Deferoxamine and Sweat Iron.* (32028)

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Numerous investigations during the last two decades have confirmed the presence of iron in sweat. The magnitude of this iron loss is largely determined by factors such as the cell composition of sweat, climatic conditions, and regional body sweating(1,2). The wide variations in estimates of 24-hour dermal iron loss are due to methods of estimation and various assumptions used in the calculations(3). Little information is available about the iron content of the skin of patients with iron overload. Pigmentation of the skin, one of the features of iron overload, is usually due to a combination of melanin pigment deposits in the basal layer of epidermis and hemosiderin in and around sweat glands and skin appendages. Measurements of the iron loss in sweat from subjects with iron overload have not been reported.

Trials with deferoxamine indicate that it is the most promising iron chelating drug for treating patients with iron overload who cannot be bled. This drug will even increase urinary iron excretion from normal subjects. The exact mechanism and site of action of deferoxamine are unknown(4). The present investigation was designed to determine: 1) the iron content of sweat in patients with iron overload, and 2) the effect of deferoxamine on the excretion of iron in sweat.

Materials and methods. Sweating was induced in 6 subjects, 3 men and 1 woman with transfusion iron overload, and 2 normal adults, using modified methods of Adams *et al* (5). Subjects sat with one arm and one foot in water kept at 42°-43°C in a steam-warmed room for 1 hour. Sweat (2-17 ml) was collected in a polyethylene bag covering the hand and lower third of the arm. The sweat was drained into a graduated tube and well mixed; equal aliquots were taken for determination of iron by Bothwell and Mallet's bathophenanthroline method(6). Similar sweat collections were made 2-3 hours after an intramuscular injection of 1 g of deferoxamine methanesulfonate. Urine was collected for 24 hours and urinary iron was measured using an acid digestion technique (7). Skin biopsies were taken from the lateral surface of the forearm and examined by light microscopy. Hemoglobin concentration, serum iron, and unsaturated iron binding capacity were measured by standard methods.

Results. In all subjects the baseline sweat iron concentrations were similar, and in the lower range of previously reported values (Table I). Sweat iron concentrations did not change appreciably after deferoxamine injection. Increases of urinary iron excretion after deferoxamine were in the range expected from patients with iron overload.

The histologic appearance of sweat glands was normal in all subjects. No detectable iron was seen in the skin biopsies of normal subjects or of patients No. 5 and 6. In patients No. 3 and 4 abundant amounts of iron were seen in macrophages around sweat glands, while in No. 3 iron was also present in epithelial cells of sweat glands and in macrophages scattered in the upper dermis.

Discussion. Increased skin pigmentation in patients with iron overload is due primarily to the presence of excessive melanin pigment in the basal layers of the epidermis and secondarily to hemosiderin-laden macrophages in the dermis near sweat glands and hair follicles. Since the iron content of epidermal cells is low, little loss of body iron would be expected from their desquamation during sweating. Mobilization of iron from the dermal macrophages surrounding sweat glands might significantly increase the iron content of sweat. Our studies indicate, however, that thermal stimulation of the forearm in 4 patients with various types of iron overload

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TABLE I. Effect of Parenterally Administered Deferoxamine (DF) on Sweat and Urinary Iron Excretion.

Subject	Sex	Diagnosis	Hgb, g/100 ml	Serum iron, μg/100 ml	TIBC, μg/100 ml	Urinary iron excretion, mg/24 hr		Sweat iron concentration, μg/100 ml	
						Baseline	After 1 g DF I.M.	Baseline	After 1 g DF I.M.
1	♂	Normal	14.8	129	309	—	—	8	7
2	♀	"	14.8	156	309	—	—	3	0
3	♂	Aplastic anemia transfusion hemosiderosis	8.6	392	392	1.02 1.10	26.69	2 0	0 0
4	♂	Aplastic anemia transfusion hemosiderosis (cured)	13.6	299	398	2.38 .64	31.08 27.16	6 2	2 2
5	♀	Sickle cell anemia transfusion hemosiderosis	10.0	381	381	1.79 .30	35.40	14 6	0 5
6	♂	Sideroachrestic anemia	7.3	293	320	0.10 .22	12.71 13.23	4 3	5 5

Hgb = hemoglobin; TIBC = total iron binding capacity; I.M. = intramuscularly.

produced sweat with iron concentrations in the same range as that of two normal subjects.

Deferoxamine causes increased excretion of iron in urine, bile, and feces(4). No previous studies have explored whether this drug causes enhanced sweat iron excretion. The amounts of iron in sweat after deferoxamine injections are very small. Even under conditions of copious sweating, this site of iron loss may be eliminated in evaluating the overall effectiveness of deferoxamine in the treatment of patients with iron overload. Failure to increase the sweat iron after deferoxamine in the patients with iron overload indicates that sweat is not an outlet for body iron mobilized by this drug.

Conclusions. Iron excretion in sweat from the forearm of normal subjects and patients with iron overload is similar, with values in the lower range of normal. Deferoxamine has no appreciable effect on sweat iron concentration.

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