union is firm, and the shortening is slightly less than half an inch.

Case 3.—A woman aged 55 had a transcervical fracture of the neck of the femur. She was operated on three days later by oblique osteotomy and fixed in plaster for three and a half months. She is now walking well without pain and with perfect stability. There is good union of all three fragments.

Case 4.—A woman aged 54 sustained a transcervical fracture of the neck of the femur. She was operated on six days later by oblique osteotomy. After three and a half months' fixation in plaster union was complete in all three fragments. The patient is now apparently normal, without disability or pain, although there was temporary stiffness in the knee-joint for three months. This was cured by massage and voluntary movements, and did not prevent the patient from walking at any time.

A POSSIBLE DISCREPANCY IN THE ESTIMATION OF ASCORBIC ACID IN URINE

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Tests have recently been evolved for the estimation of ascorbic acid in urine, and these have been used for the diagnosis of latent and subclinical scurvy. The main difficulty in their clinical application lies in the collection of specimens of urine passed during the night and early morning, since it is recognized that ascorbic acid is rapidly oxidized on standing, even when kept in dark tightly stoppered bottles; and because ascorbic acid is not excreted at a uniform rate a twenty-four-hours test at least is essential. It has been shown by Borsook *et al.* (1937) that in an alkaline medium ascorbic acid can be oxidized into dehydroascorbic acid, and further still, into 2:3-diketo-l-gulonic acid; but this latter reaction is not reversible, so that the passage of H_2S through the solution, although it converts the dehydroascorbic acid back to ascorbic acid, does not touch the diketogulonic acid, which is lost. The irreversible change from dehydroascorbic acid begins at a pH of about 4 and increases as the pH rises. In order to overcome this difficulty preservatives have been added to the urine in the form of acetic acid and sulphuric acid.

Although some workers appear to be aware of the destruction of ascorbic acid by sulphuric acid, it has seemed worth while to us to publish this paper. Youmans *et al.* (1936) used 10 per cent. 2N sulphuric acid as a preservative, and Mack and Tressler (1937) mention using 5 per cent. sulphuric acid for the inhibition of the oxidase present in vegetable juices.

The Relative Efficiency of Acetic and Sulphuric Acids

Before proceeding with the clinical application of these tests it occurred to us to examine the relative efficiency of these two acids. The micro-method of Birch *et al.* (1933) was used, with the exception of a teat pipette in place of a micro-burette. For this purpose specimens of fresh urine were employed, samples of each being tested by both methods, the urine being kept in dark bottles throughout the experiment. Control experiments with the same specimens of urine to which nothing was added were carried out simultaneously. It was found that at the end of twenty-four hours the readings of the two tests corresponded closely with a loss of 15 per cent. to 21 per

cent. of the reducing substance, the controls showing 26 per cent. to 31 per cent. loss. At the end of forty-eight hours the loss with sulphuric acid only increased by 2 per cent. or 3 per cent.; the loss with acetic acid rose to about 50 per cent., while the loss with untreated urine varied from 80 per cent. to 100 per cent.

With a view to still further checking these results the tests were repeated, but using solutions of ascorbic acid in water instead of urine, the concentration of ascorbic acid being kept similar to that usually found in urines so far tested. These tests showed that during the first five minutes the loss with solutions of 1 per cent. sulphuric acid was 20 per cent., with acetic acid 5 per cent., and with water 15 per cent. (In dealing with the aqueous solutions the acid necessary for the test was added at the moment of titration.) After twenty-four hours the loss with acetic acid varied from 27 per cent. to 36 per cent., while that occurring with sulphuric acid and unacidified solutions was in every case 100 per cent. Tests with sulphuric acid in higher concentrations up to 20 per cent. gave a correspondingly greater loss of ascorbic acid in the same time.

From these results it is clear that sulphuric acid tends to destroy rather than preserve ascorbic acid in aqueous solutions.

Reasons for Apparent Difference in Action

To account for the apparent difference in the action of sulphuric acid on ascorbic acid in aqueous solutions and those containing urine it was necessary to postulate one of three possibilities: (i) there was some reducing substance in the urine apart from ascorbic acid which was preserved by sulphuric acid; (ii) the urine in conjunction with sulphuric acid had a preservative action on ascorbic acid; (iii) the substance tested for was not ascorbic acid. In order to elucidate this problem two other tests were performed.

1. A known quantity of ascorbic acid was added to fresh urine in which the amount of reducing substance had been previously estimated, and the above tests were repeated on the resulting solutions.

2. Urine was allowed to stand until tests for the reducing substance were negative. To this were added known quantities of ascorbic acid, and the above tests again repeated, using samples of the same specimens of urine for each; in each case controls with the same amount of ascorbic acid in water, 1 per cent. sulphuric acid, and 5 per cent. acetic acid were carried out.

From these experiments the following results emerged:

In the experiment with urine containing a measured quantity of titrable substance the loss during the first five minutes with unacidified solutions and those acidified with 5 per cent. acetic acid was never more than 3 per cent., and the former always exceeded the latter by at least 1 per cent.

In the case of the solution acidified with 1 per cent. sulphuric acid the loss varied from 12 per cent. to 19 per cent., so that there appears to be an immediate destruction of ascorbic acid on the addition of sulphuric acid, the readings being only slightly lower than those obtained with ascorbic acid in water acidified with 1 per cent. sulphuric acid.

It was next found that during the following twenty-four hours the loss of titrable substance proceeded more slowly in sulphuric acid solutions than in aqueous solutions (28 per cent. compared with 45 per cent.) and only slightly more rapidly than in the case of acetic acid, which gave about 22 per cent. loss in the twenty-four hours subsequent to the first five minutes.

In the tests in which ascorbic acid was added to urine kept until all titrable substance had disappeared the results followed very closely those obtained with ascorbic acid in solution in water, sulphuric acid, and acetic acid.

These results would appear to throw doubt not only on the efficiency of sulphuric acid as a preservative for ascorbic acid but also on the nature of the reducing substance in the urine as measured by these tests. In any case an explanation is obviously required to account for the fact that ascorbic acid in the presence of urine and sulphuric acid is destroyed, while the reducing substance in urine, as measured by these tests and presumed to be ascorbic acid, is preserved by sulphuric acid of the same strength. Incidentally it may be pointed out that the loss of reducing substance in lemon juice when kept for twenty-four hours in 1 per cent. sulphuric acid is 100 per cent.

Table showing Loss of Reducing Substance in Tests with Sulphuric and Acetic Acids

	Loss of Reducing Substance	
	First Five Minutes	Subsequent 24 Hours
Ascorbic acid in water	% 10	% 100
" " 1% sulphuric acid	20	100
" " 5% acetic acid	5	29
Reducing substance in urine		31
" " " +1% sulphuric acid ..		16
" " " +5% acetic acid ..		19
Ascorbic acid and tested urine	2	45
" " " " +sulphuric acid ..	16	28
" " " " +acetic acid	1	22
Ascorbic acid and non-reducing urine		100
" " " " +sulphuric acid		89
" " " " +acetic acid ..		31

A Possible Difficulty due to Catalysis

It was suggested to us that a possible difficulty in this work is due to catalysis of the oxidation of ascorbic acid by traces of copper present either (a) in ordinary distilled water or (b) in the sulphuric acid. Stotz *et al.* (1937) also state that the sensitivity of ascorbic acid to aerobic oxidation when copper is present as a catalyst is perhaps its most striking characteristic *in vitro*. Lyman, Schultze, and King (1937) point out that the instability of ascorbic acid in weakly acid solutions is due to the copper content of the solution, and that by its strict elimination ascorbic acid solutions are stable below a pH of 7.6. These authors used metaphosphoric acid, which inhibits the copper-catalysed oxidation of ascorbic acid by decreasing the amount of copper effective in the catalysis.

However, if the copper is present in the sulphuric acid the question still remains as to why there is a difference in the rate of destruction of the reducing substance in fresh urine in the presence of sulphuric acid (? + copper) and the rate of destruction of ascorbic acid which has been added to fresh urine in the presence of the same reagent. It also fails to account for the fact that there is an immediate (five minutes) loss of ascorbic acid in fresh urine with sulphuric acid (? + copper) of about 16 per cent., while the loss in the same time with acetic acid is only 1 per cent. (The catalysis should be inhibited by fresh urine.) The only distilled water employed in these two tests is that used to dissolve the dye, and this would be present equally in all these tests. With regard

to the occurrence of copper in the distilled water used in the other tests, if it is present it would appear to make the test unreliable for clinical purposes—at any rate, where sulphuric acid is used.

Van Eekelen (1936) has pointed out that ergothioneine and thiosulphates both reduce 2:6-dichlorophenolindophenol and that these substances must be removed by precipitation with mercuric acetate. In view of the fact that even with acetic acid there is a destruction of ascorbic acid on keeping, it is quite obvious that the results obtained will be of very doubtful value, unless the titration is carried out immediately after voiding. Although to do this may appear clinically tedious, it is scientifically sound, for examination of twenty-four hours' urine is necessary.

Summary

Sulphuric acid, which was still being used to "preserve" ascorbic acid in twenty-four-hour specimens of urine at the time of writing, has been shown to destroy ascorbic acid even when used in a concentration of 1 per cent.; with stronger solutions the destructive effect is greater still.

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TREATMENT OF INFANTILE PYLORIC STENOSIS BY ANTISPASMODICS

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The majority of observers regard infantile pyloric stenosis as essentially a disorder of the neuro-muscular apparatus of the gastric outlet, rather than as the result of a hypertrophy of the pyloric muscle of unknown origin. It might have been expected, therefore, that this condition would respond well to medical treatment, but until recently experience has shown that this is not the case. Parsons (1933) states that only 20 per cent. of patients recover if treated medically, whereas a recovery rate of 80 per cent. can be anticipated if Rammstedt's operation is performed. Thompson and Gaisford (1935) in a review of 209 surgical cases find that the death rate was 14.4 per cent. Recently, it is true, Harris and Keynes (1937) have reported thirty-six cases treated surgically with only one fatality (2.8 per cent.), but these figures are exceptional in this country. As a rule surgical treatment may be expected to cure four patients out of five with this complaint, while with the older methods of medical treatment the majority of cases ended fatally.

Treatment by Eumydrine

In December, 1935, Svensgaard published the results of treating congenital pyloric stenosis with eumydrine, or atropine methyl nitrate. Only two of sixty-one patients died, giving the remarkably low mortality rate of 3.3 per cent. (or 1.6 per cent. if one death attributed to pyelonephritis is omitted). In this connexion, however, it must be remembered that foreign statistics are invariably better