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General Summary

Our basic and clinical studies have examined: the pathogenesis of cholesteatoma and adhesive otitis media, surgery of the middle ear, navigation medicine, space motion sickness, nasal allergy, endoscopic endonasal sinus surgery, sleep apnea syndrome, and deglutition reconstructive surgery for head and neck tumors.

Research Activities

Otology

We have conducted a basic experiment on regeneration of the middle ear mucosa, which plays an important role in the improvement after middle ear surgery, and a study aimed at clinical applications. We have been developing our own navigation system that uses virtual reality with the aim of safely performing surgery of the middle ear and the petrous pyramid. We have used the records of cholesteatoma operations, approximately 200 of which are performed annually, to create a database, have analyzed the pathology and surgical procedures, conducted an epidemiological survey, and evaluated the postoperative results. In otology, we have conducted a study of internal-ear lesions in metabolic diseases in experimental animals, and we have carried out a genetic analysis of patients with otosclerosis in collaboration with Shinshu University.

Cochlear implant surgery continues to be performed. Surgery for lesions of the base of the cranium, such as cholesteatoma of the pyramidal area and internal auditory meatus, is performed in cooperation with the Department of Neurosurgery to preserve hearing and facial nerve function. Approaches across the posterior cranial fossa, middle cranial fossa, or labyrinth are employed, depending on the case.

We have been measuring changes in total middle ear cavity pressure associated with transmucosal gas exchange in relation to the duration of intubation for secretory otitis media and have been deciding on the timing of extubation.

In studies of equilibrium, we have been cooperating with the Department of Neuropsychiatry in an analysis of dizziness after ingestion of ultra-short-acting and short-acting sleep-inducing agents. Dizziness was quantitatively measured with a GANGAS mobile analyzer (T & T medilogic Medizintechnik GmbH, Schoenefeld, Germany) and the film-type pressure sensors Huge-Mat and Mat-Scan (Nitta Corp., Osaka), and we have been continuing to demonstrate associations with drug concentrations in the blood and with drowsiness caused by sleep-inducing agents. In addition, we are analyzing the

results of experiments demonstrating relationships between fingertip contact pressure and posture control by means of a mobile analyzer that utilizes a force plate and analysis software.

We are assessing methods of treating patulous Eustachian tube which achieve long-term therapeutic results, such as treating the pharyngeal orifice with salicylic acid, insertion of Gelfoam or Merocel into the pharyngeal orifice, and physiological saline nose drops.

Rhinology

With the aim of expanding the indications for endoscopic sinus surgery and improving its safety, a high-tech system that superimposes stereoendoscopic images and stereonavigation is under development. We have also been assessing the involvement of fungi in the development of eosinophilic paranasal sinusitis, which is often refractory. The fungus *Alternaria* induces the production of interleukin 5, interleukin 13, and interferon γ by peripheral blood mononuclear cells isolated from patients with paranasal sinusitis, but no such responses have been observed in cells isolated from healthy subjects. We have also demonstrated that *Alternaria* directly induces activation and degranulation of isolated human eosinophils and that the aspartate protease secreted by *Alternaria* induces various immune reactions mediated by the protease-activated receptor 2 expressed on the surfaces of eosinophils and airway epithelial cells.

A comparative assessment of the association between cell expression type and clinical disease type by means of a comprehensive gene analysis of fibroblasts cultured from the inferior nasal concha of patients with perennial allergic rhinitis and healthy subjects performed to clarify pathogenetic factors in nasal allergy has shown that many of the gene expression patterns differed with the presence or absence of allergy.

We have been studying the relationship between the quality of life of patients with pollinosis and methods of oral administration of antiallergy drugs.

Head and neck cancers

The main constituents of the treatment of cancers of the head and neck are: 1. surgery, 2. radiotherapy, 3. chemoradiotherapy, and 4. radiotherapy combined with super-selective intra-arterial chemotherapy.

1. To perform curative resection designed to maximize preservation of function in cases of advance cancer, reconstruction is performed with free flaps (rectus abdominis flaps, free jejunal grafts, anterior axillary flaps, and anterolateral thigh flaps). In addition to performing reconstruction (50 to 60 cases a year), we perform partial laryngectomy for postradiotherapy recurrences (T2 to T3 cases) and strive to preserve as much of the larynx as possible.

2. Radiotherapy is primarily used to treat early cancers on an outpatient basis. In some cases chemoradiotherapy is performed by adding the oral anticancer agent S-1. In advanced cases, radiotherapy is performed as postoperative adjuvant therapy after surgical treatment.

3. Chemoradiotherapy consists of radiotherapy and simultaneous treatment with cisplatin or 5-fluorouracil as chemotherapy and is followed by adjuvant chemotherapy. Patients selected for chemoradiotherapy have cancer of the middle and lower pharynx or

the cervical portion of the esophagus and cannot undergo larynx-preserving surgery or curative resection.

4. Radiotherapy combined with superselective intra-arterial chemotherapy may be effective in cases in which curative resection is impossible, especially in highly advanced cases, and possible use in our hospital is being considered.

In addition, early diagnosis is an important factor in improving the survival rate of patients with cancers of the head and neck. We are making an effort to detect superficial cancer of the middle and lower pharynx at an early stage by means of narrow band imaging endoscopy (i.e., endoscopy performed with a narrow band filter).

Research on phonation and swallowing function

We have been performing endoscopic outpatient day surgery with flexible endoscopes, as in the past, to treat vocal cord polyps, vocal cord nodules, and vocal cord cysts.

We have also been performing atelocollagen injections as outpatient day therapy for unilateral recurrent laryngeal nerve palsy and have obtained favorable results.

Botulinum therapy, the treatment of first choice for spastic dysphonia, has been approved by the ethics committee of the university. In addition to continuing clinical assessments of diagnosis and treatment, we are assessing surgical therapy for cases in which botulinum therapy fails.

Cooperation with other departments, such as the Department of Neurology and the Department of Rehabilitation Medicine, and teamwork with co-medical staff, including nurses, are necessary to evaluate and treat dysphagia. We have been evaluating cases by means of video endoscopy and videofluoroscopy, assessing treatment policy, and implementing swallowing exercises.

Research on sleep apnea syndrome

We used acoustic rhinometry and rhinomanometry to investigate the effects of nasal breathing disorders on breathing disorders during sleep. Multivariate analysis with the apnea-hypopnea index as an objective variable and with background factors, such as body mass index and age, nasal cavity cross-sectional area, and volume variables as explanatory variables has shown that the apnea-hypopnea index increases as nasal cavity volume decreases, in other words, that breathing disorders during sleep tend to become more severe. Follow-up of children with breathing disorders during sleep who had undergone surgical treatment showed that when 2 or more years had passed since treatment, the maxillofacial morphology of many patients had improved to the standard values of healthy children, suggesting that the breathing disorders during sleep may have affected their maxillofacial morphology. Preoperative and postoperative evaluations in patients who had undergone uvulopalatopharyngoplasty suggested that the cyclic alternating pattern, a new method of analysis that differs from the conventional method of sleep electroencephalographic analysis (Rechtschaffen and Kales rules), is a very sensitive method that identifies arousal responses at the subcortical level.

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