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# Concentration of penicillin in nasopharyngeal secretions

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SUMMARY

*The penicillin concentration in the nasopharyngeal secretion after penicillin administration was studied in 33 patients undergoing tonsillectomy. Benzylpenicillin was either administrated by the intravenous or the intramuscular route in doses of 0.6–1.2 g. Phenoxymethylpenicillin was given perorally in doses of 0.5–1.0 g. The secretion from the nasopharynx was collected prior to the operation both in a disposable collector and on a filter paper disc. A serum sample was also drawn prior to and immediately after the operation. The serum penicillin concentration reached levels of 16.0 mg/l, 5.8 mg/l and 3.6 mg/l (mean values) when given by the intravenous, the intramuscular and the peroral route, respectively. The mean penicillin concentration in nasopharyngeal secretion was 1.6 mg/l, 0.3 mg/l and 0.3 mg/l for these three administration modes. In the majority of cases the concentration of penicillin in the nasopharyngeal secretion exceeded the minimum inhibitory concentration for Streptococcus pneumoniae (0.006–0.12 mg/l).*

## INTRODUCTION

Otitis prone children are often subjected to long and frequent treatment with penicillin for their acute otitis media spells. It is not unusual that these children are colonized by Streptococcus pneumoniae in their nasopharynx. Pneumococcal cultures can even be obtained during or after penicillin treatment (Kamme et al., 1970; Branefors-Helander et al., 1975). This colonization may be explained by insufficient penicillin concentration in the secretion in this compartment. The aim of this study was therefore to determine the concentration of penicillin in the secretion of the nasopharynx after administration of a single dose of penicillin.

## MATERIAL AND METHODS

### *Patients*

For practical and ethical reason otitis prone children were judged unsuitable for this study. Instead, 33 patients undergoing tonsillectomy under prophylactic

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penicillin treatment at the Ear-Nose- and Throat Department of Huddinge University Hospital were selected for this study. The age of the patients ranged from 7–51 years, with a median age of 17 years. Nine were males and 24 females.

*Methods and procedure*

Antibiotic administration

The penicillin was given as a single preoperative dose and when the sampling was finished the penicillin treatment was continued till a full course. Benzylpenicillin® (ASTRA Läkemedel AB, Södertälje, Sweden) was given intravenously and intramuscularly to 10 and 11 patients, respectively. The doses administrated by the intravenous route was 0.6–1.2 g with a mean value of 25 mg/kg bodyweight (range 11–43 mg/kg). Also the patients receiving benzylpenicillin by the intramuscular route were given 0.6–1.2 g, with a mean value of 22 mg/kg bodyweight (range 14–37 mg/kg). Twelve patients were given 0.5–1.0 g of phenoxymethylpenicillin capsules perorally with a mean value of 19 mg/kg bodyweight (range 13–25 mg/kg). To avoid contamination from the given penicillin with the secretion to be examined, capsules (specially manufactured by ASTRA Läkemedel AB, Södertälje, Sweden) were given instead of tablets. Secretory inhibiting premedication was not given until the samples had been collected.

Collection of samples

Prior to surgery nasopharyngeal secretion was collected by two different methods. One sample was obtained by dipping a filter paper disc (Biodisk, AB Biodisk, Solna, Sweden) into the nasopharyngeal secretion and holding it there for approximately 5 seconds (Rasmussen, 1969). The filter paper discs were weighed before and immediately after collecting. The other sample of the secretion was gently aspirated into a disposable collector (Xomed, Jacksonville, Florida, U.S.A.). At the same time a blood serum sample, 8–10 ml, was drawn and 30 minutes later a second one was taken. The mean time elapsing from the penicillin administration to sampling was for the intravenous route 19 minutes, for the intramuscular route 91 minutes and for the peroral route 76 minutes. All samples were frozen and stored until the penicillin concentration was analysed at the Department of Oral microbiology, by the agar well diffusion method (Jalling et al., 1972). To determine possible blood contamination in the nasopharyngeal secretion, discs were taken at random for analysis of hemoglobin content by the method described by Olsson et al., (1982). In 4 out of 11 discs the hemoglobin content was less than in plasma, in 5 of 11 discs the content was equivalent to that of plasma and in 2 of 11 discs the content of hemoglobin exceeded that of plasma. The two latter discs did also show blood contamination visible for the naked eye. All such contaminated samples, both discs and aspirated secretion were excluded from the investigation.

## RESULTS

In 30 of 33 patients the first serum concentration determination of penicillin was higher than the second one. When administrating intravenously the mean serum concentration was 16.0 mg/l (range 9.4–21.5 mg/l, when administrating intramuscularly the mean value was 5.8 mg/l (range 1.5–8.8 mg/l) and when given perorally the mean value was 3.6 mg/l (range 1.1–7.9 mg/l) (Table 1).

Table 1. Mean values of penicillin concentration (mg/l) in 33 patients.

| administration route | nasopharyngeal secretion | | |
|---|---|---|---|
| | serum | disc | aspiration |
| intravenous | 16.0 | 1.8 | 1.3 |
| intramuscular | 5.8 | 0.3 | 0.3 |
| peroral | 3.6 | 0.5 | 0 |

The penicillin given by the intravenous route and sampled on paper discs resulted in a concentration of penicillin in the nasopharyngeal secretions of 1.8 mg/l (range 0.2–3.4). When administered intramuscularly and perorally the corresponding values were 0.3 mg/l (range 0–0.9) and 0.5 mg/l (range 0–2.1) respectively. When sampling in the collector mean penicillin concentrations in the nasopharyngeal secretions of 1.3 mg/l (range 0–4.9), 0.3 mg/l (range 0–1.3) and 0 mg/l where reached for the intravenous, intramuscular and peroral administration, respectively.

## DISCUSSION

In the present investigation the serum concentration of penicillin was in good agreement with earlier published reports (Weinstein, 1965; Heimdahl and Nord, 1979). In a study of Rasmussen (1969) higher concentration of penicillin in the nasopharyngeal secretion and serum was found. The different results may be explained by different assay techniques and by the fact that both patient materials are small.

The concentration of penicillin in the nasopharyngeal secretion in the present study after intramuscular administration is low compared to values found after intravenous and peroral administration. The long time of 90 minutes elapsed from administrating to sampling is probably the explanation for this finding. Nevertheless, the concentration of benzylpenicillin in the nasopharyngeal secretion was well above the minimum inhibitory concentration for S. pneumoniae (0.006–0.12 mg/l) (Lorian, 1980) in 17 of 21 patients when using paper discs (Figure 1). When aspirating secretion only 12 of 21 patients displayed penicillin concentration values in their nasopharyngeal secretion above the minimum inhibitory concentration for S. pneumoniae (Figure 2). In no single case did aspiration give measurable concentration of phenoxymethylpenicillin, whereas sam-

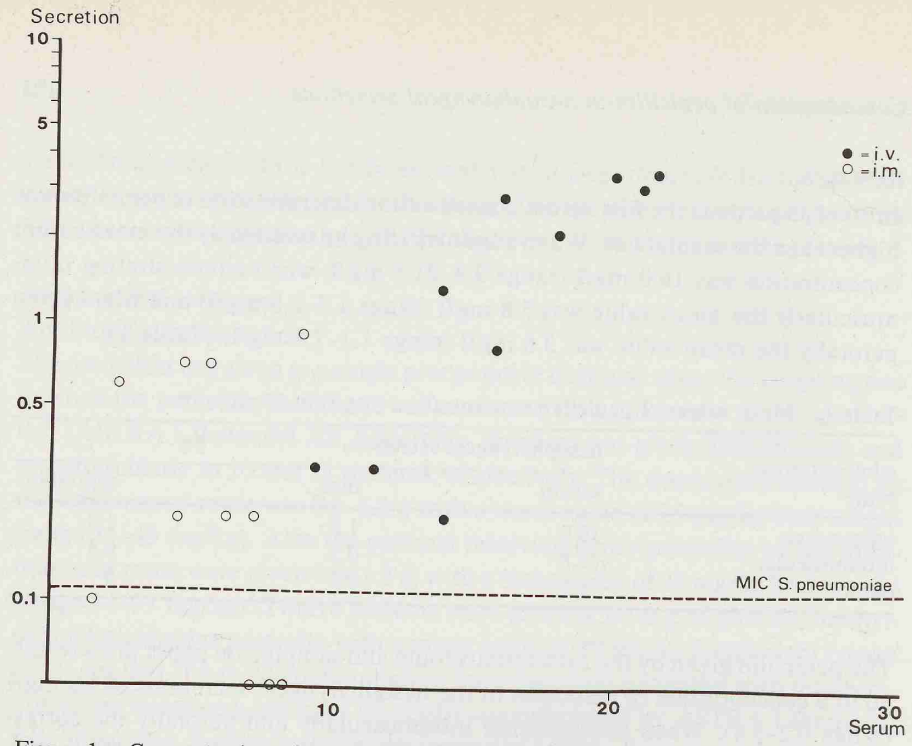


Figure 1. Concentration of benzylpenicillin (mg/l) in nasopharyngeal secretion in relation to the concentration in serum when collecting by means of paper discs.

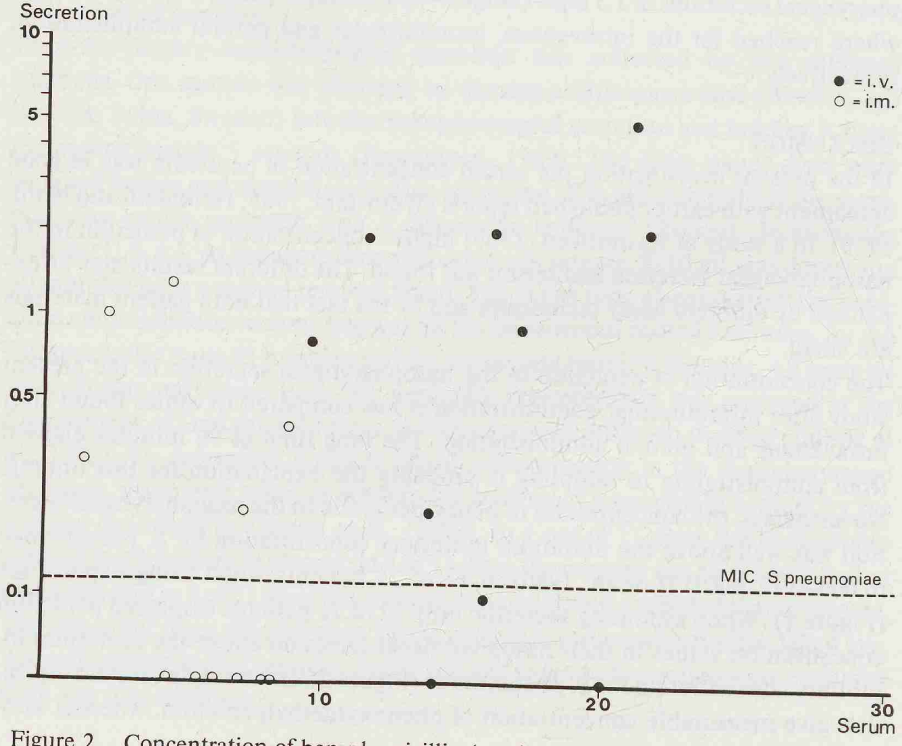


Figure 2. Concentration of benzylpenicillin (mg/l) in nasopharyngeal secretion in relation to serum concentration when aspirating secretion.

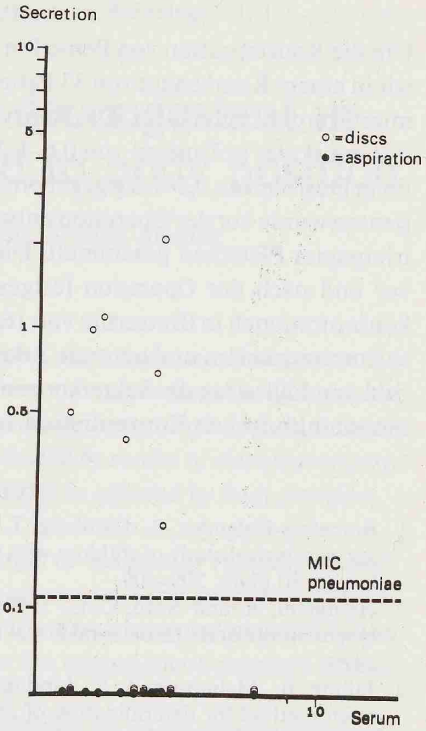


Figure 3. Concentration of phenoxymethylpenicillin (mg/l) in nasopharyngeal secretion when collecting by means of paper discs and aspiration.

pling on paper discs gave values well above the minimum inhibitory concentration for S. pneumoniae in 7 out of 12 samples (Figure 3).

There seems to be a positive correlation between the concentration of benzylpenicillin in the blood serum and in the nasopharyngeal secretion when collecting on paper discs (Figure 1). This correlation was less marked when the samples were aspirated (Figure 2). The tendency to give higher values for paper disc sampling as compared to aspiration was even more evident when phenoxymethylpenicillin was determined. Measurable concentration of penicillin was only obtained when using paper discs (Figure 3). The reason for this methodological difference is unclear. Absorption of penicillin to the material of the collector could be one explanation for the difference. One could also speculate if the water phase of the mucus is sucked into the porous paper disc thus concentration the water soluble penicillin there.

## CONCLUSION

To our opinion colonization and recolonization by Streptococcus pneumoniae of the nasopharynx during or after penicillin treatment is not caused by insufficient concentration of penicillin in the nasopharyngeal secretion and the explanation for this colonization has to be sought elsewhere.

ZUSAMMENFASSUNG

Um die Konzentration von Penicillin in Nasopharynxsekret festzustellen, haben wir in einem Krankengut von 33 Patienten die unter Penicillinschutz tonsillektomiert wurden, untersucht. Das Benzylpenicillin wurde entweder intravenös oder intramuskulär in Dosisen von 0,6–1,2 g oder peroral als Phenoxymethyl-penicillin in Dosisen von 0,5–1,0 g gegeben. Das Nasopharynxsekret von sämtlichen Patienten wurde vor der Operation entweder in einem Aspirator oder auf einem Filtrierpapier Plättchen gesammelt. Die Konzentration in Blutserum wurde auch vor und nach der Operation festgestellt. Die Patienten erriechten Penicillinkonzentrationen in Blutserum von 16,0 mg/l, 5,8 mg/l und 3,6 mg/l für intravenöse, intramuskuläre und perorale Administration, beziehungsweise. In der Mehrzahl von Fällen lag die Sekretkonzentration von Penicillin über die der minimalen inhibitorischen Konzentration von Streptococcus Pneumoniae.

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