

REVIEW

10.1111/j.1469-0691.2008.02024.x

***Alternaria* infections: laboratory diagnosis and relevant clinical features**

F. J. Pastor and J. Guarro

Unitat de Microbiologia, Facultat de Medicina i Ciències de la Salut, Universitat Rovira i Virgili, Reus, Spain

ABSTRACT

The genus *Alternaria* contains several species of melanized hyphomycetes that cause opportunistic human infections. The published literature contains 210 reported cases of human alternarioses between 1933 and the present day. The most frequent clinical manifestations are cutaneous and subcutaneous infections (74.3%), followed by oculomycosis (9.5%), invasive and non-invasive rhinosinusitis (8.1%) and onychomycosis (8.1%). Immunosuppression is frequently associated with cutaneous and subcutaneous infections and rhinosinusitis. The most important risk factors for cutaneous and subcutaneous infections are solid organ transplantation and Cushing's syndrome, and those for rhinosinusitis are bone marrow transplants. Having been exposed to soil and garbage is common in all cases of oculomycosis, with corticotherapy being a risk factor in 50% of these cases. Previous contact with soil and/or trauma to the nails is associated with most cases of onychomycosis. In general, alternariosis shows a good response to conventional antifungal drugs. On some occasions, steroid suppression or reduction is sufficient to resolve an infection. Itraconazole is the antifungal drug used most frequently to successfully treat onychomycosis and cutaneous and subcutaneous infections. Posaconazole and voriconazole are promising therapeutic options, with the latter being especially so for oculomycosis.

Keywords *Alternaria* spp., alternariosis, diagnosis, fungal infections, review, treatment

Accepted: 20 January 2008

Clin Microbiol Infect 2008; **14**: 734–746

INTRODUCTION

In the last two decades, fungal infections have become an important cause of morbidity and mortality, especially affecting immunocompromised patients. Antibacterial treatment, bone marrow and solid organ transplantation, chemotherapy and primary or acquired immunodeficiency are conditions favourable for the development of severe fungal infections [1]. Phaeohyphomycoses, which are opportunistic infections caused by melanized (dematiaceous) moulds [2], have acquired special relevance in recent years. The incidence of these infections is increasing, mainly in transplant centres [3,4]. *Alternaria* is a dematiaceous hyphomycete that is frequently involved in human infection. *Alternaria* is a very large and complex genus that encom-

passes hundreds of species, although specific data are difficult to obtain because of the proliferation of nomenclature of dubious taxonomic validity. *Alternaria* has a worldwide distribution, with many species being common saprophytes in soil, air and a variety of other habitats; some are ubiquitous agents of decay and plant pathogens [5]. *Alternaria* can also be found on normal human and animal skin [6] and conjunctiva [7]. This fungus has been associated frequently with hypersensitivity pneumonitis, bronchial asthma, and allergic sinusitis and rhinitis [8–14]. However, it can also cause several different types of human infections, e.g. paranasal sinusitis, ocular infections, onychomycosis, cutaneous and subcutaneous infections [10], and, more rarely, granulomatous pulmonary disease [15], soft palate perforation [16] and disseminated disease [17,18]. Occasionally, *Alternaria* has been reported as a contaminant of soft contact lenses [19], and has also been isolated from an emollient cream [20]. *Alternaria alternata* has been (erroneously) regarded as the most frequent species, followed

Corresponding author and reprint requests: F. J. Pastor, Unitat de Microbiologia, Facultat de Medicina, Universitat Rovira i Virgili, Carrer Sant Llorenç, 21.43201 Reus, Spain
E-mail: franciscojavier.pastor@urv.cat

by *A. tenuissima*, although identification to the species level has not been performed on many occasions [10].

This review considers all cases of alternariosis reported in the literature up to 2007, with respect to the main clinical manifestations, predisposing factors, treatment and outcome. As species identification was not performed in the majority of the reported cases, and the aetiological agent was misidentified in many other cases, some guidelines for laboratory diagnosis are also included.

LABORATORY DIAGNOSIS

Morphology

Numerous cases of alternariosis have been attributed to *A. alternata*, *A. tenuissima* and other species, when the actual causal agent was *A. infectoria* [21]. The latter is the most common clinical species, although its ability to sporulate in routine media is very poor. This fact, in conjunction with the lack of pigmentation of this species, makes its identification difficult for non-experts. Until recently, the identification of *Alternaria* isolates was performed exclusively on the basis of morphological criteria, with the most significant characteristics being the morphology of the conidia and the formation (or not) of conidial chains.

The morphological characteristics useful for distinction among the three species mentioned above are the following: in *A. alternata*, the

conidia are medium-brown with a short, cylindrical beak, and form long and profusely branched chains (ten or more conidia); the conidia of *A. tenuissima* are golden-brown, frequently tapering gradually into a beak that is up to half the length of the conidium, and occur commonly in unbranched chains of three to five conidia; in *A. infectoria*, the conidia are more scarce, as this species usually sporulates poorly in common media, with its conidia often becoming nearly tubular and occurring in strongly branched chains, with long, multiseptate secondary conidiophores often emerging (Fig. 1).

There has been anecdotal evidence of other *Alternaria* spp. being found in clinical samples, e.g. *A. chlamydospora* [22,23], *A. longipes* [24], *A. dianthicola* [25] and several other, even less common, species. These are easily distinguishable by the formation of multicelled chlamydospores in *A. chlamydospora*, conidia with only transversal septa in *A. longipes*, and conidia with very long beaks in *A. dianthicola* [5]. However, molecular methods based on the analysis of internal transcribed spacer (ITS) region sequences have demonstrated that *A. longipes* and *A. tenuissima* cannot be differentiated from *A. alternata* [21]. Therefore, it seems probable that the only two species that are isolated with any frequency in clinical samples are *A. alternata* and *A. infectoria*. The genus *Ulocladium* is morphologically very close to *Alternaria* and has also been associated with clinical infections, although more rarely [26–28].

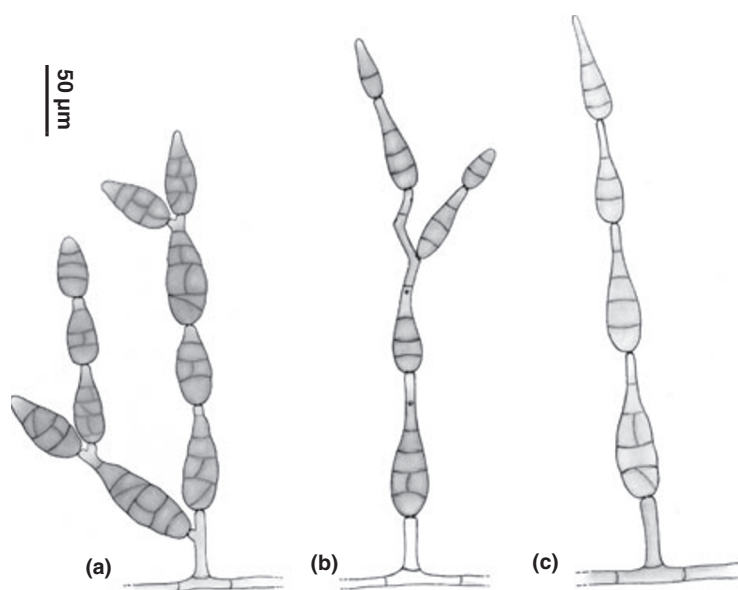


Fig. 1. Morphology of conidia of: (a) *Alternaria alternata*; (b) *A. infectoria*; and (c) *A. tenuissima*.

Ulocladium can be distinguished morphologically from *Alternaria* because its young conidia are attenuated at the base and the mature conidia are broadly ellipsoidal, whereas the young conidia in *Alternaria* are rounded at the base and the mature conidia are obclavate and rostrate.

Upon histological examination, *Alternaria* shows more or less irregular melanized hyphae that are practically indistinguishable from many other moulds that cause phaeohyphomycosis. Culture is mandatory for the correct identification of *Alternaria* spp., which grow in most routine laboratory media, although the clinically important species very soon lose their ability to sporulate. In our experience, the most suitable culture media for obtaining good sporulation of isolates from clinical specimens is potato-carrot agar.

Molecular identification

The use of molecular techniques facilitates the identification of rare pathogenic fungi, such as *Alternaria* spp., even by non-experts. Using the Basic Local Alignment Search Tool (BLAST), it is now easy to compare sequences of a given unidentified fungus, even of a non-sporulating strain, with those deposited previously in GenBank in order to find regions of similarity among sequences. However, an important problem lies in the fact that sequences within GenBank are deposited without strict quality control concerning species identification, and some sequences have therefore been deposited under erroneous names. In the case of *Alternaria*, it has been estimated that *c.* 14% of the sequences deposited in GenBank are misidentified [21]. Therefore, although the method is useful, it is important to ensure that unknown sequences are compared with the sequences of reference strains that have been identified by experts.

Amplification of the ITS region with pan-fungal primers, included in the multicopy rRNA operon, followed by downstream sequencing, has been shown to be a useful method for identification of *Alternaria* spp. Reliable ITS sequences of *Alternaria* strains deposited in GenBank, which have been checked by experts [21] and which are useful for comparison, are: *A. alternata* AF229461, AF229460 and AF071394, and *A. infectoria* AF229458, AF229480 and AJ2760558. In addition, De Hoog and Horr  [21] have provided a reliable procedure

to distinguish between *Alternaria* and *Ulocladium* spp. of clinical interest, based on a PCR method using general primers, followed by restriction enzyme digestion of the amplicons. However, the two predominant clinical species, *A. alternata* and *A. infectoria*, can easily be differentiated according to the length of the ITS1–4 amplicon, with the ITS spacer domain being *c.* 570 bp in the former species and *c.* 600 bp in the latter.

CLINICAL RELEVANCE

Alternaria infects mainly immunocompromised hosts. Although infections in immunocompetent hosts have also been reported, these rarely involve invasive disease [29]. The portal of entry of the infection is usually through corneal trauma or breakdown of the skin barrier. The majority of clinical manifestations involve cutaneous and subcutaneous infections, although other types of infections, e.g. oculomycosis, sinusitis, onychomycosis and invasive disease, have also been reported less commonly.

Ocular infections

The incidence of *Alternaria* spp. in oculomycosis ranges from 3.3% to 10.4% [30–33]. However, this can vary according to the geographical location, and is probably related to the risk of trauma caused by organic matter [33]. To date, 20 cases of ocular infections caused by *Alternaria* spp. have been reported. The patient characteristics, risk factors, treatment and outcome are summarized in supplementary Table S1. These cases were reported from the USA (four cases) and another nine countries, with one or two cases each. Male patients accounted for 13 (65%) and females for seven (35%) of the 20 cases. The median patient age was 55 years, ranging from 29 to 82 years. The majority of cases (65.0%) were cases of keratitis ($p = 0.02$), although endophthalmitis was also associated with four (20.0%) cases, and both keratitis and concomitant endophthalmitis were reported in three other cases (15.0%). In one case, keratitis was associated with onychomycosis also caused by *Alternaria* [34]. In general, patients were farmers or gardeners, and had all been exposed to soil and garbage. In many cases (55.5%), accidental or surgical ocular traumas were the predisposing factors. In two cases, the ocular injury was suffered 2–6 years before presentation [35,36]. Six

(30%) of the 20 patients had received therapy with topical and/or systemic steroids. Five (25%) patients had been treated previously with anti-fungal agents. The causative agent was identified as *A. alternata* in six cases and as *A. infectoria* in one case. In the other cases, identification to the species level was not reported.

Rhinosinusitis

Although *Aspergillus* is the most common mould causing fungal sinusitis, other fungi, such as *Alternaria*, can also be involved, albeit less commonly, in such illnesses [37–40]. Seventeen cases of invasive and non-invasive sinusitis caused by *Alternaria* spp. have been reported since 1977. Practically all of these cases were reported from the USA. Another two cases were reported as part of an epidemiological study on paranasal sinus mycoses in India, but specific clinical data for these infections were not included [40]. The patient characteristics, risk factors, treatment and outcome of these cases are summarized in supplementary Table S2. The age of the patients ranged from 13 to 56 years (median 35.6). Male patients accounted for ten (58.8%) and females for seven (41.2%) of the 17 cases. Immunosuppression was not a significant risk factor ($p = 0.09$) for rhinosinusitis caused by *Alternaria*, although this condition was present in 12 (70.6%) patients. Neutropenia was a common factor in ten of these 12 patients, who suffered from haematological malignancies, e.g. acute or chronic myeloid or lymphoblastic leukaemia (7/10), aplastic anaemia (1/10), Hodgkin's lymphoma (1/10) or solid tumour (1/10). Seven patients were bone marrow transplant recipients. The other two immunocompromised patients underwent topical and/or systemic steroid treatment. The infection was invasive in 13 (76.5%) of the 17 cases. *A. alternata* was isolated in four cases and *A. geophila* in one case; in the remaining cases, the aetiological agents were not identified to the species level.

Onychomycosis

The incidence of *Alternaria* as a causative agent of onychomycosis is low, ranging from 0.08% to 2.5% in various epidemiological studies [41–43]. However, no detailed clinical data concerning these cases have been reported. To date, only 17

cases of nail infections due to *Alternaria* spp. have been reported, with most of the patients being from Italy (10/17), followed by India (3/17) and several other countries [34,44–50]. The median patient age was 51.7 years, ranging from 7 to 76 years. Male patients accounted for 11 (64.7%) and female for six (35.3%) of 17 patients. As with onychomycosis caused by other fungi, a history of contact with soil or trauma in the nails existed in most of these cases. Two patients were diabetic [44,49] and two were receiving steroid treatment [34,49]. Clinical manifestations included dystrophy and distal subungual hyperkeratosis or onycholysis. No significant difference ($p = 0.439$) was found between the involvement of fingernails or toenails. The former were involved in nine (52.9%) of the cases, six of which affected more than one nail, and the latter were involved in seven (41.2%) cases, three of which affected more than one nail. Both fingernails and toenails were affected in one patient. Identification to the species level was reported in 14 cases, with *A. alternata* being isolated in 11 cases [45–47,49], and *A. humicola*, *A. pluriseptata* and *A. chlamydospora* in one case [44,49].

Cutaneous and subcutaneous infections

Skin is the most frequent site of infection due to *Alternaria* spp., with 156 cases of skin infection being reported to date (supplementary Table S3). Cutaneous infections are significantly more frequent than subcutaneous infections (88.4% vs. 5.8%, $p < 0.001$). Cutaneous and concomitant subcutaneous infections were both reported in nine (5.8%) cases. Most cases were from Mediterranean countries, i.e. France (38), Spain (35), Italy (15) and Greece (five). The median patient age was 53.9 years, ranging from 6 months to 94 years. These infections were clearly more frequent in males than in females (64.9% vs. 35.1%, $p < 0.001$), which may be explained by the fact that outdoor work is carried out more frequently by males, bringing with it an increased risk of minimal skin trauma [51]. Predisposing factors were described in >50% of the reported cases (128/156), with transplantation being the most common risk factor (51/128, $p < 0.001$). Among those cases, 47 involved solid organs and four involved bone marrow. Cushing's syndrome was diagnosed in ten non-recipient transplant patients (10/77, $p < 0.001$). The remaining

patients with predisposing factors (67/128, $p < 0.001$) were receiving immunosuppressive therapy.

The cases of cutaneous and subcutaneous alternariosis show a range of clinical manifestations. Most patients presented with erythema and desquamation of skin, or with red papules that developed to erosion and ulceration, particularly after steroid treatment. When the infection was associated with a penetrating trauma, clinical manifestations in the skin usually corresponded to a unilocular livid red plaque with central ulceration, which sometimes developed into a crust-ulcerous lesion, and usually affected previously healthy patients. A multilocular form of disease, with papulonodular lesions or cutaneous nodules, usually painless, was generally associated with disseminated alternariosis [52]. The most frequently isolated species was *A. alternata*, accounting for 59 (37.8%) of the 156 cases, followed by *A. tenuissima* (23 cases, 14.7%), *A. infectoria* (11 cases, 7.1%), *A. chartarum* and *A. chlamydospora* (two cases each), and *A. dianthicola*, *A. longipes* and *A. stemphylioides* (one case each). Identification at species level was not reported in the 55 remaining cases.

IN VITRO SUSCEPTIBILITY

Table 1 summarizes the scarce data available concerning the *in vitro* antifungal susceptibility of *Alternaria*. Isolates were not identified to the species level in any of the four studies [53–56] that included more than ten isolates. Amphotericin B showed variable *in vitro* activity, with MICs ranging from 0.032 to 16 mg/L. The *in vitro* activity of flucytosine against *Alternaria* spp. was practically nil [24,53,57–63]. Among the azoles, fluconazole showed no activity against *Alternaria* spp. [24,53,61,64], whereas ketoconazole MICs varied from ≤ 0.5 mg/L [53,59,61,65,66] to ≥ 2 mg/L [45,53,62,64]. In general, itraconazole, voriconazole and posaconazole showed good activity, with MICs ≤ 0.5 mg/L [54–56,67,68], although MIC₉₀ values of >8 mg/L have also been reported [54,55]. Slightly lower activity has been reported for ravuconazole, with MIC₅₀ values of 1 mg/L [54,55]. *Alternaria* seems to be susceptible *in vitro* to terbinafine [69] and to caspofungin [70], but resistant to micafungin [71], although only very limited data are available. As no comparative studies have been performed, it is not known whether significant differences exist between the antifungal

Table 1. *In vitro* susceptibility of *Alternaria* spp. to antifungal agents

Reference	No. of isolates	Antifungal agent (MICs in mg/L)											
		AMB	5FC	FLC	KCZ	MCZ	ITC	VRC	RVC	PSC	TBF	MFG	CSP
[10]	1 ^{a,b}	0.25	–	–	–	–	0.25	–	–	–	–	–	–
[24]	1 ^{c,d}	0.3	>322.7	40.0	1.6	2.5	0.24	–	–	–	–	–	–
[45]	1 ^{a,b}	3.0	10	–	3.0	–	–	–	–	–	–	–	–
	1 ^{b,e}	–	30	–	10	–	–	–	–	–	–	–	–
[53]	20 ^{d,f,g}	0.12–16	>128	16 to >64	0.5–8.0	0.5–8.0	0.12–2.0	–	–	–	–	–	–
[54]	11 ^{d,f,h}	0.25–0.50	–	–	–	–	0.25 to >8	0.25 to >8	1.0 to >8	–	–	–	–
[55]	11 ^{d,f,h}	0.25–0.50	–	–	–	–	0.25 to >8	0.25 to >8	1.0 to >8	0.12 to >8	–	–	–
[56]	13 ^{d,f,h}	0.50–4	–	–	–	–	0.50–1.0	–	–	0.125–0.25	–	–	–
[57]	1 ^{b,f}	3.2	100	–	–	–	–	–	–	–	–	–	–
[58]	1 ^{b,f}	0.3	>200	–	–	0.3	–	–	–	–	–	–	–
[59]	2 ^{b,i}	0.2	>100	–	0.4	0.4	–	–	–	–	–	–	–
[60]	1 ^{a,d}	1.0	>128	–	–	–	0.25	–	–	–	–	–	–
[61]	1 ^{d,j}	0.125	>64	64.0	0.5	–	0.125	0.5	–	–	–	–	–
[62]	1 ^{a,d}	0.5	>128	–	2.0	–	0.5	–	–	–	–	–	–
[63]	6 ^{a,k,l}	0.3–1.2	>100	–	–	–	–	–	–	–	–	–	–
[64]	1 ^{a,g}	0.4	–	50.0	50.0	0.8	0.05	–	–	–	–	–	–
[65]	1 ^{b,i}	–	–	–	0.5	–	0.05	–	–	–	–	–	–
[66]	1 ^{a,b}	0.3	–	–	0.1	–	0.07	–	–	–	–	–	–
[67]	1 ^{l,m}	0.032	–	16.0	–	–	1.5	0.23	–	–	–	–	–
[68]	4 ^{d,f,l}	0.5–4.0	–	–	–	–	0.25–1.0	1.0–2.0	–	–	–	–	–
[69]	1 ^{a,d}	–	–	–	–	–	–	–	–	0.25	–	–	–
[70]	1 ^{f,g}	–	–	–	–	–	–	–	–	–	–	–	≤ 0.09
[71]	3 ^{a,d}	0.5	–	–	–	–	≤ 0.01	–	–	–	–	>8.0	–
[81]	1 ^{a,b}	1.5	–	–	–	–	–	–	–	–	–	–	–
[82]	2 ^{b,f,l}	1.2 to >10	–	–	–	–	–	–	–	–	–	–	–
[84]	1 ^{a,d}	0.25	–	–	–	–	8.0	–	–	–	–	–	–

AMB, amphotericin B; 5FC, flucytosine; FLC, fluconazole; KCZ, ketoconazole; MCZ, miconazole; ITC, itraconazole; VRC, voriconazole; RVC, ravuconazole; PSC, posaconazole; TBF, terbinafine; MFG, micafungin; CSP, caspofungin.

^a*Alternaria alternata*. ^bSusceptibility method not reported. ^c*Alternaria longipes*. ^dMicrodilution broth method. ^e*Alternaria chlamydospora*. ^f*Alternaria* spp. ^gMacrodilution broth method. ^hMIC₅₀–MIC₉₀. ⁱ*Alternaria tenuissima*. ^j*Alternaria infectoria*. ^kAgar diffusion. ^lMIC range. ^mEstest.

susceptibilities of the two most clinically common *Alternaria* spp., i.e. *A. alternata* and *A. infectoria*.

TREATMENT AND OUTCOME

Ocular infections

Treatment and outcome of oculomycosis cases caused by *Alternaria* are summarized in supplementary Table S1. Various antifungal drugs have been used in the treatment of these infections, including topical, intravitreal and/or systemic amphotericin B, flucytosine, topical and oral fluconazole, topical ketoconazole, itraconazole, and topical and oral voriconazole. On most occasions, the infection was resolved following antifungal therapy, but surgical interventions, e.g. keratoplasty or vitrectomy, were sometimes necessary. In two cases, treatment and outcome were not described. In all but one of the cases, the infection was resolved. In one patient, the lesions persisted after antifungal and surgical treatment, but the fungus did not grow in culture [72]. Owing to the poor intravitreal penetration of amphotericin B given intravenously, intravitreal administration of this antifungal drug after vitrectomy is indicated in severe cases of fungal endophthalmitis [73]. Systemic and topical fluconazole can also be used [73]. Voriconazole, administered orally (400 mg twice daily), reaches concentrations of 0.81 and 1.13 mg/L in vitreous fluid and aqueous humour, respectively, which correspond approximately to the MIC₉₀ values required for most pathogenic fungi tested [74], including *Alternaria* spp. [56]. In addition, the clinical efficacy of voriconazole in keratitis caused by *Alternaria* has recently been reported [75,76]. Thus, this drug appears to be a useful alternative to intravitreal or topical administration [77]. In addition, therapeutic intravitreal levels of posaconazole were obtained after topical and oral administration [78]. Although there is no published clinical experience of the use of posaconazole to treat oculomycosis caused by *Alternaria*, the *in vitro* activity [55,56] and the clinical efficacy of this drug in treating ocular infections caused by other fungi [78,79] suggest that posaconazole could also be a therapeutic alternative for keratitis and endophthalmitis caused by *Alternaria*.

Rhinosinusitis

Treatments and outcomes of rhinosinusitis caused by *Alternaria* are summarized in supplementary Table S2. To date, amphotericin B has been the antifungal agent used most frequently, either alone or in combination with flucytosine and/or rifampicin. In the majority of cases, treatment with antifungal agents was combined with surgery. In two patients with no immunological impairment, the infection was recurrent despite surgical and medical treatment [80,81]. All patients were cured, with the exception of one who relapsed [58] and two who died from other causes [82].

Onychomycosis

Itraconazole was the drug used most frequently for the treatment of onychomycosis, being administered to 12 (92.3%) of the 13 patients who received antifungal therapy. In eight (72.2%) patients, the infection was cured.

Cutaneous and subcutaneous alternariosis

As for the other clinical manifestations of *Alternaria* infections, no standard treatment exists for cutaneous and subcutaneous infections. The treatments and outcomes of the reported cases are summarized in supplementary Table S3. In 21 (13.4%) of the 156 cases reported, there are no data concerning treatment. In three (2.22%) of the treated patients, infection was resolved with physical procedures, e.g. hyperbaric oxygen [83] or local heat [29,84]. The infection was resolved in nine (6.66%) cases following surgery, and suppression of steroids was sufficient for resolution in four (2.96%) of the 135 cases in which therapeutic details were provided. A variety of antifungal drugs were also used to treat those infections, including amphotericin B, azoles and terbinafine. Since the 1990s, itraconazole has been the antifungal drug most frequently used, generally with a satisfactory outcome. Voriconazole was used only on two occasions [85,86], resolving one infection [86]. No clinical experience has been reported concerning the treatment of cutaneous/subcutaneous alternariosis with posaconazole.

CONCLUSIONS

Although frequently associated with allergic respiratory diseases, *Alternaria* is an opportunistic pathogenic mould that causes mainly oculomycosis, rhinosinusitis, onychomycosis, and cutaneous and subcutaneous infections, generally in immunocompromised patients. *A. alternata* is the species reported most frequently as causing the different clinical manifestations of alternariosis, although identification to the species level is not often performed and the aetiological agent was probably often misidentified. Occupational exposure to soil and garbage, surgical and non-surgical trauma and topical or systemic steroids are predisposing factors for oculomycosis. Although rhinosinusitis has also been described in immunocompetent hosts, the majority of cases involve immunocompromised patients, most of whom have undergone bone marrow transplantation. Contact with soil or trauma of the nails are the most frequent predisposing factors for onychomycosis caused by *Alternaria* spp., although steroid treatment and diabetes should also be considered as possible predisposing factors. Immunosuppression is a common feature in cutaneous and/or subcutaneous cases of alternariosis, with most patients being solid organ transplant recipients. Cushing's syndrome has also been reported as a predisposing factor in many cases.

In general, *Alternaria* shows a good response to conventional antifungal drugs. On some occasions, steroid suppression or reduction may be sufficient to resolve the infection. Surgery alone has also been used successfully in some cases, but has been used in many other cases in combination with medical treatment. In general, cases of alternariosis have responded well to treatment with the older antifungal drugs, e.g. amphotericin B, flucytosine, fluconazole, micotazole and nystatin. Itraconazole is the antifungal drug that has been used most frequently in cases of onychomycosis and cutaneous and subcutaneous infections, with generally satisfactory results. Voriconazole could be a good alternative, especially in cases of oculomycosis, but further studies are required. On the basis of its *in vitro* activity and pharmacokinetics, posaconazole also constitutes a promising therapeutic option.

TRANSPARENCY DECLARATION

The authors declare that they have no conflicting interests in relation to this article.

SUPPLEMENTARY MATERIAL

Additional Supporting Information may be found in the online version of this article:

Table S1. Reported cases of oculomycosis by *Alternaria* spp.

Table S2. Reported cases of rhinosinusitis caused by *Alternaria* spp.

Table S3. Reported cases of cutaneous and subcutaneous infections caused by *Alternaria* spp.

Please note: Citations listed in the Supporting Information are referenced in the References below.

Please note: Blackwell Publishing are not responsible for the content or functionality of any Supporting Information supplied by the authors. Any queries (other than missing material) should be directed to the corresponding author for the article.

REFERENCES

1. Pfaller MA, Pappas PG, Wingard JR. Invasive fungal pathogens: current epidemiological trends. *Clin Infect Dis* 2006; **43** (suppl 1): S3–S14.
2. Ajello L, Georg LK, Steigbigel RT. A case of phaeohyphomycosis caused by a new species of *Phialophora*. *Mycologia* 1974; **66**: 490–498.
3. Welty KE, Perfect JR. Cutaneous mycosis in solid organ transplants. *Clin Adv Treat Fungal Infect* 1991; **2**: 1–3.
4. Clancy CJ, Wingard JR, Nguyen MH. Subcutaneous phaeohyphomycosis in transplant recipients: review of the literature and demonstration of *in vitro* synergy between antifungal agents. *Med Mycol* 2000; **38**: 169–175.
5. de Hoog GS, Guarro J, Gené J, Figueras MJ. *Atlas of clinical fungi*, 2nd edn. Baarn, The Netherlands: Centraalbureau voor Schimmelcultures, 2000.
6. Yu H. Studies on fungi of the normal skin. *Acta Dermatol (Kyoto)* 1965; **60**: 126–174.
7. Nema HV, Ahuja OP, Bal A, Mohapatra LN. Mycotic flora of the conjunctiva. *Am J Ophthalmol* 1966; **62**: 968–970.
8. Shugar MA, Montgomery WW, Hyslop NE. *Alternaria* sinusitis. *Ann Otol Rhinol Laryngol* 1981; **90**: 251–254.
9. Ogawa H, Fujimura M, Amaike S, Matsumoto Y, Kitagawa M, Matsuda T. Eosinophilic pneumonia caused by *Alternaria alternata*. *Allergy* 1997; **52**: 1005–1008.
10. Lyke KE, Miller NS, Towne L, Merz WG. A case of cutaneous ulcerative alternariosis: rare association with diabetes mellitus and unusual failure of itraconazole treatment. *Clin Infect Dis* 2001; **32**: 1178–1187.

11. Bush RK, Prochnau JJ. *Alternaria*-induced asthma. *J Allergy Clin Immunol* 2004; **113**: 227–234.
12. Cantani A, Ciaschi V. Epidemiology of *alternaria* alternata allergy: a prospective study in 6840 Italian asthmatic children. *Eur Rev Med Pharmacol Sci* 2004; **8**: 289–294.
13. Pant H, Kette FE, Smith WB, Wormald PJ, Macardle PJ. Fungal-specific humoral response in eosinophilic mucus chronic rhinosinusitis. *Laryngoscope* 2005; **115**: 601–606.
14. Stark PC, Celedon JC, Chew GL *et al.* Fungal levels in the home and allergic rhinitis by 5 years of age. *Environ Health Perspect* 2005; **113**: 1405–1409.
15. Lobritz RW, Roberts TH, Marraro RV, Carlton PK, Thorp DJ. Granulomatous pulmonary disease secondary to *Alternaria*. *JAMA* 1979; **241**: 596–597.
16. Fathallah Mili A, Boiron P, Robert D *et al.* Alternariose palatine et cutanée à *Alternaria infectoria* chez une patiente immunocompétente tunisienne. *J Mycol Med* 2003; **13**: 145–148.
17. Kucan JO, Hall S. *Alternaria* burn wound sepsis. *J Burn Care Rehabil* 1985; **6**: 501–502.
18. Revankar SG, Patterson JE, Sutton DA, Pullen R, Rinaldi MG. Disseminated phaeomycosis: review of an emerging mycosis. *Clin Infect Dis* 2002; **34**: 467–476.
19. Brooks AMV, Lazarus MG, Weiner JM. Soft contact lens contamination by *Alternaria alternata*. *Med J Aust* 1984; **140**: 490–491.
20. Millar BC, Xu J, Walker MJ, Boyd NAM, McMullan R, Moore JE. Isolation of *Alternaria alternata* from an emollient cream: implications for public health. *Mycopathologia* 2003; **156**: 273–277.
21. de Hoog GS, Horré R. Molecular taxonomy of the *Alternaria* and *Ulocladium* species from humans and their identification in the routine laboratory. *Mycoses* 2002; **45**: 259–276.
22. Bartolome B, Valks R, Fraga J, Buendía V, Fernández-Herrera J, García-Díez A. Cutaneous alternariosis due to *Alternaria chlamydospora* after bone marrow transplantation. *Act Derm Venereol* 1999; **79**: 244.
23. Chartois-Léauté AG, Wolfrom E, de Bièvre C, Geniaux M, Couprie B. Alternariose cutanée à *Alternaria chlamydospora*. *J Mycol Méd* 1995; **5**: 182–183.
24. Gené J, Azón-Masoliver A, Guarro J *et al.* Cutaneous phaeohyphomycosis caused by *Alternaria longipes* in an immunosuppressed patient. *J Clin Microbiol* 1995; **33**: 2774–2776.
25. Mitchell AJ, Solomon AR, Beneke ES, Anderson TF. Subcutaneous alternariosis. *J Am Acad Dermatol* 1983; **8**: 673–676.
26. Badenoch PR, Halliday CL, Ellis DH, Billing KJ, Mills RA. *Ulocladium atrum* keratitis. *J Clin Microbiol* 2006; **44**: 1190–1193.
27. Duran MT, Del Pozo J, Yebra MT *et al.* Cutaneous infection caused by *Ulocladium chartarum* in a heart transplant recipient: case report and review. *Acta Derm Venereol* 2003; **83**: 218–221.
28. Romano C, Maritati E, Paccagnini E, Massai L. Onychomycosis due to *Ulocladium botrytis*. *Mycoses* 2004; **47**: 346–348.
29. Gilaberte M, Bartralot R, Torres JM *et al.* Cutaneous alternariosis in transplant recipients: clinicopathologic review of 9 cases. *J Am Acad Dermatol* 2005; **52**: 653–659.
30. Chander J, Sharma A. Prevalence of fungal corneal ulcers in Northern India. *Infection* 1994; **22**: 207–209.
31. Panda A, Sharma N, Gopal D, Kumar N, Satpathy G. Mycotic keratitis in children: epidemiologic and microbiologic evaluation. *Cornea* 1997; **16**: 295–299.
32. Tanure MA, Cohen EJ, Grewal S, Rapuano CJ, Laibson PR. Spectrum of fungal keratitis at Wills Eye Hospital, Philadelphia, Pennsylvania. *Cornea* 2000; **19**: 307–312.
33. Chowdhary A, Singh K. Spectrum of fungal keratitis in North India. *Cornea* 2005; **1**: 8–15.
34. Arrese JE, Piérard-Franchimont C, Piérard GE. Onychomycosis and keratomycosis caused by *Alternaria* spp. *Am J Dermatopathol* 1996; **18**: 611–613.
35. Ferrer C, Muñoz G, Alió JL, Abad JL, Colom F. Polymerase chain reaction diagnosis in fungal keratitis caused by *Alternaria alternata*. *Am J Ophthalmol* 2002; **133**: 398–399.
36. Zahra LV, Mallia D, Hardie JG, Bezzina A, Fenech T. Case report. Keratomycosis due to *Alternaria alternata* in a diabetic patient. *Mycoses* 2002; **45**: 512–514.
37. Chakrabarti A, Sharma SC. Paranasal sinus mycoses. *Indian J Chest Dis Allied Sci* 2000; **42**: 293–304.
38. Panth H, Kette FE, Smith WB, Wormald PJ, Macardle PJ. Fungal-specific humoral response in eosinophilic mucus chronic rhinosinusitis. *Laryngoscope* 2005; **115**: 601–606.
39. Schell WA. Unusual fungal pathogens in fungal rhinosinusitis. *Otolaryngol Clin North Am* 2000; **33**: 367–373.
40. Chakrabarti A, Sharma SC, Chander J. Epidemiology and pathogenesis of paranasal sinus mycoses. *Otolaryngol Head Neck Surg* 1992; **107**: 745–750.
41. Bokhari MA, Hussain I, Jahangir M, Haroon TS, Aman S, Khurshid K. Onychomycosis in Lahore, Pakistan. *Int J Dermatol* 1999; **38**: 591–595.
42. García-Martos P, Domínguez I, Marín P, Linares M, Mir J, Calap J. Onychomycosis por hongos filamentosos no dermatofitos en Cádiz. *Enferm Infecc Microbiol Clin* 2000; **18**: 319–324.
43. Hilmioglu-Polat S, Metin DY, Inci R, Dereli T, Kilinc I, Tumbay E. Non-dermatophytic molds as agents of onychomycosis in Izmir, Turkey—a prospective study. *Mycopathologia* 2005; **160**: 125–128.
44. Wadhvani K, Srivastava K. Some cases of onychomycosis from North India in different working environments. *Mycopathologia* 1985; **92**: 149–155.
45. Singh SM, Naidu J, Pouranik M. Ungual and cutaneous phaeohyphomycosis caused by *Alternaria alternata* and *Alternaria chlamydospora*. *J Med Vet Mycol* 1990; **28**: 275–278.
46. Gianni C, Cerri A, Crosti C. Ungual phaeohyphomycosis caused by *Alternaria alternata*. *Mycoses* 1996; **40**: 219–221.
47. Glowacka A, Wasowska-Krolikowska K, Skowron-Kobos J, Kurnatowski M, Janniger CK. Childhood onychomycosis: alternariosis of all ten fingernails. *Cutis* 1998; **62**: 125–129.
48. Baykal C, Kazancioglu R, Buyukbabani N *et al.* Simultaneous cutaneous and unguinal alternariosis in a renal transplant recipient. *Br J Dermatol* 2000; **143**: 910–912.
49. Romano C, Paccagnini E, Difonzo EM. Onychomycosis caused by *Alternaria* spp. in Tuscany, Italy from 1985 to 1999. *Mycoses* 2001; **44**: 73–76.
50. Baran R, Coquard F. Combination of fluconazole and urea in a nail lacquer for treating onychomycosis. *J Dermatolog Treat* 2005; **16**: 52–55.
51. Lespessailles E, Kerdraon R, Michenet P, Barthez JP, Mille C, Benhamou CL. *Alternaria* infection of the skin and

- joints. A report of two cases involving the hand. *Rev Rhum Engl Ed* 1999; **66**: 509–511.
52. Vennewald I, Wollina U. Cutaneous infections due to opportunistic molds: uncommon presentations. *Clin Dermatol* 2005; **23**: 565–571.
 53. Pujol I, Aguilar C, Gené J, Guarro J. In vitro antifungal susceptibility of *Alternaria* spp. and *Ulocladium* spp. *J Antimicrob Chemother* 2000; **46**: 337–338.
 54. Cuenca-Estrella M, Gomez-Lopez A, Mellado E, Garcia-Effron G, Monzon A, Rodriguez-Tudela JL. In vitro activity of ravuconazole against 923 clinical isolates of nondermatophyte filamentous fungi. *Antimicrob Agents Chemother* 2005; **49**: 5136–5138.
 55. Cuenca-Estrella M, Gomez-Lopez A, Mellado E, Buitrago MJ, Monzon A, Rodriguez-Tudela JL. Head-to-head comparison of the activities of currently available antifungal agents against 3,378 Spanish clinical isolates of yeast and filamentous fungi. *Antimicrob Agents Chemother* 2006; **50**: 917–921.
 56. Sabatelli F, Patel R, Mann PA *et al.* In vitro activities of posaconazole, fluconazole, itraconazole, voriconazole, and amphotericin B against a large collection of clinically important molds and yeasts. *Antimicrob Agents Chemother* 2006; **50**: 2009–2015.
 57. Ando N, Takatori K. Keratomycosis due to *Alternaria alternata* corneal transplant infection. *Mycopathologia* 1987; **100**: 17–22.
 58. Garau J, Diamond RD, Lagrotteria LB, Kabins SA. *Alternaria* osteomyelitis. *Ann Intern Med* 1977; **86**: 747–748.
 59. Viviani MA, Tortorano AM, Laria G, Giannetti A, Bignotti G. Two new cases of cutaneous alternariosis with a review of the literature. *Mycopathologia* 1986; **96**: 3–12.
 60. Benito N, Moreno A, Puig J, Rimola A. Alternariosis after liver transplantation. *Transplantation* 2001; **72**: 1840–1843.
 61. Lo Cascio G, Ligozzi M, Maccacaro L, Fontana R. Utility of molecular identification in opportunistic mycotic infections: a case of cutaneous *Alternaria infectoria* infection in a cardiac transplant recipient. *J Clin Microbiol* 2004; **42**: 5334–5336.
 62. Sood N, Gugnani HC, Guarro J, Paliwal-Joshi A, Vijayan VK. Subcutaneous phaeohyphomycosis caused by *Alternaria* in an immunocompetent patient. *Int J Dermatol* 2007; **46**: 412–413.
 63. Mardh PA, Hallberg T. *Alternaria alternata* as a cause of opportunistic fungal infections in man. *Scand J Infect Dis* 1978; **16**: 36–40.
 64. Del Palacio A, Gómez-Hernando C, Revenga F *et al.* Cutaneous *Alternaria alternata* infection successfully treated with itraconazole. *Clin Exp Dermatol* 1996; **21**: 241–243.
 65. Contet-Audonnet N, Barbaud A, Guérin V *et al.* Alternariose cutanée et syndrome de Cushing: nouvelle observation. *J Mycol Med* 1991; **118**: 82–83.
 66. Lerner LH, Lerner EA, Bello YM. Co-existence of cutaneous and presumptive pulmonary alternariosis. *Int J Dermatol* 1997; **36**: 276–301.
 67. Dubois D, Pihet M, Le Clec'h C *et al.* Cutaneous phaeohyphomycosis due to *Alternaria infectoria*. *Mycopathologia* 2005; **160**: 117–123.
 68. Espinel-Ingroff A. In vitro fungicidal activities of voriconazole, itraconazole, and amphotericin B against opportunistic moniliaceous and dematiaceous fungi. *J Clin Microbiol* 2001; **39**: 954–958.
 69. Garcia-Effron G, Gomez-Lopez A, Mellado E, Monzon A, Rodriguez-Tudela JL, Cuenca-Estrella M. In vitro activity of terbinafine against medically important non-dermatophyte species of filamentous fungi. *J Antimicrob Chemother* 2004; **53**: 1086–1089.
 70. Del Poeta M, Schell WA, Perfect JR. In vitro antifungal activity of pneumocandin L-743,872 against a variety of clinically important molds. *Antimicrob Agents Chemother* 1997; **41**: 1835–1836.
 71. Uchida K, Nishiyama Y, Yokota N, Yamaguchi H. In vitro antifungal activity of a novel lipopeptide antifungal agent, FK463, against various fungal pathogens. *J Antibiot* 2000; **53**: 1175–1181.
 72. Hasumura K, Kondo S, Hara R, Miyajima S, Hirata A. A case of endophthalmitis due to *Alternaria* keratomycosis without corneal perforation. *Nippon Ganka Kiyo* 2006; **57**: 213–216.
 73. Rao AG, Thool BA, Rao CV. Endogenous endophthalmitis due to *Alternaria* in an immunocompetent host. *Retina* 2004; **24**: 478–481.
 74. Hariprasad SM, Mieler WF, Holz ER *et al.* Determination of vitreous, aqueous, and plasma concentration of orally administered voriconazole in humans. *Arch Ophthalmol* 2004; **122**: 42–47.
 75. Ozbek Z, Kang S, Sivalingam J, Rapuano C, Cohen E, Hammersmith K. Voriconazole in the management of *Alternaria* keratitis. *Cornea* 2006; **25**: 242–244.
 76. Bunya VY, Hammersmith KM, Rapuano CJ, Ayres BD, Cohen EJ. Topical and oral voriconazole in the treatment of fungal keratitis. *Am J Ophthalmol* 2007; **143**: 151–153.
 77. Levêque D, Nivoix Y, Jehl F, Herbrecht R. Clinical pharmacokinetics of voriconazole. *Int J Antimicrob Agents* 2006; **27**: 274–284.
 78. Sponsel WE, Graybill JR, Nevarez HL, Dang D. Ocular and systemic posaconazole (SCH-56592) treatment of invasive *Fusarium solani* keratitis and endophthalmitis. *Br J Ophthalmol* 2002; **86**: 829–830.
 79. Tu EY, McCartney DL, Beatty RF, Springer KL, Levy J, Edward D. Successful treatment of resistant ocular fusariosis with posaconazole (SCH-56592). *Am J Ophthalmol* 2007; **143**: 222–227.
 80. Shugar MA, Montgomery WW, Hyslop NE. *Alternaria* sinusitis. *Ann Otol* 1981; **90**: 251–254.
 81. Murtagh J, Smith JW, Mackowiak PA. Case report: *Alternaria* osteomyelitis: eighth years of recurring disease requiring cyclic courses of amphotericin B for cure. *Am J Med Sci* 1987; **293**: 399–402.
 82. Morrison VA, Weisdorf DJ. *Alternaria*: a sinonasal pathogen of immunocompromised hosts. *Clin Infect Dis* 1993; **16**: 265–270.
 83. Lee SS, Sun JH, Chang LY, Ueng SW, Shih CH. Limb-threatening necrotizing alternariosis salvaged by adjunctive hyperbaric oxygen therapy. *Scand J Infect Dis* 1998; **30**: 194–196.
 84. Torres-Rodríguez JM, Pérez González M, Corominas JM, Pujol RM. Successful thermotherapy for a subcutaneous infection due to *Alternaria alternata* in a renal transplant recipient. *Arch Dermatol* 2005; **141**: 1171–1173.
 85. Henn SL, Forrest GN. Photo Quiz. Febrile neutropenia associated with painful lesions of the palms and digits. *Clin Infect Dis* 2006; **43**: 747.
 86. Luque P, García-Gil FA, Larraga J *et al.* Treatment of cutaneous infection by *Alternaria alternata* with vorico-

- nazole in a liver transplant patient. *Transplant Proc* 2006; **38**: 2514–2515.
87. Azar P, Aquavella JV, Smith RS. Keratomycosis due to an *Alternaria* species. *Am J Ophthalmol* 1975; **79**: 881–882.
 88. Miño de Kaspar H, Zoulek G, Paredes ME *et al.* Mycotic keratitis in Paraguay. *Mycoses* 1991; **34**: 251–254.
 89. Rummelt V, Ruprecht KW, Boltze HJ, Nauman GOH. Chronic *Alternaria alternata* endophthalmitis following intraocular lens implantation. *Arch Ophthalmol* 1991; **109**: 178.
 90. Wenkel H, Rummelt V, Knorr H, Naumann GOH. Chronic postoperative endophthalmitis following cataract extraction and intraocular implantation. Report of nine patients. *German J Ophthalmol* 1993; **2**: 419–425.
 91. Chang SW, Tsai MW, Hu FR. Deep *Alternaria* keratomycosis with intraocular extension. *Am J Ophthalmol* 1994; **117**: 544–545.
 92. Daniel E, Mathews MS, Chacko S. *Alternaria* keratomycosis in a lepromatous leprosy patient. *Int J Lepr Other Mycobact Dis* 1997; **65**: 492–494.
 93. Koç AN, Erkiş K, Evrensel N, Coskun A. A case of *Alternaria* keratitis treated with fluconazole. *Eur J Clin Microbiol Infect Dis* 1997; **16**: 322–323.
 94. Ferrer C, Montero J, Alió JL, Abad JL, Ruiz-Moreno JM, Colom F. Rapid molecular diagnosis of posttraumatic keratitis and endophthalmitis caused by *Alternaria infectoria*. *J Clin Microbiol* 2003; **41**: 3358–3360.
 95. Verma K, Vajpayee RB, Titiyal JS, Sharma N, Nayak N. Post-LASIK infectious crystalline keratopathy caused by *Alternaria*. *Cornea* 2005; **24**: 1018–1020.
 96. Isshiki Y, Kimura T, Yokoyama M *et al.* Case of fungal endophthalmitis developed after subtenon injections of triamcinolone acetonide. *Nippon Ganka Gakkai Zasshi* 2007; **111**: 741–744.
 97. Kocatürk T, Pineda R II, Green LK, Azar DT. Post-LASIK epithelial dendritic defect associated with *Alternaria*. *Cornea* 2007; **26**: 1144–1146.
 98. Loveless MO, Winn RE, Cambell M, Jones SR. Mixed invasive infection with *Alternaria* species and *Curvularia* species. *Am J Clin Pathol* 1981; **76**: 491–493.
 99. Bassiouny A, Maher A, Bucci TJ, Moawad MK, Hendawy DS. Non-invasive antronycosis: (diagnosis and treatment). *J Laryngol Otol* 1982; **96**: 215–228.
 100. Goodpasture HC, Carlsen T. *Alternaria* osteomyelitis. *Arch Pathol Lab Med* 1983; **107**: 528–530.
 101. Zieske LA, Kopke RD, Hamill R. Dematiaceous fungal sinusitis. *Otolaryngol Head Neck Surg* 1991; **105**: 567–577.
 102. Arduino S, Villar H, Veron T *et al.* Sinusitis maxilar por *Alternaria* sp. en un paciente con trasplante de médula ósea. *Enf Infect Microbiol Clin* 1992; **10**: 68–69.
 103. Iwen PC, Rupp ME, Hinrichs SH. Invasive mold sinusitis: 17 cases in immunocompromised patients and review of the literature. *Clin Infect Dis* 1997; **24**: 1178–1184.
 104. Holmes F. Case report. *Johns Hopkins Microbiol Newslett* 2007; **17**: Available at: <http://pathology5.pathology.jhmi.edu/micro/v17n17.htm>, accessed 1 July, 2008.
 105. Chen L, Thompson K, Taky JB. Pathologic quiz case. A 56-year-old woman with anterior nasal pain and intermittent epistaxis. *Arch Pathol Lab Med* 2004; **128**: 1451–1452.
 106. Borsook ME. Skin infection due to *Alternaria tenuis*. *Can Med Assoc* 1933; **29**: 479–482.
 107. Takatsuki Y. Über eine von einer menschlichen Dermatoze isoliert Spezies von *Alternaria*. *Jpn J Dermatol Urol* 1938; **43**: 633–634.
 108. Botticher WW. *Alternaria* as a possible human pathogen. *Sabouraudia* 1966; **4**: 256–258.
 109. Delacrétaz J, Grigoriu D, Grigorio A. *Alternaria tenuis* en pathologie cutanée humaine. *Ann Dermatol* 1970; **97**: 15–20.
 110. Kawasaki H, Akagi M, Nishimura N. A case of cutaneous alternariosis. *Jpn J Med Mycol* 1970; **11**: 218.
 111. Nakama T. A case of cutaneous alternariosis. *Jpn J Med Mycol* 1970; **11**: 219.
 112. Parker JC, Klinworth GK. The pathologic anatomy of mycoses. In: Baker KD, ed. *Human infection with fungi, actinomycetes and algae*. New York, NY: Springer Verlag, 1971; 963–985.
 113. Higashi N, Asada Y. Cutaneous alternariosis with mixed infection of *Candida albicans*. Report of a patient responding to natamycin. *Arch Dermatol* 1973; **108**: 558–560.
 114. Bourlond A, Decroix J, Dobbelaere F, Lissoir A. Dermal alternariosis. *Ann Dermatol Syphiligr* 1974; **101**: 413–415.
 115. Farmer SG, Komorowski RA. Cutaneous microabscess formation by *Alternaria alternata*. *Am J Clin Pathol* 1976; **66**: 565–569.
 116. Pedersen NB, Mardh PA. Cutaneous alternariosis. *Br J Dermatol* 1976; **94**: 201–209.
 117. Fukushi G, Kameda T, Hanada K, Noguchi M. Cutaneous alternariosis. *Rinsho Derma* 1977; **19**: 227–232.
 118. Fukushima R, Kinbara T, Inoue K. Cutaneous alternariosis. *Jpn J Med Mycol* 1977; **17**: 246.
 119. Percebois G, Biava MG, Kures L. Discussion du pouvoir pathogène de certaines espèces d'*Alternaria*. A propos de trois observations. *Bull Soc Fr Mycol Med* 1978; **7**: 15–18.
 120. Mikoshiha H, Okubo S, Wakamatsu K, Nijo S. Cutaneous alternariosis. *J Dermatol* 1979; **6**: 67–73.
 121. Lucas Morante T, Rotés Mas J, Sabaté de la Cruz X, Bonin Lafuente R, Soler Ramón J. Cushing's syndrome with cutaneous alternariosis. Localization of a tumor with a body scanner. *Rev Clin Esp* 1980; **156**: 133–138.
 122. Chevrant-Breton J, Boisseau-Lebreuil M, Fréour E, Guiguen G, Launois B, Guelfi G. Les alternariosis cutanées humaines: à propos de trois cas. Revue de la littérature. *Ann Dermatol Vénéreol* 1981; **108**: 653–662.
 123. de Moragas JM, Prats D, Verger G. Cutaneous alternariosis treated with miconazole. *Arch Dermatol* 1981; **117**: 292–294.
 124. Rubio Calvo MC, Marti Lopez J, Gomez Lus R. Granuloma dérmico por *Alternaria tenuissima* en un paciente inmunodeprimido. In: Badillet G, ed. Les alternariosis cutanées. Revue de la littérature. *Ponencias 8 Congreso Nacional de Microbiología*. Madrid, Spain, 1981; 224. *J Mycol Med* 1991; **118**: 59–71.
 125. Meraud JP, Guiguen CI, Couprie B *et al.* Une alternariose cutanée d'évolution prolongée. In: Badillet G, ed. Les alternariosis cutanées. Revue de la littérature. *Abstracts of the reunion de la Société Française de Mycologie Médicale*, Tours, 1982. *J Mycol Med* 1991; **118**: 59–71.
 126. Rippon JW. Phaeoophomycosis. In: Wonsiewicz M, ed. *Medical mycology. The pathogenic fungi and pathologic actinomycetes*, 2nd edn. Philadelphia: WB Saunders Co., 1982; 668–693.
 127. Verret JL, Gaborieau F, Chabasse D, Rohmer V, Avenel M, Smulevici A. Alternariose cutanée révélatrice d'une mal-

- adie de Cushing. Un cas avec étude ultrastructurale. *Ann Dermatol Vénéreol* 1982; **109**: 841–846.
128. Del Palacio Hernandez A, Conde-Zurita JM, Reyes Pecharroman S, Rodriguez Noriega A. A case of *Alternaria alternata* Keissler infection of the knee. *Clin Exp Dermatol* 1983; **8**: 641–646.
 129. Renault JJ, Le Duigou D, Doby JM, Barrière H. Alternariose cutanée. *Presse Méd* 1983; **12**: 59.
 130. Blanc Ch, Lamey B, Lapalu J. Alternariose cutanée chez un transplanté renal. *Bull Soc Fr Mycol Med* 1984; **13**: 213–216.
 131. Bourlond A, Alexandre G. Dermal alternariosis in a kidney transplant recipient. *Dermatologica* 1984; **168**: 152–156.
 132. Panagiotidou D, Kapetis E, Chryssomallis F, Ktenides MA, Badillet G. In: Badillet G, ed. Les alternariosis cutanées. Revue de la littérature. Un cas d'alternariose cutanée. *Journées Dermatologiques de Paris*, 1984. *J Mycol Med* 1991; **118**: 59–71.
 133. Puissant A, Badillet G, Maleville J, Meyer CY, Sulimovic L. Alternariose cutanée chez un enfant. *Ann Dermatol Vénéreol* 1984; **111**: 753–754.
 134. Cohen J, Foix C, Badillet G, Weisbecker-Loyau C, Civette J. Alternariose cutanée. In: Badillet G, ed. Les alternariosis cutanées. Revue de la littérature. *Dermatologiques de Paris*, 1985, page 79. *J Mycol Med* 1991; **118**: 59–71.
 135. Galcoczy J, Simon G, Valyi-Nagy T. Case report: human cutaneous alternariosis. *Mycopathologia* 1985; **92**: 77–80.
 136. Laudren A, Chevrant-Breton J, Pichard JP, Boisseau-Lebreuil MT, Guiguen C. Alternariose chez un transplanté renal: un nouveau cas. *Ann Dermatol Vénéreol* 1985; **112**: 255–257.
 137. Levy-Klotz B, Badillet G, Cavelier-Balloy B, Chemaly P, Leverger G, Civatte J. Alternariose cutanée au cours d'un Sida. *Ann Dermatol Vénéreol* 1985; **112**: 739–740.
 138. Male O, Pehamberger H. Die Kutane Alternariose, Fallberichte und Literaturübersicht. *Mykosen* 1985; **28**: 278–304.
 139. Meraud JB, Guiguen CI, Couprie B *et al.* Une alternariose cutanée d'évolution prolongée. *Bull Soc Fr Mycol Med* 1985; **14**: 205–208.
 140. Smandia JA, Viguera J, Casanovas RM *et al.* Lesiones granulomatosas por *Alternaria*. *Acta Dermo-Sifiligr* 1985; **76**: 581.
 141. Di Silverio A, Sachi S. Cutaneous alternariosis: a rare chromohyphomycosis. Report of a case. *Mycopathologia* 1986; **95**: 159–166.
 142. Peyron F, Grillot R, Lebeau B *et al.* Alternariose cutanée chez une malade de 60 ans présentant un lupus érythémateux disséminé et un diabète insulino-dépendant. *Bull Soc Fr Mycol Med* 1986; **15**: 449–453.
 143. Schillinger F, Bressieux JM, Montagnac R, Hopfner C. Les alternarioses humaines. Analyse de la littérature à propos d'un cas personnel. *Semin Hôp Paris* 1986; **62**: 1369–1374.
 144. Simal E, Navarro M, Rubio MC, Carapeto SG. Sobre un caso de alternariosis cutánea. *Actas Dermo-Sifiligr* 1986; **77**: 252–256.
 145. Body BA, Sabio H, Johnson CE, Kahn J, Hanna MD. *Alternaria* infection with a patient with acute lymphocytic leukaemia. *Pediatr Infect Dis J* 1987; **6**: 418–420.
 146. Morin O, Pecquet C, Bouc M, Bureau B. Alternariose d'évolution prolongée chez un malade immunodéprimé. *Bull Soc Fr Mycol Med* 1987; **16**: 153–158.
 147. Stenderup J, Bruhn M, Gadeberg C, Stenderup A. Cutaneous alternariosis. Case report. *Acta Path Microbiol Immunol Scand* 1987; **95**: 79–81.
 148. Blanchet P, Bilet S, Milleron B, Grossin M, Fitoussi C, Belaich S. Alternariose cutanée associée à un cortico-surrénalome malin. In: Badillet G, ed. Les alternariosis cutanées. Revue de la littérature. *Dermatologiques de Paris*, 1988, page 49. *J Mycol Med* 1991; **118**: 59–71.
 149. Camenen I, De Closets F, Vaillant L *et al.* Alternariose cutanée à *Alternaria tenuissima*. *Ann Dermatol Vénéreol* 1988; **115**: 839–842.
 150. Iwatsu T. Cutaneous alternariosis. *Arch Dermatol* 1988; **124**: 1822–1825.
 151. Maldonado Lopez R, Sanchez Castanon J, Sanchez Yus E, Olmos Acebes L, Robledo Aguilar A. Alternariosis cutánea en un paciente con síndrome nefrótico. *Med Cutan Iber Lat Am* 1988; **16**: 466–468.
 152. Ranfaing E, Billerey C, Barale T, Brousse A, Reboud G. Alternariose cutanée. Aspects anatomo-pathologiques à propos d'un cas et revue de la littérature. *Semin Hôp Paris* 1988; **64**: 3117–3120.
 153. Aznar R, Marigil J, Puig de la Bellacasa J *et al.* Cutaneous alternariosis responding to ketoconazole. *Lancet* 1989; **i**: 667–668.
 154. Junkins JM, Beveridge RA, Friedman KJ. An unusual fungal infection in an immunocompromised oncology patient. *Arch Dermatol* 1989; **124**: 1421–1424.
 155. Miegeville M, Bureau B, Morin O, Berthelo JM, Prost A. Nouveau cas d'alternariose cutanée chez un malade sous corticothérapie. *Bull Soc Fr Mycol Med* 1989; **18**: 329–332.
 156. Wätzig V, Schmidt U. Primäre Kutane Granulomatöse Alternariose. *Der Hautarzt* 1989; **40**: 718–720.
 157. Diaz M, Puente R, Trevino MA. Response of long-running *Alternaria alternata* infection to fluconazole. *Lancet* 1990; **336**: 513.
 158. Lulin J, Lancien G, Sandron A *et al.* Alternariose cutanée: à propos d'un nouveau cas. *Nouv Dermatol* 1990; **9**: 183–184.
 159. Rovira M, Marin P, Martin-Ortega E, Montserrat E, Rozman C. *Alternaria* infection in a patient receiving chemotherapy for lymphoma. *Acta Haematol* 1990; **84**: 98–100.
 160. Sneeringer RM, Haas DW. Cutaneous alternaria infection in a patient on chronic corticosteroids. *J Tenn Med Assoc* 1990; **83**: 15–17.
 161. Drouet E, Luciani J, Frantz P, Chomette G, Ravisse P, Dupont B. Alternariose cutanée et sarcome de Kaposi chez un greffé renal. *J Mycol Med* 1991; **118**: 84–87.
 162. Guerin V, Barbaud A, Duquenne M *et al.* Cushing's disease and cutaneous alternariosis. *Arch Intern Med* 1991; **151**: 1865–1868.
 163. Kasperlik-Zaluska AA, Bielunska S. Effect of mitotane on *Alternaria alternata* infection in Cushing's syndrome. *Lancet* 1991; **337**: 53–54.
 164. Panagiotidou D, Kapetis E, Chryssomallis F, Karakatsanis G, Badillet G. Deux cas d'alternariose cutanée en Grèce. *J Mycol Med* 1991; **118**: 88–89.
 165. Lanigan SW. Cutaneous *Alternaria* infection treated with itraconazole. *Br J Dermatol* 1992; **127**: 39–40.
 166. Duffill MB, Coley KE. Cutaneous phaeohyphomycosis due to *Alternaria alternata* responding to itraconazole. *Clin Exp Dermatol* 1993; **18**: 156–158.
 167. Repiso T, Martin N, Huguet P *et al.* Cutaneous alternariosis in a liver transplant recipient. *Clin Infect Dis* 1993; **16**: 729–730.
 168. Richardson AA, Agger WA, Ringstrom JB, Kemnitz MJ. Subcutaneous alternariosis of the foot in a patient on corticosteroids. *J Am Podiatr Med Assoc* 1993; **83**: 472–474.

169. Shearer C, Chandrasekar PH. Cutaneous alternariosis and regional lymphadenitis during allogenic BMT. *Bone Marrow Transplant* 1993; **11**: 497–499.
170. Machet MC, Stephanov E, Estève E *et al.* Alternariose cutanée survenant au cours de l'évolution d'un pemphigus traité, a propos de 2 cas. *Ann Pathol* 1994; **14**: 186–191.
171. Mirkin LD. *Alternaria alternata* infection of skin in a 6-year-old boy with aplastic anemia. *Pediatr Pathol* 1994; **14**: 757–761.
172. Neumeister B, Hartmann W, Oethinger M, Heymer B, Marre R. A fatal infection with *Alternaria alternata* and *Aspergillus terreus* in a child with agranulocytosis of unknown origin. *Mycoses* 1994; **37**: 181–185.
173. Becherel PA, Chosidow O, Frances C. Cutaneous alternariosis after renal transplantation. *Ann Intern Med* 1995; **122**: 71–72.
174. Castanet J, Lacour JP, Toussaint-Gary M, Perrin C, Rodot S, Ortonne JP. *Alternaria tenuissima* plurifocal cutaneous infection. *Ann Dermatol Venerol* 1995; **122**: 115–118.
175. Chaidemenos GC, Mourellou O, Karakatsanis G, Koussidou T, Panagiotidou D, Kapetis E. Cutaneous alternariosis in an immunocompromised patient. *Cutis* 1995; **56**: 145–150.
176. Machet L, Machet MC, Maillot F, Cotty F, Vaillant L, Lorette G. Cutaneous alternariosis occurring in a patient treated with local intrarectal corticosteroids. *Acta Derm Venerol* 1995; **75**: 328–329.
177. Palencarova E, Jesenska Z, Plank L, Straka S, Baska T, Hajtman A. Phaeohyphomycosis caused by *Alternaria* species and *Phaeosclera dematioides* Sigler, Tsuneda and Carmichael. *Clin Exp Dermatol* 1995; **20**: 419–422.
178. Saez-Santamaria MC, Gilaberte Y, Garcia-Latasa FJ, Carapeto FJ. Cutaneous alternariosis in a nonimmunocompromised patient. *Int J Dermatol* 1995; **34**: 556–557.
179. Machet L, Jan V, Machet MC, Vaillant L, Lorette G. Cutaneous alternariosis: role of corticosteroid-induced cutaneous fragility. *Dermatology* 1996; **193**: 342–344.
180. Romano C, Fimiani M, Pellegrino M *et al.* Cutaneous phaeohyphomycosis due to *Alternaria tenuissima*. *Mycoses* 1996; **39**: 211–215.
181. Romano C, Valenti L, Miracco C *et al.* Two cases of cutaneous phaeohyphomycosis by *Alternaria alternata* and *Alternaria tenuissima*. *Mycopathologia* 1997; **137**: 65–74.
182. Acland KM, Hay RJ, Groves R. Cutaneous infection with *Alternaria alternata* complicating immunosuppression: successful treatment with itraconazole. *Br J Dermatol* 1998; **138**: 354–356.
183. Laumaille CI, Le Gall F, Degeilh B, Guého E, Huerre M. Infection cutanée à *Alternaria infectoria* après greffe hépatique. *Ann Pathol* 1998; **18**: 192–194.
184. Altomare GF, Capella V, Boneschi V, Viviani MA. Effectiveness of terbinafine in cutaneous alternariosis. *Br J Dermatol* 2000; **142**: 840–841.
185. Ioannidou DJ, Stefanidou MP, Maraki SG, Panayiotides JG, Tosca AD. Cutaneous alternariosis in a patient with idiopathic pulmonary fibrosis. *Int J Dermatol* 2000; **39**: 293–295.
186. Magina S, Lisboa C, Santos P *et al.* Cutaneous alternariosis by *Alternaria chartarum* in a renal transplanted patient. *Br J Dermatol* 2000; **142**: 1261–1262.
187. Romero ML, Siddiqui AH. Photo quiz. Cutaneous alternariosis. *Clin Infect Dis* 2000; **30**: 174–175.
188. Gerdson R, Uerlich M, De Hoog GS, Bieber T, Horré R. Sporotrichoid phaeohyphomycosis due to *Alternaria infectoria*. *Br J Dermatol* 2001; **145**: 484–486.
189. Gilmour TK, Rytina E, O'Connell PB, Sterling JC. Cutaneous alternariosis in a cardiac transplant recipient. *Br J Dermatol* 2001; **42**: 46–49.
190. Halaby T, Boots H, Vermeulen A *et al.* Phaeohyphomycosis caused by *Alternaria infectoria* in a renal transplant recipient. *J Clin Microbiol* 2001; **39**: 1952–1955.
191. Pereiro M, Suárez I, Monteagudo B, Abalde MT, Sánchez-Aguilar D, Toribio J. Alternariosis refractory to itraconazole in a patient suffering from bullous pemphigoid. *Dermatology* 2001; **202**: 268–270.
192. Romano C, Asta F, Miracco C, Fimiani M. Verrucoid lesions of the right hand and wrist. *Arch Dermatol* 2001; **137**: 815–820.
193. Courville P, Favennec L, Viacroze C *et al.* Co-existent cutaneous cryptococcosis of the forearm and cutaneous alternariosis of the leg in a patient with metastatic thymoma. *J Cutan Pathol* 2002; **29**: 55–58.
194. Eguino P, Aguirrebengoa K, Vilar B, Zarraga S, Ratón JA, Montejo M. Lesiones verrucosas subcutáneas en un paciente con trasplante renal. *Enferm Infecc Microbiol Clin* 2002; **20**: 129–130.
195. Mayser P, Nilles M, de Hoog GS. Case report. Cutaneous phaeohyphomycosis due to *Alternaria alternata*. *Mycoses* 2002; **45**: 338–340.
196. Miele PS, Levy CS, Smith MA *et al.* Primary cutaneous fungal infections in solid organ transplantation: a case series. *Am J Transplant* 2002; **2**: 678–683.
197. Romano C, Miracco C, Presenti L, Massai L, Fimiani M. Immunohistochemical study of subcutaneous phaeohyphomycoses. *Mycoses* 2002; **45**: 368–372.
198. Calabuig-Muñoz E, Todoli-Parra JA, Pemán-García J, Vera-Sempere FJ. Lesión cutánea papuloeritematosa tras punción con acícula de pino en paciente en tratamiento corticoideo. *Enferm Infecc Microbiol Clin* 2002; **21**: 209–210.
199. Diz S, Fortún J, Sánchez A, Marcén R. Alternariosis cutánea tras trasplante renal. *Med Clin (Barc)* 2003; **121**: 598–599.
200. Kim JO, Kim GH, Kim BC, Lee KS. Cutaneous alternariosis in a renal transplant recipient. *Int J Dermatol* 2003; **42**: 630–631.
201. Merino E, Bañuls J, Boix V *et al.* Relapsing cutaneous alternariosis in a kidney transplant recipient cured with liposomal amphotericin B. *Eur J Clin Microbiol Infect Dis* 2003; **22**: 51–53.
202. Robb CW, Malouf PJ, Rapini RP. Four cases of dermatomycosis: superficial cutaneous infection by *Alternaria* or *Bipolaris*. *Cutis* 2003; **72**: 313–319.
203. Ioannidou D, Maraki S, Krüger Krasagakis S *et al.* Cutaneous alternariosis revealing acute myeloid leukaemia in an adult patient. *Mycoses* 2004; **47**: 227–230.
204. Kazory A, Ducloux D, Reboux G *et al.* Cutaneous *Alternaria* infection in renal transplant recipients: a report of two cases with an unusual mode of transmission. *Transpl Infect Dis* 2004; **6**: 46–49.
205. Ono M, Nishigori C, Tanaka C, Tanaka S, Tsuda M, Miyachi Y. Cutaneous alternariosis in an immunocompetent patient: analysis of the internal transcribed spacer region of rDNA and *Brm2* of isolated *Alternaria alternata*. *Br J Dermatol* 2004; **150**: 773–774.

206. Ortiz J, Abad M, Bullón A, García I. Cutaneous alternariosis: cytohistological findings in a case diagnosed by fine-needle aspiration biopsy. *Diagn Cytopathol* 2004; **30**: 103–104.
207. Pereiro M, Pereiro Ferreiros MM, De Hoog GS, Toribio J. Cutaneous infection caused by *Alternaria* in patients receiving tacrolimus. *Med Mycol* 2004; **42**: 277–282.
208. Yehia M, Thomas M, Pilmore H, van der Merwe W, Dittmer I. Subcutaneous black fungus (phaeohyphomycosis) infection in renal transplant recipients: three cases. *Transplantation* 2004; **77**: 140–142.
209. Robertshaw H, Higgins E. Cutaneous infection with *Alternaria tenuissima* in an immunocompromised patient. *Br J Dermatol* 2005; **153**: 1047–1049.
210. Romano C, Vanzi L, Massi D, Difonzo EM. Subcutaneous alternariosis. *Mycoses* 2005; **48**: 408–412.
211. Uenotsuchi T, Moroi Y, Urabe K *et al.* Cutaneous alternariosis with chronic granulomatous disease. *Eur J Dermatol* 2005; **15**: 406–408.
212. Chang JY, Lee JH, Lee KH. A case of cutaneous alternariosis in liver transplant patient. *Kor J Med Mycol* 2006; **11**: 159–162.
213. Gallelli B, Viviani M, Nebuloni M *et al.* Skin infection due to *Alternaria* species in kidney allograft recipients: report of a new case and review of the literature. *J Nefrol* 2006; **19**: 668–672.
214. Marín Montín I, Camacho Fernández M, Rubio Rubio JM, Herrera A. Alternariosis cutánea en paciente inmunocomprometido. Su diagnóstico. *An Med Interna* 2006; **23**: 26–27.
215. Vieira R, Veloso J, Afonso A, Rodrigues A. Cutaneous alternariosis in a liver transplant recipient. *Rev Iberoam Micol* 2006; **23**: 107–109.
216. Garduño E, Muñoz-Lozano MT, Rovira I, Blanco-Palenciano J. Hiperplasia verrucosa en un paciente trasplantado renal. *Enferm Infecc Microbiol Clin* 2007; **25**: 341–342.