TREATMENT OF CONDYLOMATA ACUMINATA WITH TOPICAL APPLICATIONS OF INORGANIC ARSENICALS*

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The "alterative" and tonic effects of arsenicals on the general metabolism are well known. Also their empirical efficacy when given by mouth or parenterally for many dermatoses and some systemic diseases is common knowledge. But with the exception of local application of Fowler's solution and arsphenamines to the oral mucous membranes in Vincent's infection (now largely superseded by penicillin), the use of arsenic is limited to internal administration. There are very few instances in modern times where arsenicals have been applied externally for skin diseases. To cite one, W. and P. Sachs (1) recommend topical application of an aqueous solution of neoarsphenamine in the treatment of the erythroplasia of Queyrat.

In the more distant past arsenic, particularly in the form of pastes of arsenious acid, had a well deserved reputation as a good chemical caustic and was widely used in this manner for the destruction of accessible neoplasms. Thus Marsden (2) in the latter half of the 19th century enthusiastically reported successful treatment of certain forms of cancer by arsenious acid in a thick paste with mucilage of gum acacia (2 parts arsenious acid to 1 part vehicle). Ahlswede (3) lists arsenious acid among other better known caustics and states that its chief use has been for the extirpation of epitheliomas. In consequence of its fair action on superficial malignancies this arsenical has long been exploited by quacks as a cancer cure-all. Ahlswede does not cite it among other corrosive agents that are particularly recommended for condylomata acuminata like trichloracetic acid, phenol, salicylic acid, chromic acid and glacial acetic acid. Ormsby and Montgomery (4) give arsenic as a caustic, again among other substances that are more prominently mentioned. Sutton (5) does not discuss arsenic in this role at all. Houston (6) recommended a 1% solution of liquor arsenicalis, B.P. (the British equivalent of liquor potassii arsenitis, U.S.P.) for papillomas of the face and reported excellent results in 16 cases.

In the recent past acuminate warts were usually treated by extirpation with some form of scalpel-, caustic chemo- or electrosurgery. To some extent these modalities are still employed. The results with these forms of therapy leave much to be desired. Nowadays it is generally agreed that podophyllin (15—25% in oil, alcohol, collodion, tincture of benzoin, etc.) produces cures in nearly 100% of cases. We say "nearly" advisedly because every specific has occasional failures

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or inapplicabilities. There is, moreover, a more serious disadvantage to the use of podophyllin preparations in some cases. When applied indiscriminately, and sometimes unavoidably, in cases of preputial stenosis and on mucous membranes, undesirable reactions like pain, edema and even serious ulceration have been encountered. For these reasons any other substance with cure possibilities anywhere near those of podophyllin but with side effects of lesser consequence is worthy of record either as an alternative agent in rare podophyllin failures or as a safer substitute of choice where complications may be expected or feared.

For the past five years one of us (A. J. P.) has been using Fowler's solution (liquor potassii arsenitis, U.S.P., liquor arsenicalis, B.P.) in the treatment of verrucae of all varieties by topical application. We may anticipate our statistics tabulated below by stating at this point that this agent gives excellent results in acuminate warts, possibly good results in plane warts and poor results in vulgar warts.

**TECHNIC OF APPLICATION**

The speed of involution of acuminate warts from the topical use of Fowler's solution seems to be in direct proportion to the frequency of application. This is not to say that the fastest rate of involution possible is the most desirable. The size and location of the lesions to be treated are other factors determining the frequency of application and hence the rapidity of cure. For condylomata of moderate size or number and situated nearly entirely on skin surfaces the arsenical may be painted on full strength three times daily for the first two or three days and then once or twice daily depending on how well or rapidly recession is proceeding. For lesions of large size and especially for those located entirely, or to a large extent, on mucous membranes, applications twice daily to begin with for a day or two and thereafter once daily is better. The reason for this is that warts of large size and those on or near mucous membranes tend to become soft, exudative and covered with moist necrotic material both from the effect of the treatment and from the location in relation to a secreting surface. On this account a good additional hygienic measure is to order cleansing of the lesions of debris with a solution of boric acid or plain soap and water before each application of the arsenical. Both the application of the Fowler's solution and the cleansing are so simple and uncomplicated that they may safely be left for the patient to perform and only the adjustment of the rate of application need be supervised. Ordinary cotton tipped applicators are the only instruments required and no particular protection of, nor concern for, the surrounding normal tissue is necessary.

**RESULTS**

Table I is a resume of the results obtained in a recent series of cases.

Fig. I is an illustration of a case of acuminate warts that extended into the urethral meatus to a distance of 1 cm. These were given three applications daily for two days and then two applications daily for five days more. The lesions
TABLE I

Therapeutic results following topical application of Fowler's solution in various kinds of warts

<table>
<thead>
<tr>
<th>VARIETY OF VERRUCA</th>
<th>NO. OF CASES</th>
<th>CURED</th>
<th>NOT CURED</th>
<th>FREQUENCY OF APPLICATION</th>
<th>REMARKS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acuminate</td>
<td>20</td>
<td>20</td>
<td>0</td>
<td>3-2-1 times daily</td>
<td>Cure within 1-2 weeks.* 2% sod. arsenate is also effective but slower in action</td>
</tr>
<tr>
<td>Vulgar</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>On hands</td>
<td>6</td>
<td>1</td>
<td>5</td>
<td>3 times daily</td>
<td>No significant benefit even when preceded by keratolysis or paring. The one cure must be attributed to other factors.* Related inorganic arsenicals like 1% as. pentoxide and 2% sod. arsenate were also ineffective</td>
</tr>
<tr>
<td>Filiform or digitate</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>3 times daily</td>
<td></td>
</tr>
<tr>
<td>Plane</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>2 times daily</td>
<td>Cure in 2 weeks*</td>
</tr>
</tbody>
</table>

* The possibility that some of the cures may be attributable to suggestion is not to be overlooked.

Fig. I. Acuminate warts in the male urethra cured in one week with topically applied Fowler's solution.
Fig. II. An extensive case of acuminate warts on the penis cured in 12 days with topically applied Fowler's solution. Compare Fig. III.

Fig. III. The case illustrated in Fig. II after 7 days of treatment with Fowler's solution.
were entirely gone in one week. No pain, swelling or other discomfort was noted at any time during the course of treatment.

Fig. II is a case of condylomata before treatment with Fowler's solution which had recurred for the second time. One year ago they were treated with podophyllin and six months ago by electodesiccation. On this occasion Fowler's solution was applied three times daily on the first day of treatment. Slight but distinct swelling of the verrucae was seen. Consequently only one application daily was made on the following two days. No further complicating signs or symptoms appearing, the applications were increased to twice daily for the next nine days af-

Fig. IV. Photomicrograph of a section from the case illustrated in Fig. II after three days of treatment with topically applied Fowler's solution.

ter which no more lesions could be detected. This same case had perianal warts which required eight more days of treatment to eradicate completely.

Fig. III shows almost complete involution of the penile lesions of Fig. II after 7 days of treatment on the schedule of 3 applications for one day, 1 application for two days and 2 applications for four days. Five more days of treatment with 2 applications were required for complete cure. In this case a 3 mm. punch biopsy was taken after the third day of treatment. Study of the histopathology revealed slight parakeratosis, marked acanthosis of the rete with the prickle cells showing intracellular edema and vesicular nuclei. The pars papillaris was moderately infiltrated with plasma cells and small round cells. The capillary endothelium was markedly swollen but no thromboses were to be seen. This histologic picture is much what is usually found in acuminate warts but we judge it to greater in degree. That is, there was more intracellular edema, more capillary swelling and more infiltrate than usual. Nothing resembling the so-called podophyllin cells was seen. The reaction, then, is not that of a strong destructive
process, nor one of interference with cell division, but rather that of a mild hydropic degeneration. Fig. IV is a photomicrograph of the section.

**DISCUSSION**

Sollman (7) gives a good brief account of the action of inorganic arsenicals when topically applied as follows: "... Arsenic compounds act locally as mild and slow corrosives. ... Systemically they relax the capillaries and increase their permeability, thus stimulating inflammation. The arsenicals are not precipitant and therefore irritate only weakly, even on wounds and mucous membranes; but the cells die slowly after prolonged contact. This is sometimes used for killing exposed dental nerves and as salves for superficial epitheliomas. Arsenic is much more destructive to pathologic cells, so that cancerous tissue may be killed without injury to the surrounding normal tissue ..."

It is well known that some drugs in small doses or low concentrations have stimulating effects whereas in large doses or high concentrations they are destructive. This principle is well illustrated by arsenic. When taken in small amounts over short periods of time, fat hyperplasia and particularly epidermal hyperplasia are commonly observed. In fact, while excessive epidermal hyperplasia is feared, this effect plus the increase of fat and perhaps induced robustness of other tissues is what accounts for the general physical improvement and sense of well being that is sought and obtained from arsenic medication. On the other hand, large doses or prolonged administration bring on baleful effects in the form of chronic poisoning with characteristic degeneration of various tissues like epidermal keratoses and malignant changes, hepatic atrophy, gastrointestinal inflammation, etc.

In our use of Fowler's solution we have apparently taken advantage of the mild and slow corrosive action of an inorganic arsenical which has this desirable action by topical application of sufficient frequency but which is ordinarily stimulating when used systemically in proper doses. What we found clinically and histologically accords well with what has been observed before to be the surface action of arsenicals. It appears that when adequately used, inorganic arsenicals, in our experience particularly Fowler's solution, can serve well where a gentle, slow acting, painless mortifying agent is desired.

**SUMMARY AND CONCLUSIONS**

1. Fowler's solution and some other inorganic arsenicals have a selective destructive action on verrucous excrescences, particularly on those of the acuminate variety.

2. The cure rate in our series is as good as that often reported for podophyllin. The slower action on perianal warts is common to both podophyllin and arsenic.

3. While Fowler's solution must be applied more frequently than podophyllin and for more times, the less serious side actions and the ease of applications
which permits the patient's own use of the agent are distinct and compensating advantages.

4. Fowler's solution is a valuable alternative or substitute for podophyllin.

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REFERENCES