

**Publications du centre de référence des maladies rares de la peau et  
des muqueuses d'origine génétique -  
Année 2018**

1. [Clinical and haemodynamic risk factors associated with discrepancies in lower limb length with capillary malformations: data from the national paediatric French cohort CONAPE.](#) Samimi M, Durieux-Verde M, Caille A, Mazereeuw-Hautier J, Boccara O, Martin L, Chiaverini C, Eschard C, Beneton N, Vabres P, Balguerie X, Plantin P, Bessis D, Barbarot S, Dadban A, Droitcourt C, Leducq S, Lorette G, Morel B, Maruani A; Groupe de Recherche de la Société Française de Dermatologie Pédiatrique. *Br J Dermatol.* 2018 Feb;178(2):520-526.

**BACKGROUND:**

*Genetics discoveries have allowed for a better understanding of capillary malformations (CMs) associated with overgrowth syndrome. However, molecular analyses are still not easy to perform or interpret. Other analytical methods are needed.*

**OBJECTIVES:**

*To identify clinical and haemodynamic factors associated with leg length discrepancy (LLD) in children with CMs of the lower limbs.*

**METHODS:**

*Data were obtained from the multicentre French national cohort CONAPE (COhorte Nationale d'enfants atteints d'Angiome Plan de membrE inférieur), from children aged 2-12 years old with CMs of the lower limbs. Clinical characteristics were prospectively collected. Haemodynamic factors were measured by an sonographer who calculated the arterial blood flow (ABF) in both lower limbs. An ABF difference  $\geq 50\%$  between the two lower limbs was considered relevant. LLD  $\geq 2\%$  was determined by the same radiologist on centralized radiographs.*

**RESULTS:**

*We analysed data at baseline for 96 children. The mean  $\pm$  SD age was  $5.6 \pm 3.1$  years; 49 (51%) were male; and 14 (15%) showed LLD. In total, 32 patients (33%) had venous anomalies, 13 (14%) lymphatic anomalies and in one child a diagnosis of Parkes Weber syndrome was made. Only an increased circumference above the knee was more frequent with than without LLD (43% vs. 13%,  $P = 0.02$ ). In all, 10/79 patients (13%) showed a difference in ABF  $\geq 50\%$ : four had LLD. The frequency of differences in ABF  $\geq 50\%$  was greater with than without LLD [33% ( $n = 4/12$ ) vs. 9% ( $n = 6/67$ ),  $P = 0.04$ ].*

**CONCLUSIONS:**

*ABF measured by Duplex ultrasonography is a simple, low-cost and noninvasive complementary examination for help in detecting LLD, with a difference of  $\geq 50\%$  possibly associated.*

2. [Search for RASA1 Variants in Capillary Malformations of the Legs in 113 Children: Results from the French National Paediatric Cohort CONAPE.](#) Maruani A, Durieux-Verde M, Mazereeuw-Hautier J, Boccara O, Martin L, Chiaverini C, Eschard C, Bénétou N, Vabres P, Balguerie X, Plantin P, Bessis D, Barbarot S, Dadban A, Droitcourt C, Berthelot A, Lorette G, Leducq S, Samimi M, Andres C, Caille A, Vourc'h P; Groupe de Recherche de la Société Française de Dermatologie. *Acta Derm Venereol.* 2018 Feb 7;98(2):251-255.

*Patients with an inherited autosomal-dominant disorder, capillary malformation-arteriovenous malformation (CM-AVM), frequently have mutations in Ras P21 protein activator 1 (RASA1). The aims of this study were to determine the prevalence of germline RASA1 variants in a French multicentre national cohort of children, age range 2-12 years, with sporadic occurrence of capillary malformation (CM) of the legs, whatever the associated abnormalities, and to identify genotype-phenotype correlates. DNA was extracted from leukocytes in blood samples, purified and amplified, and all exons of the RASA1 gene were analysed. Among 113 children analysed, 7 had heterozygous variants (6.1%). Four different variants were identified; 2 were new. In children with RASA1 variants, CMs were more frequently bilateral and multifocal. In conclusion, RASA1 variants are rarely found in children with sporadic CM of lower limbs without CM-AVM syndrome. CMs in this study were heterogeneous, and no disease-causing relationship could be proven.*

3. [Clinical and evolutionary characteristics of a child with aquagenic keratoderma: A retrospective study of 12 patients.](#) Denos C, Dreyfus I, Chiaverini C, Labreze C, Abasq C, Phan A, Mallet S, Monteil L, Mazereeuw-Hautier J; Groupe de Recherche Clinique en Dermatologie Pédiatrique. *Ann Dermatol Venereol.* 2018 Apr;145(4):250-256.

#### **INTRODUCTION:**

*Aquagenic keratoderma (AK) is a rare condition characterized by wrinkled and edematous appearance of the skin of the hands occurring within minutes of immersion in water. Other than in a setting of cystic fibrosis, AK has rarely been reported in children, with only 13 clinical cases on record. Many clinicians are unfamiliar with AK and have fears relating to the association with cystic fibrosis. The aim of this study is to describe the characteristics and to discuss management of the disease.*

#### **METHODS:**

*Retrospective, multicentre study, including children aged under 16 years presenting AK.*

#### **RESULTS:**

*12 children were included. KA started at a mean age of 9.25 years (range: 20 months to 15 years). Clinical appearance and mode of onset were classical, with the palms being more severely affected than the soles. Pruritus or pain were reported in six cases. The median impact on daily life was 1.5/10. Some of the children underwent investigations: two had a negative sweat test, three had molecular analysis of the gene CFTR: one was negative and two had a heterozygote mutation. The course of the disease was variable: eight stabilizations, two exacerbations, one cure and one improvement.*

#### **DISCUSSION:**

*This is the first series on childhood KA. Clinical characteristics were similar to those seen in adults. Impact was moderate and the disease course was variable. Systematic medical check-up for cystic fibrosis does not appear warranted in children since to date, cystic fibrosis has not been diagnosed in any patients presenting AK alone.*

**CONCLUSION:**

*AK is rare in children and should not cause erroneous concern, and improvement can occur.*

4. [Alitretinoin reduces erythema in inherited ichthyosis.](#) Onnis G, Chiaverini C, Hickman G, Dreyfus I, Fischer J, Bourrat E, Mazereeuw-Hautier J, Orphanet J Rare Dis. 2018 Apr 4;13(1):46.

**BACKGROUND:**

*Acitretin is the main retinoid used to treat severe inherited ichthyosis. Alternatives may be considered if it results ineffective or there are side-effects, or for women of childbearing age. Our objective is evaluation of the effects and tolerance of alitretinoin. An observational retrospective multicentric study was designed to analyse patients with inherited ichthyosis treated by alitretinoin.*

**RESULTS:**

*A total of 13 patients were included, 11 of whom were receiving acitretin at inclusion. The main reason for switching to alitretinoin was a desire for pregnancy, but also because of side-effects or unsatisfactory efficacy. Starting dose was 10 mg/day, increased to 20 or 30 mg/day. Alitretinoin seemed to be more effective than acitretin at reducing erythema, but was less effective at reducing scaling or hyperkeratosis. Global efficacy was considered low for two patients, moderate for nine, and high for two. Treatment was well-tolerated, except for one patient who presented with benign intracranial hypertension leading to discontinuation of treatment.*

**CONCLUSIONS:**

*Alitretinoin may be suitable for hereditary ichthyosis with prominent erythema, especially for women of childbearing age.*

5. [Efficacy of anti-programmed cell death-1 immunotherapy for skin carcinomas and melanoma metastases in a patient with xeroderma pigmentosum.](#) Salomon G, Maza A, Boulinguez S, Paul C, Lamant L, Tournier E, Mazereeuw-Hautier J, Meyer N. Br J Dermatol. 2018 May;178(5):1199-1203.

*Xeroderma pigmentosum (XP) is an orphan disease of poor prognosis. We report one case of parallel efficacy with anti-programmed cell death-1 (PD-1) antibody on both melanoma and skin carcinoma in a patient with XP. A 17-year-old patient presented with metastatic melanoma and multiple nonmelanoma skin cancers. He was treated with pembrolizumab, a monoclonal anti-PD-1 antibody, at a dose of 2 mg kg<sup>-1</sup>, every 3 weeks. Parallel therapeutic efficacy of anti-PD-1 was observed in metastatic melanoma and skin carcinomas, and*

*maintained at week 24. This observation suggests anti-PD-1 may be considered in patients with XP and metastatic melanoma in addition to advanced nonmelanoma skin cancer.*

6. [Massive hemorrhage: A rare complication of rapidly involuting congenital hemangioma.](#) Al Malki A, Al Bluwi S, Malloizel-Delaunay J, Mazereeuw-Hautier J. *Pediatr Dermatol.* 2018 May;35(3):e159-e160.

*Rapidly involuting congenital hemangioma is a subtype of congenital hemangioma. Ulceration and bleeding are rarely reported in rapidly involuting congenital hemangioma, with only four cases reported in the literature to our knowledge. We describe a case of a newborn girl who presented with rapidly involuting congenital hemangioma complicated by ulceration and severe bleeding and discuss treatment.*

7. [KLICK syndrome: an unusual phenotype.](#) Onnis G, Bourrat E, Jonca N, Dreyfus I, Severino-Freire M, Pichery M, Fischer J, Mazereeuw-Hautier J. *Br J Dermatol.* 2018 Jun;178(6):1445-1446.
8. [Transcriptomic Analysis of Two Cdsn-Deficient Mice Shows Gene Signatures Biologically Relevant for Peeling Skin Disease.](#) Zaafour S, Pichery M, Huchenq A, Valentin F, Oji V, Mazereeuw-Hautier J, Serre G, Jonca N. *J Invest Dermatol.* 2018 Jun;138(6):1431-1435.
9. [Treatment of voluminous and complicated superficial slow-flow vascular malformations with sirolimus \(PERFORMUS\): protocol for a multicenter phase 2 trial with a randomized observational-phase design.](#) Maruani A, Boccara O, Bessis D, Guibaud L, Vabres P, Mazereeuw-Hautier J, Barbarot S, Chiaverini C, Blaise S, Droitcourt C, Mallet S, Martin L, Lorette G, Woillard JB, Jonville-Bera AP, Rollin J, Gruel Y, Herbreteau D, Goga D, le Touze A, Leducq S, Gissot V, Morel B, Tavernier E, Giraudeau B; Groupe de Recherche de la Société Française de Dermatologie Pédiatrique. *Trials.* 2018 Jun 27;19(1):340.

#### **BACKGROUND:**

*Slow-flow superficial vascular malformations (VMs) are rare congenital anomalies that can be responsible for pain and functional impairment. Currently, we have no guidelines for their management, which can involve physical bandages, sclerotherapy, surgery, anti-inflammatory or anti-coagulation drugs or no treatment. The natural history is progressive and worsening. Mammalian target of rapamycin (mTOR) is a serine/threonine kinase that acts as a master switch in cell proliferation, apoptosis, metabolism and angio/lymphangiogenesis. Sirolimus directly inhibits the mTOR pathway, thereby inhibiting cell proliferation and angio/lymphangiogenesis. Case reports and series have reported successful use of sirolimus in children with different types of vascular anomalies, with heterogeneous outcomes.*

#### **OBJECTIVE:**

*The objective of this trial is to evaluate the efficacy and safety of sirolimus in children with complicated superficial slow-flow VMs.*

## **METHODS/DESIGN:**

*This French multicenter randomized observational-phase, phase 2 trial aims to include 50 pediatric patients 6 to 18 years old who have slow-flow (lymphatic, venous or lymphatico-venous) voluminous complicated superficial VM. Patients will be followed up for 12 months. All patients will start with an observational period (no treatment). Then at a time randomly selected between month 4 and month 8, they will switch to the experimental period (switch time), when they will receive sirolimus until month 12. Each child will undergo MRI 3 times: at baseline, at the switch time, and at month 12. For both periods (observational and treatment), we will calculate the relative change in volume of the VM divided by the study period duration. This relative change weighted by the study period duration will constitute the primary endpoint. VM will be measured by MRI images, which will be centralized and interpreted by the same radiologist who will be blinded to the study period. Hence, each patient will be his/her own control. Secondary outcomes will include assessment of safety and efficacy by viewing standardized digital photographs and according to the physician, the patient or proxy; impact on quality of life; and evolution of biological makers (coagulation factors, vascular endothelial growth factor, tissue factor).*

## **DISCUSSION:**

*The main benefit of the study will be to resolve uncertainty concerning the efficacy of sirolimus in reducing the volume of VMs and limiting related complications and the safety of the drug in children with slow-flow VMs. This trial design is interesting in these rare conditions because all included patients will have the opportunity to receive the drug and the physician can maintain it after the end of the protocol if is found efficient (which would not be the case in a classical cross-over study).*

10. [Severe gynaecological involvement in Proteus Syndrome.](#) Severino-Freire M, Maza A, Kuentz P, Duffourd Y, Faivre L, Brazet E, Chassaing N, Mery-Lemarche E, Vabres P, Mazereeuw-Hautier J. Eur J Med Genet. 2018 Aug 10. pii: S1769-7212(17)30834-0.

*Proteus Syndrome is a rare complex overgrowth syndrome. We report a young female patient with Proteus Syndrome due to AKT1 mutation c.49G>A (p.Glu17Lys), presenting with a severe gynaecological involvement which necessitated a complete hysterectomy and a left adnexectomy. Cases of gynecological involvements in Proteus Syndrome are rare, not well known by physicians while they can be potentially severe.*

11. [Factors associated with delayed referral for infantile hemangioma necessitating propranolol.](#) Onnis G, Dreyfus I, Mazereeuw-Hautier J. J Eur Acad Dermatol Venereol. 2018 Sep;32(9):1584-1588.

## **BACKGROUND:**

*Oral propranolol is the gold standard to treat infantile hemangiomas. There is better efficacy and a lower risk of sequelae if therapy is started before the end of the growth phase, but most children are referred too late. Herein, we report the first study to investigate the delay and its associated factors when referring infants with infantile hemangiomas that need propranolol therapy.*

## **OBJECTIVES:**

*The primary objective was to determine the delay in referral (time between age at referral [first phone contact] and the optimal age for referral (fixed at 75 days). The second objective was to determine the*

impact of weighted factors associated with delayed referral assessed by logistic regression performed on two subgroups (referral  $\leq 75$  vs.  $>75$  days).

#### **METHODS:**

Monocentric, retrospective, observational study included infants with infantile hemangiomas treated with oral propranolol between August 2014 and May 2017.

#### **RESULTS:**

Eighty-two children (83% females) were included. Before referral, 81 (99%) children had seen another physician (a paediatrician in 67% of cases). Median age at referral was 99 days [2-478] and 63% phoned after 75 days. Median age at the first visit was 111 days [2-515], and median age when propranolol was started was 128 days [32-541]. After adjustment, in multivariate analyses, location on the lips (OR (CI 95%): 4.21[1.19-14.89]) and superficial hemangioma (OR (CI 95%): 4.19 [1.55-11.34]) emerged as the most significant factors to influence referral before 75 days.

#### **CONCLUSIONS:**

This study adds to our understanding regarding delayed referral and has identified targets for future information campaigns.

12. [Childhood pilomatricomas: Associated anomalies.](#) Richet C, Maza A, Dreyfus I, Bourrat E, Mazereeuw-Hautier J. *Pediatr Dermatol.* 2018 Sep;35(5):548-551.

*Pilomatricoma is a common benign tumor in children. We present a review of the literature with the aim of helping clinicians manage these patients. A detailed review of the literature was performed in the PubMed database using an exhaustive list of Medical Subject Heading words. One thousand four hundred fifty-eight children were described in retrospective series and case reports. An associated disease was found in 32 children (2.2%), most of whom had several pilomatricomas (n = 23); 9 had a single lesion. Based on this literature review, we recommend reassuring the family and then conducting a detailed interview regarding past medical and family history and a thorough clinical examination for signs of Turner syndrome, constitutional mismatch repair deficiency, Kabuki syndrome, Steiner's myotonic dystrophy, or Gardner syndrome. Regular long-term clinical follow-up is recommended. Specific paraclinical examinations should be performed only in cases of other clinical anomalies or a positive family history. Pilomatricoma requires management because it may be associated with other potentially serious diseases, especially when multiple lesions are present.*

13. [Ichthyosis prematurity syndrome: Two new cases.](#) Severino-Freire M, Bing Lecointe AC, Bourrat E, Pichery M, Jonca N, Chiaverini C, Mazereeuw-Hautier J. *Ann Dermatol Venereol.* 2018 Oct;145(10):603-606.

#### **BACKGROUND:**

*Ichthyosis prematurity syndrome is a rare syndromic form of ichthyosis caused by mutations in FATP4, which plays a central role in the transport and activation of fatty acids in the epidermis and in epidermal barrier function. Despite stereotypical clinical presentation in the neonatal period, the diagnosis is not well known by clinicians. Herein we report two new cases.*

## **PATIENTS AND METHODS:**

Case no. 1: a boy born prematurely (33weeks of gestation) to non-consanguineous French parents presented at birth with respiratory distress necessitating admission to intensive care. His skin was covered by a thick caseous vernix, especially on the scalp, eyebrows and 4 limbs. At the age of 4years, the boy's skin appeared normal. Case no. 2: a boy born prematurely to consanguineous Moroccan parents (34weeks of gestation) presented at birth with respiratory distress requiring admission to intensive care. At clinical examination, he had a whitish thick skin giving an impression of vernix caseosa, with involvement of the scalp, forehead, 4 limbs and abdomen. At the age of 2 years, his skin was normal.

## **CONCLUSION:**

The clinical presentation of this syndrome is typical. It is important to make the diagnosis to enable genetic counseling and planning of adequate neonatal care in the event of future pregnancies.

14. [Familial chilblain lupus: Four cases spanning three generations.](#) Beltoise AS, Audouin-Pajot C, Lucas P, Tournier E, Rice GI, Crow YJ, Mazereeuw-Hautier J. *Ann Dermatol Venereol.* 2018 Nov;145(11):683-689.

## **BACKGROUND:**

Familial chilblain lupus is a hereditary form of cutaneous lupus erythematosus seen in young children. It shows autosomal dominant inheritance due to mutations in the *TREX-1* gene, or, more rarely, *SAMHD1* or *TMEM173* (*STING*). It belongs to the type I interferonopathies, i.e. inflammatory diseases associated with excessive interferon production and characterized by a positive "interferon signature". This is a rare entity with fewer than 10 families described to date. We report a new family followed over several years.

## **PATIENTS AND METHODS:**

The patients were four subjects from the same family and spanning three generations (a brother and sister aged 17 and 15 years, their 39-year-old mother, and their 60-year-old grandfather). The initial cutaneous lesions on the extremities were described as papular, erythematous, purplish, infiltrated, hyperkeratotic, pruritic and/or painful. They occurred in childhood, improved during summer and stabilized over time. Immunological abnormalities such as positive antinuclear antibodies were noted. The interferon signature was positive in all patients. Molecular analysis of *TREX-1*, *SAMHD1* and *STING* genes in both children showed no evidence of mutation.

## **DISCUSSION:**

The cutaneous involvement was classic except for absence of the scarring and mutilating progression, photosensitivity and vasculopathy reported in other families. There was no intrafamily variability other than unconstant immunological abnormalities. At the molecular level, no mutations in the known genes were identified. A complementary molecular analysis is in progress.

## **CONCLUSION:**

We report a new case of familial LEF, thus adding to knowledge about this very rare form of lupus erythematosus

15. [Dermatological manifestations in Noonan syndrome: a prospective multicentric study of 129 patients positive for mutation.](#) Bessis D, Miquel J, Bourrat E, Chiaverini C, Morice-Picard F, Abadie C, Manna F, Baumann C, Best M, Blanchet P, Bursztejn AC, Capri Y, Coubes C, Giuliano F, Guillaumont S, Hadj-Rabia S, Jacquemont ML, Jeandel C, Lacombe D, Mallet S, Mazereeuw-Hautier J, Molinari N, Pallure V, Pernet C, Philip N, Pinson L, Sarda P, Sigaudy S, Vial Y, Willems M, Geneviève D, Verloes A, Cavé H. *Br J Dermatol.* 2018 Nov 12.

#### **BACKGROUND:**

*Data on dermatological manifestations of Noonan syndrome (NS) remain heterogeneous and are based on limited dermatological expertise.*

#### **OBJECTIVES:**

*To describe the dermatological manifestations of NS, compare them with the literature findings, and test for dermatological phenotype-genotype correlations with or without the presence of PTPN11 mutations.*

#### **METHODS:**

*We performed a large 4-year, prospective, multicentric, collaborative dermatological and genetic study.*

#### **RESULTS:**

*Overall, 129 patients with NS were enrolled, including 65 patients with PTPN11-NS, 34 patients with PTPN11-NS with multiple lentigines (NSML), and 30 patients with NS who had a mutation other than PTPN11. Easy bruising was the most frequent dermatological finding in PTPN11-NS, present in 53.8% of patients. Multiple lentigines and café-au-lait macules ( $n \geq 3$ ) were present in 94% and 80% of cases of NSML linked to specific mutations of PTPN11, respectively. Atypical forms of NSML could be associated with NS with RAF1 or NRAS mutations. In univariate analysis, patients without a PTPN11 mutation showed (i) a significantly higher frequency of keratinization disorders ( $P = 0.001$ ), including keratosis pilaris ( $P = 0.005$ ), ulerythema ophryogenes ( $P = 0.0001$ ) and palmar and/or plantar hyperkeratosis ( $P = 0.06$ , trend association), and (ii) a significantly higher frequency of scarce scalp hair ( $P = 0.035$ ) and scarce or absent eyelashes ( $P = 0.06$ , trend association) than those with PTPN11 mutations.*

#### **CONCLUSIONS:**

*The cutaneous phenotype of NS with a PTPN11 mutation is generally mild and nonspecific, whereas the absence of a PTPN11 mutation is associated with a high frequency of keratinization disorders and hair abnormalities.*



16. [Creation and pilot test results of the dermatology-specific proxy instrument: the Infants and Toddlers Dermatology Quality of Life.](#) Chernyshov PV, Boffa MJ, Corso R, Pustišek N, Marinovic B, Manolache L, Salavastru CM, Tiplica GS, Kakourou T, Alexopoulos A, Nasi L, Wojciechowska-Zdrojowy M, Seniuta J, Szepietowski JC, Erkens A, Fölster-Holst R, Sampogna F, Chernyshov AV, Jemec GB, Esmann S, Mazereeuw-Hautier J, Merlos M, Tomas-Aragones L, Marron SE. *J Eur Acad Dermatol Venereol.* 2018 Dec;32(12):2288-2294.

**BACKGROUND:**

*Until now, there was no validated dermatology-specific health-related quality of life (HRQoL) instrument to be used in youngest patients.*

**OBJECTIVE:**

*To create dermatology-specific proxy instrument for HRQoL assessment in children from birth to 4 years.*

**METHODS:**

*International focus groups, item selection and pilot tests were utilized. In order to avoid the problem of cross-cultural inequivalence, focus group work and pilot tests were planned simultaneously in all national centres of the project. Comprehensibility, clarity, acceptance and internal consistency of new instrument were checked.*

**RESULTS:**

*The title 'Infants and Toddlers Dermatology Quality of Life' was chosen for our new instrument with the proposed acronym 'InToDermQoL'. Focus group work was completed in seven national centres (Croatia, Germany, Greece, Malta, Poland, Romania and Ukraine). A total of 170 families of children with different skin diseases were interviewed, and a pilot version of the instrument was created. Centres from France, Denmark and Spain have joined the project at this stage. Parents of 125 children with skin diseases filled in the pilot versions of the instrument. Good comprehensibility, clarity, acceptance and internal consistency of the InToDermQoL were confirmed. The pilot test results showed that the InToDermQoL questionnaire well differentiates severity-dependent differences. It was also checked and confirmed during the pilot test that no significant information was missed in the questionnaire. Three age-specific versions of the InToDermQoL questionnaire with 10, 12 and 15 items, respectively, were approved for field tests.*

**CONCLUSION:**

*The pilot test results showed that the InToDermQoL questionnaire has good comprehensibility, clarity, acceptance and internal consistency and well differentiates severity-dependent differences. Further validation of the InToDermQoL during international field test will be performed.*

[17. Multiple hypochromic or achromic macules in children and risk of tuberous sclerosis.](#) Battini M, Casassa E, Maza A, Dreyfus I, Mazereeuw-Hautier J. *Ann Dermatol Venereol.* 2018 Dec;145(12):741-748.

**AIM:**

*To describe in a large paediatric cohort the characteristics of hypopigmented and depigmented (hypochromic and achromic) macules with no clear diagnosis but potentially evocative of tuberous sclerosis (TS).*

**PATIENTS AND METHODS:**

*This was a retrospective multicentre study performed between 2010 and 2017 at a reference centre for rare skin diseases; it included all children consulting for hypochromic and achromic macules. A descriptive analysis was made of the characteristics of macules with no clear diagnosis, enabling them to be classified in three secondary groups: TS certain, TS ruled out, TS uncertain.*

**RESULTS:**

*Of the 3300 children seen during this 7-year period 7,265 were consulting for hypochromic or achromic macules, with no clear diagnosis in 18 cases: 7 girls and 11 boys of median age at 7.21 years (range: 4 months to 16 years and 7 months). The lesions were congenital in 7 cases. The number of macules varied, with over 20 in some cases. The majority were in the form of ash-leaf spots, followed by the oval form. Two children were diagnosed at clinical examination, and 16 underwent it is not examinations, resulting in a diagnosis of certain ST in 6 of these cases. No particular characteristics of the macules appeared to guide the clinical examination towards ST or isolated lesions. Café-au-lait spots were more frequent in the group in which ST was ruled out than in the other two groups: 67% vs. 33% and 33%. Neurologic involvement was more common in children with certain or uncertain ST than in children in whom ST was ruled out (83% and 67% vs. 11%).*

**CONCLUSION:**

*No identified characteristics of stains enabled the clinical examination to confirm or rule out tuberous sclerosis. Screening for acute any signs of ST is essential. Diagnostic efficacy is enhanced by additional exams.*

[18. What's new in pediatric dermatology?](#) Mazereeuw-Hautier J., *Ann Dermatol Venereol.* 2018 Dec;145 Suppl 7:VIIS32-VIIS46.

*In order to describe the latest news in Pediatric dermatology (pathophysiology, clinical aspects and therapy), a literature review was performed from September 2017 to September 2018. This article is not an exhaustive review but present the new data that may influence the daily practice. The results are presented by disease that may be common or rare. Some references are available as supplements.*

[19. Creation and pilot test results of the dermatology-specific proxy instrument: the Infants and Toddlers Dermatology Quality of Life.](#) Chernyshov PV, Boffa MJ, Corso R, Pustišek N, Marinovic B, Manolache L, Salavastru CM, Tiplica GS, Kakourou T, Alexopoulos A, Nasi L, Wojciechowska-Zdrojowy M, Seniuta J, Szepietowski JC, Erkens A, Fölster-Holst R, Sampogna F, Chernyshov AV, Jemec GB, Esmann S,

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[20. Multiple hypochromic or achromic macules in children and risk of tuberous sclerosis.](#) Battini M, Casassa E, Maza A, Dreyfus I, Mazereeuw-Hautier J. Ann Dermatol Venereol. 2018 Dec;145(12):741-748.

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### **CONCLUSION:**

*No identified characteristics of stains enabled the clinical examination to confirm or rule out tuberous sclerosis. Screening for acute any signs of ST is essential. Diagnostic efficacy is enhanced by additional exams.*