Epidermolysis Bullosa

Eisenberg, Stevens and Schofield, *Australian Journal of Dermatology* (1978), studied the effects of PHT on the collagenolytic system in tissue samples from patients with dystrophic epidermolysis bullosa. The collagenolytic system is known to be excessive in this disorder. PHT was found to inhibit the excessive activity.

As a result of these findings, two children with dystrophic epidermolysis bullosa were given PHT. Marked improvement in skin fragility resulted. The authors concluded that the clinical effects of PHT on both blister formation and collagenase activity are consistent with the protective effect observed *in vitro* and suggested that PHT is useful in the management of this disease.

Bauer, Cooper, Tucker and Esterly, *The New England Journal of Medicine* (1980), citing the work of Eisenberg, Stevens and Schofield, studied the effect of PHT on the collagenolytic system *in vitro*, and clinically in seventeen patients with recessive dystrophic epidermolysis bullosa. With PHT there was a significant decrease in blistering in all patients. In twelve patients the reduction was from 46% to 90%. The clinical study was controlled in that all patients underwent a period without PHT during which they experienced a notable exacerbation in blistering. The authors state that the correlation of the clinical responsiveness and *in vitro* inhibition of collagenase indicates that PHT represents a therapeutic option of relatively low risk in a disease for which there has been no rational method of therapy.

Bauer and Cooper, *Archives of Dermatology* (1981), reported an extended study (76 to 99 weeks) of nine patients with moderate or severe recessive dystrophic epidermolysis bullosa. In seven of the nine patients, the decrease in blisters and erosion with PHT was 70%. In the other two patients, blistering decreased 24% to 40%. (See also Refs. 2176, 2188, 2247.)

Bandmann and Perwein, *Zeitschrift fur Hautkrankheiten* (1982), in a detailed case report, describe a patient with the rare Gedde-Dahl type of epidermolysis bullosa, with severe blistering, erosions, and dysphagia due to esophageal stenosis. With PHT, fewer blisters developed, and blisters and erosions already present healed more quickly. (See also Ref. 2863.)

Wirth, Nesch, Ostapowicz and Anton-Lamprecht, *Zeitschrift fur Hautkrankheiten* (1983), state that they have used oral PHT in the treatment of eleven patients with recessive dystrophic epidermolysis bullosa (Hallopeau-Siemens and Inversa type) since 1978. The authors detail six
of their cases, ages six weeks to sixty-one years. Treatment with PHT, at blood levels of 8-15 mg/ml, resulted in definite reduction in blistering and lessened skin fragility. The authors report that four of their patients had esophageal stenosis, one with complete obstruction. With PHT, improvement was such that esophageal dilation could be performed in all four.

Cooper and Bauer, Archives of Dermatology (1984), 2409 studied the effects of PHT in twenty-two patients with recessive dystrophic epidermolysis bullosa. Therapeutic response was defined as mean decrease in blistering of more than 40%. The authors stated that, with this strict criterion, fourteen of the twenty-two patients had 46% or more reduction of blistering. PHT, 100-300 mg/day, was adjusted to maintain blood levels if at least 8 mg/ml. To determine if prolonged treatment altered response, nine of the patients were studied for periods longer than seventy-five weeks. Seven of these patients continued to have a mean decrease in blistering of at least 40%. The authors noted that with PHT patients had an enhanced sense of well-being.

See Refs. 2247, 2491, 2532, 2546, 2560, 2602,2617, 2643, 2658, 2793, 2818, 2876, 3009, 3087. Also, regulatory effect of PHT on collagen synthesis and breakdown, Refs. 172, 501, 502, 811, 1867, 1882, 2107, 2571, 2581.

Fine and Johnson, *Archives of Dermatology* (1988), treated four children (two with generalized atrophic benign epidermolysis bullosa [GABEB] and two with Herlitz disease) with two 16-20-week treatment periods with phenytoin separated by an 8-12-week drug-free period. Oral dosages of phenytoin were adjusted to achieve a blood level of 8 mg/l. No other medications were used. Each patient was assessed before PHT therapy and at 2-4-week intervals during treatment. Serial counts were made of lesions (blisters, crusts and erosions) and surface areas of granulation tissue, when present, were also serially measured. Changes in the percentage of surface area involved with scarring, as well as changes in extracutaneous disease activity, were similarly assessed.

Both patients with GABEB showed excellent responses during each course of phenytoin, with average reductions in lesion counts of 70% and 38%. The healing times also appeared to be reduced. During the "wash-out" period, total lesional counts returned toward pretreatment levels. PHT did not appear to benefit the two patients with the Herlitz form of EB. Both GABEB patients received PHT for an additional two years with continued excellent response.

Pappu-Katikaneni and Wiest, *Pediatric Research* (1988), report the phenytoin dosing requirements for a patient having junctional epidermolysis bullosa. A decrease in blister formation was observed when the patient received 39 mg/kg/day of phenytoin. The authors suggest that the loss of drug in blister fluid represents an extra pathway of PHT elimination and could account for the excessive dosage requirements in this patient.

Lin, Stern, Caldwell-Brown and Carter, *Clinical Research* (1989), report the results of the oral phenytoin treatment of twenty-six patients with recessive dystrophic epidermolysis bullosa. Patients received either phenytoin or placebo for five to seven months. After a 2-month washout period, the patients who received phenytoin were switched to placebo, and vice versa, for an additional five to seven months. Blood phenytoin levels were monitored in an attempt to maintain levels of 8 µg/ml. The phenytoin-treated patients showed improvement in the size of involved sites, number of blisters and erosions, although the difference was indicative of a trend rather than statistical significance.

Caldwell-Brown, Stern, Lin and Carter, *New England Journal of Medicine* (1992), continued their evaluation of phenytoin's therapeutic effectiveness in thirty-six patients with recessive dystrophic epidermolysis bullosa in a randomized, double-blind, placebo-controlled, crossover trial. Each treatment was given for five to seven months separated by a two-month period. The total number of blisters, and erosions on the entire body, the size of three plaques containing blisters and erosions, and the number of blisters and erosions in three plaques at the beginning and end of each treatment period were measured in each patient. Twenty-two patients completed both courses of therapy; seven patients completed one course; and seven patients withdrew before completing a single course. The number of blisters and erosions on the entire body showed a 7% decrease with phenytoin and a 6% increase with placebo. The area of the three designated plaques decreased by 0.4% with phenytoin and increased by 0.2% with placebo. The number of blisters and erosions in the designated plaques decreased by 12% with phenytoin and increased by 31% with placebo. Although a trend favoring the use of phenytoin was evident, it was not statistically significant and the authors concluded that phenytoin is not effective in patients with recessive dystrophic epidermolysis.
bullosa. The authors caution that their study does not indicate whether or not phenytoin may be effective in some subsets of this disease.


Masgrau-Peya, Lacour and Saloman, *Dermatology* (1995), 3336 evaluated 8 patients (2 males, 6 females) aged 1 through 40 years suffering from local epidermolysis bullosa simplex (EBS). During a period of 6 - 36 months, a phenytoin cream was applied topically twice daily at the sites of bulla formation (hands and feet). While in all cases, there was an increase in the rate of wound healing, it was faster in 3 of the 8 patients. For one 2-year-old girl who was unable to walk due to severe EBS, the application of PHT overnight led to marked improvement and allowed physical activity. There was no PHT detected in two patients whose plasma levels were measured. The authors conclude that their open trial of topical PHT showed that patients with a mild form of EBS had a quicker rate of healing of their lesions and felt improved over a long period of time. They note that phenytoin is inexpensive and suggest further controlled trials.


Fine, *International Journal of Dermatology* (1986), 3337 reports on various clinical aspects, pathology and recent advances in epidermolysis bullosa (EB) research and highlights PHT as a notable form of topical therapy for some cases of EB. In a study of seventeen patients with recessive dystrophic EB where patients were treated with oral PHT, twelve patients were shown to have at least a 45% reduction in blistering and a correlation between reduction of blistering and higher PHT levels was noted. It was suggested that PHT is beneficial in patients with recessive dystrophic EB due to its effects on collagenase synthesis.


Nawaz, Matta, Jacobsz and Al-Salem, *Pediatric Surgery International* (2000), 3338 report on the use of phenytoin in a six-day-old full-term female newborn with both junctional epidermolysis bullosa (EB) and congenital pyloric atresia (CPA). Surgical correction of the pyloric atresia was performed successfully, and with phenytoin treatment, the patient’s skin condition showed immediate signs of improvement. She was discharged from the hospital at age 35 days.


See also Refs.


