Clinical and experimental aspects of tracheal stenosis
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Summary and Conclusions
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Mechanical interventions on the airway, either in the form of surgery or intraluminal distension, have evolved little in their concept over the last decades, although the technological and biological armamentarium has progressed vastly and is still in evolution. Results in terms of mortality have drastically improved and are more than satisfactory; however, morbidity and the inexplicable occurrence of granulation tissue are disappointing.

Efforts at reducing morbidity have therefore been directed towards minimizing granulation tissue, either by adapting surgical technique, suture and repair materials, choice of prosthetic implants, or by topical treatments at the surgical anastomotic site to enhance healing. In this study, many of these aspects were looked at, and the following observations were made:

Congenital tracheal stenosis is a rare but life-threatening disease, presenting in infancy and childhood with varying degrees of clinical and anatomical severity, and whose diagnostic work-up, operative treatment, and postoperative care should involve a committed multidisciplinary team, most appropriately in a tertiary referral center (Chapter 2). The relative rarity of the patients and the dispersed effort in research and clinical experimentation may play a role in the continuing frustrating results (hypothesis). The centralization of referral towards specialized teams and their respective research centers could accumulate knowledge, and implicate the power of numbers and financial resources, to boost the current know-how and improve the results in these difficult, rare and demanding patients (hypothesis).

Congenital vascular rings and pulmonary arterial slings are a relatively more frequent cause of tracheal compression and airway compromise, whose surgical approach and technique are standardized and yield excellent operative and long-term results (Chapter 3a). With an appropriately high index of clinical suspicion, the diagnostic work-up is straightforward and allows for sufficient preoperative information without undue delay or expense, and should lead to prompt surgical correction without the unnecessary hi-tech temptation of modern era imagery (Chapter 3a). In case of doubt with the more rare types of vascular anomalies, however, the available technology should be pursued until a correct surgical approach can be performed with near certainty (Chapter 3b).

Airway narrowing is not uncommonly associated with intracardiac disease or vice versa, and needs to be appropriately assessed prior to cardiac surgery, so as to plan on concomitant
repair in one elective setting (Chapter 4). When reoperation on the airway for recurrent stenosis is deemed difficult or is contraindicated in the presence of an anatomical difficulty, hemodynamic or cardiac instability, or generalized unfavorable condition of the patient, intraluminal tracheal stenting may be considered as a life-saving bail-out measure or as mid-term palliation. This has given good long-term results in selected patients, making it an alternative “treatment” modality (Chapter 4).

Granulation tissue is an omnipresent and apparently unavoidable “complication”, if not the natural history after surgical interruption of the respiratory epithelium. Following the hypothesis that an improvement of local blood supply at the time of surgical insult to the tracheal wall could enhance healing, and hence reduce postoperative granulation tissue, an animal model tested an experimental angiogenic substance, vascular endothelial growth factor (VEGF) (Chapter 5). When applied to the trachea of rabbits during surgery, topical pretreatment with VEGF resulted in improved local healing of the tracheal wall, as assessed histologically by reduced inflammation, edema, and absence of granulation tissue, as compared to controls (Chapter 5).

Various repair materials and intraluminal stents are used in clinical surgical practice to perform tracheal repair or achieve airway patency. The relative efficiency of repair or stenting was compared histologically in a rabbit model, with regards to pretreatment with topical VEGF (Chapter 6). Autograft patch repair, namely the use of autologous trachea as patch material, resulted in the best healing pattern, further enhanced by topical VEGF, as compared to xenopericardium or intraluminal stents. The diffuse granulation tissue and fibrosis after stent insertion resulted in premature death of all animals studied, and was unhindered by topical VEGF. Finally, besides the topical VEGF treatment, local VEGF production by the tracheal wall is not excluded, probably in plasmocytes and in submucosal glands, and whose role in healing and prevention of granulation tissue remains to be determined (Chapter 6).

Extensive lesions of the trachea that preclude repair may need to be bridged by synthetic prostheses, when allografts are unavailable or unsuitable. A new composite silicone-metallic prosthesis with a biocompatible inner lining was tested in a rabbit experimental model, and produced satisfactory temporary results in some of the rabbits. Overgrowth of epithelium did occur on the biocompatible inner lining, but not extensively or in an organized fashion, leaving the possibility for granulation tissue to occur (Chapter 7). Improvements in prosthesis design
and in the biocompatible lining are still in order, before clinical application is deemed safe (Chapter 7).

The repair or replacement of the airway remains a formidable challenge, despite the tremendous amount of progress made, both in terms of diagnostic workup, peri-operative management, surgical technique, and the innovative research done in materials and adjuncts to healing. After initial satisfactory clinical results, the mid to long-term problems of recurrent stenosis and the need for reoperation illustrate the improvements which still remain to be achieved. Classical repair materials remain relevant in that they are easy to use, readily available, and whose healing may be favorably influenced by the adjunct of topical growth factors such as VEGF. When repair is not feasible in more extensive lesions, the optimal means for replacement of the airway remains to be found. All fully synthetic tracheal prostheses developed to date have a long list of immediate or latent failures. The role of inert synthetic materials in prostheses should be questioned, and their use should probably be altogether abandoned in the ideal bioengineering future (hypothesis).

Biocompatibility and namely bioactive coatings represent a tremendous promising step in reconstruction not only of the major airway, but in other organs as well. Along these lines, future development involves total replacement of the major airway by biological compounds, by xenograft cell cultures of chondrocytes on sheets of biodegradable polyglycolic acid (PGA), or by autologous human fetal chondrocytes seeded on PGA, amongst others, to create high-quality cartilage constructs. Continuing research is still required to enhance the initial spectacular results, both towards a strive for its use in human trials, and to render the as of yet cumbersome and costly process of tissue bioengineering more available and readily applicable.

References