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**Advances in microbiology, infectious diseases and public health: Refractory *Trichophyton rubrum* infections in Turin, Italy: a problem still present**

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*Original Citation:*

*Availability:*

This version is available <http://hdl.handle.net/2318/1617533> since 2018-01-19T13:19:46Z

*Publisher:*

Springer International Publishing

*Published version:*

DOI:DOI 10.1007/5584\_2015\_5012

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## Metadata of the chapter that will be visualized online

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Chapter Title Advances in Microbiology, Infectious Diseases and Public Health ~~Short Data Report/Revised Version~~

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Chapter Sub Title  **Refractory *Trichophyton rubrum* Infections in Turin, Italy: A Problem Still Present**

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Author Family Name **Tullio**  
Particle  
Given Name **Vivian**  
Suffix  
Division Bacteriology and Mycology Laboratory, Department of Public Health and Pediatrics  
Organization University of Torino  
Address via Santena 9, 10126 Turin, Italy

---

Author Family Name **Cervetti**  
Particle  
Given Name **Ornella**  
Suffix  
Division Department of Medical Sciences  
Organization University of Turin  
Address Turin, Italy

---

Author Family Name **Roana**  
Particle  
Given Name **Janira**  
Suffix  
Division Bacteriology and Mycology Laboratory, Department of Public Health and Pediatrics  
Organization University of Torino  
Address via Santena 9, 10126 Turin, Italy

---

Author Family Name **Panzone**  
Particle  
Given Name **Michele**  
Suffix  
Division A.O.U. Città della Salute e della Scienza  
Organization San Lazzaro Hospital  
Address Turin, Italy

---

Author Family Name **Scalas**

Particle  
Given Name **Daniela**  
Suffix  
Division Bacteriology and Mycology Laboratory, Department of  
Public Health and Pediatrics  
Organization University of Torino  
Address via Santena 9, 10126 Turin, Italy

---

Author Family Name **Merlino**  
Particle  
Given Name **Chiara**  
Suffix  
Division Bacteriology and Mycology Laboratory, Department of  
Public Health and Pediatrics  
Organization University of Torino  
Address via Santena 9, 10126 Turin, Italy

---

Author Family Name **Allizond**  
Particle  
Given Name **Valeria**  
Suffix  
Division Bacteriology and Mycology Laboratory, Department of  
Public Health and Pediatrics  
Organization University of Torino  
Address via Santena 9, 10126 Turin, Italy

---

Author Family Name **Banche**  
Particle  
Given Name **Giuliana**  
Suffix  
Division Bacteriology and Mycology Laboratory, Department of  
Public Health and Pediatrics  
Organization University of Torino  
Address via Santena 9, 10126 Turin, Italy

---

Author Family Name **Mandras**  
Particle  
Given Name **Narcisa**  
Suffix  
Division Bacteriology and Mycology Laboratory, Department of  
Public Health and Pediatrics  
Organization University of Torino  
Address via Santena 9, 10126 Turin, Italy

---

Corresponding Author	Family Name	<b>Cuffini</b>
	Particle	
	Given Name	<b>Anna Maria</b>
	Suffix	
	Division	Bacteriology and Mycology Laboratory, Department of Public Health and Pediatrics
	Organization	University of Torino
	Address	via Santena 9, 10126 Turin, Italy
	Email	annamaria.cuffini@unito.it

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**Abstract**      Dermatophytosis caused by *Trichophyton rubrum* is the most common cutaneous fungal infection in industrialized countries and worldwide with high recurrence and lack of treatment response. In addition, patients with cutaneous and concurrent toenail lesions are often misdiagnosed and therefore treated with an inappropriate therapy. In this study, we evaluated five previously misdiagnosed cases of *T.rubrum* chronic dermatophytosis sustained by two variants at sites distant from the primary lesion. Our patients were successfully treated by systemic and topical therapy, and 1 year after the end of therapy follow-up did not show any recurrence of infection.

Our data indicate that the localization of all lesions, the isolation and the identification of the causative fungus are essential to establish the diagnosis and the setting of a correct therapeutic treatment to avoid recurrences.

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**Keywords (separated by '-')**      *Trichophyton rubrum* - Chronic dermatophytosis - Misdiagnosis

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## Advances in Microbiology, Infectious Diseases and Public Health ~~Short Data Report/Revised Version~~

Refractory *Trichophyton rubrum* Infections in Turin, Italy: A Problem Still Present

Vivian Tullio, Ornella Cervetti, Janira Roana, Michele Panzone, Daniela Scalas, Chiara Merlino, Valeria Allizond, Giuliana Banche, Narcisa Mandras, and Anna Maria Cuffini

### Abstract

Dermatophytosis caused by *Trichophyton rubrum* is the most common cutaneous fungal infection in industrialized countries and worldwide with high recurrence and lack of treatment response. In addition, patients with cutaneous and concurrent toenail lesions are often misdiagnosed and therefore treated with an inappropriate therapy. In this study, we evaluated five previously misdiagnosed cases of *T. rubrum* chronic dermatophytosis sustained by two variants at sites distant from the primary lesion. Our patients were successfully treated by systemic and topical therapy, and 1 year after the end of therapy follow-up did not show any recurrence of infection.

Our data indicate that the localization of all lesions, the isolation and the identification of the causative fungus are essential to establish the diagnosis and the setting of a correct therapeutic treatment to avoid recurrences.

### Keywords

*Trichophyton rubrum* • Chronic dermatophytosis • Misdiagnosis

V. Tullio, J. Roana, D. Scalas, C. Merlino, V. Allizond, G. Banche, N. Mandras, and A.M. Cuffini (✉)  
Bacteriology and Mycology Laboratory, Department of Public Health and Pediatrics, University of Torino, via Santena 9, 10126 Turin, Italy  
e-mail: [annamaria.cuffini@unito.it](mailto:annamaria.cuffini@unito.it)

O. Cervetti  
Department of Medical Sciences, University of Turin, Turin, Italy

M. Panzone  
A.O.U. Città della Salute e della Scienza, San Lazzaro Hospital, Turin, Italy

30 Chronic dermatophytosis is a condition in which  
31 the clinical symptoms persist for more than 1 year  
32 with episodes of exacerbation and remission (Hay  
33 1982; Zaias and Rebell 2003; Prasad et al. 2005).  
34 The main etiologic agent is *Trichophyton rubrum*  
35 responsible for 90 % of chronic infections (Di  
36 Chiacchio et al. 2014; Nenoff et al. 2014).  
37 Chronicity is probably related both to fungal cell  
38 wall components, such as mannan, that play an  
39 important role in the process of down-modulation  
40 of cell-mediated immune response of the host and  
41 to a lack of treatment response (Blake et al. 1991;  
42 Sato and Tagami 2003; Waldman et al. 2010).  
43 Patients with cutaneous and concurrent toenail  
44 lesions are often misdiagnosed and, therefore,  
45 treated with an inappropriate therapy (Larruskain  
46 et al. 2005).

47 In this study, we evaluated previously  
48 misdiagnosed cases of *T. rubrum* chronic  
49 dermatophytosis in five patients admitted to the  
50 Medical Sciences Department, University of  
51 Torino (Italy), through an investigation of clinical  
52 and mycological infection aspects.

53 **Case 1** A 42-year old male, born in Ecuador,  
54 reported a 7-year history of itchy and squamous  
55 lesions on the soles, toenails, palms and the nail  
56 plates, before arriving in Italy (Fig. 1a–d). Despite  
57 therapies with topical antibacterial agents in his  
58 native country, the patient had extensive erythema  
59 with painful papules, pustules and crusts in the  
60 chin and beard (Fig. 1e, f). Incomplete alopecia,  
61 associated with follicular nodules most prevalent  
62 above the upper lip was seen. Hands and  
63 fingernails examination revealed hyperkeratosis  
64 and distal onycholysis.

65 **Case 2** A Caucasian male of 48 years presented  
66 erythematous and squamous lesions on the feet  
67 and toenails. A closer examination revealed scal-  
68 ing lesions on the inguinal area and buttocks,  
69 hands and fingernails plate hyperkeratosis and  
70 distal onycholysis.

71 **Case 3** A Caucasian female of 78 years reported  
72 a 2-week history of extensive erythema with  
73 papules and fine pustules appearing at the

opening of hair follicles in the inguinal region 74  
(Fig. 2a, b). An intense erythema involved both 75  
buttocks and thighs (Fig. 2c). Examination of the 76  
left foot revealed sole and toenail/fingernail 77  
hyperkeratosis, with nail plate thickened, friable 78  
and yellowish (Fig. 2e, f). The left knee (Fig. 2d) 79  
and the right leg were also involved with flaking 80  
in net margins. 81

**Case 4** A Caucasian female of 69 years, with 82  
rheumatoid arthritis, treated for 20 years with 83  
therapeutic cycles of methotrexate (7.5 mg/ 84  
week) and prednisone (5 mg/day), presented a 85  
chronic erythematous scaly dermatitis extended 86  
to the lower back and rear thigh area, diagnosed 87  
as psoriasis (Fig. 3e). Since 2006, she was treated 88  
with emollient cream and topical steroids with- 89  
out benefit. On physical examination, the patient 90  
revealed *tinea pedis* and *tinea unguium* with sole 91  
and toenails plate hyperkeratosis (Fig. 3a, b), 92  
squamous lesions on the elbow, on the back and 93  
left palm (Fig. 3c, d, g). Involvement of the scalp 94  
with flaking dandruff and thinning hair was 95  
observed (Fig. 3f). 96

**Case 5** A Caucasian female of 68 years, with 97  
rheumatoid arthritis, treated for several years 98  
with prednisone (25 mg/day), presented a history 99  
of chronic erythematous scaly dermatitis 100  
diagnosed as psoriasis and treated with emollient 101  
cream without benefit. A closer examination 102  
revealed an intense lamellar desquamation of 103  
the toenails and fingernails, hyperkeratosis of 104  
the soles and the palms, scaling lesions with 105  
sharp margins in the breast, abdomen, inguinal 106  
area, buttocks and thighs, neck and chin. 107

Mycological analysis of all patient lesions 108  
was performed. Skin and nail samples were col- 109  
lected, examined under a light microscope (20 % 110  
KOH + 40 % DMSO preparation) and 111  
inoculated into Mycobiotic agar (Merck, 112  
KGAA, Germany) to detect dermatophytes. 113  
Molds identification was based on macroscopic 114  
and microscopic characters of the colonies after 115  
15 days of incubation at 25 °C. 116

All patients had dermatophytosis and concur- 117  
rent lesions caused by two variants of *T. rubrum*: 118



**Fig. 1** Case 1. A 42-year old, male, born in Ecuador. Squamous lesions on the soles, toenails, palms and nail plates (a–d); extensive erythema in the chin and beard with follicular nodules above the upper lip (e, f)

119 downy white-colored colonies with reverse pig- 126  
 120 ment brownish-yellow (Cases 1, 2, and 3) or deep 127  
 121 wine-red (Cases 4, and 5). Scant teardrop-shaped 128  
 122 microconidia along septate hyphae were 129  
 123 observed on microscopic colonies examination. 130  
 124 The primary lesion was localized always in 131  
 125 the foot (*tinea pedis*), in agreement with other 132

studies (Larruskain et al. 2005). Secondary 126  
 lesions distributed in other sites were the main 127  
 demand for medical consultation; in all five 128  
 cases, the anatomical sites mainly interested 129  
 were the inguinal area, buttocks, palms and 130  
 fingernails (*tinea unguium*). In only one case, 131  
*tinea capitis* was observed (Case 4). Patient 132



**Fig. 2** Case 3. A 78-year old, female, Caucasian. Extensive erythema with papules at the opening of hair follicles in the inguinal region (a, b), buttocks and thighs (c); left

knee with flaking in net margins (d); toenail and fingernail hyperkeratosis (e, f)

133 4 under methotrexate therapy and patient  
 134 5, under corticosteroid therapy had risk factors  
 135 predisposing them to fungal spread. *Tinea* in  
 136 such cases tends to be chronic and extended,  
 137 mimicking various skin diseases, such as psoria-  
 138 sis, eczema, etc., as in Patients 4 and 5 (Atzori  
 139 et al. 2012; Tan et al. 2014).

For all patients a successful treatment with 140  
 topical (azoles) and systemic (terbinafine hydro- 141  
 chloride 250 mg/day) antimycotics was carried 142  
 out. In details, in patient 1, after 4 weeks of 143  
 treatment, all skin lesions were completely 144  
 healed and culture results were negative; both 145  
 direct mycological and culture were negative 146





**Fig. 3** Case 4. A 69-year old, female, Caucasian, with rheumatoid arthritis. Sole and toenails hyperkeratosis (a, b); back and left palm squamous lesions (c, d); extensive

erythema on lower back and rear thigh area diagnosed as psoriasis (e); scalp with flaking dandruff and thinning hair (f); squamous lesions on the elbow (g)

147 also for nails after 3 months. In patient 2, all  
148 lesions were completely healed and culture  
149 results were negative after 12-weeks of treat-  
150 ment. In patient 3, all skin lesions were  
151 completely healed after 6 weeks of treatment;  
152 both direct mycological and culture were nega-  
153 tive for nails after 4 months. In patient 4, after  
154 4-weeks of treatment, all skin lesions were  
155 completely healed; both direct mycological and  
156 culture were negative also for nails and scalp  
157 after 5 months. In patient 5, after 6-weeks of  
158 treatment, all skin lesions were completely  
159 healed and culture results were negative; the  
160 nail lesions were alleviated after 5-months  
161 therapy.

162 The five clinical cases reported in this study  
163 are considered dermatophytosis, affecting both  
164 immunocompetent and immunodeficient  
165 patients, and fulfilled the diagnostic criteria of  
166 *T.rubrum* chronic dermatophytosis, as indicated  
167 by the literature (Zaias and Rebell 1996;  
168 Böhmer and Korting 1999; Kick and Korting  
169 2001; Balci and Cetin 2008; Piñeiro  
170 et al. 2010; Kong et al. 2015). Since in our  
171 group of patients from the beginning a correct  
172 therapeutic treatment was not carried out or  
173 misapplied, a gradual spread of the infection  
174 occurred to the toenails, as secondary site  
175 involved, constituting the reservoir of infection  
176 that spread later to other sites, such as legs,  
177 groin, hands, face and scalp. On the other  
178 hand, it has to be underlined that *tinea unguium*  
179 is an infection usually more resistant to treat-  
180 ment, whose eradication is difficult even with  
181 appropriate therapy (Gupta and Cooper 2008).

182 For fungal infection eradication, diagnosis  
183 must be based on both a correct patient history  
184 and an adequate microbiological study that  
185 includes the identification of the species isolated.  
186 Therefore, it is essential a careful examination of  
187 the patient *in toto* to avoid inappropriate or  
188 wrong therapeutic treatment. In fact, as in the  
189 first patient, the antibiotic treatment was  
190 established solely on the observation of highly  
191 inflammatory facial injuries that did not present  
192 the typical clinical features of *T.rubrum* infection  
193 (Yin et al. 2011); hence, the treatment being  
194 wrong was ineffective.

In conclusion, our data indicate that in all  
cases of suspected syndrome or when skin  
involvement is extended to multiple sites, the  
localization of all lesions, the isolation and the  
identification of the causative fungus are essen-  
tial to establish the diagnosis, prognosis and the  
setting of a correct antifungal therapy to avoid  
recurrences.

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Uncorrected Proof

# Author Queries

Chapter No.: 5012      0002619843

Queries	Details Required	Author's response
AU1	Please check the article title and article sub title.	
AU2	The citations Di Chiacchio et al. (2012), Tan et al. (2013), Piñeiro et al. (2009), Kong et al. (2014) have been changed to Di Chiacchio et al. (2014), Tan et al. (2014), Piñeiro et al. (2010), Kong et al. (2015). Please check if okay.	OK

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