

Effects of sulphur on the skin.

Clinical and Experimental Observations with an Aqueous Solution of Polythionic Acids («Polythiosol»).

By

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A new sulphur preparation, Euthiosol, was described in «Ugeskrift for Læger» No. 9, 1940. It consists of a colloidal sulphur solution corresponding to about 7 per cent sulphur and possesses considerable advantages: It has a powerful therapeutic effect, and is convenient to use. The small quantities of sulphur required can scarcely be seen on the skin. The chief sphere for the therapeutical employment is Seborrhoea faciei et corporis, especially if complicated with Acne vulgaris. It is also useful for the scalp, but it gives the hair a slightly dusty appearance.

Euthiosol has gradually come into wide use, and justly so. In particular, young ladies with Acne vulgaris seem to appreciate it. A minor drawback must be mentioned: On becoming warm, or in the presence of impurities Euthiosol may precipitate a compact sediment of sulphur. Thereby the advantage of the fine sulphur emulsion is lost. The sediment cannot be shaken into suspension again.

As to the question why an obviously better therapeutic effect is obtained with this remedy as compared with older, wellknown sulphur preparations, the explanation must be the extremely fine suspension of the sulphur, and the consequently very great active surface. Another possibility was suggested by Mr. M. B. Sc. NEESBY (Svoga laboratories), the originator of the preparation. He drew our attention to the fact, that the liquid containing the colloidal sulphur is a strongly acid solution of polythionic acids in varying

quantities. These polythionic acids might have some part to play, and from this point of view we started in September 1940 on therapeutical experiments with a simple solution of polythionic acids containing only a trace of colloidal sulphur.

This solution is practically clear and therefore still easier and more agreeable to use on the skin than is Euthiosol; it is easy to apply not only to the skin but just as readily to the hair, where the seborrhoea and pityriasis steatodes in the scalp form a large and important therapeutic field. Some few patients complain of a slight smarting on the skin, the solution being rather acid (P_h 0.64), but the smarting always passes over quickly. In such cases it may be advisable to leave the preparation on for only a short time, i. g. two hours, and then to wash it off with ordinary water. No dermatitis in the proper sense of the term is observed, apart from the ordinary sulphur dermatitis, with redness, crackling and scaling of the skin, the classical appearance of which is so well known in all forms of treatment with sulphur.

In this respect this solution of polythionic acid, which we call *Polythiosol*, has exactly the same effect as the usual sulphur preparations. It is always the same patients that react, both to the usual preparations and to *Polythiosol*. Sometimes there is the difference that the dermatitis is particularly pronounced after *Polythiosol*, which may indicate that the therapeutic effect is particularly strong.

We have seen only two cases of true hyper-sensitive eczema. *Idiosyncratic eczema develops very rarely* under sulphur treatment, and if so analysis will often show that it is the sulphur compound employed, and not the metalloïd sulphur itself, that acts as the eczematogenous substance. We have observed this a few times in connection with a preparation that has recently come into use, *Septiolan*. On closer investigation the hypersensitivity with this remedy proved to be due to dibenzoyl-disulphide, not to the sulphur.

The therapeutical experiments with *Polythiosol*, and with *Sulfo-siccol*, — an almost identical preparation made by Mr. NÆESBY (who originally was connected with Svoga and is now working in Norway), — have been extended over about 18 months at the pri-

vate clinic of one of us (LOMHOLT). We preferred to perform these experiments on a private clientele because this has evident advantages compared with a policlinical material: The patients follow the instructions more precisely, they are more interested, come more regularly, and particularly are more given to observing themselves and reporting on the effects of the preparation, for example capable of estimating its value in relation to other sulphur preparations, which most patients have tried before.

In these 18 months the number of patients using polythiosol or sulfosiccol was 175. The polythiosol has been subjected to a careful chemical analysis at the laboratory for anorganic chemistry of the Technical Highschool by Mr. PILEGAARD HANSEN under the supervision of Prof. I. A. CHRISTIANSEN.

The result of these analyses was as follows:

Polythiosol is an acid, colourless, faintly turbid fluid. The turbidity is due to a content of very small quantities of colloidal sulphur. The specific gravity is 1.006 g per cm^3 i. e., very nearly the same as that of distilled water. The solution is 0.23 normal, its degree of acidity: pH 0.64. The total content of sulphur is 1.4 per cent. The composition of the remedy was found to be the following:

1. Colloidal sulphur 0.03 per cent.
2. Sulphur from tetrathionic acid ($\text{H}_2\text{S}_4\text{O}_6$): 0.65 %.
3. » » pentathionic acid ($\text{H}_2\text{S}_5\text{O}_6$): 0.72 %.
4. In addition, polythiosol contains traces of sulphurous acid (H_2SO_2), thiosulphuric acid ($\text{H}_2\text{S}_2\text{O}_3$), trithionic acid ($\text{H}_2\text{S}_3\text{O}_6$), hexathionic acid ($\text{H}_2\text{S}_6\text{O}_6$) and sulphuretted hydrogen (H_2S). The last three acids are present in quantities so small that they are just demonstrable. The solution also contains traces of sulphuric acid.

As stated, about 175 patients have used the polythionic acid solution (Sulfosiccol-Polythiosol). In about 75 per cent of the cases the result was definitely satisfactory. The patients preferred decidedly this remedy to other sulphur preparations. For about 15 per cent there was no apparent improvement from the treatment, which was accordingly stopped. Finally, about 10 per cent found that the acid liquid irritated the skin and felt better when using Euthiosol, which is somewhat milder in its action.

Several patients (about 30 per cent of the whole) stated that they felt a rather sharp but quite brief smarting (10 to 20 seconds),

but only few wished to abandon the treatment for that reason. The smarting was particularly severe on areas where the skin is thin and where the seborrhoea is least pronounced (around the eyes, cheek bones and temples). No discomfort was felt when these areas were left untreated.

One difficulty encountered in judging the therapeutic value of a preparation like this is that it is impossible to find exact measures of the effect: Complete cure is exceptional. Generally there is merely a certain improvement, though it may often be quite considerable; moreover, it must be remembered that a disease such as *Acne vulgaris* is frequently rather capricious in its course.

On the other hand, with a commonplace disease like *Acne vulgaris* an experienced dermatologist will have no difficulty after a suitable time has elapsed (and 18 months must be regarded as a suitable time in this connection) in judging whether a new preparation of a group so thoroughly tested as that of sulphur, has any outstanding advantage over the old, familiar preparations. We are convinced that this is the case with *Polythiosol* (Sulfosiccol), with the reservation that the difference as regards *Euthiosol*, which also contains polythionic acid, is very slight except for the fact that *Polythiosol* is easier to apply and is therefore used more consistently. Here the advantage lies just in its extremely convenient form (the aqueous solution which cannot be seen on the skin), in its greater stability and in its economy, for *Polythiosol* is much cheaper to make than *Euthiosol*.

To quote merely one example: Before the preparation was put into the market most patients came back faithfully for a new bottle of that »splendid» remedy when the old one was used up.

Having arrived at this stage where we considered it justifiable to record it as an established fact that a simple solution of polythionic acids in water possessed the familiar effect of sulphur, though it only contained metalloïd sulphur in minute quantities, there came the interesting problem of how this is to be explained.

Discussion.

Since very early times metalloid sulphur has been employed in the treatment of skin diseases in cases where an antiseptic and defatting effect is desired. This effect has long been known, but there is still much that is vague about the action of sulphur. In most dermatological and pharmacological text-books it is stated that the effect is due to the formation of sulphuretted hydrogen, in others also the formation of sulphides and polysulphides, e.g. disulphides. Only in one the hypothesis is discussed that the effect on the skin might be due to polythionic acids, especially pentathionic acid (GOODMANN, A. GILMANN: *The Pharmacological Basis of Therapeutics*. 1940).

There seems to be general agreement that unconverted, chemically pure sulphur is therapeutically inactive. The therapeutic effect does not appear until there has been a conversion. In view of the great practical importance of this question, it is surprising how few experimental investigations have been published; and of these few most part occupy themselves exclusively with particular sulphur preparations such as bathing water containing sulphuretted hydrogen (MALIWA), and so provide no information on the subject as a whole.

Clinicians are quite familiar with the antiseptic affect of sulphur on staphylococci on the skin. For the purpose of obtaining an approximate idea of which sulphur compounds possess a particularly strong antiseptic effect on staphylococci, one of us (MØLLER) performed the following experiment:

To a concentrated suspension of *Staphylococcus aureus* was added sufficient pure sulphur sublimate to form a thick gruel of sulphur. This was sown on an agar plate 1) *immediately after* mixing, 2) *18 hours* after, and 3) *24 hours* after. In all cases there was a vigorous growth of *Staphylococcus aureus*, just as luxuriant as on plates sown at the same time with staphylococci which had not been affected by sulphur.

The next series comprised a similar, concentrated suspension of staphylococci, through which sulphuretted hydrogen was bubbled for 15 minutes, whereafter it was stoppered so that there remained a gas with a high content of sulphuretted hydrogen over the liquid. After being sown on agar plates the same vigorous growth of bacteria was obtained 1) *immediately after* bubbling, somewhat less so 2) *after 18 hours* and 3) *after 24 hours*.

In a final series, 0.2 cm³ of a ca. 2 per cent solution of polythionic acids (Polythiosol) was added to 10 cm³ of a concentrated suspension of *Staphylococcus aureus*. After sowing on agar there was no growth at all, no matter whether it was done 1) *immediately after* adding the polythionic acid solution, 2) *18 hours* or 3) *24 hours later*. In order to make sure that this

was not due simply to acid effect, controls were started with *hydrochloric acid*, the same quantity being added as that of polythionic acid solution and of the same acidity (normality). After sowing on agar there was vigorous growth immediately, decreased growth after 18 hours, and only after 24 hours was there no growth at all.

These preliminary experiments suggest that polythionic acids are a particularly active form of sulphur in sulphur treatment. The experiments are being continued.
