CHEMOTHERAPY OF CHRONIC SINUSITIS,
Especially by Continuous administration of large doses of Penicillin

By

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The following is derived from joint works of the senior author and his colleagues; Drs. M. Hosui, T. Higuti, K. Akaike, R. Otsuka, Y. Sakai and Y. Nakamura.

There are many applicable methods in the treatment of chronic sinusitis with penicillin and there are some conflicting opinions about the results. In order to determine the degree of effectivity and the limitation of penicillin therapy in chronic sinusitis, the authors carried out some studies in patients.

1. Basic Studies

Ten cases, chosen at random, of chronic sinusitis had after admission into the hospital, their maxillary sinus exposed. After macroscopic and bacteriological studies, as well as excision of bioptic sections counter opening was created. Instead of being followed by a radical operation the exposed sinus was closed, penicillin instilled and the progress observed. 100,000 units of mix penicillin was used in from 5 to 6cc. of distilled water. From 25,000 to 50,000 units was given once every day. This procedure was followed until no further improvement was observed by its use. The amount of penicillin employed by this procedure was from 1,200,000 to 1,050,000 units over a period of about 10 days. The result was the change of the nasal discharge from purulent to mucous in character as well as great reduction in quantity even sometimes to complete disappearance, diminished swelling of the mucous membrane, opening of the meatus nasi media and fissura olfactoria, lessening or disappearance of such nervous symptoms as headache, weariness, nervousness, sleeplessness and also disturbance of the sense of smell.

2. General Treatment

30,000 units of mix penicillin was given intramuscularly every three hours to ten cases admitted to the hospital. Great difference was not noted in these cases compared with the cases in which basic experiments were carried out except that result was slightly poorer and the amount of penicillin used a little more. Of the ten cases, four had previously radical operations performed on, the result of which had not been very satisfactory but on this medication they improved to the point where the patients were satisfied.

3. By the above two experiments we noted the superioritry of penicillin in
chronic sinusitis and were thus encouraged to carry on this method. This is the so called mass dosage continuous administration therapy by which the nasal findings were improved by a general administration followed by local administration of penicillin after the method of Prötz. The principle of this method lies in the continuous use of penicillin over a certain length of time. In chronic cases and where one is confronted with an anatomical difficulty such as a sinus, the problem is one of poor penicillin absorption and drainage. In 21 cases (including some who have had radical operations) the figures in the following chart goes to prove the effect of this theoretically based therapeutic method.

<table>
<thead>
<tr>
<th>Result</th>
<th>Cases</th>
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<tbody>
<tr>
<td>Excellent</td>
<td>12 (52%)</td>
</tr>
<tr>
<td>Good</td>
<td>7 (38%)</td>
</tr>
<tr>
<td>Satisfactory</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>No change</td>
<td>0</td>
</tr>
</tbody>
</table>

Now when the 38% with good result are added to the 52% with excellent result a high cure rate of 90% is shown. The total units of penicillin used were from 1,000,000 to 4,990,000 units with an average of 1,700,000 units. These were used over a period of from ten to fourteen days. Since the use of 30,000 units of penicillin intramuscularly every three hours in out-clinic patients was impracticable, 300,000 units of penicillin in oil was used every day over a period of a week. The result was comparable with that of the afore mentioned series.

4. In five cases in which no improvement was noted immediately after a radical operation, penicillin was used as a complement to operative procedures. Although from 200,000 to 600,000 units of penicillin were used locally and systematically the result was not so very good. This fact points out that those cases which do not show much improvement subsequent to operative procedures belong to a group in which either penicillin or surgery could not have been of definite help.

5. As control experiment against our procedure of mass dosage continuous administration we carried out a series in which the Prötz method alone was used. We studied 11 hospital cases. The results of this method did not compare with those obtained in method (3), for it obtained excellent progress in only 20% of the cases, while in seven cases no improvement was noted. The total amount of penicillin used was 700,000 units. This shows that the local application method is much more inferior compared with our method in which mass dosage continuous administration was used in combination.

6. There is often in chronic sinusitis a loss or diminution of sense of smell. Of the forty one patients in which we carried out our experiments with penicillin, twenty nine cases (70%) complained of total loss or diminished sense of smell. In twelve cases (65%) in which penicillin was used there was
improvement or complete recovery from the above complaints. Of this number seven with complete loss of smell recovered almost completely with the use of approximately 4,030,000 units. Recovery of this sense generally takes the most time and is usually the last of the nervous symptoms to disappear and that only after many units of penicillin used. Recovery of the olfactory sense was interpreted to be due to opening of the fissura olfactoria.

7. From the above experimental therapy we found that there is a limit in the effect of penicillin. Below are our findings concerning the limitations of this method.

An unsuccessful attempt was made to determine this limitation by the use of the X ray. In but 20% of the cases which had markedly improved did we note signs of increase in translucency in the sinus X-ray pictures.

8. The relation in chronic sinusitis between therapeutic results and histopathological findings.

The cases were studied on this connection. It is very difficult to determine what constitutes major or minor changes in the histopathological findings in chronic sinusitis. When change in the ciliary epithelium was used as a criterion for penicillin to be used, most of the cases did not show high degree of metaplasia or cell destruction. In cases where changes were severe we found that treatment was of little avail. We found, however that changes in the ciliary epithelium alone could not be used as a criterion in choosing cases in which penicillin was to be used.

9. In forty one cases of chronic sinusitis we studied the relation between the bacteria found and the penicillin dosage. The bacteria found in the greatest numbers were the staphylococci with the gram positive and negative macro- and microdiplococci next in number. Besides these were the gram negative bacilli, cornebacterium, B. proteus, streptococci and other gram positive organisms. Only few cases carried a single type of bacteria exclusively. Most cases had a mixed infection by two or more forms. Penicillin had its greatest effect in cases with gram positive forms, especially where they were of a single species. Cases where there was a mixture of gram positive and gram negative organisms responded less readily to penicillin while cases with gram negative bacteria alone responded even less. Where penicillin failed to work favorably, streptomycin and flacin also failed to obtain effective response in most cases.

One of the factors limiting the use of penicillin in the treatment of chronic sinusitis seems definitely to do with the kind of bacteria one deals with.

10. From clinical findings we have attempted to classify chronic sinusitis into the following five types.

1. Purulent granulomatous type.
2. Purulent type.
3. Mucous purulent type.
4. Fungous edematous type.
5. Allergic purulent type.

If an allergy factor plays a part in the manifestations of chronic sinusitis, type 2 to type 5 may be thought of as stages in which this factor plays an increasingly larger part. Type no. 1 in relation to the mass dosage continuous administration method did not at all respond favorably. The response to penicillin became more and more marked as we moved from type 2 down on to type 5.

11. Remote results are recorded here:

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Complete recovery</td>
<td>23</td>
<td>74%</td>
</tr>
<tr>
<td>No changes</td>
<td>8</td>
<td>26%</td>
</tr>
<tr>
<td>Change for worse</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>31</td>
<td></td>
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</tbody>
</table>

The period of observation was from one to nineteen months, with an average of 3.3 months or 99 days. Cases who felt themselves completely cured numbered 74%. There were no cases in which a turn for the worse occurred. Where sense of smell was used as a criterion 55% are still in satisfactory condition.


Concentrations of penicillin in samples of biological fluids were determined by superposition method. When 30,000 units of penicillin was given intramuscularly in 30 minutes 0.03 units was noted in the nasal discharge while 0.21 units (highest value) was noted in three hours. From the discharges from the superior maxillary sinus in an hour was noted 0.12 units and in two hours 0.09 units. Employing the Prötz method the highest value of 0.22 units of penicillin was noted in an hour when 50,000 units of penicillin was administered into one sinus. The Prötz method was found to excell the superior maxillary instillation method in that it showed a faster and higher increase in penicillin concentration in the blood; for greater penetration of penicillin across the mucous membrane from the sinus cavity to the blood or vice versa suggests a greater concentration of penicillin available to the epithelium cells.

These experiments we carried out in the treatment of chronic sinusitis are regarded to give adequate proof of the value of the mass dosage continuous administration method.