# Large discrepancies in otomycosis treatment in private ear, nose, and throat clinics in Denmark

Elisabeth Arndal[1], Henrik Glad[2] & Preben Homøe[2]


## ABSTRACT

**INTRODUCTION:** Otomycosis is a fungal infection of the external ear canal that can involve the middle ear in case of tympanic membrane perforation and also extend to the auricle. Fungi cause 7-15% of external otitis. Diagnosing otomycosis is often based entirely on non-specific clinical signs and symptoms. A multitude of antifungal drugs are available. Some are ototoxic in animals, a few are proven safe, but the ototoxicity of many drugs remains unknown. The aim of this study was to describe how otomycosis was diagnosed and treated by private ear, nose, and throat (ENT) consultants in Denmark and to investigate if the patient's immune status and the presence of a tympanic membrane perforation affected the chosen treatment modality.

**METHOD:** A questionnaire on the treatment of otomycosis was sent to 147 private ENT consultants.

**RESULTS:** In total, 103 (70%) responded. 95% performed intensive aural cleaning using an otomicroscope. The initial diagnosis was based on symptoms as only 20% required to see fungal hypha. 42% sent material for culture and sensitivity (C + S) before starting treatment and 92% sent for C + S if treatment failed. 89% used a variety of topical antifungal drugs as the first line of medical treatment. Antiseptics were used in 5%. The presence of a tympanic membrane perforation did not alter the treatment modality. Only 13% treated immunocompromised patients differently.

**CONCLUSION:** The initial diagnosis was based on non-specific symptoms and there were large discrepancies in the chosen antifungal treatment. Topical antifungal drugs were preferred. Additional research is needed.

**FUNDING:** Department of Otorhinolaryngolgy and Maxillofacial Surgery, Zealand University Hospital, Køge, Denmark. The Danish Association of Research-interested Otorhinolaryngology Consultants: Kim Werther, Peter Tingsgaard, Mads Stougaard, Steen Telmer, Henrik Møller, Liviu Guldfred.

**TRIAL REGISTRATION:** No trial registration was necessary as the questionnaire was anonymous and contained no patient data.


Otomycosis is a fungal infection of the external ear canal that may involve the middle ear in case of tympanic membrane perforation and also may involve the auricle [1-3]. The main causative fungi are yeasts (*Candida* spp.), molds (*Aspergillus* spp.) and dermatophytes [1, 4, 5]. Fungi cause 7-15% of external otitis and the treatment is often long and cumbersome [6-8]. Predisposing factors include a warm humid climate, frequent swimming, eczema, excessive use of cotton tips, a narrow ear canal, allergy, chronic drainage, irradiation, obstructing ear wax, a radical cavity after mastoidectomy, dermatomycosis, a weakened immune system, earplugs and secondary to prolonged use of topical antibacterial treatment [1, 6, 9, 10]. Immunocompromised patients have an increased risk of developing fungal necrotising otitis externa [11, 12]. The diagnosis is often based entirely on the clinical signs and symptoms such as swelling, redness of the skin, itching, detritus, moisture, pain and discharge. Unfortunately, these symptoms are unspecific with the obvious exception of visible fungal growth [8, 13, 14]. Culture and sensitivity (C + S) testing can help secure the diagnosis [15, 16]. A multitude of antifungal drugs, dyes and antiseptics are used [1, 6, 17, 18]. Some (acetic acid and gentian violet) are known to be ototoxic in animal studies, a few are proven safe (clotrimazole, miconazole and nystatin), but the ototoxicity status of many drugs remains unknown [1]. Treatment is mainly topical. In Denmark, the diagnosis and treatment of otomycosis is primarily provided by private ear, nose, and throat (ENT) clinics. The aim of the present study was to investigate how otomycosis is diagnosed and treated by private ENT consultants. We also investigated if the patient's immune status and the presence of a tympanic membrane perforation affected the chosen treatment.

## METHOD

The Danish Healthcare Services' website [19] identified 147 active private ENT consultants who were sent a two-page anonymised questionnaire electronically. Subsequently, we also sent the questionnaire by surface mail to non-responders (**Table 1**). The questionnaire was designed so that the answers were mainly yes/no or the name of a treatment in order to facilitate data entry and reduce the time needed to fill in the questionnaire as most private ENT consultants have a tight schedule. No validated questionnaire on the diagnosis and treatment of otomycosis was found in the literature. Therefore, we designed a questionnaire specifically for this study. The Danish Association of Research-interested Otorhinolaryngology Consultants (SAFSOD) tested the questionnaire

ORIGINAL ARTICLE

1) Ear, Nose, and Throat Department, Rigshospitalet
2) Ear, Nose, and Throat Department, Zealand University Hospital, Køge, Denmark

Dan Med J 2016;63(5):A5231

and adjustments were made according to their comments. No further validation was conducted. Data were entered and analysed in IBM SPSS Statistics 22. Differences between groups were tested by Fisher's exact test. Random samples were checked for input errors.

*Trial registration:* No trial registration was necessary as the questionnaire was anonymous and contained no patient data.

## RESULTS

The questionnaire response rate was 70%. The number of otomycosis patients seen per year per consultant is shown in **Table 2**. The diagnosis was generally based on the clinical otomicroscopic presentation as only 20% required to see fungal hyphae. However, it should be noted that yeasts do not produce hyphae [20]. At the primary visit, 42% sent material for C + S testing and immediately started treatment. However, 92% sent material for C + S testing if the primary treatment failed and 95% performed intensive aural cleaning using an otomicroscope. A variety of medical treatments with or without antiseptics, dyes, hydrocortisone and antibacterial drugs were used (**Table 3**). Treatment was changed if the primary and/or secondary treatment was ineffective. The diversity seen in the initial treatment continued when treatment was changed. The treatment received by those who did not experience treatment failure showed the same diversity as was seen in the other groups.

The results for antifungal drug administration in immunocompetent patients are shown in **Table 4**. 2% without tympanic membrane perforation (–p) and 5% with tympanic membrane perforation (+p) were treated with systemic antifungal drugs. There was no statistical difference between the two groups (p = 0.45, Fisher's exact test). The same applied to the use of topical antifungal drugs (90% –p/85% +p; p = 0.84, Fisher's exact test). Thus, the presence of a tympanic membrane perforation did not alter the drug administration route. The preferred antifungal drugs were miconazole, clotrimazole, ketokonazole and econazolnitrate (topical imidazoles); fluconazole and itroconazole (systemic imidazoles); and nystatin (topical polyene) and terbinafine (topical allylamine).

27% –p /23% +p were treated with antiseptics alone or in combination with other antifungal drugs as the primary treatment. There was no statistically significant difference between the two groups (p = 0.75, Fisher's exact test). Thus, the presence of a tympanic membrane perforation did not affect the use of antiseptics. Methylrosanilin (gentian violet) was the preferred antiseptic dye. Atamon and Vioform were the second and third preferences, respectively. 27% –p/19% +p used hydrocortisone alone or in combination with other drugs as the initial treatment.

13% reported that they treated immunocompromised patients differently. The main difference was that 77% sent material for C + S at the first visit compared with 23% if the patients were immunocompetent (p = 0.17). The primary line of treatment was still topical antifungal drugs which showed the same diversity as was seen in the immunocompetent patients. However, if the primary treatment failed, treatment was intensified with systemic antifungal drugs, more frequent aural cleaning, conference with a microbiologist and referral to hospital.

## DISCUSSION

Treatment of otomycosis can be troublesome and may

**TABLE 1**

Questionnaire about the diagnosis and treatment of otomycosis (answered by 103 out of 147 ENT consultants in Denmark).

| Question no. | Question |
|---|---|
| 1 | How many otomycosis patients do you see per year? |
| 2 | Do you demand to see fungal hyphae to diagnose otomycosis? |
| 3 | Do you perform C + S testing at the first consultation? |
| 4 | Do you perform C + S testing if the initial treatment is ineffective? |
| 5 | Do you use an otomicroscope to clean the external ear canal? |
| 6 | What is you first line of treatment for otomycosis without[b] perforation of the tympanic membrane? |
| 7 | Do you use mesh treatment? |
| 8 | Do you swab the external ear canal with an antifungal drug? |
| 9 | Do you use both mesh and swab? |
| 10 | Do you only use antifungal eardrops? |
| 11 | Do you use other forms of treatment? |
| 12 | What is you 2nd line of treatment for otomycosis, without[b] perforation of the tympanic membrane, if the initial treatment was ineffective? |
| 13 | What is you 3rd line of treatment for otomycosis, without[b] perforation of the tympanic membrane, if the secondary treatment was ineffective? |
| 14[a] | Do you treat an immunocompromised[c] patient with otomycosis differently? |

C + S = culture and sensitivity; ENT = ear, nose, and throat.
a) If respondents answered yes to question no. 14 they were asked to repeat question no. 3-13 for the immunocompromised patient.
b) The question was repeated for otomycosis with a perforated tympanic membrane.
c) The individual ENT consultant decided which patients they considered to be immunocompromised.

**TABLE 2**

Number of otomycosis patients seen per year per private ear, nose, and throat consultant in Denmark.

| Patients/consultant, n | Consultants, % (N = 103) |
|---|---|
| 0-10 | 13 |
| 11-50 | 47 |
| 51-100 | 6 |
| > 100 | 3 |
| No answer | 31 |

involve several treatment modalities. It is therefore important to collect systematic knowledge about the diagnostic habits and potential variations concerning treatment in order to improve the quality of the diagnosis as well as the treatment.

In the present study, we found that 80% treated otomycosis based on non-specific clinical signs without visible hyphae. 42% performed C + S testing before starting therapy, while 92% did C + S testing if the initial therapy failed. 95% performed otomicroscopic intensive aural cleaning. 89% used topical drugs, while only 2% used systemic treatment. 80% used antifungal drugs initially, while 5% used antiseptics only. The use of antiseptics increased to 10% if treatment failure was experienced. Perforation of the tympanic membrane did not influence the choice of treatment.

### Diagnosis and symptoms

Previous studies have found that clinical symptoms of otomycosis were unspecific and recommended C + S testing unless characteristic fungal hyphae were seen (yeasts do not produce hyphae). Saunders et al [7] made a retrospective study of 170 patients with external otitis and found that fungi were involved in 20% with a mixed bacterial and fungal aetiology, while 5% were positive for fungi alone. Only 38% of positive fungal cultures had clinical signs of fungi. Kurnatowski & Filipiak [8] studied 249 patients with external otitis and found that 15% had a mixed bacterial and fungal aetiology, while 13% were caused by fungus alone. The most frequent symptoms were pain and wet grey debris. In addition, Ho et al [9] and Kaur et al [15] found unspecific symptoms such as pruritus, aural fullness, hearing loss, tinnitus, discharge and pain.

### Culture and sensitivity testing

Vennewald & Klemm [1] recommended a sterile swab and debris sample from the ear canal for C + S testing. The reliability of C + S results was questionable if it was only performed when treatment failed. The frequent aural cleaning and topical antifungal treatment before C + S may explain why no causative agent was found.

### Antifungal drugs

In our study, 80% of the initial treatment (Table 3) was antifungal drugs alone or in combination with antiseptics and or hydrocortisone. The use of topical imidazoles, mainly clotrimazole and miconazole, were preferred. Imidazoles have a broad spectrum against yeasts (*Candida* spp.), molds (*Aspergillus* spp.), dermatophytes and gram-positive bacteria and are safe in animal studies. However, the ototoxicity in humans has not been tested. The same is true for the polyene nystatin. Terbinafine is an allylamine which primarily works against dermatophytes, but its ototoxicity has not been tested [1]. Some of the treatment failures experienced in our study may result from a relatively frequent use of terbinafine in combination with only 42% performing C + S testing before starting treatment. Patient compliance and a too short period of treatment may also affect treatment efficacy.

### Antiseptics

27% used some kind of antiseptic therapy. The preferred antiseptic was methylrosanilin (gentian violet), which is ototoxic in animal models [1], but no studies have been made on humans. This dye was regularly used, and we

**TABLE 3**

Treatment of immunocompetent patients with otomycosis without tympanic membrane perforation in private ear, nose, and throat practices in Denmark (N = 103). The values are %.

| Treatment | Primary treatment | If primary treatment failed | If secondary treatment failed |
|---|---|---|---|
| *Antifungal drugs* | | | |
| Without hydrocortisone | 45 | 27 | 15 |
| With hydrocortisone | 12 | 12 | 0 |
| Subtotal | 57 | 39 | 15 |
| *Antifungal drugs and antiseptics* | | | |
| Without hydrocortisone | 13 | 11 | 5 |
| With hydrocortisone | 9 | 2 | 2 |
| Subtotal | 22 | 13 | 7 |
| *Antiseptics* | | | |
| Without hydrocortisone | 2 | 6 | 6 |
| With hydrocortisone | 3 | 4 | 1 |
| Subtotal | 5 | 10 | 7 |
| Hydrocortisone only | 3 | 1 | 0 |
| According to culture | 1 | 15 | 20 |
| Other[a] | 6 | 6 | 11 |
| No treatment failure | 0 | 8 | 15 |
| No answer | 6 | 8 | 25 |
| Total | 100 | 100 | 100 |

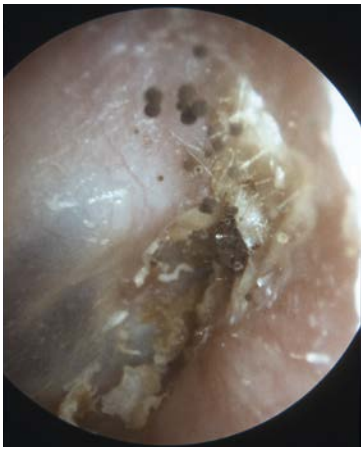
a) Non-specified local or systemic treatment, referral to hospital, advising no water in the ear or considering non-fungal aetiology.

**TABLE 4**

Antifungal drug administration against otomycosis in immunocompetent patients as reported by 103 ear, nose, and throat consultants in Denmark. The values are %.

| Drug administration | Primary treatment | If primary treatment failed | If secondary treatment failed |
|---|---|---|---|
| Topical antifungal drugs | 89 | 53 | 28 |
| Topical and systemic antifungal drugs | 1 | 3 | 0 |
| Systemic antifungal drugs | 2 | 7 | 4 |
| Other[a] | 2 | 29 | 43 |
| No answer | 6 | 8 | 25 |
| Total | 100 | 100 | 100 |

a) According to culture and sensitivity, unspecified antifungal treatment, referral to hospital, considering bacterial aetiology, advising no water in the ear, no treatment failure.



Otomycosis in the external ear canal, *Aspergillus niger* growth.

assume that the ENT consultants did not experience obvious deterioration in the patients' hearing. The application method of methylrosanilin was most often basting of the external ear canal skin with a cotton stick soaked in methylrosanilin and the method was therefore also considered safe even in patients with tympanic membrane perforation.

**Hydrocortisone**

Hydrocortisone is known to reduce oedema and the immunological response and may therefore have a place in otomycotic treatment of itching and pain. It may also be beneficial for patients who are susceptible to otomycosis due to an underlying skin disease.

**Tympanic membrane perforation**

In our study, the presence of a tympanic membrane perforation did not alter the choice of treatment. Hurst [3] studied 22 cases of otomycosis with tympanic membrane perforation. Patients were treated with a combination of topical clotrimazole, hydrocortisone and antibacterial drugs. All but one patient with a completely disintegrated tympanic membrane recovered without persistent hearing loss. Given that the ototoxicity of the majority of antifungal drugs used remain unknown, the failure to consider a tympanic membrane perforation may not be advisable. Recommendation of frequent cleaning and the use of antifungal drugs that have been proven safe in animal studies may therefore be advisable.

**Immune status**

In accordance with Rutt & Staloff [13] and Viswanatha et al [10], immunocompromised patients can be treated efficiently and safely with topical antifungal drugs, but vigilance and prompt treatment is recommended. In this study, the 13% who chose to treat immunocompromised patients differently also consulted early on with a microbiologist and were referred to hospital in case of signs of treatment failure.

**Strengths and limitations of our study**

This study is the first of its kind in Denmark. The response rate was 70% (103 out of 147), which we find acceptable. There are a number of limitations in our study. Among these are recall bias when filling in the questionnaire and selection bias of responders and non-responders. A response rate above 80% would have been preferable, but as this study demonstrates a very large diversity in the used treatments, it seems very unlikely that a higher response rate would have changed this conclusion. Before using the questionnaire, it was tested by a group of private ENT consultants who formed part of the target group.

**Future research**

No existing guideline or randomised controlled efficacy and outcome studies for the treatment of otomycosis were found in the literature. Future studies may include: diagnostic criteria, when to perform C + S, the optimal way to sample material for C + S testing, interval for aural cleaning, preferred initial treatment (including dosis), length of therapy and choice of therapy in case of treatment failure. Furthermore, recommendations are needed on whether a tympanic membrane perforation or immunosuppression should alter treatment.

## CONCLUSION

The diagnosis of otomycosis in private ENT clinics was based on non-specific clinical signs. 42% performed C + S testing at the first visit. Initial treatment was empirical and in case of failure 100% performed C + S. Almost all performed intensive otomicroscopic aural cleaning.
A large variety of antifungal drugs, hydrocortisone, antiseptics, dyes and antibacterial drugs were administered topically. Tympanic membrane perforation did not affect choice of treatment. 13% treated immunocompromised patients more vigorously. This study revealed large discrepancies in how otomycosis is diagnosed and treated. Additional research is needed to provide advice and to ensure evidence-based diagnosis and treatment of otomycosis.

**CORRESPONDENCE:** *Elisabeth Arndal.* E-mail: elisabetharndal@hotmail.com
**ACCEPTED:** 29 February 2016
**CONFLICTS OF INTEREST:** Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk

**LITERATURE**

1. Vennewald I, Klemm E. Otomycosis: diagnosis and treatment. Clin Dermatol 2010;28:202-11.
2. Munguia R, Daniel SJ. Ototopical antifungals and otomycosis: a review. Int J Pediatr Otorhinolaryngol 2008;72:453-9.
3. Hurst WB. Outcome of 22 cases of perforated tympanic membrane caused by otomycosis. J Laryngol otol 2001;115:870-80.
4. Morinaka S. Dermatophytosis of the ear. Otolaryngol Head Neck Surg 2005;133:113-5.
5. Ozcan M, Ozcan KM, Karaarslan A et al. Concomitant tomycosis and dermatomycoses: a clinical and microbiological study. Eur Arch Otorhinolaryngol 2003;260:24-7.
6. Anwar K, Gohar MS. Otomycosis; clinical features, predisposing factors and treatment implications. Pak J Med Sci 2014;30:564-7.

7. Saunders JE, Raju RP, Boone JL et al. Antibiotic resistance and otomycosis in the draining ear: culture results by diagnosis. Am J Otolaryngol 2011;32:470-6.
8. Kurnatowski P, Filipiak J. Otitis externa: the analysis of relationship between particular signs/symptoms and species and genera of identified microorganism. Wiad Parazytol 2008;54:37-41.
9. Ho T, Vrabec JT, Donals Y et al. Otomycosis: clinical features and treatment implications. Otolaryngol Hed Neck Surg. 2006;135:787-91.
10. Viswanatha B, Sumatha D, Vijayashree MS. Otomycosis in immunocompetent and immunocompromised patients: Comparative study and literature review. Ear Nose Throat J 2012;91:114-21.
11. Tarazi A, Al-Tawfiq JA, Abdi RF. Fungal malignant otitis externa: pitfalls, diagnosis and treatment. Otol Neurotol 2012;33:769-73.
12. Hamzany Y, Soudry E, Preis M et al. Fungal malignant external otitis. J infect 2011;62:226-31.
13. Rutt AL, Staloff RT. Aspergillus otomycosis in an immunocompromised patient. Ear Nose Throat J 2008;87:622-3.
14. Bardanis J, Batzakakis D, Mamatas S. Types and causes of otorrhea. Auris Nasus Larynx 2003;30:253-7.
15. Kaur R, Mittal N, Kakkar M et al. Otomycoses: a clinicomycologic study. Ear Nose Throat J 2000;79:606-9.
16. Kurnatowski P, Filipiak A. Otomycosis: prevalence, clinical symptoms, therapeutic procedure. Mycoses 2001;44:472-9.
17. Karaaslan A, Arikan S, Ozcan M et al. In vitro activity of terbinafine and itraconazole against Aspergiullus species isolated from otomycosis. Mycoses 2003;47:284-7.
18. Kaya AD, Kiraz N. In vitro susceptibilities of Aspergillus spp. causing otomycosis to amphotericin B, voriconazole and itraconazole. Mycoses 2007;59:447-50.
19. https://www.sundhed.dk/find-behandler/?action=Search&Name=%C3%B8re+n%C3%A6se+hals&OrganizationTypeId=4&Street=&ZipCode=&City=&MunicipalityId=&RegionId=0&Sex=0&AgeGroup=0&DisabilityFriendlyAccess=false&EMailConsultation=false&EMailAppointmentReservation=false&EMailPrescriptionRenewal=false (1 Mar 2016).
20. Lowman DW, Greene RR, Bearden DW et al. Novel structural features in Candida albicans hyphal glucan provide a basis for differential innate immune recognition of hyphae versus yeast. J Biol Chem 2014;289:3432-43.