of drowning and 8 other causes). The mean age was 127 days, range 25–348 days.

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Table 1 Group 1 (47 cases)

Specimen	Mean Reid index	Min./max. Reid index	Standard deviation
Trachea ($n=44$)	0.37	0.20–0.55	0.08
Bifurcatio ($n=39$)	0.38	0.27–0.51	0.06
Bronchioli HE ($n=36$)	0.39	0.27–0.60	0.08
Bronchioli PAS ($n=25$)	0.36	0.28–0.49	0.06

Table 2 Group 2 (50 cases)

Specimen	Mean Reid index	Min./max. Reid index	Standard deviation
Trachea ($n=50$)	0.40	0.23–0.61	0.07
Bifurcatio ($n=47$)	0.38	0.22–0.58	0.07
Bronchioli HE ($n=41$)	0.38	0.22–0.58	0.06
Bronchioli PAS ($n=36$)	0.36	0.26–0.51	0.06

Table 3 Group 3 (23 cases)

Specimen	Mean Reid index	Min./max. Reid index	Standard deviation
Trachea ($n=19$)	0.39	0.24–0.60	0.08
Bifurcatio ($n=18$)	0.38	0.25–0.54	0.07
Bronchioli HE ($n=19$)	0.41	0.17–0.58	0.10
Bronchioli PAS ($n=19$)	0.37	0.16–0.52	0.10

The following sites in the respiratory tree were sampled: transverse sections of the trachea, bifurcation/main bronchi and bronchioli. Paraffin sections were cut at 7 μ and stained with haematoxylin and eosin (HE) and, in the case of the bronchioli with periodic acid-Schiff (PAS).

The gland/wall ratio was determined by measuring the diameters of both the bronchial wall from the inner aspect of the perichondrium to the basal membrane of the epithe-

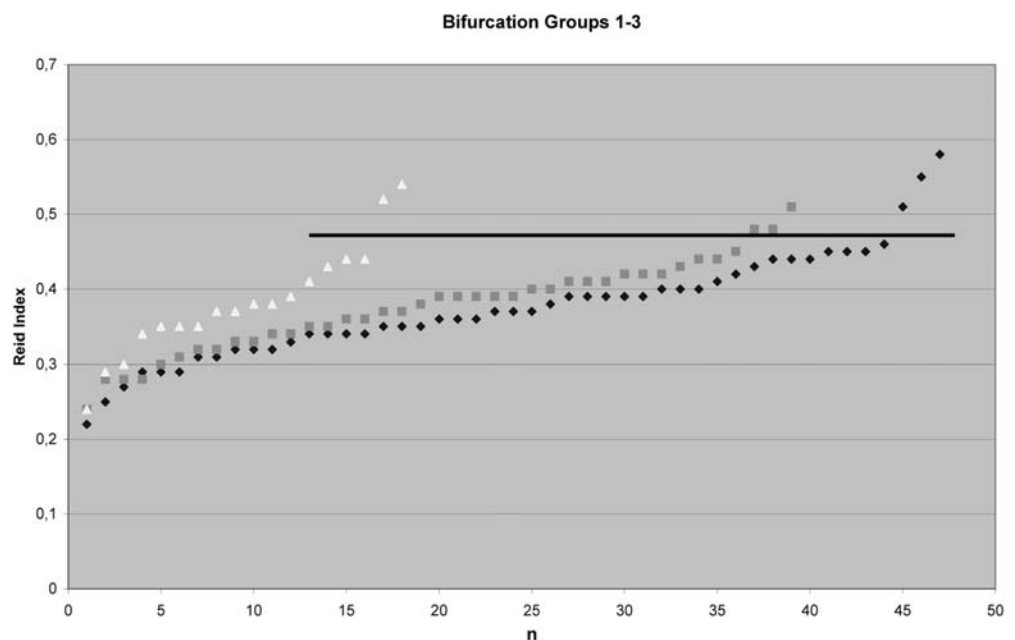
lium and of the bronchial gland layer in that plane. Sites where the mucosa and the cartilage were parallel were chosen [2, 3]. The number of measurements per slide commonly was 10 because it has been shown [5] that this number is sufficient to duplicate the results of volumetric measurements [9, 10, 11]. After choosing the field by optic microscopy (magnification 10 \times), the image was recorded by a colour video camera (Sony Trinitron) and analysed on a PC by Hipax Diocom 3 medical imaging software. A statistical analysis of the mean ratios was performed.

Results

The results of the morphometric measurements are depicted in Tables 1, 2 and 3. The mean Reid index varied from 0.36 to 0.41 and the standard deviation from 0.06 to 0.10. There was no statistically significant difference between groups 1, 2 and 3. The distribution of the individual index values is exemplified in Fig. 1 for one anatomical site (bifurcation/main bronchi). In all three groups, the distribution was unimodal and there was no tendency of age or gender preference. A special analysis of the outlying groups also did not yield any indication of age or gender preference but the histology of the upper outliers ($n=8$, marked in Fig. 1) showed some irregularities as follows:

- Acute leucocyte-rich inflammation in one control case (bleeding, group 3)
- Pronounced oedema without cell increase in one control case (shaken infant, group 3)
- Acute inflammation with interstitial oedema and focal leucocyte infiltration in two cases (group 2)
- Proliferative inflammation with increase of fibroblasts, myoblasts and macrophages in one case (group 2)
- Hypertrophy of the internal muscle layer without cell increase in one case (group 1).

Fig. 1 The distribution of the individual Reid indices exemplified for bifurcation/main bronchi. Group 1 *grey squares*, group 2 *black squares*, group 3 *triangles*. The highest outliers in the three groups located above the horizontal bar ($n=8$) were analysed in detail



Discussion

The standard deviation of the mean Reid index was low in all three groups and at every anatomical level investigated. Also, the mean Reid indices remained constant independent of the anatomical site. This demonstrates that the Reid index is stable throughout the respiratory tree even including the trachea, where the Reid index had not been determined before.

Reid [7] originally compared a group of patients having a clear clinical diagnosis of chronic bronchitis with a control group. Reid was able to discriminate between controls (mean ratio 0.26, range 0.14–0.36) and bronchitics (mean ratio 0.59, range 0.41–0.79) and thus determined a cut-off value of 0.41. Successors could not determine a precise cut-off value due to considerable overlapping [3, 5, 8, 9, 12] but the mean value was always higher in bronchitics [9, 10].

Compared to Reid's cut-off value of 0.41, the mean Reid indices of the three subgroups in this study were lower but there were Reid indices in every group and at every anatomical site which clearly surpassed 0.41 (Fig. 1). In addition, the mean Reid indices in this infant study (0.36–0.41) were higher than those of adult control groups which varied from 0.14 to 0.36 [7]. It can therefore be concluded that the Reid index is age-dependent. The mean Reid index tends to be higher in infants than in adults, which is probably due to anatomical characteristics of infants such as megalosplanchny.

The mean Reid index in the control group was not statistically different from those in the two SIDS-groups. This demonstrates that morphometric changes of the bronchial glands and thus the Reid index itself have no significance in the vast majority of SIDS cases. A small group of upper outliers is associated with pathological findings either indicating acute dysregulation (oedema) or inflammatory processes but these were also present in the control group. Furthermore, the mean Reid indices of groups 1 and 2 were not statistically different. It can therefore be concluded that acute inflammation of the respiratory tract commonly does not produce major morphometric changes of the glands.

Conclusions

Irrespective of age, the Reid index is suitable for morphometric investigations of the complete respiratory tract but there is a higher ratio in infants for anatomical reasons. Neither acute inflammatory changes nor death from SIDS are commonly associated with morphometric changes of the bronchial glands.

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