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Post-Intubation Tracheal Stenosis - Morphological-Clinical Investigations

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The authors observed 42 patients with post-intubation tracheal stenosis who had been treated surgically. The report presents late morphological lesions within the trachea that constituted the causes of such stenosis.

Introduction

Tracheal stenosis often has an iatrogenic origin and results from artificial ventilation combined with intubation or tracheostomy employed as a life-saving, emergency procedure. In spite of a considerable improvement in the conditions of managing patients with life-threatening conditions, the issue of tracheal stenosis is ever present, although investigators both in Poland and abroad are reluctant to engage in clinical and pathomorphological discussion on the subject [11]. The incidence of post-intubation tracheal stenosis in patients on prolonged controlled ventilation is estimated as occurring in 0.1 - 20% of chronic intubation cases [18, 30]. Usually patients report to a physician when the stenosis involves approximately 70% of the normal tracheal lumen, and thus the lower incidence value refers to symptomatic individuals that usually require surgical treatment, while the remaining ones represent patients with stenosis of lesser degrees [3, 6]. Other causes of tracheal stenosis may involve a direct injury or be a consequence of an external compression of the trachea as a result of a neoplastic or inflammatory process; such cases have been excluded from the investigated series.

One should also bear in mind that in numerous patients, especially in those with lower degrees of stenosis, the establishment of an appropriate diagnosis is difficult and such individuals are often incorrectly treated for bronchial asthma, chronic bronchitis or respiratory and circulatory insufficiency. This is why in patients who report intubation in the past the physician should always consider the possibility of tracheal stenosis [18, 29].

Material and Methods

In the period between 1997 and 2000, 46 patients with post-intubation tracheal stenosis were managed surgically at the Thoracic Surgery Ward, John Paul II Hospital of Kraków [25]. In 38 cases the authors succeeded in obtaining complete clinical information on the course of the disease. The patients ranged in age from 4 to 71 years of life. The cause of original intubation was most often multiple trauma (8 cases), head injury (5 cases), myocardial infarction and circulatory arrest (5 cases) and acute pancreatitis (3 cases). In addition, intubation resulted from shock (1 case), post-medication shock (1 case), diabetic coma (1 case), viral meningitis (1 case) and injuries defined as traffic accidents (13 cases).

The mean duration of intubation was 17 days, ranging from 4 to 65 days. The time interval between primary intubation and resolution of stenosis oscillated between 3 weeks to 2 years (mean, 24 weeks).

The operation consisted in excision of the stenosed tracheal segment, 1cm to 4cm in length. The internal diameter of the stenotic segment was 3mm to 10mm. The remaining tracheal fragments were anastomosed end-to-end. The postoperative course was uneventful and the patients demonstrated a clear improvement in tracheal patency and resolution of clinical symptoms.

The excised stenotic tracheal segment was fixed in formalin; the entire material was embedded in paraffin and the sections were stained with hematoxylin and eosin.

In histologic examination, the material revealed numerous characteristic lesions. The predominant cause of stenosis of the tracheal lumen was a considerable thickening of the mucosa and submucosa, while the surrounding cartilage was intact. The thickening resulted from a markedly increased amount of fibrous tissue, which in this location had undergone hyalinization. The mucosa, which is normally smooth within the trachea, showed clear wrinkling, what was interpreted by some authors as polyps (Fig. 1). Irrespectively of the time lapse after intubation, the mucosa demonstrated

extensive ulceration, with ulceration foci devoid of epithelium and layered with granulation tissue with numerous small capillary vessels and various infiltrating cells, mostly neutrophils (Fig. 2). In addition, the tracheal sections showed old ulceration sites, also devoid of epithelium, which we defined as decubitus sores characterized by a considerable proliferation of connective tissue fibers, hyalinization and the presence of focal clusters of thin-walled blood vessels layered with endothelium, but showing a scant amount of inflammatory cells. In the majority of cases, the thin-walled vessel were sinusoidally distended and resembled cavernous hemangiomas. Within these lesions, which we termed "decubitus sores", there was observed inflammatory infiltration predominantly containing infrequent lymphocytes and plasma cells. The margin of ulceration and decubitus sore often demonstrated squamous cell metaplasia of the stratified glandular epithelium - in the later phase, the same type of epithelium often covered the resected segment (Fig. 2) - as well as regenerative lesions of the re-epithelization type noted at some locations, within which the glandular epithelium was flattened and devoid of the cilia. In some cases one could observe cystic distension of the tracheal mucous glands; the glands themselves were additionally atrophic (Fig. 3). We believe the distension of the glands to result from hindered drainage in consequence of connective tissue proliferation, edema and inflammatory infiltration. The distended glands, similarly as the aforementioned sinusoid blood vessels, could also have contributed to the tracheal stenosis.

The above-mentioned lesions leading to segmental tracheal stenosis mostly involved the mucosa and submucosa. Oftentimes, also the deeper elements of the tracheal wall were involved, mostly the tracheal cartilage and tissues situated outside the cartilage. The cartilage itself demonstrated degenerative lesions and ossification, seen mostly in younger patients in the third decade of life; at times bone marrow tissue was present within the ossification foci (Fig. 4). In some cases one could also note cartilage wrinkling resulting from scar contraction, what clearly potentiated the stenosis of the examined tracheal segment (Fig. 5).

In some cases the cartilage showed clusters of distended, thin-walled vessels filled with blood without any concomitant inflammatory infiltration (Fig. 6). Fibrosis, hyalinization and clusters of sinusoidally distended blood vessels were seen in some instances also outside the cartilage. The presence of recent hemorrhages, edema and congestion, which were often encountered in the investigated specimens, is difficult to interpret, since some of these lesions may indicate chronic inflammation or else result from a surgical injury during tracheal resection.

Morphological-clinical correlation

Ulcerations with granulation tissue layering their fundus were seen chiefly in patients, in whom the time interval between the original intubation and the resection of the stenotic tracheal segment was short (12 - 18 weeks), but at times such phenomena were also encountered after a longer interval (above 30 weeks). Abundant, chronic inflammatory infiltration was noted within the stenotic segment as late as two years after the intubation.

Fibrosis and hyalinization were demonstrated mostly in patients in whom the time between the onset of tracheal stenosis and the excision of the stenotic segment was prolonged, although in a specimen collected from an individual operated on 4 weeks following the onset of stenosis (the shortest interval in the investigated group), the predominant feature was the proliferation of connective tissue, while the inflammatory infiltration was scant.

A more clear association seems to occur between the duration of intubation itself and the morphological presentation. In patients intubated for longer periods, histology revealed mostly intense inflammatory infiltration with ulceration and granulation tissue.

The presence of distended blood vessels in the investigated material seems to be independent of the duration of intubation and the interval between intubating the patient and the surgical resection of the stenotic tracheal segment. Numerous sinusoidally distended vessels filled with blood were observed both in cases with predominant recent inflammatory lesions and in specimens with predominant fibrosis and hyalinization.

Discussion

Reports on post-intubation tracheal stenosis and its management describe both isolated cases [1, 5, 7, 10, 20, 21, 28] and larger series of patients originating from centers involved in surgical treatment of such complications, also dealing with pediatric patients [2, 12, 18, 32, 35].

The etiology of post-intubation tracheal stenosis is probed into numerous publications, but to-date has not been fully elucidated. Various authors consider mechanical damage to the tracheal mucosa, and especially compression and ischemia-associated necrosis of the stenotic segment, to be the main cause of stenosis [2, 18]. Nevertheless, also such issues are taken into consideration as local infections, low blood pressure in the period of intubation, steroid administration, sensitivity of the patient to the employed intubation materials and chemical agents used to sterilize the intubation tube, as well as an individual idiosyncratic reaction [7, 16, 17, 24]. Some authors suggest a role played by aspirated gastric juice, what has been confirmed in experiments performed in dogs [21]. Balluch [4] believes the cause of tracheal stenosis to be a transient, acquired deficit of fibrin-stabilizing factor XIII. Fishman et al. [12] emphasize the role of appropriate patient care in the case of intubated individuals, the use of sterile gloves and catheters, as well as decreasing the pressure in the intubation balloon for 5

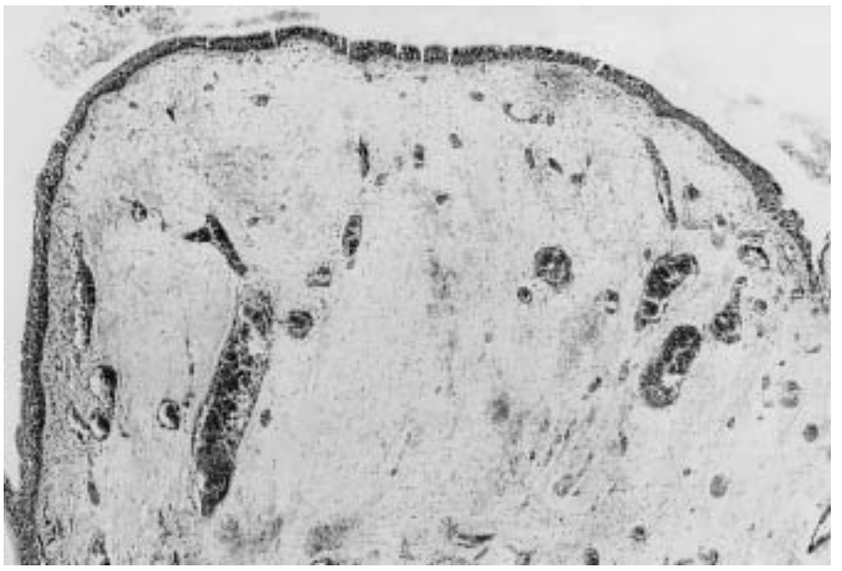

Fig. 1. A polypoid fragment that narrows the tracheal lumen, layered predominantly with glandular stratified epithelium with hyalinized stroma showing numerous thin-walled, sinusoidally distended blood vessels. HE.

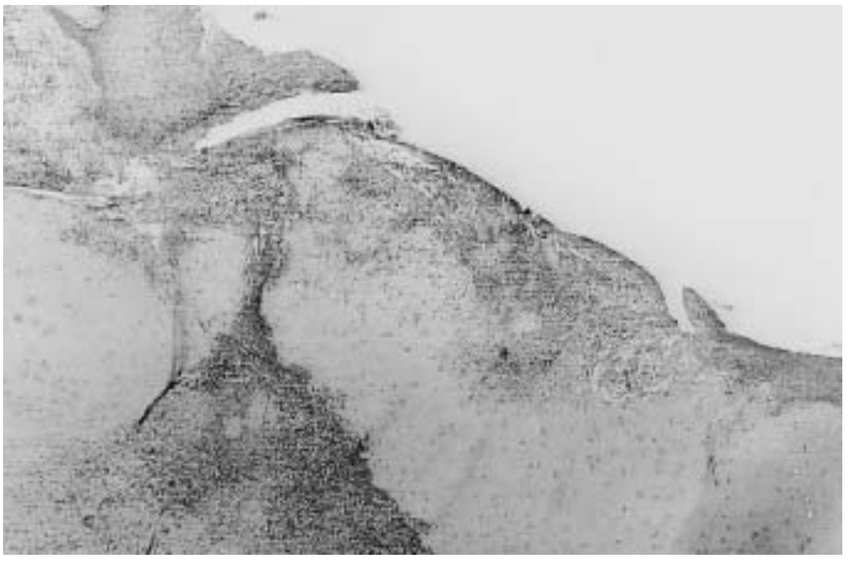

Fig. 2. Tracheal ulceration with an extensive, polymorphous inflammatory infiltration involving the adjacent tracheal cartilage. In the marginal zone note the epithelial layer showing squamous cell metaplasia. HE.

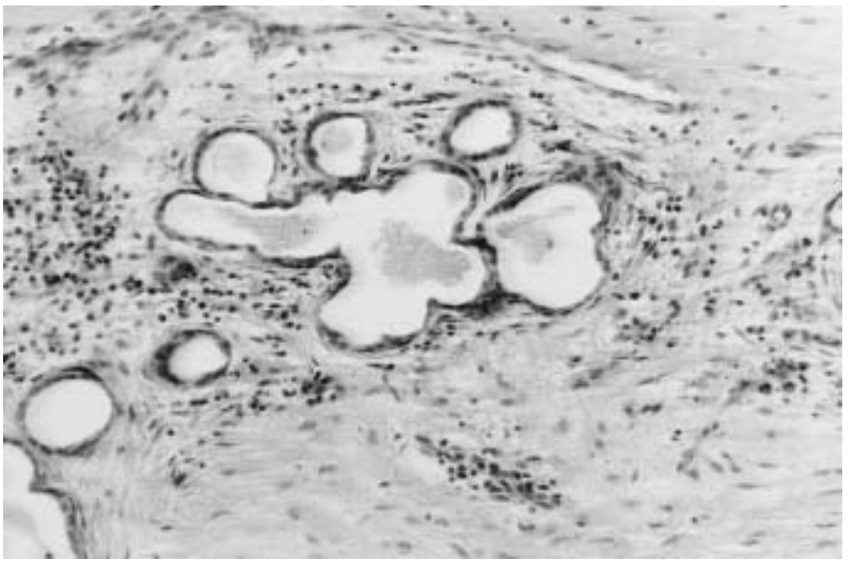

Fig. 3. Distended glands within the tracheal wall are filled with mucus and surrounded by fibrous tissue. Note a scarce chronic inflammatory infiltration in the vicinity of the glands. HE.

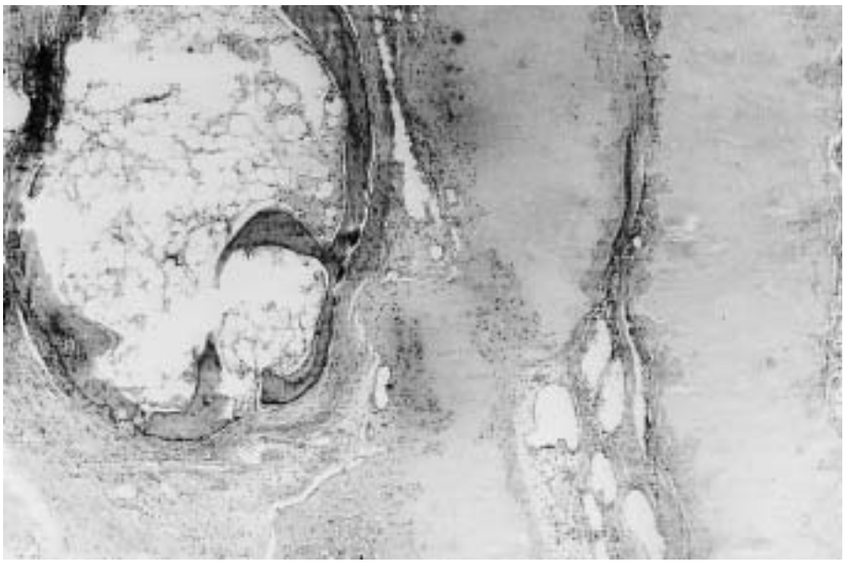

Fig. 4. Tracheal cartilage with ossification and bone marrow foci. Note numerous thin-walled blood vessels adjacent to the deformed cartilage. HE.

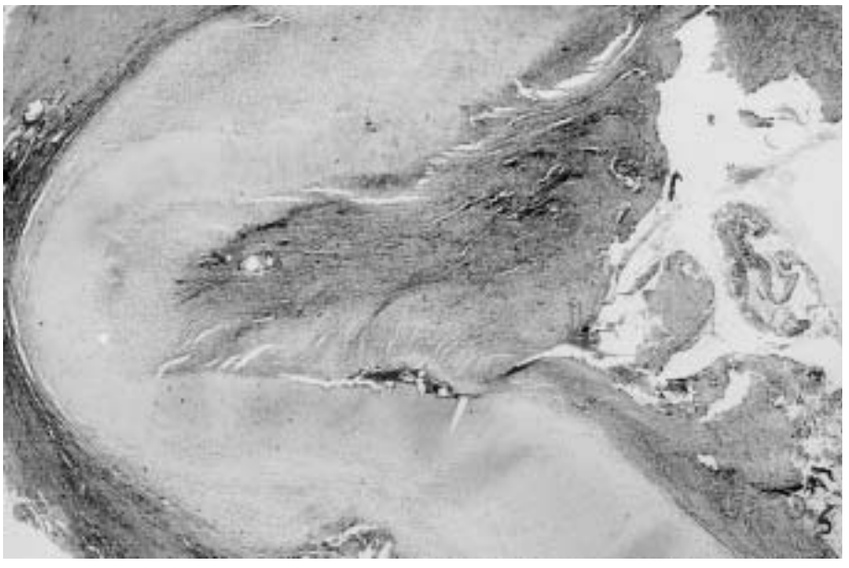

Fig. 5. Tracheal cartilage wrinkling resulting from contraction of a post-ulceration scar (a common cause of tracheal stenosis). HE.

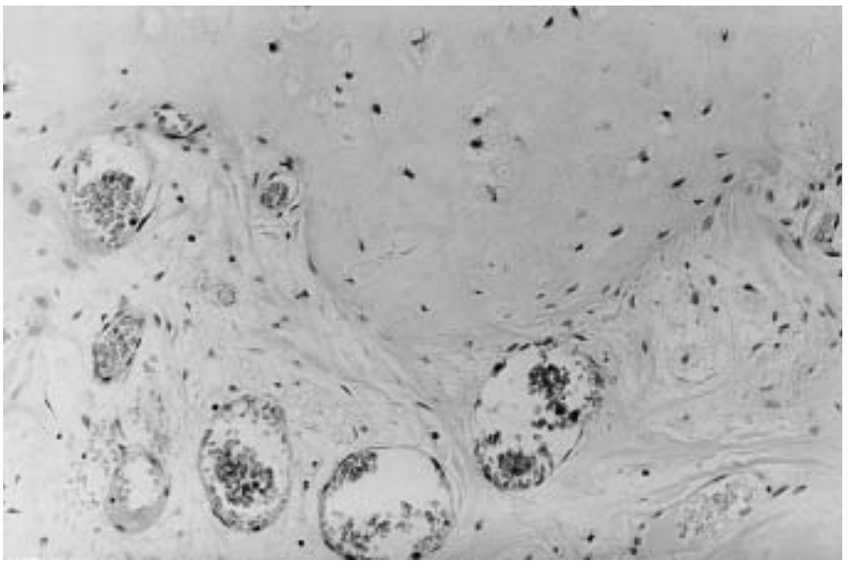

Fig. 6. A fragment of the submucosa with numerous thin-walled, sinusoidally distended blood vessels that grow into the tracheal cartilage. HE.

minutes every hour combined with controlling the pressure within the balloon (the value should not be too high). To explain the etiology of tracheal stenosis numerous experimental studies have been carried out in animal models [8, 21, 22, 24, 27, 33, 34], wherein the investigators have observed similarities between lesions encountered in animals (dogs and rabbits) and in humans.

Zagalo et al. [35] performed statistical studies in a series of 20 patients and demonstrated that there was no statistical correlation between the length of the stenotic tracheal segment and the duration of intubation, as well as between the time lapse since intubation and the onset of stenosis. Dikkers [10] presented a case of tracheal stenosis developing 20 years after intubation, but early lesions, occurring after 10 - 12 hours, have been also reported [2]. In the material described by Zagalo et al. [35] no correlation was demonstrated between the extent of lesions and the age of the patient, yet the authors presented 20 patients only and the group seems not to be sufficiently large to allow for unequivocal statistical analysis.

In early post-intubation tracheal lesions one can observe mostly the mucosa being turned ischemic, as well as edema, congestion, hemorrhages and traces of fibrinous exudate [2]. In the majority of cases these lesions promptly regress within 12 to 48 hours. According to Stein et al. [31], they are the most pronounced in the first week, and subsequently undergo gradual regression. Nevertheless, some patients often manifest deep focal ulcerations with subsequent healing; the latter may be asymptomatic, but in a part of patients it may lead to cicatrical stenosis of the trachea. An undoubtedly significant issue is the duration of intubation - the longer the procedure lasts, the greater likelihood of tracheal wall damage and subsequent stenosis; nevertheless, it is impossible to abandon intubation in patients with life-threatening conditions [2, 31]. Yang [36] described tracheal stenosis that developed as early as after 24 hours of intubation. Spittle and Beavis [28] believed that generally each intubated patient should be taken into consideration and examined as potentially at risk of tracheal stenosis. Numerous morphological studies on tracheal lesions in intubated patients were also carried out in autopsy materials [24, 31]; these investigations revealed that the tracheal damage was similar to early post-intubation lesions. As it was reported by Stein et al. [31], in such cases the lesions were more common and affected 79% of patients.

According to the literature on the subject, what has been confirmed by our observations, a morphological determinant of delayed tracheal stenosis that occurs later after intubation is the thickening of the mucosa and submucosa. Mucosal ulceration has been always noted in the stenotic tracheal segments [2, 12, 35].

The presented morphological lesions in the trachea show a morphological similarity to lesions observed by one of the authors (BP) in the esophagus and stomach as a consequence of postchemical stenosis, what seems to indicate similar repair mechanisms in chronic damage to the mucosa, regardless where the mucosa is situated.

The investigated material originated from patients who had been intubated in various centers (only two individuals from the group in question were intubated in the same ward), mostly located in the south of Poland (the Małopolskie, Śląskie and Podkarpackie provinces) and central Poland (the Mazowieckie and Pomorsko-Kujawskie provinces), and thus one cannot conclude that only in some hospitals are post-intubation lesions more common in association with inadequate patient care.

The analysis of world literature published within the past two decades indicates that the number of reports on post-intubation tracheal stenosis is lower than it used to be. This fact confirms the improvement of patient care in intensive care units worldwide and in Poland, what allows for avoiding this serious complication, requiring surgery, at least in some percentage of cases.

Apart from resecting a post-intubation stenotic tracheal segment, the management also includes the administration of corticosteroids in the early stages of the disease, as well as laser therapy and stenting in more advanced cases, yet it appears that resection is the best method, although at times recurrent tracheal stenosis is observed and a repeated surgical procedure is required.

References

1. *Ahmad I, Pahor AL:* Post-intubational tracheal stenosis. Hospital Medicine 2000, 61, 508-509.
2. *Albert W, Stasiak K:* Pointubacyjne zmiany histologiczne w tchawicy. Pol Przeg Chir (supl) 1979, 25-30.
3. *Andrews MJ, Pearson FG:* Analysis of 59 cases of tracheal stenosis following tracheostomy with cuffed tube and assisted ventilation, with special reference to diagnosis and treatment. Br J Surg 1073, 60, 208-212.
4. *Balluch H:* Zur Ätiopathogenese der Trachealstenosen nach Langzeitintubation bei Polytraumatisierten. HNO 1983, 31, 395-398.
5. *Bradbeer TL, James ML, Sear JW et al:* Tracheal stenosis associated with low pressure cuffed endotracheal tube. Anaestesia 1976, 31, 504-507.
6. *Brichet A, Verkindre C, Dupont J et al:* Multidisciplinary approach to management of postintubational tracheal stenosis, Eur Respir J 1999, 13, 888-893.
7. *Byrn F, Davies CK, Harrison GK:* Tracheal stenosis following tracheostomy. Brit J Anesth 1967, 39, 171-173.
8. *Cooper JD, Grillo H:* Experimental production and prevention of injury due to cuffed tracheal tubes. SGO 1969, 129, 1235-1241.
9. *Couraud L, Moreau JM, Velly JF:* The growth of circumferential scars of the maior airways from infancy to adulthood. Eur J Cardiothorac Surg 1990, 4, 521-525.
10. *Dikkers FG:* Tracheal stenosis can occur 20 years after intubation. Br Med J 2001, 322, 362.
11. *Ducavage JA, Koriwachak MJ:* Open surgical techniques for laryngotracheal stenosis. Otol Laryngol Clin North Am 1995, 28, 785-795.

12. *Fishman NH, Dedo HH, Hamilton WK et al:* Postintubational tracheal stenosis. Ann Thoracic Surg 1969, 8, 47-57.
13. *Gavilan J, Cerdeira MA, Toledano A:* Surgical treatment of laryngotracheal stenosis: a review of 60 cases. Ann Otol Rhinol Laryngol 1998, 107, 588-592.
14. *Grillo HC:* Circumferential resection and reconstruction of the mediastinal and cervical trachea. Ann Surg 1969, 162, 374-386.
15. *Grillo HC, Donahue DM, Mathisen OJ et al:* Postintubation tracheal stenosis: treatment and results. J Thorac Cardiovasc Surg 1995, 109, 486-489.
16. *Grillo HC, Donahue DM:* Post intubation tracheal stenosis. Seminars in Thoracic and Cardiovascular Surgery 1996, 8, 370-380.
17. *Hawkins DB:* Pathogenesis of subglotic stenosis from endotrachal intubation. Ann Otol Rhinol Laryngol 1987, 96, 116-117.
18. *Juszczyński M, Gąsiorek T, Dziatkowiak A et al:* Niektóre aspekty pointubacyjnych zwężeń tchawicy. PTL 1984, 39, 289-292.
19. *Klainer AS, Turndorf H, Wu WH et al:* Surface alterations due to endotracheal intubation. Am J Med 1975, 58, 674-683.
20. *Kreienbuhl G:* Trachealstenose nach nasotracheal Langzeitintubation mit Plastiktubus mit vorgedehntem (prestretched) Cuff. Anaestesist 1973, 22, 243-244.
21. *Little FB, Koufman JA, Kohut RI, Marshal RB:* Effect of gastric acid on the pathogenesis of subglottic stenosis. Ann Otol Rhinol Laryngol 1985, 94, 516-519.
22. *Marshak G, Doyle WJ, Bluestone ChD:* Canine model of subglotic stenosis secondary to prolonged endotracheal intubation. Laryngoscope 1982, 92, 805-809.
23. *McCaffrey TV:* Management of subglottic stenosis in the adult. Ann Otol Rhinol Laryngol 1991, 100, 90-94.
24. *Miller DR, Sethi G:* Tracheal stenosis following prolonged cuffed intubation. Ann Surg 1970, 171, 283-293.
25. *Papla B, Dyduch G, Olechnowicz H:* Postintubational tracheal stenosis - morphological and clinical study. XV Zjazd Pol Tow Patol. Kraków 21-23 June, 2001. Pol J Pathol 2001, 52, 88(abs).
26. *Sara C:* Histological changes in the trachea and bronchi with tracheostomy. Med J Aust 1967, 1, 35-39.
27. *Shelly WM, Dawson RB, May IA:* Cuffed tubes as a cause of tracheal stenosis. J Throc Cardiovasc Surg 1969, 57, 623-627.
28. *Spittle CSN, Beavis SE:* Post-intubation tracheal stenosis. Hospital Medicine 2001, 62, 54.
29. *Spittle N, McCluskey A:* Tracheal stenosis after intubation. Br Med J 2000, 321, 1000-1002.
30. *Stauffer JL, Olson DE, Petty TL:* Comlications and consequences of tracheal intubation and tracheostomy. A prospective study of 150 critically ill adult patients. Am J Med 1981, 70, 65-76.
31. *Stein AA, Quebral R, Boba A, Landmesser Ch:* A post mortem evaluation of laryngotracheal alterations associated with intubation. Ann Surg 1960, 151, 131-138.
32. *Wiel E, Vilette B, Darras JA et al:* Laryngotracheal stenosis in children after intubation. Report of five cases. Paed Anaesth 1997, 7, 415-419.
33. *Zagalo C, Grande N, Santos J et al:* Experimental autotransplantation of the trachea: structural changes studied in the rabbit with reference to human trachal stenosis. Eur J Anat 2000, 4, 69-81.
34. *Zagalo C, Grande N, Santos J et al:* Tracheal transplantation: cytological changes studied by scanning and electron microscopy in the rabbit. Laryngoscope 2001, 111, 657-662.
35. *Zagalo C, Santiago N, Grande NR et al:* Morphology of trachea in benign human tracheal stenosis: a clinicomorphological study of 20 patients undergoing surgery. Surg Radiol Anat 2002, 24, 160-168.
36. *Yang KL:* Tracheal stenosis after a brief intubation. Anesth Analg 1995, 80, 625-627.

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