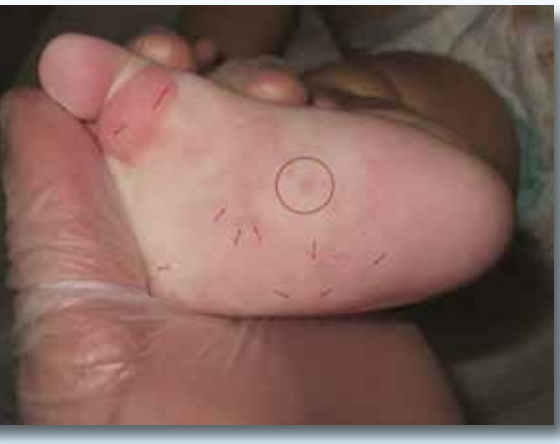

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Scabies: myths to dispel

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Scabies: myths to dispel

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Contents

1. Old and new modalities of transmission

Sarcoptes scabiei var. *hominis* does not fly or jump: it crawls at the rate of 0.5-3 mm/day on warm skin.[1]

Scabies is usually transmitted by direct skin-to-skin contacts or intercourses.[1-4] Fifteen to 20 minutes of direct skin-to-skin contact are necessary to transfer the mites from one person to another.[3] The more mites on a person, the greater the likelihood and speed of transmission.[1] According to many authors, intercourses are a common transmission modality of the infestation. In a study on risk factors for scabies in a sexually transmitted diseases unit, high-risk persons included men who had sex with men and, curiously, men with sporadic sexual contacts.[5] Scabies can be therefore considered as a true sexually transmitted disease.[1,4,6] Scabies is less commonly transmitted by clothes, sheets and towels.[1,4] Furthermore, living mites have been found on floors and furniture.[2,7] In a study by Arlian et al. [7], 44% of dust samples of patients' homes contained mites, and 64% of them were vital. Fomite transmission of the infestation is therefore considered as possible. This modality of transmission is more frequent in crusted scabies.[1] Some studies documented survival of mites, at a temperature of 21°C and 40-80% of relative humidity, for more than three days.[7-10] In particular, it was demonstrated that low temperatures and high relative humidity values favoured survival of mites, whereas high temperatures and low relative humidity led to early death.[9] Transmission among family members and in institutional settings is very common.[1,3] Risk factors are overcrowding, poor environmental and personal hygiene, poor nutritional status, homelessness, severe neurological and psychiatric diseases.[3]

Transmission occurs by means of the gravid female, more rarely by larvae and nymphs.[4] Males of *Sarcoptes scabiei* var. *hominis* are not able to transmit the infestation. Latency time depends by mite burden and host immunity. It ranges between 3 weeks and 3 months: in most patients it ranges between 3 to 4 weeks.[2,4] This is the latency time in patients infested for the first time: in re-infestations, signs and symptoms arise after 1 to 5 days.[2,4,11] This means that, although scabies does not induce a true definitive immunity, a certain degree of cell immunity occurs, possibly towards keratolytic enzymes produced by females for the construction of the burrows and/or as a sensitization towards

metabolic products released by mites during their growth or at their death and/or as a sensitization towards saliva and/or faeces.[4]
The genetic predisposition for susceptibility or resistance to *Sarcoptes scabiei* var. *hominis* infestation has been hypothesized to be correlated with the dominance of an IgE-driven Th2 response in crusted scabies or an interferon-γ-dominated Th1 response that induces a mite control.[12]

Cuban scabies

Approximately twenty years ago, we observed several cases of scabies in Italian patients returning from vacations in Cuba.[13] These patients had some similar features:

a) almost all patients were males aged between 25 and 55 years, in good general health, immunocompetent, not in therapy with systemic drugs, and heterosexual;
b) the latency time was often long or very long (even more than three months);
c) dermatological examination revealed almost exclusively lesions due to scratching, without burrows, papules and vesicles;
d) almost all patients complained of chronic and severe pruritus: it was widespread, but shoulders, back, thighs and legs were less frequently and severely involved;
e) the search for the mite was positive in about 25% of patients, even by means of epiluminescence microscopy: in these cases, the mite appeared of normal morphology and size. In all the other patients the diagnosis of scabies was possible by means of the medical history and by exclusion of other diseases causing pruritus;
f) laboratory examinations were within normal ranges in all patients;
g) many patients were resistant to the topical treatments which were used in Italy at those times: 25% benzyl benzoate, 10% potassium polysulfur (Milian ointment), Helmerich-Hardy ointment or Helmerich paste (containing 17-30% sulfur), bis-butil carboethylene and 10% crotamiton.[13] In Italy, at those times, lindane, malathion and permethrin were not on the market; furthermore, the use of ivermectin was allowed only in veterinary medicine.

This clinical variety of scabies was named *Cuban scabies*.[13] Some hypotheses were suggested about this scabies. The hypothesis according to which this scabies was not caused by mites or was caused by a mite other than *Sarcoptes scabiei* var. *hominis* was subsequently excluded.[13] This variety of scabies is superimposable to a variety that was named in the past *scabies of the cultivated*[14,15] or *scabies in the clean*[16] or *scabies in clean persons*[17] or *scabies of the cleanly*:[18] this variety is seen in individuals who wash themselves very often or even are obsessed with cleanliness.[19] However, in some cases, *Cuban scabies* actually is a chronic dermatitis due to an irritant/ allergic reaction to metabolic products of mites in hyper-reactive or frankly allergic individuals.[19]

Scabies acquired in Chinese massage centers

We observed three patients who contracted scabies at Chinese massage centers.[20] The caselist consists of three Caucasian males, aged 29, 46 and 56 years, respectively, heterosexuals, in good general health, not in therapy with systemic drugs. All three patients were regular customers of Chinese massage centers (the same center for two of these patients). A clinical diagnosis of allergic contact dermatitis was made at other dermatological centers for all three patients. A treatment with topical corticosteroids and oral anti-histamines was unsuccessful.
In all patients medical history was negative for previous scabies. In all patients, history also allowed to exclude other possible sources of infestation (intercourses, direct contacts with patients affected by scabies, direct contacts with fomites belonging to patients with scabies, in the last three months before our examination). Latency time ranged from 3 to 6 weeks.
Clinical picture was typical: squamous-crusted lesions at interdigital folds of the hands, burrows and papular-vesicular lesions on wrists, axillae, chest, abdomen, pubis, penis and buttocks. Pruritus was widespread and severe.
Microscopical examinations were positive for mites, eggs and faeces in all patients.
It is possible that in these patients scabies was transmitted by the sheets that covered the futon or by the towels used by the patients after the shower. It is unlikely that scabies has been transmitted by the oil used for the massage.

As Chinese massage centers are very numerous in Italy, we believe that cases of scabies caused by massages will be observed more frequently in the next future.[20]

Contact sports and scabies

Scabies has been very rarely reported in contact sports: to our knowledge, only reviews, and no case reports, have been published.[21-25]
A 38-year-old Caucasian male was admitted with a clinical diagnosis of widespread itching. The patient stated that he was in good general health and that was not in therapy with systemic drugs. He also declared that itching had appeared approximately three weeks before at the right hand, and subsequently reached the right wrist, forearm and elbow. The patient was unsuccessfully treated at another center with hydrocortisone butyrate cream and cetirizine.
Dermatological examination revealed some pink to brown, round papules on the right wrist, some serpiginous, erythematous burrows on the abdomen and some excoriations on the chest, breasts and abdomen. A clinical diagnosis of scabies was made. Microscopical examinations showed adults and eggs of *Sarcoptes scabiei* var. *hominis*. Medical history revealed that the patient was an amateur arm wrestler: this explained the reason for which itching appeared initially on the right hand, wrist and forearm: the patient used his right hand for arm wrestling. No other possible sources of infestation were detected.
Cutaneous infections and infestations, such as herpes gladiatorum, molluscum contagiosum, warts, tinea capitis, barbae and gladiatorum, impetigo, folliculitis and pediculosis are well-known in contact sports.[21-25] To our knowledge, no cases of scabies in arm, greco-roman and all-in wrestlers have been reported so far. The patient we have described very likely is the first case of scabies acquired in arm wrestling. It is also very likely that in this patient the infestation occurred through direct human-to-human contact with another arm wrestler. It is evident that, in this case, the guidelines for removal of an infected athlete from play, until he/she is no longer contagious, have not been followed.[26]

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2. Where to look for the scabies mite

Common locations of scabies are axillae, elbows, wrists, interdigital folds of the hands, breasts, penis, scrotum and buttocks.[1-3] Literature data about nail involvement are poor and limited to anecdotical cases.[4-8] However, subungual skin of fingers is much more frequently involved than previously thought.[9]
Eighty-nine Caucasian immunocompetent patients (51 males and 38 females, aged 18-74 years), with a clinical diagnosis of scabies, were subjected to microscopical examinations in order to confirm the diagnosis. In all patients, fourteen locations (chest, breasts, axillae, elbows, wrists, interdigital folds of the hands, subungual skin of fingers, abdomen, pubis, penis, scrotum, vulva, back and buttocks) were evaluated. Microscopical examination was considered positive when mites and/or eggs and/or faeces were observed.[9]
In males, more frequently involved area was penis (34/51 = 66.7%), followed by scrotum (26/51 = 51%), subungual skin of fingers (21/51 = 41.2%), interdigital folds of the hands (16/51 = 31.4%), wrists and abdomen (13/51, respectively = 25.5%). In females, microscopical examination was positive in breasts (23/38 = 60.5%), followed by axillae (15/38 = 39.5%), subungual skin of fingers (14/38 = 36.8%), abdomen (13/38 = 34.2%), buttocks (12/38 = 31.6%), interdigital folds of the hands (11/38 = 28.9%) and wrists (10/38 = 26.3%).[9] Results are reported in Table 1.
The results of this study confirm that in males common locations of scabies are penis, scrotum, interdigital folds of the hands, wrists and abdomen, while in females they are breasts, axillae, subungual skin of fingers, abdomen, buttocks, interdigital folds of the hands and wrists. However, in both genders, the subungual skin of fingers was very commonly involved (third location both in males and females).
In all patients, neither burrows nor other lesions (i.e. papules, nodules, vesicles, pustules, excoriations) in subungual skin of fingers were observed. In 5/21 males (23.8%) and 2/15 females (13.3%) only very mild subungual scales were observed. In addition, no patient complained of itching in peri- and subungual skin of fingernails.[9]
Nail involvement is well known in crusted scabies.[10] It is characterized by yellow pigmentation of the nail plate and nail bed hyperkeratosis.[10] However, as previously mentioned, nail involvement was very rarely reported in classic scabies.[4-9]

In conclusion, subungual skin of fingernails is a frequent location of scabies, although no typical lesions, except for rare thin scales in some patients, were observed in these areas, and no symptoms, in particular itching, were reported by patients. It is possible that scabies mites find a favourable environment beneath the free edge of nail plates.[6]
These observations strongly suggest to treat carefully also peri- and subungual skin of fingers in all patients with scabies. The fingernails should be trimmed very short, scrubbed with a brush and treated with the specific therapy.[5-7,9] This procedure can reduce the incidence of relapse after therapy.[9]

Table 1. Locations of scabies in males and females.

	Males 51	Females 38
Chest	2	2
Breasts	2	23
Axillae	3	15
Elbows	1	2
Wrists	13	10
Interdigital folds of the hands	16	11
Subungual skin of fingers	21	14
Abdomen	13	13
Pubis	4	5
Penis	34	-
Scrotum	26	-
Vulva	–	3
Back	2	4
Buttocks	16	12
Total	153	114

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3. Why is the back so rarely involved in scabies?

In a study carried out at the Dermatology Unit of the University of Milan, it was observed that the back was involved by scabies in 2/51 males (3.9%: the 2nd last location) and in 4/38 females (10.5%: the 3rd last location).[1] This observation confirmed what reported in the literature: the back is very rarely affected in scabies: only a few cases with back involvement were reported in children,[2,3] pregnants[4] and malnourished or immunocompromised patients.[5-7]

Why is the back so rarely involved in scabies? Is the back an unfit environment for scabies mites? If so, why? It is difficult to state that the skin of the back is an unfit environment because it is similar, according to the histological point of view, to the skin of the chest, the anterior pillars of axillae, the abdomen, the hips and the buttocks: all these areas are frequently involved in scabies.[1] It is possible that in the skin of the back the nerve endings that convey the itching are less numerous and/or less developed: however, we found no data to support this hypothesis. We suggest a possible and simple hypothesis. Diffusion of scabies is by autoinoculation: the latter is caused by scratching: the latter is carried out by fingernails. It is rather difficult to reach and scratch the back! This, of course, cannot be considered as the only hypothesis, because some areas of the skin surface, such as the face and feet, which are easily reachable by hands, in adults are rarely affected by scabies.[8]

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4. Nodular scabies versus postscabies prurigo

The literature about nodular scabies is extremely confusing.[1-30]
Nodular scabies is an uncommon clinical variety of scabies. It is characterized by papules and nodules located mainly on the axillae, groins, penis, scrotum and buttocks. These lesions are round, reddish to brown in colour, up to 1.5 cm in diameter, accompanied by severe pruritus.[1] Microscopical, dermoscopic or histopathological examinations allow to observe mites or fragments of them and/or eggs and/or scybala. In particular, dermoscopy acquired in the last years a great importance for the diagnosis.[16,23,26] Permethrin and oral ivermectin are considered as the most effective treatments.[1,31] More or less used synonyms of nodular scabies are persistent nodular scabies,[7] persistent nodules in scabies,[3,4,7,15] persistent scabious nodules,[2,5,9] scabietic nodules[10,20] and scabious nodules.[14]
Postscabietic nodules were first described in 1963 by Samman.[2] They are uncommon complications of scabies. In an Indian study, these nodules occurred in 29 out of 544 patients (5.3%) with previous scabies.[9] Postscabietic nodules are caused by a delayed, chronic hypersensitivity reaction to antigens of the mite.[10,15,18,19,21,22] The diagnosis of postscabietic nodules is possible when:

a) there is a history of scabies which has been successfully treated;
b) reddish-brown, round, papular-nodular lesions are present (also in non typical locations for scabies). In the previously cited Indian study, scrotum (96.5% of patients) and penis (69%) were the commonest affected sites, followed by axillae (37.9%) and groins (17.2%);[9]
c) patients complain of severe pruritus;
d) microscopical, dermoscopic and histopathological examinations are negative for mites or parts of them, eggs and scybala;
e) specific anti-scabies therapy is ineffective;
f) the disease may persist for weeks or months.[15]

Postscabietic nodules are more frequent in males[9,10] and children.[3,5,9,15] Recovery is possible by means of potent topical or intralesional corticosteroids.[4,15,19,27] Pimecrolimus[17] and tacrolimus[25,27] are also sometimes effective. Cryotherapy[29] and surgical excision (!)[4] have also been used.
In 2011, Czeschik et al.[22] suggested to separate nodular scabies, i.e. the infestation in the strict sense of the word, from postscabietic nodules, i.e. the

chronic hypersensitivity reaction after scabies recovery. We totally agree with this division.[31] However, as postscabietic nodules are not always only nodules, but often also papules,[5,18,19,21-24,27,28] and in consideration of the clinical picture, we believe that the name "postscabies prurigo" is proper. In fact, this entity is characterized by reddish-brown, round papular-nodular lesions, accompanied by severe pruritus. Clinical course is chronic-relapsing, with improvement by means of potent topical corticosteroids. In conclusion, postscabies prurigo is a true prurigo with a known aetiology.[31]

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5. Pruritus in scabies

Scabies and nocturnal pruritus

Pruritus of scabies is due to a delayed type IV T cell-mediated reaction to *Sarcoptes scabiei* var. *hominis*, its saliva (in particular keratolytic enzymes that are produced by females for the construction of the burrows), products released by the mite during its life cycle, eggs and excrements.[1-4] Movements of the mite also induce pruritus.[4]

According to literature data, scabies pruritus is more frequent and severe at night.[3-15] In a French study on children with scabies, nocturnal pruritus was present in 82.5% of patients.[11] These results were confirmed in an Indian study: 79.4% of patients reported a worsening of pruritus at night.[13] Nocturnal pruritus can cause severe sleep disturbances:[4,11] in the previous cited French study, 22.4% of patients reported sleep disturbances.[11]

A survey on nocturnal pruritus in a group of African migrants with scabies gave interesting results.

A total of 36 male adult patients were visited from October 2018 to February 2019 (18 patients) and from May to September 2019 (18 patients). The two groups were similar for gender, age and duration of the infestation (3 to 4 months, according to medical history). The diagnosis of scabies was confirmed by microscopical examinations: they were considered positive when adults or fragments of them or eggs of *Sarcoptes scabiei* var. *hominis* or faeces were visible. In all patients, scabies was contracted in their countries (Niger, Mali, Senegal, Gambia, Guinea, Eritrea and Somalia) or during the trip from these countries to Italy. A questionnaire about pruritus was given to all patients. The two questions were: «Is your pruritus more severe at night?» and «Do you wake up from the sleep because of pruritus?». All patients were treated with 5% permethrin cream (one application/day for two consecutive days: the treatment was repeated 7-10 days later).[16]

The answer to the first question was "Yes" in 13/18 patients (72.2%) visited from October 2018 to February 2019 and in 6/18 patients (33.3%) visited from May to September 2019. The answer to the second question was "Yes" in 11/18 patients (61.1%) of the first group and in 5/18 patients (27.7%) in the second group.

According to the results of this survey, pruritus worsens during night much

more in patients observed in autumn and winter than in patients observed in spring and summer. It is not easy to explain these results. Almost all epidemiological studies on scabies (in United Kingdom,[17,18] Denmark,[19] Turkey,[20] Israel,[21,22] India[1] and New Zealand[23]) conclude that the incidence of this infestation is higher in autumn and winter. However, in a study carried out in Saudi Arabia, it was observed that recurrence rate of scabies was higher from May to August.[24] The higher incidence of scabies in autumn and winter has been explained with the fact that cold weather encourages overcrowding.[2,18] Poor hygiene is also important.[1]

We previously stated that, according to our results, pruritus worsens during night much more in patients observed in autumn and winter than in patients observed in spring and summer. We think that nocturnal pruritus of scabies is associated with pyjamas, heavy sheets and blankets: they induce an increase of the temperature of the skin: the heat stimulates movements and activity of the mite.[4,7] This would be in contrast with the fact that females and nymphs of *Sarcoptes scabiei* var. *hominis* can survive in a heated home environment up to 5 days, and longer in a cooler weather.[2,17,18] However, this was actually demonstrated only for *Sarcoptes scabiei* var. *canis*.[25,26] The second part of our study was carried out from May to September, when the climate is warm and people usually sleeps without blankets, with light sheets and pyjamas or not having a stitch on. In a Korean study, the authors observed that, in a group of 82 patients with scabies, the commonest aggravating factor of pruritus was heat (40.2% of patients) and that the most important alleviating factor was cool environment (32.9% of patients).[15]

We believe that nocturnal pruritus in scabies is due to the temperature of the skin surface: when it is high, because of the use of pyjamas, heavy sheets and blankets, pruritus increases; when it is low, as in the summertime, when people usually sleeps without blankets, with light sheets and pyjamas or not having a stitch on, pruritus is less frequent and severe.[27]

Pruritus sine materia and scabies

Pruritus sine materia is an important symptom caused by systemic diseases (cholestasis, chronic renal insufficiency, hypothyroidism, hematological diseases, iron deficiency) or psychiatric and neurological disorders.[28-30] In pruritus sine materia there is no evidence of primary cutaneous lesions.

In the period 1996-2019 we observed 23 patients for whom a previous diagnosis of pruritus sine materia was made at other dermatology centers; however, in all these patients a final diagnosis of scabies was made. The caselist consists of 23 Caucasians [9 males and 14 females, with an age ranging from 43 to 73 years (mean age: 53.3 years)]. All patients had been previously studied, treated and followed at different dermatology centers in Italy and Switzerland. In all patients a diagnosis of pruritus sine materia was made because no lesions on the skin were visible; furthermore, all laboratory and instrumental examinations were within normal ranges or negative. All patients had been unsuccessfully treated with topical and oral corticosteroids and oral anti-histamines. In addition, one patient each was treated with capsaicin, naltrexone, cyclosporin and narrow band UVB.

On admission to our Dermatology Unit, all patients complained of more or less widespread and severe pruritus. Dermatological examinations were negative for burrows, papules, vesicles, nodules and crusts in all patients: only some small excoriated lesions were visible in 9 patients (39.1%). Laboratory examinations revealed only mild increase (≤7%) of eosinophils in 5 patients (21.7%). Microscopical examinations for the research of *Sarcoptes scabiei* var. *hominis* or its fragments or eggs were carried out in all patients in fourteen locations: chest, breasts, axillae, elbows, wrists, interdigital folds of the hands, subungual skin of fingers, abdomen, pubis, penis, scrotum, vulva, back and buttocks, i.e. the most frequently involved areas in scabies.[31] The examinations were positive in 11 patients (47.8%). We decided to treat all patients, both those with positive microscopical examinations and those who were negative, by means of 5% permethrin cream (one application/day for two consecutive days; the treatment was repeated 7 days later).[16] Complete recovery was observed in all patients, although two to three courses were necessary in 6 patients (26.1%). Follow up (≤6 months) was possible in 17 patients and was negative in 15 of them.

We think that all these patients, for whom a previous diagnosis of pruritus sine materia was made, were actually affected by scabies. In 11 patients (47.8%), microscopical examinations allowed to observe mites or eggs. In the other 12 patients, the therapy with permethrin and the subsequent complete disap-

pearance of pruritus, with a long follow up, also allowed to make a diagnosis of scabies.[32]

This variety of scabies is characterized by the absence of burrows as well as other typical lesions, such as papules, vesicles, nodules and crusts. Only some excoriated lesions caused by scratching are visible in a minority of patients.[32] Contrariwise, pruritus is present in all patients, with different degrees of severity.[32] This variety of scabies is superimposable to a variety that was named in the past *scabies of the cultivated*,[33,34] *scabies in the clean*,[35] *scabies in clean persons*[36] or *scabies of the cleanly*:[12] this variety is observed in individuals who wash themselves very often or even are obsessed with cleanliness. This occurrence was possible in 15 (56.5%) of our patients: it is possible that repeated cleanings mechanically destroy the burrows. Furthermore, this variety of scabies is very similar to the so called *Cuban scabies*. As previously mentioned, its observation was very common in Italy approximately 20 years ago.[37]

It is possible that pruritus sine materia actually is, at least in some cases, a clinical variety of scabies. For this reason, we suggest to perform, in all patients with pruritus sine materia, microscopical examinations or dermoscopy. We also suggest to prescribe a specific anti-scabies treatment also in those patients with negative microscopical exams. As previously mentioned, a complete remission of the disease was observed in 12 patients with negative microscopical examinations.[32]

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6. Entodermoscopy
The Philosophy of Dermoscopy in Scabies

Why should scabies also be submitted to the hegemony of the ever-present dermatoscope?
It is the first consideration that a dermatologist could make on the basis of his/her university studies during which the clinic of this infestation has always been sufficient to guide to diagnosis.
This consideration in itself is very correct but unfortunately in scabies the "exception to the rule" is exactly the rule so much so that in some older books scabies was nicknamed "the great simulator",[1] a definition generally used for Syphilis!
This means that any scrupulous dermatologist, while examining a patient who complains of an unexplainable itch, should dedicate at least 15 minutes of his/her visit to scraping and performing microscope observation. Nothing to complain about, except for the fact that few colleagues have a microscope in their own offices, and in particular few of them have the experience needed to recognize scybala (feces pellets) and eggs which, in the absence of a mite (a very frequent occurrence), would make any examination useless.
Dermoscopy (DS) thus becomes the most suitable tool which nowadays can combine the universal availability of the instrument to diagnostic reliability in scabies diagnosis.[2]
Thus in 2006[3] a thought current which chooses to call the diagnostic act of skin infestations "entodermoscopy" (EDS), i.e. a blend between entomology and dermatology, was born. Nothing complex but it is inevitable, when examining a parasite in its natural habitat (us), to refine one's diagnostic skills by learning what no optical microscope has ever allowed to examine: the *in situ* and *in vivo* interaction between parasites and the human skin, in the anatomical respect of both.
This is an important step not only for diagnosis but also to understand the most intimate parasite-host relationships from which new strategies for therapy or prevention could also come.

Description of the mite-gallery unit (MGU)

Also in scabies it is possible to use global and local dermoscopical descriptors. It was even more interesting though to understand that their origin is

closely linked to the biological cycle of the mite which is a slow-but-not too slow dynamic event. Surprisingly, in this micro-world emerges that another movement as well must be taken into account, and that is the substrate (our skin) which, in its turnover, leads to a micro environment that *entodermoscopy* suggests to study.

A new way of seeing the old "burrow" develops in an anatomical-functional integrated structure called Mite-Gallery Unit (MGU). The MGU, though simply in its intuition, emphasizes something never explored before in the literature, namely that the mite moves horizontally on a ground which in turn has a vertical movement.[4] It is just from this interaction that the dermatoscopic descriptors derive. Probably the reason of this "absence" in previously published literature depended on the fact that when the parasite is put on the slide, the micro-habitat is disassembled, subtracting any trace that could have suggested from the beginning how the more superficial layer of the epidermis reacts to a foreign body (sarcoptes) when crossing by it.

Consequently, *entodermoscopy* allows us to better observe what happens *in vivo*, provided that dermatologists develop a more friendly approach to entomology, a somewhat complex matter.

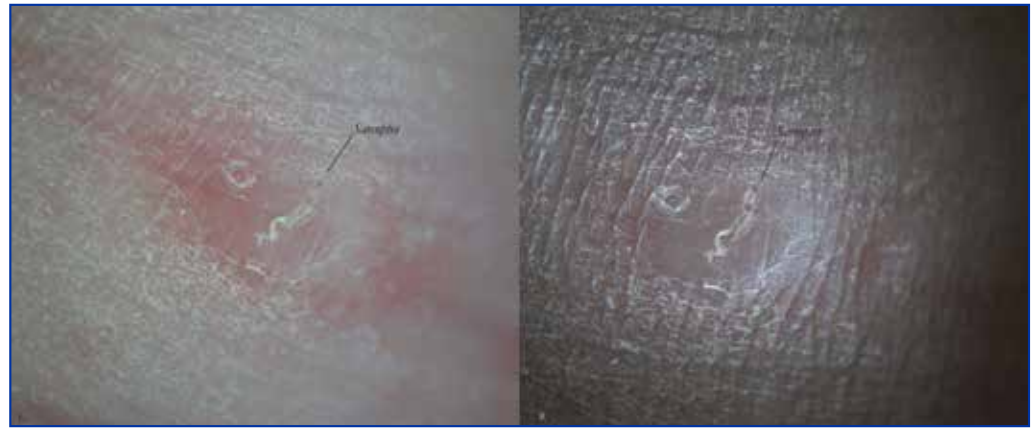
Instrumental procedure (Figs. 1-3)

The instrumental procedure in *entodermoscopy* is the same as that of general dermatoscopy but some essential points need to be strengthened:

1. Non-contact dermatoscopy (dry-dermoscopy; d-DS) represents the first moment of the examination because it allows to leave the observation field totally intact, an indispensable condition to have an exact representation of the parasite-human interaction. In this set, some parameters of the surface texture treated below can be better appreciated.
2. Contact dermatoscopy with plate and liquid interface (wet-dermoscopy; w-DS) follows immediately after because it allows a greater penetration of light as a result of the skin surface compression but especially thanks to the help that the liquid (generally mineral oil) provides to the reading of the MGU of which the interior components and some organs of the body of the mite can be better appreciated.
3. At what magnification should one operate? The magnification that the dermatoscope provides (10x) is only used to identify the global descriptors to confirm the clinical suspicion of a burrow. For the local descriptors it is necessary to use a magnification between 30 and 50x at least. Those who use a compact digital camera to capture images have no difficulty in reaching such magnification using the optical zoom. This

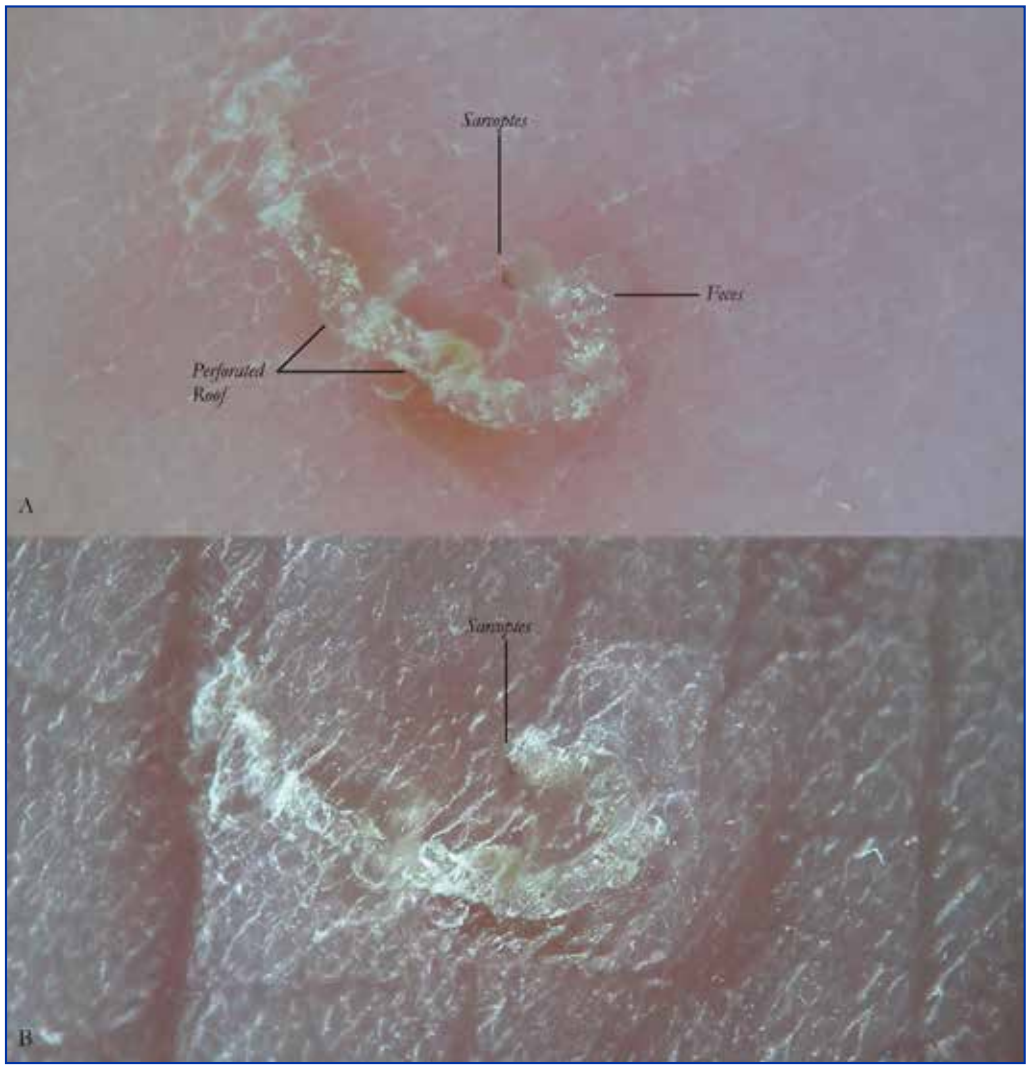
FIGURE 1. *Some instrument used for an entodermoscopic examination. Particular attention was paid to the protection of tools with disposable transparent film.*

FIGURE 2. *Contactless dermoscopy (d-DS). Comparison between two different types of lighting. On the left an image with polarized light, on the right the same lesion with non-polarized tangential light.*



set may be referred to as enhanced dermatoscopy. Digital zoom is generally not recommended as it generates artifacts and unsatisfactory resolution. On the other hand, those who have a video-dermatoscope can work easily using the appropriate optics that can even exceed 50x.

FIGURE 3. *Contactless dermoscopy (d-DS). Above polarized light image allows to recognize the mite and feces inside the tunnel. Under the same image with tangential light that enhances the surface texture of the whole skin, highlighting the discontinuity of the gallery roof.*



4. Recently some articles have appeared in the literature in which low cost video-microscopes have been used instead of the common expensive dermatoscopes. Although these devices are limited in image quality, they have showed to be able in supporting clinical diagnosis in contexts with insufficient economic resources (emerging countries). [5]
5. In *entodermoscopy*, however, magnification is not everything. It is also particularly useful to have the ability to illuminate the lesion with a tangentially oriented light, because in this way dry-dermoscopy is able to better capture the smallest anomalies of the epidermal surface texture and better identify the anatomical structures of the mite. No commercial dermatoscope has this illumination which therefore must be produced by devices built for such purpose, devices inside which LEDs are arranged parallel to the skin surface. When this and other utilities such as micromanipulators for in field operations will be available, the ideal "entodermatoscope" will be reached for every research of parasites *in vivo* and *in situ*.

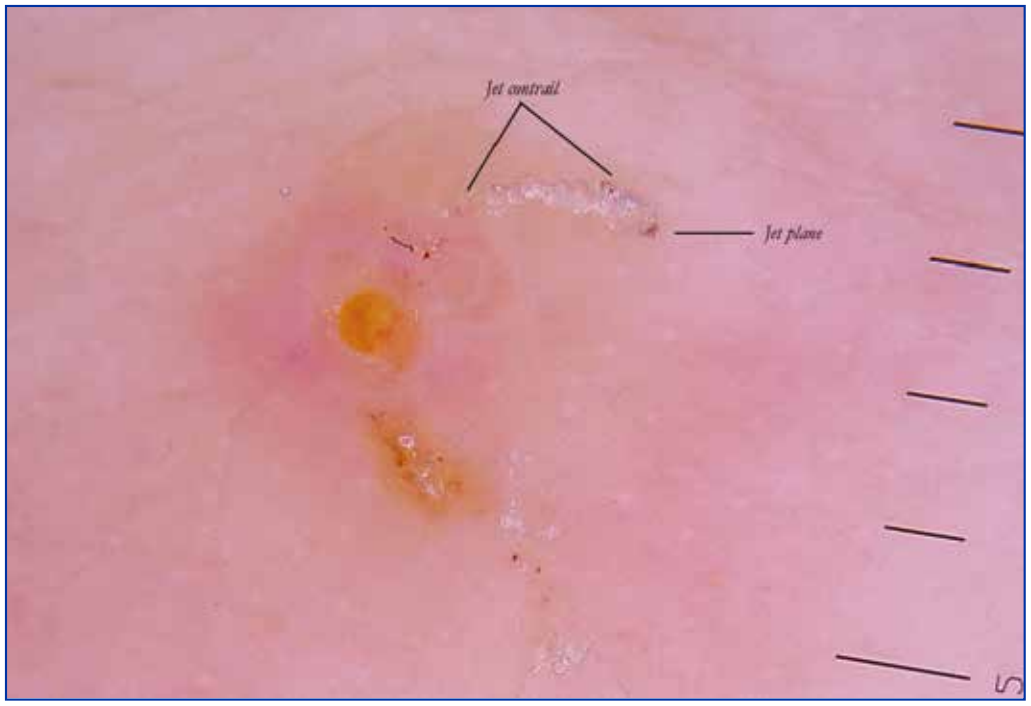
Dermatoscopic semeiotics (Figs. 4-6)

Global descriptors

The global descriptors are represented by what in the literature is described as a jet plane (delta wing) followed by its white contrail.[6] Although this sign is mentioned everywhere, little has been said regarding the real cause of this phenomenon. The mite has only one refractive part visible under DS that corresponds to the *gnathosome* (the buccal apparatus) and the first pair of legs placed immediately behind. The rest of the body is totally invisible at low magnification.

The anterior part of the mite, when examined under the dermatoscope, roughly appears as a smooth rounded dark *triangular sign* whose vertex is directed towards the tunnel's progression point. Immediately behind is the tunnel which takes on a whitish refraction recalling the jet contrails. But beware of the fact that this "picture" is not intrinsic to the lesion itself but rather depends by which dermoscopic procedure is used.

FIGURE 4. *Contact dermoscopy (w-DS). The front of the parasite is recognized as a dark triangle resembling a delta wing of a jet. Immediately after, the tunnel produces a series of micro bubbles that remain trapped under the glass plate of the dermatoscope simulating the jet contrail.*



Let us start to consider plate and liquid medium dermoscopy (w-DS). The first report in the literature[6] comes exactly from this set which made possible to distinguish a reflective triangle (the mite) and a white trail along the entire tunnel. The trail is determined by micro bubbles which, reflecting the light, produce a sign that is far easier to recognize than the front part of the mite. The frontal part of the mite generally has a faded brown appearance which must be searched carefully, so the gallery is the *global descriptor* that best guides the dermatologist's gaze in his/her diagnosis.
But what happens if the observation is repeated on the same lesion because of some doubt or because another photo needs to be taken? The trail disappears completely and what remains is only the triangle of the

mite. It is difficult to find the description of this phenomenon if one is not close to the world of *entodermoscopy* but it is needful to know that such phenomenon exists due to the fact that after the first contact with the plate the bubbles trapped between the glass and the skin vanish and the liquid medium enters into the gallery completely. It is precisely for this reason that the tunnel's refractivity disappears, simply because the roof of the tunnel becomes transparent and the tunnel completely floods inside.[7]

FIGURE 5. *Contactless dermoscopy (d-DS). The initial part of the tunnel where the mite resides has an intact roof. It is important to note that the gallery has instead a roof interrupted by holes from which air bubbles come out when switching to the w-DS (plate + liquid medium).*

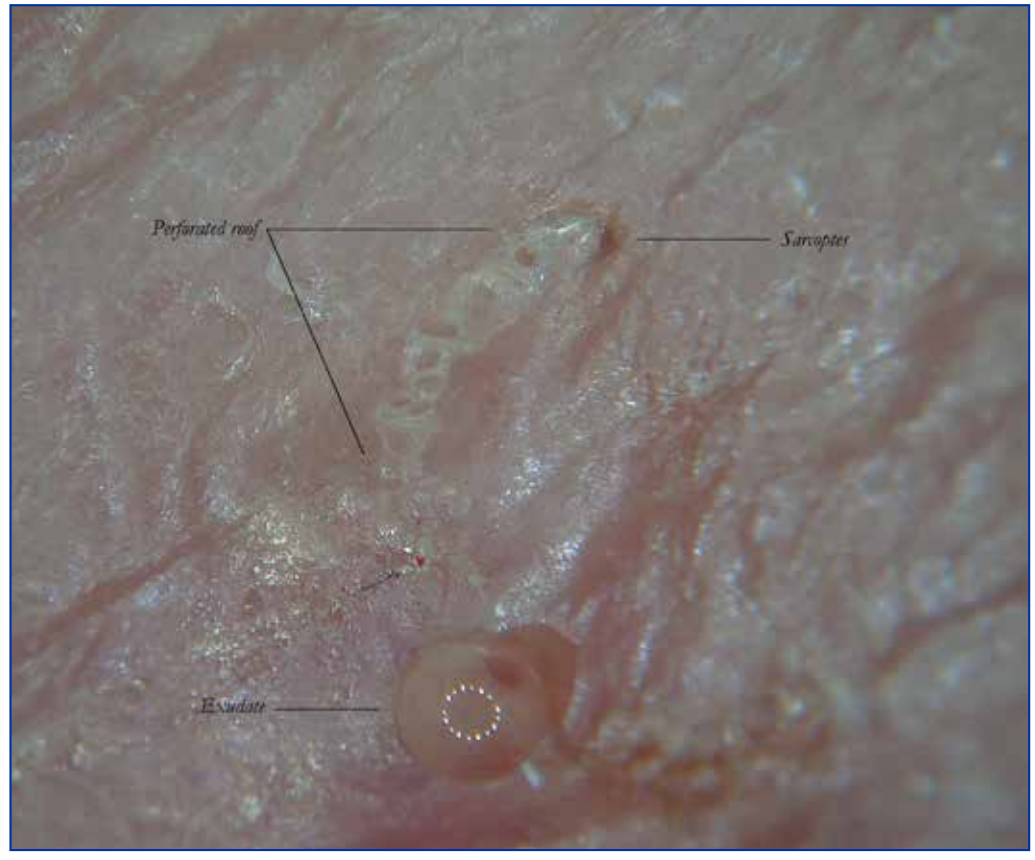
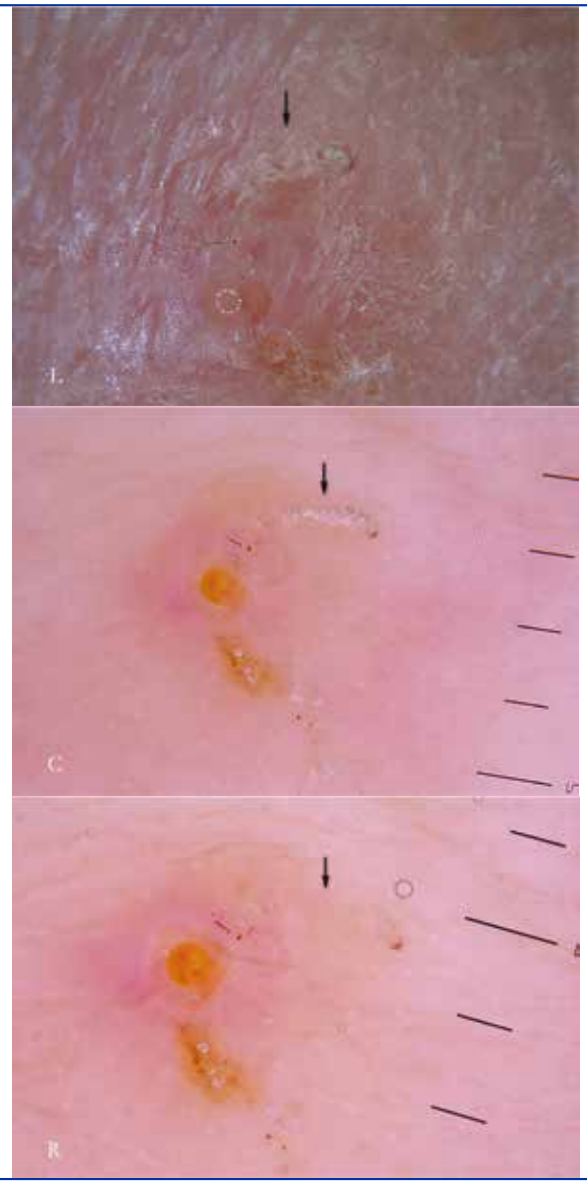


FIGURE 6. *Contactless versus contact dermoscopy of the same Mite-Gallery Unit. In d-DS the roof of the tunnel appears interrupted by several holes that allow the air to exit (Left). The first description of an MGU resembling a white jet contrail was determined by the trapped air between the tunnel and the glass plate of w-DS (Center). After having discontinued dermoscope contact, the gallery disappears as all of air bubbles escape and the liquid medium passes inside it (Right).*

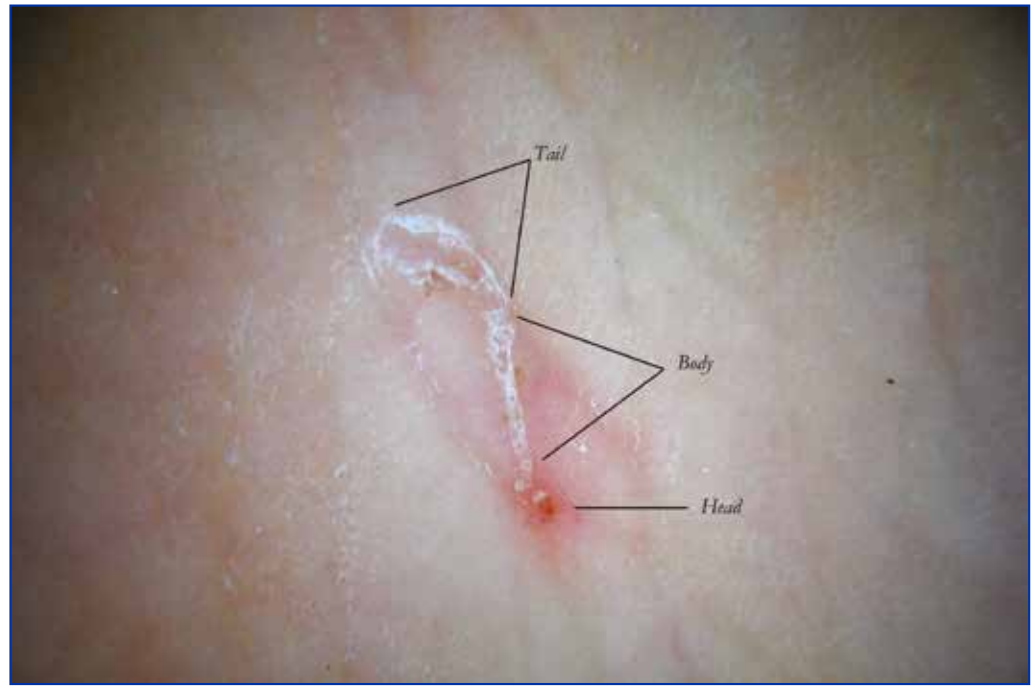


The practical consequence is that the *global descriptor* of scabies has a life time limited to the first observation after which only the front of the mite may remain visible which not always it is distinguishable from the background especially when the observer's eye is poorly trained or if only 10x magnification is used.

Local descriptors (Fig. 7)

These parameters are strongly correlated to the life cycle of the *sarcoptes*, to its horizontal movement, to its interaction with the turnover of the epidermis, in other words to everything introduces the new concept of MGU,[7] in which 3 anatomo-functional parts are recognized: *head, body and tail*. The analysis of these descriptors necessarily requires magnifications around 30-50x.

FIGURE 7. *The Mite-Gallery Unit under contactless dermoscopy (d-DS). The Mite-Gallery Unit (MGU) structure can be divided into three parts. The Head hosting the mite, the Body which represents what clinically is defined as the burrow containing eggs and feces of the parasite and the Tail at the end of structure, which is an incomplete gallery because without roof but made of keratinic collarettes visible only in d-DS. An erythema is present in the background around and immediately behind the mite.*



MGU head (Figs. 8-10)

MGU always has a polarity. In fact, the part named "head" represents the true origin of the tunnel. In the literature, some authors define the origin of the burrow as the first point where the mite begins to dive. But although this can be correct when thinking about the timeline, from a functional point of view the gallery begins only where the mite forms it by digging[7]. It would be better to use this logical sequence so as not to be confused during future descriptions. In dry dermoscopy, the head of the MGU houses the entire body of the mite which, when using magnification >10x, appears as a brown and barely raised area on the epidermis level. In this part of the gallery the corneum layer of the roof is intact.

FIGURE 8. *Contactless dermoscopy (d-DS). The initial part of the MGU is the head. This part of the gallery houses the mite which is recognized by a small triangular area with the vertex oriented towards healthy skin where it will proceed. The head of gallery has a roof intact.*

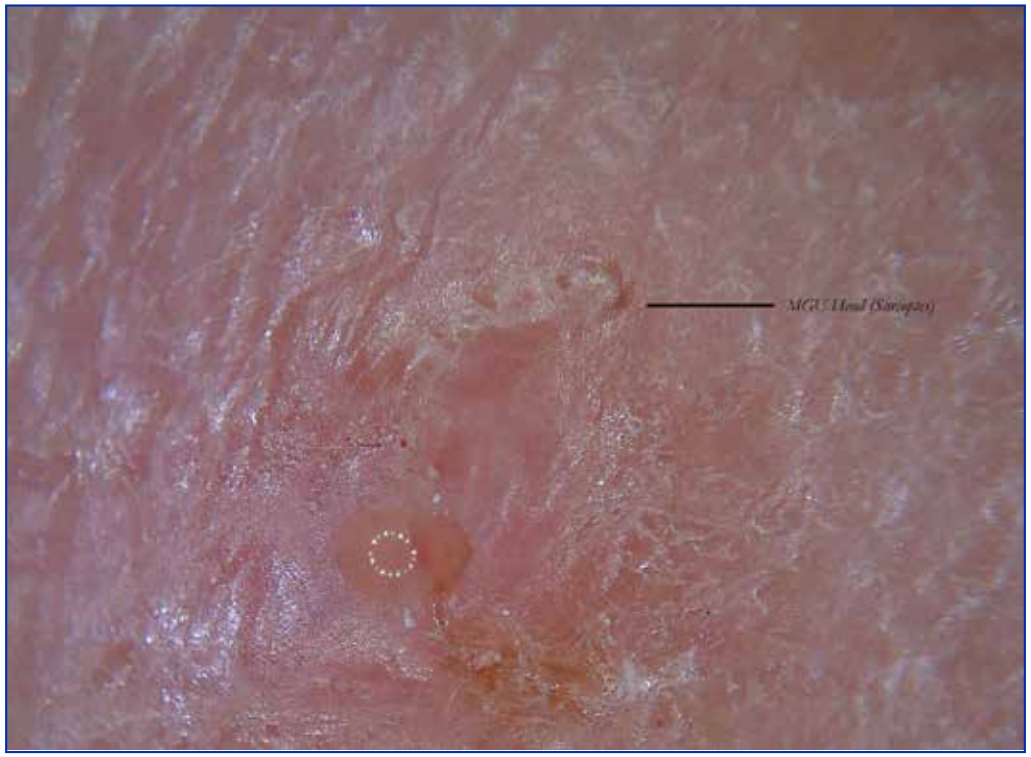
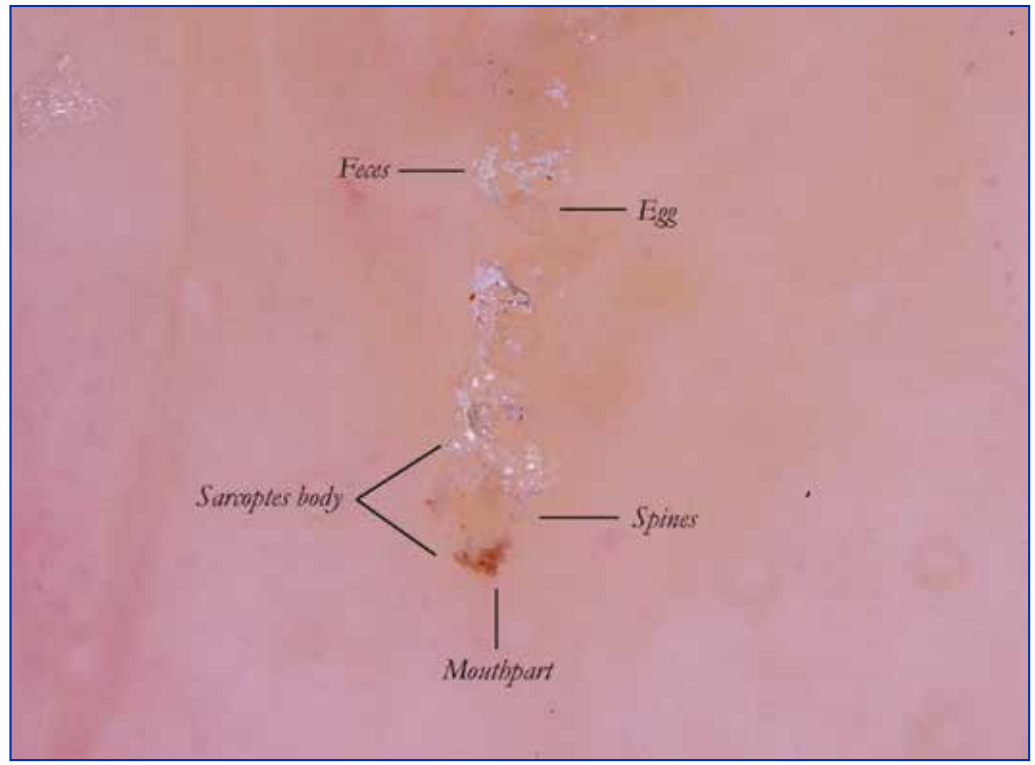


FIGURE 9. *Enhanced contact dermoscopy of an MGU in w-DS mode. The Body of the mite. In addition to refraction of its anterior part, Sarcoptes scabiei shows an opalescent body with several scattered little dark dots (ladybug sign). These formations correspond to the "bristles" on the body that guarantee, among other functions, the adherence of the mite within the tunnel.*



In wet-dermoscopy it is possible to recognize not only the anterior part of the acarus as previously described, but also somatic ultramicroscopic structures which are visible as a series of dark little dots whose appearance resembles a ladybug (*ladybug sign*). These dots under the scanning microscope correspond to specific bristles (*spine-like type*) by which the mite anchors itself to the tunnel walls working also as mechanical receptors.[8] This example demonstrates *entodermoscopy* potentiality.

FIGURE 10. *Enhanced contact dermoscopy (w-DS). The body of the mite has a slight opalescence which may be detected only at higher magnifications. The front part corresponds to the gnatosoma and the first pair of legs. The body of the mite is marked by little dark dots that correspond to the bristles of the back (mechano-sensory receptors) that give rise to the dermoscopic sign "ladybug".*

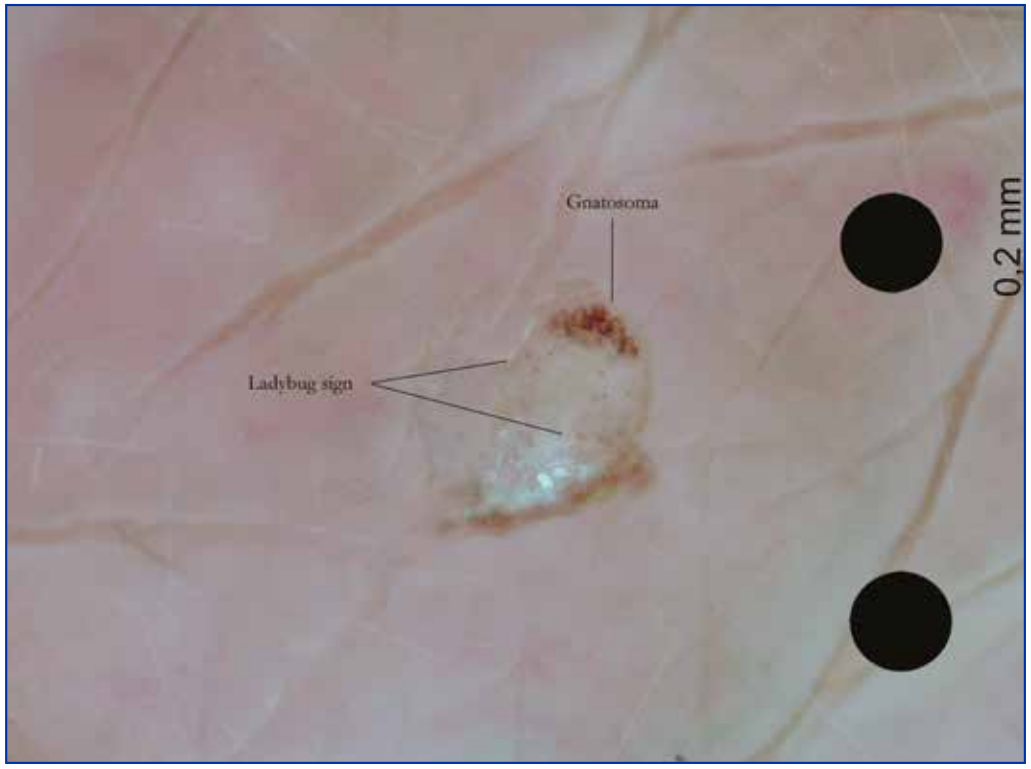
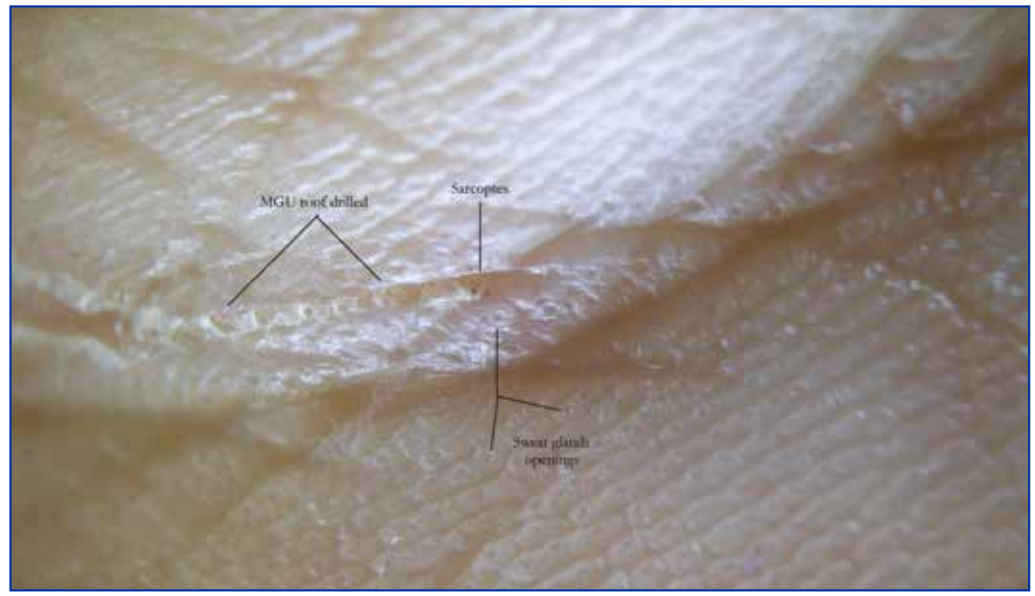


FIGURE 11. *Contactless dermoscopy (d-DS) with lateral light. The body of the MGU corresponds to the main part of the tunnel on the bottom of which the mite eggs are glued. The roof of the tunnel is clearly interrupted by holes from which the larvae are supposed to come out but which could also be the result of the detachment of the sweat gland openings.*



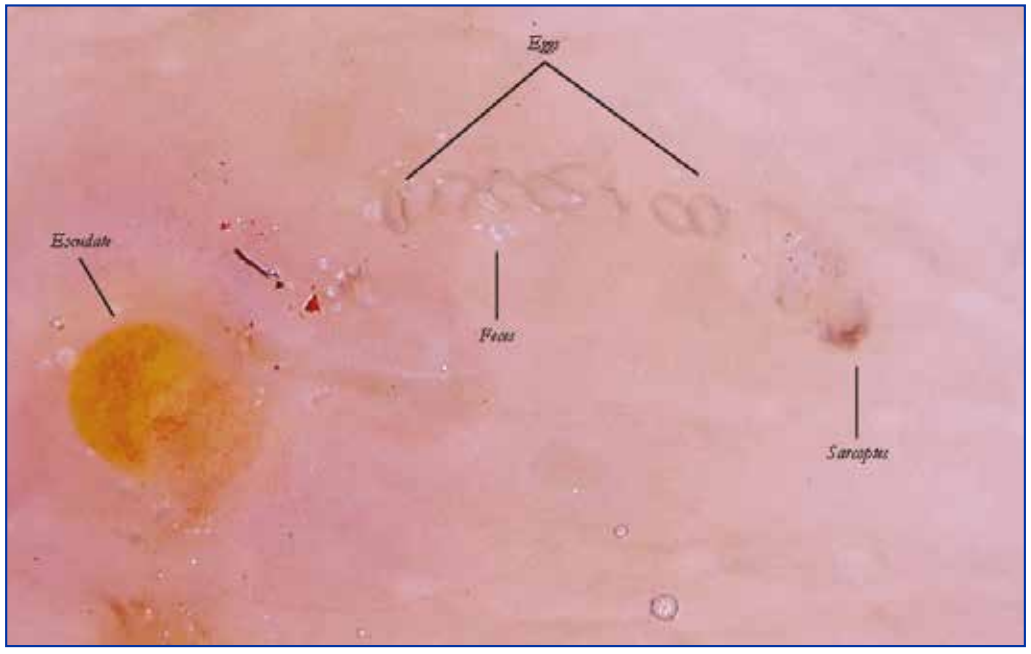
MGU body (Figs. 11,12)

The MGU body indicates the most part of the tunnel which develops behind the mite.

In dry-dermoscopy it appears to consist of a whitish roof marked by holes or little openings. Some authors argue that their origin depends on the escape of the larvae that move away to create a new burrow elsewhere.[9] Another hypothesis is that the holes, often of the same size, are nothing more than the ostia of the sweat glands ducts separated by the passage of the parasite which would act as a wedge.[7] The two hypotheses are not mutually exclusive. *Entodermoscopy* once again adds new elements.

In wet-dermoscopy the body segment of the MGU can be seen precisely because the air inside the tunnel escapes from the holes of the roof remaining entrapped under the plate. But if one detaches the dermatoscope, at the next examination of the same area, the bubbles vanish and the liquid medium goes into the tunnel, making the very thin roof transparent. In this case, as previously mentioned, only the head part of the tunnel will remain recognizable. Something interesting happens though, when the roof becomes transparent, as this transparency leaves the base and the content of the gallery previously hidden by the air bubbles free to be seen. Here two descriptors are found, one of which is represented by oval formations which correspond to the eggs and the other one by numerous whitish points which correspond to the fecal pellets left by the mite inside the tunnel. It is useful to remind that under optical microscopy the feces

FIGURE 12. *Enhanced contact dermoscopy of an MGU in w-DS mode. Content of the gallery. The absence of bubbles and the penetration of the liquid film in the tunnel, makes the roof transparent and allows to glimpse a row of eggs otherwise not accessible. The white dots are the feces of the mite. A serum-purulent drop is located on the left.*

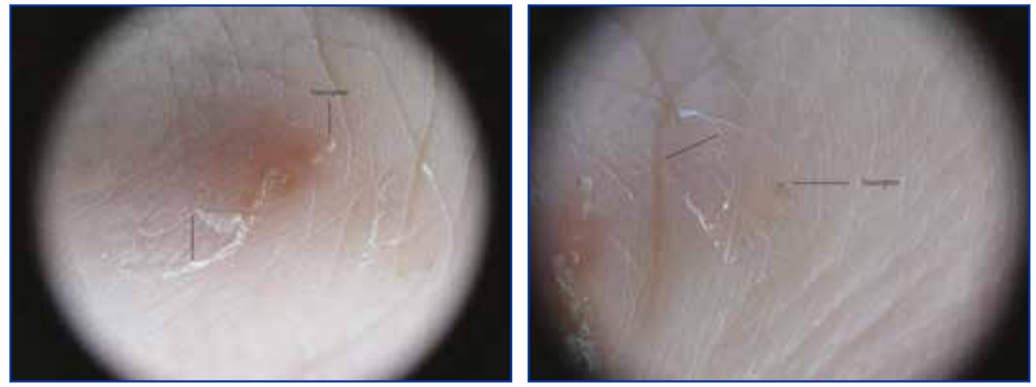


appear as "dark bullets" because they are not crossed by light. In dermatoscopy, where incident light is used, their color is instead grayish-white. Another new piece of information coming from *entodermoscopy*.

MGU tail (Figs. 7,13)

MGU tail is the final part of the tunnel, which however coincides temporally with the beginning when the mite dips into the epidermis. Being the oldest part of the burrow, it rarely remains intact because it lacks the roof normally present in the rest of the MGU. In dry-dermoscopy the tail is defined by two keratin edges progressively diverging and fading into surrounding healthy skin. In wet-dermoscopy this part does not appear because under the glass plate and liquid interface the edges lose all refraction.

FIGURE 13. *Contactless dermoscopy (d-DS). The rear of the MGU is no longer a gallery because it lacks the roof. In its place one can recognize two keratin edges that move away from each other. This phenomenon could be attributable to the turnover of the outer layers of the skin that replace the older part of the tunnel with new skin.*



The explanation for this segment of the MGU lies in the parasitic movement that advances horizontally[10] while the skin turnover produces a vertical movement, because of which the oldest part of the tunnel is the first part to be eliminated[11] by the renewal of epidermis, regardless of any scratches of the host. The latter is not involved at all because the tail is surrounded by normal skin without any sign of nails trauma. In literature the tail has never been described both because of the lack of a morpho-functional interpretative model as the MGU and above all because the ordinary descriptions have been made with a liquid medium (w-DS) which renders the subtle keratin edges defining the MGU tail completely invisible. Another example of *entodermoscopy* utility.

Variations of the MGU. Atypical MGUs (Figs. 14,15)

The description of MGU made so far has not considered some additional factors represented by the host's inflammatory response, secondary infections, hyperkeratotic reaction, itchy nodules and juvenile forms of the mite whose role in the scab pathogenesis is still completely unknown. In these situations other local descriptors are identifiable and are summarized in the concept of *atypical* MGU.

FIGURE 14. *Contactless dermoscopy (d-DS) of an atypical MGU. The refractive part of the mite (arrow) is evident, behind which there is an aggregate of scales rather than an ordinary gallery.*

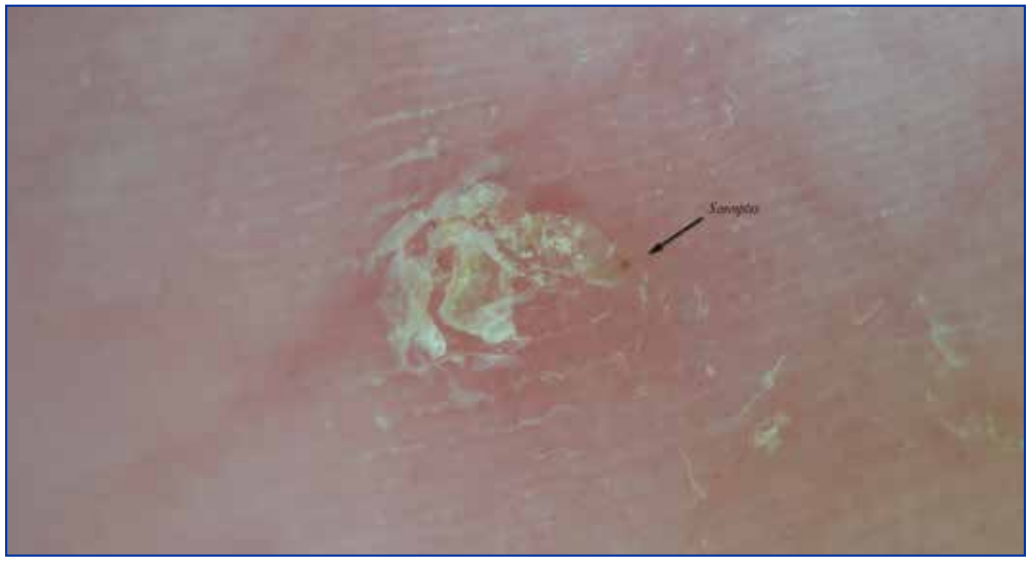
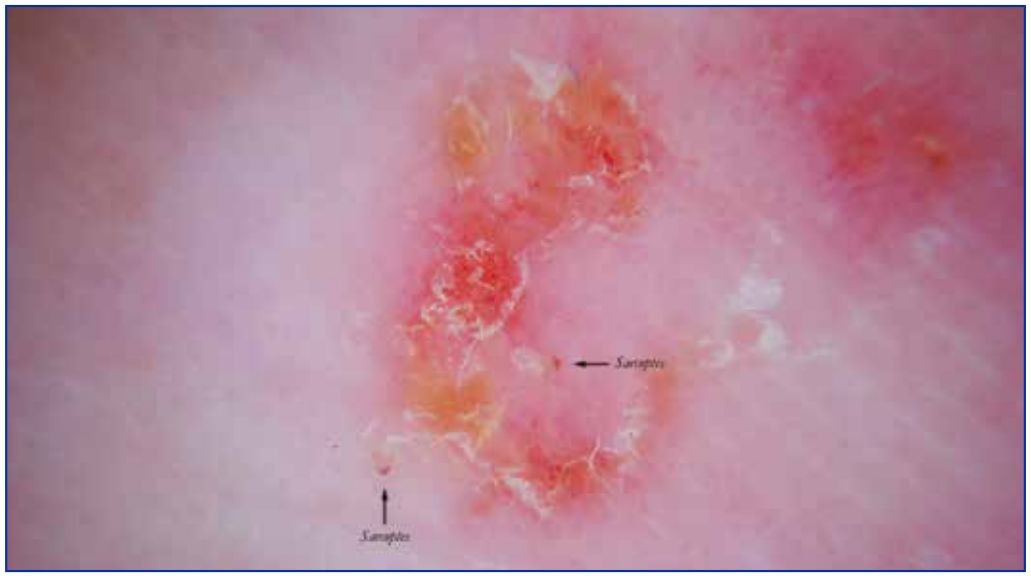


FIGURE 15. *Contacless dermoscopy (d-DS) with polarized light of an atypical MGU. Two mites (arrows) can be recognized behind which there is no tunnel but an erythematous area with polycyclic borders.*



MGU complicated by flogosis or hyperkeratosis (Figs. 16-18)

It is well known that scabies represents a risk to develop streptococcal infection. In the poorer regions of the globe or where climatic conditions increase scabies diffusion, renal failure or post-streptococcal endocarditis represent a feared com-

FIGURE 16. *Contactless dermatoscopy (d-Ds). (A) tangential light, (B) polarized light. The images show an MGU in which can be appreciated the delta wing sign produced by the mite and the following body of the gallery. A pink area is visible around MGU which corresponds to the inflammatory response that the mite products induce in the host.*

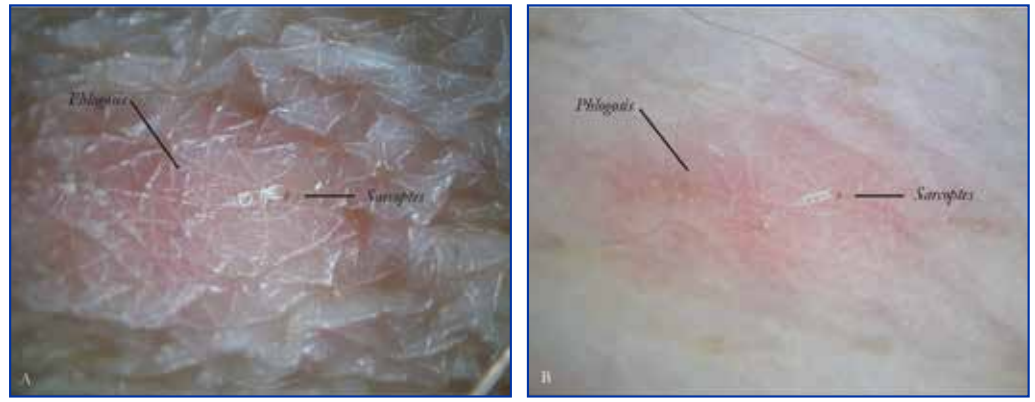


FIGURE 17. *Phlogistic response to an MGU observed with polarized light contactless dermoscopy (d-DS). Next to the mite (black arrows, L-R) the skin is normal, while in the central part of the gallery an erythematous halo (red arrow, L) is evident. Immediately behind the mite, phlogosis can also occur in micro-vesicles trapped in the epidermis (red arrow, R). The tail of the galleries is characterized by keratinic collarettes.*

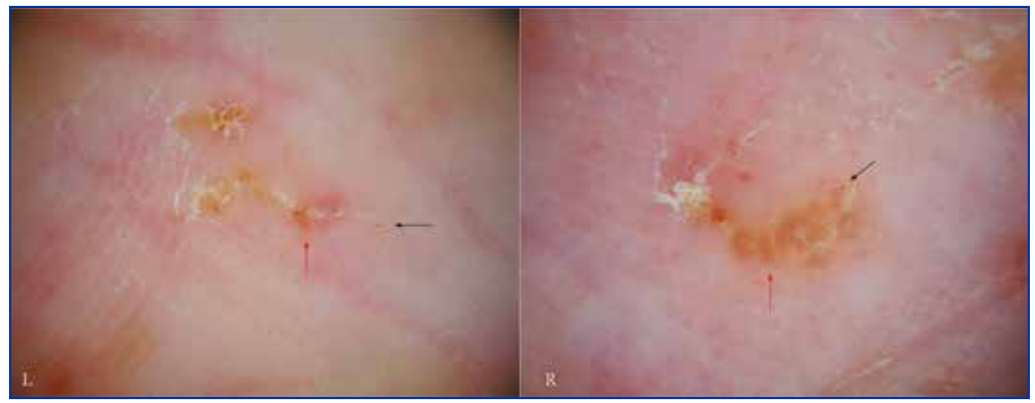
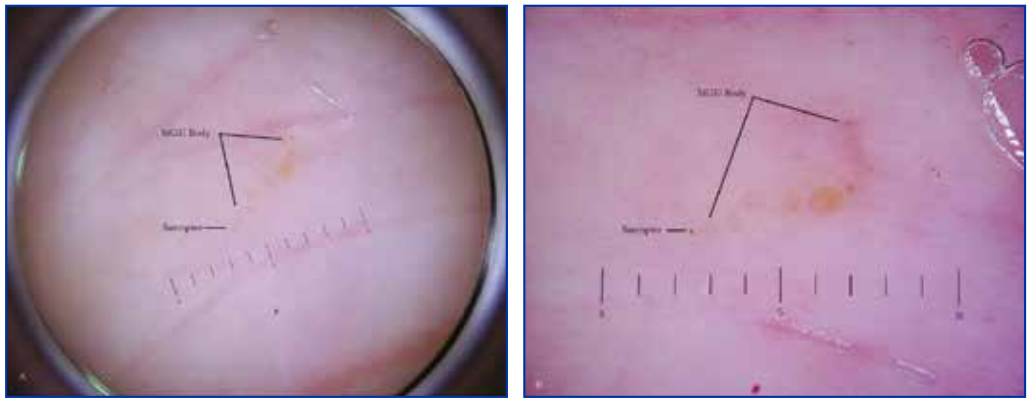


FIGURE 18. *Contact dermoscopy (w-DS). The inflammatory response is an exudation that can remain trapped in skin thickness as a dyshidrotic-like appearance. In these images, the bubbles of MGU gallery were intentionally eliminated by moving the dermatoscope in order to better observe the phlogistic phenomenon.*



plication.[12] Moving on to the microscopic scale of the burrow, the inflammation is recognized as an pink-reddish veil generally located around the burrow or by a drop of serous exudation on skin surface[13] or also as deep semitransparent (*dyshidrotic-like*) spongiotic vesicle[14] where keratin is thicker, as in palms or soles. If phlogosis is very intense, it disrupts the basic morphology of the MGU, especially erasing the body and the tail of the tunnel.
During its path, the *sarcoptes* activates various immune signals including interleukin IL6[15] which increases the rate of turnover and therefore allows the accumulation of keratinocytes on the surface as yellowish scales variable in shape and thickness. The erythematous response that is found around the MGU, if not complicated by secondary infections, can be at first concentrated at the level of the head of the tunnel where the mite releases antigenic proteolytic enzymes. The dermatoscopic diagnosis of scabies must necessarily take into account *atypical* MGUs since they resembling secondary/unspecific lesions can induce the observer to erroneously exclude them from a dermoscopic examination.
Generally in *atypical* MGUs it is no longer possible to find the mite-gallery couple but mainly only the mite. Since the representation of the latter is less "clear" than in the uncomplicated MGU, it requires a careful look to recognize the parasites among scales-crusts and exudates collections, which are able to mask sarcoptes very easily.

MGU of nodules (Figs. 19,20)
Nodular scabies is almost a separate chapter because in the multiplicity expressivity of the disease it poses an unresolved question. Why does an intensely itchy nodule form in specific parts of the body instead of an ordinary tunnel? The prevailing idea is that it depends on a cell-mediated hyper-reactivity[16] favored by local conditions such as friction, pressure and humidity that can probably allow a deeper penetration of antigens (intradermic) in areas undergoing a physical pressure.[7]
What are the dermoscopic descriptors of this form of scabies?
MGU can still be recognized only in more recent (younger) nodules mainly through the presence of the *sarcoptes* itself rather than a whole burrow. However, if the nodule is older, the traces of the MGU disappear completely and it is possible to speak of an "uninhabited nodule" on which is useless to make an etiological diagnosis by dermatoscopy.

FIGURE 19. *Enhanced contactless dermatoscopy (d-DS). Mite and gallery are clearly recognized in a recent papulo-nodular lesion.*

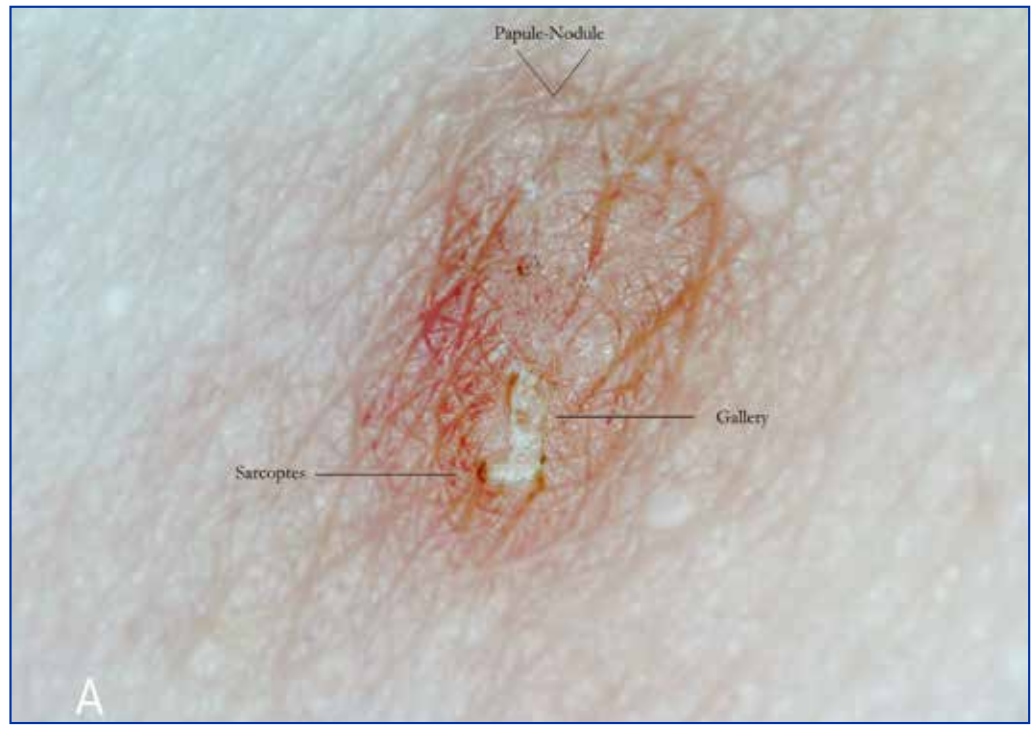
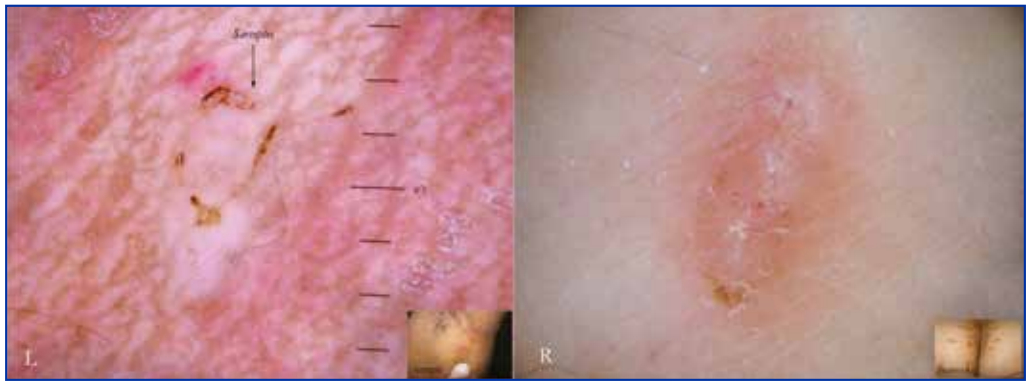


FIGURE 20. *Nodular scabies observed in contact dermoscopy (w-DS) and contactless (d-DS) polarized light dermoscopy. A mite is recognizable in one of the axillary (L inset) papules of a subject of African ethnicity. A buttock (R inset) nodule present for a few weeks appears uninhabited instead.*



MGU of mite youth forms (Figs. 21-23)

The life cycle of the mite requires an egg which gives birth to a young individual as a 6-legged larvae which then matures into an 8-legged nymphs of the same shape as an adult but smaller in size.[17] This maturation takes place outside the mother burrow and precisely in a dimple that the young mite digs to find shelter and remain there. In this case it does not form a burrow but a small pocket for moulting and mating. Once the mature stage is reached, the female waits to be reached by a male to be fertilized and finally she begins to dig a definitive tunnel as it is known in temperate climates.[18] The fate of the male after fertilization is not known and in any case it does not produce burrows.

What dermoscopic descriptor identifies these juvenile forms? In the literature no clinical symptoms can be traced back to them but it is certain that the skin surface is the place of many interactions among the juvenile forms which not producing a real gallery, could never be recognized either with the naked eye or by any dermoscopic jet contrail. The descriptors of the juvenile forms therefore coincide with the mere presence of a tunnel-free mite regardless of the mode of observation (wet or dry dermoscopy).

In a local context where there is a MGU with a full gallery developed by an adult mite, a tunnel-less mite nearby, very probably is a juvenile form. In some entomological texts[19] it is said that even the hair follicles can be exploited as

FIGURE 21. *Moulting pocket in contactless dermoscopy (d-DS) with non-polarized (L) and polarized light (R). In this structure the complete Mite-Gallery Unit does not develop because the mite remains stationary until the moulting process is completed or mating happens. There is instead only a small whitish raising (arrows, L-R) corresponding to the whole body of the Sarcoptes behind which a real tunnel is not formed. Around the pocket, an area of erythema with blurred borders is recognizable.*

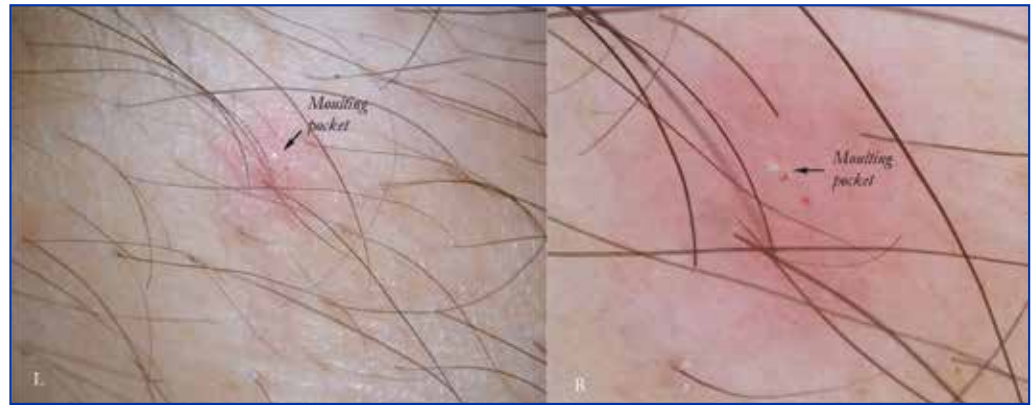


FIGURE 22. *Contact dermatoscopy (w-DS). Some moult pockets are found in proximity to an adult head MGU which size is about twice larger than immature forms.*

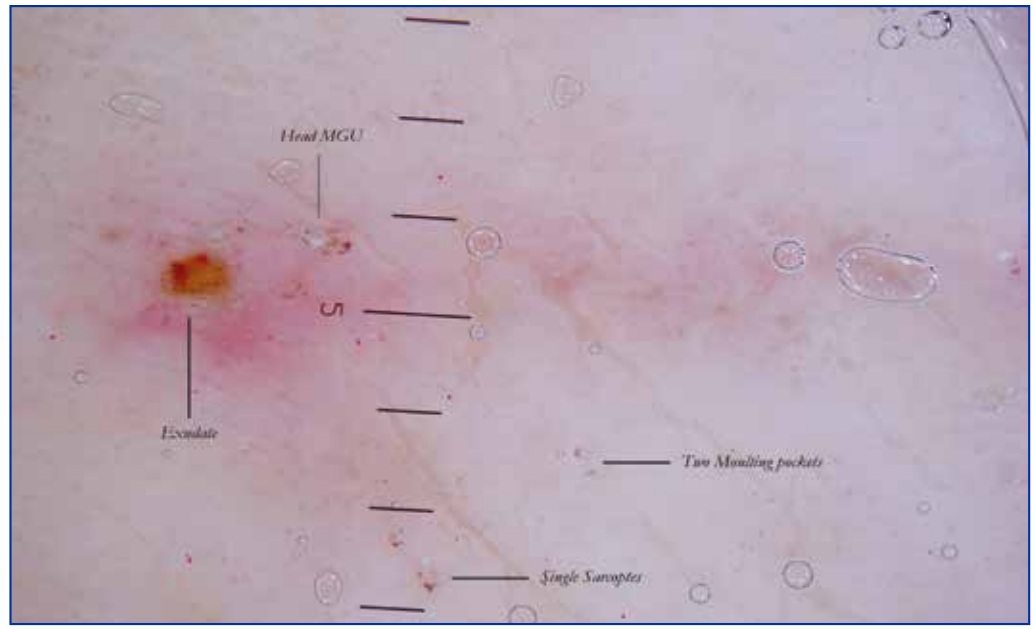
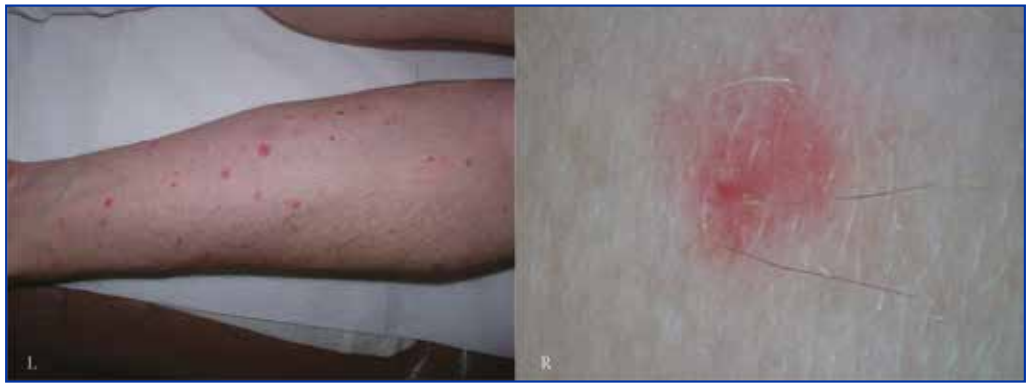


FIGURE 23. *Scabies pseudo-follicular eruption observed under contactless dermoscopy (d-DS). Folliculitis-like lesions (L) are commonly considered non-specific sign of scabies. Under dermoscopy, only a peri-follicular erythematous halo is appreciated with some pinpoints-like vessels inside it (R). There are no signs of any complete or atypical MGU.*



moulting/mating niches but at the moment there is no dermatoscopic evidence in the literature. If confirmed, this hypothesis could explain the nature of the pseudo-follicular rash which could turn from non-specific to a specific sign of scabies.

MGU evolution at the end of mite life cycle or after therapy. Ghost gallery (Figs. 24,25)

When the formation of new parts of the tunnel stops, due to therapy or to exhaustion of mite life cycle, after a few days all the MGU will be remodeled. It will be replaced only by its traces in the form of polycyclic keratinic borders appearing as a "ghost gallery". Post-inflammatory phenomena and local superinfections can also contribute to its formation. Detection of phantom gallery might be useful in hypothesizing scabies when the therapeutic anamnesis is uncertain or in the absence of active MGU, to confirm the success of a therapy, itching being a subjectively variable criterion.

In conclusion, it is possible to say that *entodermoscopy*, despite some apparent complexities, adds new descriptors which, together with clinical evaluation (always the base of any decisional process) increase the reliability of the diagnosis. It brings practical advantages because of the easy availability of derma-

FIGURE 24. *Contactless dermoscopy (d-Ds). In these pictures it is possible to follow the natural evolution of the oldest part of the MGU. (A) The tail of the MGU is constituted by a gallery which progressively loses the roof and of which only its bases remain as two keratinic edges. Subsequently they diverge to become areas of skin limited by thin polycyclic keratin flaps (B) in which the gallery is no longer recognizable (ghost gallery).*

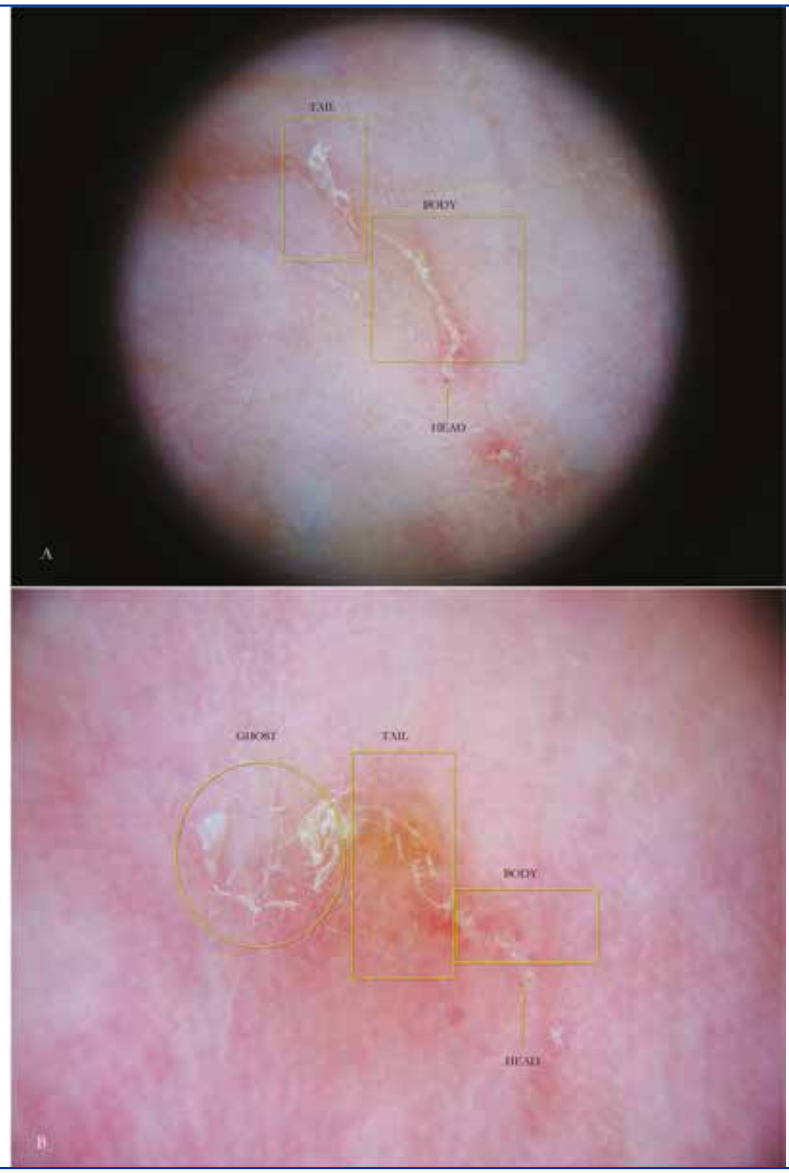
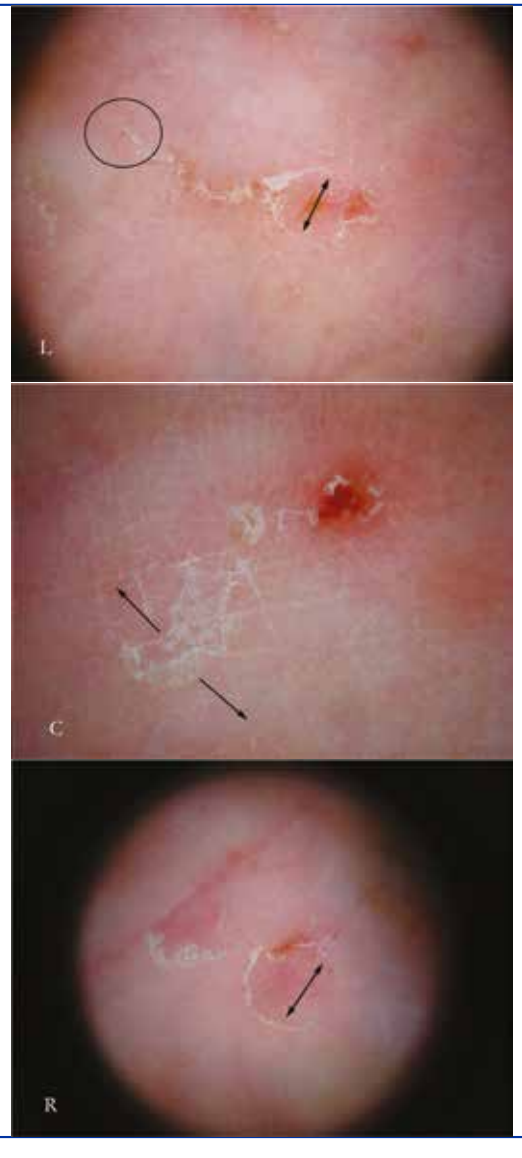


FIGURE 25. *Evolution of an MGU towards a "ghost gallery" under polarized contactless dermoscopy (d-DS). A mature MGU ends with a tail made up of keratinic collarettes that progressively move away from each other (black arrow, L). Sarcoptes is recognized in the front part of burrow (circle, L). When the mite is at the end of its life cycle or after therapy also the other parts of the tunnel undergo the normal processes of rearrangement of the skin (C) becoming thin and polycyclic keratinic edges of a ghost gallery (C,R).*



toscopes but especially for the time saved, which is not very different from the examination of a multiple melanocytic nevi patient. After a short training each dermatologist will be able to recognize triangles (mites) isolated or associated to white trails or to identify other local signs belonging to the micro-environment that develops between humans and parasites. *Entodermoscopy* is able to disclosure something that no traditional microscopic examination has ever had access to, becoming for the first time a key part of the clinical diagnosis.

All dermoscopic photos can be downloaded in full format from the following link:
https://www.gaetanoscanni.it/SCABIES_MYTHS_TO_DISPEL

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7. Skin bacterial superinfections in scabies

Skin bacterial superinfections in patients with scabies are very common in some Tropical and Subtropical countries. Several studies have been carried out in India,[1,2] some countries of Pacific area (Fiji,[3-5] Australia,[6-10] Samoa,[11] and Solomon Islands[12,13]) and Trinidad.[14] However, only very rare epidemiological-bacteriological studies have been performed in immunocompetent patients with scabies living in Western countries.[15,16]

We present the results of a bacteriological study in immunocompetent adult patients with scabies living in Milan.

Eighty-nine Caucasian immunocompetent patients with scabies [51 males and 38 females, with an age ranging from 21 to 63 years (mean age: 36.7 years)], were subjected to bacteriological examinations of the skin for aerobic and anaerobic bacteria. Clinical diagnosis of scabies was confirmed in all patients by means of microscopical examinations: they were considered positive when adults or eggs or faeces of *Sarcoptes scabiei* var. *hominis* were visible. In all patients, six skin swabs (three for aerobic and three for anaerobic bacteria) were taken in three different areas before the beginning of a treatment with 5% permethrin cream: one application/day for two consecutive days; the treatment was repeated 7-10 days later.[17] The choice of the areas which were subjected to bacteriological examinations was made on the basis of the most frequently involved areas: penis, scrotum and subungual skin of fingers in males, and breasts, axillae and subungual skin of fingers in females.[18] In our experience, penis, scrotum, breasts and axillae are also the most itchy areas.

No clinical manifestations of bacterial superinfection were observed. Bacteriological examinations were positive in 5/89 patients (5.6%) [4/51 males (7.8%) and 1/38 females (2.6%)]. Bacteriological cultures were positive for *Staphylococcus aureus* in all 5 patients; in one patient they were positive also for *Escherichia coli*. No growth of anaerobic bacteria was recorded. According to antibiograms, all patients were successfully treated with amoxicillin (2-3 g/day for 10 days). Daily cleanings with chlorhexidine were also prescribed.[19]

The importance of skin bacterial superinfections in patients with scabies is due to the fact these infections can cause severe systemic diseases, such as glomerulonephritis, rheumatic fever and sepsis.[4]
In Tropical and Subtropical countries, the prevalence of bacterial superinfections in patients with scabies varies from country to country, but it is overall high. In an Indian study, secondary pyoderma was detected in 42.8% of children with scabies.[2] Three studies were carried out in Fiji Islands.[3-5] The first one showed that impetigo was more common in indigenous Fijian children when compared with children of other ethnicities.[3] In the second study, the prevalence of impetigo in patients with scabies was 19.6%, with a peak of 34.2% in children aged 5 to 9 years.[4] In the last study, it was observed that people with scabies were 2.8x more likely to develop impetigo. Households with four or more people sharing the same room were more likely to develop scabies and impetigo compared to households with rooms occupied by a single individual.[5] In indigenous communities in Northern Australia, the prevalence of superinfected scabies in children aged less than 5 years was 12%.[8] Furthermore, 84/508 (16.5%) children randomized to receive treatment for impetigo were affected by scabies. On the whole, scabies ranged from 14.3% to 20%.[9,10] In American Samoan children with scabies, 53% of them had a bacterial superinfection.[11] In Solomon Islands, 41.1% of patients with impetigo also had scabies.[13] The close relationship between scabies and skin bacterial superinfections was demonstrated by two studies which were performed in an Australian Aboriginal community[6] and Solomon Islands,[12] respectively. In the first one, following a treatment with permethrin cream, the prevalence of scabies in adults was reduced from 28.8% to <10%, and from 32.3% to <10% in children. The initial prevalence of pyoderma in children was 69.4%, which was reduced and maintained at approximately one-half.[6] In the second study, the prevalence of scabies dropped from 25% to less than 1% after therapy with ivermectin; prevalence of pyoderma decreased from 40% to 21%.[12]
In two Indian studies, *Staphylococcus aureus* was the commonest microorganism responsible for pyoderma in patients with scabies.[1] It was isolated in pure culture from 48% of patients, followed by group A beta-hemolytic streptococci (36%). A combination of both bacteria was observed in 16% of patients.[2] In Fiji Islands, the majority of cases of post-scabies impetigo was caused by group A *Streptococcus pyogenes*; *S. aureus* was also a common cause (57.4% in school aged children and 69% in infants).[3] Also in Australia, children with scabies were more likely to develop *S. pyogenes* superinfections of the skin.[9] In Trinidad, 50% of schoolchildren and 93% of adults with scabies had pyoderma caused by group A *Streptococcus*.[14]
It was demonstrated that scabies mite complement inhibitors, such as SMSB4, increase *S. pyogenes* survival rates in vitro by 2-15 fold.[20-22] Furthermore, scabies mite promotes growth of opportunistic pathogens in a porcine model.[21]
As previously mentioned, we surprisingly found only very rare studies about skin bacterial superinfections in immunocompetent patients with scabies living in Western countries.[15,16] In a study carried out in Washington, aerobic and anaerobic bacteria grew from specimens obtained from 30 children with scabies. Aerobic bacteria were present in 14 (47%) patients, anaerobic bacteria in 6 (20%) patients and a mixed anaerobic-aerobic flora in 10 (33%) patients. Fifty isolates were recovered: 27 were aerobic and 23 were strict anaerobes. The predominant aerobic and facultative bacteria were *S. aureus* (nine isolates), group A streptococci (five isolates), and *Pseudomonas aeruginosa* (three isolates). The predominant anaerobes were *Peptostreptococcus* sp. (nine isolates), *Prevotella* sp. and *Porphyromonas* sp. (four isolates each).[15]
According to the results of our study, skin bacterial superinfections in adult immunocompetent patients with scabies living in Milan are uncommon. Contrariwise, impetigo is rather common in the metropolitan area of Milan, in particular in children aged 4 to 8 years. *S. aureus* is responsible for approximately 95% of all cases. It is possible that our results are due to the climate (in Milan winter usually begins at the end of October and ends at the end of March) and adequate personal and housing hygienic conditions of the population. It is well known that both scabies and pyoderma occur in people living in poverty, with low income, overcrowding, lack of sanitation, poor environmental and personal hygiene and malnutrition.[23]

Skin bacterial cultures may therefore be considered an unnecessary routine procedure in adult immunocompetent patients with scabies living in some Western countries.

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A new treatment regimen with permethrin

Permethrin is a combination of pyrethrins isomers. It causes depolarization of nerve cell membranes and disrupting neurotransmission.[1] The selective neurotoxic effect of permethrin in invertebrates is due to structural differences in voltage-gated sodium channels between vertebrates and invertebrates.[1]
Eighty-nine adult immunocompetent patients with scabies were treated with 5% permethrin cream: 42 patients were treated with a single application (group I); 47 patients were treated with one application/day for two consecutive days (group II). This second regimen was adopted because we observed in the past very good clinical and parasitological results in patients in whom permethrin had been applied once daily for two consecutive days.[2]
Clinical diagnosis of scabies was confirmed in all patients by means of microscopical examination: it was considered positive when adults or eggs or faeces of *Sarcoptes scabiei* var. *hominis* were visible.
The cream was stored in refrigerator and applied cool on the entire skin surface, including nails. The cream was left on the skin for 24 hours. Approximately 90 g/day of cream were applied. No other topical and/or systemic drugs were allowed, except for a cleanser with 0.4% chlorhexidine digluconate (one washing/day). The treatment with permethrin was repeated in all patients 7-10 days later.
Follow up duration was two months after the end of the treatment. Statistical study was carried out by calculating the percentage of recovered patients, both clinically and microscopically, in both groups. Data were evaluated by means of X^2 test. $P<0.05$ values were considered as statistically significant.
Seventy-three out of 89 patients (82%) were considered evaluable: 34/42 patients (81%) in the group I and 39/47 patients (83%) in the group II.
Twenty-one out of 34 patients (61.8%) in the group I and 34/39 patients (87.2%) in the group II were considered recovered both clinically and microscopically. X^2value was 6.31544. The difference of percentage of recovered patients in both groups was statistically significant ($p<0.05$).
Three patients (7.1%) in the group I and 4 patients (10.2%) in the group II developed a mild irritant contact dermatitis, characterized by worsening of

pruritus, burning sensation and erythema. In all these patients, it was unnecessary to stop the treatment.
During follow-up, three patients (7.1%) in the group I and two patients (4.2%) in the group II developed a recurrence or a re-infestation (it was impossible to distinguish one from the other), confirmed by microscopical examination.
The results of this multicentre, controlled, randomized, sponsor-free study may be summarized as follows:

a) 5% permethrin cream, when applied once daily for two consecutive days, is statistically more effective than when it is applied once daily;
b) the application of permethrin as cold cream improves significantly patients' compliance: it reduces pruritus and the incidence and severity of irritant contact dermatitis;
c) the storage of permethrin in refrigerator does not influence its clinical activity: it was demonstrated that both cis and trans isomers of permethrin are highly stable at different temperatures;[3]
d) in humans, lethal oral dose of permethrin is 1-2 g/kg. After topical application, permethrin is rapidly metabolized in the skin, is absorbed in small amounts, and is almost completely excreted in the urine.[4] Elimination is complete after one week: no risks of tissue storage exist. Therefore, to leave permethrin on the skin for 24 hours does not induce a systemic absorption. This is important because in many leaflets of permethrin products marketed in Europe, it is suggested to apply the cream for not more than 6-8 hours. As cis isomer of permethrin is considered more toxic (it is excreted at a lower rate and more slowly than trans isomer), preparations with lower quantity of cis-permethrin are preferable; in particular, the ratio cis/trans should be 25:75.[4-7] Permethrin we used in this study has this ratio.

The results of this study showed that 5% permethrin, when applied as cold cream, once daily for 24 hours and for two consecutive days, is more effective than the single application in adult immunocompetent patients with scabies.[8]

Treatment of crusted scabies with acitretin

An 83-year-old woman was examined because of a crusted dermatitis. The patient was in therapy with metoprolol and levodopa/benserazide for essential arterial hypertension and Parkinson's disease. The patient stated that the dermatitis had appeared approximately six months earlier. It was diagnosed as allergic contact dermatitis and unsuccessfully treated with topical and oral corticosteroids, and oral anti-histamines. Three months later, a diagnosis of scabies was made. The patient was treated at other centres with benzyl benzoate (two courses: one application/day for 10 days), permethrin (two courses: one application/day, repeated 7 to 10 days later) and synergized pyrethrins (one course: one application/day, repeated 7 to 10 days later). However, skin lesions did not improve and microscopical examinations were again and again positive for scabies mites.
Dermatological examination revealed the presence of isolated or confluent crusts and scales on a slightly erythematous base involving the elbows, forearms, wrists, hands, knees, legs and feet. The patient complained of mild pruritus. A clinical diagnosis of crusted scabies was made.
General physical examination revealed essential arterial hypertension, and fecal and urinary incontinence. Neurological examination confirmed the diagnosis of Parkinson's disease.
Laboratory tests showed increase in white blood cells (9.900/mm^3) with eosinophilia (8%) and erythrocyte sedimentation rate (ESR) (43 mm at the 1st hour). Microscopical examinations of the skin were positive for *Sarcoptes scabiei* var. *hominis* adults, eggs and faeces. Bacteriological and mycological examinations were negative.
A therapy with acitretin (30 mg/day), associated with a cream containing 15% glycerine, was started. Two weeks later, improvement of the lesions was observed. Six weeks later, complete remission was observed. Microscopical examinations were negative. Neither important side effects, except for cheilitis, nor laboratory abnormalities were recorded. Acitretin was continued for a total of eight weeks. Follow up (ten months) was negative.
A 78-year-old man was seen because of a crusted dermatitis. He was affected by essential arterial hypertension, type II diabetes mellitus and benign prostate hypertrophy. He was in therapy with atenolol, metformin and tamsulosin. The patient stated that the dermatitis had appeared approximately nine months earlier. It was diagnosed at other centres as allergic contact dermatitis and psoriasis, and unsuccessfully treated for six months with topical corticosteroids and oral anti-histamines.

Dermatological examination revealed isolated or confluent crusts and scales on a slightly erythematous base involving the scalp, elbows, forearms, wrists, hands, knees, legs and feet. The patient complained of mild pruritus. A clinical diagnosis of crusted scabies was made.
General physical examination revealed essential arterial hypertension. Laboratory examinations showed increase in white blood cells (11.200/mm^3) with eosinophilia (9%), blood glucose (136 mg/dl), ESR (68 mm at the 1st hour) and prostate specific antigen (6.1 ng/ml).
Microscopical examinations of the skin were positive for *Sarcoptes scabiei* var. *hominis* adults and eggs. Bacteriological and mycological examinations were negative.
The patient was unsuccessfully treated with permethrin (two courses: one application/day for two days, repeated 7 to 10 days later), followed by synergized pyrethrins (two courses: one application/day for two days, repeated 7 to 10 days later). However, skin lesions did not improve and microscopical examinations were repeatedly positive.
A therapy with acitretin (30 mg/day), associated with a 15% glycerine cream, was started. Two weeks later, improvement of crusted lesions was seen. Six weeks later, complete remission was observed. Microscopical examinations were negative. Cheilitis and increase in triglycerides were recorded. Acitretin was continued for a total of eight weeks. Follow up (13 months) was negative.
According to literature data,[9-14] topical permethrin is the most effective treatment for scabies: it is more effective than topical crotamiton and lindane. Permethrin also appears to be more effective in reducing itch than either crotamiton and lindane. No significant differences were detected in the number of treatment failures between crotamiton and lindane, lindane and sulfur, benzyl benzoate and sulfur, and benzyl benzoate and synergized pyrethrins. Also oral ivermectin is considered as an effective treatment. However, it is not licensed in several countries, such as Italy. Acitretin was never used for the therapy of scabies. We decided to use this drug because all previous treatments were ineffective in both patients. It is well known that oral retinoids increase the desquamation and inhibit the differentiation of keratinocytes. Furthermore, a reduction in filaggrin expression was observed in mouse keratinocyte cultures treated with retinoids.[15] In addition, human keratinocyte cultures grown in the presence of retinoids at concentrations that inhibit differentiation, contain neither filaggrin nor profilaggrin.[15] Keratinocyte cultures expressing the 56.5 and 67 kD keratins express profilaggrin, but not filaggrin. According to these data, retinoids can alter filaggrin expression at the level of profilaggrin synthesis and/or at the level of post-translational processing of profilaggrin to filaggrin.[15] Filaggrin is very important for mite survival because it was demonstrated that it is the main "food" for mite.[16]
It is possible that acitretin was active in these patients thanks to its keratolytic action, but also thanks to its inhibitory action on filaggrin synthesis. Furthermore, it is known that some arthropods have retinoid receptors, such as the retinoid X receptor.[17,18]

Treatment of recalcitrant scabies with tretinoin cream

A 62-year-old Caucasian man was seen because of a clinical diagnosis of scabies. The patient was in therapy with candesartan (32 mg/day), bisoprolol (5 mg/day) and simvastatin (20 mg/day). The patient stated that in the last four months he had been unsuccessfully treated with two courses each with 5% permethrin, 25% benzyl benzoate, pyrethrins associated with piperonylbutoxide and 10% crotamiton. Microscopical examinations were constantly positive for adults and/or eggs of *Sarcoptes scabiei* var. *hominis*.
General physical examination revealed mild arterial hypertension. Dermatological examination showed the presence of some small, roundish, erythematous papules involving the wrists, hands, penis, scrotum and buttocks. The patient complained of severe pruritus. Laboratory examinations showed slight increase in leucocytes with eosinophilia, and ESR. Furthermore, total cholesterol, triglycerides and glucose levels were increased. Microscopical examination of the skin was positive for adults and eggs of scabies mite.
We treated the patient according to the previously cited regimen (5% permethrin cream: one application/day for two consecutive days; the treatment was repeated 7-10 days later).[8] In our experience, this regimen induces a clinical and microscopical recovery in 87.2% of patients.[8] However, also this treatment was unsuccessful. We therefore decided to treat the patient with 0.05% tretinoin cream (one application/day) and 8% calamine cream (2-3 applications/day). Acitretin was ruled out because of high levels of total cholesterol

and triglycerides. Pruritus improved five days later. Complete remission of pruritus was reported ten days later. The patient complained of burning sensation on the penis, scrotum and inguinal folds. Tretinoin and calamine were used for a total of three weeks. Microscopical examinations became negative from the 7th day of treatment. Subsequently, they were always negative. Follow up (nine months) was negative.

As previously mentioned, we successfully treated two patients affected by crusted scabies with acitretin.[18] Acitretin was active in these two patients thanks to its keratolytic action, but also thanks to its inhibitory action on filaggrin synthesis.[15,16,18] The case we have described is the first one successfully treated with tretinoin. We subsequently treated three additional patients, for whom traditional treatment were unsuccessful.

Treatment of postscabies prurigo with diflucortolone and chlorquinaldol in a group of African refugees

The term "postscabies prurigo" (PSP) has been recently suggested by us in place of postscabietic nodules, because it can be considered as a true prurigo with a known etiology.[19] PSP was first described in 1963 by Samman with the name of "persistent scabious nodules".[20] PSP is a rare complication of scabies. In an Indian study, this prurigo occurred in 29/544 patients (5.3%) previously affected by scabies.[21] PSP is caused by a delayed, chronic hypersensitivity reaction to unknown antigens of the mite.[22-27] The diagnosis of PSP is possible when all the following criteria are present:

a) there is a history of scabies which has been successfully treated;
b) round, reddish-brown, papular-nodular lesions are present (also in non typical locations of scabies): in the previously cited Indian study, scrotum (96.5% of patients) and penis (69%) were the commonest affected sites, followed by axillae (37.9%) and groins (17.2%);[21]
c) patients complain of severe itching;
d) microscopical, dermoscopic and histopathological examinations are negative for mites or fragments of them, eggs and scybala;
e) specific anti-scabies therapy is ineffective;
f) the disease persists for weeks or months.[23] PSP is more frequent in males[21,22] and children.[21,23,24,28,29] Recovery is possible by means of potent topical or intralesional corticosteroids.[23,25,30,31] Pimecrolimus[32] and tacrolimus[30,33] are sometimes effective. Cryotherapy[34] and surgical excision (!?)[31] have also been used.

We present the results of a sponsor-free study on the anti-itching effectiveness and tolerability of a cream containing diflucortolone valerate and chlorquinaldol in the treatment of PSP.

Eighteen African refugees [15 males and 3 females, with an age ranging from 18 to 46 years (mean age: 31.8 years)] were enrolled in the period March-September 2018. These patients had arrived from Niger, Mali, Senegal, Gambia, Guinea, Eritrea and Somalia. All patients had been affected by scabies confirmed by microscopical examinations: the latter were considered positive when adults or fragments of them or eggs of *Sarcoptes scabiei* var. *hominis* were visible. All patients had been successfully treated with 5% permethrin cream (one application/day for two consecutive days; the treatment was repeated 7-10 days later).[8]

The diagnosis of PSP was made by negative microscopical and dermoscopic examinations. Thirteen out of 18 patients had been previously, although unsuccessfully, treated with 0.05% clobetasol proprionate cream (2 applications/day on each lesion for two weeks). This treatment was decided because it is usually effective. In addition, it is cheaper in comparison with pimecrolimus and tacrolimus, and technically easier in comparison with intralesional corticosteroids and cryotherapy. All patients were therefore treated with 0.1% diflucortolone valerate/1% chlorquinaldol cream (2 applications/day on each lesion for two weeks). No other topical and/or systemic drug was used. Primary objective of the study was the evaluation of itching at the end of the second week of treatment. Itching severity was evaluated by means of a 1-100 visual analogue scale (VAS).[35] Secondary end points were the changes of the morphology of the lesions at the end of the second week of treatment.

Fifteen patients (83.3%) were considered evaluable. All patients reported improvement of itching: before the beginning of the treatment, mean VAS was 86/100; at the end of the treatment, mean VAS was 29/100 (-57/100). In 6/15 patients (40%), a mild improvement of the lesions was observed: they appeared less infiltrated. No systemic or local adverse events were reported or observed. Six out of 15 patients (40%) judged the smell of the cream as rank. Chlorquinaldol, or hydroxydichloroquinaldine (5,7-dichloro-2-methyl-8-quin-

olinol), is a derivative of 8-hydroxyquinoline. It showed a good activity, both *in vitro* and *in vivo*, against yeasts, dermatophytes, Gram-positive bacteria, *Neisseria gonorrhoeae* and *Chlamydia trachomatis*.[36-41] In a recent study, staphylococci resulted to be the most sensitive bacteria to chlorquinaldol, with MIC-values ranging from 0.016 to 0.5 mg/l. A lower activity was observed against Gram-negative bacteria: 77% of the isolates were inhibited at concentrations ranging from 128 to 512 mg/l. Chlorquinaldol showed a bactericidal activity after 24-48 h of incubation.[42] Furthermore, an important anti-itching action of chlorquinaldol has been hypothesized.[43-45]

A possible limitation of our study is the small number of patients; however, as previously mentioned, PSP is a rare complication of scabies. The results of our study may be summarized as follows:

a) the association diflucortolone/chlorquinaldol can be considered for the treatment of itching in PSP. This was demonstrated by a significant reduction of VAS after two weeks of treatment;
b) it is possible that this anti-itching action is due also to chlorquinaldol. Its presence seems to be important, because 13/18 patients had been previously, although unsuccessfully, treated with clobetasol; a synergistic anti-itching action of chlorquinaldol with diflucortolone is possible;
c) at the end of the treatment, a mild improvement of infiltration of the lesions was observed;
d) thanks to the antibacterial action of chlorquinaldol, the association diflucortolone/chlorquinaldol can be considered in the prevention of bacterial superinfections in scabies and PSP.[45]

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