

slightly for each allergen in each patient.

Conclusion

When the Sensi-Pen or the Coss Scarifier is used, skin tests can be performed relatively rapidly and painlessly, but false-negative and false-positive results are common. Prick tests, although more time-consuming and more painful, are still the most accurate and specific tests for delineation of type I hypersensitivity.

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Ecthyma gangrenosum

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Ecthyma gangrenosum, a relatively uncommon condition pathognomonic of *Pseudomonas* septicemia, is usually seen in immunocompromised patients, particularly those with underlying malignant disease.¹⁻⁴ In the past year we have seen two such cases at the Children's Centre in Winnipeg — one in a child with intractable diarrhea and one in an apparently well child. Prompt recognition of the skin lesions and immediate institution of appropriate antibiotic therapy may be lifesaving in this potentially fatal illness. For this reason, and because many physicians may be unfamiliar with the clinical presentation, we are reporting these two cases.

Case reports

Case 1

A 5½-month-old girl was well

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until an upper respiratory tract infection, otitis media and gastroenteritis developed. She was treated orally with amoxicillin for 5 days, but symptoms persisted and she was admitted to a local hospital with mild bronchopneumonia. The leukocyte count was $14.9 \times 10^9/L$ with a normal differential count. She was treated with parenteral administration of fluids, and intravenous penicillin therapy was begun 2 days prior to transfer to the Children's Centre.

At the time of transfer the infant was afebrile, pale, irritable, lethargic and 5% dehydrated. Bilateral otitis media and mild pneumonia of the right upper lobe were diagnosed. Pathogens could not be cultured from specimens of stool, urine or tracheal secretions. Despite intravenous administration of fluids and ampicillin she became progressively more lethargic. The diarrhea persisted despite a variety of trial feedings, and after 8 days the ampicillin was discontinued.

The following day an area of induration 1.5 cm in diameter that was

thought to be an abscess was noted on the right buttock. Because of co-existent recurrent otitis media, ampicillin therapy was resumed. Two days after its appearance the skin lesion had become more severe and new lesions were forming on both legs and buttocks. The total leukocyte count was $1.5 \times 10^9/L$, with 4% mature and 10% immature polymorphonuclear cells. Gentamicin and cloxacillin were added to the antibiotic regimen, and later that day, after the possibility of ecthyma gangrenosum was considered, carbenicillin was added. The skin lesions became more extensive, however, and the child died. On the day of death *P. aeruginosa* was cultured from the blood, and *Escherichia coli* and *P. aeruginosa* from the stool.

Postmortem examination showed anatomic features of shock with cutaneous purpura, and *P. aeruginosa* was noted in the walls of cutaneous vessels at the sites of the purpuric lesions. There were no lesions in the gastrointestinal tract.

Case 2

A 22-month-old boy had been seen by his private physician 10 days prior to admission for an upper respiratory tract infection and secondary infection of a recurrent diaper rash. He was given cloxacillin therapy, but diarrhea and anorexia developed. Four days prior to admission a chest roentgenogram revealed right middle lobe pneumonia, and erythromycin was substituted for cloxacillin. The diarrhea increased, and the morning of admission the child's mother noted fever and large

purplish ulcers on the buttocks.

At the time of admission to hospital the child was pale and irritable and looked ill. Pertinent physical findings were confined to the skin of the buttocks. There were three deep black necrotic ulcers with erythematous bases approximately 2 cm in diameter on the left buttock, a raised purplish nodule on the right buttock, a crater 1 cm in diameter on the left posterior thigh, and a diffuse erythematous papular rash over the remainder of the buttocks (Fig. 1). The leukocyte count was $8.1 \times 10^9/L$, with 5% mature and 16% immature

polymorphonuclear cells. Gram-staining of material from the skin lesions showed a slight amount of pus and gram-negative rods.

A tentative diagnosis of ecthyma gangrenosum was made and therapy instituted with gentamicin and carbenicillin. *P. aeruginosa* sensitive to both antibiotics was subsequently cultured from blood and material from the skin lesions. The early hospital course was complicated by a transient fall in the platelet count, but the clotting parameters remained normal. Neutropenia developed during the second week of hospitalization, with absolute counts of polymorphonuclear cells below $0.4 \times 10^9/L$, but this gradually resolved. During the 2 weeks of therapy *Pseudomonas* continued to be cultured from material from the skin lesions.

At a follow-up examination 1 month after discharge the child appeared healthy and the lesions had healed by granulation. Subsequent investigations demonstrated that he had severe hypogammaglobulinemia.

Discussion

Ecthyma gangrenosum has most frequently been described in patients with chronic disease and impaired defence mechanisms. In adults it is known to be a rare complication of malignant disease^{1,5} and burns,² and has been described in a heroin addict.⁶

In children it has also been known to complicate burns,⁷ and isolated cases have been reported in association with bowel rupture, congenital agammaglobulinemia, aplastic anemia⁸ and congenital megacolon;⁹ it has also been described in the newborn.^{3,9,10} One important factor predisposing infants and children to *Pseudomonas* septicemia appears to be antibiotic therapy, particularly when several antibiotics are given. Children receiving antibiotics who have ecthyma gangrenosum have also had preceding diarrhea,^{3,10} and one can only speculate whether the antibiotic therapy resulted in a change in bowel flora. It appears, then, that *Pseudomonas* septicemia is infrequent without some change in host susceptibility. Immunologic studies, how-



FIG. 1—Typical ulcers of ecthyma gangrenosum and lesions representing deeper abscesses in patient of case 2.

ever, have not generally been reported for adults or children with ecthyma gangrenosum, and it is impossible to know if specific immune defects are commonly present.

The first patient in this report was certainly debilitated from her lengthy illness and intractable diarrhea, and had been receiving antibiotic therapy intermittently for 1 month. The second patient, however, had minimal diarrhea and had received a relatively short course of antibiotic therapy. His underlying hypogammaglobulinemia was first documented after his illness, which suggests that perhaps all patients with ecthyma gangrenosum should undergo immunologic investigation.

Classic lesions of ecthyma gangrenosum are deep ulcers with ecchymotic and gangrenous centres and bright red areolae. Typically the ulcer has raised, purplish, indurated and rolled edges (Fig. 1). In addition, there may be erythematous, violaceous, elevated and indurated nodules with fluctuation, or similar lesions without fluctuation that are actually deeper abscesses (Fig. 1). These lesions have been shown to harbour organisms for long periods, even while the patient is receiving antibiotic therapy, and may require incision and drainage.⁸ More nonspecific vesicles, small papules and cellulitis can also be present. Characteristically there is very little inflammatory response.

Lesions can occur anywhere, but are commonly found in the anogenital region, the inner aspect of the thighs, the abdomen and the axillae. Two cases of noma-like lesions have been reported,^{3,10} and autopsies have shown that typical lesions may be present in the gastrointestinal tract with or without simultaneous skin involvement.^{3,4,9} The portal of entry is commonly the skin, but may also be the gastrointestinal tract.⁴ Lesions may progress rapidly from one form to another, and in one documented case the sequence of edema, erythema, hemorrhagic bullae and frank necrosis evolved in a 12-hour period, with various forms coexisting at any given time.⁵

Leukopenia, as in both our patients, has been documented previously in patients with *Pseudomonas* septicemia.⁴ Teplitz¹¹ noted that the maturation arrest of marrow neutrophils, with resultant peripheral leukopenia, occurred in both rats and humans during the terminal phase of overwhelming *Pseudomonas* sepsis and might be an important factor contributing to the minimal neutrophilic response found in many septic lesions. This "agranulocytic angitis" is usually a terminal event. However, with early diagnosis and institution of appropriate antibiotic therapy in addition to incision and drainage of nodular lesions, most patients with *Pseudomonas* septicemia and ecthyma gangrenosum should survive.

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Warnings The following warnings apply to Anafranil and other tricyclic antidepressants:

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Electrocardiographic studies suggest that Anafranil should not be used in the presence of pronounced cardiac or circulatory failure, recent myocardial infarction or ischaemic heart disease. Anafranil also has a hypotensive action which may be detrimental in these circumstances. The drug should, therefore, be used with caution in patients who are susceptible to hypotensive episodes.

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Particularly in the elderly and in hospitalized patients the tricyclic antidepressants may give rise to paralytic ileus and therefore appropriate measures should be taken if constipation occurs.

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Precautions In seriously depressed patients the possibility of suicide should be borne in mind and may persist until significant remission occurs. Therefore, these patients should be carefully supervised during treatment with Anafranil, and hospitalization or concomitant electro-convulsive therapy may be required.

Activation of latent schizophrenia or aggravation of existing psychotic manifestations in schizophrenic patients may occur; patients with manic-depressive tendencies may experience hypomanic or manic shifts; and hyperactive or agitated patients may become over-stimulated. A reduction in dose or discontinuation of Anafranil should be considered under these circumstances.

Since Anafranil may produce sedation, particularly during the initial phase of therapy, patients should be cautioned about the danger of engaging in activities requiring mental alertness, judgement and physical coordination.

It should be borne in mind that Anafranil may block the pharmacological effects of hypotensive drugs, such as guanethidine and similar agents.

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Adverse Reactions The following adverse reactions have been reported with Anafranil or other tricyclic antidepressants:

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Behavioural Effects: agitation, excitement, hypomania or manic episodes, activation of psychosis, confusion, disturbed concentration, visual hallucinations.

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Haematological and Other Toxic Effects: agranulocytosis has been reported; it represents a hypersensitivity reaction. Eosinophilia may also occur. Obstructive jaundice, allergic skin reactions, photosensitization, occasional disturbances of appetite, abdominal pain, changes in libido, and weight gain.

Dosage and Administration EXCEPT IN ELDERLY PATIENTS AND ADOLESCENTS: One tablet (25 mg) 3 times daily initially, increase up to six tablets (150 mg) daily, or more, as required.

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