Bullous Disease of Dialysis

Bullous dermatosis of dialysis is a syndrome of cutaneous fragility and blistering. The skin lesions clinically and histologically resemble those of porphyria cutanea tarda. Lesions predominantly occur in sun-exposed skin, most often on the dorsal hands, of individuals treated for chronic renal failure with maintenance dialysis regimens. This mechanobullous disorder has been observed in
end-stage renal disease patients treated with chronic ambulatory peritoneal dialysis and with hemodialysis. Porphyrin levels in urine and stool are normal. Plasma porphyrin levels are normal or only minimally elevated, thus excluding a true porphyria, which, in anephric individuals, would result in grossly abnormal values.

Blistering and mechanical fragility of skin subjected to sunlight and incidental trauma typically begin only after several months or years of dialysis therapy.

The frequency of this disorder among dialysis populations in the United States has not been accurately determined but may be similar to that reported from several European surveys.

In a large French survey, 6 of 500 individuals who underwent hemodialysis were affected. Among 66 individuals who incurred hemodialysis for more than 10 years in France, 27% reported cutaneous fragility and pseudoporphyria (presumably bullae) was noted in 13%. In 2 additional French surveys, 16 of 100 and 6 of 136 dialysis patients were affected. Three patients with blistering were found among 70 patients at an Irish dialysis center.

These cutaneous lesions are cosmetically distressing and interfere with use of the hands. They may be painful, become secondarily infected, and eventuate in scarring, but are not life threatening.

Although no racial predilections have been reported, individuals with less melanin pigmentation of the skin have less natural photoprotection and may be more likely to develop dialysis-related cutaneous fragility and blistering.

Although some surveys report a predominance of males, a higher female-to-male ratio has also been noted. In none of these surveys was the sex composition of the underlying population stated; thus, the male-to-female data reported may be reflections of different sex frequencies in
their source populations.

Most reported cases have involved adults; however, this may reflect the predominance of older individuals with end-stage renal failure among populations treated with chronic dialysis regimens.

Individuals with chronic renal failure who are afflicted with bullous dermatosis of dialysis typically develop these lesions only after months to years of maintenance dialysis regimens. The lesions are more florid after sunlight exposure; however, patients often are unaware of the role of sunlight in evoking the lesions since they do not note discomfort in the skin during the exposure.

Vesicles and bullae filled with clear or hemorrhagic fluid and exudative erosions occur chiefly on the dorsal hands, although the scalp, face, and neck also may be affected. Healing of crusted erosions leaves atrophic scars. Milia, dyspigmentation, and hypertrichosis occur infrequently.

The etiology of bullous dermatosis of dialysis remains unclear, although the propensity for sunlight aggravation of the bullae and fragility suggests a phototoxic mechanism.

Because plasma porphyrin levels in individuals with chronic renal failure may be mildly elevated, porphyrin photosensitization might play a contributory role in some cases. However, porphyrin photosensitization is not likely to be the primary cause because many dialysis patients with similarly mild elevations of plasma porphyrin levels do not develop photocutaneous lesions. Speculations that photosensitizers encountered during dialysis (eg, compounds emanating from plastic tubing) are responsible remain unproven. Concomitant use of therapeutic agents with phototoxic potential (eg, furosemide) cannot be identified in most cases. Effects of high aluminum concentrations from therapeutic or environmental sources on enzymes of heme biosynthesis, leading to overproduction of porphyrins, have been suggested as possible etiologies but remain unproven.

**Treatment**
Any photosensitizing drug that the patient may be using should be identified and discontinued, if possible. N-acetylcysteine, a glutathione precursor used orally as a radiotherapy protector, was administered to 2 patients in a clinical trial; resolution of blistering and fragility followed after several weeks. Another patient successfully treated with oral N-acetylcysteine was reported by Cooke and McKenna in 2007.

Sunlight avoidance, use of long ultraviolet and visible light topical sunblock formulations, and protection of exposed skin from mechanical trauma may help reduce the severity of the lesions. Intermittent treatment of secondarily infected bullae or erosions with topical or systemic antibiotics may be required.

Recommend avoidance of sunlight exposure and protection of hands from mechanical trauma.

No specific systemic therapy is known to be consistently effective.

Anecdotally, 2 patients treated with oral N-acetylcysteine were reported to have clearing of blistering and fragility after 1-2 months of daily therapy.

**N-acetylcysteine (Mucomyst, Mucosil)**

Glutathione precursor that may be effective as a photoprotector by increasing availability of glutathione, a potent antioxidant.

**Adult**
Doses reported in 2 cases: 200 mg PO qid and 600 mg PO bid

**Pediatric**

Doses used for acetaminophen toxicity: 70 mg/kg PO q4h