Transmyringical Middle Ear Ventilation

An Experimental Approach to Evaluation of its Benefits
and Consequences

by

OVE SÖDERBERG

1985
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ABSTRACT

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University of Umeå Medical Dissertations
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Ove Söderberg, M.D., Department of Otolaryngology & Head and Neck Surgery, University of Umeå, S-901 85 Umeå, Sweden

A prerequisite for a functioning middle ear is an air-filled middle ear cavity. Aeration of the middle ear cavity is controlled by the Eustachian tube. Dysfunction of the Eustachian tube has long been acknowledged as a significant etiological factor in disorders of the middle ear, especially middle ear effusions. Artificial ventilation of the middle ear through the tympanic membrane has been practised for almost two centuries, but with varying degrees of success. In 1954, Armstrong reintroduced the method of inserting a transmyringeal tympanostomy tube into the ear drum. Since that time this ventilatory device has gained wide popularity and several types of tube have been designed. However, an increasing number of clinical reports have shown treatment with tympanostomy tubes to be followed by complications such as tympanosclerosis, atrophy, persistent perforations and cholesteatomas.

In the present thesis, experiments were outlined in which the tympanostomy tube - tympanic membrane interaction was studied and in which tympanostomy tubes were also applied in a well-defined type of otitis media. Furthermore, alternative transmyringeal ventilatory procedures such as myringotomies with a delayed healing time were investigated. The results were evaluated with morphological and microbiological methods.

Repeated tympanostomy tube insertions in ears of healthy rats caused a remarkable thickening (about 30-fold) of the tympanic membrane of the tubulated quadrants, but even the untouched quadrants were affected. The thickened areas were characterized mainly by an increase in dense connective tissue which also contained sclerotic plaques. The structural changes in the tympanic membrane were still present 3 months after the final ventilation episode.

Cleavage of the rat soft palate caused an immediate accumulation of effusion material in the tympanic cavity due to disturbance of Eustachian tube function. The fluid turned purulent within one to two weeks. The microbial flora of the middle ear cavity correlated well with that of the nasopharynx, indicating an ascending infection. Insertion of a tympanostomy tube could prevent the accumulation of effusion material in the meso- and hypotympanon and significantly suppress bacterial growth in the middle ear cavity.

Thermal energy-inflicted myringotomies were tested as an alternative method for establishing transmyringeal ventilation. Myringotomies performed either with a CO₂-laser or by diathermy showed a delayed healing pattern, most probably due to widespread destruction of the outer keratinized squamous epithelium and damage to the vascular supply. Upon comparison, laser myringotomies appeared more favourable due to their longer closure times, whereas the perforations accomplished by diathermy were often complicated by otorrhea and showed more advanced structural changes.

Key words: Middle ear, tympanic membrane, otitis media, heat myringotomy, laser myringotomy, tympanostomy tube, transmyringeal ventilation.
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ABBREVIATIONS

ET .................................................... Eustachian tube
MEC .................................................. Middle ear cavity
NPH ................................................... Nasopharynx
TM ..................................................... Tympanic membrane
TP ..................................................... Tubulation period
TT ..................................................... Tympanostomy tube
INTRODUCTION

Generally speaking, middle ear function requires an air-filled middle ear cavity (MEC). Ventilation of the MEC is controlled by the Eustachian tube (ET) and dysfunction of the tube has long been acknowledged as a significant cause in disorders of the middle ear, especially of middle ear effusion processes.

The relation between an impaired ET ventilation of the MEC and middle ear disease was recognized as early as 1801 by Sir Astley Cooper. His by now famous paper was entitled "Farther Observations on the Effects which take Place from the Destruction of the Membrana Tympani of the Ear; with an Account of an Operation for the Removal of a particular Species of Deafness." He reported that a small opening in the tympanic membrane (TM) "would be sufficient to admit a free passage of air to and from the tympanum, perhaps a substitute might be thus easily found for the Eustachian tube".

Early in the 19th century, myringotomies became more and more popular for treatment of different kinds of loss of hearing, even those that were due to neurogenic disturbances. Poor results as well as a high frequency of postoperative infections led to disrepute for this surgical procedure. In the 1860s, artificial ventilation by myringotomy was reintroduced following reports by Schwartz and Politzer, among others. For prolonged ventilation of the MEC, Politzer inserted a hard rubber eyelet into the opening of the TM. However, the eyelets and similar devices of silver, aluminium or gold were soon abandoned because of their early extrusion from the ear drum, often in association with suppuration. Another strategy for keeping the MEC ventilated included removal of whole segments of the TM. These large punctures gave way to other operative procedures on the TM, e.g. electrocautery and cautery with acids. These procedures had setbacks comparable to
those in which a foreign body had been inserted into the myringotomy opening.\textsuperscript{1,80,81}

The concept of a permanent opening in the TM for treatment of secretory otitis media was rediscovered by Armstrong. Thus, in 1954 he reported on the use of a vinyl plastic tube, inserted into the TM, for ventilation of the middle ear.\textsuperscript{6} In his original paper the device had been used only in chronic cases that had resisted treatment. The method gained wide popularity and numerous types of ventilating tubes have been reported.\textsuperscript{7,26,38,46,71} To give an idea of their comprehensive use, each year an estimated 2 million tubes are inserted into ear drums of American children.\textsuperscript{72}

However, various complications related to the use of tympanostomy tubes (TTs) have steadily been reported and reviewed.\textsuperscript{10,12,31,42,49,60,67} Tympanosclerosis and atrophic scars are very common after tube treatment in chronic secretory otitis media. Whether or not these pathological changes are due to the underlying disease or to the tympanostomy tube treatment itself has been debated.\textsuperscript{15,58,68,103} Some recent prospective studies on unilateral tube treatment in cases of bilateral secretory otitis media have shown that ears subjected to tube treatment display the previously mentioned TM changes to a significantly higher degree than do intact ear drums.\textsuperscript{15,54,95} Although some of these reports indicate a slightly impaired hearing in the tube-treated ear,\textsuperscript{15,54} the importance of structural changes in the TM as regards auditory function remains to be elucidated. Persistent perforations\textsuperscript{50,51,73} and cholesteatomas\textsuperscript{16,22,25,30,92} have also been reported after tube treatment. During the tubulation period the most common accompanying feature is otorrhea.\textsuperscript{8,9,37}

The TTs were originally applied in the treatment of secretory otitis media. However, they have also been used for the prevention of recurrent purulent otitis media.\textsuperscript{23,89} Their role in preventing bacterial infection of the middle ear has also been studied in animal experiments, but the results are contradictory.\textsuperscript{65,66}
Simple TM perforation (a myringotomy) without insertion of a TT has also been employed in the treatment of secretory otitis media. However, these perforations will usually close spontaneously well before the underlying middle ear disease is cured. Thus it would seem logical to investigate alternative myringotomy methods by which the healing process of the perforation can be delayed. One such method could be the thermal energy inflicted perforation, since it is well known from clinical practice that a welding injury to the TM heals slowly or results in a persistent perforation. Against this background, heat myringotomies have been performed. In the most recent report on this subject it is concluded that this type of myringotomy, adequate in size, should be useful for the treatment of chronic secretory otitis media. However, in none of the clinical studies cited above, has the repair process of or persistent damage to the TM, caused by heat, been characterized.

Studies that can elucidate the possible benefits and consequences of various transmyringeal ventilation procedures are difficult to carry out in man. One reason for this is purely ethical; others are the diversities encountered in clinical treatment of ear diseases. At present, experimental studies in animal models appear to be the only possible approach to this important problem.

The rat has recently gained importance as a suitable animal model for experimental middle ear research. It has been demonstrated that the rat TM shows a great similarity to that of man. Generally speaking, the pars tensa consists of three different major layers. On the outer meatal side there is an epidermal layer of a keratinizing stratified squamous epithelium, 3-7 cells thick. Facing the MEC the TM is covered by a layer of simple squamous epithelium. Interposed between these two epidermal layers lies the lamina propria, a connective tissue layer composed mainly of collagen fibres. The latter are arranged in a pattern of inner circular and outer radial fibres. Not only is the structure of the TM well known, but also its healing pattern after a central traumatic perforation has been carefully
studied in various animals. In brief, a perforation is initially overbridged by a proliferating stratified squamous epithelium exhibiting a marked production of keratin. The epithelium rests on a highly vascularized granulation tissue. Our thorough knowledge of the structure of the TM and its healing properties in the rat model would appear to facilitate an experimental study of the benefits and consequences of various transmyringal ventilation procedures.

AIMS OF THE STUDY

The specific aims of the present study were:

- to determine the consequences for the tympanic membrane structure in a healthy ear of repeatedly inserting a tympanostomy tube;

- to evaluate the benefits of transmyringal ventilation in a well defined type of otitis media;

- to study the effects of alternative myringotomy methods - diathermy and CO\textsubscript{2}-laser - on the healing pattern of a central tympanic membrane perforation;
MATERIALS AND METHODS

EXPERIMENTAL ANIMALS

Healthy, male Sprague-Dawley rats weighing 250-350 g were used. The animals were maintained under standard laboratory conditions throughout the study and were fed a conventional diet for laboratory rodents. The animals had access to water ad libitum.

SURGICAL PROCEDURES

For the surgical procedures the animals were anesthetized with a short-lasting barbiturate, hexabarbital (BrietalR). The drug was administered through a tail vein in repeated boluses.

Myringotomies were performed either with a myringotomy lancet (I, III, IV, V, VI), a diathermy device (Hyphrecator, 80 W) (V) or a CO₂-laser (Coherent 400 CO₂, 0.1s, 10 W) (VI). The myringotomies engaged the whole upper rear quadrant of the TM and were of equal size irrespective of the technique used. In the case of repeated myringotomies, these were performed upon four different occasions at intervals of 5 weeks.

Insertion of tympanostomy tubes (I, III, IV). Biflanged tympanostomy tubes (TTs) made of polyethylene (polyethylene tubing, IntramedicR; I.D. 0.28 mm and O.D. 0.61 mm) were inserted into myringostomas performed in the upper rear quadrant of the TM of the right ear. In order to study the effects of repeated insertions of TTs a primary myringotomy was performed and a TT inserted. After 2 weeks the TT was removed. The animals were left for 3 weeks and at the end of this period they were again subjected to myringotomy and tube insertion. The tubing-detubing sequence was repeated three times.
Cleavage of the soft palate (II, III, IV). This procedure will interfere with the normal ventilation of the MEC through the ET. Under sterile conditions the soft palate of the animals was cleft with a scalpel along the midline from the hard palate to the posterior free border.

Occlusion of the Eustachian tube (II). Through a hole drilled in the lateral wall of the tympanic bulla the tympanal orifice of the ET was hermetically sealed with a polyethylene plug which was squeezed into the orifice. Partial occlusion of the ET was accomplished by insertion of a polyethylene tube (I.D. 0.28 mm and O.D. 0.61 mm).

MORPHOLOGICAL METHODS

Otomicroscopy. The TMs were examined through an ear speculum with the aid of an otomicroscope (Zeiss OpMi).

Tympanic membrane photography. For photography a 2.7 mm otoendoscope 30° (Storz), connected to an Olympus OM2 camera via an objective lens (Wolf; f=95 mm) was used. A flow-light source (Wolf 5105) was connected to the endoscope and the film used was Kodak Ectachrome 400.

Histological techniques. Animals anesthetized with a pentobarbital (Mebumal, 40 mg/kg bodyweight) were sacrificed by perfusion through the left heart ventricle of 2% glutaraldehyde in cacodylate buffer. After fixation the TMs were excised together with adjacent external auditory canal skin. The specimens were postfixed in 1% OsO₄, dehydrated in graded ethanol solutions and embedded in Epon. For the light microscopical (LM) studies semithin sections (0.5-1.0 μm) were cut in an ultramicrotome, mounted on glass slides and stained with toluidine blue. For the transmission electron microscopy (TEM) studies (I), ultrathin sections (70 nm) were cut in an LKB Ultratome. After counterstaining with uranyl acetate and lead citrate the sections were examined and photographed in a JEOL transmission electron microscope 100 CX. For the scanning electron microscopical (SEM) studies (II, VI), the
specimens were dehydrated in increasing concentrations of ethanol and ethanol-amylacetate up to 100% amylacetate and dried with the critical point method. The specimens were mounted on specimen holders and coated with gold. The TMs were then studied in a Cambridge Stereoscan S4 scanning electron microscope.

**Morphometry (I).** In a light microscope equipped with a 10 mm eyepiece micrometer disc, the anterior-posterior distance of the TM from the handle of the malleus to the annulus was determined. This distance was then divided into four equal parts and the three points of division were selected for measurement of the thickness of the pars tensa. Based on three measuring points at five different superior-inferior levels, the thickness of the pars tensa was calculated from 15 different measuring points in each upper quadrant.

**MICROBIOLOGICAL AND BIOCHEMICAL METHODS**

**Microbiological sampling (III, IV)** was performed according to a technique described by Thore et al. In brief, the animals were decapitated and the MECs were opened via the tympanic bulla under sterile surgical conditions. Effusion material from the MEC was aspirated and transferred to glass vials containing 5 ml of a thioglycolate broth. The samples were stored at +15°C and were further processed within 24 h. After appropriate dilution, the samples were spread over blood agar plates and incubated under aerobic and anaerobic conditions at +37°C for 48 h. Colonies that appeared were counted and identified according to standard techniques. Into MECs without visible effusion material, into the nasopharynx (NPH) and into the external ear canal, roughly 50 μl of thioglycolate broth was instilled, aspirated and then processed and analysed as described above.

**Histamine determination (III)** was performed according to the fluorimetric assay of Shore et al. A rinsing solution (about 50 μl of saline) was injected into the MEC through the punctured TM (intact ears)
or through a tympanic membrane perforation. The fluid was retrieved by aspiration and analysed for histamine content.

STATISTICAL METHODS

Values obtained by measuring TM thickness were subjected to one-way analysis of variance and contrast analysis according to Scheffé (I).

RESULTS

THE STRUCTURE OF THE TYMPANIC MEMBRANE AFTER REPEATED TYPANOSTOMY TUBE INSERTIONS COMPARED TO REPEATED MYRINGOTOMIES (I).

After repeated insertions of TTs, the TM lost its transparency. White chalky structures were incorporated in the TMs and at the end of the experiment extensive masses of an opaque sclerotic material were seen. These tissue changes were located mainly in the tubulated quadrants. Similar changes, albeit less pronounced and exclusively restricted to the myringotomized quadrants, were noted also after repeated myringotomies without tube insertions.

In the light microscope, 3 weeks after the last tubulation period (TP), the thickness of the tubulated quadrants was compared with a normal age-matched TM and was roughly 150 µm versus 5 µm. The tissue changes were observed mainly in the connective tissue layer which was characterized by whorled masses of densely packed, collagen-rich connective tissue. Scattered in the latter tissue, groups of keratinizing squamous epithelial cells were constantly found. Such cells were also noted
within areas of the epithelial surface facing the MEC. The untouched anterior quadrants also exhibited a thickened (about 10-fold) collagenous connective tissue layer.

Three months after the last TP the thickness of the tubulated quadrants was still evident. In certain areas of the connective tissue layer, bone-like tissue was observed. At this time squamous epithelial cells were only occasionally noted in the connective tissue layer and they were completely absent from the epithelial lining facing the MEC. The untouched anterior quadrants were still thickened compared with corresponding quadrants in normal age-matched TMs.

The TMs that had been subjected to repeated myringotomies without TT insertion exhibited similar structural changes, although not as advanced as those observed in tubulated ears. The thickness was considerably increased, compared with controls at 3 weeks. The histological picture was dominated by a dense fibrous connective tissue which, 3 months after the final myringotomy, contained discrete areas of bone-like material. Keratinizing squamous epithelial cells were also present in the lamina propria of these TMs, but not as frequently as in the tubulated TMs. The untouched anterior quadrants of the repeatedly myringotomized ears showed only a slight thickening 3 weeks after completion of the experiments, but were of normal thickness after 3 months.

**EFFUSION MATERIAL IN THE MIDDLE EAR CAVITY CORRELATED TO A DISTURBED EUSTACHIAN TUBE FUNCTION (II, III, IV)**

In paper II it was described how different types of effusion material, serous and purulent, were intimately related to the type of surgical procedure used to interfere with the ET function. Thus, total obstruction of the tympanal orifice led to a serous otitis media whereas cleavage of the soft palate gave rise to a purulent otitis media. Furthermore, it was found in the study that partial obstruction of the ET did not lead to production of any effusion material. In papers III
and IV cleavage of the soft palate was undertaken to cause purulent otitis media in order to study the possible advantages of transmyringeal ventilation in an infected middle ear.

Cleavage of the soft palate led, within 2 days, to a maximally retracted pars flaccida and an accumulation of amber-coloured effusion material in the attic. This effusion material contained considerable amounts of histamine (III). After 6 days the whole MEC was filled with effusion material, which in most cases was opalescent. The TMs displayed markedly dilated vessels. Two weeks later the effusion material of all ears was otomicroscopically classified as purulent.

Samples from the fluid in the MEC and from the NPH were removed and subjected to microbial analysis at various time intervals (days 0, 2, 7 and 21). At day 0, no bacteria were detected in the MECs, but on day 2, 3 out of 10 ears gave positive cultures. The dominant bacteria were gram-positive cocci. On day 7, 7 out of 10 ears gave growth of bacteria of both gram-positive and gram-negative character. On day 21, all MECs were infected, with a marked predominance of gram-negative bacteria. At the beginning of the experiment and on day 2, the bacterial flora of the NPH was dominated by gram-positive cocci. However, on day 7, gram-negative bacteria had increased and after 3 weeks they were predominant. The study demonstrated that a changing flora in the NPH is paralleled by similar changes in the bacterial flora of the MEC.

EFFECTS OF ARTIFICIAL TRANSMYRINGEAL VENTILATION ON PURULENT OTITIS MEDIA EVOKED BY CLEAVAGE OF THE SOFT PALATE (III, IV)

Animals with a cleft soft palate were subjected to artificial ventilation of their MECs either by myringotomy alone or combined with insertion of a TT. As long as the myringostoma persisted (III) or the TT remained unclogged (III, IV), no effusion material appeared in the meso- and hypotympanon. Compared with ears with intact TMs, ventilation with TTs reduced the degree of infection of the MECs. Thus on day 7, 3
out of 10 tubulated ears gave growth of bacteria. In intact ears the figures were 7 out of 10. On day 21, 4 out of 10 tubulated ears showed infection whereas 10 out of 10 intact ears were infected. In the infected tubulated ears, bacterial counts were markedly lower as compared with corresponding infected intact ears. It should be noted that in both ventilated and non-ventilated ears a transient episode of fluid production in the attic space always occurred during the first 4 days after an impaired ET function.

THE HEALING PATTERN OF TM PERFORATIONS MADE BY DIATHERMY AND CO₂-LASER (V, VI)

In the preceding papers artificial ventilation of the MEC was accomplished by inserting a transmyringeal device. In papers V and VI attempts were made to effectuate transmyringeal middle ear ventilation by delaying the healing of a TM perforation. For this purpose, myringotomies were performed by diathermy (V) and a CO₂-laser (VI).

Perforations made with a myringotomy lancet healed within 9-12 days (V). In histological, light microscopical studies, this type of perforation was observed to be gradually sealed by a proliferation of the squamous epithelium at the rim of the opening. The advancing hyperplastic epithelium rests on a bed of richly vascularized connective tissue.

The diathermy-induced myringotomies (V) healed within 12-18 days. Microscopy revealed that diathermy destroyed the keratinizing squamous epithelium, not only within the perforated area, but also at a considerable distance from the edge of the perforation. The heat also damaged blood vessels in the surrounding tissue. The early stages of healing were in some cases complicated by otorrhea. In sectioned material, inflammatory cells were seen to invade the damaged areas of the TM. Although the healing process was delayed in this type of myringotomy, the healing pattern, once apparent, was similar to that observed after myringotomies performed with a lancet. Not until day 9, when the
proliferating squamous epithelium reached the perforation edge, did the tissue defect start to diminish in size. With respect to the connective tissue layer it was definitely thickened, and remained so not only in the perforated quadrants but also in the surrounding areas initially denuded by the heat.

Myringotomies performed with the CO\textsubscript{2}-laser (VI) were characterized by a very long healing period (15-24 days). The laser beam not only produced a perforation of the TM but also damaged the keratinizing squamous epithelium over large areas of the anterior upper quadrant. In addition, blood vessels along the handle of the malleus were severely affected. In contrast to the diathermy-inflicted myringotomies, the laser perforations were only in one single case accomplished by otorrhea and the invasion of inflammatory cells into the damaged tissue was negligible. The healing pattern was similar to that described for the other types of myringotomy. Once the perforations had healed, the epidermal layer returned to its usual thickness and appearance. The connective tissue layer, on the other hand, remained thickened and furthermore, the connective tissue reaction was restricted to the perforated quadrants despite the fact that the squamous surface epithelium had been damaged over a fairly large area.
Ventilation tubes have been extensively used for clinical purpose since they were reintroduced by Armstrong in 1954. It is rather surprising that so few reports concerning their effects on TM structure have been published. Since such studies are difficult to perform in the human, animal models would seem to provide a possible way of carefully assessing the changes that take place in the TM and the MEC in various pathological conditions and after different types of treatment. The structure of the TM has been shown to be strikingly similar in numerous species, including man. The rat has recently been shown to be a suitable animal model for the study of structural changes in the TM, especially with respect to experimental ear drum perforations and subsequent healing processes. It has also proved useful in studies on the pathogenesis of experimentally induced otitis media with effusion. In the present thesis, knowledge gained from these studies has formed the basis for an investigation of the benefits and consequences of different transmyningeal ventilation procedures in healthy and diseased rat middle ears.

It is well established that disturbance of the ET function in an experimental animal will cause an accumulation of effusion material in the MEC. Cleavage of the soft palate led to middle ear effusion (II, III, IV). The initial production of a sterile effusion material always starts in the attic. Recently the middle ear mucosa, especially that of the pars flaccida, has been shown to contain numerous mast cells and these cells have been suggested to participate in the onset of otitis media with effusion. In this context it is interesting to note increased histamine levels in the effusion material occurring at 1 and 2 days after cleavage of the soft palate (III).
Between days 7 and 21 all middle ear cavities were filled with an effusion material which gradually became purulent. It would thus seem that one type of otitis media (serous) may pass over into another (purulent). However, it remains to be established whether purulent otitis media invariably arises from a serous ear effusion and whether a small amount of effusion material is a prerequisite for bacterial invasion and growth.

It was interesting to note that the bacteria found in the MECs were identical with those of the NPH and that a change in the MEC flora reflected a changed NPH flora. These data clearly support the assumption that purulent otitis media can develop as an ascending infection from the NPH.

**TRANSMYRINGEAL MIDDLE EAR VENTILATION**

**Effects on the TM of repeated ventilation procedures**

Repeated insertions of TTs (I) caused marked structural damage to the TM. Of the sideeffects related to the use of TTs noted clinically, only tympanosclerosis could be provoked. That atrophy, persistent perforations and manifest cholesteatomas did not occur in the present study could have been due to differing reactions in different species. Another possible explanation may be that TTs only induce these pathological changes when inserted into diseased middle ears. The tympanosclerosis-like changes were frequently observed also in the untouched quadrants. Similar findings have been made clinically.

The persistent changes were strictly confined to the connective tissue layer of the TM. This is consistent with previous findings in the rat and in the chinchilla. The damaged areas showed little or no improvement throughout the observation period. The thickened connective tissue layer contained whorled masses of collagen and patches of degenerated, sclerotic material. It has recently been proposed that forces created
by superfluous quantities of connective tissue fibres may contribute more to the extrusion of TTs from TM than does a migrating keratinizing squamous epithelium.\textsuperscript{14,24}

An interesting finding was that tubulated TM, 3 weeks after the last tubal removal, exhibited islands of keratinizing squamous epithelium scattered in the thickened connective tissue. Similar epithelial structures within the TM connective tissue have been reported to occur in homografts following tympanoplasty.\textsuperscript{13} In some TMs, keratinizing squamous epithelium was interposed between the epithelial cells lining the tympanic surface. According to histopathological definition this displaced epithelial tissue should be classified as a cholesteatoma.\textsuperscript{19} However, this keratinizing squamous epithelium did not seem to survive and at 3 months after the last tubal removal the cells had disappeared. It is tempting to suggest that keratinizing squamous epithelium introduced into the MEC may survive under certain conditions and develop into clinically manifest cholesteatomas.

After repeated myringotomies without tube insertion, the untouched quadrants were of normal thickness but exhibited a horseshoe-shaped blanching, clearly seen through the otomicroscope. The upper rear quadrant was thickened and showed histological features similar to those observed after repeated TT insertions. However, the damage to the TM structure was less pronounced. Thus it seems evident that the extensive changes following treatment by tube must be related to the inserted foreign device.

\textbf{Benefits}

In paper IV the rat animal model was used to evaluate the effects of transmyringoeal ventilation in cases of purulent otitis media. A myringotomy, with or without insertion of a TT, prevented effusion material from collecting in the meso- and hypotympanon. As long as the ventilation was effective, most of the MECs remained sterile. These findings lend support to the idea that TTs may be of value in the treatment of
Artificial ventilation of the MEC did not, however, prevent the initial accumulation of a histamine-rich effusion material in the attic. Whatever mechanisms are involved in this early stage of effusion production (e.g. vasoactive substances released from mast cells, or autonomic nerves), they appear to be effective in a ventilated middle ear. One important question arises: what factors prevent the MECs from being extensively invaded by bacteria when the MECs are sufficiently aerated? The function of the Eustachian tube is definitely disturbed by cleavage of the soft palate, probably due to impairment of the opening-closing procedure. In consequence, the pressure conditions of the MECs are altered and a reduced oxygen tension of the MEC may affect the mucociliary system. This may in turn render the ear more prone to bacterial invasion from the NPH. Another possible mechanism might be that, if ventilation occurs through the ET when there is a high negative middle ear pressure, bacteria-containing NPH secretions could be aspirated into the MEC. With a TT inserted, the middle ear pressure and the gas composition maintain equilibrium with that of the ambient atmosphere and are maintained regardless of the tubal function. This appears to have a positive effect on the antimicrobial defence mechanisms of the middle ear.

ALTERNATIVE PROCEDURES TO VENTILATION TUBE TREATMENT

In papers III and IV it was shown that artificial ventilation of the MEC could prevent effusion material from filling up the tympanic cavity. These experimental findings agree closely with the ideas of Politzer, and later on Armstrong, who advocated artificial transmyringeal middle ear ventilation as a treatment for a fluid-filled MECs. However, as mentioned in the Introduction, numerous clinical studies have shown that ventilation tubes cause severe damage to the ear drum. On the other hand, the duration of transmyringeal ventilation through a single myringotomy without insertion of a device has proved to be too short in many cases, i.e. the perforation closes before the
middle ear disease is cured. It would be advantageous if less harmful and more effective methods for middle ear ventilation could be developed. An ideal method could be one which causes not only minimal damage to the TM but also does not require general anesthesia.

It is well-known among clinicians that welding injuries sustained by the TM in welding accidents heal slowly or may even result in a permanent perforation. Therefore in papers V and VI thermal energy was utilized in an attempt to accomplish TM perforations that would be slow in healing. Both diathermy and laser-inflicted perforations showed a considerable delay in healing compared with myringotomies made with a lancet. The delay was due mainly to destruction of the keratinizing squamous epithelium far beyond the perforation edge and damage to the vascular supply of the TM. According to Armstrong, artificial ventilation of the MEC for 2-3 weeks is sufficient to restore the middle ear status in most cases of secretory otitis media. Should the healing pattern reported in the rat prove to be similar to that in man, it would be tempting to suggest that thermic methods may prove a useful alternative to the ventilating tube. Some promising results pointing in this direction have recently been reported. These authors describe the use of a battery-powered heat myringotomy device for clinical use. However, judging from results obtained in the present studies (V, VI) the laser technique appears to have certain advantages compared with heat myringotomy. The latter technique caused more pronounced damage to the TM and was frequently complicated by otorrhea. Another advantage of the laser technique is that the energy can be extremely well controlled. A pulse just sufficient to destroy the TM layers within a restricted area can easily be accomplished. Although the laser technique has been clinically applied to a few patients, CO₂-laser-made myringotomy should be carefully evaluated with respect to possible inner ear damage before being more widely used in clinical practice. The risk of inner ear damage would seem to be minimal, however, as the laser energy is rapidly absorbed in a fluid-filled middle ear cavity.
CONCLUSIONS

I. Repeated tympanostomy tube insertions cause long lasting structural changes in the tympanic membrane. These changes include the appearance of tympanosclerosis-like inclusions and a marked thickening of the connective tissue layer of the tympanic membrane. Changes brought about by repeated myringotomies without tube insertion are less pronounced and are restricted to the quadrants manipulated.

II. Cleavage of the soft palate in the rat provokes middle ear effusion, which is initially serous but gradually turns purulent. Serous and purulent otitis media occur as a continuum. Throughout the study the microbial flora of the purulent middle ear effusions becomes identical with that of the nasopharynx, thus gradually changing from gram-positive to gram-negative strains. Obviously the infected middle ears were invaded by bacteria ascending from the nasopharynx.

III. Transmyringal middle ear ventilation in the cleft palate model prevents effusion material from collecting in the meso- and hypotympanon and represses bacterial growth in the middle ear cavity.

IV. Myringotomies inflicted by thermal energy (diathermy and CO₂-laser) both cause a considerable delay in healing due to widespread destruction of the outer stratified, squamous epithelium and pronounced vascular damage. Upon comparison, however, the laser method has certain advantages, namely a prolonged period of perforation and a minimal discharge of middle ear fluid (otorrhrea) throughout the healing process.
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