laboratory tests.[8] The elevation of CK in patients undergoing isotretinoin therapy is usually mild and asymptomatic[3] and its incidence is variable (5.5% to 37.3%).[3,4] In addition, some patients with symptoms of pain and muscle weakness have CK within the normal range.[3,7]

CK levels are influenced by the level of physical activity. They are higher in athletes than in physically active nonathletes and higher in the latter than in sedentary people.[9] Some authors have suggested that normal ranges should take into account the level of physical activity of the individual. The upper limit of the normal range could be 350-532 IU/L in physically active male nonathletes.[9]

It is believed that isotretinoin and exercise can have a synergistic effect in causing muscle damage,[3] a hypothesis that could explain the differences in CK levels found in different studies. Landau et al[4] found elevated levels of CK in 37.3% of patients in a study performed on soldiers, whose physical activity is higher than that of the general population. On the other hand, Kaymac[3] found elevated levels of CK in only 5.5% of patients from the general population treated with isotretinoin.

There are disagreements concerning the management of isolated CK elevation. Although some authors recommend not starting isotretinoin therapy if the baseline CK is elevated and discontinuing therapy if CK rises during therapy,[10] most prefer to decrease the dose or temporarily discontinue therapy until the enzyme levels return to normal.[3,4] In patients performing strenuous exercise, avoidance of this activity may be sufficient.[3,4]

In conclusion, we present a case of rhabdomyolysis in a patient treated with isotretinoin. We believe that the dermatologist should be able to recognize this adverse effect and know how to manage it. It is recommended to avoid strenuous exercise during isotretinoin therapy and CK levels should be determined in the routine laboratory tests in athlete patients to detect asymptomatic cases. Although we discontinued the isotretinoin therapy, it may be sufficient to avoid exercise, decrease the dose, or interrupt therapy until CK has returned to normal levels.

References

1. Chatzizisis YS, Misirli G, Hatzitolios AI, Giannoglou GD. The syndrome of rhabdomyolysis: complications and treatment. Eur J Intern Med. 2008;19:568-74.
2. Melli G, Chaudhry V, Cornblath DR. Rhabdomyolysis: an evaluation of 475 hospitalized patients. Medicine (Baltimore). 2005;84:377-85.
3. Kaymac Y. Creatine phosphokinase values during isotretinoin treatment for acne. Int J Dermatol. 2008;47:398-401.
4. Landau M, Mesterman R, Ophir J, Mevorah B, Alcalay J, Harel A, et al. Clinical significance of markedly elevated serum creatine kinase levels in patients with acne on isotretinoin. Acta Derm Venereol. 2001;81:350-2.
5. Guttman-Yassky E, Hayek T, Muchnik L, Bergman R. Acute rhabdomyolysis and myoglobinuria associated with isotretinoin treatment. Int J Dermatol. 2003;42:499-500.
6. McBurney EI, Rosen DA. Elevated creatine phosphokinase with isotretinoin. J Am Acad Dermatol. 1984;10:528-9.
7. Hodak E, Gadoth N, David M, Sandbank M. Muscle damage induced by isotretinoin. Br Med J (Clin Res Ed). 1986;293:425-6.
8. Trauner MA, Ruben BS. Isotretinoin induced rhabdomyolysis? A case report. Dermatol Online J. 1999;5:2.
9. Mougios V. Reference intervals for serum creatine kinase in athletes. Br J Sports Med. 2007;41:674-8.
10. Chroni E, Monastirli A, Tsambaos. Neuromuscular adverse effects associated with systemic retinoid dermatotherapy: monitoring and treatment algorithm for clinicians. Drug Saf. 2010;33:25-34.

S. Gómez-Bernal,* L. Rodríguez-Pazos, M.T. Rodríguez-Granados, J. Toribio

Departamento de Dermatología, Complejo Hospitalario Universitario, Facultad de Medicina, Santiago de Compostela, Spain

*Corresponding author.
E-mail address: sil.gomez@gmail.com (S. Gómez-Bernal).

Physiological Desquamation of the Newborn: Epidemiology and Predisposing Factors

Descamación fisiológica en el recién nacido: epidemiología y factores predisponentes

To the Editor:

Physiological desquamation is the name given to surface scaling that appears in most newborn infants within a few days after birth. It begins on the ankles in the first 24 to 48 hours after birth and can remain localized, often confined to the hands and feet, or gradually spread. It is usually most intense and widespread between the sixth and tenth days.[1,2]

When involvement is generalized or more intense it must be distinguished from certain forms of ichthyosis or hypohidrotic ectodermal dysplasia, which are rare conditions with a very different clinical course and management. Furthermore, newborns with physiological desquamation do not present findings consistent with ichthyosis, such as poor general condition, ectropion, family history, characteristic distribution, continuous flaking, or erythema of the underlying skin. It is important to recognize this transitory benign skin condition in order to avoid unnecessary tests and treatment and parental anxiety.[3]

Although physiological desquamation is a common disorder, few studies have analyzed the frequency and predisposing factors involved. Our aim was to determine the prevalence of physiological desquamation and the areas of the body affected in 1000 newborn infants in our health care district, and how neonatal and maternal parameters, time of examination, and mode of delivery influence its appearance.

We undertook a descriptive study of 1000 newborn infants seen in the perinatology outpatient clinic of the

Table 1 Location of Physiological Desquamation and Percentage of Body Area Affected According to Gestational Age

Variables	Preterm		Term		Post-term		Total	
	No.	%	No.	%	No.	%	No.	%
Total	75	7.5	912	91.2	13	1.3	1000	100
Total with PD	16	21.3	392	43	7	53.8	415	41.5
More than 1 area	4	5.3	165	18.1	4	30.7	173	17.3
Head and neck	3	4	120	13.1	4	30.7	127	12.7
Trunk	4	5.3	221	24.2	4	30.7	229	22.9
Limbs	16	21.3	331	36.3	7	53.8	354	35.4
Proportion of BSA affected, %(mean [SD])	5.593 (19.9631)		17.962 (33.0599)		33.077 (46.6288)		17.231 (32.6533)	

Abbreviations: BSA, body surface area; PD, physiological desquamation.

Pediatrics Department of Hospital Arquitecto Marcide, La Coruña, Spain. All infants born at hospitals in the health care district of Ferrol are seen in this department within 3 days of birth. In each case we applied a data collection protocol that included the following: a) age (in hours) at the time of examination; b) mode of delivery; c) maternal factors (age, number of previous pregnancies and diseases, pharmacological treatments, and drinking or smoking during pregnancy); and d) neonatal parameters (gestational age, sex, parents' ethnic group or geographical origin, Apgar score at 1 and 5 minutes, noncutaneous diseases and malformations, the presence of neonatal toxic erythema and vernix caseosa, and the presence, localization, and percentage of body surface with physiological desquamation).

The diagnosis of physiological desquamation was made clinically. The percentage of body surface area was calculated according to the Lund and Browder Chart for children under 1 year of age.[4] The data corresponding to quantitative variables were categorized into groups, while the qualitative variables were presented as percentages and analyzed using the χ^2-square test. The statistical analysis was carried out using the SPSS software package version 15.0. Statistical significance was set at a *P* value of less than .05.

The 1000 newborn infants were recruited over 19 months (between May 2008 and November 2009) and 41.5% presented physiological desquamation: 35.4% on the limbs, 22.9% on the trunk, and 12.7% on the head and neck. More than 1 body area was involved in 17.3% of the infants. Table 1 details the site and percentage of body area affected according to gestational age.

Table 2 shows the frequency of physiological desquamation according to the different maternal and neonatal factors, mode of delivery, and the age in days at the time of examination. The prevalence barely varied according to sex, parents' ethnic or geographical group, Apgar score at 1 and 5 minutes, presence of neonatal toxic erythema or other diseases or malformations of the newborn infants, or the maternal history of disease or pharmacological treatments (dietary supplements or otherwise). A higher frequency of physiological desquamation was observed in the following situations: a) term or post-term neonate weighing over 2500 g at birth, and with vernix caseosa; b) primiparous mother, under 30 years of age, alcohol or tobacco consumption (particularly smoking); c) vaginal delivery; and d) examination on the first day. These differences were statistically significant for gestational age, birth weight, presence of vernix caseosa, number of previous pregnancies, and mode of delivery.

The prevalence of physiological desquamation varies according to the series, from 1.9% reported by Moosavi et al[1] to 87.7% reported by Griffiths.[2] The data in our series—prevalence of 41.5%—would therefore fall midway between the 2 extremes. These variations could be justified by differences in the time of examination, the follow-up period of the infants,[1,5] and the terminology used; while some registries defined desquamation alone, others included xerosis and desquamation.[9,8] As for clinical morphology, our results agree with the findings reported by Griffiths[2]: a high frequency of physiological desquamation from the first day of life that, though most commonly affecting distal parts of the limbs, frequently spread to the trunk and head, affecting more than 1 body area.

There is, however, some debate about the existence of differences in the incidence of physiological desquamation depending on sex or parents' geographical origin.[6] Some studies report a slight predominance in males.[5] Boccardi et al[7] observed a higher frequency in South American and Asian newborns and, as in our case, a lower frequency in those of north African origin. However, the differences in prevalence observed in our series could be due to the small sample size available in each non-white racial group and we must therefore be cautious when interpreting these results.

Although this is a controversial topic,[6,7] most studies associate a higher prevalence of physiological desquamation with a higher gestational age[1,2,5,8,9] and higher birth weight.[5,8] For other authors, such as Rivers et al,[6] only the time of appearance of the condition varies: post-term infants are born in a desquamative phase, infants born at term develop fine desquamation at 24 to 48 hours of life, and premature infants do so 2 or 3 weeks later. Our results confirm that a higher gestational age is associated with an increase in the prevalence of physiological desquamation in all body areas, in the number of body areas involved, and in the extent of body surface affected. We observed that this condition is not rare in preterm neonates, but is usually limited to the distal area of the limbs.

There is an association between the disappearance of the vernix caseosa and the appearance of desquamation. In

Table 2 In 1000 Neonates, Frequency of Physiological Desquamation According to Neonatal and Maternal Parameters, Mode of Delivery, and Day of Examination

Variables	Neonates, No.	Neonates With Physiological Desquamation, No. (%)	χ^2	P[a]
Sex				
Male	528	218 (41.3)	0.021	0.886
Female	472	197 (41.7)		
Parental geographical origin or ethnic group				
White	922	382 (41.4)		
Roma/gypsy	29	14 (48.2)	3.608	0.730
Hispanic	23	7 (30.4)		
Arab	7	4 (57.1)		
Asian	7	4 (57.1)		
Black	7	2 (28.5)		
Mulatto	5	2 (40)		
Gestational age				
Preterm (<37 wk)	75	16 (21.3)		
Term (37-41 wk)	912	392 (43)	14.206	0.001[b]
Post-term (≥42 wk)	13	7 (53.8)		
Birth weight				
Low (≤2500 g)	69	18 (26.1)		
Normal (2501-3999 g)	869	371 (42.7)	7266	0.026[b]
High (≥4000 g)	62	26 (42)		
Apgar score at 1 minute				
≤8	184	72 (39.1)	0.522	0.470
≥9	816	343 (42)		
Apgar score at 5 minutes				
≤9	173	72 (41.6)	0.001	0.972
10	827	343 (41.5)		
Diseases or noncutaneous malformations in the newborn				
No	956	399 (41.8)	0.500	0.479
Yes	44	16 (36.4)		
Vernix caseosa				
No	508	235 (46.2)	9.636	0.002[b]
Yes	492	180 (36.6)		
Neonatal toxic erythema				
No	833	345 (41.4)	0.014	0.905
Yes	167	70 (42)		
Maternal age				
≤29 y	407	183 (45)		
30-34 y	353	145 (41.8)	4.761	0.092
≥35 y	240	87 (36.2)		
No. of previous gestations				
0	498	225 (45.2)		
1	328	119 (36.3)	6.494	0.039[b]
≥2	174	71 (41)		
Maternal diseases during gestation				
No	723	306 (42.3)	0.729	0.393
Yes	277	109 (39.3)		
Drinking and smoking				
No	782	313 (40)	3.212	0.073
Yes	218	102 (46)		
Supplements[c]				
No	182	72 (39.5)	0.345	0.557
Yes	818	343 (42)		

Table 2 *(Continuation)*

Variables	Neonates, No.	Neonates With Physiological Desquamation, No. (%)	χ^2	P[a]
Drugs (not supplements)				
No	744	308 (41.4)	0.012	0.911
Yes	256	107 (41.8)		
Mode of delivery				
Vaginal delivery	783	341 (43.5)	6.249	0.012[a]
Cesarean	217	74 (34.1)		
Day of examination				
1st	835	355 (42.5)		
2nd	107	44 (41.1)	4.986	0.083
3rd	58	16 (27.6)		

[a]Asymptotic significance (2-tailed).
[b]Statistically significant ($P<.05$).
[c]Includes iron, folic acid, and iodine.

post-term neonates and those born by vaginal delivery, less of the body surface is covered by vernix and physiological desquamation is therefore more common.[10] As the vernix caseosa diminishes, there is increased maceration of the stratum corneum in the uterus, increased transepidermal water loss, and a subsequent dehydration of the stratum corneum in the first days of life, thereby triggering desquamation.[2] This theory has been criticized by Rivers et al[6] as it does not justify the greater acral involvement observed in many newborns with physiological desquamation.

Contrary to the previously evaluated variables, maternal parameters played an insignificant part in predicting physiological desquamation in our series. This situation was also reported by Boccardi et al,[7] who found no statistically significant relationship between physiological desquamation and maternal age, diseases, and pharmacological treatments (including dietary supplements). Our results concerning the value of the number of previous pregnancies differ from the study by Sachdeva et al,[5] who observed a higher frequency of physiological desquamation in multiparous women, while in our study it was more common in the first offspring.

In conclusion, we found physiological desquamation in 41.5% of the 1000 neonates included in the study. The limbs were the most affected areas, though spread to other regions was not uncommon. A higher prevalence was observed in higher birth weight and higher gestational age neonates born by vaginal delivery, without vernix caseosa, and with a primiparous mother.

References

1. Moosavi Z, Hosseini T. One-year survey of cutaneous lesions in 1,000 consecutive Iranian newborns. Pediatr Dermatol. 2006;23:61-3.
2. Griffiths AD. Skin desquamation in the newborn. Biol Neonat. 1966;10:127-39.
3. Lucky AW. Transient benign cutaneous lesions in the newborn. In: Eichenfield LF, Frieden IJ, Esterly NB, editors. Neonatal Dermatology. 2nd ed. Philadelphia: Saunders Elsevier; 2008. p. 85-97.
4. Lund CC, Browder NC. The estimation of areas of burns. Surg Gynecol Obstet. 1944;79:352-8.
5. Sachdeva M, Kaur S, Nagpal M, Dewan SP. Cutaneous lesions in new born. Indian J Dermatol Venereol Leprol. 2002;68:334-7.
6. Rivers JK, Frederiksen PC, Dibdin C. A prevalence survey of dermatoses in the Australian neonate. J Am Acad Dermatol. 1990;23:77-81.
7. Boccardi D, Menni S, Ferraroni M, Stival G, Bernardo L, La Vecchia C, et al. Birthmarks and transient skin lesions in newborns and their relationship to maternal factors: a preliminary report from Northern Italy. Dermatology. 2007;215: 53-8.
8. Ferahbas A, Utas S, Akcakus M, Gunes T, Mistik S. Prevalence of cutaneous findings in hospitalized neonates: a prospective observational study. Pediatr Dermatol. 2009;26:139-42.
9. Gokdemir G, Erdogan HK, Koslu A, Baksu B. Cutaneous lesions in Turkish neonates born in a teaching hospital. Indian J Dermatol Venereol Leprol. 2009;75:638.
10. Visscher MO, Narendran V, Pickens WL, LaRuffa AA, Meinzen-Derr J, Allen K, et al. Vernix caseosa in neonatal adaptation. J Perinatol. 2005;25:440-6.

B. Monteagudo,[a,*] J. Labandeira,[b] E. León-Muiños,[c] R. Romarís,[c] M. Cabanillas,[a] D. González-Vilas,[a] A. Acevedo,[d] R. Fernández-Prieto,[c] J. Toribio[b]

[a]*Servicio de Dermatología, Hospital Arquitecto Marcide, Área Sanitaria de Ferrol, SERGAS, Fundación Novoa Santos, Ferrol, La Coruña, Spain*
[b]*Servicio de Dermatología, Complexo Hospitalario Universitario de Santiago de Compostela (CHUS), SERGAS, Facultad de Medicina, Santiago de Compostela, La Coruña, Spain*
[c]*Servicio de Pediatría, Hospital Arquitecto Marcide, Área Sanitaria de Ferrol, SERGAS, Fundación Novoa Santos, Ferrol, La Coruña, Spain*
[d]*Unidad de Formación Continuada, Hospital Arquitecto Marcide, Área Sanitaria de Ferrol, SERGAS, Fundación Novoa Santos, Ferrol, La Coruña, Spain*

*Corresponding author.
E-mail address: benims@hotmail.com (B. Monteagudo).