

## Erythrocyte Glutathione Peroxidase Activity in Acne vulgaris and the Effect of Selenium and Vitamin E Treatment

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The glutathione-peroxidase (GSH-Px) activity in erythrocytes was determined in 42 men with severe acne and 47 women with acne—26 of a moderate degree and 21 severe.

The male acne patients had significantly lower GSH-Px levels than the controls. The women with acne did not differ significantly from the controls in this respect when patients and controls using oral contraceptives were excluded. Both the female controls and the women with acne using oral contraceptives had significantly higher GSH-Px values than the corresponding groups not using the pill. The pubertal acne girls had the same high GSH-Px activity as women on oral contraceptives.

In an open trial 29 patients were given 0.2 mg of selenium (as Na<sub>2</sub>Se O<sub>3</sub>) + 10 mg of tocopheryl succinate for their acne twice daily for 6-12 weeks. A good result was obtained, especially in patients with pustular acne and low GSH-Px activity, and the beneficial effect was usually paralleled by a slow rise of the GSH-Px activity. Some 6-8 weeks after withdrawal of the treatment the GSH-Px values had returned to the pretreatment levels. *Key words: Glutathione peroxidase; Acne; Oral contraceptives; Selenium.* (Received March 15, 1983.)

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The role of selenium in human health and disease has been discussed in several publications in recent years (1 for ref.). In particular, the possible association between selenium deficiency and both cancer and increased mortality from cardiovascular diseases has been a matter of debate.

Selenium is usually quantitated either directly by neutron activation or indirectly by measuring the activity of the selenium-dependent glutathione peroxidase (GSH-Px, E.C. 1.11.1.9). Methods of determination by atomic absorption spectrometry have also been developed in recent years.

Selenium can be demonstrated in all tissues. In skin, Molokhia (2) found a mean value of 0.52 µg/g dry weight in the epidermis and 0.39 in the dermis. Molin & Wester (3) reported somewhat higher epidermal values, around 1 µg/g dry tissue. The precise role of selenium in skin function has not been defined. Selenium-containing preparations have long been used topically in the treatment of seborrhoeic scalp disorders.

Preliminary screening of blood GSH-Px activity in various skin disorders was recently undertaken by Juhlin et al. (4). They observed significantly lower mean activity in several groups of patients, e.g. those with psoriasis, atopic dermatitis and dermatitis herpetiformis.

This paper deals with blood GSH-Px activity in acne vulgaris. The results of an open, preliminary study of treatment of acne with oral selenium combined with vitamin E, including the influence of this treatment on the GSH-Px activity, are also reported.

## MATERIAL

### Patients

The study was performed on 42 young men (aged 16–25 years) and 46 young women (6 of them 13–15 years old and still with ongoing puberty, stages II–IV, the others 16–25 years old) with acne. With the exception of the pubertal girls, most patients had had their acne for 3–10 yrs. In all patients the acne was of the inflammatory type. Its severity was estimated by grading on a 0–10 scale as described by Jones et al. (5) and also by counting the various types of lesions. All the male patients had fairly severe acne (grade 2.5–4.5). Among the 46 women, 19 postpubertal and 6 pubertal patients had moderate acne (grade 1–2.5) and 21 had a more severe form (grades >2.5–4.5). The acne grades refer to the patients' facial acne. Many patients, especially the boys, also had acne on the back and/or chest. Three acne patients also had mild seborrhoeic dermatitis. About 35% of the patients had previously been treated with oral tetracyclines or zinc citrate. Eight patients were taking oral tetracyclines, 250–500 mg daily and 5 were taking zinc citrate (45–90 mg zinc 2+) when the GSH-Px was checked. Thirteen of the 19 women with moderate and 4 of the 21 with severe acne used oral contraceptives. Apart from their acne, the patients were healthy. None of them were vegetarians or had alcohol problems.

### Controls

Twenty-two men and 28 women, all healthy, most of them 20–30 years old, served as controls. The majority were medical students or belonged to the medical staff. Five of the female controls were using oral contraceptives. They were taking no extra vitamins or mineral tablets.

## METHODS

**Blood sampling.** Blood was drawn into 10-ml Vacutainer glass tubes (Becton-Dickinson A 4716) containing 144 U of heparin; 0.5 ml of the blood was hemolysed in 2.5 ml of distilled water and frozen at  $-25^{\circ}\text{C}$  within 3 hours of sampling. Samples were taken simultaneously for hematocrit determination.

**GSH-Px determination.** The method of Paglia & Valentine with slight modifications was used (6), cumenehydroperoxide being used as the substrate. The method is a linked reaction in which the oxidized glutathione is regenerated to reduced form enzymatically with glutathione reductase and NADPH. Reaction rates are followed by continuously measuring the decrease of the NADPH concentrations at 340 nm. The activity was determined in an LKB 8600 Reaction Rate Analyser (LKB; Bromma, Sweden).

The intra- and interassay precisions for the range of activity measured in this study were 2.4 and 7.5%, respectively.

### Treatment

In order to study the effect of selenium on acne, 29 patients were treated with tablets containing 0.2 mg of selenium (as  $\text{Na}_2\text{SeO}_3$ ) and 10 mg of tocopheryl succinate, taken twice daily with meals. In

Table I. GSH-Px activity in patients with acne

See results for *p*-value

	Number	GSH-Px, $\mu\text{kat/l}$ (mean $\pm$ SD)
Controls (young men)	22	323.4 $\pm$ 45.9
Controls (all women)	28	325.0 $\pm$ 51.4
Controls (young women no ocs)	23	302.2 $\pm$ 49.8
Controls (young women ocs)	5	353.4 $\pm$ 30.8
Acne (young men severe acne)	42	267.4 $\pm$ 37.4
Acne (young women severe acne no ocs)	17	282.7 $\pm$ 36.6
Acne (women, severe acne, ocs)	4	295.8 $\pm$ 15.1
Acne (women, moderate acne, no ocs)	6	286.8 $\pm$ 32.5
Acne (women, moderate acne, ocs)	13	357.7 $\pm$ 33.9
Acne (pubertal girls)	6	363.8 $\pm$ 38.4

ocs = oral contraceptives

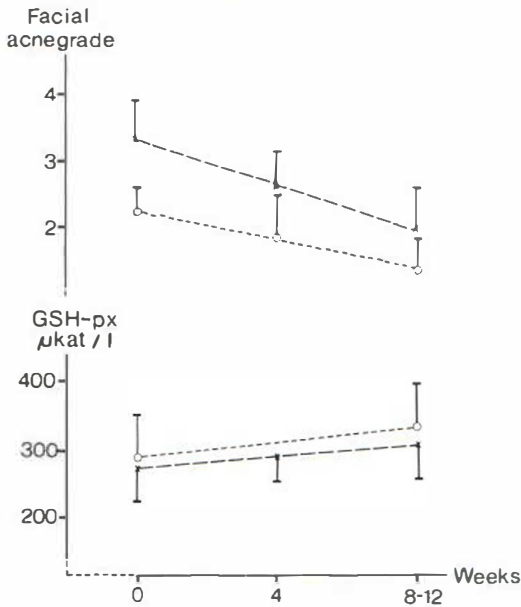


Fig. 1. Effect of 0.2 mg of selenium and 10 mg of vitamin E orally twice daily on facial acne and GSH-Px activity. Initial acne grade 2-3, ○---○; >3, X—X

most of the patients the GSH-Px value was not known until after the end of the trial. Sixteen patients had selenium and vitamin E as the only oral treatment, whereas the 8 patients on tetracyclines and the 5 on zinc continued with these medications during the selenium treatment, but their acne activity had been found to be stationary for a long time.

## RESULTS

Table I shows the mean GSH-Px activities. The male acne patients, all of whom had acne grades >2.5, had a significantly lower mean activity than the controls ( $p < 0.001$ ).

The data for female patients are more difficult to interpret, as the GSH-Px values seem to be influenced by hormonal factors. Thus, controls using oral contraceptives (ocs) had significantly higher values than the controls not using ocs ( $p < 0.025$ ). Likewise, women with moderate acne using the Pill had a much higher mean value ( $p < 0.001$ ) than the women with moderate acne not using ocs. The same tendency was observed in the 4 patients with severe acne, using ocs. Furthermore, the mean GSH-Px value for the 6 pubertal girls with moderate acne was significantly higher ( $p < 0.0025$ ) than that of the postpubertal women with a moderate acne not using ocs. In fact the pubertal girls with acne had the same high mean GSH-Px value as both the controls and patients with acne using ocs.

However, when patients and controls on oral contraceptives were excluded, the two mean GSH-Px values for the moderate and the severe acne group did not differ significantly from each other or from that of the control group.

In 12 patients (not treated with selenium) the GSH-Px activity was checked repeatedly during a period of 6 months to one 1 year. In 9 of the patients the activity remained almost the same ( $\pm 10 \mu\text{kat/l}$ ), but in 3 of them a marked worsening of the acne with pustular reactions coincided with a decrease in the GSH-Px level (by 40–100  $\mu\text{kat/l}$ ). The GSH-Px value increased when the acne improved.

Treatment with selenium was given to 29 patients for 6–12 weeks. The mean degrees of acne severity and the GSH-Px activity during the treatment are shown in Fig. 1. A good

response was observed, especially in some patients with pustular acne and low GSH-Px activity. Five patients on tetracyclines were able to stop this medication during the selenium treatment. In 3 patients who had had moderate acne for years, complete healing took place during selenium therapy. These patients had previously been treated with oral zinc (2) and tetracyclines (1) with good improvement but without complete healing. One patient with severe acne also had a one-year history of depression and had received psychotherapy, with little effect. After a few weeks on selenium the depression disappeared and her acne also improved markedly. Since then (now 2 years) she has been free from depressive tendencies. In 3 patients who also had mild seborrhoeic dermatitis, this condition improved.

In 5 patients, no improvement was noted during the first 4–6 weeks of treatment, and in 3 of them the GSH-Px level also remained unchanged. Three of these 5 patients had initial GSH-Px values above 345  $\mu$ kat/ml.

In one patient the acne worsened markedly, with the occurrence of new pustules, during the first 4 weeks of treatment. At the same time his GSH-Px activity fell from 262 to 209  $\mu$ kat/l. Another patient had transient acne exacerbation between the fourth and tenth week of treatment and also showed a decrease in GSH-Px activity, from 340 to 220  $\mu$ kat/l during this period. Both patients said that they had taken their tablets.

Some 6–8 weeks after withdrawal of selenium, the GSH-Px activity was checked in 13 of the 29 patients. In all but one the GSH-Px activity had fallen to the pretreatment value. No other change in the medication had been made in these patients. Clinically one patient had improved at the follow-up, whereas the others were unchanged or slightly worse. The patient with improved acne was found to be the only one in whom the GSH-Px activity had increased.

## DISCUSSION

In humans the relationship between erythrocyte GSH-Px and erythrocyte selenium content has been found to be positive and closely correlated (7), poorly correlated (8), or not correlated (9). This may to some extent be explained by the relatively low amount of the erythrocyte selenium concentration which is associated with GSH-Px. This figure is reported to be 10–15% in humans (10) as compared with e.g. 75% in sheep (11). In the present study no attempts were made to relate GSH-Px activity to the selenium content in erythrocytes or blood plasma. It is noteworthy, however, that most of the patients treated with selenium responded with an increased GSH-Px activity.

Hormonal factors also seem to influence the GSH-Px levels. Thus Capel et al. (12) noted significantly increased GSH-Px activity in subjects taking oral contraceptives for longer than 6 months. They found no correlation between enzyme activity and selenium concentration in this group. Their results have been questioned by Pleban et al. (8) who, however, studied only 4 women. The results of our study confirm that users of oral contraceptives, both among controls and among women with moderate acne, have significantly higher GSH-Px activity in their blood than corresponding groups not taking contraceptive pills. Likewise the pubertal acne girls had higher GSH-Px values than the postpubertal women with acne. When evaluating the correlation between the selenium concentration and enzyme activity it is probably essential to be aware of the influence of hormonal factors.

In this study a significantly lower GSH-Px value was found for the young men with acne than for the healthy male controls. On the other hand there was no significant difference between the values for the women with acne and for the controls, when the contraceptive pill users were excluded. In some patients GSH-Px was determined several times. Usually the activity was about the same, but in a few patients it was markedly lower during

episodes of increased inflammation and pustule formation than on other occasions. Whether this might be a cause or a consequence of the deterioration is not known.

The influence of exacerbations of inflammatory conditions on the GSH-Px activity does not seem to have been reported. However, low enzyme activity has also been reported in several groups of inflammatory skin disorders, e.g. psoriasis and atopic dermatitis (4). Low selenium values have been found in chronic inflammatory conditions such as rheumatoid arthritis (13). Further investigations are required to establish whether there is a bodily need for more selenium in inflammatory conditions—or whether a relative selenium deficiency may be induced by inflammatory reactions.

The beneficial effects of oral selenium in some acne patients, especially those with low initial GSH-Px activity, were encouraging. With two exceptions the GSH-Px activity increased during selenium treatment. Both the low GSH-Px activity and the influence of the selenium on the acne lesions and the enzyme activity indicate that the selenium status in the acne patients may not be optimal. Sweden is known to have low contents of selenium in crops and selenium deficiency among pigs and other domestic animals has been a serious problem. Fortification of the fodder with selenium has recently been proposed. The amount of selenium in human food has also often been lower than recommended. This may be of particular importance in adolescence when requirements are probably higher than during other periods of life.

There is no satisfactory explanation for the lower GSH-Px activity in the male acne patients than in the control group. We have previously found significantly lower serum zinc values in male acne patients, without any obvious reason (14). It might be speculated that acne patients are especially sensitive to some trace metal deficiencies, as is the case with zinc (15). Another conceivable explanation is that for some reason the absorption of zinc and selenium in acne patients is decreased. A further possibility might be that both GSH-Px activity and the zinc level are influenced by the inflammatory process in a non-specific way.

Both selenium and zinc are essential for the function of the neutrophils and for the metabolism of arachidonic acid and the prostaglandins, and they also influence lipid metabolism. At present it seems likely that selenium deficiency may be one of several contributory factors in inflammatory acne, but further information on selenium levels, both in controls and in patients, is needed. It would also seem worthwhile to check the GSH-Px activity in acne patients and to undertake a double-blind study on the effects of selenium in those patients who have low GSH-Px activity.

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