Abstract
Any drug can cause any rash! Cutaneous adverse drug reactions (CADRs) are great mimickers and can be included in the differential diagnosis of any inflammatory dermatoses. Several drugs can cause rash of similar morphology and the same drug can cause rash of different morphology. While some common and specific drug reaction patterns are recognized easily by the clinicians, many a times unusual and interesting patterns can be induced by drug(s), thus leading to erroneous diagnosis and mistreatment. This review aims to familiarize clinicians with some rare, yet interesting patterns of CADR.

Key words: Adverse cutaneous drug reactions, emerging cutaneous adverse drug reactions, newer targeted therapy, rare

Introduction
Adverse drug reactions are one of the major preventable public health problems. They are common but are underreported and underrecognized cause of morbidity and mortality. As the longevity of population increases with a large subset belonging to elderly on multiple drugs and with the advent of newer drugs, the probability of encountering drug reaction is on the rise. The world of cutaneous adverse drug reactions (CADRs) is wide and enigmatic and almost any inflammatory or noninflammatory dermatosis can be mimicked. Thus, the aphorism – “Anything you see, anything you think, and something that you don’t even think of could be due to drugs!!”

In this article, we have included some rare, unusual, interesting, and diagnostically challenging adverse drug reactions. For the sake of convenience, they are classified into:
• ADRs to commonly used drugs which are generally considered safe
• Atypical presentations of some common classical ADR
• Typical CADRs, although not very common, which are interesting morphologically
• CADR to newer targeted therapy/emerging CADR
• Drugs causing induction of malignancy
• Some interesting hair- and nail-related ADR and
• Paradoxical drug reactions (PDRs).

Adverse drug reactions to commonly used drugs generally considered safe
This group comprises drugs which are commonly used, sometimes over-the-counter, are usually considered safe and often excluded when a patient on multiple drugs develop a drug reaction. Some of these drugs are frequently used in the treatment of adverse drug reactions, so clinicians should have a high index of suspicion and should be aware of the possibility of reactions to these drugs.

Anaphylaxis to ranitidine
So far, at least 10 cases of anaphylaxis have been reported with ranitidine, both oral[1] and intravenous
preparation (bolus\(^2\) as well as slow infusion\(^7,8\)). Most of the reactions have occurred within minutes; in one case though, it was delayed up to 90 min.\(^9\) The clinical manifestations include skin rash, pruritus, angioedema, wheezing, dyspnea, tachycardia, hypotension, irritability, deterioration or loss of consciousness, drowsiness, and right bundle branch block in varying combination. Most of the patients can be resuscitated with inotropic and ventilator support. One patient, however, died within 30 min despite intensive resuscitation attempts.\(^7\) Oral challenge test, skin prick test, intradermal test, and specific serum IgE are used for confirmation of diagnosis.

**Omeprazole-induced gynecomastia**

The first case was reported in 1991 when a 53-year-old male developed bilateral gynecomastia and mastodynia following 8 weeks of omeprazole therapy for duodenal ulcer.\(^9\) The gynecomastia regressed after 4 weeks of drug termination and was reproduced 6 weeks after drug reintroduction. In a retrospective review of cases of gynecomastia from the “Spanish Pharmacovigilance system,”\(^10\) 24 patients on treatment with omeprazole were identified as having gynecomastia in the 2007 year database. Here, the relative odds ratio for omeprazole exposure showed a statistically significant elevation in comparison to those with no exposure.

**Hypersensitivity reactions to glucocorticoids**

Glucocorticoids and the excipients contained in commercial corticosteroid formulations are able to induce severe immediate type as well as delayed type hypersensitivity reactions. The overall prevalence of type I steroid hypersensitivity is estimated to be 0.3%–0.5%.\(^11\) Allergic contact dermatitis is the most commonly reported nonimmediate hypersensitivity reaction and usually follows topical corticosteroid (CS) application but has also been reported with parenteral CS.\(^12\) As glucocorticoids are the most widely used drugs for the treatment of hypersensitivity, it is even more so important to consider an allergy to CS in patients with worsening anaphylactic symptoms after administration of systemic CS.

**Fixed drug eruption to antihistamines**

Antihistamines form a sizeable proportion of dermatology prescriptions. There have been a few reports of fixed drug eruption (FDE) with piperazine derivatives (hydroxyzine,\(^13,14\) cetirizine,\(^15,16\) and levocetirizine\(^17\)) and they are also known to show cross-reactions on patch test.\(^18\) This cross-reaction is not observed with piperidine derivatives (fexofenadine, ebastine, loratadine, and astemizole). Multilocalized bullous FDE has also been described with cetirizine.\(^15\)

**Atypical presentation**

This group includes atypical morphological variants of common adverse drug reactions which can pose diagnostic challenge at times.

**Nonpigmenting fixed drug eruption**

Residual pigmentation is one of the characteristic features of FDE and is often a supportive diagnostic clue in patients with recurrent episodes. Nonpigmenting FDE has been reported in association with pseudoephedrine,\(^19\) co-trimoxazole,\(^20\) tetrahydrozoline, diflunisal, thiopental, piroxicam,\(^21\) iothalamate, arsephenamine, paracetamol, intra-articular triaminolone acetone, eperisone hydrochloride,\(^22\) furazolidone, and acetonaphen. Recently, reports of nonpigmenting FDE to euprazinone, sorafenib,\(^21\) tadalafil,\(^22\) esomeprazole, and fluoroquinolones\(^23\) have also been described. The lesions can be as large as over 10 cm and multiple lesions possibly represent abortive variant of toxic epidermal necrolysis (TEN).

**Postcoital fixed drug eruption**

A 34-year-old male patient developed FDE on the glans penis after sexual intercourse with wife on trimethoprim-sulfamethoxazole.\(^24\) Similar reaction has also been reported with wife using sulfathiazole/sulfacetamide/sulfabenzamide (triple-sulfa) vaginal cream.\(^27\)

**Bullous Sweet’s syndrome**

An HIV-positive patient developed a bullous eruption soon after each cycle of interleukin-2 (IL-2). Histopathology was suggestive of Sweet’s syndrome. The same patient developed pseudolymphatous reaction on restarting the therapy after 5 years, and it resolved after discontinuation.\(^28\)

**Acute localized exanthematous pustulosis**

Acute localized exanthematous pustulosis (ALEP) is a rare variant of AGEP (acute generalized exanthematous pustulosis). A pregnant female developed sterile pustules localized over right breast, fever, and malaise with oral clindamycin.\(^29\) Other medications which are reported to cause ALEP include amoxicillin,\(^30\) amoxicillin-clavulanic acid, cephalosporins, sulfamethoxazole-trimethoprim, levofloxacin, paracetamol,\(^31\) ibuprofen, nimesulide, finasteride,\(^32\) docetaxel, and sorafenib.

**Cutaneous adverse drug reactions with interesting morphology**

**Symmetrical drug-related intertriginous and flexural exanthema or Baboon syndrome**

Baboon syndrome is a distinctive skin reaction, in which the patient typically develops erythematous buttocks that appear similar to those of a baboon. The noncontact allergic variant of Baboon syndrome is also referred to as symmetrical drug-related intertriginous and flexural
exanthema (SDRIFE). The diagnostic criteria of SDRIFE include:

a. Exposure to a systemically administered drug either at the first or repeated dose
b. Sharply demarcated erythema of the gluteal/perianal area and/or V-shaped erythema of the inguinal/perigenital area
c. Involvement of at least another intertriginous/flexural localization
d. Symmetry of affected areas
e. Absence of systemic symptoms and signs.

SDRIFE has been reported with multiple medications including antibacterials (erythromycin, penicillins, and aminoglycosides), antifungals, allopurinol, antiallergic treatments (aminophylline, terbutaline), and radiographic media.[33-35]

**Flagellate erythema and pigmentation**

Flagellate erythema is a distinctive morphologic presentation of linear, whiplash-like pattern, red streaks on the skin which usually leaves residual postinflammatory hyperpigmentation behind. It has been described with antineoplastic agents including bleomycin[36-44] (most commonly), bendamustine,[45] docetaxel,[46] peplomycin,[47] and trastuzumab.[48] Other conditions which may lead to flagellate dermatoses include chikungunya fever, parvovirus B19 infection, hypereosinophilic syndrome, infections and abuse, phytophotodermatitis, paederus dermatitis, toxin-induced (mushroom, shiitake), and rheumatologic conditions (SLE, dermatomyositis, and adult-onset Still's disease).[49]

**Red man syndrome**

Red man syndrome encompasses a constellation of symptoms ranging from a mild reaction such as flushing, urticarial rash, and/or pruritus to a serious reaction such as generalized erythema, intense pruritus, and even hypotension.[40] Signs appear about 4–10 min after start of infusion or may begin soon after its completion. It is often associated with rapid (<1 h) infusion of the first dose of vancomycin.

**Capillary leak syndrome**

Capillary leak syndrome (CLS) is characterized by acute episodes of generalized edema, hemoconcentration, hypoproteinemia, and severe hypotension. The etiopathogenesis is unclear. Scintigraphy with labeled albumin showed increased vascular permeability and albumin retention in extravascular space. Many drugs are known to induce CLS, including IL-2, IL-11, gemcitabine, doxorubicin, granulocyte colony-stimulating factor, interferon, and acitretin.[50,51]

**Hand-foot skin reaction**

Classic hand-foot syndrome has been described with the use of various chemotherapeutic agents, including sunitinib, cabozantinib, sorafenib, regorafenib, cytarabine, capecitabine, doxorubicin hydrochloride, and fluorouracil.[52,53] It generally starts with prodromal symptoms of tingling and numbness on the palms and soles, and sometimes a painful sensation induced on touching hot objects, hence also known as palmoplantar erythrodyssesthesia. This is followed by three phases: the inflammatory phase, characterized by erythema, desquamation and blisters with a perilesional erythematous rim; the hyperkeratotic phase, marked by the appearance of new lesions that become hyperkeratotic and development of pain in the older, hyperkeratotic areas; and the resolution phase, typified by clearing of the lesions as a result of dose modification or drug termination.[54]

**Cutaneous adverse drug reactions to newer targeted therapy/emerging cutaneous adverse drug reactions**

The past several decades have seen the advent and rapidly expanding use of biological agents in the treatment of chronic diseases. As increasingly, large pools of patients have been enrolled in treatment protocols using these agents, physicians have become acquainted with both desired and adverse events associated with their use. Dermatologists frequently encounter patients affected by cutaneous drug reactions associated with the use of biological agents, and should therefore be familiar with the full range of side effects. Table 1 enlists CDRs to newer targeted chemotherapeutic drugs.

**Drugs inducing malignancies**

Immunosuppressed patients experience an increased incidence of cutaneous neoplasms including melanoma, nonmelanoma skin cancer, and cutaneous lymphoproliferative disorders. The common drugs[55] which are associated with induction of malignancy are mentioned in Table 2. The ones with definite risk are mentioned in bold.

**Hair- and nail-related adverse drug reactions**

Drug can affect hair in many ways, most common being in the form of hair loss. Table 3 enumerates some unusual ADRs related to hair and the drugs commonly implicated in their causation.

Nail abnormalities due to drugs generally occur as a part of symptom complex with coexistent skin and mucosal lesions. Pigmentary abnormalities and asymptomatic growth rate changes are the most commonly observed nail changes and reverse on discontinuation of the causative agent. The changes are often more readily observed on the nails of the thumbs and great toes, and on the fingernails, than on the toenails. The clinical features are dependent on the area of nail unit damaged. Table 4 enlists some of the unusual ADRs related to nail and their causative agent.
Table 1: Cutaneous adverse drug reactions to targeted chemotherapy

| Drug class      | Drugs                               | CADR                                                                 |
|-----------------|-------------------------------------|----------------------------------------------------------------------|
| EGFR Inhibitors | Erlotinib, gefitinib, lapatinib, cetuximab, panitumumab | Papulopustular rash/acroform eruption-most common, surrogate marker of tumor response[^56,58]  
Xerosis-35%[^57,68]  
Nail changes (17.2%)[^55,58]  
Paronychia  
Onycholysis  
Pyogenic granuloma-like lesions  
Dyspigmentation and brittle nails  
Hair changes[^55,58,59]  
Scalp hair-slow growth, fine brittle, and kinky  
Eyelash-trichomegaly and trichorrhesis  
Eyebrows-hypertrichosis  
Hirsuitism in females  
Alopecia with/without scalp inflammation  
Telangiectasias[^57]  
Photosensitivity and hyperpigmentation of exposed areas of skin[^58,60]  
Mucositis[^55,65]  
Oral aphthae, xerostomia, geographic tongue  
Nasal ulcers  
Vaginal dryness, vulvovaginitis, balanitis  
Conjunctivitis and keratitis  
Increased severity of radiation dermatitis[^57]  
Pruritus[^56]  
Other skin lesions[^55,56]  
Transient acantholytic dermatosis  
Necrolytic migratory erythema-like skin lesion (gefitinib)  
Sycosis (gefitinib)  
Pyoderma gangrenosum-like lesions (gefitinib)  
 Purpuric drug eruption  
Hand-foot syndrome/acral erythema[^56]  
Hyposalivation and taste abnormalities[^58]  
Hand-foot syndrome/palmoplantar erythodysesthesia[^57]  
Facial erythema and seborrheic dermatitis-like rash[^66,67]  
Transient yellow discoloration of skin (sunitinib)^[56]  
Subungal splinter hemorrhages[^57]  
Hair changes[^55,57]  
Alopecia  
Reversible hair depigmentation  
Xerosis[^55]  
Eruptive benign nevi[^55]  
Pruritus[^56]  
Inflammatory eruptions[^55]  
Disseminated morbilliform rash  
TEN  
DHS  
Papulopustular rash (~3%)  
Stomatitis and cheilitis[^61,63]  
Pyoderma gangrenosum-like ulcerations (sunitinib)^[66]  
Hyperkeratotic squamoproliferative lesion (sorafenib)^[56]  
Blue-gray macules of dyspigmentation (vandetanib)[^55]

Contd...
| Drug class                        | Drugs                        | CADR                                                                 |
|----------------------------------|------------------------------|----------------------------------------------------------------------|
| **BRAF inhibitors**              | Vemurafenib, dabrafenib      | Keratinocytic neoplasia/proliferations^{64,65}                        |
|                                  |                              | Verrucal keratosis (50%-86%)                                        |
|                                  |                              | Keratoacanthoma (20%-30%)                                           |
|                                  |                              | SCC                                                                 |
|                                  |                              | Morbilliform skin rash^{64,65}                                      |
|                                  |                              | Photosensitivity-UVA sensitivity^{66}                               |
|                                  |                              | Pruritus^66                                                          |
|                                  |                              | Palmoplantar dyesthesia-hyperkeratotic hand-foot reaction - up to (60%) |
|                                  |                              | Keratosis pilaris-like reaction (33%)^{64,65}                       |
|                                  |                              | Seborrheic dermatitis-like eruption                                  |
|                                  |                              | Melanocytic lesions^{64-66}                                         |
|                                  |                              | Changes in preexisting nevi and eruptive nevi                        |
|                                  |                              | Primary melanoma                                                     |
|                                  |                              | Painful lobular panniculitis^{67}                                    |
|                                  |                              | Exanthematous morbilliform eruption (46%-74%)^{57,64}               |
|                                  |                              | Papulopustular rash with pruritus^{67}                              |
|                                  |                              | Xerosis cutis with erythema^{57,64}                                 |
|                                  |                              | Paronychia^{57}                                                      |
|                                  |                              | Reduced hair pigmentation^{57}                                       |
|                                  |                              | Alopecia-17%^{57,62}                                                |
|                                  |                              | Hyperpigmentation^{57}                                              |
|                                  |                              | Trichomegaly^{57}                                                   |
|                                  |                              | Telangiectasia^{57,64}                                              |
| **MEK/ERK inhibitors**           | Selumetinib, trametinib      | Exanthematous morbilliform eruption (46%-74%)^{57,64}               |
|                                  |                              | Papulopustular rash with pruritus^{67}                              |
|                                  |                              | Xerosis cutis with erythema^{57,64}                                 |
|                                  |                              | Paronychia^{57}                                                      |
|                                  |                              | Reduced hair pigmentation^{57}                                       |
|                                  |                              | Alopecia-17%^{57,62}                                                |
|                                  |                              | Hyperpigmentation^{57}                                              |
|                                  |                              | Trichomegaly^{57}                                                   |
|                                  |                              | Telangiectasia^{57,64}                                              |
| **BCR-ABL tyrosine kinase inhibitors** | Imatinib, dasatinib, nilotinib | Facial edema^{56}                                                    |
|                                  |                              | Generalized pruritic morbilliform rash (7%-21%)^{55,54}             |
|                                  |                              | Pigmentary changes^{55,54}                                           |
|                                  |                              | Patchy and diffuse hypopigmentation                                  |
|                                  |                              | Worsening of preexisting vitiligo                                   |
|                                  |                              | Patchy hyperpigmentation                                             |
|                                  |                              | Repigmentation of gray hair^{56}                                     |
|                                  |                              | Pruritus^{56}                                                        |
|                                  |                              | Acne (dasatinib)^{56}                                               |
|                                  |                              | Inflammatory eruptions^{55,56}                                       |
|                                  |                              | Acute generalized exanthematous pustulosis                           |
|                                  |                              | Mycosis fungoides-like reaction                                     |
|                                  |                              | SJS, DRESS                                                           |
|                                  |                              | Lichenoid reaction                                                  |
|                                  |                              | Pityriasis rosea-like eruption                                       |
|                                  |                              | Psoriasiform dermatitis                                             |
|                                  |                              | Acute neutrophilic eruptions                                         |
|                                  |                              | Pseudolymphoma                                                       |
|                                  |                              | Porphyria cutanea tarda                                             |
|                                  |                              | Small-vessel vasculitis                                             |
|                                  |                              | Panniculitis                                                         |
|                                  |                              | Perforating folliculitis                                             |
|                                  |                              | Erythroderma                                                        |
|                                  |                              | Alopecia-nilotinib                                                  |

Contd...
Therapeutic paradox

PDRs are nonallergic drug reactions with an outcome of treatment opposite to the expected one. Common examples of PDRs include:

1. Jarisch–Herxheimer reaction (JHR): The reproduction or aggravation of infectious disease symptoms following antibiotic treatment is known as JHR. The clinical symptoms include chills, fever, headache, myalgia, and exacerbation of mucocutaneous lesions. JHR has been described for syphilis, borreliosis, leptospirosis, mycobacterial diseases, and Q-fever among others.[97]

2. Immune reconstitution inflammatory syndrome (IRIS): noted in HIV/AIDS patients during highly active antiretroviral therapy. Symptoms include fever, progressive lymphadenopathy, and worsening or newly detected radiological findings of tuberculosis.

3. Chloroquine and hydroxychloroquine are antimalarial drugs used to treat polymorphic light eruption.[98] In rare cases, however, these drugs can cause photodermatosis resembling polymorphic light eruption.[99]

4. Azathioprine and methotrexate are used in the treatment of Stevens–Johnson syndrome/TEN (SJS/TEN), but are also known to induce it.[100,101] TNF-α inhibitors have become an established therapy for moderate-to-severe plaque-type psoriasis also used for systemic lupus erythematosus and SJS/TEN. However, plaque psoriasis, nail psoriasis, intertriginous, erythrodermic, and palmoplantar pustular psoriasis may be induced or aggravated with a mean time of 9.5 months after initiation of TNF-α inhibitors.[102] TNF-α inhibitors induced lupus-like syndrome is also reported,[103] and these drugs may also induce SJS/TEN in rare cases.[104,105]

5. Tumor necrosis factor α (TNF-α) inhibitors have become an established therapy for moderate-to-severe plaque-type psoriasis also used for systemic lupus erythematosus and SJS/TEN. However, plaque psoriasis, nail psoriasis, intertriginous, erythrodermic, and palmoplantar pustular psoriasis may be induced or aggravated with a mean time of 9.5 months after initiation of TNF-α inhibitors.[102] TNF-α inhibitors induced lupus-like syndrome is also reported,[103] and these drugs may also induce SJS/TEN in rare cases.[104,105]

6. Inhibitors of epidermal growth factor receptor (EGFR) are targeted chemotherapeutic agents approved for different cancer entities including squamous cell carcinoma of the head and neck. Hair follicles express EGFR. Trichomegaly and hypertrichosis are adverse effects. PDR include nonscarring alopecia in the form of patchy or frontal alopecia which occurs usually with a delay of 2–3 months after initiation of treatment.[106]

7. Inhibitors (vemurafenib and dabrafenib) are used for the treatment of advanced melanoma. Related to a paradoxical activation of mitogen-activated protein-kinases signal transduction, patients can
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Learning points
1. There are no biologically safe drugs and any drug can cause any rash
2. Drugs being used in the treatment of drug reactions such as antihistamines, steroids, and inotropic drugs can also cause CADR and a high index of suspicion is required as continuing them can have serious consequences
3. Some drug reactions have typical morphology which helps the clinician in making the diagnosis, deviation from which leads to diagnostic dilemma and delay in withdrawal of offending agent and treatment. Nonpigmenting FDE is a common example of such scenario
4. Morphological patterns of some CADRs make them interesting. These include flagellate pigmentation, SDRIFE, capillary leak syndrome, and hand-foot skin reaction. The presentation may be benign as in flagellate pigmentation or associated with grave prognosis as in capillary leak syndrome
5. Newly introduced drugs are continuously adding to the already vast variety of CADRs indicating even more so that they are something to be closely looked for
6. Induction of cutaneous malignancy is a serious side effect of some immune-modulatory drugs including biologicals
7. Hair and nail changes, especially when occur in isolation or as initial manifestation, are often refuted to be caused by drugs. Pigmentary abnormalities and asymptomatic growth rate changes are the most commonly observed nail changes and reverse on discontinuation of causative agent. Others are infrequent and include transient nail shedding to permanent nail deformities
8. PDRs are no rarities. In particular, paradoxical IRIS and induction of psoriasis by biologicals are being observed in increasing numbers
9. It is almost disheartening and cruel that what may appear like an interesting drug reaction or observation to a clinician is never interesting for the patient.

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There are no conflicts of interest.

Table 3: Some unusual and uncommon hair-related adverse drug reactions and common causative drugs

| Some unusual hair-related ADRs | Drugs implicated |
|-------------------------------|-----------------|
| Darkening of hair             | Indinavir, bromocriptine, levodopa/carbidopa, arsenic, minoxidil, PABA, PG analogs, zidovudine, tamoxifen, acitretin, etrolitin |
| Lightening/graying            | Benzoyl peroxide, cyclosporine, hydroquinone, interferon-α, tamoxifen, imatinib, valproic acid, phenols, parapenphenylenediamine, corticosteroids (inhaled), etrolitin |
| Straightening                | Interferons, lithium |
| Curling                      | Cytotoxic/chemotherapy, indinavir, systemic retinoids, verumafenib, and valproic acid |

ADR: Adverse drug reactions, PABA: Para-aminobenzoic acid, PG: Prostaglandin

Table 4: Unusual nail-related adverse drug reactions and drugs implicated in causation

| Some unusual nail-related ADRs | Causative drugs |
|-------------------------------|-----------------|
| Onycholysis                   | Taxanes (docetaxel, paclitaxel), rituximab, doxorubicin, sirolimus, etoposide, retinoids, captorpl, chloramphenicol, thiazide diuretics, and selenium toxicity |
| Photo-onycholysis             | Tetracyclines, psoralens, fluoroquinolones, antipsychotics, NSAIDs, diuretics, griseofulvin |
| Paronychia                    | Taxanes, Systemic retinoids, Topical retinoids, namely, tretinoin, tazarotene, protease inhibitors, EGFR inhibitors, Capectabine, Less commonly lamivudine, Phenolphthalein, Cephalosporins |
| Pyogenic granuloma-like lesions | EGFR inhibitors, Retinoids, Protease inhibitors |
| Curly nails                   | Ettretinate |

NSAID: Nonsteroidal anti-inflammatory drugs, EGFR: Epidermal growth factor receptor

Some unusual and interesting adverse cutaneous drug reactions include acantholytic dyskeratosis resembling Grover’s disease. Such reactions can develop in a variety of settings and may be associated with a wide range of drugs. The presentation of cutaneous adverse drug reaction is not always typical. The clinician should therefore be familiar with unusual and rare presentations as well. Many drugs considered safe may cause adverse drug reactions, many of which may be serious. Many newer and targeted agents often believed to be safe, can have bizarre and unusual presentation of adverse drug reactions. A possibility of paradoxical drug reactions should be kept in mind when a primary disease gets worsened with a drug used to treat that disease; the examples include immune reconstitution inflammatory syndrome (IRIS) with antiretroviral therapy and induction and/or worsening of psoriasis by TNF-alpha inhibitors.

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What is new?
The presentation of cutaneous adverse drug reaction is not always typical. The clinician should therefore be familiar with unusual and rare presentations as well.

• Many drugs considered safe may cause adverse drug reactions, many of which may be serious.
• Many newer and targeted agents often believed to be safe, can have bizarre and unusual presentation of adverse drug reactions.

A possibility of paradoxical drug reactions should be kept in mind when a primary disease gets worsened with a drug used to treat that disease; the examples include immune reconstitution inflammatory syndrome (IRIS) with antiretroviral therapy and induction and/or worsening of psoriasis by TNF-alpha inhibitors.
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