Extensive Dermatitis due to Warfarin Sodium (Coumadin)

By Crawford W. Adams, M.D., and Bernard J. Pass, M.D.

Warfarin Sodium, 3-(alpha-acetoxybenzyl)-4-hydroxycoumarin sodium, (Coumadin) is one of several popular anticoagulant agents used to delay intravascular clotting by depression of the prothrombin level of the blood. This drug is often used in instances in which there is an acute thrombophlebitis, pulmonary and peripheral embolism, coronary and cerebral thrombosis, and it is employed prophylactically to prevent arterial embolization and thrombosis.1-4

Excessive lowering of circulating prothrombin with spontaneous hemorrhage is the important complication in the use of this prothrombinemic agent.4,5 Five per cent of the patients who receive anticoagulant therapy develop mild hemorrhagic manifestations such as hematuria, hemoptysis, epistaxis, and ecchymosis. These are readily controlled by the administration of vitamin K1. Approximately 2 per cent of patients develop more severe hemorrhagic phenomena such as hemarthrosis, gastrointestinal, cerebral, or subarachnoid hemorrhage, or purpura. These complications demand early recognition and the prompt use of vitamin K1 or blood transfusion.6,8

Sheps and Gifford9 first reported an allergic manifestation of warfarin sodium. In that instance, transient urticaria appeared in a 50-year-old man, 40 minutes after the oral administration of 50 mg. of warfarin sodium. Subsequently,bishydroxycoumarin was administered without reaction. Extensive dermatitis has not previously been reported as a complication of warfarin sodium therapy.

Case Report

A 63-year-old white man developed an acute inferior myocardial infarction 7 weeks prior to the onset of an acute cerebral arterial thrombosis with aphasia and hemiplegia.

While hospitalized for the myocardial infarction, the patient was treated withbishydroxycoumarin for 17 days. There were no complications, and the patient had an uneventful recovery. Following the extensive cerebral thrombosis, anticoagulant therapy was again initiated. Initially 75 mg. of warfarin sodium were administered, and after 36 hours, the prothrombin level was reduced to 20 per cent of normal. Subsequent prothrombin levels were maintained between 25 and 30 per cent of normal, with a daily dosage of 7.5 mg. of warfarin sodium. After 27 days of anticoagulant therapy, a pruritic, maculopapular, erythematous eruption developed on the face, neck, hands, and forearms. There was no evidence of cutaneous hemorrhage. Examination of the mouth revealed superficial erosions on the buccal mucosa. The eruption on the face and neck resembled the dermatitis seen following unusual exposure to the sun or ultraviolet radiation. There was no previous personal or family history of allergy. The patient was also taking ascorbic acid, nicotinic acid, and phenobarbital, and these were discontinued. Warfarin sodium was continued but the skin manifestations progressed. Three days later, warfarin was discontinued and a combination of pyrrobutamine and thienylpyramine (Copyronil) was administered for 2 days without improvement. Prednisolone, 40 mg., was initiated with a progressive daily reduction in dosage. The oral and the skin lesions immediately improved and disappeared completely 14 days after onset, or 5 days after the initiation of steroid therapy.

After an interval of 10 weeks, 5 mg. of warfarin sodium were again administered daily. After 3 days, the patient again developed pruritus and a recurrence of the oral and superficial cutaneous lesions. Warfarin was discontinued, and the eruption disappeared. A saturated solution of warfarin sodium on sterile gauze was placed upon the patient’s forearm for 48 hours. An area, 1.5 x 2.0 cm., of erythema developed without pruritus or induration. Control applications remained clear.

Because of the generalized arterial disease, treatment with bishydroxycoumarin was initiated, and the prothrombin time was maintained between 25 and 30 per cent of normal with 50 mg. daily. After 5 months of therapy there has been no recurrence of allergic manifestations.

The administration of another chemically related anticoagulant, bishydroxycoumarin, without similar allergic manifestations, suggests an absence of cross sensitivity, as noted by Sheps and Gifford.9

From the Department of Medicine, Vanderbilt University, School of Medicine, Nashville, Tenn.

Circulation, Volume XXII, November 1960 947
Conclusion

Severe dermatitis involving the skin and mucous membranes followed the use of warfarin sodium (Coumadin). Lesions disappeared with steroid therapy but recurred upon challenge with warfarin sodium. Upon elimination of this drug, the skin and oral lesions disappeared. The patient had no allergic manifestations following the administration ofbishydroxycoumarin.

Summario in Interlingua

Dermatitidis sever, afficiente le pelle e le membranas mucose, sequente le uso de warfarina a natrium (Coumadina). Le lesiones dispareva con le uso de un therapia steroidic, sed illos recurreva post le provocation con warfarina a natrium. Post le suspension del droga, le lesiones cutanee e oral dispareva. Le patiente habeva nulle manifestaciones allergice post le administration de bishydroxycoumarina.

References


Of the three characteristics of living tissue—adaptation, growth, and reproduction—the last, reproduction, provides the most searching question to be asked if we want to test for vitality and continuity. Keepers of zoos begin to feel at ease when their more exotic animals succeed in producing their own kind in captivity. Since medical education replenishes the professions that provide medical care, and since medical care is changing in important ways, we must be on guard to make sure that none of the new factors or practices of medical care threatens the continuity of medical education.—ALAN GREGG, M.D. Challenges to Contemporary Medicine, New York, Columbia University Press, 1956, p. 87.
Extensive Dermatitis due to Warfarin Sodium (Coumadin)
CRAWFORD W. ADAMS and BERNARD J. PASS

Circulation. 1960;22:947-948
doi: 10.1161/01.CIR.22.5.947

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1960 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/22/5/947.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/