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# Acute generalized exanthematous pustulosis (AGEP) – A clinical reaction pattern

**Background:** A wide range of diseases or reactions can cause pustular eruptions of the skin. In this spectrum there seems to be a subgroup with characteristic clinical features and a typical course which is mostly caused by drugs for which the term acute generalized exanthematous pustulosis (AGEP) has been established.
**Objective:** To describe the clinical features of AGEP.
**Methods:** The authors' experience from a multinational epidemiological study on severe cutaneous adverse reactions and a comprehensive review of the literature were used to provide an overview of the disease and it's possible causes. An algorithm for validating cases which was established for this study is also presented.
**Results:** AGEP typically presents with at least dozens of non follicular sterile pustules occurring on a diffuse, edematous erythema predominalty in the folds and/or on the face. Fever and elevated blood neutrophils are common. Histopathology typically shows spongiform subcorneal and/or intraepidermal pustules, a marked edema of the papillary dermis, and eventually vasculitis, eosinophils and/or focal necrosis of keratinocytes. Onset is acute, most often following drug intake, but viral infections can also trigger the disease. Pustules resolve spontaneously in less than 15 days.
**Conclusion:** The diagnosis AGEP should be considered in cases of acute pustular rashes and detection of the causative drug should be strived for. Knowledge of the clinical features and usual course of this disease can often prevent unnecessary therapeutical measures.

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When Baker and Ryan described a series of 104 cases of pustular psoriasis in 1968[1] they detected a subgroup of 5 patients who had no history of psoriasis and in which the episode of pustular eruption was very acute, resolved quickly and did not recur. This group was named *exanthematic pustular psoriasis* and already then the authors suspected drugs and/or infections as trigger for the pustular skin reaction. In the meantime many cases with similar clinical features were described under different denominations such as *toxic pustuloderma*[2] and *pustular drug rash*,[3] or were interpreted as special variants of other pustular diseases. In 1980 Beylot et al.[4] introduced the term *pustuloses exanthématique aiguës généralisés* (PEAG) to the French literature and it's translation *acute generalized exanthematous pustulosis* (AGEP) is now broadly used in cases of pustular eruptions showing the clinical features discussed below. We will use the term AGEP throughout this paper well aware, that many reported cases of toxic pustuloderma are dealing with the same disease. A clear distinction has to be made from the term *pustulosis acuta generalisata*, which describes a post-

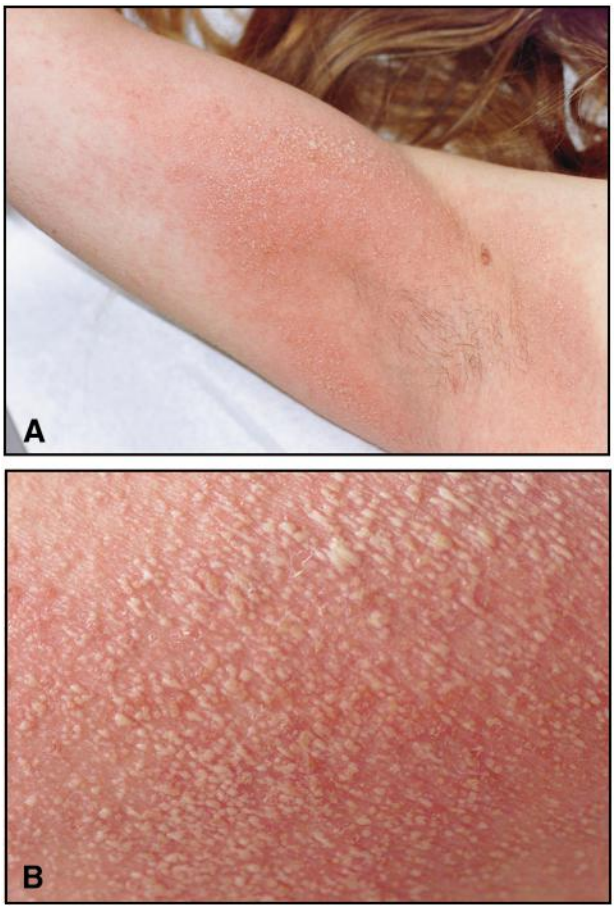


*Fig. 1.* A) Diffuse erythema in the axilla with hundreds of pustules. B) Close-up view of the same region showing hundreds of small, non-follicular, partially confluent pustules.

streptococcal disease arising mainly in children and different from AGEP.[5]

## Clinical features, course, and laboratory findings

Mostly beginning in the intertriginous areas or in the face a diffuse, often edematous erythema develops very acutely. Patients often describe a burning or itching sensation. On this – often widespread – erythema soon dozens to hundreds of small (pinhead sized, <5 mm) non follicular sterile pustules arise mainly in the folds (Fig. 1). Sometimes confluence of pustules may mimic a positive Nikolsky's sign and thus lead to a misinterpretation as toxic epidermal necrolysis (TEN). Other skin symptoms like marked edema of the face, purpura lesions (especially on the legs), Stevens-Johnson-syndrome-like "atypical targets", blisters and vesicles have been described but are not typical for AGEP. Mucous membrane involvement may occur in about 20% of the cases but usually is mild and remains limited to one location (mostly oral).

Skin symptoms are almost always accompanied by fever above 38° Celsius and leucocytosis mostly due to blood neutrophil counts above $7\times10^9$/l. A mild eosinophilia may be present in about one third of the patients.[6] Lymphadenopathy has been reported in some cases.[7] Apart from a slight reduction of the creatinine clearance (<60 ml/min in ~30% of the cases) and a mild elevation of aminotransferases, no involvement of other internal organs has to be expected.

The combination of high fever, leucocytosis and pustules is often misinterpreted as acute infectious disease. Early diagnosis of AGEP is important to avoid unnecessary investigations and/or the administration of expensive and sometimes risky antibiotics.

Pustules resolve spontaneously within a few (~4 to 10) days and are – in typical cases – followed by a characteristic postpustular pin-point desquamation (Fig. 2). The overall prognosis is good in AGEP although high fever or superinfection of skin lesions can sometimes lead to life-threatening situations in patients of old age or poor general condition.

## Histopathology

The typical histopathology of AGEP shows spongiform subcorneal and/or intraepidermal pustules, an often marked edema of the papillary dermis and perivascular infiltrates with neutrophils and exocytosis of some eosinophils.[8] Vasculitis and/or some single cell necroses of keratinocytes may be present. Psoriatic changes like acanthosis and papillomatosis are usually absent.[9]

## Differential diagnosis

A wide spectrum of cutaneous diseases or reactions can cause pustular eruptions. Most of them can easily be differentiated from AGEP: all follicular eruptions like bacterial folliculitis, furunculosis, acne and acnei-

*Fig. 2.* Typical pinhead-sized postpustular desquamation.

form pustules, localized pustular contact dermatitis, dermatophyte infections, pyoderma vegetans, varicella, Kaposi's varicelliform eruption, Sweet's syndrome, impetigo, impetiginized eczema, pemphigus foliaceus and other autoimmune bullous disorders, infantile chronic acropustulosis, migratory necrolytic eruption of glucagonoma, bowel bypass syndrome, Behcet's disease or staphylococcal scalded skin syndrome and others. Yet a couple of diseases remain where differentiation from AGEP may cause problems both, clinically and conceptually.

### Pustular psoriasis (von Zumbusch type)

One of the main issues in the discussion whether AGEP (or toxic pustuloderma) is an entity of it's own or not is it's clinical similarity with pustular psoriasis of the von Zumbusch type, the morphology of the pustules often being indistinguishable in both diseases. Many authors have addressed this issue and until now no clear-cut rules for the differentiation of both entities exist but a list of differences seems to justify the distinction between AGEP and pustular psoriasis (Table 1).

### Subcorneal pustular dermatosis (Sneddon-Wilkinson)

Sneddon-Wilkinson disease is characterized by larger, flaccid blisters with hypopyon formation often arranged in a circinate distribution pattern. In addition, evolution of the disease is far less acute than in AGEP.

### Pustular vasculitis

Bullous and/or pustular lesions may arise in purpura lesions of leucocytoclastic vasculitis. In addition there seems to be a special variant of leucocytoclastic vasculitis which is characterized by the development of many small pustules which – as opposed to AGEP – are localized mainly on the dorsum of the hands and which might also be drug-induced. A marked leucocytoclastic vasculitis can be detected in histology.[10,11] Confusion may occur due to the report of some cases of pustular vasculitis under the term pustulosis acuta generalisata[5,12] or due to the occasional presence of vasculitis in AGEP.

### Drug hypersensitivity syndrome

Drug hypersensitivity syndrome, also referred to as DRESS (an acronym for drug rash with eosinophilia and systemic symptoms) may also show papulo-vesicles and/or papulo-pustules, the pustular component being usually less pronounced than in AGEP. In addition patients show fever, lymphadenopathy, eosinophilia, mononucleosis and often severe visceral involvement like hepatitis, nephritis, pneumonitis, and/or myocarditis.

### Toxic epidermal necrolysis (TEN)

The presence of "atypical" target lesions and the confluence of pustules mimicking a positive Nikolsky-sign may suggest the diagnosis of TEN in severe cases of AGEP. In general the distinction can be easily made by experienced physicians as, among other criteria, epidermal detachment in AGEP is much more superficial, and mucous membrane involvement is much more pronounced in TEN. Whereas differentiation in some cases might be difficult on clinical grounds alone, histology is significantly different in TEN typically showing full thickness epidermal necrosis and only a very sparse inflammatory infiltrate. Yet, in our experience even some overlap cases might exist that fulfil the criteria for both diseases both clinically and histologically.

## Scoring system

As a conclusion from a retrospective analysis of 63 cases the following five criteria have been suggested for the definition of AGEP: 1) several dozens of small, mostly non follicular pustules arising on a widespread edematous erythema; 2) histopathologic changes as described above; 3) fever (>38 °C); 4) blood neutrophil counts above $7\times10^9$/L; and 5) acute evolution

Table 1. Differentiation between AGEP and pustular psoriasis

| | AGEP | Pustular psoriasis |
|---|---|---|
| History of psoriasis | Possible | Mostly |
| Distribution pattern | Predominance in the folds | More generalized |
| Duration of pustules | Shorter | Longer |
| Duration of fever | Shorter | Longer |
| History of drug reaction | Usual | Uncommon |
| Recent drug administration | Very frequent | Less frequent |
| Arthritis | Rare | ~30% |
| Histology | Spongiform subcorneal and/or intraepidermal pustules, edema of papillary dermis, vasculitis, exocytosis of eosinophils, single-cell necrosis of keratinocytes | Subcorneal and/or intraepidermal pustules, papillomatosis, acanthosis |

Table 2. AGEP validation score of the EuroSCAR study group

| | |
|---|---|
| **Morphology** | |
| Pustules | |
| Typical* | +2 |
| Compatible** | +1 |
| Insufficient*** | 0 |
| Erythema | |
| Typical | +2 |
| Compatible | +1 |
| Insufficient | 0 |
| Distribution/pattern | |
| Typical | +2 |
| Compatible | +1 |
| Insufficient | 0 |
| Postpustular desquamation | |
| Yes | +1 |
| No/insufficient | +0 |
| **Course** | |
| Mucosal involvement | |
| Yes | −2 |
| No | 0 |
| Acute onset (≤10 d) | |
| Yes | 0 |
| No | −2 |
| Resolution ≤15 days | |
| Yes | 0 |
| No | −4 |
| Fever ≥38 °C | |
| Yes | +1 |
| No | 0 |
| PNN ≥7000/mm$^3$ | |
| Yes | +1 |
| No | 0 |
| **Histology** | |
| Other disease | −10 |
| Not representative/no histology | 0 |
| Exocytosis of PNN | +1 |
| Subcorneal and/or intraepidermal *non* spongiform or NOS pustule(s) *with* papillary edema or subcorneal and/or intraepidermal *spongiform* or NOS pustule(s) *without* papillary edema (NOS=not otherwise specified) | +2 |
| *Spongiform* subcorneal and/or intraepidermal pustule(s) *with* papillary edema | +3 |

Interpretation: ≤0: no AGEP, 1–4: possible, 5–7: probable, 8–12: definite.
Remarks: Patients are not included in the study, if only localized pustules are reported, the pustular rash already lasts longer than 3 weeks or a clear alternative diagnosis has been made by a dermatologist.
*Typical: typical morphology as described in the "clinical features" section
**Compatible: not typical, but not strongly suggestive of other disease.
***Insufficient: lesions can not be judged (mostly because of late stage of the disease or poor quality of pictures).

with spontaneous resolution of pustules in less than 15 days.[6] While performing a multinational epidemiological case-control study on severe cutaneous adverse reactions (EuroSCAR-project) we realized, that these criteria were not precise enough, especially when dealing with the retrospective assessment of cases. We therefore elaborated a more sophisticated scoring system presented in Table 2.

## Epidemiology

From the current data males and females seem to be equally affected and AGEP can occur at any age. In one study HLA B51, DR11 and DQ3 were found to be more frequent than in the average population.[13]

Table 3. Anti-infective and non-anti-infective drugs as causes of AGEP

| Anti-infectives | References |
|---|---|
| **A) Anti-infectives as causative drugs for AGEP** | |
| β-Lactam antibiotics | 4, 6, 8, 18–22 |
| Macrolides | 6, 23, 24 |
| Cephalosporins | 7, 18, 25–30 |
| Quinolones | 31, 32 |
| Tetracyclins | 6, 18, 33 |
| Other antibiotics | |
| Chloramphenicol | 3, 34 |
| Gentamycin | 35 |
| Imipenem | 36 |
| Isoniazid | 37 |
| Metronidazol | 38 |
| Trimethoprim sulfamethoxazole | 39, 40 |
| Vancomycin | 6 |
| Antimycotics | |
| Griseofulvin | 18 |
| Itraconazol | 41, 42 |
| Nystatin | 43, 44 |
| Terbinafine | 45–47 |
| Other antiinfectives | |
| (Hydroxy-)chloroqine | 48–52 |
| Diaphenylsulfone | 8 |
| Nifuroxazide | 53 |
| Pyrimethamine | 3 |
| Protease inhibitors | 54 |

**B) Non-anti-infective drugs as causes of AGEP (in alphabetical order)**

| Agent | References |
|---|---|
| Acetylsalicylic acid | 55 |
| Allopurinol | 56, 57 |
| Amoxapine | 58, 59 |
| Buphenine | 60 |
| Bufexamac | 6 |
| Calcium channel blockers | 61–64 |
| Carbamazepine | 2, 6, 65 |
| Carbutamide | 6 |
| Chemotherapy (high dose) | 66 |
| Chromium picolinate | 67 |
| Cimetidine | 8 |
| Clemastine | 68 |
| Clobazam | 6 |
| Clozapine | 69 |
| Dexamethasone | 70 |
| Disulfiram | 71 |
| Enalapril | 18, 72 |
| Eprazinon | 73 |
| Fenoterol | 74 |
| Furosemide | 3 |
| Lansoprazole | 75 |
| Nadoxolol | 6, 76 |
| Nifedipine | 6 |
| Mercury | 6, 77, 78 |
| Paracetamol | 6, 79, 80 |
| Prostaglandine E1 | 81 |
| Piperazine ethionamate | 3 |
| Pneumococcal vaccine | 82 |
| Quinidine | 4, 6 |
| Sulbutiamine | 6 |
| Sulfasalazine | 83, 84 |
| Thalidomide | 85, 86 |
| Topical agents | 6, 87 |
| PUVA | 88 |

From the inclusion rate in the EuroSCAR study we estimate the incidence rate of AGEP to be in the range of 1 to 5 cases per million per year, but reliable data is missing.

## Etiology and pathogenesis

It seems that more than 90% of cases with AGEP or toxic pustuloderma are drug induced. A wide range of drugs has been suspected of causing these reactions in case reports and larger series (Table 3A, B), antibacterials being the most frequent triggers. A high proportion of these cases have been attributed to aminopenicillins or macrolides but interestingly not to sulfonamides, who have a high potential of causing other cutaneous drug reactions. Also an increasing number of cases attributed to antimycotic drugs is being reported. In the group of non-antiinfective drugs especially calcium channel blockers, carbamazepine and paracetamol have been reported as culprit agents in several cases. In a minority of cases viral infections[6,14–16] have been suspected to trigger AGEP.

After administration of a new drug it may take 1 to 3 weeks until – probably as result of a primary sensitization – skin symptoms arise. Yet there is a second group of patients where the interval between drug intake (especially antibacterials) and skin symptoms may be as short as a few hours to 2–3 days. Such rapid onsets have been described in patients who were rechallenged with the same drug after a first episode of AGEP or patients with a known previous sensitization to topical antibacterials. More often than in other drug reactions patch testing shows positive, sometimes strong and even pustular reactions.[17] Furthermore *in vitro* tests like the macrophage migration inhibition factor (MIF) test and the mast cell degranulation (MCD) test have been shown to be helpful in detecting the causative drugs in AGEP (18). Although the mechanisms of AGEP have not been investigated some of the mentioned features suggest an immunologic recall phenomenon where in particular memory T cells producing neutrophil promoting cytokines like interleukin (IL)-3 and IL-8 play an important role.

## Therapy

Obviously the causative drug has to be discontinued and antibiotics are not to be given unless there is a clear and well-documented associated infection. Due to the benign, self-limited course of the disease a specific treatment, especially systemic corticosteroid treatment which is often taken into consideration is usually not necessary. Symptomatically systemic antipyretics can be given if not suspected as causative drug for the disease.

## References


1. Baker H, Ryan TJ. Generalized pustular psoriasis. A clinical and epidemiological study of 104 cases. Br J Dermatol 1968; 80: 771.
2. Staughton RC, Payne CM, Harper JI, McMichen H. Toxic pustuloderma – a new entity? J R Soc Med 1984; 77 (Suppl 4): 6.
3. Macmillan AL. Generalised pustular drug rash. Dermatologica 1973; 146: 285.
4. Beylot C, Bioulac P, Doutre MS. Acute generalized exanthematic pustuloses (four cases) (author's transl). Ann Dermatol Venereol 1980; 107: 37.
5. Auer-Grumbach P, Pfaffenthaler E, Soyer HP. Pustulosis acuta generalisata is a post-streptococcal disease and is distinct from acute generalized exanthematous pustulosis. Br J Dermatol 1995; 133: 9.
6. Roujeau JC, Bioulac-Sage P, Bourseau C, et al. Acute generalized exanthematous pustulosis. Analysis of 63 cases. Arch Dermatol 1991; 127: 1333.
7. Eeckhout I, Noens L, Ongenae K, al Sarraf Z, Schelfhout A, Naeyaert JM. Acute generalized exanthematic pustulosis: a case with a lymphoma-like presentation. Dermatology 1997; 194: 408.
8. Burrows NP, Russell Jones RR. Pustular drug eruptions: a histopathological spectrum. Histopathology 1993; 22: 569.
9. Beylot C, Doutre MS, Beylot-Barry M. Acute generalized exanthematous pustulosis. Semin Cutan Med Surg 1996; 15: 244.
10. Röckl H. Leukocytoclastic vasculitis due to drug allergy presenting as generalized pustular exanthema. Hautarzt 1981; 32: 467.
11. Strutton G, Weedon D, Robertson I. Pustular vasculitis of the hands [see comments]. J Am Acad Dermatol 1995; 32: 192.
12. Braun-Falco O, Luderschmidt C, Maciejewski W, Scherer R. Generalized acute pustulosis. An unusual presentation of leukocytoclastic vasculitis. Hautarzt 1978; 29: 371.
13. Bernard P, Lizeaux-Parneix V, Miossec V, et al. HLA et prédisposition génétique dans les pustuloses exanthématiques (PEAG) et les exanthémes maculo-papuleux (EMP). Ann Dermatol Venerol 1995; 122: S38.
14. Rouchouse B, Bonnefoy M, Pallot B, Jacquelin L, Dimoux-Dime G, Claudy AL. Acute generalized exanthematous pustular dermatitis and viral infection. Dermatologica 1986; 173: 180.
15. Naides SJ, Piette W, Veach LA, Argenyi Z. Human parvovirus B19-induced vesiculopustular skin eruption. Am J Med 1988; 84: 968.
16. Feio AB, Apetato M, Costa MM, Sa J, Alcantara J. Acute generalized exanthematous pustulosis due to Coxsackie B4 virus. Acta Med Port 1997; 10: 487.
17. Wolkenstein P, Chosidow O, Flechet ML, et al. Patch testing in severe cutaneous adverse drug reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis. Contact Dermatitis 1996; 35: 234.
18. Lazarov A, Livni E, Halevy S. Generalized pustular drug eruptions: confirmation by *in vitro* tests. J Eur Acad Dermatol Venereol 1998; 10: 36.
19. Epelbaum S, Benhamou PH, Lok C, et al. Acute generalized exanthematous pustulosis. Pediatrie 1989; 44: 387.
20. Shuttleworth D. A localized, recurrent pustular eruption following amoxycillin administration. Clin Exp Dermatol 1989; 14: 367.
21. Armster H, Schwarz T. Drug reaction to amoxicillin simulating toxic pustuloderma. Hautarzt 1991; 42: 713.
22. Gebhardt M, Lustig A, Bocker T, Wollina U. Acute generalized exanthematous pustulosis (AGEP): manifestation of drug allergy to propicillin. Contact Dermatitis 1995; 33: 204.

23. Bernard P, Amici JM, Catanzano G, Beretti B, Touraine P, Bonnetblanc JM. Generalized acute pustular drug dermatitis. Apropos of a case induced by josamycin. Ann Dermatol Venereol 1989; 116: 31.
24. Trevisi P, Patrizi A, Neri I, Farina P. Toxic pustuloderma associated with azithromycin [Letter]. Clin Exp Dermatol 1994; 19: 280.
25. Kalb RE, Grossman ME. Pustular eruption following administration of cephradine. Cutis 1986; 38: 58.
26. Stough D, Guin JD, Baker GF, Haynie L. Pustular eruptions following administration of cefazolin: a possible interaction with methyldopa [Letter]. J Am Acad Dermatol 1987; 16: 1051.
27. Jackson H, Vion B, Levy PM. Generalized eruptive pustular drug rash due to cephalexin. Dermatologica 1988; 177: 292.
28. Fayol J, Bernard P, Bonnetblanc JM. Pustular eruption following administration of cefazolin: a second case report [Letter]. J Am Acad Dermatol 1988; 19: 571.
29. Rustin MH, Robinson TW, Dowd PM. Toxic pustuloderma: a self-limiting eruption. Br J Dermatol 1990; 123: 119.
30. Ogoshi M, Yamada Y, Tani M. Acute generalized exanthematic pustulosis induced by cefaclor and acetazolamide. Dermatology 1992; 184: 142.
31. Shelley ED, Shelley WB. The subcorneal pustular drug eruption: an example induced by norfloxacin. Cutis 1988; 42: 24.
32. Tsuda S, Kato K, Karashima T, Inou Y, Sasai Y. Toxic pustuloderma induced by ofloxacin. Acta Derm Venereol 1993; 73: 382.
33. Trueb RM, Burg G. Acute generalized exanthematous pustulosis due to doxycycline. Dermatology 1993; 186: 75.
34. Lee AY, Yoo SH. Chloramphenicol induced acute generalized exanthematous pustulosis proved by patch test and systemic provocation [Letter]. Acta Derm Venereol 1999; 79: 412.
35. Sawhney RA, Dubin DB, Otley CC, Kwan TH, Bowers KE. Generalized exanthematous pustulosis induced by medications. Int J Dermatol 1996; 35: 826.
36. Escallier F, Dalac S, Foucher JL, Lorcerie B, Lucet A, Lambert D. Acute generalized exanthematic pustulosis. Imputability of imipenem (Tienam). Ann Dermatol Venereol 1989; 116: 407.
37. Yamasaki R, Yamasaki M, Kawasaki Y, Nagasako R. Generalized pustular dermatosis caused by isoniazid [Letter]. Br J Dermatol 1985; 112: 504.
38. Watsky KL. Acute generalized exanthematous pustulosis induced by metronidazole: the role of patch testing [Letter]. Arch Dermatol 1999; 135: 93.
39. Macdonald KJ, Green CM, Kenicer KJ. Pustular dermatosis induced by co-trimoxazole. Br Med J (Clin Res Ed) 1986; 293: 1279.
40. Bissonnette R, Tousignant J, Allaire G. Drug-induced toxic pustuloderma. Int J Dermatol 1992; 31: 172.
41. Heymann WR, Manders SM. Itraconazole-induced acute generalized exanthemic pustulosis. J Am Acad Dermatol 1995; 33: 130.
42. Park YM, Kim JW, Kim CW. Acute generalized exanthematous pustulosis induced by itraconazole. J Am Acad Dermatol 1997; 36: 794.
43. Kuchler A, Hamm H, Weidenthaler-Barth B, Kampgen E, Brocker EB. Acute generalized exanthematous pustulosis following oral nystatin therapy: a report of three cases. Br J Dermatol 1997; 137: 808.
44. Rosenberger A, Tebbe B, Treudler R, Orfanos CE. Acute generalized exanthematous pustulosis, induced by nystatin. Hautarzt 1998; 49: 492.
45. Dupin N, Gorin I, Djien V, et al. Acute generalized exanthematous pustulosis induced by terbinafine [Letter]. Arch Dermatol 1996; 132: 1253.
46. Kempinaire A, De Raeve L, Merckx M, De Coninck A, Bauwens M, Roseeuw D. Terbinafine-induced acute generalized exanthematous pustulosis confirmed by a positive patch-test result. J Am Acad Dermatol 1997; 37: 653.
47. Condon CA, Downs AM, Archer CB. Terbinafine-induced acute generalized exanthematous pustulosis [Letter]. Br J Dermatol 1998; 138: 709.
48. Friedman SJ. Pustular psoriasis associated with hydroxychloroquine [Letter]. J Am Acad Dermatol 1987; 16: 1256.
49. Lotem M, Ingber A, Segal R, Sandbank M. Generalized pustular drug rash induced by hydroxychloroquine. Acta Derm Venereol 1990; 70: 250.
50. Assier H, Auffret N, Beltzer-Garelly E, Faures-Quenet B, Binet O. Acute generalized exanthematous pustulosis induced by hydroxychloroquine. Ann Dermatol Venereol 1993; 120: 848.
51. Assier-Bonnet H, Saada V, Bernier M, Clerici T, Saiag P. Acute generalized exanthematous pustulosis induced by hydroxychloroquine [Letter]. Dermatology 1996; 193: 70.
52. Janier M, Froidevaux D, Lons-Danic D, Daniel F. Acute generalized exanthematous pustulosis due to the combination of chloroquine and proguanil [Letter]. Dermatology 1998; 196: 271.
53. Machet L, Jan V, Machet MC, Lorette G, Vaillant L. Acute generalized exanthematous pustulosis induced by nifuroxazide. Contact Dermatitis 1997; 36: 308.
54. Aquilina C, Viraben R, Roueire A. Acute generalized exanthematous pustulosis: a cutaneous adverse effect due to prophylactic antiviral therapy with protease inhibitor. Arch Intern Med 1998; 158: 2160.
55. Ballmer-Weber BK, Widmer M, Burg G. Acetylsalicylic acid-induced generalized pustulosis. Schweiz Med Wochenschr 1993; 123: 542.
56. Yu RC, Chu TC. Allopurinol-induced toxic pustuloderma. Br J Dermatol 1993; 128: 95.
57. Boffa MJ, Chalmers RJ. Allopurinol-induced toxic pustuloderma [Letter; comment]. Br J Dermatol 1994; 131: 447.
58. Larbre B, Kanitakis J, Savy C, Besnard V, Faure M, Claudy A. Acute exanthematous pustulosis during amoxapine treatment. Ann Dermatol Venereol 1994; 121: 40.
59. Loche F, Durieu C, Bazex J. Acute generalized exanthematous pustulosis induced by amoxapine [Letter]. Acta Derm Venereol 1998; 78: 224.
60. Spindler E, Janier M, Bonnin JM, Carlotti A, Daniel F. Generalized exanthematous pustulosis caused by buphenine: report of a case. Ann Dermatol Venereol 1992; 119: 273.
61. Lambert DG, Dalac S, Beer F, Chavannet P, Portier H. Acute generalized exanthematous pustular dermatitis induced by diltiazem [Letter]. Br J Dermatol 1988; 118: 308.
62. Blodgett TP, Camisa C, Gay D, Bergfeld WF. Acute generalized exanthematous pustulosis secondary to diltiazem therapy. Cutis 1997; 60: 45.
63. Wakelin SH, James MP. Diltiazem-induced acute generalised exanthematous pustulosis. Clin Exp Dermatol 1995; 20: 341.
64. Vicente-Calleja JM, Aguirre A, Landa N, Crespo V, Gonzalez-Perez R, Diaz-Perez JL. Acute generalized exanthematous

pustulosis due to diltiazem: confirmation by patch testing [Letter]. Br J Dermatol 1997; 137: 837.
65. Commens CA, Fischer GO. Toxic pustuloderma following carbamazepine therapy [Letter]. Arch Dermatol 1988; 124: 178.
66. Valks R, Fraga J, Munoz E, Bartolome B, Garcia-Diez A, Fernandez-Herrera J. Acute generalized exanthematous pustulosis in patients receiving high-dose chemotherapy [Letter]. Arch Dermatol 1999; 135: 1418.
67. Young PC, Turiansky GW, Bonner MW, Benson PM. Acute generalized exanthematous pustulosis induced by chromium picolinate. J Am Acad Dermatol 1999; 41: 820.
68. Feind-Koopmans A, Van der Valk PG, Steijlen PM, Van de Kerkhof PC. Toxic pustuloderma associated with clemastine therapy. Clin Exp Dermatol 1996; 21: 293.
69. Bosonnet S, Dandurand M, Moati L, Guillot B. Acute generalized exanthematic pustulosis after intake of clozapine (leponex). First case. Ann Dermatol Venereol 1997; 124: 547.
70. Demitsu T, Kosuge A, Yamada T, Usui K, Katayama H, Yaoita H. Acute generalized exanthematous pustulosis induced by dexamethasone injection. Dermatology 1996; 193: 56.
71. Larbre B, Larbre JP, Nicolas JF, Fauvet N, Faure M, Thivolet J. Bullous toxic dermatitis due to disulfiram. Apropos of a case. Ann Dermatol Venereol 1990; 117: 721.
72. Ferguson JE, Chalmers RJ. Enalapril-induced toxic pustuloderma. Clin Exp Dermatol 1996; 21: 54.
73. Faber M, Maucher OM, Stengel R, Goerttler E. Eprazinone exanthema with subcorneal pustulosis. Hautarzt 1984; 35: 200.
74. Koehler AV, Schunter M, Weber L, Gall H. Acute generalized exanthematous pustular eruption due to fenoterol. Allergologie 1999; 22: 675.
75. Dewerdt S, Vaillant L, Machet L, de Muret A, Lorette G. Acute generalized exanthematous pustulosis induced by lansoprazole [Letter]. Acta Derm Venereol 1997; 77: 250.
76. Bernard P, Bedane C, Catanzano G, Robbe J, Bonnetblanc JM. Acute generalized exanthematic pustulosis. An atypical case due to nadoxolol? Dermatologica 1991; 182: 115.
77. Barrazza V, Meunier P, Escande JP. Acute contact dermatitis and exanthematous pustulosis due to mercury. Contact Dermatitis 1998; 38: 361.
78. Bolzinger T, Ducombs G, Labreze C, Taieb A, Maleville J. Acute generalized exanthematous pustulosis in a child and epicutaneous tests with mercurials. Ann Dermatol Venereol 1993; 120: 223.
79. De Coninck AL, Van Strubarq AS, Pipeleers-Marichal MA, Huyghens LP, Suys ET, Roseeuw DI. Acute generalized exanthematous pustulosis induced by paracetamol. A case with severe hemodynamic disturbances. Dermatology 1996; 193: 338.
80. Leger F, Machet L, Jan V, Machet C, Lorette G, Vaillant L. Acute generalized exanthematous pustulosis associated with paracetamol [Letter]. Acta Derm Venereol 1998; 78: 222.
81. Gallego I, Badell A, Notario J, Gallardo F, Servitje O, Peyri J. Toxic pustuloderma induced by intracavernous prostaglandin E1 [Letter]. Br J Dermatol 1997; 136: 975.
82. Correia O, Nunes JP, Vaz-da-Silva MJ, Pires S, Brandao F, Mesquita-Guimaraes J. Acute exanthematous pustular dermatitis after pneumococcal vaccine [Letter]. Dermatology 1993; 187: 217.
83. Marce S, Schaeverbeke T, Bannwarth B, Marty L, Dehais J. Generalized acute exanthematous pustulosis after ingestion of sulfasalazine [Letter]. Presse Med 1993; 22: 271.
84. Kawaguchi M, Mitsuhashi Y, Kondo S. Acute generalized exanthematous pustulosis induced by salazosulfapyridine in a patient with ulcerative colitis. J Dermatol 1999; 26: 359.
85. Darvay A, Basarab T, Russell-Jones R. Thalidomide-induced toxic pustuloderma. Clin Exp Dermatol 1997; 22: 297.
86. Rua-Figueroa I, Erausquin C, Naranjo A, Carretero-Hernandez G, Rodriguez-Lozano C, De la Rosa P. Pustuloderma during cutaneous lupus treatment with thalidomide [Letter]. Lupus 1999; 8: 248.
87. Dooms-Goossens A, Loncke J, Michiels JL, Degreef H, Wahlberg J. Pustular reactions to hexafluorosilicate in foam rubber. Contact Dermatitis 1985; 12: 42.
88. Yip J, Sheehan-Dare R, Cotterill J. Toxic pustuloderma due to PUVA treatment [Letter]. Br J Dermatol 1991; 125: 401.